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PREFACE

Veterinary ophthalmology has no deficiency of textbooks or atlases, and the available titles are all very good. However, *Small Animal Ophthalmology Secrets* is different from the other textbooks in the field. The format of The Secrets Series® relies on the authors to pose a question that is commonly asked on exams or in the clinic and then follows up with an answer that is founded on years of the authors' experience. The goal of this text is not to be all-inclusive; the standard texts serve that purpose. The format and the content of this text provide key information in a way that will save readers time and energy concerning topics that they need to know.

It is my hope that The Secret Series® will expand to include other veterinary ophthalmology titles, such as large animal species and exotic species, because ophthalmology still turns me on. It has been enjoyable working with my colleagues to complete this text, and their contributions are much appreciated. In addition, we are all indebted to our animal patients, clients, students, interns, residents, and, last but certainly not least, veterinary technicians.

Ronald C. Riis, DVM, MS, DACVO

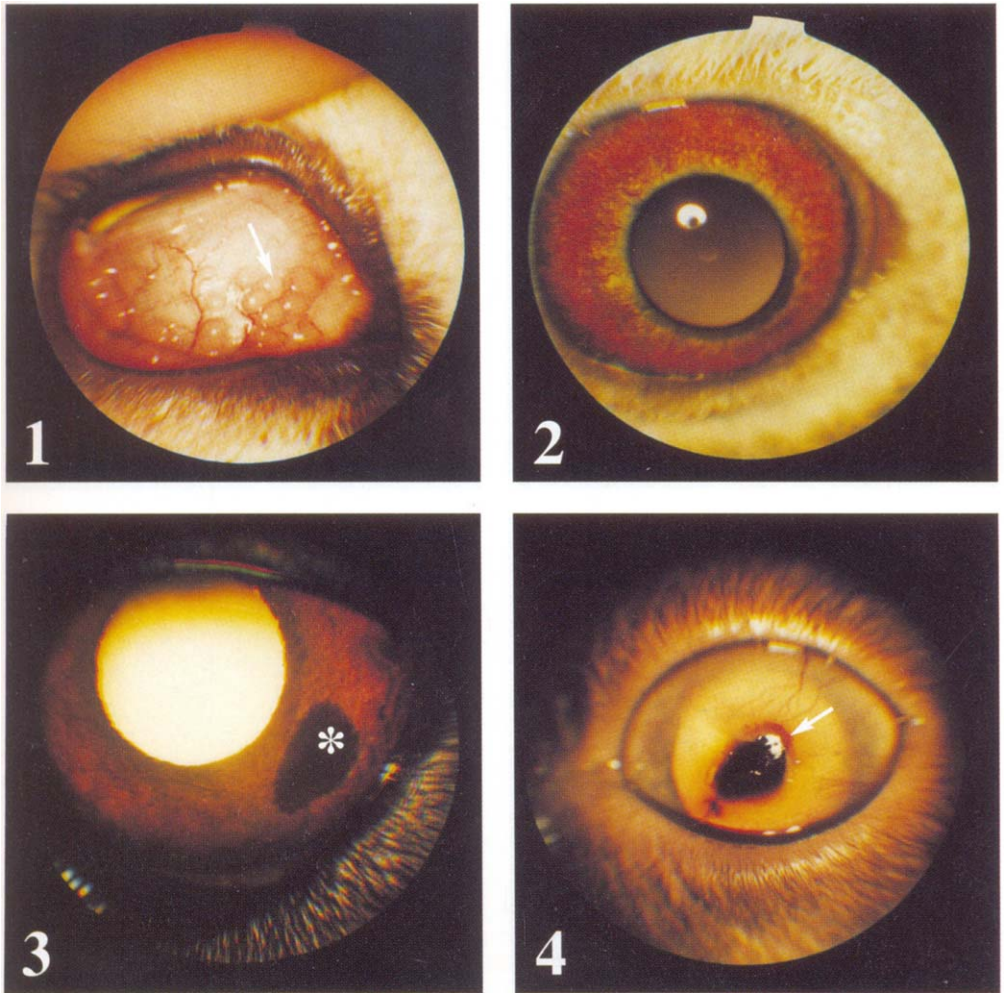


FIGURE 1. Dog nictitans. Diagnosis: follicular hyperplasia.

FIGURE 2. Pigeon iris. Diagnosis: normal "eye sign."

FIGURE 3. Dog iris with focal pigmentation. Diagnosis: iris nevus.

FIGURE 4. Cat cornea with central pigment and neovascularization. Diagnosis: sequestrum.

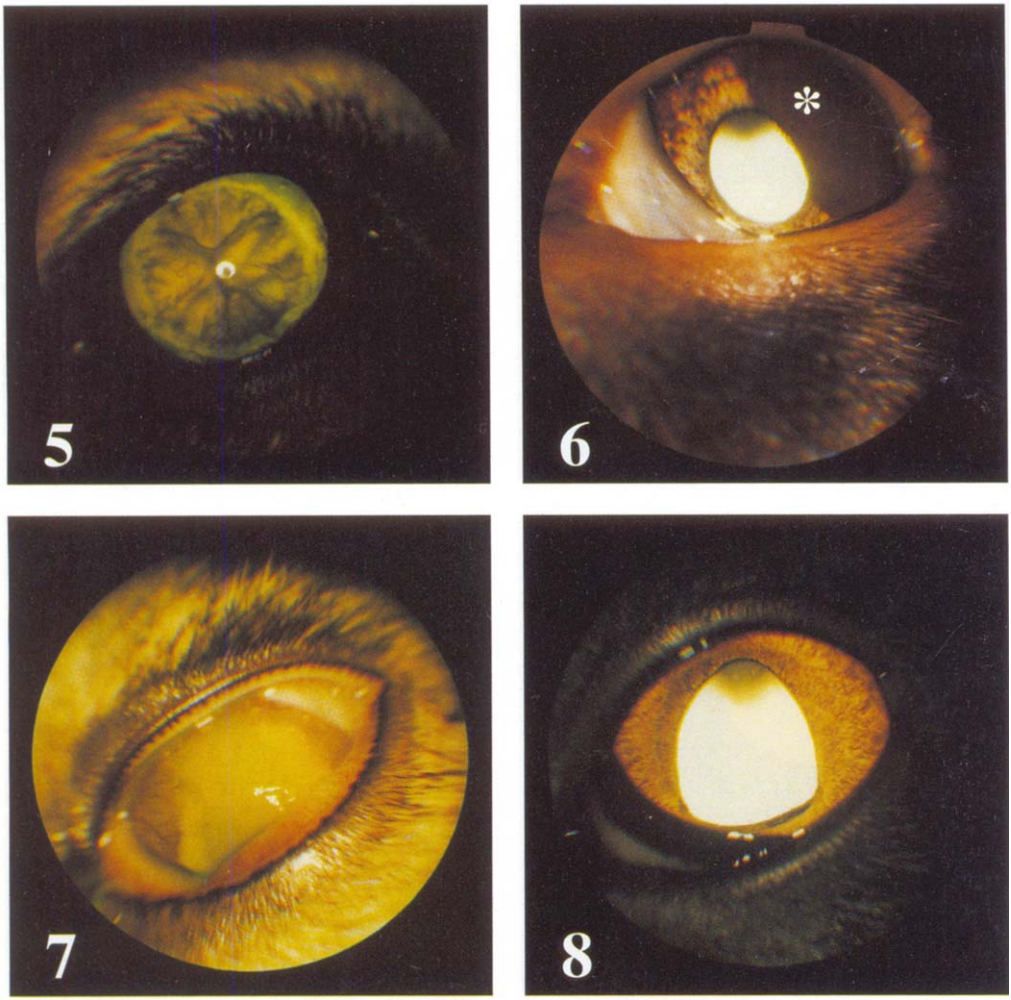


FIGURE 5. Dog eye with lens opacity. Diagnosis: cortical and perinuclear cataract.

FIGURE 6. Dog iris bulging pigemented tumor. Diagnosis: anterior uveal melanoma.

FIGURE 7. Cat cornea with neovascularization infiltrate. Diagnosis: stromal abscess.

FIGURE 8. Cat iris, unusual shape. Diagnosis: typical iris coloboma.

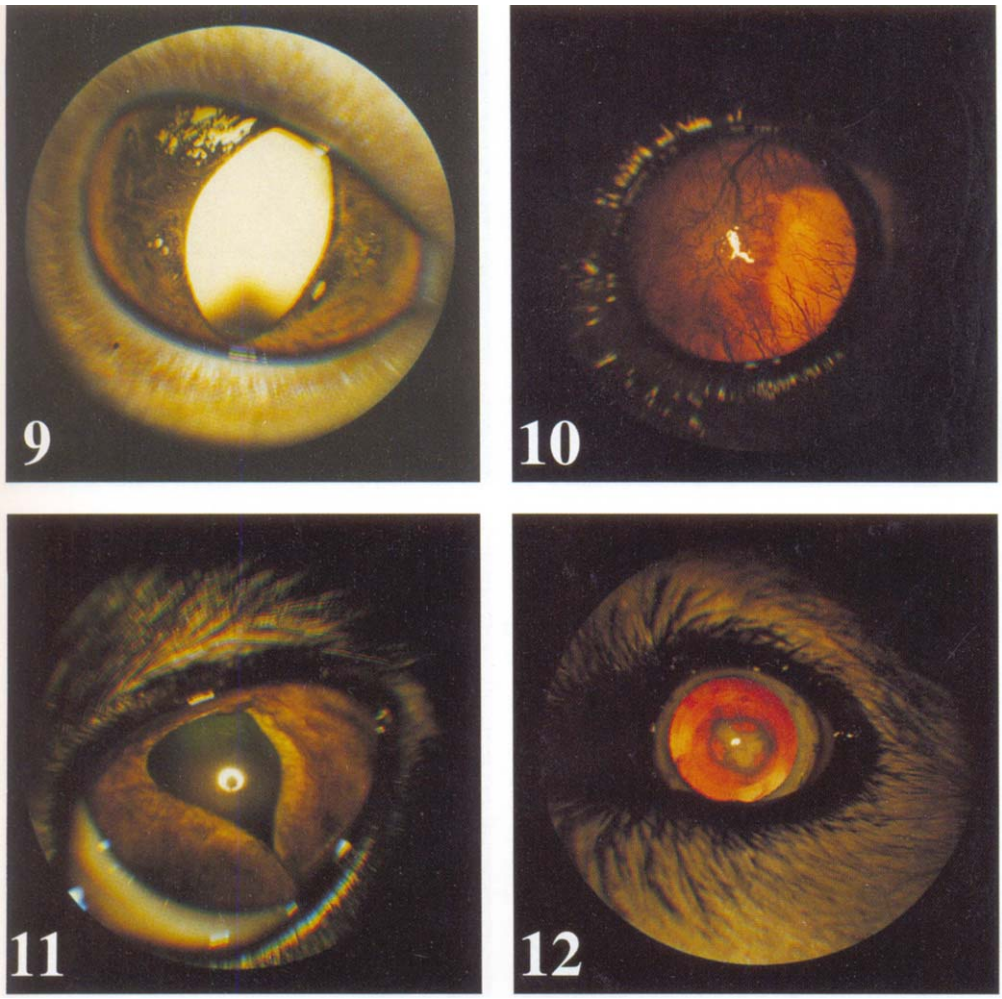


FIGURE 9. Cat iris with stromal rarification. Diagnosis: senile iris atrophy.

FIGURE 10. Dog cornea with extensive neovascularization. Diagnosis: keratoconjunctivitis sicca.

FIGURE 11. Dog iris, swollen and disfigured. Diagnosis: ocular manifestation of lymphoma.

FIGURE 12. Dog lens opacity. Diagnosis: congenital inherent cataracts.

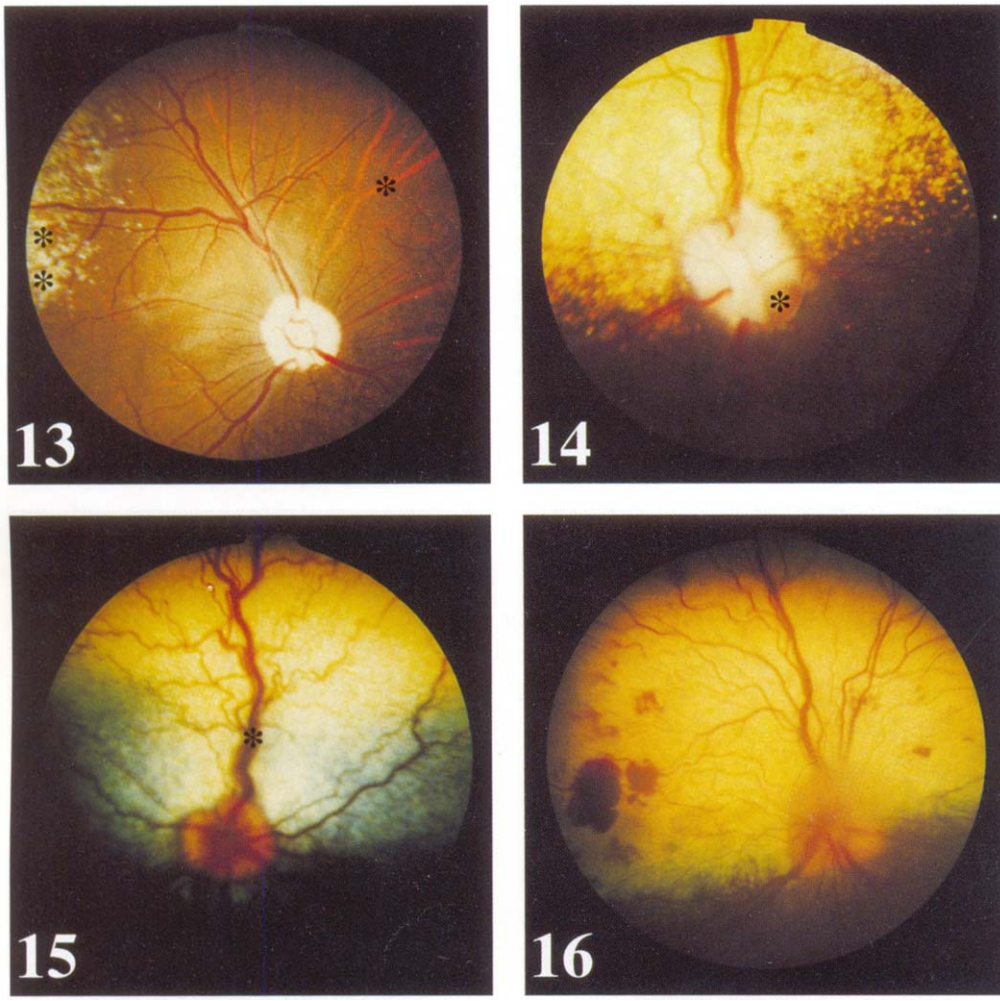


FIGURE 13. Chocolate Labrador retriever fundus. Normal variation. Note choroidal vessels (*) and small tapetal islands (**).

FIGURE 14. Tri-collie fundus. Diagnosis: small optic disc coloboma (*).

FIGURE 15. Dog fundus. Diagnosis: uveitis associated with pyometra (*).

FIGURE 16. Dog fundus with hemorrhage. Diagnosis: hemorrhage secondary to thrombocytopenia. Note: hemorrhage is located in the intraretinal and photoreceptor layers, vitreal haziness over disc secondary to plasmoid effusion.

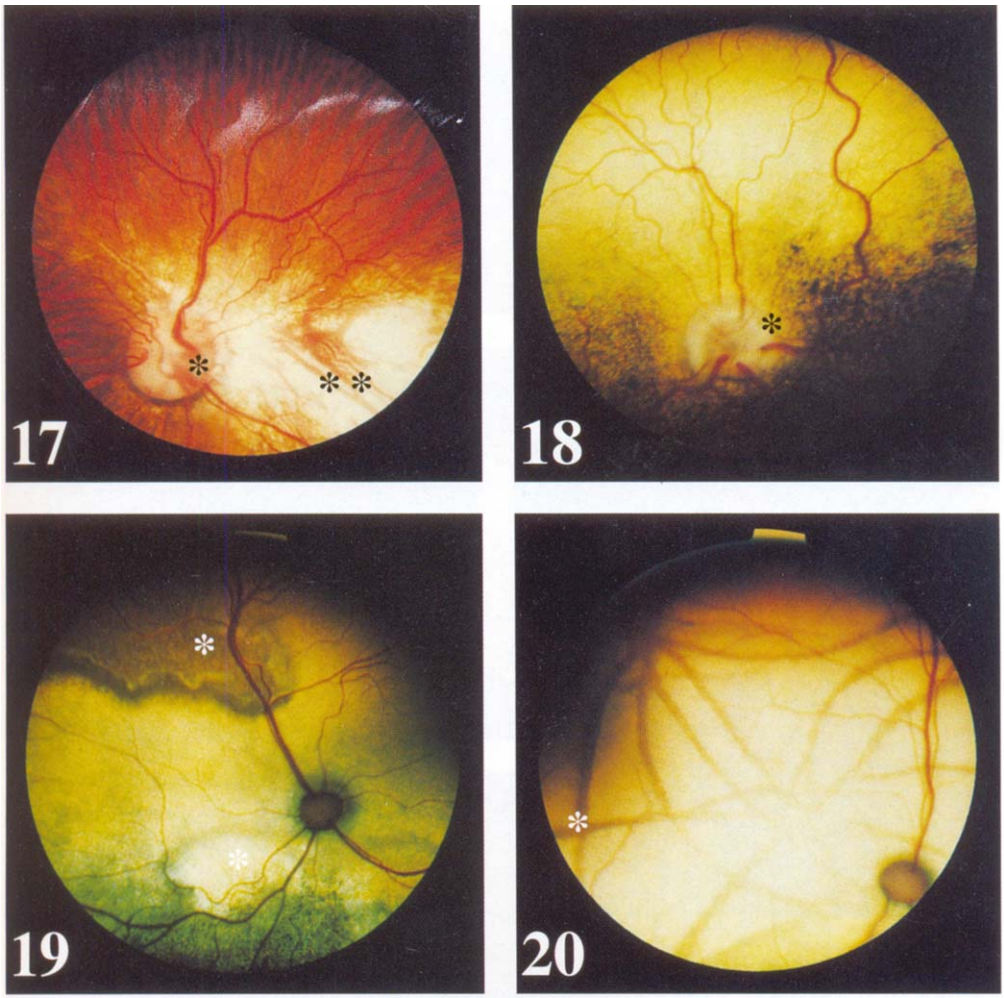


FIGURE 17. Merle collie fundus. Diagnosis: subalbinotic with small optic disc coloboma (*) and choroidal hypoplasia (**).

FIGURE 18. Golden retriever. Diagnosis: normal variant. Note excessive myelination of optic disc (*) (pseudopapilledema).

FIGURE 19. Cat fundus with large areas of altered reflectivity (*). Diagnosis: chorioretinal scars. Rule out toxoplasmosis.

FIGURE 20. Cat fundus with linear scars (*). Diagnosis: ophthalmomyiasis (larvae tracks).

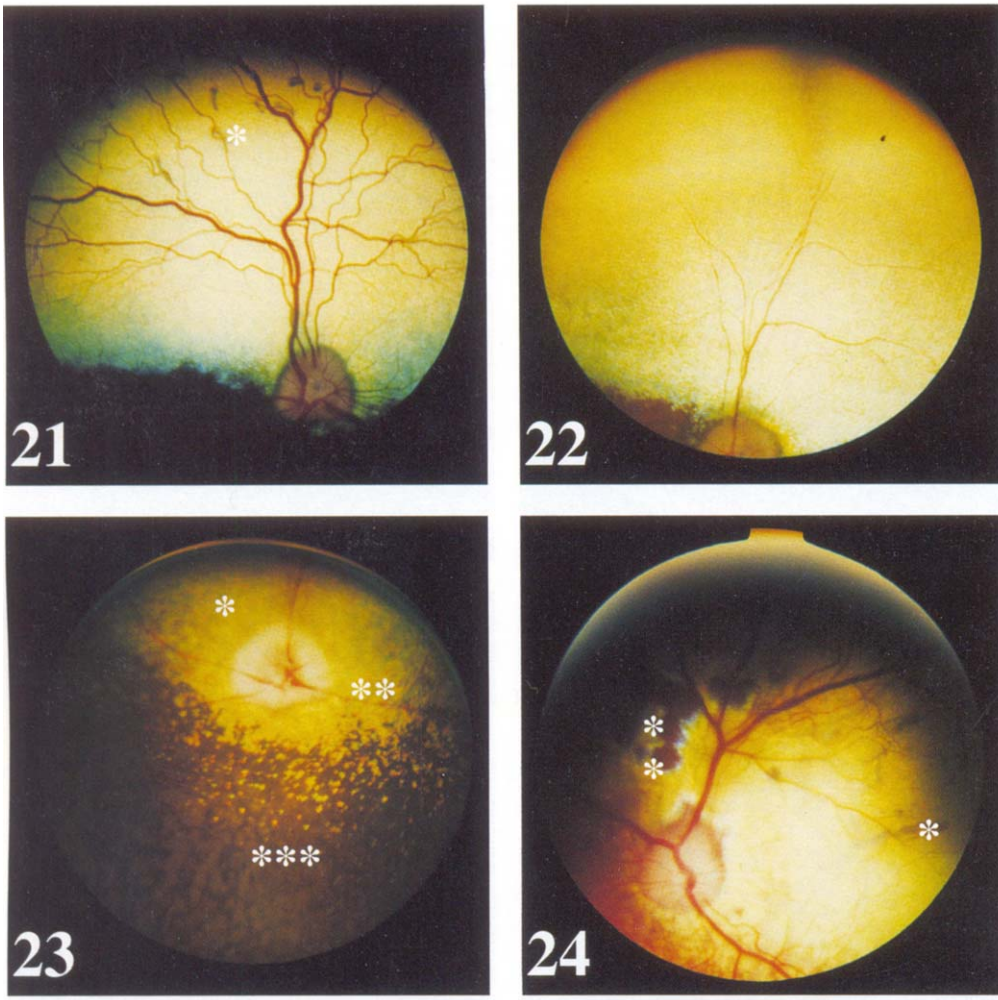


FIGURE 21. Cocker spaniel fundus with linear scars (*). Diagnosis: retinal folds or retinal dysplasia.

FIGURE 22. Portuguese water dog tapetal fundus showing vascular attenuation and hyperreflectivity. Diagnosis: progressive retinal atrophy.

FIGURE 23. Labrador retriever fundus with tapetal hyperreflectivity (*), vascular attenuation (**), and nontapetal pigmentation (***). Diagnosis: progressive retinal atrophy.

FIGURE 24. Springer spaniel fundus with scarring, unpigmented (*) and pigmented (**). Diagnosis: retinal dysplasia.

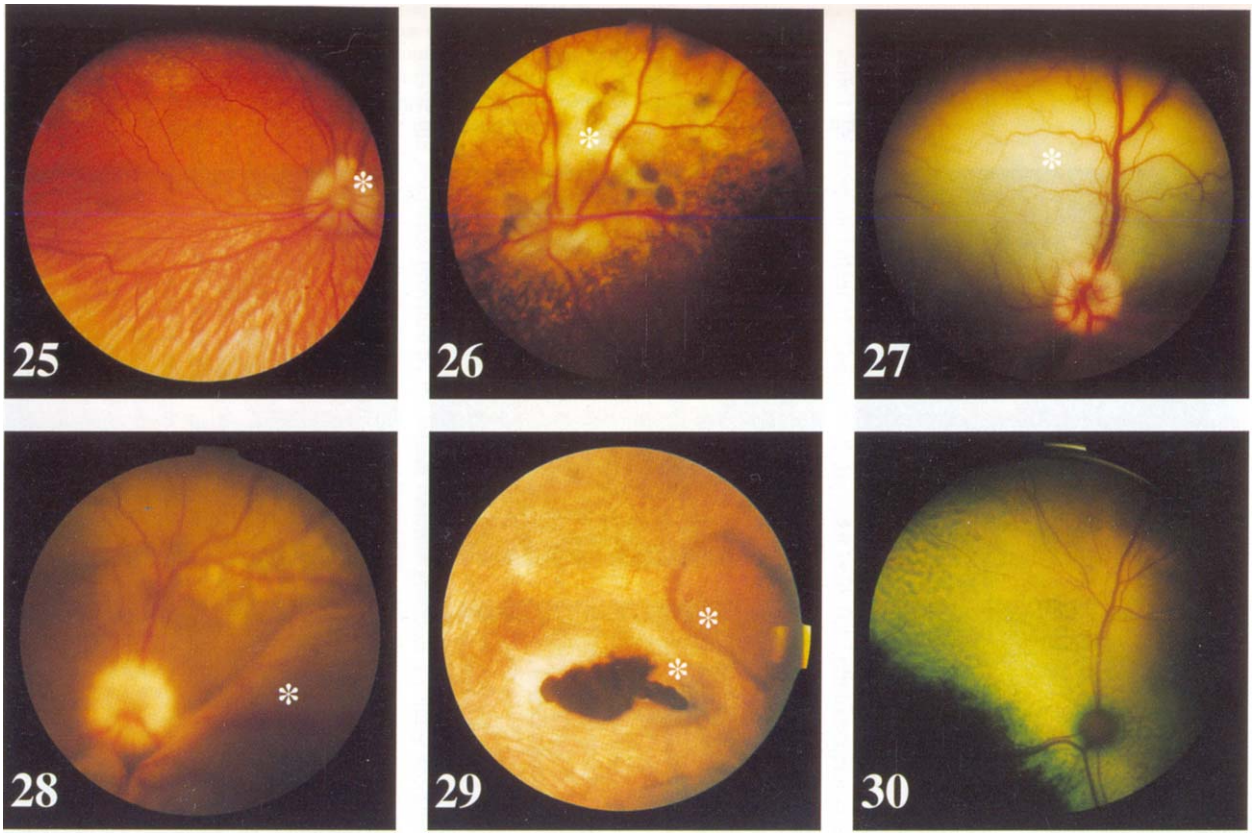


FIGURE 25. Siberian husky with an albinotic tigroid fundus. Diagnosis: Bergmeister's papilla (*) (pearl-gray spherical body in center of optic disc).
FIGURE 26. Springer spaniel fundus. Diagnosis: retinal dysplasia (*) and optic disc hypoplasia.
FIGURE 27. German shepherd fundus. Diagnosis: flat retinal detachment (*).
FIGURE 28. Dog fundus. Diagnosis: bullous retinal detachment (*).
FIGURE 29. Owl fundus. Diagnosis: retinal hemorrhage (*) adjacent to and involving pecten secondary to trauma.
FIGURE 30. Cat fundus. Diagnosis: multifocal retinal detachments secondary to antifreeze toxicity.

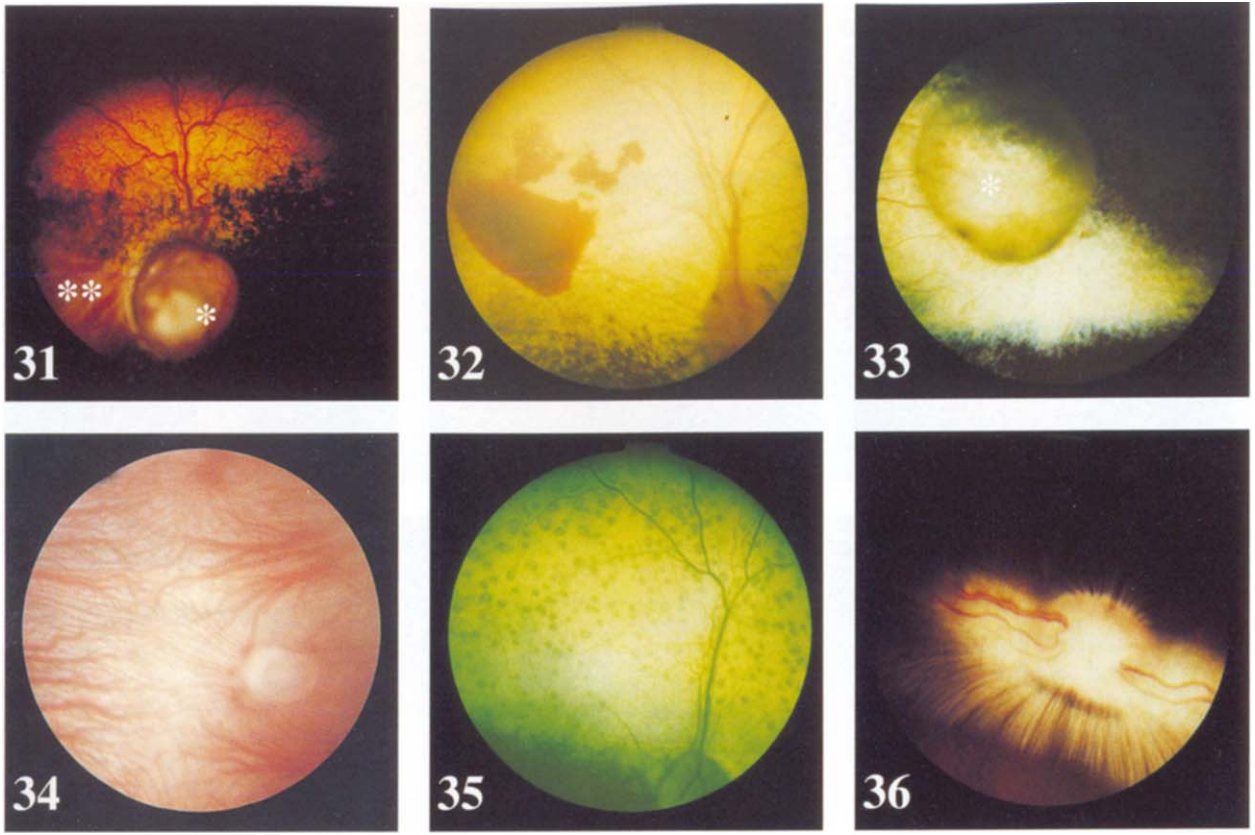


FIGURE 31. Sable collie fundus. Diagnosis: large optic disc coloboma (*) and choroidal hypoplasia (**).
FIGURE 32. Dog fundus. Diagnosis: choroidal hemorrhage secondary to hypertension.
FIGURE 33. Dog fundus. Diagnosis: focal retinal detachment (*).
FIGURE 34. Chinchilla fundus. Diagnosis: normal.
FIGURE 35. Dog fundus. Diagnosis: multiple retinal scars secondary to distemper.
FIGURE 36. Rabbit fundus. Diagnosis: central optic disc depression and myelinated nerve fibers.

I. General

1. ELECTRICAL ACTIVITY OF THE VISUAL SYSTEM: THE ERG AND THE VER

Ellis R. Loew, Ph.D.

1. What is the electroretinogram (ERG)?

The first step in the process of vision is the absorption of light by the primary receptor cells and the transduction of this event into a membrane potential change. This change in potential is called the receptor potential. The primary receptor cells (i.e., photoreceptor cells) of the visual system are the rods and cones. They are derived from ciliated cells and respond to a light increase with a membrane hyperpolarization due to the closing of Na+ channels. There is also a redistribution of ions in the inter- and intracellular spaces that results in extracellular currents. The membrane potential change leads to a change in transmitter release that affects the electrical activity of neuronal elements proximal to the photoreceptors. These subsequent changes also produce extracellular currents in the retina. In the end, stimulation of the ganglion cells leads to the production of action potentials that move over the inner retinal fiber layer and exit the eye via the optic nerve. Only the ganglion cells produce action potentials. All other electrical activity in the retina is graded. By measuring the changes in retinal activity in response to known stimuli, one can deduce many of the characteristics of retinal processing underlying the visual process.

2. What is the electrical basis of the ERG?

There are always ions flowing within the retina because of the action of pumps, membrane leakage and other potential differences. Moving charges are called a current, and a current flowing through the resistance provided by the retinal structure produces a voltage according to Ohm's law ($E = IR$ where E is voltage, I is current, and R is resistance). To measure voltage, place two electrodes attached to some kind of voltmeter at two points in the current path separated by some distance. If the line joining the electrodes is parallel to the current path, the full ohmic voltage is measured. If the line joining the electrodes is normal to the path, and the current flow is uniform along the path, then no voltage is measured. The magnitude of the measured voltage is a sine function of the electrode axis relative to the current path. This is of great importance in measuring neuronal potentials because it points out the importance of electrode geometry in making accurate measurements.

The electrical events recordable from the retina are of two types. Intracellular recordings make use of microelectrodes and can measure the activity of single cells. The main voltage source being measured is the transmembrane membrane "battery." Extracellular recording measures the potential differences that arise between different parts of a cell or between cells. In these cases, the electrodes do not pierce the cell membrane, and, in fact, the electrodes can be quite large and remote from the cells of interest. Extracellular measurements of retinal activity take advantage of the geometry of the retina, the location of "voltage sources," and the presence of a resistive layer (remember, current flowing through a resistor produces a voltage—that is Ohm's law). Remember that there is a continuous extracellular dark-current flowing from the inner segment to the outer segment of rods and cones. This current is moving in a radial direction. Electrodes placed at the ends of the photoreceptor cell would record a voltage that was proportional to the current and the extracellular resistance (from Ohm's law!). If the electrodes were placed on either side of the outer segment, no po-

tential difference would be recorded. If we imagine a layer of parallel outer segments with the electrodes "bridged" to the ends of all the cells using a conductive solution, the voltage we measure would be the sum of the contributions from all the cells. This is called a mass-cell potential. The concept to be gained from the above example is that those cells having currents flowing radially in the eye can be recorded with the electrodes placed across the retina, whereas the cells whose extracellular currents flow in the plane of the retina will not be measured. Also, the potential seen by distant electrodes represents the sum of all the radial currents flowing through the retinal resistance.

3. How is the ERG performed?

The vertebrate ERG takes advantage of the above geometrical considerations so that the response of the retina or whole eye can be recorded using external electrodes. In practice, a reference electrode is placed on some part of the animal unresponsive to light but close to the eyes (e.g., the forehead or the bridge of the nose), while a second, active electrode is placed in contact with the cornea. Because the eye is filled with conductive solution and also sits in a conductive "pocket," these electrodes are effectively recording across the whole retinal layer. The active and reference electrodes are connected to a differential amplifier whose output is the difference between these two inputs. In this way, any signals such as motion artifacts or power line noise are minimized or eliminated since signals common to the two inputs will cancel each other out. A third, common or ground electrode placed on the ear or nape of the neck establishes the zero level of the system.

4. What are the ERG components?

The retina responds to a flash of light with a series of electrical changes representing the passage of the stimulus through the retinal circuitry. As cells in the information pathway change their electrical state, they contribute to the overall current flow within and across the retina. The recording electrodes sum these changes in space and time so that the potential measured at any instant in time represents the activity of all the cell types electrically active at that time. This leads to the appearance of a complex waveform of varying amplitude and polarity recorded under the corneal electrode (Fig. 1). In order to understand what is happening in the retina in response to a stimulus, it is necessary to ascertain how each contributing current generator in the retina responds separately. Theoretically, if one knew the response characteristics of each cell type in isolation, the complex ERG waveform could be reproduced by simple summation. There are three main components, or processes (P), that sum to produce the ERG: PI, PII, and PIII following the designation of Granit (for a more detailed discussion of these and a number of minor components the reader is directed to reference 3). PI is a slow, cornea positive wave that appears to be generated by the pigment epithelium. It is not normally used in veterinary ERG diagnostics and will not be further considered. PII is a fast cornea positive wave localized to the bipolar and Müller cells. PIII is a cornea negative wave issuing from the photoreceptors.

5. How do the components sum to produce the multiphasic ERG?

Figure 1 demonstrates how these components sum. The generation of the ERG proceeds from the absorption of a photon train (a flash of light) by the photoreceptor cell outer segments. This leads to activation of PIII, which pulls the corneal potential negative resulting in the initial negative deflection of the ERG. The electrical changes in the photoreceptors, reflected in PIII, lead to a change in transmitter release that, after a time delay, result in changes in bipolar and horizontal cell activity as well as changes in extracellular ion concentrations activating PII. The horizontal cell currents flow mainly in the plane of the retina and thus contribute little to the ERG. The rise-time of PII is faster and its amplitude greater than PIII because of amplification between the photoreceptors and the more proximal cells. This leads to a rapid increase in corneal positivity and a resulting negative peak in the ERG, producing the a-wave. PII peaks rapidly and with its decay produces another peak and identifiable wave, the b-wave. Because the decay of PII is faster than that of PIII, there is often a late negativity in the ERG. Note that the only part of the ERG that can be unequivocally correlated with the activity of a single cell type is the descending limb of the a-wave, which is a pure photoreceptor cell.

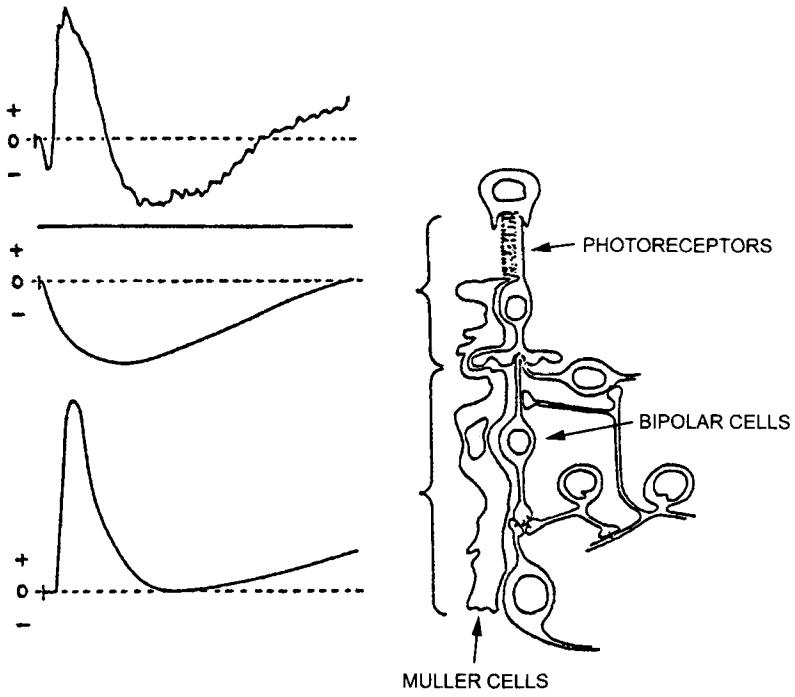


Figure 1. Component analysis of the vertebrate ERG. As seen, the negative monophasic wave generated by the photoreceptor cells sums with the positive monophasic wave generated by the Müller/bipolar cells to produce the multiphasic ERG at the top.

The waveforms and amplitudes of the components depend on the intensity, duration, and wavelength of the stimulus as well as adaptation state. As for all sensory responses, rise times and amplitudes are proportional to the log of the stimulus intensity (i.e., as the stimulus intensity increases response amplitude increases and the time-to-peak decreases). For the ERG, this means that the amplitudes of the a- and b-waves will increase as the stimulus intensity increases and their time-to-peak or implicit times will decrease. These changes can be seen in Figure 2. Over a defined range, stimulus duration multiplied by stimulus amplitude is a constant. However, with increasing duration, there is the risk of initiating adaptational processes that can affect ERG waveform. Wavelength affects response characteristics because of the spectral sensitivity of the photoreceptors as determined by their contained visual pigments.

6. What kinds of stimuli are best for eliciting the ERG?

Although the retina can follow slowly changing stimuli, a rapid rise time stimulus such as that produced by a photographic strobe, fast shutter, or light emitting diode (LED) ensures a rapid activation of the transductional cascade and good temporal segmentation of the ERG waves. The geometry of the stimulus is also important. The ERG is a mass cell response. Therefore, the best responses will occur when the entire retina is stimulated. This is best achieved by placing the eye in an integrating sphere ensuring that the visual field is filled with a uniform stimulus (a Ganzfeld stimulator). A uniformly irradiated, frosted contact lens covering the pupil is a good approximation of a true Ganzfeld. Sources that do not stimulate the entire retina can also be used successfully as long as they stimulate a large retinal area. Intraocular scatter will ensure that areas not directly stimulated will ultimately contribute to the ERG (this is particularly true for tapetal animals).

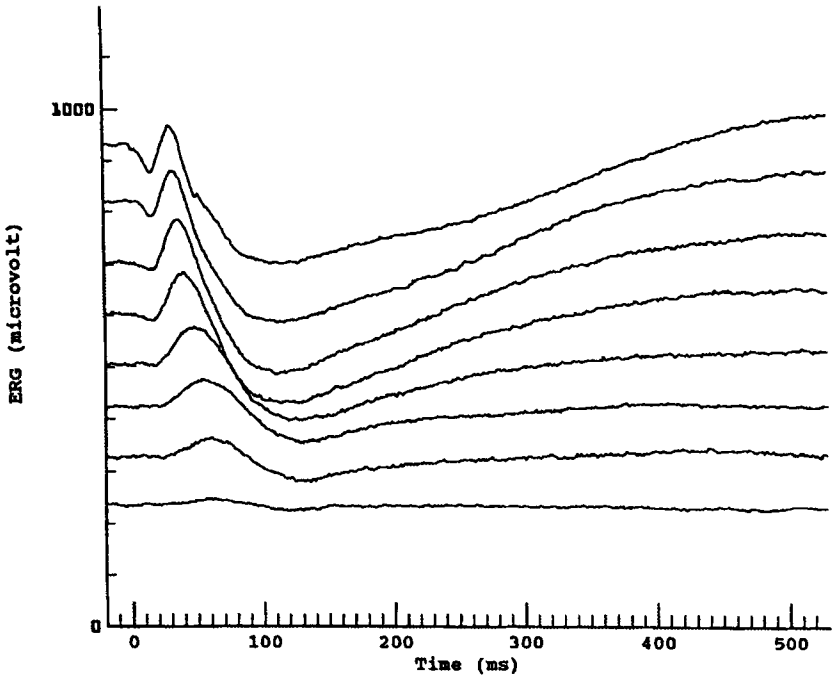


Figure 2. The effect of increasing stimulus intensity on the canine ERG (brightest at top). Note the a- and b-wave amplitude increases and decreases in implicit times. The stimulus was a 50-msec flash from a 470-nm blue LED.

7. What are the minor ERG components?

A number of minor components and ERG features may be of diagnostic significance in certain situations:

The **c-wave.** This is a slow, positive wave arising from PI and is believed to be due to changes in RPE activity. It is best produced using long duration stimuli on the order of seconds. It is also sensitive to adaptation state. Because it is a slow wave, it is best recorded using a direct current (DC) amplifier or one with a long time constant—both of which require stable preparations.

The **d-wave.** This is an off effect again seen with long stimuli. Interestingly, it usually has the same polarity as the normal "on" ERG event and is therefore not a typical rebound effect. This may come from the fact that on and off responses are carried by different retinal pathways and show different response properties. The d-wave shows the same changes with stimulus amplitude as the on event.

The **e-wave.** This is a late event coming many seconds after an appropriate stimulus. Unlike other waves, the implicit time of the e-wave increases with increasing stimulus intensity. It has been associated with afterimage activity as the result of bright flashes given under defined adaptation states.

Oscillatory potentials (P waves). Under conditions of fast rise times and bright stimuli, oscillations may be seen on the ascending limb of the b-wave extending over the peak. These arise from local feedback circuits operating between the retinal layers.

8. What parameters are measured in the clinical ERG and how do they relate to retinal abnormalities?

In order to use the ERG diagnostically, it is necessary to establish normal values for the ERG parameters most likely to be affected by retinal pathologies. This means generating ERGs with

known and accepted stimuli and cataloging associated waveform parameters. The most obvious parameters to record are the amplitudes and implicit times of the ERG wavelets. These can be used to generate slopes, which in some cases may be more useful than their parent parameters. For example, the slope of the descending limb of the a-wave is sensitive to changes in the transductional cascade that are often associated with primary photoreceptor cell degenerations. Before proceeding, it should be remembered that in some cases it is only important to determine that the retina is responding to light with a qualitatively normal-looking response. This "all-or-none" ERG is most commonly used for evaluation of prospective cataract extraction patients.

Some examples of possible ERG abnormalities can illustrate the utility of the test:

- Because the ERG is a mass cell response, it will be affected by a decrease in the number of stimulated cells or by changes in their response characteristics. In the case of primary photoreceptor cell degenerations, such as canine PRA, abnormal transduction and degenerative changes lead to a decrease in PIII for a given stimulus intensity. This would be seen as decreased a-wave amplitude, increased implicit time, and decreased a-wave slopes. Because activation of PII depends on PIII, the b-wave is also affected with decreasing slopes and amplitudes and increased implicit times. However, a-wave changes often may precede b-wave changes owing to the gain between PIII and PII. An intensity series also shows changes in the normal pattern of ERG changes with stimulus intensity.
- Processes such as optic neuritis may differentially affect the inner and outer retinal layers. In some cases this can lead to decreases in PII with a sparing of PIII. This leads to a "negative" ERG with only PIII contributing substantially. As the neuritis resolves, the ERG may return to normal with the return of PII. Increased intraocular pressure may also isolate PIII as the blood supply to the inner layers is reduced. Transient or early glaucoma can produce the negative ERG waveform.
- PIII activates PII so that anything interfering with this activation will lead to a decrease in b-wave with an increase in negativity. This kind of pattern is seen in some forms of congenital stationary night blindness where there is a defect in synaptic transmission.
- The ERG results from retinal currents flowing through the retinal resistance (following Ohm's law). A decrease in retinal resistance would lead to decreased ERG amplitudes with implicit times staying normal. Changes in retinal resistance can be produced by structural defects or metabolic changes in the resistive elements, such as the retinal pigment epithelium (RPE). One way to differentiate between amplitude decreases due to photoreceptor cell pathologies or resistive changes is to calculate the a- to b-wave ratio and compare it to normal values.
- One may stimulate the eye and get no recordable ERG as is seen in sudden acquired retinal degeneration (SARD) and advanced progressive retinal atrophy (PRA). Simply put, no photoreceptor cells, no ERG!

9. What are the limitations of the clinical ERG?

Although the ERG can be used to differentiate among a number of retinal pathologies, it cannot be used to diagnose blindness. For example, imagine a situation where 90% of the retina has been wiped out with only a small central 10% area remaining. With such a small number of cells, the ERG could be lost in the noise and yield no response even though the animal can still function visually. It is also possible to have a perfectly normal ERG in a functionally blind animal. Remember that the usual ERG is an outer layer retinal phenomenon. A pathology of the ganglion cells or their axons (i.e., optic neuritis) could stop information flow and cause blindness. Obviously, central lesions could also produce blind animals with normal ERGs. The lesson here is that, for the ERG to be useful in all but the all-or-none situation, it should be evaluated in the light of other factors such as pedigree, ocular exam, and behavior.

10. What is the visual evoked response (VER)?

VER, also known as the visual evoked cortical potential (VECP or VEP), represents the activity of cortical areas resulting from retinal stimulation.

11. How is the VER measured?

The exact protocols may vary, but the general idea is to place an active electrode over the occipital region and reference this to an electrode placed at the vertex or nasion. Stimuli from a strobe lamp, an ultrabright LED, or pattern stimulator are presented to the eyes and the responses averaged over a second. The VER is seen as a series of waves occurring after the main ERG components, which are usually present as an artifact.

12. How is the VER used diagnostically?

In human medicine, VER is used to confirm the patency of the visual pathways, measure visual acuity, check for albinism, and measure progression of multiple sclerosis by using delays in the appearance of VER peaks. However, in companion animals, the VER normally is used only to test for visual pathway patency.

13. Why is the VER not a standard diagnostic tool for companion animals?

Although it is easy to obtain a VER from a companion animal, standardization and the development of normal patterns to be used diagnostically are problematic. The measurement of the VER is not as straightforward as the ERG because of large variations in the geometry of the skull and the three-dimensional nature of the VER "generator"—the visual cortex. Variations among breeds have not been cataloged nor have there been adequate age studies. The lack of quantitative data limits the usefulness of the VER. There is also the problem of electrode placement standardization. In humans, the standard 10–20 EEG positions are used with the electrodes over the visual cortex (O_1 and O_2) being successively connected to one side of an amplifier whereas reference electrodes are attached to the other. Standardization is possible because head dimensions vary very little when expressed as percentage distances between landmarks such as the inion and nasion and preauricular depressions. However, this is not the case for dogs and cats where different breeds can have radical differences in head dimensions and placement of the head relative to the rest of the body. This makes it almost impossible to develop a standard for dogs or cats. In addition, interference from the ERG is a problem. In some breeds the relationship between skull shape and eye placement makes it difficult to distinguish between late ERG components and the VER, especially when bright flashes are used as stimuli. Although late VER waves can usually be detected, any value of the early components is lost because of this uncertainty.

BIBLIOGRAPHY

1. Armington JC: The Electroretinogram. New York, Academic Press, 1974.
2. Fishman GA: The Electroretinogram and Electrooculogram in Retinal and Choroidal Disease. Rochester, NY, American Academy of Ophthalmology, 1975.
3. Heckenlively JR, Arden GB (eds): Principles and Practice of Clinical Electrophysiology of Vision. St. Louis, Mosby, 1991.

2. COLOR VISION IN ANIMALS

Ellis R. Loew, Ph.D.

1. What is color vision?

Light illuminating an object can be reflected, transmitted, or absorbed. These interactions impart information about the object onto the light field that emanates from the object. The visual system is adapted to extract object information from the two-dimensional light field and use it to detect, recognize, and distinguish such objects from other objects and from the background. Differences between objects and backgrounds integrated over the spectral bandwidth of the illuminating light subserve brightness detection and discrimination. Spectral changes in the illuminant due to interactions with objects are interpreted as color. Color vision is the ability to recognize and distinguish objects based on their spectral reflectance as opposed to their relative broad-band intensity variations.

2. What are the requirements for color vision?

The most fundamental requirement for color vision is the presence of at least two photoreceptor cell populations (usually cones) differing in spectral sensitivity. Having two different visual pigment opsins expressed in each of the populations satisfies this requirement. However, spectral sensitivity may also be adjusted by interposing filters in front of the outer segments (e.g., oil droplets as in birds and reptiles) or through optical means (e.g., wave-guiding). In addition to the two spectrally different detectors, there must be a neural network capable of comparing the outputs of these two detector classes and extracting color or chromaticity signals from them. Lastly, there must be interpretive centers that can "paint" the color information onto the perceptual map of the visual world.

3. Why is color vision adaptive?

This is actually a question of the evolution of color vision by a species, which must improve the probability that an individual having the capability will survive to reproduce. The need for chromatic discrimination may not extend over the whole of the available spectrum but may only have to be active over a particular spectral region of particular importance to the organism. We often hear that this or that animal has color vision but it is not as "good" as ours. This is a meaningless statement since "good" can only be judged within the context of the visual world in which the organism in question lives.

4. How does one determine if an animal has color vision?

As mentioned above, the presence of at least two spectral classes of photoreceptor is a prerequisite for color vision. Given this, it might be thought that if one could confirm the presence of two or more classes, color vision could be assumed. Unfortunately, this is not the case for it is possible to have sensitivity in different spectral regions without extracting the information necessary to name colors. Nonetheless, finding more than one class is certainly suggestive of color vision and often points the way toward experiments that can confirm color vision.

The two most common ways of checking the retina for different spectral classes of photoreceptor are **microspectrophotometry** (MSP) and **electrophysiology.** In MSP, a retina is isolated in the dark and the cells dispersed by maceration. Microbeams are shown through the outer segments of the rods and cones and the contained visual pigment measured. The absorption spectrum of the visual pigment, together with any pre-outer segment filters, sets the spectral sensitivity of the cell. Once the visual pigment complement has been identified, the capabilities of a color vision system based on these pigments can be modeled.

Electrophysiologic methods can be applied at any point in the visual pathway to measure spectral sensitivity that can be referred back to the retinal photoreceptors. The paradigm is one in

which stimuli that differ in color are used to excite the system, and the response is analyzed in terms of the spectral nature of the stimulus. Constant response criteria are preferred, but constant stimulus intensity series are also useful. If done at the level of the photoreceptor with either intracellular or suction electrodes, the data should be similar to that obtained using MSP, which seems to be the case. If done at higher levels the responses are much more complex, but information about color capabilities is still possible. Recently Jacobs and his collaborators have used a flicker method to isolate and number the spectral sensitivity channels in a number of vertebrates including companion animals. The paradigm involves alternating a colored stimulus with a broadband white one and asking the question, "what intensity colored stimulus is required to match the response to the white stimulus?" This is done for a series of colored stimuli from the red to the near ultraviolet (UV). The series is then repeated, only this time in the presence of a background light chosen to desensitize red-sensitive cells. If such cells are present, there will be a change in the spectral sensitivity curve, and by subtracting one from the other the spectral sensitivity of the red channel can be calculated. In this way, Jacobs has found evidence that the majority of mammals are dichromats—they have two spectral sensitivity channels. Trichromacy, as seen in humans and several other primates, is relatively rare.

Most recently, molecular techniques have been used to check for color vision. Starting with the excellent studies of Nathans (1986) on the human color vision system, steady progress has been made in examining many other species. The basic technique involves determining the opsins (the protein moiety of the visual pigment) expressed in the retina by isolating mRNAs, making cDNAs, using probes to pick out likely opsin candidates, and obtaining their nucleotide sequences. These can be translated into amino acid sequences. Once the amino acids present at specific "tuning" sites are known, the spectral absorption of the visual pigment that uses the opsin can be calculated. It is also possible to insert a constructed opsin gene into an expression system and then reconstitute the visual pigment by adding vitamin A aldehyde to the expressed opsin. The absorption spectrum of the reconstituted visual pigment can be measured directly. This technique has been most successfully applied to primates and rodents.

Of course, the best test for color vision is to demonstrate it behaviorally. That is, can an animal discriminate among objects based only on spectral characteristics as opposed to brightness differences? In a typical test, animals would be trained to always go to a red card verses a white card using classical conditioning techniques. Once the animal was operating at a reasonable confidence level, it would be asked to discriminate the red card from cards of other colors and brightnesses. The whole process would then be repeated after training to another color. In this way a color space could be constructed indicating which colors could be discriminated and how different they had to be to be discriminated. Although this sounds straightforward, it is fraught with difficulties. Training the animal is difficult, and there are problems controlling for other cues such as texture, position, or even odor. Only a few cases of behavioral testing have been unequivocal in demonstrating color vision.

5. What about color vision anomalies?

It is well known that humans can suffer from alterations to their color vision system rendering them incapable of making color discriminations in particular spectral regions—that is, they are color blind. It is now known for certain that color blindness results when one of the normally present visual pigments is absent due to a mutation that eliminates one of the opsins. For example, a person lacking the opsin for the red photoreceptor cannot distinguish between reds and greens and is called a protanope. Loss of the green or blue opsins leads to discrimination loss in other spectral regions. It is to be expected that such mutations would be present in nonprimates. However, behavioral color blindness has not been confirmed in any other species.

Of greater interest are mutations that alter the opsin at the sites that spectrally tune the visual pigment. In these cases the normal number of opsins are present, but they are not in the "normal" spectral position. This leads to a distortion of the color space meaning that these individuals would see the world differently from their "normal" conspecifics. In humans such amino acid differences

lead to conditions such as protanomaly and deuteranomaly. There is behavioral evidence that this occurs in animals, particularly primates.

6. What do other animals see?

This is a common question and one that captures the imagination of animal owners and practitioners. If asked within the context of television, it can be said with certainty that our color television sets do not "work" for dogs and cats. Color television is designed specifically around the human system and appears as color nonsense to other animals with different visual pigments and spectral sensitivities. This does not mean that animals cannot recognize things on a television screen, only that they cannot use color as a recognition cue. If one knew enough about the color vision system of an animal, a true color television system could be made that would provide the full richness of color we expect from our system. Only for the honeybee has such a system been constructed, but once the canine genome is available, some enterprising person will probably fill the void and offer a pet color television system complete with synthesized color movies for the pet's enjoyment. Cat and horse television cannot be far behind!

7. What about color vision in other vertebrates?

Remembering the minimum requirements for color vision, it is not surprising that nonmammalian vertebrates also have color vision systems. Among the best studied are fish, reptiles, and birds. However, whereas three color channels appears to be the maximum number for mammals, it is not uncommon for other animals to have four, five, or even six color channels. A good example from fish is the goldfish, which has four visual pigments in four separate classes of cones including double cones. There are three cones sensitive in the human visible range as well as an ultraviolet sensitive cone. In fact, most diurnal nonmammals have an ultraviolet cone leading to the potential for quadrachromatic vision at higher order color vision systems. The goldfish is also interesting because instead of using vitamin A_1 as the chromophore for making visual pigment, it uses vitamin A_2. The substitution of vitamin A_2 for vitamin A_1 shifts the absorption spectrum for visual pigments toward the red end of the spectrum. In general, freshwater fish use vitamin A_2 for making visual pigments, and marine species use vitamin A_1. For example, a switch to vitamin A_2 in humans would push the long-wave pigment from a λ_{max} of 565 nm to approximately 625 nm. As a consequence, the spectral range over which the goldfish color vision system operates is greater than for humans and other mammals, extending from the ultraviolet to the infrared. The same is true for many tropical coral reef fish.

However, it is in reptiles and birds where vertebrate color vision really expands. Diurnal reptiles not only have up to five visual pigments, some using vitamin A_2 as the visual pigment chromophore, but they also can have a variety of highly colored oil droplets in their cones that act as filters that change their spectral sensitivity (Fig. 1). These droplets act as cut-off filters that can improve the spectral resolution in certain spectral regions. The combinations of pigments and droplets can lead to as many as six different chromatic channels before chromophore type even comes into play!

The presence of so many color channels in other vertebrates begs the question of what we are missing by having only trichromatic color vision that excludes the ultraviolet and infrared parts of the spectrum. Spectroradiometric measurements of many natural objects show reflectance differences extending into the UV and the infrared. For example, many fruits have substantial UV reflectance that not only could improve contrast, but also could add to the already available color information in the visible spectrum to increase recognition cues for frugivores. It is also known that many animal parts, such as the feathers in birds and the dewlaps in lizards, show variable UV reflectance. At the other end of the spectrum, chlorophyll-containing plant parts are highly reflective in the infrared with the spectral character of this reflectance depending on such factors as chlorophyll concentration, age, prior light exposure (plants can tan!), or disease. We can only guess at how rich in color the world would appear if we could look at it through the eyes of other animals.

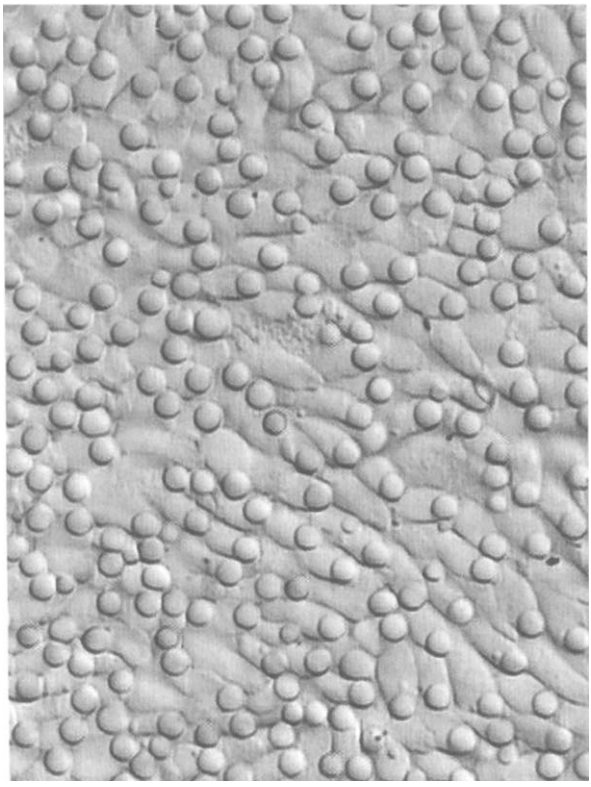


Figure 1. Oil droplets from the eye of a lizard (*Anolis cristatellus*). There are four classes of oil droplet in almost all fully diurnal lizards: a yellow, a green, and two colorless droplets, one of which absorbs in the ultraviolet. These are placed immediately in front of the outer segments and act as filters (800×).

BIBLIOGRAPHY

1. Boynton RM: Human Color Vision. New York, Holt, Rinehart & Winston, 1979.
2. Cronly-Dillon JR, Gregory RL: Evolution of the Eye and Visual System. Boca Raton, FL, CRC Press, 1991.
3. Jacobs GH: Comparative Color Vision. New York, Academic Press, 1981.
4. Jacobs GH: Photopigments and seeing: Lessons from natural experiments. Invest Ophthalmol Vis Sci 39:2205–2216, 1998.
5. Loew ER: Determinants of visual pigment spectral location and photoreceptor cell spectral sensitivity. In Djamgoz MBA, Archer SN, Vallerga S (eds): The Outer Retina. London, Chapman & Hall, 1995, pp 57–78.
6. Lythgoe JN: The Ecology of Vision. Oxford, Clarendon Press, 1979.
7. Mollon JD, Sharpe LT: Colour Vision: Physiology and Psychophysics. London, Academic Press, London, 1983.
8. Nathans J, Thomas D, Hogness DS: Molecular genetics of human color vision: The genes encoding blue, green, and red pigments. Science 232:193–203, 1986.
9. Smythe RH: Vision in the Animal World. London, MacMillan, London, 1975.

3. OPHTHALMIC IMAGING

David A. *Wilkie*, D.V.M., M.S., *and* A. *Michelle Willis*, D.V.M.

1. What imaging techniques are available for imaging the eye and orbit?

Many varied imaging modalities can be applied in ophthalmology to assess the architectural structure of the globe, adnexa, orbit, and visual system. Traditional imaging modalities include radiography and ultrasound, but as access to sophisticated equipment becomes more commonplace, computed tomography (CT) scan and magnetic resonance imaging (MRI) are becoming routine procedures in the assessment of clinical patients. In addition, newer imaging modalities are allowing access to in vivo ultrastructure and multidimensional views of the globe to permit a better understanding and earlier diagnosis of ocular disease. The clinician must remember that ocular imaging is an addition to, not a replacement for, routine ophthalmic and physical examination.

Routine Imaging Modalities	*New Imaging Modalities*
Radiographs	Ultrasound biomicroscopy
Plain	Color Doppler ultrasound
Contrast studies	Confocal microscopy
Ultrasonography	Confocal scanning laser ophthalmoscopy
MRI	Nerve fiber analyzer
CT scan	Optic coherence tomography
Fluorescein angiography	
Fundus photography	

2. How do I decide which imaging technique to use?

The decision on the imaging modality depends on several factors. Availability and cost are often the two most important factors because access to many of these tests is limited and many require sophisticated and expensive equipment and diagnostic expertise in the interpretation of results. The area of anatomic interest is also a factor. Imaging of the anterior and posterior aspects of the globe require the ability to view soft tissue with high resolution while having a different requirement for depth of axial resolution. Although B-scan ultrasound can image the entire globe and orbital contents, the axial resolution of ultrasound biomicroscopy and confocal microscopy is limited in imaging the anterior-most aspect of the globe. Imaging of the adnexa and orbit varies depending on whether the soft tissue or bony structures are of interest. In general, radiographs and CT scans are preferred for evaluation of the bony orbit and nasal and sinus cavities whereas MRI and ultrasound are superior for the globe and orbital soft tissue, and MRI is best for central nervous system evaluation. Evaluation of the nasolacrimal apparatus and vascular anatomy can be performed using contrast radiographs and techniques such as dacryocystorhinography. Fundus photography is used to document retinal vascular and optic nerve head changes for future comparison. When combined with the technique of fundus photography, fluorescein angiography allows visualization of retinal arterial and venous blood flow and optic nerve and choroidal blood flow (Fig. 1). Areas of delayed filling, nonperfusion, leakage, and blocked fluorescence are evaluated.

Selection of an orbital imaging technique requires a thorough understanding of pertinent anatomy applied to relevant clinical history and detailed ophthalmic examination. The clinical findings should direct the clinician to the imaging study that provides maximum information and narrows diagnostic considerations for the individual patient.

3. Which imaging modalities are clinically applicable and which are research tools?

In addition to a routine ophthalmic examination, ocular ultrasonography is perhaps the most useful diagnostic imaging modality, allowing for rapid examination of the globe and orbit without requiring chemical restraint. Radiographs are also a common and useful aid, especially in

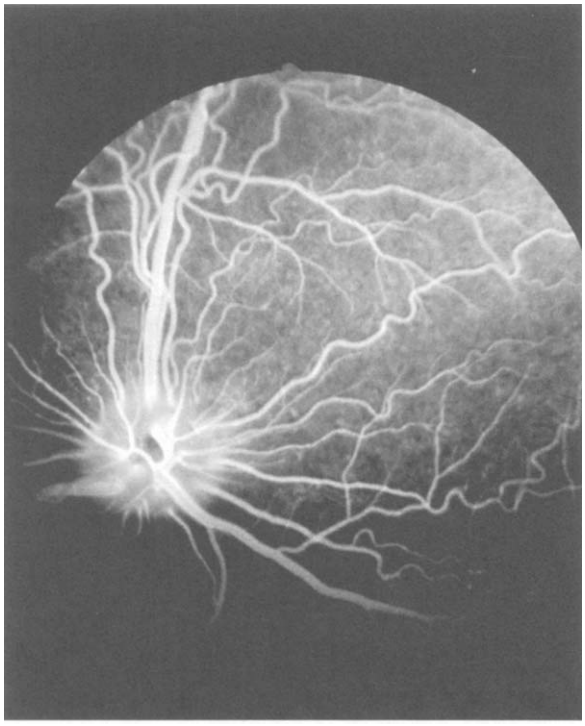


Figure 1. Late-venous phase fluorescein angiogram of a normal canine retina.

evaluating orbital and sinus disease. In recent years, MRI and CT scan have become more readily available and are considered routine in most specialty practices.

While currently only available in limited facilities, the newer imaging modalities are offering insight into disease pathogenesis and allowing accurate evaluation of extent of damage. Ultrasound biomicroscopy and confocal microscopy are applicable for anterior segment disease, and the nerve fiber analyzer, confocal scanning laser ophthalmoscope, and optical coherence tomographer examine the posterior segment and are most applicable in the understanding of glaucomatous retinal and optic nerve damage. Color Doppler ultrasonography allows evaluation of ophthalmic and orbital blood vessels to assess blood velocity and vascular resistance. This has applications in diseases with altered hemodynamics such as glaucoma and diabetes mellitus.

4. What is the goal of performing ophthalmic imaging?

The goal of the clinician should be to assess intraocular and periocular structures not visible by routine biomicroscopy or indirect ophthalmoscopy, to evaluate the extent of intra- and extraocular involvement in a disease process, and to examine structures that relate to the visual process such as optic nerve, optic chiasm, optic tracts, and visual cortex that cannot be adequately evaluated by routine examination. In addition, imaging techniques may help obtain a diagnosis, formulate a treatment plan, or give a more accurate prognosis of outcome.

5. What are the indications for skull radiographs in ophthalmology?

Radiographs of the skull are indicated to evaluate orbital trauma, to evaluate nasal, sinus, and oral disease with periorbital or intraorbital extension, and to look for bony destruction (Fig. 2). The variation in the inter- and intraspecies (especially canine) anatomy of the skull combined with the superimposition of structures often makes interpretation difficult. Use of lateral, dorsoventral, ventrodorsal, oblique, skyline, and open-mouth views is often required to fully evaluate the orbital and periorbital anatomy.

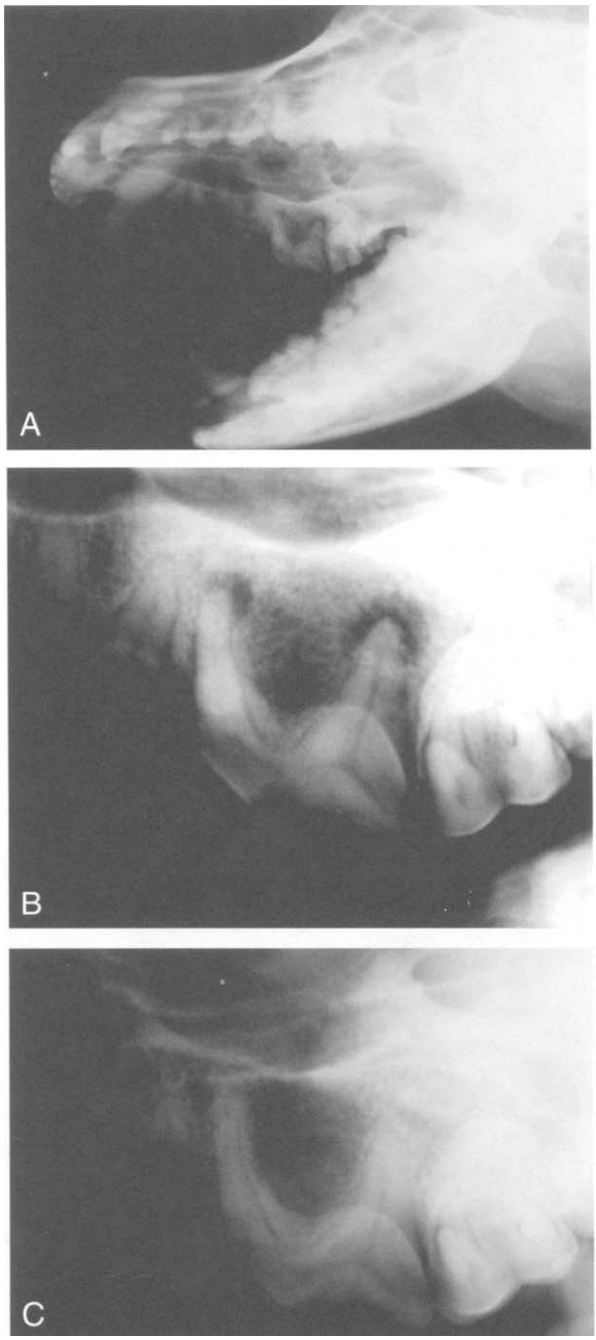


Figure 2. A, Plain radiograph of a 10-year-old canine with a swelling ventral to the right eye. Lucency surrounding rostral and caudal roots of right maxillary PM4, compatible with apical abscessation is noted. B, Close-up of abnormal right rostral and caudal roots of maxillary PM4. C, Close-up of normal left premolars. (Courtesy of J. Reichle.)

6. When do I choose contrast as compared to plain radiographs?

Plain radiographs are indicated to evaluate the bony orbit, nasal and sinus cavities, and skull (Fig. 3). They are obtained following head trauma, with exophthalmos and orbital disease, to evaluate nasal and sinus cavity disease resulting in or affected secondarily to orbital disease and to

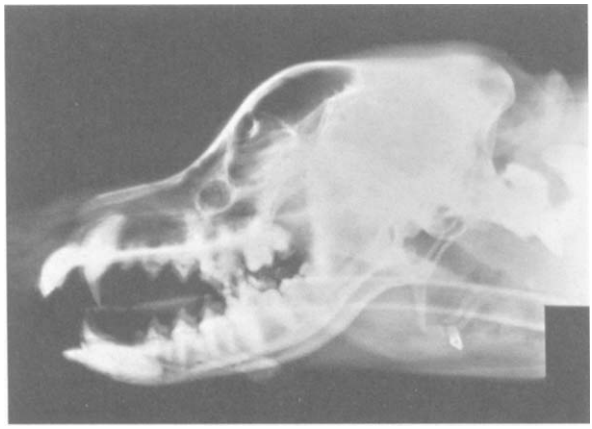


Figure 3. Plain lateral radiograph of a dolicocephalic dog. A circular area of bony sclerosis is visible anterior to the orbit above the molars.

evaluate for radioopaque foreign bodies such as pellets. General anesthesia is advised, and dorsal, lateral, and oblique views should be obtained. Evaluate the radiographs for fractures, bony lysis/proliferation, and increased soft tissue density.

Following plain radiographs, contrast radiographs can be used to evaluate the nasolacrimal apparatus, performing a dacryocystorhinography, and the vascular anatomy, using orbital venograms and arteriograms. Dacryocystorhinography is performed by cannulating the superior punctum and slowly injecting 1–2 ml of a radiopaque contrast agent into the nasolacrimal apparatus while occluding the inferior punctum (Fig. 4). The contralateral side is used as a normal control if possible. In general, use of other contrast radiographic techniques to further evaluate the orbit has been replaced by CT and MRI. In addition, CT and MRI are better suited to ascertain the extent of involvement of nasal, sinus, and orbital neoplasia prior to surgical or radiation therapy.

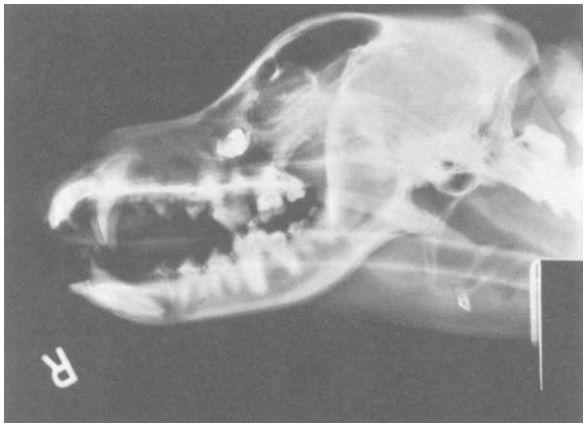


Figure 4. Contrast material has been used to perform a dacryocystorhinogram of the dog in Figure 3. The radiopaque contrast agent is pooling in the area of previously noted bony sclerosis, identifying a cystic dilation of the nasolacrimal duct.

7. What are the indications for ophthalmic ultrasonography?

Ultrasonography is an inexpensive, noninvasive, safe procedure that allows evaluation of the intraocular and retrobulbar tissue without sedation or general anesthesia. Ocular ultrasonography is indicated whenever opacity of the transmitting media of the eye (cornea, aqueous humor, lens, vitreous humor) prevents a complete ophthalmic examination. Ultrasound aids in evaluation of intraocular mass lesions, differentiation between solid and cystic structures, evaluating the extent of damage following ocular trauma, examination for a foreign body, axial length determination,

and examination of retrobulbar orbital structures. The most common clinical indications for ocular ultrasound are to evaluate for the presence of a retinal detachment in eyes with a cataract, to assess posterior segment damage and examine for the presence of a foreign body following trauma, and to evaluate intraocular structures in eyes with severe corneal opacification. In addition, orbital evaluation can be performed in instances of exophthalmos or orbital trauma. New ultrasound technologies include three-dimensional imaging, tissue characterization, and very high frequency (50 MHz) ultrasound biomicroscopy. For a further discussion of ocular ultrasonography, please see Chapter 4.

8. What is ultrasound biomicroscopy?

Ultrasound biomicroscopy is similar to a conventional B-scan ultrasound, but uses an operating frequency of 40–100 MHz to provide a high-resolution image of the cornea and anterior segment. The axial resolution is 2–5 mm, but the image resolution is similar to a histopathologic section. The cornea, sclera, limbus, iris, anterior chamber, iridocorneal angle, lenticular zonules, and ciliary processes are all imaged. This technique is most useful in evaluation of the iridocorneal angle in glaucoma and assessment of anterior uveal neoplasms, and it may prove useful in the determination of the depth of corneal involvement of squamous cell carcinoma or other infiltrative corneal diseases.

9. What is the difference between CT and MRI?

CT, or CAT, stands for *c*omputer *a*xial *t*omography. In general, CT scans provide high detail cross-sectional images with excellent contrast resolution compared with conventional radiographs. In addition the information can be manipulated to view the anatomy in any desired plain of section. Like radiographs, CT scans rely on a radiation source to transmit x-rays, but do so by rotating the source to create cross-sectional, two-dimensional scans. The data is then digitized and analyzed to create a gray-scale reconstructed image. The lighter the appearance of the area imaged (e.g., bone, muscle) the greater the absorption of x-rays; conversely, the darker the image (e.g., fat, liquids), the lower the x-ray absorption. CT scans are excellent for evaluation of the orbit, nasal, and sinus cavities and are good for the intraorbital portion of the optic nerve. CT is not as good as MRI for soft tissue (globe, optic nerve) or intracranial examination. CT is most often used to evaluate the extent of neoplastic involvement of the orbit and adjacent structures prior to surgical and radiation therapy (Figs. 5 and 6).

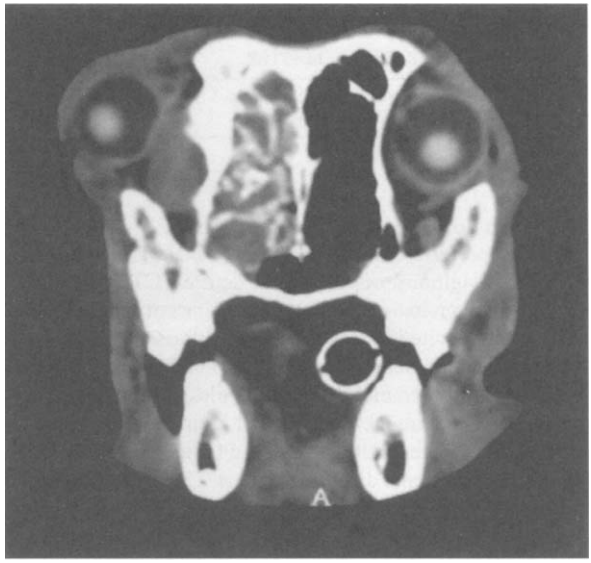


Figure 5. A CT scan of an 11-year-old canine with progressive exophthalmos and strabismus of the left eye of 1 month duration. A soft tissue mass with bone production and destruction is evident in the left orbit/nasal cavity. Diagnosis: chondrosarcoma. (Courtesy of J. Reichle and Colorado State University.)

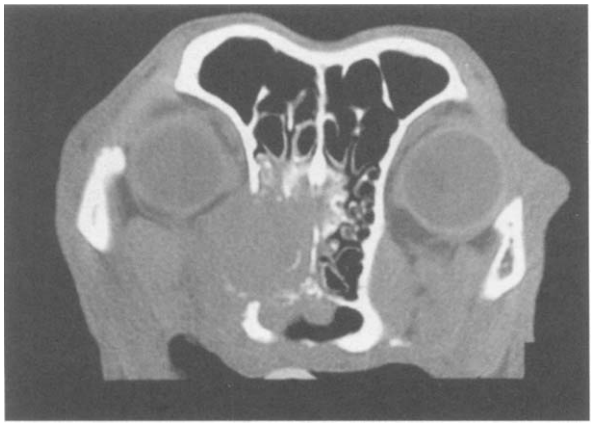


Figure 6. A CT scan of a 13-year-old canine. A soft tissue mass arising from right nasal cavity with bone destruction and invasion into orbit and is evident. Diagnosis: probable nasal adenocarcinoma (Courtesy of J. Reichle.)

MRI like CT allows information to be reformatted and viewed in any plain of section. Contrast and spatial resolution are excellent and permit differentiation of soft tissue and fluid. MRI images are obtained using a strong, static magnetic field that causes hydrogen protons to align with the magnetic field. Radiofrequency pulses are then applied, changing the axis of rotation of the protons, which then return to their previous alignment when the pulse is discontinued. This generates a signal that is used to create an image. The image depends on proton-density and proton-relaxation dynamics representative of the chemical and physical tissue properties. With MRI, proton-density, T1-weighted, and T2-weighted images are used with proton-density best for discriminating between gray and white matter, T1-weighted images better for anatomic detail and contrast enhancement, and T2-weighted for identifying masses, edema, and other fluids. T2 images of the globe are easily identified by the white, high-density vitreous signal. In addition, contrast enhancement using gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA) may help to highlight areas of blood-brain barrier breakdown.

Appearance on MRI of Various Tissues

	WATER	GRAY MATTER	WHITE MATTER	FAT	BONE	CORNEA	LENS CAPSULE	LENS	VITREOUS
T1	Black	Light gray	Medium gray	White	Black	Gray	White	Black	Light gray
T2	White	Dark gray	Dark gray	White	Black	White	Not seen	Black	White

10. When do I choose CT versus MRI?

CT is preferred for evaluation of orbital trauma, foreign body detection, and evaluation of osseous, cartilaginous, or calcified structures. CT is most often used to evaluate the extent of neoplastic involvement of the orbit and adjacent structures prior to surgical and radiation therapy. MRI is better suited for assessment of soft tissues (Fig. 7). It is indicated to assess extraocular extension of an intraocular neoplasm; evaluate orbital soft tissue, optic nerve, and optic chiasm; and examine for intracranial disease (neoplasia, inflammatory). Use of fat-suppression and contrast-enhancement techniques makes MRI a superior technique over CT for intraocular and optic nerve images. MRI is generally considered to be contraindicated when a metallic foreign body is suspected. An additional difference is that CT is generally significantly less expensive than MRI and more widely available.

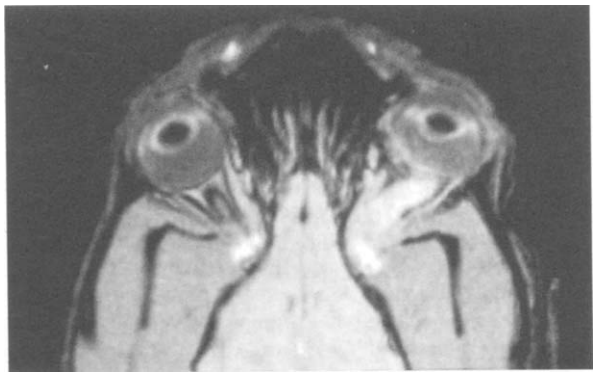


Figure 7. MRI of a 5-year-old canine, blind in the left eye with peripapillary retinal separation and retinal hemorrhage. Enlargement and increased intensity of the left optic nerve on the dorsal (coronal) view is seen. (Courtesy of J. Reichle and UC Davis.)

BIBLIOGRAPHY

1. Brooks DE: Ocular imaging. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 1998, pp 467–482.
2. Byrne SF, Green RL: Ultrasound of the Eye and Orbit. St. Louis, Mosby, 1992.
3. Koplin RS, Gersten M, Hodes B: Real Time Ophthalmic Ultrasonography and Biometry: A Handbook of Clinical Diagnosis. Thorofare, NJ, Slack, 1985.
4. Morgan RV, Daniel GB, Donnell RL: Magnetic resonance imaging of the normal eye and orbit of the dog. Vet Radiol Ultrasound 35:102–108, 1994.
5. van der Woerdt A, Wilkie DA, Myer CW: Ultrasonographic abnormalities in the eyes of dogs with cataracts: 147 cases (1986–1992). J Am Vet Med Assoc 203:838–841, 1993.
6. Wilkie DA, Gilger BC: Equine diagnostic ocular ultrasonography. In Rantanen NW, McKinnon AO (eds): Equine Diagnostic Ultrasonography. Baltimore, Williams & Wilkins, 1998, pp 637–643.
7. Williams J, Wilkie DA: An alternate modality for the examination of opaque eyes: Ophthalmic ultrasonography. Comp Cont Educ 18:667–677, 1996.
8. Williamson TH, Harris A: Color Doppler ultrasound imaging of the eye and orbit. Surv Ophthalmol 40:255–267, 1996.

4. OPHTHALMIC ULTRASONOGRAPHY

David A. *Wilkie*, D.V.M., M.S., *and* A. *Michelle Willis*, D.V.M.

1. What are the indications for ophthalmic ultrasonography?

Ultrasonography is a noninvasive, safe procedure that allows evaluation of the intraocular and retrobulbar tissue without sedation or general anesthesia. Ocular ultrasound is an addition to, not a replacement for, routine ophthalmic examination.

Ocular ultrasonography is indicated whenever opacity of the transmitting media of the eye (cornea, aqueous humor, lens, vitreous humor) prevents a complete ophthalmic examination. Ultrasound aids in evaluation of intraocular mass lesions, differentiation between solid and cystic structures, evaluation of the extent of damage following ocular trauma, examination for a foreign body, axial length determination, and examination of retrobulbar orbital structures.

The most common clinical indications for ocular ultrasound are to evaluate for the presence of a retinal detachment in eyes with a cataract, to assess posterior segment damage and examine for the presence of a foreign body following trauma, and to evaluate intraocular structures in eyes with severe corneal opacification. In addition, orbital evaluation can be performed in instances of exophthalmos or orbital trauma.

New ultrasound technologies, including three-dimensional imaging, tissue characterization, and very high frequency (50 MHz) ultrasound biomicroscopy, have become available recently.

2. What type of ultrasound probe do I need?

When performing ocular ultrasonography, it is desirable to have high resolution, but it is not essential to have deep tissue penetration. It is best to use a sector scanner with a small scan head diameter (footprint) to facilitate optimal placement on the cornea. Transducer probes are available in a range of frequencies. A low-frequency transducer (5 MHz) gives greater tissue penetration but poor near-field axial resolution, and a high-frequency transducer (10 MHz) gives lower tissue penetration but high near-field axial resolution. In simple terms, the higher the transducer frequency the better the visualization of superficial structures such as those found within the eye. The optimal ophthalmic transducer is a 10–15 MHz with a focal range of 3–4 cm. This probe will provide adequate depth of penetration to visualize the retrobulbar structures, enhanced resolution, and ability to visualize the anterior intraocular structures such as the iris, ciliary body, and anterior and posterior chambers. Alternately, a 7.5-MHz transducer will give good ophthalmic images of the lens, posterior segment, and retrobulbar structures, but the anterior segment will be lost in the near-field reverberation artifact. To overcome the near-field loss a stand-off device, using increased sterile coupling gel or performing the ultrasound examination through closed eyelids may help when using a 7.5-MHz transducer.

3. What is the gain setting?

Gain is measured in decibels and is also known as the sensitivity setting. In effect, increasing gain is similar to turning up the volume on a radio. By increasing the gain, you alter the intensity of the returning echo that is displayed on the screen, but do not alter the energy signal that is emitted. This allows amplification of weaker signals such as those in the vitreous. Increasing the gain setting too high will amplify background noise and result in false interpretation of structures such as the vitreous. Decreasing the gain allows only the strong echoes to remain and effectively increases axial and lateral resolution and decreases depth of sound penetration because deeper, weak echoes are not displayed.

4. How do I perform an ophthalmic ultrasound?

Topical anesthesia of the cornea (proparacaine 0.5% [Alcaine, Alcon Laboratories]) and manual restraint is usually all that is required for ultrasonographic ophthalmic examination in most

small animal patients. Sterile ultrasound coupling gel or K-Y Jelly is placed on the transducer tip or on the corneal surface. Cellulose-based coupling gels should be avoided because they may cause corneal irritation. The transducer is placed directly on the cornea, or the scan may be performed through closed eyelids or an offset device. Performing the examination through the eyelids or an offset device will facilitate examination of the anterior portions of the globe, whereas direct corneal contact provides a superior image of the posterior segment and orbit. When imaging through eyelids or an offset device, it may be necessary to increase the gain setting, and significant reverberation artifact may occur from air in the offset or that is trapped under the hair. The globe is imaged in both the horizontal and vertical planes through the visual axis. Oblique positioning of the probe should also be used for a complete examination. A temporal approach has also been described that entails placing the probe caudal to the orbital ligament and directing it ventrally to evaluate the retrobulbar structures. This technique allows superior visualization of the optic nerve, extraocular muscles, and orbital fissure. At the completion of the study the coupling gel should be irrigated from the eye and conjunctiva using sterile eyewash.

The image is projected to and viewed on a built-in monitor and can be output to a television, VCR, thermal printer, computer, or other image capture device.

5. What does a normal ultrasound look like?

In general, ultrasonographic images are described as hyperechoic, hypoechoic, and anechoic. There are four major ocular acoustic echoes within a normal eye: anterior cornea, anterior lens capsule, posterior lens capsule, and the retina/choroid/sclera (Fig. 1). When ultrasound energy travels across these interfaces, energy will be reflected back to the transducer in the form of an echo and will be seen as an echodensity. The iris, corpora nigra, ciliary body, optic nerve, orbital fat, muscles, and other orbital structures may generate additional echodensities. The optic nerve head or lamina cribrosa appears as a hyperechoic structure with the optic nerve itself seen as a hypoechoic structure extending posteriorly from the optic nerve head. The orbital muscle cone appears as an echodensity extending posteriorly from the equatorial region of the globe and converging toward the orbital apex. The anterior and posterior chambers, lens cortex and nucleus, and vitreous chamber are normally anechoic.

6. What is the difference between A and B scan ultrasonography?

Ocular ultrasonography as a diagnostic tool includes both amplitude-mode (A-scan) and brightness-mode (B-scan) ultrasound. In veterinary ophthalmology, B-scan ultrasound provides a two-dimensional, cross-sectional, real-time image and is the most common mode of ultrasound

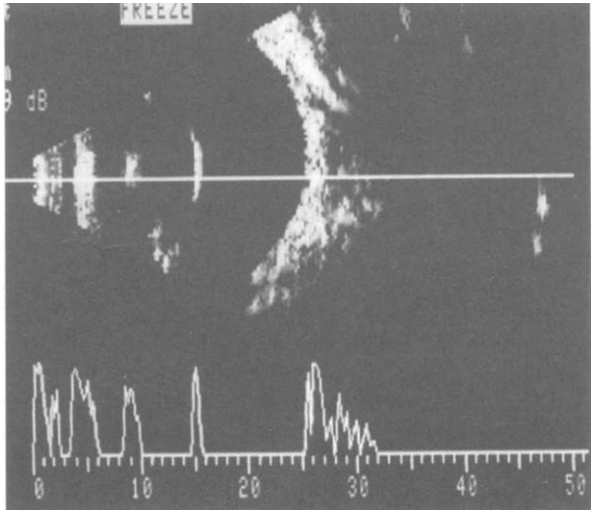


Figure 1. 10-MHz B-scan (*top*) and A-scan (*bottom*) ultrasound of a normal canine eye. The B-scan echodensities, from left to right, are cornea, anterior lens capsule, posterior lens capsule, and posterior eye wall. Corresponding A-scan peaks are evident below. A portion of the anterior uvea (iris, ciliary body) and retrobulbar tissues are also evident.

used in a clinical setting to obtain architectural information. A-scan is a one-dimensional, time-amplitude display and is used to determine axial length measurements, calculate intraocular lens power for lens replacement surgery, and quantify the echodensity (tissue characterization) of a structure. Most dedicated ophthalmic ultrasound units will display A-scan and B-scan images simultaneously (see Figure 1).

7. What features are evaluated during the ultrasound examination?

The eye should be examined from anterior to posterior in both the horizontal and vertical planes. The examiner evaluates the image in real-time allowing a mental three-dimensional composite to be created. First, determine that all normal structures are present, in normal position and of normal echogenicity. This includes the anterior chamber, iris, axial anterior and posterior lens capsule, vitreous, posterior eye wall, optic nerve, and orbital tissues. Evaluate for the presence of echogenic material in a normally anechoic space such as the anterior chamber, lens cortex and nucleus, and vitreous cavity. Determine the axial length of the lens and globe. Is the position of the lens normal with respect to the iris and posterior eye wall? Interpretation of orbital tissues is more difficult, but the contralateral orbit often can be used as a control, thereby aiding in the interpretation.

8. How is ultrasound used in the preoperative cataract patient?

Prior to cataract surgery, an ocular ultrasound should be performed to evaluate the axial length of the lens and the posterior segment. Specifically, lens resorption, vitreous degeneration, retinal detachment, persistent hyperplastic primary vitreous, and persistent hyaloid remnant may be noted. When cataractous, the entire lens circumference is visible and internal echos are seen (Fig. 2).

In one retrospective study, the combination of cataract and retinal detachment was present in 13% and cataract and vitreous degeneration in 21% of dogs evaluated prior to cataract surgery. Retinal detachment was seen in 7% of the eyes with immature cataract, in 9% of the eyes with mature cataract, and 19% of the eyes with hypermature cataract (Fig. 3). Vitreous degeneration was seen in 7%, 20%, and 28% of eyes with immature, mature, or hypermature cataract, respectively.

A-scan is also used to measure the axial length of the globe, which is required for intraocular lens power determination. This is more common in human cataract surgery.

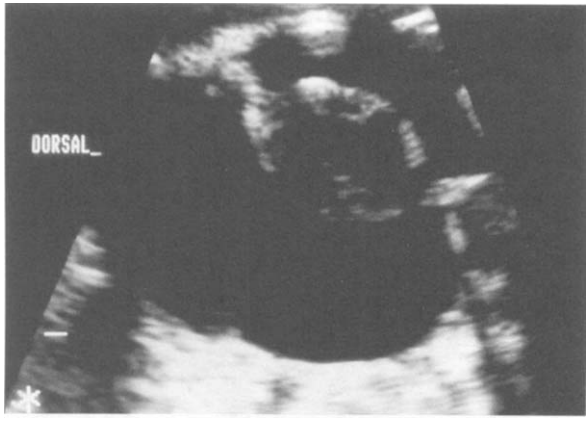


Figure 2. Ultrasound (7.5 MHz) of a canine eye with a mature cataract.

9. How is ultrasound used in hyphema?

Hyphema can be the result of trauma, hypertension or hyperviscosity, bleeding disorders, intraocular neoplasia, congenital abnormalities, and anterior uveitis. If the hyphema is severe enough to prevent a complete ophthalmic examination, ultrasound may aid in determination of the etiology and the prognosis. Hemorrhage in the posterior segment or a retinal detachment are

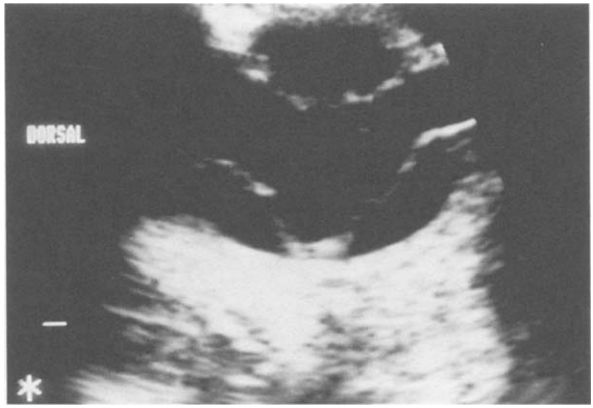


Figure 3. Ultrasound (7.5 MHz) of a canine eye with a cataract and a complete retinal detachment. This is the contralateral eye of the dog in Figure 2. Note the subretinal space is anechoic.

both negative prognostic indicators for vision. Intralenticular echo indicates a cataract. The eye should be evaluated for the presence of a foreign body or mass lesion suggesting a neoplasm. It is important to assess the posterior eye wall in eyes with traumatic hyphema because expulsive rupture of the posterior globe can occur.

10. How is ultrasound used in retinal detachment?

The diagnosis of retinal detachment is made based on the presence of an echodense linear structure in the posterior segment. Many of these remain attached at the optic disk and ora ciliaris retinae. During B-scan ultrasonography, a waving motion of the detached retina may be noted after the eye has stopped moving, termed **aftermovement.** The presence of echogenic material in the subretinal space suggests hemorrhagic or exudative detachment (Fig. 4).

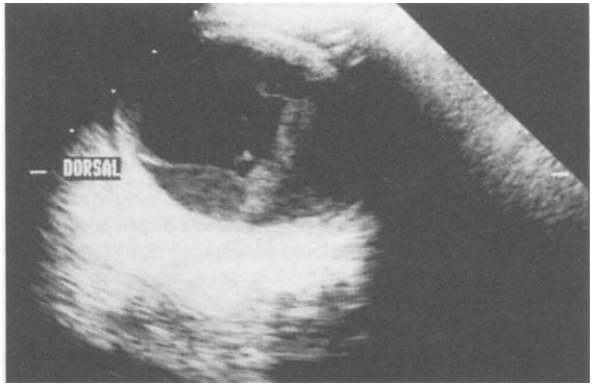


Figure 4. Ultrasound (7.5 MHz) of a canine eye with a complete retinal detachment secondary to intraocular blastomycosis. Note the exudative material in the subretinal space.

11. How is ultrasound used in orbital disease?

Ultrasound examination of the orbit is best performed using a 7.5-MHz probe, which allows deeper tissue penetration than is obtainable with a 10-MHz probe. Typically, orbital ultrasonography is performed in instances of exophthalmos to examine for retrobulbar space-occupying lesions, to evaluate the optic nerve (Fig. 5), or following orbital trauma to assess type and extent of damage. If an orbital mass lesion is present on ultrasonography, an attempt is made to characterize it as cystic or solid and to determine its location within the orbit. If a mass lesion is detected, it is possible to then obtain an ultrasound-guided fine-needle aspirate or biopsy to assist in diagnosis. A temporal approach may be of benefit in evaluating orbital disease.

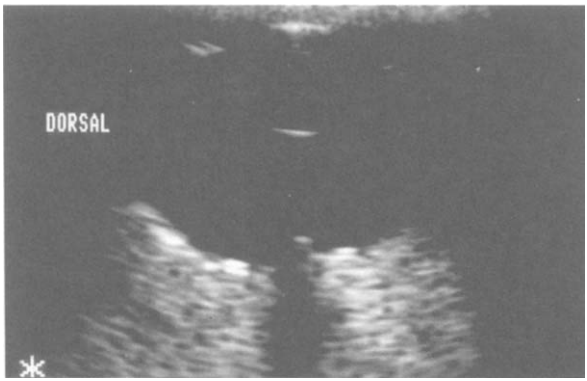


Figure 5. Optic neuritis with intravitreal projection of the optic nerve head and widening of the optic nerve shadow.

12. How is ultrasound used in intraocular neoplasia?

Ultrasound can be used to diagnose a mass lesion in eyes with hyphema or other opacities of the transmitting media. With ultrasound, the extent of a mass can be determined and the image used to help owners understand what is happening inside the eye. In addition, many ultrasound units will allow area and volume calculations of the mass. This information is used to assess response to therapy, such as laser photocoagulation, or progression of an untreated tumor.

13. What do vitreous echoes indicate?

Liquefaction of the vitreous (syneresis) occurs in vitreous degeneration. The liquefaction may be variable within the vitreous cavity resulting in tissues with different acoustic impedance. Therefore, multiple echogenic lines or areas will be seen ultrasonographically in the vitreous cavity. The detection of vitreal syneresis depends on the gain setting of the ultrasound probe. By increasing the far field gain, subtle differences in echogenicity will be more pronounced, making vitreous syneresis easier to detect. If the ocular examination is not performed at various gain levels, vitreous degeneration may go unnoticed.

Asteroid hyalosis is the accumulation of calcium and phospholipid particles. It is more common in older dogs, in association with diabetes mellitus, retinal degeneration, and intraocular neoplasia. Ultrasonographically, asteroid appears as many echodense structures suspended in the vitreous (refer also to Chapter 45).

Vitreous hemorrhage may be seen in association with ocular trauma, hyphema, retinal detachment, and hypertension (Fig. 6). It is a negative prognostic indicator because it indicates more severe ocular damage and may progress to fibrosis of the vitreous with resulting contraction and retinal detachment.

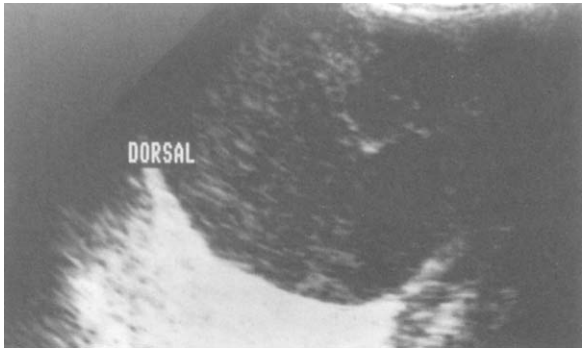


Figure 6. Trauma with hyphema and intravitreal echodensity suggestive of intravitreal hemorrhage.

14. When is ultrasound indicated in ocular trauma?

Ultrasonography helps to determine the extent and severity of the injury, evaluate position of the lens, assist in treatment selection, and allow the clinician to give a more accurate prognosis. In many instances, ultrasonography is the only examination method of value in an eye that is otherwise severely painful and opaque. In instances of severe eyelid swelling, the examination can be performed directly through the eyelids. Care should be taken to avoid further traumatizing the globe through excessive pressure exerted on the globe by the ultrasound probe. In addition, avoid exposure of intraocular contents to the coupling gel in instances of corneal laceration or uveal prolapse.

Sequelae of penetrating trauma include shallow anterior chamber, fibrin in the anterior chamber, lens capsule rupture, hyphema, retinal detachment, vitreous hemorrhage, and possibly posterior eye wall rupture. Blunt or concussive trauma causes a rapid increase in the intraocular pressure and often results in an expulsive rupture of the weak areas of the globe such as the limbus or posterior pole. Such an expulsive rupture will expel intraocular contents (lens, uvea, vitreous, and retina) out of the eye and onto the face or into the surrounding environment. In addition, hyphema, vitreous hemorrhage, retinal detachment, cataract, lens (sub)luxation and rupture, and choroidal detachment can all occur with blunt trauma. It is important to assess the posterior eye wall in eyes following blunt trauma because expulsive rupture of the posterior globe can occur.

15. What is ultrasound biomicroscopy?

Ultrasound biomicroscopy is similar to a conventional B-scan ultrasound, but it uses an operating frequency of 40–100 MHz to provide a high-resolution image of the cornea and anterior segment. The axial resolution is 2–5 mm, but the image resolution is similar to a histopathologic section. The cornea, sclera, limbus, iris, anterior chamber, iridocorneal angle, lenticular zonules, and ciliary processes are all imaged. This technique is most useful in evaluation of the iridocorneal angle in glaucoma and assessment of anterior uveal neoplasms, and it may prove useful in the determination of the depth of corneal involvement of squamous cell carcinoma or other infiltrative corneal diseases.

16. Are artifacts or false readings possible?

The normal lens acts to refract the sound waves from the transducer, resulting in a faster passage of sound through the peripheral compared with the central lens. This fact may result in the posterior eye wall appearing to be closer to the probe and will be seen as two discrete retinal elevations at the retinal surface, the size of which will vary with the scan angle. This artifact has been termed "Baum's bumps."

Reduplication echoes result from the echo passing from an intraocular structure to the transducer and back again. Because it will take longer for this echo to reach the probe and return into the eye to be imaged, the artifact always appears deeper in the globe than the tissue of origin. The typical reduplication echo occurs from the lens capsule to the transducer and back again and appears as linear hyperechodensities in the mid to posterior axial vitreous and can be confused with vitreous hemorrhage, inflammatory debris, or degeneration.

Absorption artifact occurs when a dense structure such as a cataract or intraocular foreign body results in an acoustic shadow. This occurs because of the almost complete reflection of sound from the dense structure with little or no sound passing beyond to image the deeper tissues. This appears as an anechoic area some distance posterior to the hyperechoic structure and can be confused with a mass lesion.

Additional artifacts occur when there is a failure to use adequate coupling gel resulting in a gap between the transducer and the eyelid or cornea.

BIBLIOGRAPHY

1. Brooks DE: Ocular imaging. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 1998, pp 467–482.

2. Byrne SF, Green RL: Ultrasound of the Eye and Orbit. Mosby, St. Louis, 1992.
3. Koplin RS, Gersten M, Hodes B: Real Time Ophthalmic Ultrasonography and Biometry: A Handbook of Clinical Diagnosis. Thorofare, NJ, Slack, 1985.
4. Penninck D, Daniel GB, Brawer R, et al: Cross-sectional imaging techniques in veterinary ophthalmology. Clin Tech Small Anim Pract 16:22–39, 2001.
5. Stuhr CM, Scagliotti RH: Retrobulbar ultrasound in the mesaticephalic and dolichocephalic dog using a temporal approach. Vet Comp Ophthalmol 6:91–99, 1996.
6. van der Woerdt A, Wilkie DA, Myer, CW: Ultrasonographic abnormalities in the eyes of dogs with cataracts: 147 cases (1986–1992). J Am Vet Med Assoc 203:838–841, 1993.
7. Wilkie DA, Gilger BC: Equine diagnostic ocular ultrasonography. In Rantanen NW, McKinnon AO (eds): Equine Diagnostic Ultrasonography. Baltimore, Williams & Wilkins, 1998, pp 637–643.
8. Williams J, Wilkie DA: An alternate modality for the examination of opaque eyes: Ophthalmic ultrasonography. Comp Cont Ed 18:667–677, 1996.

II. Cornea and External

5. THE RED EYE

Daniel R. Priehs, D.V.M., and Amy Knollinger, D.V.M.

1. What is the most common clinical sign of ocular disease recognized by the owner?

The red eye. Most cases of the red eye are benign. However, some cases can be vision threatening. Understanding the anatomy of the eye is important to diagnosing the etiology of the red eye.

2. What are the main causes of the "red eye"?

Conjunctivitis	Keratitis
Episcleritis	Scleritis
Uveitis	Erosions/ulcers
Glaucoma	Hyphema

3. Is localization of the redness important?

Yes, the redness may be focal or generalized. It may involve the eyelid, conjunctiva, episclera, sclera or corneal tissue. It may also involve the intraocular structures (Fig. 1).

4. What is the first step when a dog or cat presents with a "red eye"?

A thorough history and physical examination is mandatory. Important questions to ask include:

- Is there any history of trauma?
- Has there been any medication administered or change in current medication?
- Is there any illness to which your pet is currently being treated for?
- Any history of known or potential toxin exposure?
- Any history of previous eye surgery (nictitans gland removal, entropion, or eyelash surgery)?
- Has there been any significant behavior changes?
- Any significant medical problems (nose bleed, blood in the feces or urine, generalized malaise)?

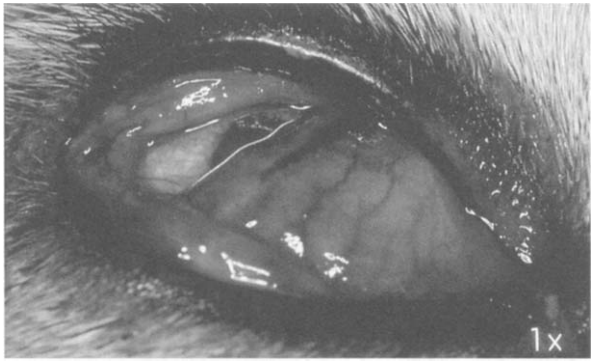


Figure 1. Acute FHV-1 conjunctivitis/keratitis in a kitten. Note the hyperemia and intense chemosis.

5. What is the next step?

A complete ocular examination is warranted. Localization of the redness is very important.

- Is it a focal or generalized problem?
- Does it involve the adnexa and/or is the redness intraocular?

Once the area involved is localized, a differential diagnosis can be made and further diagnostics and therapeutic modalities can be initiated.

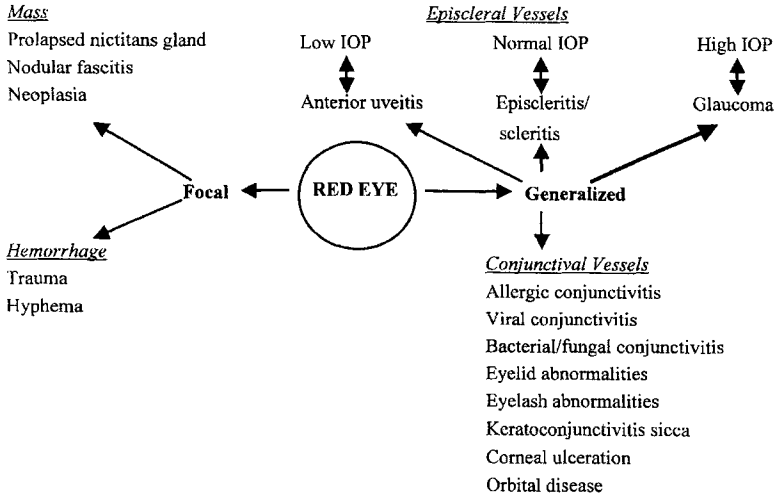


Figure 2. Algorithm for Determining the Cause of a Red Eye in the Dog or Cat

6. How can I tell if the redness involves the conjunctival or episcleral vessels?

The conjunctival vessels are generally smaller and less intensely red. They are more mobile than the episcleral vessels and blanch when 1% epinephrine or 2.5% phenylephrine is applied. Although not a hard and fast rule, generalized conjunctival hyperemia is associated with extraocular disease, and episcleral vessel engorgement is associated with intraocular disease.

7. What are the most common causes of conjunctivitis in the feline?

Conjunctivitis is usually infectious in the cat. Many times there will be a history of or concurrent upper respiratory infection (URI). The most common cause of conjunctivitis is feline herpesvirus-1 (FHV-1), although *Chlamydia* and *Mycoplasma* may be the offending pathogen (Figs. 3 and 4).

Figure 3. Chronic and severe FHV-1 infection in a kitten.

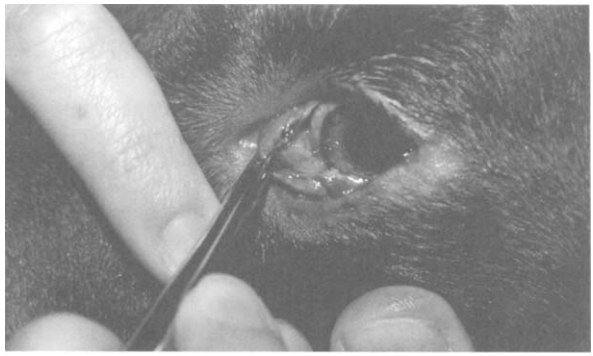


Figure 4. A grass awn was located in the bulbar surface of the nictitans, although this case presented as bacterial conjunctivitis.

8. How is FHV-1 diagnosed?

FHV-1 should be suspected any time a cat has conjunctivitis. FHV-1 is usually observed in younger cats, although clinical signs can be seen at any age. It can be a bilateral or unilateral problem. The presence of dendritic corneal ulcerations is highly suspicious of FHV-1, but these are not commonly observed. Many times the history and presence of conjunctivitis that is nonresponsive to antibiotics are all the clinician has to use to make a clinical diagnosis.

9. Are there any laboratory tests that can be done to diagnose FHV-1?

Virus isolation, immunofluorescence assay (IFA), and serology are all available diagnostic tests. Virus isolation is impractical and cost-prohibitive in the clinical setting. IFA has been proven to be insensitive for FHV-1 and therefore not usually used. Serology is also not practical because of lack of predictable rising titers and cross-reactivity to antibodies that are produced by vaccination.

10. Are there new testing techniques available?

Yes, polymerase chain reaction (PCR) testing is becoming more available to clinicians. PCR has high sensitivity and specificity for viral DNA and should be the test of choice for diagnosing FHV-1. Conjunctival swabs or corneal or conjunctival scraping are simple diagnostic procedures and all that are needed for testing. As more laboratories perfect this technique and make this test available, FHV-1 will be an easy and accurate diagnosis.

11. How is feline conjunctivitis treated?

In the event of an acute case, treatment starts with topical antibiotics administered three times a day. Tetracycline and chloramphenicol are the first-line antibiotic therapies. If there is no response to this medical management after 3–4 days, consider concurrent use of antiviral medications such as trifluridine (1% (Viroptic), a commercially available topical antiviral medication. This medication is expensive and can cause some irritation after application. Additionally, this medication needs to be applied 5–6 times a day during an acute outbreak. Another antiviral medication is idoxuridine (0.1%), which must be compounded by a pharmacist. This medication is more cost-effective and causes less conjunctival irritation. Although some laboratory evidence suggests that trifluridine is more effective, it is preferable to start with 0.1% idoxuridine administered 4–6 times daily. Vidarabine monohydrate 3% (Vira A) ointment is also available and may be applied topically 3–4 times a day. Oral antiviral medications appear to be effective with human and rabbit herpes virus outbreaks, but they do not seem to have the same effect over FHV-1. Acyclovir shows the most promise for control of FHV-1, but at this time it is not approved for use in felines because the full spectrum of side effects has not been established. This therapy should be reserved for the most resistant of FHV-1 infections.

12. Are there any good oral supplements that can be used?

Some evidence suggests that the oral supplementation of L-lysine (250 mg capsule, every 12 hours) mixed in the food may lessen the severity of the herpetic lesions and lengthen the time be-

tween recurrences. L-lysine is an arginine inhibitor that slows the replication of FHV-1. This amino acid is commonly used by humans with oral herpes problems.

13. If after using these medications, the eye has not responded, what should be done next?

FHV infections can be very frustrating for the clinician, the owner, and the animal. Refractory or nonresponsive cases should be referred to a veterinary ophthalmologist. New antiviral medications along with the use of oral or topical interferon may provide some control of FHV-1. Although it is recommended never to administer topical or systemic corticosteroids with FHV-1 infections, some forms of stromal herpetic keratitis require anti-inflammatory therapy or nonsteroidal anti-inflammatory solutions.

14. Conjunctivitis is present, but white plaques have formed on the conjunctiva and cornea of a cat. What should I do?

A conjunctivial or corneal scraping is warranted. This is a common presentation of an eosinophilic conjunctivitis and keratitis. The predominate cell type is usually the eosinophil, although plasma cells and lymphocytes may be present (see Chapter 9).

15. What causes this and how should it be treated?

The etiology of eosinophilic conjunctivitis/keratitis is unknown; however, a large percentage of these cats are positive for FHV-1. Allergies and other viruses have been implicated but never confirmed. The treatment is directed toward decreasing the immune response around the eye. Topical corticosteroids (0.1% dexamethasone phosphate) may be all that is needed to control the inflammation. Treatment should be started every 8 hours and tapered by the response. Concurrent FHV-1 must be monitored, and, if suspected, antiviral medications may need to be administered. If the infiltrates are nonresponsive to therapy, give 20 mg of methylprednisolone (Depo-Medrol) subcutaneously, and a dramatic response is seen. Occasionally, systemic megestrol acetate can be used at the dosage of 5 mg PO every 24 hours for 5 days and then tapered. Megestrol acetate is a last resort for control of feline eosinophilic conjunctivitis/keratitis because of the systemic effects caused by long-term usage, such as diabetes mellitus and pyometra.

16. Is canine conjunctivitis as difficult to treat as it is in the feline patient?

No. Vary rarely is canine conjunctivitis associated with a viral infection. Bacterial and fungal conjunctivitis is uncommon and usually secondary to eyelid abnormalities and keratoconjunctivitis sicca. Allergic conjunctivitis is also commonly seen and is often associated with atopy. The use of a topical antibiotic and corticosteroid solution (neomycin-polymixin-dexamethasone) is usually sufficient to control inflammation. Of course, it is necessary to rule-out a corneal ulceration with a fluorescein stain test before application of a topical corticosteroid. Corneal cultures may be warranted if infectious conjunctivitis is suspected. Other causes of conjunctivitis in the dog need to be explored.

The ocular examination is very important. Any conformational eyelid abnormality such as entropion or ectropion could cause conjunctival irritation. If they are present, appropriate surgical correction is warranted. The presence of distichiasis, trichiasis, or ectopic cilia will cause significant irritation. Very close ocular examination is needed because these cilia are difficult to visualize. The use of Rose Bengal stain is helpful in the localization of the offending cilia. Rose Bengal stains devitalized corneal epithelial cells. A corneal ulceration does not need to be present to have a positive Rose Bengal stain. Always be careful not to overlook a conjunctival foreign body. Grass awns or other plant material hide behind the nictitans and cause an intense hyperemia (Fig. 4).

17. Excessive mucoid discharge is present. In fact, the owners reports that they need to clean the discharge from the eye hourly. What should I do?

A Schirmer tear test (STT). An STT of less than 10 mm/min for dogs and less than 5 mm/min for cats is diagnostic of keratoconjunctivitis sicca (KCS). Many breeds such as cocker spaniels, West Highland white terriers, bulldogs, shih tzus, and Lhaso apsos are predisposed and KCS

should be considered in any red eye problem. Treatment of topical cyclosporine (Optimmune) should be started. Adjunct therapy of tear supplementation, antibiotic, or antibiotic-corticosteroid combination therapy should be used as indicated by the severity of the inflammation.

18. Are there any other causes of KCS?

Yes. Iatrogenic causes of KCS include the systemic use of sulfonamides and the surgical removal of the third eyelid. Systemic disease such as hypothyroidism, diabetes mellitus, Cushing's syndrome, canine distemper, and chronic blepharoconjunctivitis should be considered. Systemic nonsteroidal anti-inflammatory medication has recently been implicated as a cause of KCS. Further data are needed to confirm the association of KCS with their administration. KCS is rare in cats but can be associated with chronic FHV-1 infections (see Chapter 10).

19. Along with the red eye, the globe appears to be pushed forward. What should I do?

Exophthalmos is an indication of orbital disease. A common mistake is to confuse exophthalmia with buphthalmia (enlargement of the globe). If the globe itself is normal, the possibility of retrobulbar disease needs to be explored. Anatomic variations can give the appearance of exophthalmos and must be considered in the brachycephalic breeds. Lagophthalmia can also contribute to this variation.

20. What diagnostic tests should be done?

A complete ophthalmic examination is needed to assess the extent of the pathology present. Increased resistance on digital retropulsion indicates an orbital mass. Pain observed on manual opening of the oral cavity may indicate a retrobulbar lesion. A thorough examination is needed to evaluate the soft palate especially in the area of the second molar. Ocular or orbital ultrasonography will help to define the retrobulbar lesions. Radiographs, MRI, and CT scan may be warranted (see Chapter 3).

21. What are the major categories of the orbital disease?

Inflammatory, cystic, and neoplastic causes should be considered. Orbital abscesses can cause a red, exophthalmic globe. Once the diagnosis is obtained, appropriate therapy should be initiated.

22. Are there any extraocular neoplastic disease that can cause a red eye?

As previously discussed, orbital neoplasia needs to be considered. Although rare, conjunctival neoplasia is possible, and any mass identified should be biopsied and resected. Appropriate adjunct therapy should be considered as determined by the type of neoplasia. Neoplasia of the nictitans is more commonly observed. Biopsy should be considered prior to removal of the entire third eyelid because the gland is responsible for 20–30% of tear production. Therefore, the removal of the third eyelid could predispose the animal to KCS (Fig. 5).

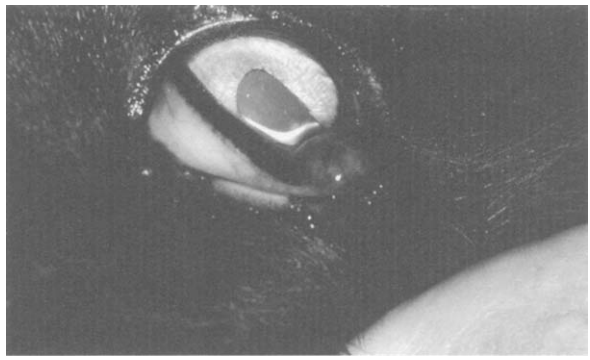


Figure 5. A melanoma located at the leading edge of the nictating membrane.

23. Neoplastic cells were not reported on my conjunctival biopsy. A diagnosis of episcleritis was given. What does it mean?

Inflammatory diseases of the episcleral tissue are rare and can be difficult to define. The first thing to do is to eliminate other causes of episcleral tissue inflammation. Keratitis, uveitis, and glaucoma must be ruled out. Episcleritis is thought to be an underlying autoimmune disorder although the etiology is frequently not determined. Episcleritis is defined as generalized, necrotizing, or nodular. Generalized episcleritis is usually responsive to topical corticosteroids. Necrotizing episcleritis is extremely challenging, rare, and a topic unto itself. Nodular episcleritis is more difficult to treat and is characterized by raised nodules usually at the limbus. Many names such as nodular episcleritis, nodular fascitis, fibrous histiocytoma, and others have been given to this condition. The criteria for naming this condition can be confusing, and the type and number of cell types (plasma cells, histiocytes, lymphoytes, and fibroblasts) are used to classify the lesion. It is possible that all these lesions are essentially the same, just at different stages of development (see Chapter 48).

24. Although naming the condition of episcleritis is important, how do you treat it?

This can be a very difficult disease to manage. Along with topical corticosteroids, systemic immunosuppressive medications are warranted. Topical 0.1% dexamethasone can be used 3–4 times daily along with a tapering dose of oral prednisolone (1 mg/kg every 12 hours for 4 days, than 1 mg/kg every 24 hours for 4 days, and then 1 mg/kg every other day). If the inflammation is severe, use azathioprine at a dosage of 1–2 mg/kg daily for 2 weeks and then taper as dictated by response to the medication (Fig. 6).

25. It appears nodules could just be surgically resected. Is medical treatment necessary?

For isolated nodules, the inflammatory tissue can be debulked surgically followed by use of liquid nitrogen to freeze the area of concern. However, systemic immunosuppressive medication should still be used in conjunction with the surgery. Reoccurrence is commonly observed, and multiple cryosurgery procedures may need to be performed (Fig. 7).

26. What is scleritis?

Scleral inflammation is associated with the stromal elements of the sclera. This has a deep red or bluish-red appearance. The engorged vessels are not movable. Scleritis can be quite uncomfortable and, when the necrotizing form is present, quite devastating to the eye. Etiology is assumed to be autoimmune, and systemic immunosuppressive medications should be used as discussed with episcleritis (Fig. 8).

27. Are engorged, deep episcleral or scleral vessels always considered scleritis?

No. Glaucoma and uveitis are also possibilities that need to be considered. The redness can be intense and associated with considerable discomfort with both of these disease processes. The

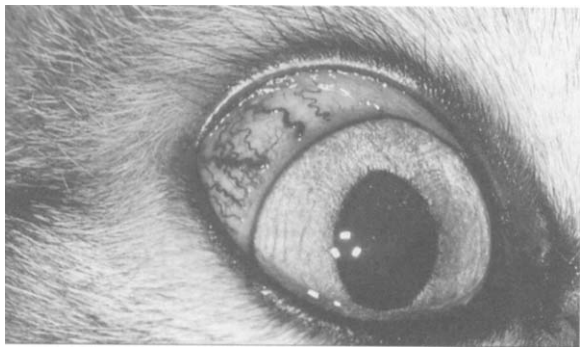


Figure 6. Episcleritis in a mature cat. It was partially responsive to topical corticosteroid therapy.

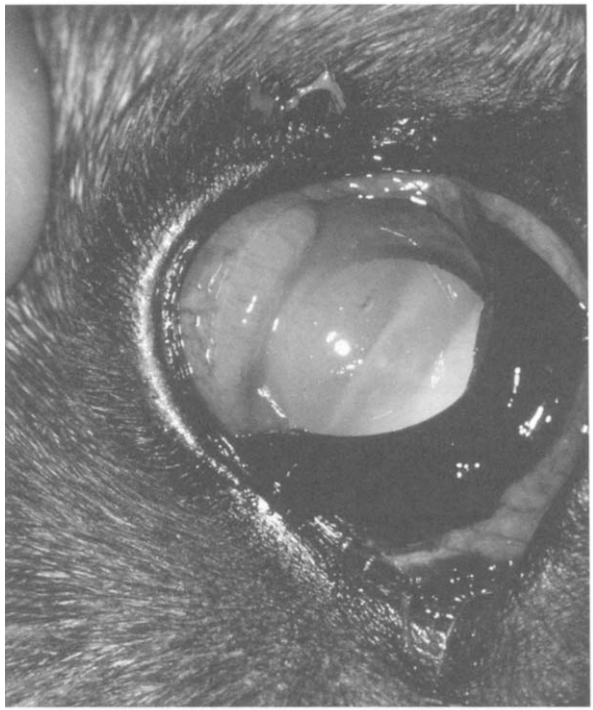


Figure 7. Nodular episcleritis in a collie.

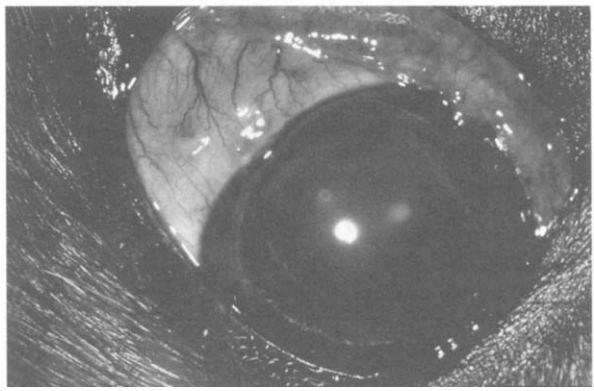


Figure 8. Generalized scleritis in a Labrador retriever.

measurement of intraocular pressure (IOP) is critical to differentiate uveitis from glaucoma. Glaucoma is associated with IOP > 22–25 mmHg. Corneal edema, epiphora, and light sensitivity can be associated with both disease processes. However, the presence of a dilated nonresponsive pupil is usually indicative of glaucoma. The measurement of IOP in conjunction with clinical signs should help you to key in on your clinical diagnosis. (For further discussion on glaucoma and uveitis, see Chapters 13–15.)

28. Are there any other external ocular causes of a red eye?

Of course, we cannot forget to discuss the most common corneal problem. Corneal abrasions or ulcerations are very common and can cause an intensely red and painful eye. The use of fluorescein stain will help to aid in this diagnosis. The type of ulceration is important to discern so appropriate therapy can be started. Ulcers that are refractory to treatment and do not heal within

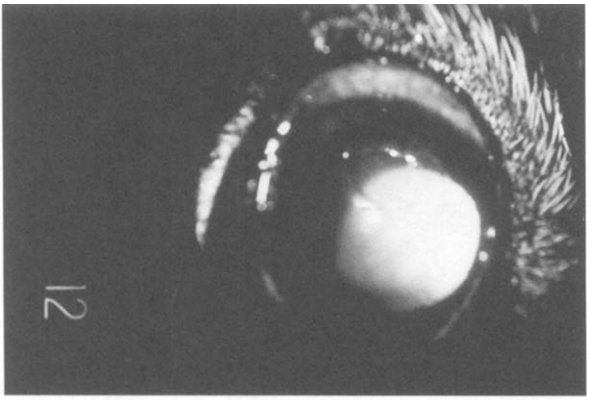


Figure 9. Indolent ulceration in a boxer. Note the epithelial lipping present.

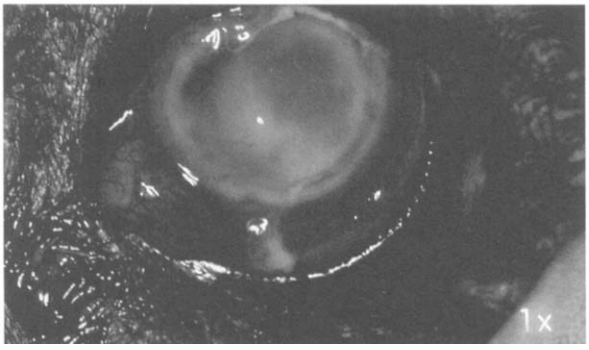


Figure 10. Infected corneal ulceration in a canine. *Pseudomonas aeruginosa* was cultured.

5–7 days may be considered an indolent ulcer or erosion. Indolent ulcers require epithelial debridement and a superficial punctate keratotomy to be performed to help stimulate healing. Appropriate antibiotic and anticollagenase medication may be necessary for treatment of infected ulcerations (see Chapter 7) (Figs. 9 and 10).

29. What is hyphema?

Hyphema, or blood within the eye, will definitely cause the eye to appear red. Hyphema can result from trauma, retinal detachment, coagulopathies, or vasculitis from uveitis or neoplasia. Retinal detachment as a sequela to systemic hypertension can result in hyphema. A very thorough physical examination is warranted to evaluate for other systemic problems. If systemic problems are identified, proper treatment should be started immediately. Ocular treatment is focused on decreasing any existing uveitis to prevent secondary glaucoma (see Chapter 35).

BIBLIOGRAPHY

1. Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Philadelphia, Lea & Febiger, 1999.
2. Hendrix DV: Differential diagnosis of the red eye. In Bonagura J (ed): Kirk's Current Veterinary Therapy, 13th ed. Philadelphia, W.B. Saunders, 2000, p 1042.
3. Murphy CJ: Disorders of the cornea and sclera. In Bonagura J (ed): Kirk's Current Veterinary Therapy, 11th ed. Philadelphia, W.B. Saunders, 1992, p 1101.
4. Nasisse MP: Feline herpesvirus ocular disease. Vet Clin North Am Small Anim Pract 20:667, 1990.
5. Nasisse MP: Ocular feline herpesvirus-1 infection. In Bonagura J (ed): Kirk's Current Veterinary Therapy, 13th ed. Philadelphia, W.B. Saunders, 2000, p 1057.

6. CORNEAL DYSTROPHIES

Alexandra van der Woerdt, D.V.M., M.S.

1. What are the clinical characteristics of corneal dystrophy?

Corneal dystrophy is usually a bilateral, symmetrical, familial, noninflammatory corneal disease that is not associated with systemic disease.

2. What is the most common owner complaint?

Owners will often notice a "white spot" in the cornea without ocular discomfort.

3. Describe the clinical appearance of corneal dystrophy in general.

Corneal dystrophy usually appears as a very focal, well-demarcated, white, crystalline or metallic-like lesion in the (para) central cornea. The lesion is often in the anterior stroma, and the epithelium covering the dystrophic area is usually intact. Affected dogs do not experience any ocular discomfort if the epithelium is intact. It is usually bilateral. One eye may be affected prior to the other eye becoming affected (Figs. 1 and 2).

4. How do I distinguish corneal dystrophy from corneal fibrosis?

Corneal fibrosis has a diffuse gray-whitish appearance and is always the result of some sort of insult to the cornea such as trauma, previous ulceration, or chronic Keratoconjunctivitis sicca (KCS). These lesions usually have neovascularization. Corneal dystrophy has an intense white appearance and consists of multiple little crystal-like opacities rather than a diffuse opacity (Fig. 3).

5. How do I distinguish corneal dystrophy from corneal edema?

Corneal edema may be either focal or involve the entire cornea. Corneal dystrophy is always a focal lesion. An edematous cornea has a hazy, bluish appearance, and a grid pattern can be seen with magnification. The dystrophic area in the cornea has a bright white appearance, and multiple crystal-like structures can be seen on close inspection. Corneal edema is often associated with other (intra)ocular diseases such as glaucoma, anterior uveitis, lens luxation, and corneal ulceration. Corneal dystrophy is not usually associated with other intraocular diseases.

6. In which layers of the cornea is the dystrophic material located?

The subepithelial stroma is most commonly affected. In the beagle and Siberian husky, deeper layers of the stroma may be affected as well.

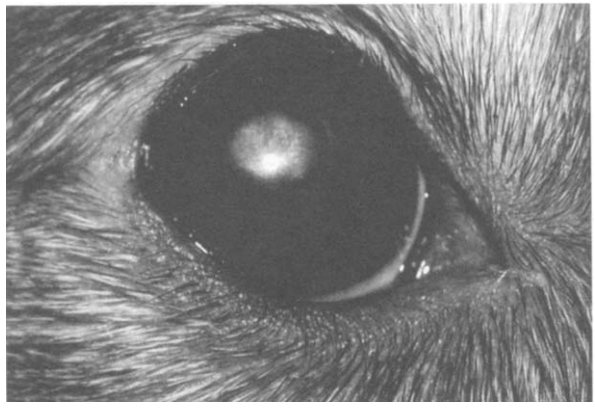


Figure 1. Circular superficial lipid corneal dystrophy. This lesion was found in both eyes by the owner. No discomfort was noted.

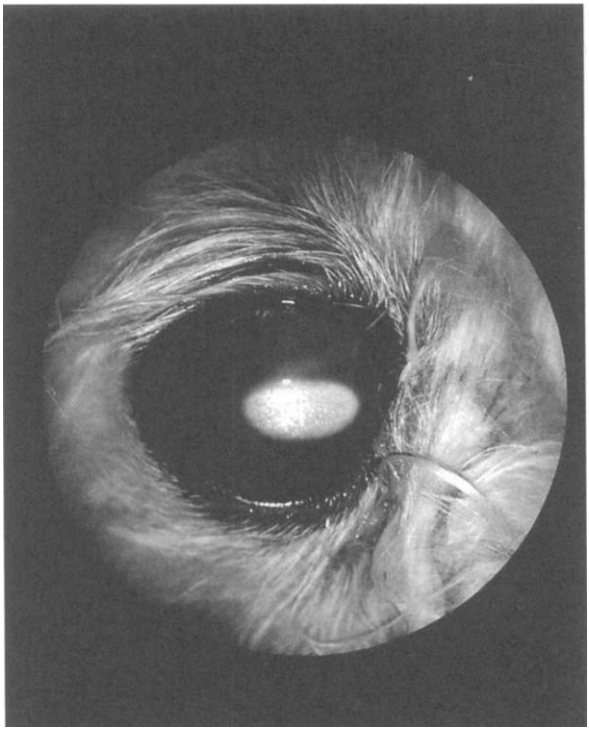


Figure 2. Elliptical (race track) superficial lipid corneal dystrophy. No neovascular response, which is typical of these dystrophies.

7. What is the biochemical composition of the infiltrate in corneal dystrophy?

The infiltrate in the cornea consists of a combination of cholesterol, cholesterol esters, phospholipids, and neutral fat.

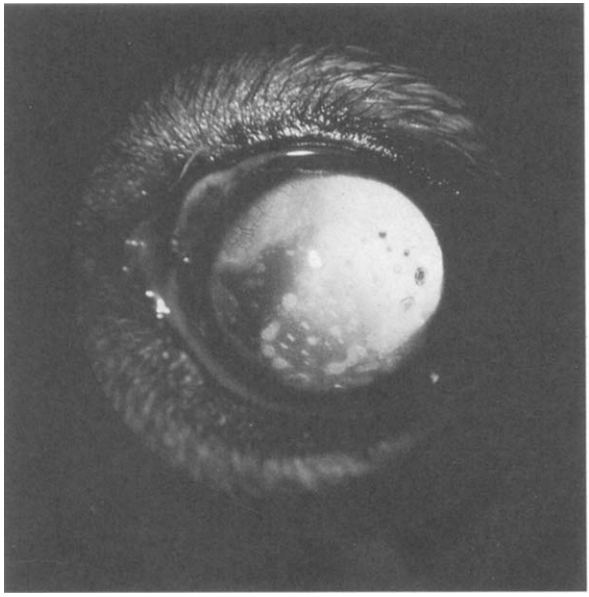


Figure 3. Multiple punctate lipid corneal dystrophy.

8. What additional diagnostic tests should be performed?

A biochemistry profile including cholesterol, high-density lipoprotein, low-density lipoprotein, and triglycerides is recommended. Evaluation of adrenal and thyroid function may be indicated as well. Addressing any abnormalities found may help arrest the dystrophy.

9. Describe the treatment for corneal dystrophy.

Medical treatment is usually not effective in corneal dystrophy. A superficial keratectomy may be used to remove the affected area of the cornea. Excimer laser therapy has been used to treat selected cases of corneal dystrophy.

Some superficial epithelial dystrophies exfoliate the outer layers of the cornea enough to cause hypersensitivity to the sensory nerves, inducing squinting and possibly tearing. These cases heal in a matter of days. Artificial tears used frequently reduces the sensitivity and aids in the healing process.

10. Which breeds of dogs are most commonly affected?

Although this disease has been reported in many breeds, the breeds in which this disease has been described in most detail are the beagle and the Siberian husky. Other breeds include the Shetland sheepdog, Cavalier King Charles spaniel, and Airedale terrier.

Corneal Dystrophy in the Dog: Affected Breeds[6,10]

BREED	AGE OF ONSET	LOCATION IN CORNEA	INHERITANCE
Airedale terrier	6–11 months	Axial, all layers	Sex-linked, recessive
Alaskan malamute	> 2 years	Similar to beagle	
Beagle	3.5 years	Nebular: anterior stroma Race track: all layers White arc: stroma and subepithelial plaques	
Bearded collie	> 1 year	Subepithelial	
Bichon frise	> 2 years	Subepithelial	
Cavalier King Charles spaniel	2–5 years	Anterior stroma	
Collie (rough)	1–4 years	Anterior stroma	
English toy spaniel	2–5 years	Stroma	
German shepherd	1–6 years		
Golden retriever	< 2 years	Anterior stroma	
Lhasa apso		Subepithelial	
Mastiff		Subepithelial	
Miniature pinscher	1–2 years	Subepithelial	
Pointer		Similar to Siberian husky	
Poodle (miniature)	> 1 year	Epithelial	Suspect recessive
Samoyed	5 months-2 years	Stroma	
Shetland sheepdog	4 months	Subepithelial, superficial stroma	
Siberian husky	0.4–2 years	All layers of cornea Ring-shaped	Autosomal recessive Variable expression
Weimaraner	1–8 years	Subepithelial	
Whippet	3–5 years		

Other Breeds Affected[6,10]

Afghan hound	Chinese shar pei	Labrador retriever
Basenji	Cocker spaniel	Nova Scotia duck tolling retriever
Belgian sheepdog	Curly coated retriever	Rottweiler
Boston terrier	Dachshund	Standard schnauzer
Boykin spaniel	English setter	Vizsla
Boxer	English springer spaniel	Yorkshire terrier
Briard	German pinscher	
Chesapeake Bay retriever	Irish wolfhound	

11. Describe the clinical appearance of corneal dystrophy in the beagle.

The lesions are oval, horizontal and on average 3 × 5 mm in size. Three clinical types have been described.

1. The **nebular form** is located in the anterior third of the stroma and has a uniform ground glass appearance.
2. The **race-track form** involves the stroma full thickness and has a dense outer ring surrounding a lighter center.
3. In the **white-arc form,** white plaques located subepithelially are overlying a nebular or race track form lesion. The epithelium is usually intact.

The opacities may progress from nebular through race-track to white-arc patterns.

12. What is the clinical appearance of corneal dystrophy in the Siberian husky?

Corneal dystrophy in the Siberian husky can manifest itself in five different patterns depending on the location within the corneal stroma. The infiltrate may be present (1) in the anterior part of the stroma, (2) as refractory crystals in the posterior stroma, (3) as homogenous deposits in the posterior stroma, (4) as a combination of both anterior and posterior stroma, or (5) as full-thickness corneal dystrophy (the most severe form). The infiltrates are present in a doughnut-shaped pattern (Fig 4).

13. Why is corneal dystrophy in the Shetland sheepdog different from corneal dystrophy in most other breeds of dogs?

Corneal dystrophy in the Shetland sheepdog is characterized by multifocal, superficial irregular rings 1–3 mm in diameter that are initially located in the (para)central cornea. Recurrent corneal erosions may occur associated with the dystrophic lesions, making this a potentially painful disease. Distichiasis, decreased tear film break up time, low T4 levels, and abnormal lipid profiles have been reported in affected dogs. Treatment consists of treating the corneal ulcerations associated with the dystrophy using topical antibiotics with or without atropine, cyclosporine, or hyperosmotic agents. These ulcers may behave as indolent ulcers and additional treatments such as grid keratotomy, punctate keratotomy, or soft contact lens placement may be required. A viral etiology has been suggested, but not proven, to be present. Antiviral therapy, such as idoxuridine, has been suggested in treatment of this disease.

14. Do dogs go blind from corneal dystrophy?

Corneal dystrophy rarely results in visual impairment with the possible exception of the Siberian husky and the Airedale terrier. The dystrophy can involve a large area of the cornea in these breeds resulting in visual impairment.

15. Is corneal dystrophy inherited?

There appears to be a genetic predisposition in certain breeds. It is presumed to be caused by

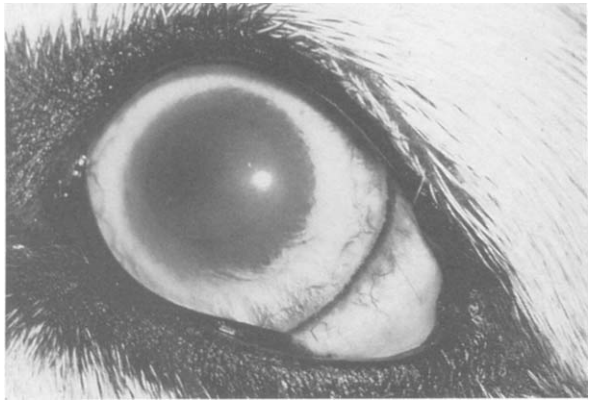


Figure 4. Siberian husky corneal dystrophy. This dystrophy is deep stromal and a little more difficult to visualize.

a recessive gene with variable expression in the Siberian husky. A possible sex-linked, recessive inheritance has been suggested in the Airedale terrier. A recessive mode of inheritance is suspected in the miniature poodle.

16. Do I need to recommend against breeding a dog that has corneal dystrophy?

The Canine Eye Registration Foundation (CERF) in cooperation with the American College of Veterinary Ophthalmologists has established guidelines for breeding advice for each individual breed of dogs. Contact your veterinary ophthalmologist for further details on specific breeds.

17. What are the characteristics of corneal degeneration?

Corneal degeneration may affect one eye or both eyes. It is a secondary change in the cornea. It is often asymmetrical if it involves both eyes. It is usually associated with inflammation in the cornea, and it may be associated with systemic diseases. In addition to lipids and cholesterol, calcium may be present in corneal degeneration as well. Corneal ulceration and vascularization of the affected area is common.

18. Name a few systemic diseases that may be associated with corneal lipid or calcium infiltration.

Hypothyroidism	Hyperlipoproteinemia
Cushing's disease	Diabetes mellitus
Pancreatitis	Hypercalcemia
Uremia	Hypervitaminosis D

19. What is the treatment for corneal lipid infiltration?

Diagnosis and treatment of the underlying disease may or may not result in spontaneous resolution of the lipid infiltration. Corneal lipid infiltration secondary to hypercholesterolemia may respond to a fat-restricted diet.

20. What is endothelial dystrophy?

Endothelial dystrophy or endothelial degeneration refers to the premature loss of endothelial cells that is most commonly seen in the Chihuahua, Boston terrier, and dachshund. The loss of endothelial cells results in progressive corneal edema and may lead to bullous keratopathy and nonhealing corneal ulcers (Figs. 5 and 6).

21. How do you determine that endothelial dystrophy is the cause of corneal edema?

This is a diagnosis by exclusion. Other important causes of corneal edema such as glaucoma, anterior uveitis, anterior lens luxation, or corneal ulceration need to be excluded. Diagnostic tests include measurement of the intraocular pressure, fluorescein staining of the cornea, careful ex-

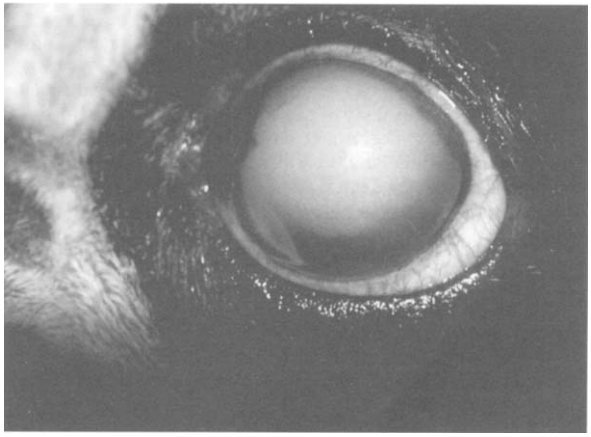


Figure 5. Boston terrier with endothelial dystrophy. The graying of the cornea is stromal edema. Note the clear (normal) zone ventrally.

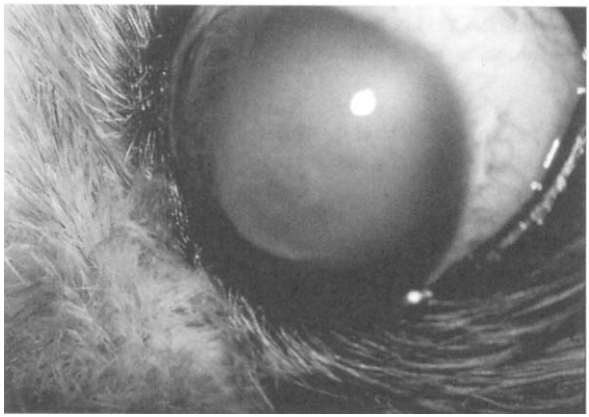


Figure 6. This endothelial dystrophy caused so much edema centrally that the cornea bulged forward (keratoconus). Also present are multiple blister-like areas (bullous keratopathy). Some resolution was obtained by the use of hyperosmotic ointments.

amination of the eye for the presence of signs of anterior uveitis (i.e., conjunctival hyperemia, aqueous flare, miosis), or lens luxation (lens in the anterior chamber, deep anterior chamber if the lens has luxated posteriorly). Specular microscopy may reveal a decreased number of endothelial cells, but this is not usually available in a clinical setting.

Examination tip: Globe digital pressure applied through the lids will temporarily cause hypertension within the globe to increase the density of the corneal edema if endothelial degeneration is present).

22. What is the treatment for endothelial dystrophy?

There is no treatment for the disease itself. The loss of endothelial cells is permanent. The secondary corneal edema can be treated using hypertonic solutions or ointments (2.5–5% NaCl ointments). Corneal ulcers associated with the corneal edema will often behave as indolent ulcers and may need to be treated as such (see Chapter 7). Thermokeratoplasty may be beneficial in advanced stages of the disease. Penetrating keratoplasty is the treatment of choice in human beings. Its use in veterinary ophthalmology is limited, mainly because of donor cornea availability.

23. What is posterior polymorphous dystrophy and in which breed of dog does this occur?

This is a focal dysfunction of corneal endothelial cells resulting in multifocal posterior corneal opacities. This has been reported in the American cocker spaniel.

BIBLIOGRAPHY

1. Cooley PL, Dice PF: Corneal dystrophy in the dog and cat. Vet Clin North Am Small Anim Pract 20:681–692, 1990.
2. Crispin SM, Barnett KC: Dystrophy, degeneration and infiltration of the canine cornea. J Small Anim Pract 24:63–83, 1983.
3. Ekins MB, Waring GO, Harris RR: Oval lipid corneal opacities in beagles. Part II: Natural history over four years and study of tear function. J Am Anim Hosp Assoc 16:601–605, 1980.
4. Genetics Committee, American College of Veterinary Ophthalmologists: Ocular Disorders Presumed to be Inherited in Purebred Dogs, 3rd ed. city, ACVO, 1999.
5. Linton LL, Moore CP, Collier LL: Bilateral lipid keratopathy in a boxer dog: Cholesterol analyses and dietary management. Prog Vet Comp Ophthalmol 3(1):9–14, 1993.
6. MacMillan AD, Waring GO, Spangler WL, et al: Crystalline corneal opacities in the Siberian husky. J Am Vet Med Assoc 175:829–832, 1979.
7. Ward DA, Martin CL, Weiser I: Band keratopathy associated with hyperadrenocorticism in the dog. J Am Anim Hosp Assoc 25:583–586, 1989.
8. Waring GO, MacMillan A, Reveles P: Inheritance of crystalline corneal dystrophy in Siberian huskies. J Am Anim Hosp Assoc 22:655–658, 1986.
9. Waring GO, Muggli FM, MacMillan A: Oval corneal opacities in beagles. J Am Anim Hosp Assoc 13:204–208, 1977.
10. Whitley RD, Gilger BC: Diseases of the canine cornea and sclera. In Gellatt K (ed): Veterinary Ophthalmology, 3rd ed. Baltimore, Lippincott Williams & Wilkins, 1999, pp 635–674.

7. CORNEAL EROSIONS (INDOLENT ULCERS)

Alexandra van der Woerdt, D.V.M., M.S.

1. What is an indolent ulcer?

An indolent ulcer is a nonhealing superficial corneal ulcer or erosion with nonadherent epithelial edges.

2. Name a few other terms that are used to describe an indolent ulcer.

Boxer ulcer
Recurrent erosion
Refractory corneal ulcer
Rodent ulcer

3. In how many days does an uncomplicated ulcer usually heal?

An uncomplicated corneal ulcer should heal within 3–5 days. Erosions are called *persistent* if they have been present for more than 14 days.

4. In which species have indolent ulcers been reported?

Dogs, cats, and horses.

5. What breeds of dogs most commonly develop indolent ulcers and at what age?

The boxer is the breed in which this condition has been most extensively studied. Other breeds that appear to be predisposed include the Australian cattle dog, Boston terrier, English springer spaniel, golden retriever, Labrador retriever, miniature poodle, miniature schnauzer, and Welsh corgi. The average age of affected dogs is approximately 9 years.

6. Describe the histopathologic abnormalities in a cornea with an indolent corneal ulcer.

Ultrastructural examination of affected corneas has revealed abnormalities in the basal cell-basement membrane complex with a lack of hemidesmosomes and a thickened and irregular corneal epithelial basement membrane. A thin superficial acellular zone of hyalin collagen, which may act as a barrier to epithelial adhesion, has also been shown to be present in affected areas.

7. What are the most common complaints of owners of dogs with an indolent ulcer?

Dogs with an indolent corneal ulcer usually present with the complaints of redness of the eye, chronic discharge from the eye, and mild blepharospasm. If the dog has already been treated by another veterinarian, owners may indicate a lack of response to treatment with topical antibiotic ointment or solution with or without atropine. A dog with an indolent corneal ulcer may show surprisingly little discomfort considering the size of the ulcer.

8. How are indolent ulcers diagnosed?

An indolent ulcer is diagnosed by clinical signs and exclusion of other etiologies of a nonhealing superficial ulcer. The tear production should be measured using a Schirmer tear test to rule out keratoconjunctivitis sicca (KCS). A careful examination of the conjunctiva and eyelids should be performed looking for the presence of distichiae or ectopic ciliae. The conjunctival cul-de-sac should be inspected for the presence of a foreign body. After application of a topical anesthetic, the loose epithelium can easily be removed from the edges of the ulcer using a dry cotton swab.

9. List the most common ophthalmic abnormalities in an eye with an indolent ulcer.

Ophthalmic examination may reveal the following abnormalities:
Mild blepharospasm
Mild epiphora

Conjunctival hyperemia
Superficial corneal ulcer with redundant epithelial edges

A reflex miosis of the pupil usually does not occur in dogs with an indolent ulcer, and the pupil is usually of normal size. Fluorescein stain may migrate under the loose epithelial edges. In general, indolent ulcers are superficial and do not involve the stroma, and there is no cellular infiltration into the ulcer. Cytology may be normal or show nonseptic inflammation (Figs. 1–3).

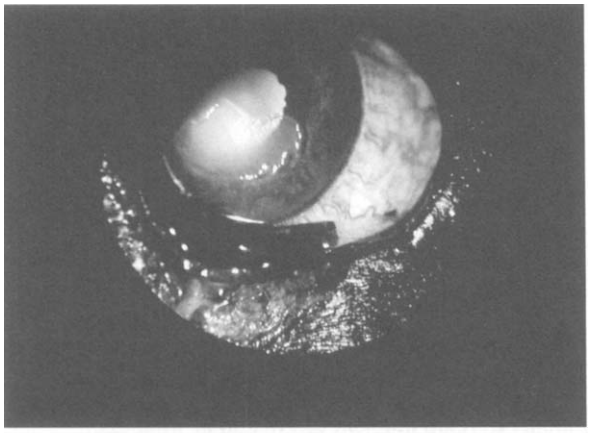


Figure 1. Corneal erosion showing the irregular edges of the epithelial exfoliation.

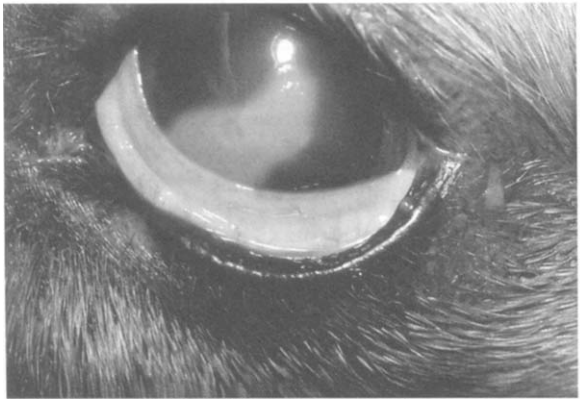


Figure 2. A corneal erosion showing the roughened epithelium at the edges of a fluorescein-stained lesion. Note the stain is positive beyond the edges of the loosened epithelium. Once the loose epithelium is removed, the original erosion is made considerably larger.

10. What is the differential diagnosis of an indolent ulcer?

Other causes of nonhealing ulcers include:

- Decreased tear production
- Goblet cell deficiency
- Distichiae
- Ectopic ciliae
- Other eyelid abnormalities (e.g., entropion, eyelid tumors)
- Exposure keratitis
- Lagophthalmos
- Neurotrophic keratitis
- Presence of a foreign body
- Infection

Endothelial cell degeneration with secondary corneal edema predisposes the cornea to the development of bullous keratopathy (blisters), which may progress to superficial corneal ulcers.

11. What additional diagnostic tests should be performed?

Tear production should be measured. The conjunctival cul-de-sac should be carefully inspected for the presence of abnormal hairs or foreign bodies. Evaluate a thyroid panel. Approximately 44%

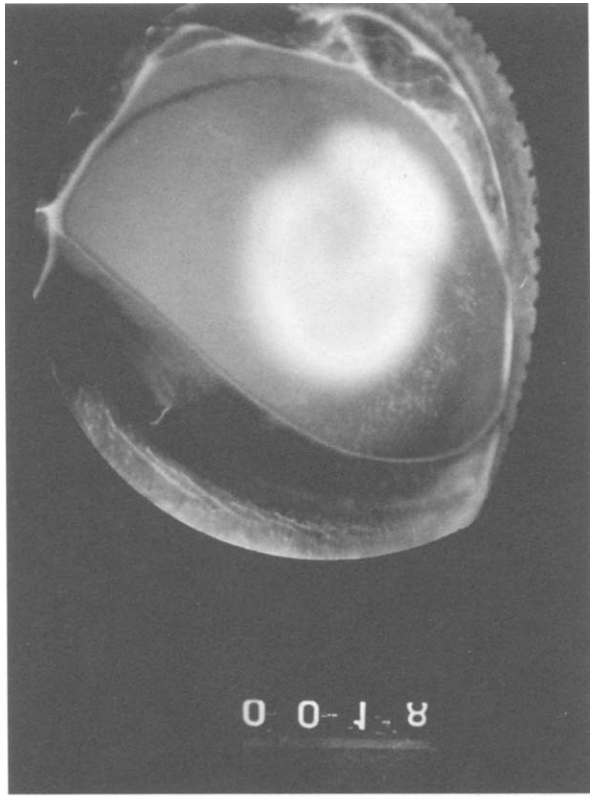


Figure 3. An erosion stained with fluorescein showing the stain uptake under the visible edges of the lesion.

of the erosions evaluated in boxers also had hypothyroidism. Supplemental thyroxine decreased healing time and prevented either recurrence or the opposite eye from developing an erosion.

12. How is an indolent ulcer treated?

The loose epithelium needs to be debrided using dry cotton swabs after application of topical anesthetic to the cornea. After debriding the cornea, the resulting ulcer is usually significant larger than the original ulcer. Aftercare consists of topical antibiotic solution or ointment three to four times a day with or without topical atropine. (**Therapy tip:** Keep in mind that some antibiotics, especially the "mycins," inhibit epithelial mitosis and cell migration—so don't over medicate).

Additional procedures that can aid in healing of these ulcers include a grid keratotomy using a 25-gauge needle or punctate keratotomy using a 20-gauge needle and placement of a soft contact lens or collagen shield. The dog may experience some discomfort after these procedures, which can be treated with an oral nonsteroidal anti-inflammatory drug (NSAID) such as buffered aspirin at a dose of 10 mg/kg/body weight once or twice daily.

Additional medications that have been used to aid in healing include 5% NaCl ointment or solution if significant corneal edema is present, autogenous plasma or serum, fibronectin, aprotinin, epidermal growth factor, and polysulfated glycosaminoglycans. Ophthalmic tissue adhesives and superficial keratectomies have also been used in the management of these lesions (Figs. 4 and 5).

An Elizabethan collar is indicated if excessive rubbing of the eye occurs.

13. Describe the mechanism of action of aprotinin in treatment of an indolent ulcer.

Aprotonin inhibits the enzymes (chymo)trypsin, plasmin, and kallikrein. Excessive plasmin levels have been shown to be present in animals with persistent corneal erosions.

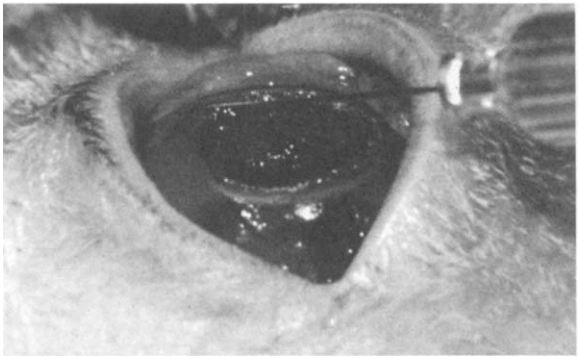


Figure 4. A central ulcer being strengthened by tissue adhesive (N-butylcyanoacrylate). Note that the adhesive should be a thin overlay allowed to extend to the edges of the erosion.

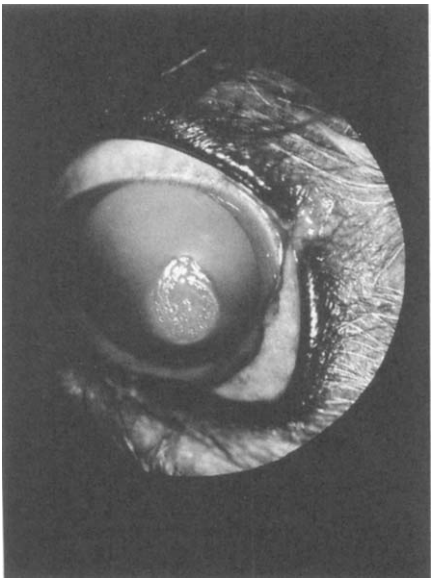


Figure 5. Tissue adhesive in place over an erosion. Approximately 2–3 weeks are required for healing and rejection of the glue.

14. Why do polysulfated glycosaminoglycans have a beneficial effect on healing in some dogs with an indolent ulcer?

Polysulfated glycosaminoglycans act by inhibiting protease activity. The proteolytic activity of lacrimal fluid in eyes with an indolent ulcer has been shown to be significantly higher in a high percentage of affected dogs than the proteolytic activity of lacrimal fluid of normal eyes.

15. Explain the beneficial effect of epidermal growth factor on healing of indolent ulcers.

Epidermal growth factor (EGF) stimulates mitosis in the corneal epithelium. Topical application of EGF resulted in resolution of an indolent ulcer in 8 out of 10 affected dogs within 2 weeks, compared to 2 out of 10 dogs treated with a placebo.

16. How is grid keratotomy performed?

Topical anesthetic is applied to the cornea, and the abnormal epithelium is removed using a dry cotton swab. A 25-gauge needle is used to make multiple superficial microincisions (scratches) into the cornea in a grid pattern, 1–2 mm apart. The grid should cover the entire ulcer and extend a few millimeter into normal cornea.

17. What is a punctate keratotomy?

Punctate keratotomies can be performed with a 20-gauge needle or a Yag laser. Prepare the surface as with the grid procedure. The objective is to disrupt the exposed stroma by superficially fracturing the collagen. The needle technique superficially penetrates the stroma from a 45–60° angle then exits the stroma at 90°. This produces a ticking sound. Each site leaves a stellate white abrasion, which serves as an anchor site for migrating epithelium to adhere onto. The entire area should be treated. Once healed, these punctate sites become imperceptible except on slit lamp examination (Fig. 6).

18. Which surgical procedures have been used in the management of indolent ulcers?

Chemical cauterization, temporary tarsorrhaphy, nictitans and conjunctival flap procedures and superficial lamellar keratectomy have all been reported in the management of indolent ulcers. A nictitans flap was found to have no beneficial effect in one study. A superficial keratectomy may be highly beneficial in refractory cases, with the disadvantage of requiring specialized equipment and general anesthesia.

19. What is the reported success rate of debridement with a cotton swab only?

In one large retrospective study, 84% of indolent ulcers healed with one or more debridement procedures of the cornea in an average of 23.4 ± 11.1 days. Sixteen percent needed additional surgical procedures to heal.

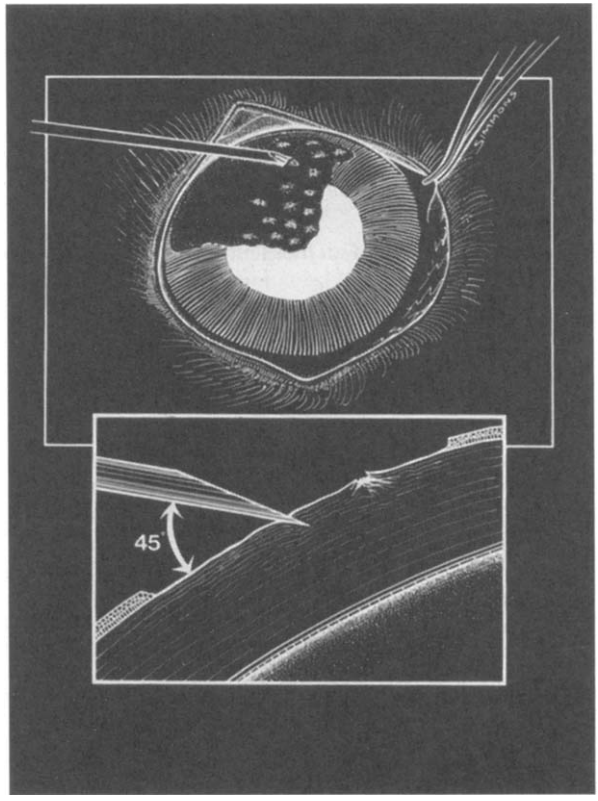


Figure 6. Punctate keratotomy procedure.

20. What is the reported success rate of debridement followed by grid keratotomy?

In one large retrospective study, all ulcers treated with debridement and grid keratotomy healed, although 17% of cases required more than one procedure. Average healing time was 13.4 ± 5.1 days. Similar findings were obtained with punctate keratotomy.

21. What is the reported success rate of superficial keratectomy?

In one large retrospective study, all ulcers treated with superficial keratectomy healed with one treatment in an average of 9.3 ± 3.9 days.

22. Explain the mechanism through which grid keratotomy and superficial keratectomy encourage healing of an indolent ulcer.

Abnormal hyalin collagen is present in the corneal stroma in the area of an indolent ulcer that acts as a barrier to epithelial adhesion. Both grid keratotomy and superficial keratotomy will disrupt this barrier, allowing migrating corneal epithelial cells to be exposed to the subepithelial type I collagen. This will lead to a more effective attachment between the epithelium and the stroma.

23. Why might an ulcer appear to be healed but then recur?

The epithelium may migrate over the ulcer bed but fail to properly attach to the underlying basement membrane and stroma. This may give the impression that the ulcer has healed, but the weak epithelium will quickly retract from the stroma creating the impression of a recurrence when in fact the original ulcer has never healed properly.

24. What can be done to prevent these ulcers from recurring?

There has been little information reported in the literature regarding prevention of indolent corneal ulcers. Application of a lubricating ophthalmic ointment twice daily may help to protect the cornea from environmental irritants and may help to decrease the forces applied to the corneal epithelium by the eyelids during normal blinking.

25. What infectious agent may be associated with indolent ulcers in cats?

Geographic corneal ulcers associated with feline herpes virus type 1 may behave as indolent corneal ulcers.

26. Is the treatment of an indolent ulcer the same for dogs and cats?

No. The use of a grid keratotomy has been associated with the development of a corneal sequestrum in cats. Repeated debridement of the cornea using a cotton tipped applicator is indicated in the treatment of a nonhealing ulcer in the cat. Antiviral therapy is indicated when herpes virus is suspected to be an etiologic factor.

BIBLIOGRAPHY

1. Champagne ES, Munger RJ: Multiple punctate keratotomy for the treatment of recurrent epithelial erosions in dogs. J Am Anim Hosp Assoc 28:213–216, 1992.
2. Chavkin M, Riis RC: Management of persistent corneal erosion in a boxer dog. Cornell Vet 80:347–356, 1990.
3. Cook C, Wilcox B: A clinical and histological study of canine persistent superficial corneal ulcers. Proc Am Coll Vet Ophthalmol 26:139, 1995.
4. Cooley PL, Wyman M: Indolent-like corneal ulcers in 3 horses. J Am Vet Med Assoc 188:295–297, 1986.
5. Gelatt KN, Samuelson DA: Recurrent corneal erosions and epithelial dystrophy in the boxer dog. J Am Anim Hosp Assoc 18:453–460, 1982.
6. Kirschner SE, Niyo Y, Betts DM: Idiopathic persistent corneal erosions: Clinical and pathological findings in 18 dogs. J Am Anim Hosp Assoc 25:84–90, 1989.
7. Kirschner SE: Persistent corneal ulcers: What to do when ulcers won't heal. Vet Clin N Am Small Anim Pract 20(3):627–642, 1990.
8. Kirschner SE, Brazzell RK, Stern ME, et al: The use of topical epidermal growth factor for treatment of nonhealing corneal erosions in dogs. J Am Anim Hosp Assoc 27:449–452, 1991.

9. La Croix NC, van der Woerdt A, Olivero D: Nonhealing corneal ulcers in cats: 29 cases. Proc Am Coll Vet Ophthalmol 30:84, 1999.
10. Miller WW: Using polysulfated glycosaminoglycan to treat persistent corneal erosions in dogs. Vet Med 91:916–922, 1996.
11. Morgan RV, Abrams KL: A comparison of six different therapies for persistent corneal erosions in dogs and cats. Vet Comp Ophthalmol 4:38–43, 1994.
12. Pickett JP: Treating persistent corneal erosions with a crosshatch keratotomy technique. Vet Med 90:561–572, 1995.
13. Stanley RG, Hardman C, Johnson BW: Results of grid keratotomy, superficial keratectomy and debridement for the management of persistent corneal erosions in 92 dogs. Vet Ophthalmol 1:233–238, 1998.
14. Willeford KO, Miller WW, Abrams KL, et al: Modulation of proteolytic activity associated with persistent corneal ulcers in dogs. Vet Ophthalmol 1:5–8, 1998.

8. FELINE CORNEAL SEQUESTRUM

Ronald C. Riis, D.V.M, M.S.

1. What is unique about feline corneal sequestrum?

It is a keratopathy seen predominantly in the feline species.

2. What other names have been given to this condition?

Corneal mummification
Corneal nigrum
Corneal necrosis
Necrotizing keratitis
Corneal sequestrum.

3. What are the characteristic clinical signs?

A dark brown-to-black spot in the central or paracentral cornea. Depending on chronicity, the cornea may or may not have neovascularization. The surface of the sequestrum has no epithelium. Fluorescein stain does not light up sequestra, only around the sequestra. Sequestra usually present with minor blepharospasm and little mucopurulent discharge but with brownish tears. They are usually initially unilateral with the opposite eye at high risk. Recurrence is also possible. The highest incidence of occurrence of sequestra is found in brachycephalic cats (Figs. 1–4).

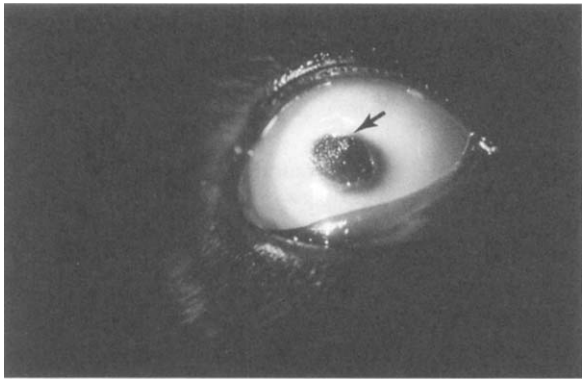


Figure 1. Central corneal sequestrum with associated diffuse corneal edema. Fluorescein stain is positive only around the pigment.

4. What is the etiology of these sequestra?

Corneal sequestra have not been reproduced in experimental studies. Prolonged exposure of the central cornea from causes such as neuroparalytic or neurotrophic conditions and sicca have been suggested. Sequestrum following a bout of rhinotracheitis (FVH-1) has been reported clinically and experimentally; polymerase chain reaction (PCR) herpesvirus DNA have been found in keratectomized samples.

5. What is the treatment for sequestra?

Removal by superficial keratectomy is recommended. It is difficult to judge the depth of the sequestrum prior to surgery. Therefore, the keratectomy may begin as a superficial procedure and end with a more radical procedure if the majority of the corneal thickness has to be removed. Because more radical procedures involve many options, it is much easier to keratectomize small, superficial sequestra than to wait and see if the cornea will vascularize to reject the sequestrum.

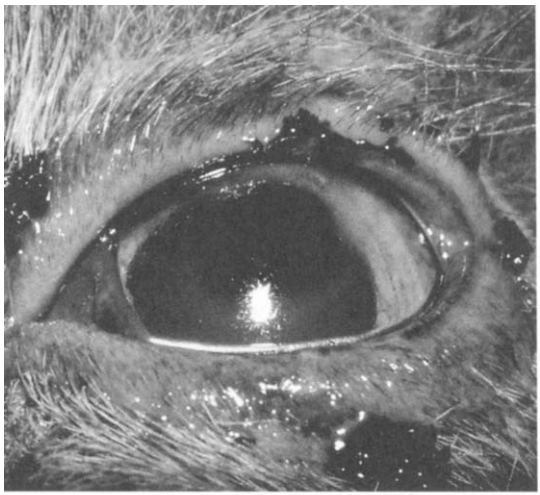


Figure 2. Large superficial sequestrum that was not noted by owner; however, the dark discharge was a complaint.

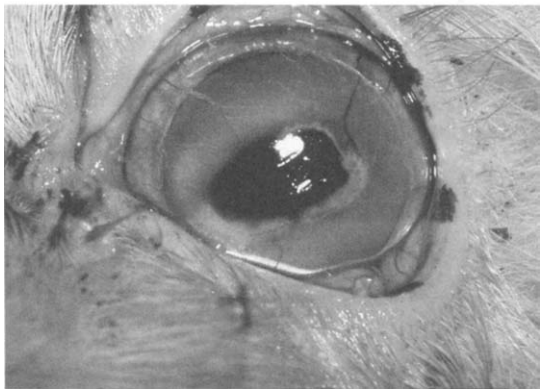


Figure 3. Large superficial and deep sequestrum present for 6 months. Note the neovascularization and scarring. Surgical keratectomy required a free Tenon's grafts to support the compromised cornea.

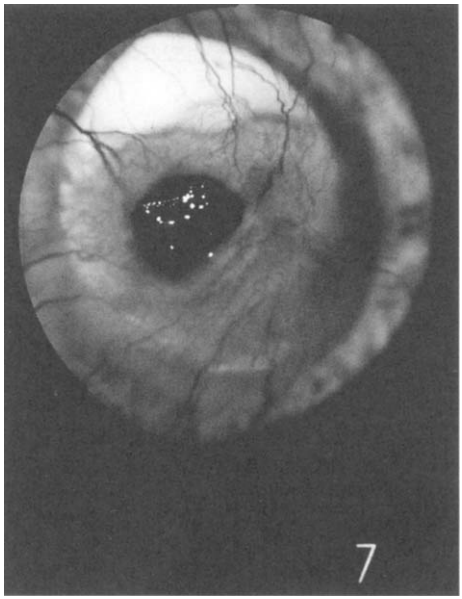


Figure 4. Sequestrum that was finally extruded after 9 months. Note the damage to the cornea generated by months of reaction as evidenced by neovascularization and scarring.

6. What other procedures may be necessary to remove sequestra?

If the surgical site needs to be supported with additional tissues, the options are numerous. Conjunctival flaps (180–360° and pedicle), Tenon's free graft, sliding corneal conjunctival graft, corneal grafts, and surgical adhesives all do the job. If donor corneas are available, both full-thickness and lamellar keratoplasties give postsurgical results that have clear central corneas as do the sliding corneal-conjunctiva grafts. Leukomas are usually the sequelae of grafts from Tenon's capsule, flaps, and glues (Figs. 5–8).

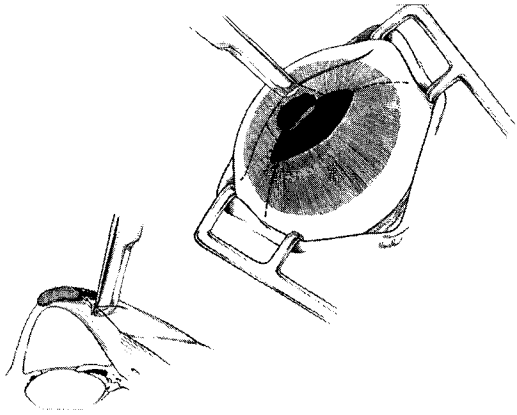


Figure 5. Deep keratectomy of a central corneal sequestrum showing the incision extending away from the sequestrum into the conjunctiva.

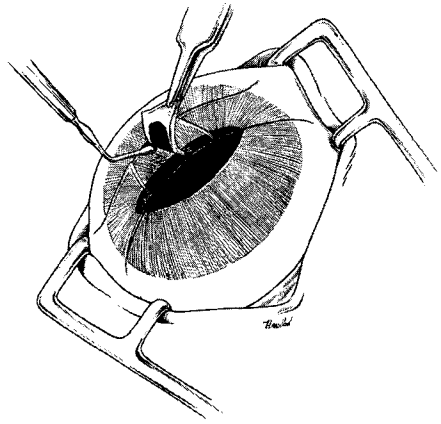


Figure 6. The sequestrum is removed by lamellar undermining with a Martinez spatula. The corneal splitting is carried beyond the limbus into the conjunctiva.

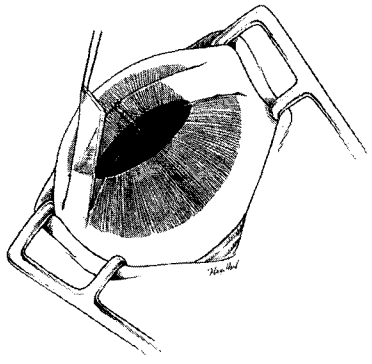


Figure 7. The split corneal layers are repositioned to appose together into the void left by the excised sequestrum.

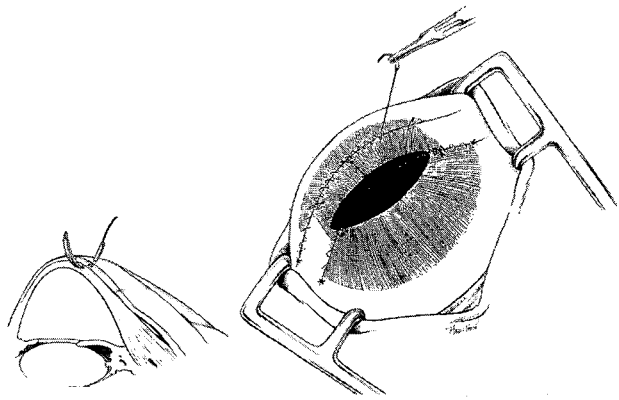


Figure 8. The sliding conjunctival-corneal graft is sutured to the adjacent cornea with 8–0 Vicryl. Note the central cornea now has clear tissue, but the periphery of the graft is opaque from the conjunctiva.

7. Following the surgical procedure elected, is it necessary to medicate the eye topically?

Yes, most ophthalmologists prefer to medicate a corneal wound with a broad-spectrum antibiotic. Culture and sensitivity tests from the surgical site should be submitted on all keratectomy cases. The results many times are negative, possibly because the patient has been on topical antibiotics presurgically. Those that have resulted in positive cultures have a high incidence of *Micrococcus*, which usually will respond to antibiotics, such as tobramycin (Tobrex) or ciprofloxacin (Ciloxan). Ointments are preferred mainly for their longevity. Allografts and heterografts should also be treated with 0.2% cyclosporine (Optimmune) twice a day for 3–6 months, depending on acceptance of the graft. In addition to the above, topical corticosteroids (dexamethasone) should be used for regression of neovascularization once the healing has taken place.

8. Should atropine be used postoperatively?

Initially, mydriasis is indicated, so a dose of 1% atropine pre- and postoperatively usually lasts 3–5 days. If atropine solution is used frequently and over days to weeks, the medication causes adverse effects that outweigh the desired effects.

9. If some pigment remains in the deep stroma after the keratectomy, is that bad?

The incomplete removal of the stromal pigment does not have adverse long-term consequences. A faint tint of brown may be the worst remaining consequence, but the healing will progress.

10. Where does the pigment come from?

It is not known for sure. It may arise from the lacrimal gland or from the conjunctival flora. The pigment, whatever its source, can be noted in the tears. It can stain the hairs around the eyes; it can be absorbed onto tissue paper; and, if you treat an ulcerated cornea with a soft contact lens, it will densely stain the contact. Attempts to identify the stain have proven the pigment to be a protein (Fig. 9).

11. In which cat breeds are sequestra most prevalent?

The breeds of highest incidence of sequestrum occurrence are the Burmese, Himalayan, and Persian. These breeds all have shallow orbits and protruding eyes, which make their corneas particularly vulnerable to microtrauma from trichiasis, entropion, lagophthalmia, and associated diseases of the adnexa.

12. Is there anything that can be done to prevent recurrence if the diagnosis of sequestration has been made and surgical treatment instigated?

Although there are no guarantees, it is helpful to start a topical antiviral at the first indication of corneal irritation and confirmation of an ulcerative process. Also, vaccines should be main-

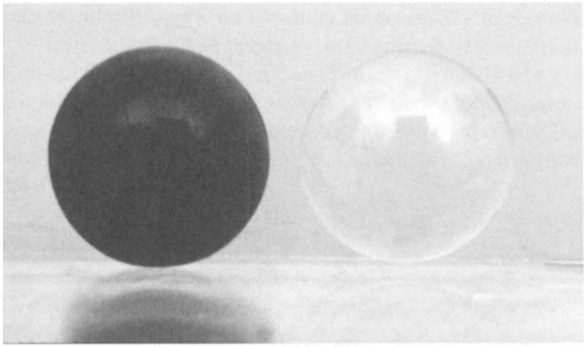


Figure 9. Contact lens removed from a postkeratectomized cat's cornea after only 2 days of placement. The pigment absorbed into the contact on the left with such affinity that it could not be washed away.

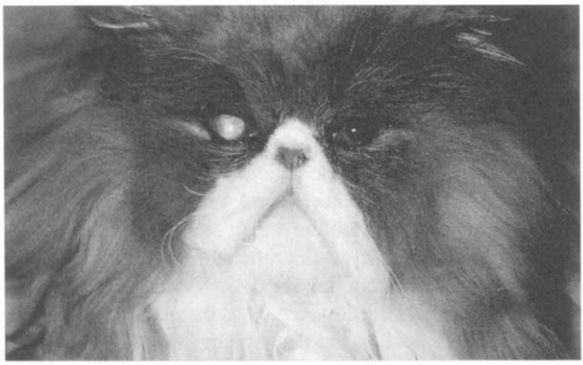


Figure 10. Champion Persian with unilateral sequestrum.

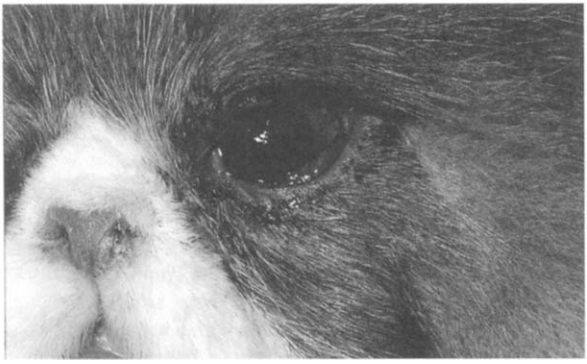


Figure 11. Champion Persian close-up of the left eye sequestrum shown in Figure 10.

tained faithfully to keep the titer high. Supplemental oral lysine can be considered. Antivirals can be used in conjunction with antibiotics. Even Champion Persians are susceptible (Figs. 10 and 11).

BIBLIOGRAPHY

1. Andrew SE, Tou S, Brooks D: Corneoconjunctival transposition for the treatment of feline corneal sequestra; A retrospective study of 17 cases (1990–1998). Vet Ophthalmol 4:107–111, 2001.
2. Blogg JR, Stanley RG, Dutton AG: Use of conjunctival pedicle grafts in the management of feline keratitis nigrum. J Small Anim Pract 30:678–684, 1989.
3. Gimenez MTD, Farina IM: Lamellar keratoplasty for the treatment of feline corneal sequestrum. Vet Ophthalmol 1:163–166, 1998.

4. Morgan RV: Feline corneal sequestration: A retrospective study of 42 cases (1987–1991). J Am Anim Hosp Assoc 30:24–28, 1994.
5. Nasisse MP, Guy JS, Davidson MG, et al: Experimental ocular herpesvirus infection in the cat. Invest Ophthalmol Vis Sci 30:1758–1768, 1989.
6. Pentlarge VW: Corneal sequestration in cats. Comp Cont Educ Pract Vet 11:24–32, 1989.
7. Schmidt GM, Whitley RD: Management of feline corneal sequestration: Medical therapy and surgical therapy. Vet Med Report 1:258–261, 1989.
8. Startup FG: Corneal necrosis and sequestration in the cat: a review and record of 100 cases. J Small Anim Pract 29:476–286, 1988.
9. Wilkie DA, Whittaker G: Surgery of the cornea. Vet Clin N Am Small Anim Pract 27:1067–1107, 1997.

9. FELINE PROLIFERATIVE KERATOCONJUNCTIVITIS

Ronald C. Riis, D.V.M, M.S.

1. **Is the feline species the only species to acquire proliferative keratoconjunctivitis?**
   No, the equine species also has a similar syndrome.

2. **Have these syndromes been identified?**
   Collectively, they have been called **eosinophilic keratitis.**

3. **Why is that term used?**
   The typical lesion is pink to white and is proliferative, from the surface of the cornea, conjunctiva, or nictitans. It is irregular on the surface and in shape. Transillumination of the eye displays dense neovascularization reacting to the involved areas. If cytology is performed from the lesions that are whitish and raised, the cellular response has high numbers of eosinophils among a mixed population of other inflammatory cells (Figs. 1–5).

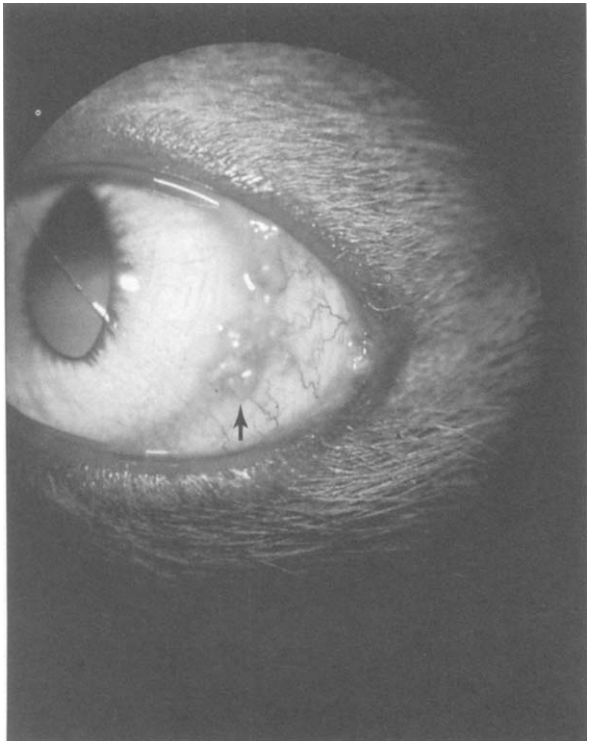


Figure 1. Note the proliferations at the limbus. This is an early manifestation of the syndrome.

4. **What factors might confuse the interpretation of the cytology of proliferative keratoconjunctivitis?**
   Inflammatory cells and high numbers of free rod-like bodies sometimes appear similar to rod bacteria. Comparing the intact numbers of eosinophils found with other cells will clarify whether

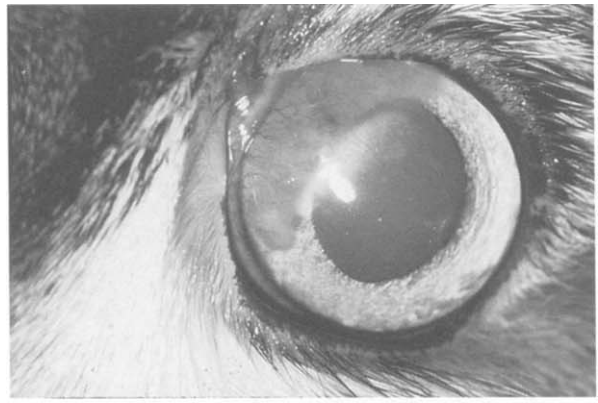


Figure 2. This pink thickening of the medial cornea is a rather smooth infiltration of proliferative keratitis.

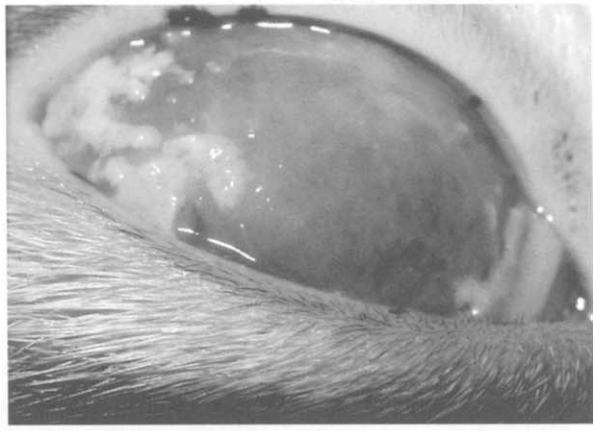


Figure 3. The proliferative component of this keratoconjunctivitis looks severe, but complete resolution was obtained with treatment.

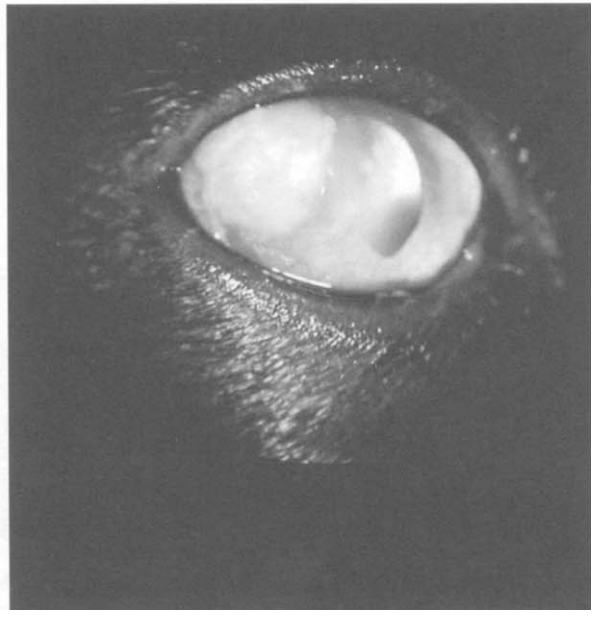


Figure 4. The appearance of this lesion is raised enough to rule out *in situ* neoplasms, but cytology confirmed tremendous numbers of eosinophils. The response to treatment was excellent.

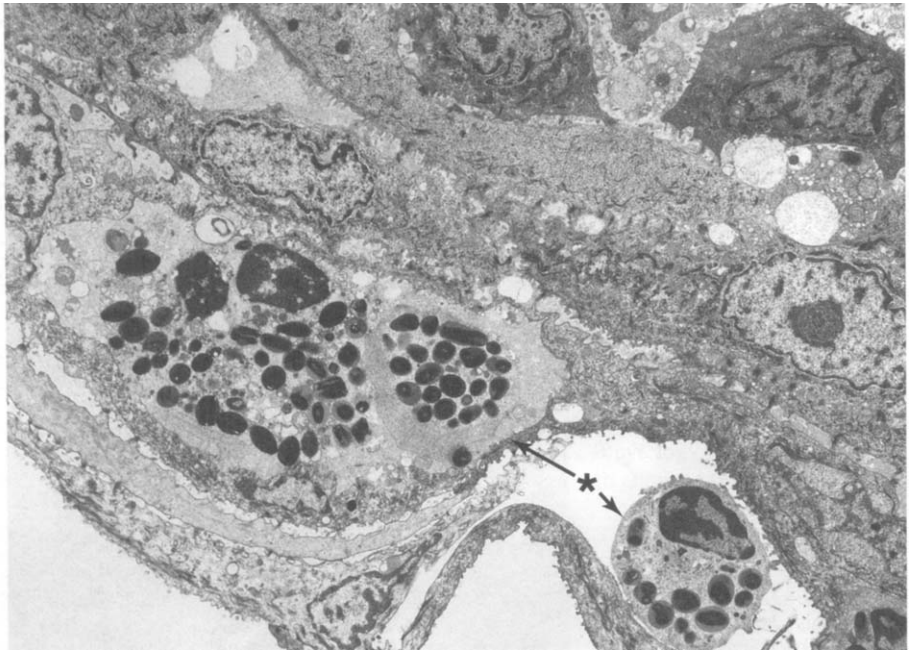


Figure 5. Electron microscopy of feline proliferative keratopathy. The inflammatory cells on the surface are eosinophils with their characteristic cytoplasmic granules (7,117×).

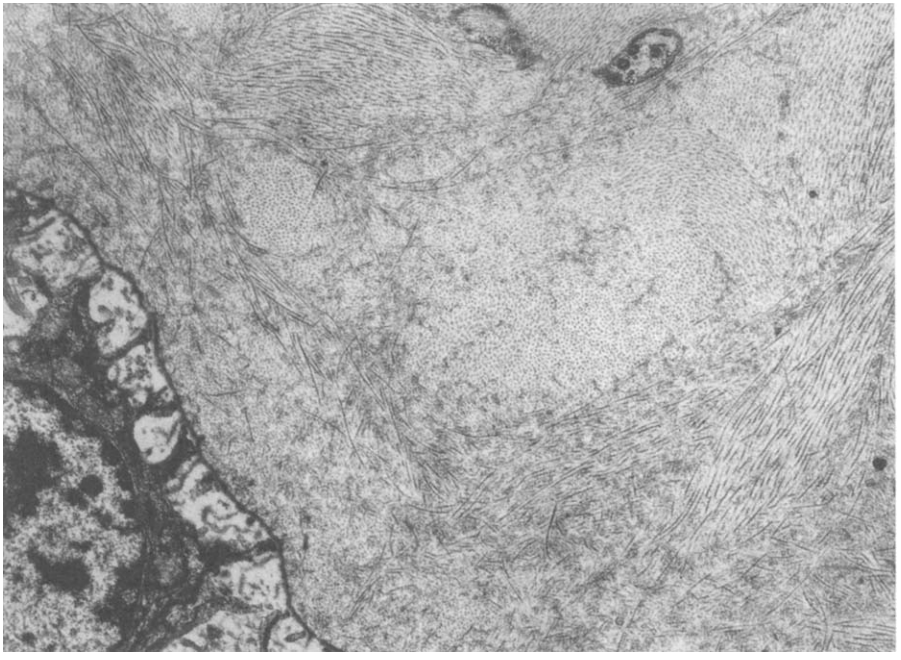


Figure 6. Electron microscopy at the edge of a lesion of feline proliferative keratopathy. Epithelial degeneration with vacuolation at the basement membrane and stromal collagen disorganization (115,300×).

eosinophils have released their cytoplasmic granules. The slide preparation technique may cause this traumatic fracture of the cells; a gentle blotting or rolling of the material gathered usually yields more intact eosinophils.

5. Are the eye manifestations in any way related to the dermatologic syndromes?
No, the ocular lesion is unique.

6. Is there any consistency to ocular involvement or breeds involved?
Usually, the condition presents as a unilateral problem; however, it has been seen bilaterally. Previously diagnosed cases can re-present with the opposite eye involved. There is no breed or sex predilection.

7. What is the etiology of proliferative keratoconjunctivitis?
The etiology is uncertain, however, one study found PCR-positive results against feline herpesvirus-1 (FHV-1) in 76.3% of the surgical samples taken from proliferative lesions. To add to the uncertainty, this author has diagnosed and treated specific-pathogen free (SPF) cats with proliferative keratoconjunctivitis.

8. What is the treatment for proliferative keratoconjunctivitis?
The lesions respond to corticosteroids. Depending on how aggressive you choose to be, topical, subconjunctival, and oral medications all are effective. If the cat is difficult to treat and the lesions are large, all three routes can be used. Initially, give 0.1 ml of 40 mg/ml of methylprednisolone (Depo-Medrol) subconjunctivally. Oral megestrol acetate should be prescribed: 5 mg/day for 1 week, then 5 mg/every other day for 1 week, then 5 mg/every third day for 2 weeks, and tapering off after 6 weeks. Minor lesions need to be treated only with the topical medication.

9. Are there concerns over the use of megestrol acetate?
Yes, owners should be warned about possible polydipsia-polyuria signs. Most cats lose these adverse signs once the dose is reduced or stopped. Some weight gain has also been noted on Ovaban, which is now off the market.

10. Causing a flare-up of FHV is a concern with corticosteroids use. Do nonsteroidal anti-inflammatories work?
Topical 0.1% diclofenac, 0.03% flurbiprofen, 1.0% indomethacin, and 1.0% Suprefen all reduce the neovascularization and, therefore, slow the proliferative course of the disease. These medications need to be used 4–6 times per day for several months, but the results still may not be as good as with corticosteroids. Another drawback is that cats become tired of frequent, long-term eye medications, and their owners feel they cause a bonding loss with this ritual.

11. Can a different therapy approach be used other than corticosteroids?
Yes, immunomodulators have been used.

12. Which immunomodulator has worked?
Interferon alfa-2a has been successful when used at an oral dose of 1000 IU/day/week, followed by no treatment for 1 week, then again back on medication. This alternating schedule is continued as necessary, but eventually the treatment is completely cancelled. In severe cases, oral interferon is supplemented with topical steroids.

13. How is the interferon prepared?
Interferon alfa-2a (Roferon-A Roche Pharmaceuticals) is sold in units containing 3 million IU. Aliquots are made up with 10,000 IU/ml and dispensed with directions to give oral 0.1 ml (1000 IU)/day.

14. Are there any adverse effects from interferon in cats?

The only reported side effect is a reduced white blood cell level, which returns once the interferon is stopped. The alternating weekly dose helps keep the white blood cell level.

BIBLIOGRAPHY

1. Bedford P, Cotchin E: An unusual chronic keratoconjunctivitis in the cat. J Small Anim Pract 24:85, 1983.
2. Larocea RD: Eosinophilic conjunctivitis, herpesvirus, and mast cell tumor of the third eyelid in a cat. Vet Ophthalmol 3:221–225, 2000.
3. Nasisse M, Luo H, Wang Y, et al: The role of feline herpesvirus-1 (FHV-1) in the pathogenesis of corneal sequestration and eosinophilic keratitis. Proc Am Coll Vet Ophthalmol 27:80, 1996.
4. Pentlarge VW, Riis RC: Proliferative keratitis in a cat: a case report. J Am Anim Hosp Assoc 20:477, 1984.
5. Pentlarge V. Eosinophilic conjunctivitis in 5 cats. J Am Anim Hosp Assoc 27:21, 1991.
6. Prasse K, Winston S: Cytology and histopathology of feline eosinophilic keratitis. Vet Comp Ophthalmol 6:74, 1996.

10. KERATOCONJUNCTIVITIS SICCA

Seth A. Koch, V.M.D., M.M.Sc., and John Sykes, D.V.M.

1. What is Keratoconjunctivitis sicca (KCS)?

KCS (*kerato* means "cornea" and *sicca* means "dry") is a disease in which the primary lacrimal gland has, for a variety of reasons, stopped functioning. The primary lacrimal gland supplies the aqueous portion of the precorneal tear film.

2. Describe the portions of the precorneal tear film.

Of the three parts of the precorneal tear film, the aqueous layer is the most copious, the lipid layer and the mucin layer are produced by the tarsal glands and the conjunctival goblet cells, respectively. The aqueous layer is responsible for causing KCS.

3. What is the primary lacrimal gland?

There are two lacrimal glands in the canine and feline. The primary lacrimal gland is located at the lateral aspect of the upper lid (2–3 mm from the lid margin). The ducts of the lacrimal gland bathe the corneal surface. The secondary or accessory lacrimal gland, or gland of the third eyelid, is responsible for about 30% of the total aqueous tear production. This gland can be negligently or mistakenly removed when it becomes swollen ("cherry eye"). Removal of this gland may result in significant decrease in tear production. In susceptible patients (breed related), there will be a resultant "dry eye" syndrome. A number of accepted surgical techniques should be used to ensure appropriate cosmesis and continued function of the gland. For discussion of the various surgical techniques see Chapter 12.

4. Which breeds are susceptible to KCS?

A number of breeds are disproportionately affected with KCS. The English bulldog, cocker spaniel, Pekingese, West Highland white terrier, schnauzer, and Yorkshire terrier are the most common breeds observed with the syndrome. The Yorkshire terrier has been reported to have congenital acinar hypoplasia as a genetic defect, and KCS is, therefore, seen in the young "Yorkie."

5. What are the clinical findings of KCS?

As with many other ocular irritative diseases involving the conjunctiva and cornea, the patient will exhibit discomfort, photophobia (discomfort in bright light), blepharospasm (blinking), copious ropey mucopurulent discharge, crusting of the lid margins, corneal neovascularization, ulcers, and keratinization (pigment deposition) (Figs. 1 and 2).

6. This sounds just like a conjunctivitis. Where's the sicca?

The sicca part of the KCS is what makes the diagnosis of the disease definitive. Any case of conjunctivitis seen in practice should have a Schirmer tear test performed to distinguish KCS from the other conjunctivitides.

7. What is the Schirmer tear test?

The tear test is a piece of filter paper of a specific type that is usually dye-impregnated for ease of reading. The strip of paper is bent at the indicated crease and inserted into the inferior conjunctival cul-de-sac at the lid margin. The amount of wetting that occurs in 1 minute is the recorded result. The conjunctival cul-de-sac should be cleansed with a dry cotton-tipped applicator to remove the debris prior to doing the test.

8. What's a normal reading for the Schirmer tear test?

Using the dye-impregnated strips, a finding of 12–15 mm of wetting in 1 minute is considered normal.

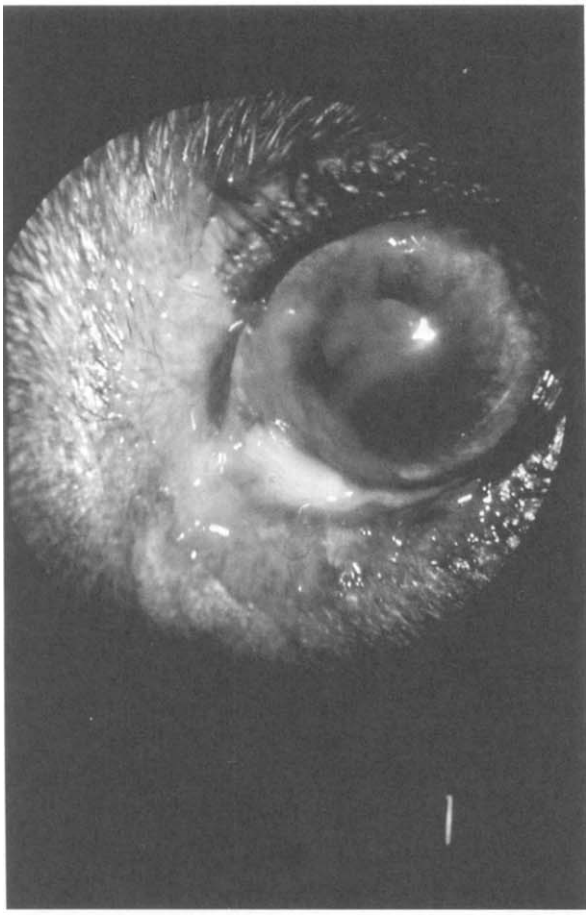


Figure 1. Dog eye with classical mucopurulent discharge. Note the dryness of the cornea allowing the discharge to stick to the surface and accumulate in the medial canthus.

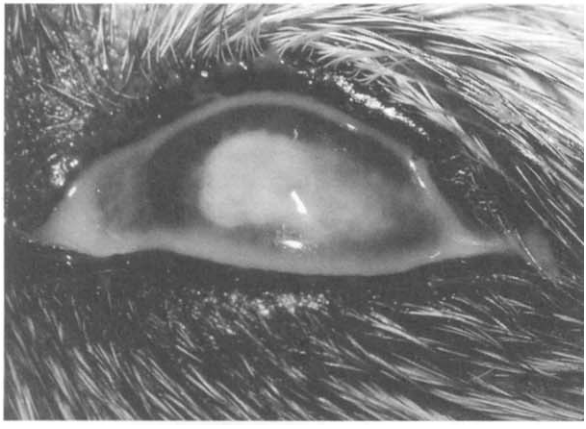


Figure 2. Dog eye with chronic keratoconjunctivitis sicca. The cornea is densely pigmented with a central leukoma. The eye is very red and the discharge mucopurulent.

9. Does the disease occur only in dogs?

No. KCS occurs in cats as well. In fact, any case of conjunctivitis in the cat should have a Schirmer tear test performed. The normal Schirmer tear test for a cat is 10 mm/1 minute.

10. What causes KCS?

There are many etiologies. The most commonly stated is immune deficiency disease. Other etiologies include viral distemper; congenital acinar hypoplasia (Yorkshire terrier); iatrogenic, either by drug-induced disease (sulfa class of drugs) or by removal of the secondary gland ("cherry eye") (30% of the tear film production); trauma; neurologic; endocrinopathy (thyroid, Cushing's, diabetes); and, of course, neoplasia.

11. How is KCS treated??

If the primary etiology can be determined and it is treatable, then obviously it should be treated. For example, KCS from thyroid disease may resolve with thyroid therapy. In addition or if the etiology is not known, the eye must be kept moist. The modalities for a "wet eye" are artificial tears, cyclosporine, pilocarpine, antibiotics, and corticosteroids.

The consensus is that many KCS cases are immune related, and **cyclosporine** is the modality of choice for this etiology. Cyclosporine stimulates the lacrimal gland by its action as a T-cell immunosuppressant.

Artificial tears have an effective life of 8–10 minutes, so it takes a lot of applications to keep an eye moist. If both "mom" and "dad" are working 8 hours a day, not much is accomplished with artificial tears. **Topical antibiotics** and **antibiotic-corticosteroid combinations** are used to reduce infection and inflammation wherever appropriate (if there is an accompanying corneal ulcer, antibiotic-corticosteroid is contraindicated).

Pilocarpine is a parasympathomimetic that can stimulate the lacrimal gland to function, if there is any gland to stimulate. It must be given in high enough doses to have a systemic effect, and therefore it can also negatively affect the respiratory and cardiovascular systems. Some have advocated its use topically as an irritant to cause reflex tearing and as a direct parasympathomimetic. These authors are opposed to pilocarpine for KCS treatment.

12. Is KCS a hard disease to treat?

It takes a lot of work: clean-up, treating, and "staying on top of it." A 60-day trial period of topical therapy will be enough to determine the efficacy of the therapy. If, at the end of 60 days, there hasn't been a dramatic change, then surgery is indicated. If there has been a positive change in 60 days, medication must be continued indefinitely. Cyclosporine is only effective for short periods of time and must be given continuously. Other supportive therapy is also necessary.

13. Are some KCS cases just not responsive to cyclosporine treatment?

A few breeds of dogs seem to be unresponsive. The German shepherd, samoyed, and West Highland terrier top the list.

CONTROVERSIES

14. Is cyclosporine indicated when the etiology of KCS is known *not* to be immune deficiency?

Probably no more than 60–70% of the patients treated with cyclosporine respond significantly.

15. Is surgery a good option for KCS?

Surgery to treat KCS involves transposing the parotid gland duct (PDT) from the mouth to the inferior cul-de-sac so the animal in effect "spits" in the eye. This keeps the affected eye "wet." The question then becomes, Is an excessively "wet eye" from PDT surgery better than a dry eye that needs constant medication? Many authors say that the surgery has insurmountable side effects. Others, including these authors, believe it is better to deal with the minimal problems of a wet eye than having to deal constantly with a nonresponsive dry eye. This applies to the cat as well. Before the advent of cyclosporine, PDT surgery was frequently performed. Because cyclosporine is not the "wonder drug" it was once thought to be, surgery is once again being performed with some degree of regularity.

BIBLIOGRAPHY

1. Gilger B, Allen J: Cyclosporine A in veterinary ophthalmology. Vet Ophthalmol 1:181–187, 1998.
2. Moore CP: Qualitative tear film disease. Vet Clin N Am Small Anim Pract 20:565–581, 1990.
3. Morgan R, Duddy JM, McClurg K: Prolapse of the gland of the third eyelid in dogs: A retrospective study of 89 cases (1980–1990). J Am Anim Hosp Assoc 29:56–60, 1993.
4. Salisbury MA, Kaswan RL, Ward DA, et al: Topical application of cyclosporine in the management of keratoconjunctivitis sicca in dogs. J Am Anim Hosp Assoc 26:269–274, 1990.

11. OCULAR PROPTOSIS

Dennis K. Olivero, D.V.M.

1. Define proptosis.

Proptosis is the rostral displacement of the globe with entrapment of the eye forward of the eyelid margins. Subsequent orbicularis oculi muscle spasm rapidly compromises blood supply to the displaced eye.

2. What causes proptosis?

Trauma frequently is involved in the development of ocular proptosis in animals. Blunt trauma to the head and neck causes forward displacement of the globe. Small dogs grasped by the neck and shaken by larger dogs have developed unilateral or bilateral proptosis. Excessive restraint of brachycephalic breeds of dogs can result in proptosis, but most proptosis cases result from injury from other animals or people or contact with moving automobiles.

3. Are certain breeds predisposed to proptosis?

Brachycephalic breeds of dogs comprise the majority of the cases of ocular proptosis. Macropalepbral fissure and shallow orbits offer little resistance to forward displacement of the globe with blunt injury to the head or neck. When proptosis occurs in dolichocephalic breeds of dogs or in cats, severe trauma is involved and the patient should be carefully evaluated for other injuries not involving the eye.

4. What is the most important first-response measure following proptosis?

When the veterinary client calls the clinic to report that the eye has "popped out," veterinary staff should stress the importance of preventing exposure and dessication of the cornea. If saline is available in the home, a soft towel or gauze squares can be soaked in saline and gently placed around the eye during transportation. Any antibiotic or tear replacement eye ointment can also be used to prevent drying of the cornea. Even petroleum jelly (Vasolene) can be applied on the eye if no ocular lubricating agents are available.

5. What steps should be taken when the patient arrives at the hospital?

If the globe has not been lubricated, liberally apply antibiotic or tear replacement ointment to the exposed ocular tissues. Next, evaluate the patient as a whole. Remember, in dolichocephalic breeds of dogs and in cats, excessive trauma is required to displace the globe from the orbit. If an automobile accident caused the injury, carefully evaluate the neurologic, cardiovascular, and pulmonary status of the patient. Administer IV fluids and corticosteroids for shock if necessary. Some patients will not be immediately ready for anesthesia and globe replacement, depending on the extent of their other injuries.

6. What is the prognosis for vision following proptosis of the globe?

In general, the prognosis for vision following ocular proptosis is guarded. Only 20% of patients experiencing ocular proptosis have any useful vision in the involved eye following treatment. The prognosis specifically depends on the amount of force required to displace the globe. Dogs with exaggerated brachycephalic conformational anatomic features can experience proptosis with minimal trauma and sometimes as a complication of excessive restraint. If the globe is immediately repositioned, vision is generally not affected. In most patients, however, more severe trauma is involved in globe displacement, and this affects the prognosis for vision (Fig. 1).

7. When is the prognosis for vision favorable?

A favorable prognosis for vision is offered for patients when the eye is displaced for a very short period of time and those in which the displacement was associated with minimal trauma.

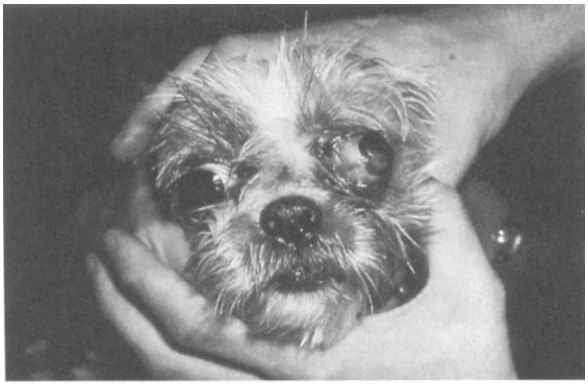


Figure 1. This 7-year-old female shih tzu dog suffered proptosis of the left globe after being attacked by a larger dog. Lateral deviation of the globe is evident with medial rectus muscle avulsion, but the anterior segment is clear and there is minimal orbital hemorrhage. The globe was salvaged but was not visual.

These patients show intact pupillary light reflexes or a miotic pupil in the affected eye with an indirect pupillary response to the contralateral eye. Minimal or no hyphema and minimal orbital hemorrhage are present in patients who continue to have useful vision following proptosis. Intact visual responses with a normal-appearing fundus confer a favorable prognosis.

8. When is the prognosis for vision grave?

When severe trauma resulted in globe displacement and it is accompanied by marked hyphema, vitreal hemorrhage, or retinal detachment, the prognosis for future vision is grave.

9. Are there any ancillary tests that can be done to determine the prognosis for vision?

Most veterinary referral centers provide ultrasound imaging of the globe and orbit. Hyphema in the absence of marked vitreal hemorrhage and retinal detachment would suggest a better prognosis compared with vitreal hemorrhage and complete retinal detachment. Blindness following proptosis, however, is frequently the result of optic nerve injury. Visual evoked potentials can be measured with specialized equipment, indicating the transmission of electrical signals from the retina to the occipital (visual) cortex. This type of testing requires a clear ocular media and is rarely considered in the emergency situation, but it can be useful in combination with electroretinography after the globe has been salvaged to determine amount of vision present (see Chapter 1).

10. Is it always possible to salvage the globe?

Some patients present with severe tissue damage to the globe and orbit. Patients with rupture of the cornea, collapse of the globe, complete loss of extraocular muscle attachments to the orbit (Fig. 2), or excessive corneal injury associated with drying and exposure are often scheduled for

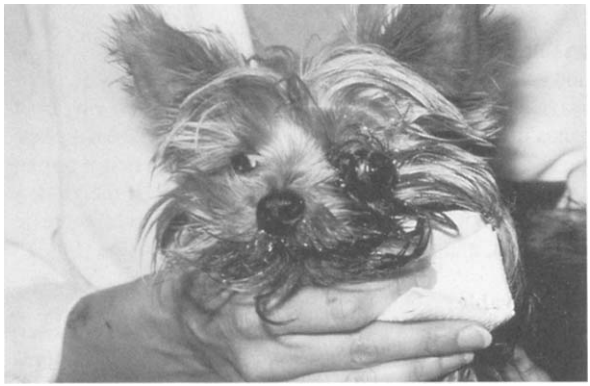


Figure 2. This 8-year-old male Yorkshire terrier dog was attacked by a German shepherd dog resulting in proptosis of the left eye. No extraocular muscle attachments remained intact, and marked orbital hemorrhage is evident. The eye was enucleated shortly after presentation.

enucleation as soon as the patient is able to withstand general anesthesia. Enucleation can be considered at any time during the course of treatment, however, and because of this most clinicians attempt initially to salvage the globe. The prognosis for vision should be discussed with clients, because some will prefer enucleation to rapidly resolve the medical situation if there is no hope for future vision. Even if the globe is salvaged, chronic medical treatment may be necessary to keep the patient comfortable.

11. Is there any danger of injury to the contralateral eye?

Most dogs with proptosis of the globe exhibit unilateral injury. There are case reports of blindness in the contralateral eye that shows no visible evidence of displacement or traumatic injury. It is assumed that optic nerve tearing at the level of the optic chiasm results in contralateral injury. Excessive traction on ocular tissues, especially in cats, can result in further optic nerve injury with potential involvement of the second eye. Some degree of vision loss in the contralateral eye may occur more frequently than is realized because there is no easy way to assess partial vision loss in veterinary patients.

12. What steps are taken to reposition the globe into the orbit?

General anesthesia is required in most cases to reposition the globe. If proptosis develops as a result of restraint, the hairs can be grasped on the lids and pulled out away from the globe, allowing the eye to fall back into the orbital space. In this situation, anesthesia may not be necessary. With most traumatic cases of globe proptosis, excessive tissue swelling and orbital hemorrhage will complicate globe repositioning and necessitate chemical restraint. Blood and debris are removed from the periocular tissues prior to globe replacement.

When excessive tissue swelling and orbital hemorrhage are evident, a lateral canthotomy not only will ease repositioning of the eye but also will immediately relieve vascular stasis to the globe. Various techniques have been described for globe replacement. Essentially the eyelid margins must be elevated and rotated away from the globe while gentle pressure is placed on the cornea. Stay sutures can be placed in the eyelid tissue near the lid margin to allow manipulation of the eyelids, or tissue clamps (Allis) can be used. Split-thickness mattress sutures of 3–0 to 4–0 nonabsorbable material supported with stents are preplaced and gradually tightened to close the lids around the displaced globe. Caution is used while placing sutures to avoid needle contact with the cornea. Just prior to lid closure, all debris should be thoroughly flushed from the conjunctival fornices using sterile saline. Most clinicians leave a gap medially or laterally for placement of antibiotic and atropine ophthalmic ointments. If a lateral canthotomy is made, it is closed routinely after eyelid closure and stabilization of the globe.

13. Should there be supportive medical treatment after closure of the eyelids?

Following recovery from general anesthesia and in the absence of other severe injuries, most patients with proptosis can be released for home care soon after replacement of the globe. An Elizabethan collar is often necessary and recommended to prevent self-injury or removal of the sutures. Supportive medical care should include rest, oral antibiotics, and oral corticosteroids. Corticosteroids are used at the anti-inflammatory level to help resolve panuveitis and optic nerve injury in addition to orbital inflammation and swelling. If an opening was left between the eyelids to facilitate application of medications, triple antibiotic ophthalmic ointment is applied 3–4 times daily and atropine ophthalmic ointment is applied 1 or 2 times daily to control pain associated with ciliary spasm and anterior uveitis. Atropine ointment should be used judiciously because it will contribute to sicca, which is frequently a complication of proptosis in dogs.

If the cornea is ulcerated at the time of globe replacement, evaluation of the ocular discharge emerging from the medial or lateral eyelid opening is an important way to monitor for secondary corneal bacterial infection. If copious white discharge emerges from the opening and the patient shows excessive and progressive discomfort, the sutures can be temporarily removed to further assess the condition of the cornea. Microscopic evaluation of debris collected from the ulcer bed can categorize the inflammation and aid in appropriate changes in antimicrobial therapy.

14. How long should the eyelids be left closed after repositioning of the globe?

In general, the eyelids should be left closed for at least 2 weeks. Clients should be instructed to evaluate the lid closure daily. As tissue swelling resolves, gaps may develop between the upper and lower eyelid margins, allowing suture contact with the cornea. This may necessitate altering the tension on the sutures or replacing them. After 2 weeks, the sutures are removed and the globe is assessed for vision and any other irreversible injury that is evident. If excessive lagophthalmos and exophthalmos persist, the lids should be closed again for an additional 2 weeks.

15. What complications are commonly encountered after the eyelids are opened several weeks following the injury?

Common complications following ocular proptosis include strabismus associated with extraocular muscle injury, both ulcerative and nonulcerative keratitis, keratoconjunctivitis sicca, lagophthalmos, and blindness. Traumatic cataract, iris bombé glaucoma secondary to hyphema, retinal detachment, and phthisis bulbi can occur additionally.

16. Why does strabismus occur following proptosis?

The medial rectus muscle frequently is torn from the globe at its insertion when the eye is accelerated forward. This results in lateral strabismus in most dogs following proptosis. Reportedly, the strabismus improves with time, presumably associated with readjustment of tension on the remaining viable extraocular muscles (Fig. 3). Although clients have requested reattachment of the medial rectus muscle, finding and reattaching fragments of torn muscle is not likely to be successful following proptosis injury.

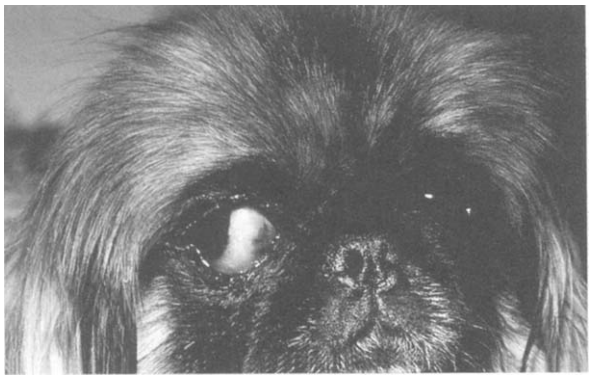


Figure 3. This 3-year-old female Pekingese dog suffered proptosis of the right eye 6 weeks prior to this photograph. The final outcome of treatment is evident with lateral strabismus but a quiet, comfortable eye. The strabismus will probably partially resolve in the following months.

17. Why is keratitis frequently a problem following proptosis?

Ulcerative keratitis develops rapidly secondary to exposure after injury. Following treatment of proptosis using a temporary tarsorrhaphy, keratitis can result from poor tear production and lagophthalmos. Poor tear production can result from direct injury to lacrimal glands or as a result of nerve damage or vascular damage supplying these structures. Treatment with ophthalmic cyclosporine ointment (Optimmune) may or may not improve tear production because sicca following traumatic proptosis of the globe is frequently neurogenic in origin.

Anesthesia of the cornea is common following proptosis, presumably associated with loss of function of the cranial nerve five sensory endings in the cornea. This also contributes to lagophthalmos and sicca because blinking and tearing are at least partially controlled by reflexes originating in the corneal stroma. Lack of sensation in the cornea in addition to exposure and sicca will promote ulcerative keratitis, referred to as **neurotropic keratitis.** Ulcers associated with anesthesia of the cornea frequently are very slow to resolve with supportive treatment alone, and other surgical procedures may be necessary.

18. Are there any steps that can be taken to prevent proptosis?

Dogs that experience proptosis with minor trauma frequently have exaggerated brachycephalic anatomic features that provide little support or protection for the globe. Reduction of the excessive palpebral fissure size with lateral or medial canthoplastic procedures can reduce the chances of proptosis in the future. After loss of vision in one eye, many veterinary clients will consider palpebral reduction surgical procedures to protect the second eye.

CONTROVERSIES

19. Should the medial rectus muscle be reattached during globe replacement to minimize postoperative strabismus?

For repair of the medial rectus muscle: Repair of the medial rectus muscle prior to globe replacement can minimize or resolve strabismus, which is common following proptosis injury in animals. After induction of general anesthesia, a lateral canthotomy can be immediately performed to reduce vascular stasis to the globe. Medial rectus muscle is reattached to the sclera at its insertion prior to performing the temporary tarsorrhaphy.

Against repair of the medial rectus muscle: Traumatic proptosis of the globe in animals is usually associated with marked orbital edema and hemorrhage, which prohibits identification of medial rectus fragments for attempted repair. It is questionable whether or not the extended anesthetic time required for extraocular muscle repair and further manipulation of an already traumatized eye is warranted when repositioning of the globe and stabilizing of the patient are of paramount importance. Emergency clinic veterinarians and primary care veterinarians are more likely to initially manage ocular proptosis cases than specialists, and these individuals are not likely to have available specialized surgical instrumentation for strabismus surgery.

20. Should every effort be made to salvage the globe for a cosmetic appearance?

For salvage of the globe whenever possible: Emergency clinic and primary care veterinarians initially manage the majority of cases of ocular proptosis in animals. If the eye is irreversibly damaged, enucleation is discussed and recommended. In all other situations the eye is replaced in the orbit in hopes of future vision. Specialists later become involved in case management, and with more sophisticated equipment the prognosis for vision can be clearly established. Emergency and primary care veterinarians are reluctant to recommend enucleation in the absence of such information.

Against salvage of the globe when blindness is inevitable: Most veterinary ophthalmology references indicate that every effort should be made to salvage the globe even if enucleation may be necessary at some later point. This advice may be hard to justify in light of the overall poor prognosis for vision in most cases of traumatic proptosis of the globe. The recommendation becomes even more difficult to justify when consideration is made of the time of patient discomfort following salvage versus enucleation and when medical expenses are considered for the various approaches to treatment. Obviously, enucleation is not recommended if there is any hope for vision, but enucleation perhaps should be considered early on for hopelessly blind eyes when clients are more concerned with patient discomfort and/or medical expenses than the final cosmetic appearance. Following enucleation of the globe, most animals have fully recovered from inflammation and discomfort 5 days after surgery. Traumatized eyes may be inflamed and painful for weeks or months after injury. Most veterinary clients are not well informed on the usual appearance of salvaged globes, and the "cosmetic" appearance of laterally deviated and oftentimes phthisical eyes can be debated. After induction of general anesthesia to replace the proptosed globe, ultrasonography can be performed quickly. If this shows excessive ocular hemorrhage and retinal detachment, then enucleation can be strongly considered to rapidly alleviate patient discomfort.

BIBLIOGRAPHY

1. Fritsche, J, Spiess BM, Ruehli MG, et al: Prolapsus bulbi in small animals: A retrospective study of 36 cases. Tierarztl Prax 24:55–61, 1996.

2. Gilger BC, Hamilton HL, Wilkie DA, et al: Traumatic ocular proptoses in dogs and cats—84 cases (1980–1993). J Am Vet Med Assoc 206:1186–1190, 1995.
3. Kern TJ: The Canine orbit. In Gellatt K (ed): Veterinary Ophthalmology, 2nd ed. Philadelphia, Lea & Febiger, 1991, pp 243–244.
4. Lindley DM, Ringle M, Moorthy R, et al: Efficacy of lateral canthotomy and cantholysis in orbital hemorrhage. Vet Pathol 29:473, 1992.
5. Ramsey DT, Fox DB: Surgery of the orbit: Surgical management of ocular disease. Vet Clin North Am 27:1244–1247, 1997.
6. Slatter DH: Ocular emergences. In Fundamentals of Veterinary Ophthalmology. Philadelphia, W.B. Saunders, 1990, p 538.
7. Spiess BM, Wallin-Hakanson N: Diseases of the canine orbit. In Gellatt K (ed): Veterinary Ophthalmology, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 1999, pp 520–522.

12. NICTITANS ABNORMALITIES AND THERAPIES

James F. Swanson, D.V.M., M.S., and M. Kohle Herrmann, D.V.M.

1. Some owners notice a pigment band on the dorsal bulbar conjunctiva of their pets' eyes. What are they seeing?

At times, the third eyelid will extend dorsally. Owners may think that there is a tumor or some other disease process. By manually prolapsing the third eyelid, one can see the extension of this structure (Fig. 1). It does not cause any problems and the owners should be reassured that this can be normal. This is not a fault in show dogs. The American cocker spaniel seems to be the most common breed with the encircling third eyelid.

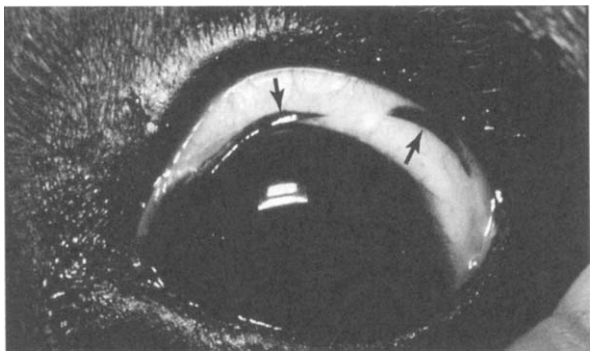


Figure 1. American cocker spaniel; note linear pigment outlining the dorsal encirclement of the third eyelid.

2. Are there any problems with a nonpigmented third eyelid?

A nonpigmented edge of the third eyelid may be unilateral or bilateral. The hair coat color has a bearing on the degree of pigmentation. Dogs that have white hair coats or a merling factor have the highest incidence. Usually a nonpigmented third eyelid does not cause any problems. Owners may complain that the affected eye looks larger or that it seems redder. There may be a slightly higher incidence of conjunctivitis, which can be treated with topical antibiotic-steroid combinations. Dogs' and cats' nictitans may be at increased risk for squamous cell carcinomas when the third eyelid is not pigmented.

3. Can dermoid cysts occur on the third eyelid?

Dermoid cysts of the third eye lid are rare but do occur. Dermoids are found in both dogs and cats with Burmese cats exhibiting the highest incidence. Dermoids can cause chronic irritation due to cilia rubbing on the cornea. These lesions should to be excised, and the conjunctiva sutured to ensure no cartilage is exposed. Be certain to either bury your knot or tie your knot on the anterior surface of the third eyelid. Suture such as 6–0 Vicryl works well.

4. If the third eyelid has been lacerated, what should I do?

If the tear is small, involving only the edge, and no cartilage exposed, the defect may be trimmed or just left in place. When lacerations are more extensive or involve the cartilage, the defect should be repaired. Make sure the conjunctiva is positioned, and suture to cover any exposed cartilage. All knots should be buried, as in a subcuticular pattern, or brought to the anterior surface of the third eyelid. Again, 6–0 Vicryl suture is preferred.

5. Do eosinophilic granulomas involve the third eyelid?

Eosinophilic conjunctivitis may affect the third eyelid. Most of the time there is concomitant corneal involvement. Feline herpesvirus infection may be the underlying cause for this lesion in cats. Cytology will reveal eosinophils and, at times, mast cells. Topical corticosteroids can be used first if there are no herpetic lesions on the cornea. Oral steroids can be used in resistant cases. Megestrol acetate can also be used and works very well (see Chapter 9).

6. What does a prolapsed third eyelid mean?

Usually there is an underlying disease process. This could include a retrobulbar mass, hemorrhage, myositis, ocular pain, tetanus, loss of orbital fat, or a neurologic disorder.

With a retrobulbar mass the globe will not retropulse back into the orbit. Ocular retropulsion is accomplished by gently pressing on the globe to determine if it will recede back into the orbit. Always compare both eyes. In painful orbital conditions such as orbital cellulitis, the animal exhibits pain when the globes are retropulsed or the mouth is opened.

If there is orbital hemorrhage, the globe often does not retropulse normally. Examine the mucus membranes for evidence of petechiation or pale coloration as would be seen with clotting disorders.

Inflammation of the extraocular muscles and temporal muscle myositis can cause the third eyelid to prolapse (Fig. 2). Usually there is swelling and sometimes pain noted in the muscles of mastication. Opening the mouth is often painful, also.

Ocular pain can cause the animal to retract the eye and prolapse the third eyelid. This can be seen with corneal ulcers, glaucoma, and uveitis.

Loss of orbital fat in older animals or animals with chronic orbital cellulitis can cause the globe to sink into the orbit, allowing the third eyelid to prolapse. Although various implants have been used to reverse the signs of enophthalmos, to date all have met with only limited success.

Systemic disease, such as tetanus, can cause the animal to have elevated third eyelids. Usually the ears will be upright and the animal will have a wide palpebral opening. There is often history of a wound or injury.

Neurologic disorders such as Horner's syndrome, idiopathic prolapse of the third eyelid of cats, and generalized dysautonomia may cause the third eyelid to be elevated (Fig. 3). Horner's syndrome is caused by preganglionic or postganglionic sympathetic nerve injury. The most common is a postganglionic lesion originating at the craniocervical ganglion or above. Lesions may involve the cavernous sinus, middle ear, or orbit. The middle ear seems to be the most common site of involvement. By using 10% phenylephrine drops, one can test for pre- or postganglionic lesions. It usually takes 40 minutes or more to dilate the pupil in a preganglionic lesion. Only about 20 minutes are needed to dilate the pupil with a postganglionic lesion. The third eyelid will usually go back to a nearly normal position. If there are some visual problems then 2.5% phenylephrine can be used (see Chapter 24).

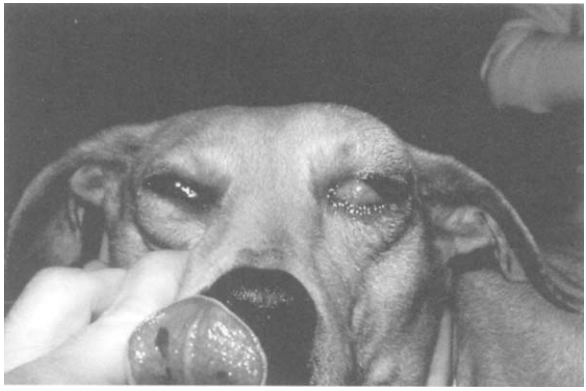


Figure 2. Mixed breed dog with temporal myositis exhibiting temporal muscle swelling and third eyelid prolapse.

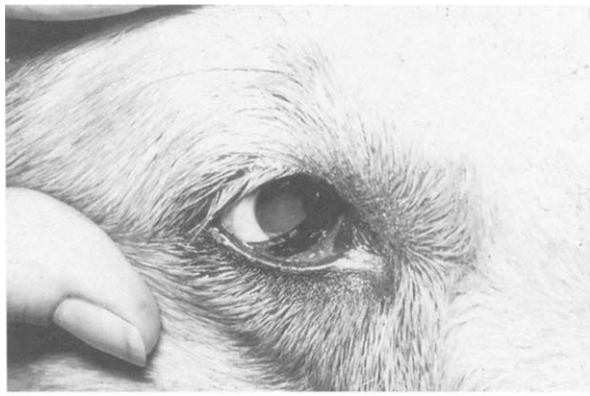


Figure 3. Third eyelid protrusion and miosis caused by Horner's syndrome.

Cats may have an idiopathic protrusion of the third eyelid referred to as "haws." Rarely is the cause known, and it is usually bilateral with no pupillary involvement. Sometimes there is a history of gastrointestinal problems. A drop of 2.5% phenylephrine will cause the third eyelid to return to its normal position and can be used 2–4 times a day if visual problems are occurring.

Generalized dysautonomia or Key-Gaskell syndrome in cats can cause a protrusion of the third eyelid. The pupils are usually dilated and unresponsive to light. There is also a decrease in tear production. Other systemic signs are seen with this disease.

7. Is there any reason to remove the third eyelid?

The only reason to remove the third eye lid is neoplasia. The most common third eyelid tumors we see are melanosarcoma (Fig. 4), adenocarcinomas, hemangiomas, hemangiosarcomas, and squamous cell carcinomas of the gland of the third eyelid (Fig. 5). It is advisable to rule out metastasis before excising the tumor. When the third eyelid is removed, be sure to suture the bulbar conjunctiva to the palpebral conjunctiva. This will close off the space leading to the retrobulbar area.

Occasionally a portion of the third eyelid may be removed when it has interfered with vision, leaving the gland of the third eyelid. These cases were older animals that were enophthalmic or had long-standing Horner's syndrome.

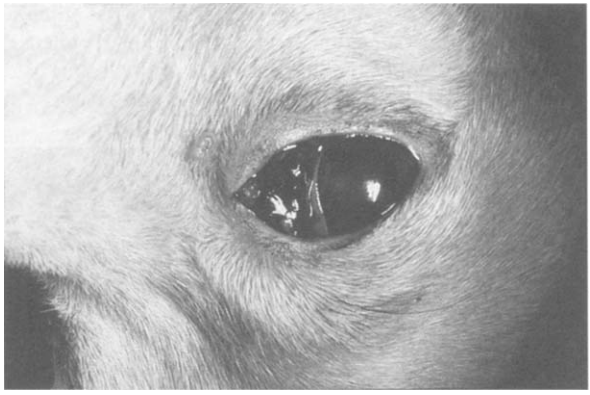


Figure 4. Malignant melanoma of the third eyelid in a dog.

8. How does a foreign body of the third eyelid present?

The animal will most often exhibit sudden onset of lacrimation and blepharospasm. The third eyelid can be prolapsed and thickened. A corneal ulcer may be present along with a mucopurulent discharge. Always be sure to use a topical anesthetic and look behind the third eyelid. Grass

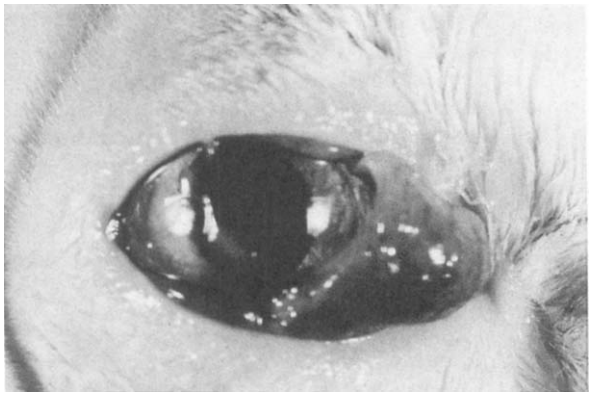


Figure 5. Squamous cell carcinoma of a nonpigmented third eyelid in a cat.

awns and plant material seem to be the most common foreign bodies. Pieces of porcupine quills or cactus thorns may also be lodged in the third eyelid.

9. Are third eyelid flaps of any benefit?

Third eyelid flaps can be helpful when treating corneal ulcers in the cat. In some cats there is a loss of corneal sensation and a superficial ulcer develops. Protection of the cornea by a third eyelid flap often speeds healing. Third eyelid flaps may also be beneficial in the treatment of nonmelting midstromal ulcers. When performing a third eyelid flap, be sure to scarify the bulbar surface to create some bleeding. The resulting serum exuded helps to heal the ulcer more rapidly. Size 5–0 nylon suture is used in a mattress pattern to place up the flap. The sutures are brought out close to the upper fornix, and a stint (intravenous tubing or rubber band) is used to take tension off the sutures to prevent pulling through the upper eyelid. Usually three sutures are used and are left in place for at least 2 weeks. Topical medication can still be placed in the eye.

10. What does a thickened, meaty-looking third eyelid indicate?

If the dog is a German shepherd or a greyhound, the condition is probably a variant form of pannus (Fig. 6). Cytologic examination reveals primarily plasma cells along with fewer numbers of lymphocytes. The condition can be controlled with topical steroids or cyclosporine. Another entity resulting in similar appearance is follicular conjunctivitis. The inner surface of the third eyelid looks like raw hamburger meat (Fig. 7). The etiology is not known but could be a form of chronic low-grade infection or allergic reaction to pollens. Treatment is symptomatic using corticosteroid-antibiotic combinations. If the follicles persist, sedation and debridement of the affected surface with a gauze sponge usually bring improvement.

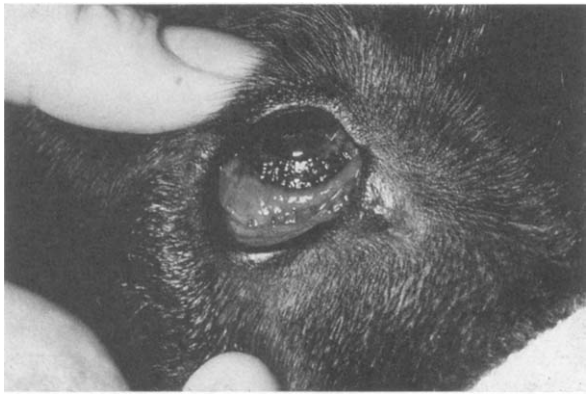


Figure 6. Depigmentation and follicle formation on the third eyelid of a German shepherd affected with atypical pannus.

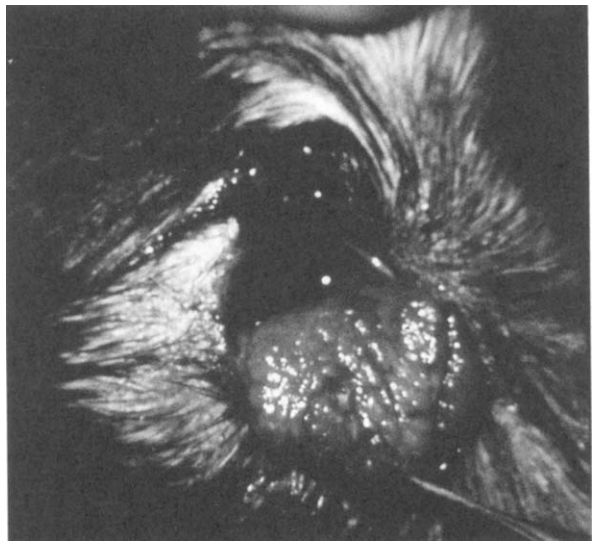


Figure 7. Severe follicular conjunctivitis affecting the inner aspect of the third eye.

11. How is a prolapsed gland of the third eyelid treated?

The gland of the third eyelid contributes a significant proportion of the aqueous tear film, therefore the gland should be preserved. Prolapse of the gland is due to a lack of the connective tissue band that fixes the gland to the periorbital tissues or from pressure due to an inflamed and swollen gland. This appears to have an inherited basis and is seen in the beagle, bulldog, cocker spaniel, great dane, Lhasa apso, Pekingese, and shih tzu. Burmese cats with this condition have been observed with severe keratoconjunctivitis sicca when the gland has been excised, so the gland should be surgically replaced.

Surgery is the treatment of choice, because the glands will not normally go back to their position at the base of the cartilage with medication. In dogs, removing the gland can be considered, but the owners need to be informed that the animal runs the risk of developing dry eye (keratoconjunctivitis sicca) if the third eyelid is entirely removed. Surgical repositioning of the gland is recommended. The pocket technique described by Dr. Morgan works nicely in the majority of the cases and is used when the gland is not excessively swollen. Be sure to separate the conjunctiva from the cartilage, because this will allow you to suture the conjunctiva without incorporating the cartilage. Dr. Gross's technique anchors the gland to the inferior sclera, and this procedure can be used when the gland is enlarged. At times, a combination of these two techniques works best. Another frequently used procedure is Kaswan and Martin technique. Our suture of choice is 6–0 Vicryl with a tapered needle to avoid cutting the conjunctival or scleral tissue. Be sure to bury your knots.

12. Are there any anatomic defects that occur with the cartilage of the third eyelid?

The third eyelid has a T-shaped cartilage that gives definition to the third eyelid. This cartilage can bend due to trauma or a congenital defect (Fig. 8). When the cartilage bends away from the globe (eversion) the inner surface of the third eye lid is exposed and can become inflamed and infected. The animal may develop a mucoid ocular discharge. It is best to remove the deformed vertical portion of the cartilage to allow the third eye lid to resume its normal position. As long as the cartilage is exposed, you must suture the conjunctiva. In the larger breeds of dogs, it is advisable also to perform a pocket procedure (see above) to prevent subsequent prolapse of the third eyelid gland. For suturing, 6–0 Vicryl can be used to close the conjunctiva. At times, the cartilage can be sutured together.

Some animals will have a slight bend in the horizontal portions of the T cartilage (the horns). It is rarely necessary to treat this defect. Some veterinary ophthalmologists will trim these areas. It is not usually necessary to do any suturing.

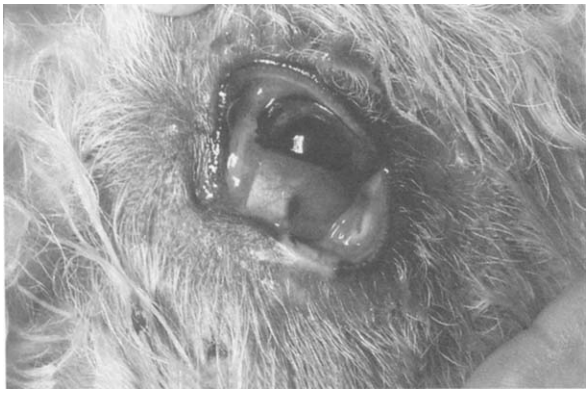


Figure 8. Deformed stem of the cartilage in the third eyelid.

BIBLIOGRAPHY

1. Gross SL: Effectiveness of a modification of the Blogg technique for replacing the prolapsed gland of the canine third eyelid [abstract]. Proc Am Coll Vet Ophthalmol 14:38–42, 1983.
2. Kaswan RL, Martin CL: Surgical correction if third eyelid prolapse in dogs. J Am Vet Med Assoc 186:83, 1985.
3. Morgan RV, Duddy JM, McClurg K: Prolapse of the gland of the third eyelid in dogs: A retrospective study of 89 cases (1980 to 1990). J Am Anim Hosp Assoc 29:56–60, 1993.
4. Severin GA: Severin's Veterinary Ophthalmology Notes, 3rd ed. Fort Collins, CO, College of Veterinary Medicine, 1996, pp 207–221.
5. Ward DA: Diseases and surgery of the canine nictitating membrane. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd. Philadelphia, Lippincott Williams & Wilkins, 1999, pp 609–618.

III. Glaucoma

13. GLAUCOMA OVERVIEW

Seth A. Koch, V.M.D., M.M.Sc., and John Sykes, D.V.M.

1. What does the word *glaucoma* mean?

The word itself comes from the Greek (*glaukoma*) and means "blue" or "glazed." It was the appearance of the pupil that prompted the word. It took a while for the ancients to distinguish glaucoma from cataracts. Cataract was a fixable entity; glaucoma wasn't.

2. What is glaucoma?

The answer to this question is complex. Glaucoma is not merely an increase in intraocular pressure, it is a disease of multiple etiologies that results in destruction of ocular structure and function.

3. If glaucoma isn't a pressure disease, then what is the problem?

Glaucoma is a disease of the optic nerve, and perhaps "glaucomatous optic neuropathy" is a better term for the disease entity. This neuropathy may or may not be accompanied by a change in intraocular pressure.

4. What do you mean by "glaucomatous optic neuropathy"?

The optic nerve is really a continuation of the axons of the ganglion cells of the retina. Glaucoma is a degeneration of the ganglion cells and because of this change we can consider the disease to be of the optic nerve.

5. So what is the ultimate cause of glaucoma?

We don't know. Risk factors other than change in intraocular pressure play a role in the pathogenesis. What is clear is that the optic nerve is damaged independently of the level of the intraocular pressure. The current thought is that apoptosis of the retinal ganglion cells occur. The mechanism triggering the apoptosis is still unknown.

6. Well, what about all we've learned about intraocular pressure?

At some point in the development of the disease there may or may not be a change in the intraocular pressure (IOP). In humans, peripheral visual field loss and an observed change in the appearance of the optic nerve occur with or without a change in the IOP. In the domestic species we do not currently have a way of assessing peripheral visual field loss. We also do not appreciate a minimal change in the appearance of the optic nerve. We rely on increases in IOP to reach a diagnosis of glaucoma. We miss the initial changes detectable in humans and may not make a diagnosis until we observe the pressure change. In cases where there may be glaucoma without a change in IOP, we may even see an animal with just unexplained visual loss.

7. How is IOP measured?

There are two ways. The first method is Schiotz tonometry in which a fixed amount of weight is applied to the cornea and indentation is measured. The second method is applanation tonome-

try where a known force is applied to the cornea and the resistance to change is measured. Applanation tonometry is more reliable, is easier to use, and can be used in all species.

8. What is normal IOP?

The mean is around 20 mm Hg, and pressure above 30 mm in the dog is considered to be abnormal.

9. What are we really measuring?

IOP represents a balance between aqueous production and outflow. IOP is the ocular tension maintained by globe connective tissue and the intraocular fluids within.

10. What is the iridocorneal angle?

This is an anatomic space in which aqueous produced by the ciliary body percolates out of the eye into the subconjunctival space (Fig. 1).

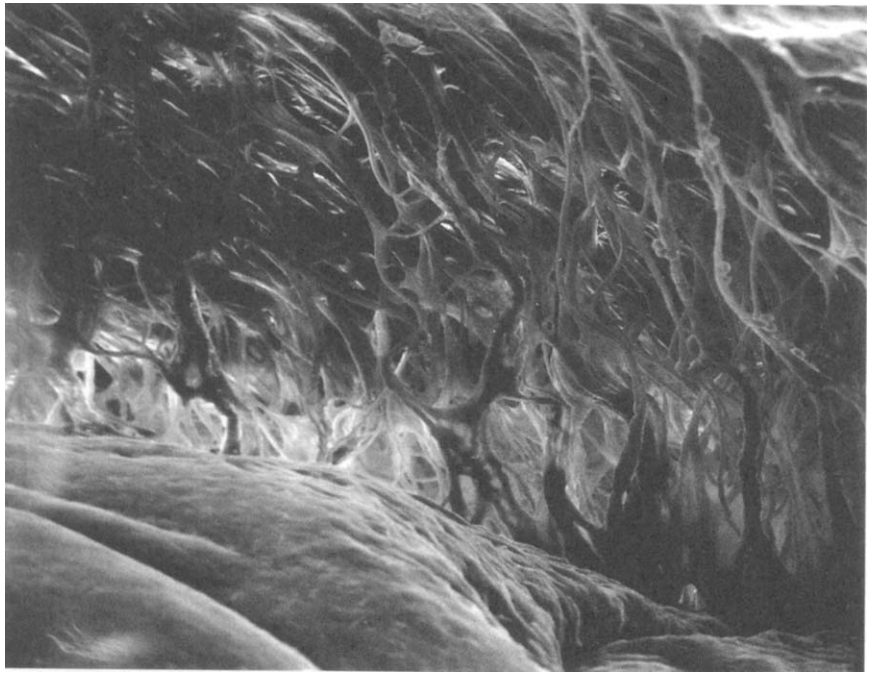


Figure 1. The iridocorneal angle of a cat. The trabecular fibers form a meshwork between the iris on the bottom and the cornea on the top. Scanning electron microscopy.

11. Can we see the angle?

A special lens called a goniolens is used to view the angle, which is at the anterior aspect of the ciliary cleft and the peripheral base of the iris. This area communicates with the anterior chamber and contains the trabecular meshwork that allows the fluid to flow through it. The width of the angle (open or closed) is used as a predictor for potential glaucoma. A narrow angle may indicate susceptibility to glaucoma or it may be meaningless (Figs. 1–4).

12. What makes the eye susceptible to glaucoma?

Probably the most important factor is genetics. A number of breeds are prone to the disease because of angle deformities or other causal factors. The breeds most commonly affected with

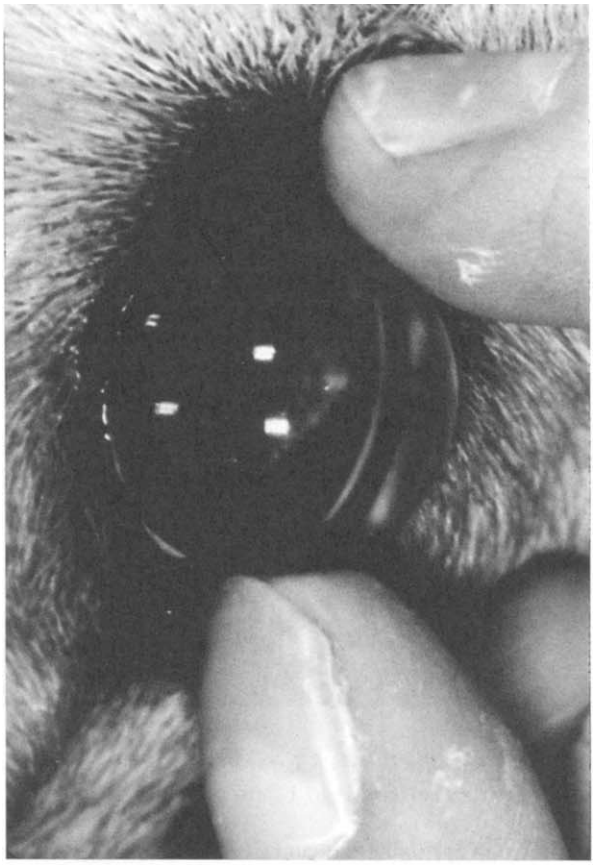


Figure 2. A goniolens used to view the iridocorneal angle. This lens is applied to the corneal surface after topical anesthesia. Methylcellulose is used to protect the cornea.

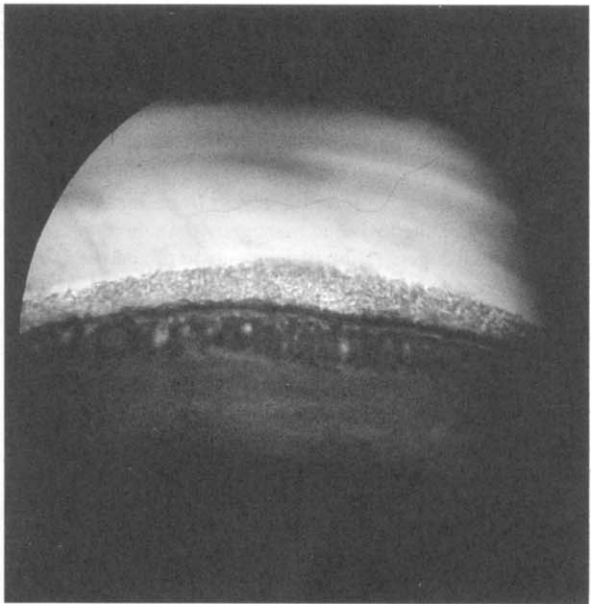


Figure 3. A view through the goniolens of an open angle in a dog.

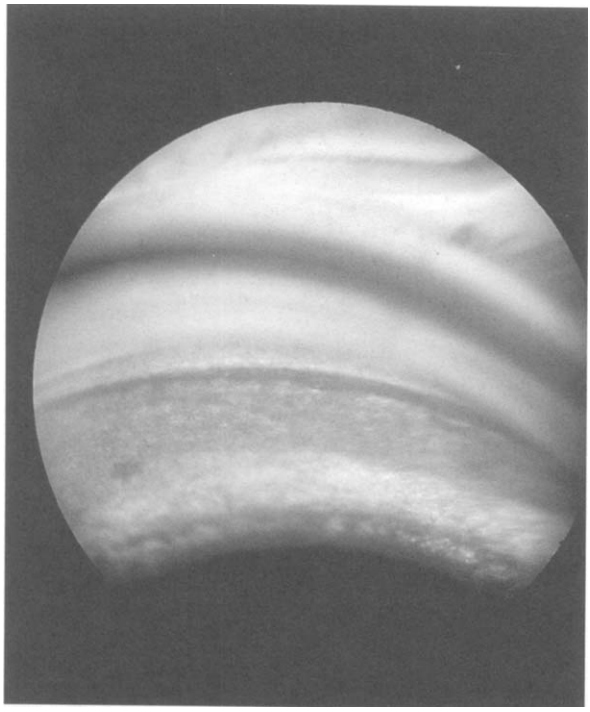


Figure 4. A view through the goniolens of a closed angle in a dog.

primary glaucoma are the cocker spaniel, basset, beagle, Boston terrier, dalmatian, miniature poodle, Norwegian elkhound, and chow chow.

13. What is primary glaucoma?

Glaucoma is classified as either primary or secondary. Primary glaucoma comprises those cases in which there is no apparent inciting cause and the iridocorneal angle appears open and normal in appearance.

14. What is secondary glaucoma?

Secondary glaucoma is attributed to some other inciting cause. Trauma, uveitis, and lens luxations are some examples of secondary causes.

15. What is the prognosis for vision in patients with glaucoma?

Terrible. Diagnosis and management in the domestic species has focused on IOP. However, ganglion cell degeneration is independent of and not caused by pressure changes. Controlling the pressure slows down the degenerative process but does not halt it. The end point is inevitable. The underlying ganglion cell degeneration has already preceded the pressure changes and is irreversible, which may very well be the reason the disease is so difficult to manage.

16. Why is pressure control important?

If the pressure is reduced by a substantial amount early in the course of the disease, the progression of the degeneration that occurs is delayed.

17. What is the relationship among IOP, angle deformity, and the reality of the ganglion cell degeneration?

This remains an unanswered question. What causes the ganglion cell degeneration? What is the real meaning of IOP? If the ganglion cell degeneration is the real cause for the visual loss, can

we really ever cure glaucoma? All of these questions require answers, and until we have them, glaucoma will remain the number one cause for blindness in both man and animals.

BIBLIOGRAPHY

1. Brooks DE: Glaucoma in the dog and cat. Vet Clin North Am Small Anim Pract 20:775–797, 1990.
2. Collaborative Normal-Tension Glaucoma Study Group: Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. Am J Ophthalmol 126:487–497, 1998.
3. Gelatt K, MacKay E: Distribution of IOP. Vet Ophthalmol 1:109–114, 1998.
4. Roberts SM: Glaucoma in companion animals: Current management and new trends. Calif Vet 48:9–16, 1994.
5. Wax M, Tezel G, Edward PD: Clinical and ocular histopathological findings in a patient with normal-pressure glaucoma. Arch Ophthalmol 116:993–1001, 1998.

14. SECONDARY GLAUCOMA

James E. Gaarder, D.V.M.

1. How is secondary glaucoma distinguished from primary glaucoma?

Glaucoma occurs when elevated intraocular pressure (IOP) impairs normal function of the eye. In canine and feline glaucoma, IOP is elevated due to the reduced or absent egress of aqueous from the anterior chamber. Glaucoma destroys vision by killing ganglion cells with the direct effects of increased pressure and the indirect effects of impaired intraocular circulation. Unlike primary glaucoma, secondary glaucoma is associated with concurrent and identifiable ocular disease such as inflammation (uveitis), neoplasia, hemorrhage, and lens luxation. Careful examination of the anterior and posterior segments with a focal light source, magnification, and indirect or direct ophthalmoscopy will usually identify these underlying disorders.

2. Why is it important to distinguish these two types of glaucoma?

Primary glaucoma is, by definition, ultimately **bilateral.** Therefore, the normal fellow eye is at risk and the owner needs to be aware of this. Primary glaucoma in dogs is an **incurable** disorder that, at best, can be managed effectively for variable periods of time. It is also an **inherited** disease, and affected dogs should not be used for breeding.

Secondary glaucoma is usually a unilateral disease and can sometimes be successfully treated with preservation of vision if the underlying cause can be identified and corrected. Therefore, the prognosis as well as the goal of treatment differs depending on the primary diagnosis, both for the affected eye and the fellow eye.

3. How does uveitis cause secondary glaucoma?

Glaucoma secondary to uveitis results from decreased aqueous outflow due to peripheral anterior synechiae, posterior synechiae, or iridocorneal angle occlusion with inflammatory debris. It is important to recognize that the uveitic eye is usually a soft or hypotensive eye. This is why a precise and objective method of estimating IOP such as applanation (e.g., TonoPen) or indentation (Schiotz) tonometry is essential for evaluating any red eye without an obvious corneal defect. If there are signs of active anterior uveitis, such as ciliary injection, miosis, aqueous flare, or photophobia, one would expect to find an IOP significantly lower than that in the normal eye (usually less than 10 mmHg). A normal or elevated IOP in an actively inflamed eye should alert the clinician to the possibility of the development of secondary glaucoma. The eyes must be closely monitored, and immediate medical therapy should be instituted should the pressure become elevated.

4. How do intraocular tumors cause secondary glaucoma?

Secondary glaucoma can occur when an intraocular tumor grows anteriorly to a size that impedes aqueous outflow or when exfoliated tumor cells obstruct the iridocorneal angle. The most common intraocular tumor resulting in secondary glaucoma in dogs and cats is the **melanoma.** These pigmented tumors are often not diagnosed until they are quite large because they are not obvious to the owner and do not cause ocular pain or redness until secondary glaucoma occurs. If diagnosed early, they can sometimes be effectively treated or cured with surgical excision or laser surgery. If not diagnosed until after the development of secondary glaucoma, usually the only option is enucleation.

5. Is secondary glaucoma a concern when hyphema is present?

Yes, because free blood can also obstruct the drainage apparatus. Intraocular pressure must be carefully monitored in eyes with anterior uveal hemorrhaging, and topical atropine should be used judiciously in these cases because pupillary dilation can further impede aqueous outflow in dogs and cats. The two most common causes of hyphema are ocular **trauma** and intraocular **tu-**

mors. Other causes of hyphema include coagulopathies, severe uveitis, and retinal detachment (see Chapter 35).

6. Does lens luxation cause glaucoma or does glaucoma cause lens luxation?

Although lens luxation does cause glaucoma, glaucoma can also cause lens luxation. As with glaucoma, lens luxation can be divided into primary and secondary categories. Primary lens luxation occurs in certain predisposed breeds (e.g., terriers, Norwegian elkhounds, Brittanies, Welsh springer spaniels, poodles, beagles). Although this form of glaucoma is usually considered secondary to lens luxation, several characteristics of this syndrome in these breeds resemble primary glaucoma. First, although the diagnosis of glaucoma in these breeds often coincides with lens luxation, removing the luxated lens in most cases does not cure glaucoma and glaucoma often precedes overt anterior lens luxation. Second, primary lens instability or luxation, like primary glaucoma, is an inherited disease. Third, and most importantly, primary lens instability or luxation is a bilateral disease, and the normal, unaffected eye is at risk. In contrast, in most nonterrier breeds, lens luxation is secondary to zonular disinsertion in a buphthalmic globe with chronic glaucoma (Figs. 1 and 2).

Figure 1. Fox terrier with bilaterally luxated lenses causing acute glaucoma. Transillumination helped define the lens in the anterior chamber despite the corneal edema.

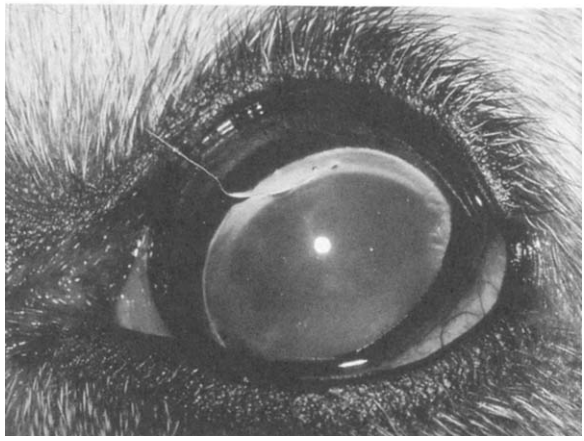


Figure 2. Luxated lens—always posing the question whether glaucoma caused the luxation or the luxation caused the glaucoma.

7. How does a luxated lens cause glaucoma?

Most often, a lens luxates anteriorly, producing a pupillary block. Aqueous, which is produced posterior to the iris in the ciliary body, is then prevented from gaining access to the anterior chamber. Alternatively, the anteriorly luxated lens can fill the anterior chamber and directly

block the iridocorneal angle. Whereas posteriorly luxated lenses and lens subluxations are warning signs of an impending problem, the anterior lens luxation is an acute medical and often surgical emergency. Usually, these lenses must be surgically removed in order to successfully manage this type of glaucoma.

8. What are the clinical signs that distinguish acute anterior lens luxation causing secondary glaucoma from lens luxation secondary to chronic glaucoma?

In most cases of acute anterior lens luxation, the lens is clear, the eye is very red (ciliary injection and episcleral congestion), and the eye is very painful (blepharospasm and photophobia). The optic nerve and retina are initially normal ophthalmoscopically. There is usually an intact consensual pupillary light response (PLR) from the affected eye to the normal eye, and the lens can be viewed clearly in the anterior chamber. When these clinical signs are apparent, this should be considered an ocular emergency, and medical treatment should be instituted to lower IOP while discussing referral to a veterinary ophthalmologist for lensectomy. With lens luxation secondary to chronic glaucoma, the eye is markedly enlarged (buphthalmic) and blind. Ocular pain is less obvious, and there is neither an intact direct nor indirect/consensual PLR. An aphakic crescent can often be seen in addition to stretched and displaced lenticular zonules and a deep anterior chamber. The lens is more commonly subluxated or posteriorly luxated than anteriorly luxated in these cases, and the lens is often cataractous or opaque. This type of lens luxation is not an ocular emergency.

9. What factors are most important when assessing a glaucomatous globe?

After establishing a diagnosis of glaucoma with objective tonometric measurements, the **vision potential** of the affected eye must be determined before appropriate therapy can be employed. Eyes with **chronic** glaucoma are usually irreversibly blind and uncomfortable. Blind eyes with **acute** glaucoma may still have potential for vision provided the IOP can be normalized in a timely manner and the disease is still in its early stages. Because greatly elevated IOP can cause irreversible damage to the visual potential of the eye within hours, acute glaucoma, whether primary or secondary, is an ocular emergency.

10. What are the most common clinical signs associated with acute glaucoma?

Early in its course, glaucoma causes acute **blindness,** ocular **pain,** conjunctival and **episcleral** vascular congestion, and **diffuse corneal edema.** The pupil is usually **dilated** and unresponsive or sluggishly responsive to direct light stimulation. In addition, proteinaceous aqueous flare and ciliary injection, an intraocular space-occupying mass, hemorrhage, and lens displacement are also seen if the glaucoma is secondary to uveitis, neoplasia, hemorrhage, or lens luxation. Although these clinical signs are very suggestive, it is important to remember that there are no pathognomonic signs of acute glaucoma (in contrast to chronic glaucoma). Therefore, tonometry is essential for accurate diagnosis (Figs. 3 and 4).

11. How can it be determined whether an affected eye has vision potential?

Careful assessment of the direct and especially the **consensual pupillary light response** (from the affected eye to the normal eye) is very helpful. The **dazzle reflex** can be used in evaluating the optic nerve. A very strong light source (e.g., a fiber optic or Finhoff transilluminator) when directed into the eye at close range should produce a rapid blink referred to as the dazzle reflex. With acute glaucoma, these initial tests should be performed and repeated when IOP is normalized. Sometimes a simple test such as blindfolding the normal fellow eye and assessing functional vision using an obstacle course can be helpful. In acute glaucoma, the fundus, when it can be seen, is usually normal.

FAVORABLE PROGNOSTIC SIGNS FOR VISION	UNFAVORABLE PROGNOSTIC SIGNS FOR VISION
Normal direct and/or consensual PLRs	Absent direct and/or consensual PLRs
Normal dazzle reflex	Absent dazzle reflex
Normal menace or functional vision	Lack of detectable functional vision or history of blindness for more than 3–5 days

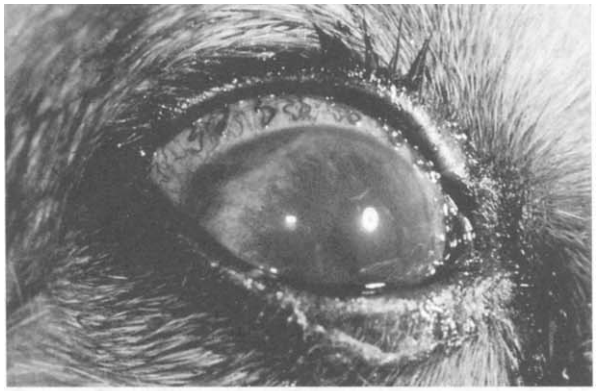


Figure 3. Acute glaucoma in a beagle. This breed can present with normal pupils despite elevated IOP. This dog's anterior chamber was very narrow.

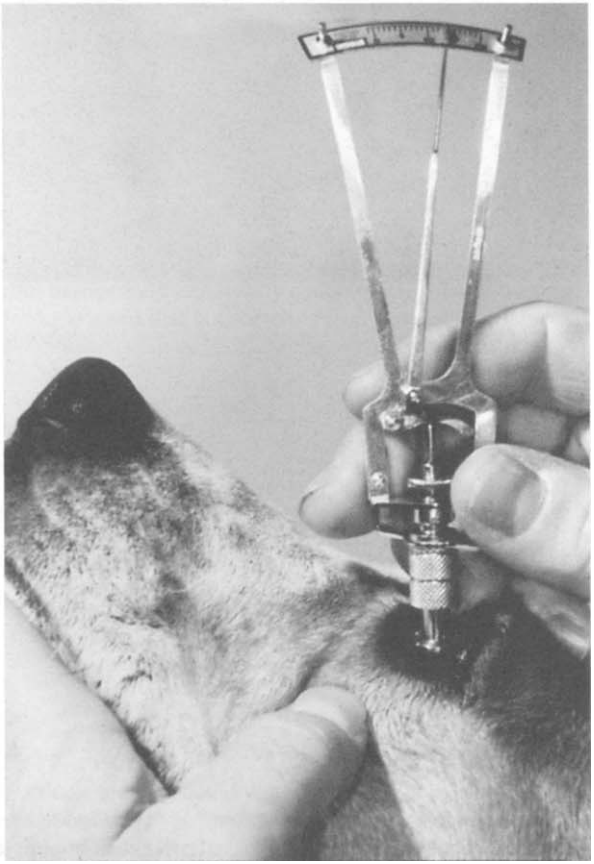


Figure 4. Tonometry being performed with a Schiotz tonometer. Instrumental tonometry is essential for the diagnosis and management of glaucoma.

12. How is chronic glaucoma distinguished from acute glaucoma?

The classic and pathognomonic clinical signs of chronic glaucoma include buphthalmia, corneal striae, and optic disk "cupping." **Buphthalmia** occurs due to the stretching and thinning of collagen fibers that compose the cornea and sclera. With buphthalmia, the cornea stretches and linear tears occur in Descemet's membrane, allowing aqueous to enter the corneal stroma. These linear breaks or tears are referred to as **corneal striae,** Descemet's striae, or Haab's striae and ap-

pear as single or multiple parallel lines or bands deep within the cornea, usually spanning the entire corneal diameter. Optic nerve head **cupping** appears as a dark and depressed or recessed optic disk due to axonal degeneration and posterior displacement of the lamina cribrosa. This change is best appreciated with indirect ophthalmoscopy, comparing the normal eye with the affected eye. It should be emphasized that by the time IOP has been elevated long enough to cause buphthalmia, irreversible damage has been done to the retina and optic nerve. Therefore, the big eye is almost always a blind eye (Figs. 5 and 6).

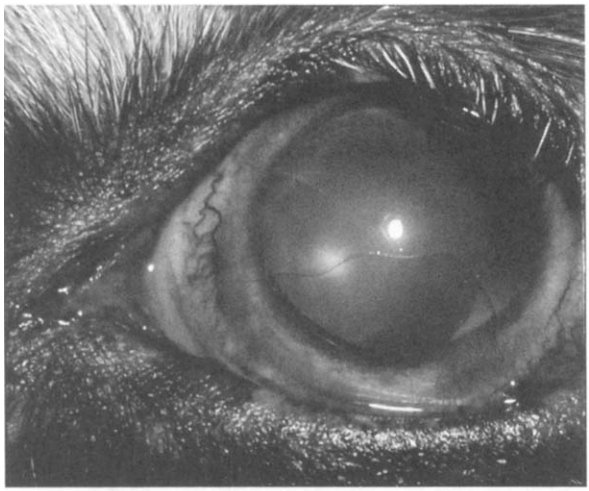


Figure 5. A buphthalmic globe with an aphakic crescent laterally. The optic disc was cupped. This was a blind eye poorly responsive to antiglaucoma medication.

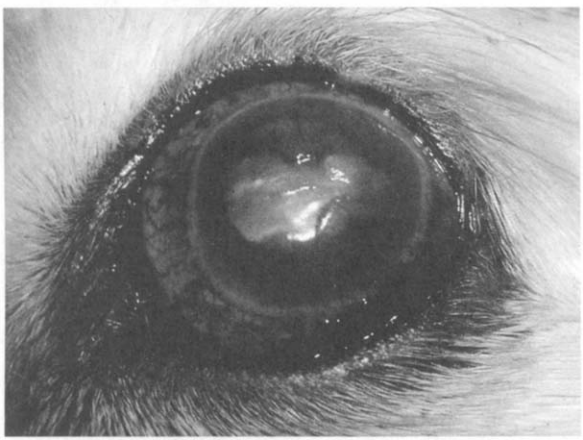


Figure 6. Buphthalmic globes are candidates for many complications. This eye had ulcerative keratitis secondary to exposure.

13. Are there any exceptions to the "big eye, blind eye" rule?

An exception to this rule is occasionally seen in puppies. In the juvenile dog, buphthalmia can occur within days due to the marked elasticity of the cornea and sclera in young animals. In puppies, this elasticity may protect the retina because the eye can enlarge with even moderate increases in IOP. This makes IOP alone an unreliable indicator of glaucoma in young animals. Buphthalmia in puppies may be reversible if IOP is normalized. Glaucoma is relatively uncommon in young dogs. Additional exceptions to this rule are occasionally seen in Chinese shar-peis, chow chows, and beagles diagnosed with corneal striae and buphthalmia in sighted eyes affected with primary glaucoma. This preservation of vision in enlarged eyes may be due to mucinosis of collagen fibrils in the former two breeds, increasing the elasticity of the sclera and cornea and the

insidious nature of primary open angle glaucoma, which almost exclusively affects the latter breed.

14. What are some common diagnostic considerations when presented with a uveitic and glaucomatous eye?

With secondary glaucoma, it is most important to identify and treat the underlying cause. For glaucoma secondary to uveitis, the intraocular inflammation must be addressed to control the glaucoma. A complete physical examination and routine laboratory work (CBC, serum chemistry profile, urinalysis) must be performed to look for systemic illness. Radiographs and ultrasound can also be helpful. Depending on the geographic location and animal's travel history, infectious diseases must be considered. For dogs, leptospirosis, brucellosis, ehrlichiosis and the systemic mycoses are important considerations. In cats, feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis (FIP), toxoplasmosis, and the systemic mycoses should be considered. Despite extensive diagnostic testing, etiologic determination can prove elusive. Symptomatic therapy to control intraocular inflammation and elevated IOP is imperative.

15. How does medical therapy for glaucoma secondary to uveitis differ from medical therapy for primary glaucoma for sighted or potentially sighted eyes?

Therapy for uveitis involves using topical and systemic corticosteroids and nonsteroidal anti-inflammatory medications. Corneal epithelial integrity (fluorescein dye testing) must be assessed before using topical corticosteroids. The drugs selected, dosages, frequencies, and routes of administration will vary with severity of the inflammation. Some drugs that can be useful for primary glaucoma should *not* be used if uveitis is present. For example, topical pilocarpine, a direct-acting cholinergic miotic, echothiophate iodide (Phospholine Iodide, Wyeth-Ayerst), and demecarium bromide (Humorsol, Merck) should not be used in uveitic eyes because they potentiate the breakdown of the blood aqueous barrier and can intensify concurrent uveitis. In addition, atropine, a strong mydriatic and cycloplegic agent that is generally recommended as adjunctive therapy for uveitis, should not be used in hypertensive eyes because pupillary dilation will further impair an already compromised iridocorneal angle.

16. Is glaucoma secondary to an intraocular tumor treatable?

If an intraocular tumor has grown large enough to occlude the iridocorneal angle and cause secondary glaucoma, surgical resection with preservation of vision is impossible. The key to successful management of these cases is early detection and referral to a veterinary ophthalmologist. Some uveal melanomas exfoliate cells that can occlude the iridocorneal angle. Remission and even cure is possible in some cases using transcorneal laser (diode or Nd:YAG) surgery. Sector iridectomy or iridocyclectomy has been successful in curing some intraocular neoplasms. These procedures are usually applicable to tumors in their early stages, before secondary glaucoma has developed. Unfortunately, in the majority of glaucoma cases secondary to an intraocular neoplasm, enucleation is the only treatment option. It is critical to have the enucleated globe examined by a veterinary pathologist in these cases to further quantify the nature of the tumor and the potential for recurrence or metastasis.

17. What are special considerations when treating hyphema and secondary glaucoma?

The underlying cause of the hemorrhage must be determined. Ocular trauma and ocular tumors are the two most common causes. However, hyphema may also be secondary to thrombocytopenia, coagulopathies, severe iritis, congenital ocular anomalies (e.g., retinal detachment, retinal dysplasia), and chronic glaucoma. Ocular ultrasonography is valuable in assessing the intraocular structures if the posterior segment cannot be visualized ophthalmoscopically. Symptomatic treatment of hyphema is similar to that of anterior uveitis except that systemic nonsteroidal anti-inflammatory agents such as aspirin, flunixin meglumine, and topical ocular nonsteroidals should be avoided. As with treating uveitis with secondary glaucoma, topical mydriatic or cycloplegic agents such as atropine should not be used. Topical corticosteroids such as prednisolone acetate and dexamethasone are useful in controlling related inflammation. For traumatic hyphema, once the intraocular bleeding has stopped and a stable clot has formed, intracameral tis-

sue plasminogen activator (tPA)—a fibrinolytic agent—can be useful. Surgical removal of the blood is also used in select cases but should be performed by a veterinary ophthalmologist.

18. When is lensectomy indicated as part of the treatment regimen for glaucoma secondary to lens luxation?

Surgical management of sighted or potentially sighted eyes with early lens luxation/subluxation is controversial. There is little doubt that acute anterior lens luxation in a sighted eye requires emergency therapy consisting of medications to reduce IOP and intracapsular lensectomy to relieve the associated pupillary block glaucoma. There is controversy among veterinary ophthalmologists, however, regarding the management of the subluxated lens remaining in the patellar fossa posterior to the iris. This author believes that intracapsular lensectomy in these eyes has an unacceptably high complication rate, including vitreous presentation due to adhesion of the anterior vitreous to the posterior lens capsule and secondary retinal detachment. These eyes remain sighted for longer periods of time with conservative medical treatment with miotic antiglaucoma medications to decrease the access of the lens to the anterior chamber than with early lensectomy. Despite medical therapy, many of these lenses eventually luxate into the anterior chamber and must be surgically removed.

19. What types of medical therapy are appropriate for managing blind and painful eyes due to chronic secondary glaucoma?

Medical therapy has no place in the long-term management of blind and painful glaucomatous eyes. Most antiglaucoma medications are expensive and generally ineffective for long-term use. More importantly, all antiglaucoma medications, including topical drugs, have the potential for systemic toxicity and side effects. The oral carbonic anhydrase inhibitors are the most effective antiglaucoma drugs, but they also have the greatest potential for severe side effects such as polyuria/polydipsia, metabolic acidosis, depression, anorexia, vomiting, and diarrhea. Many humans receiving pilocarpine therapy complain of a brow-ache and blurred vision. Topical beta-blockers can cause cardiovascular and respiratory compromise.

The expense and potential for side effects of antiglaucoma medications are warranted as long as there is vision or at least potential for vision. However, if the eye is irreversibly blind and painful, the animal and the owner are better served by a salvage procedure to make the eye comfortable and eliminate the need for chronic medications.

20. When should surgery be performed and what types of surgery are available for blind, end-stage glaucomatous eyes?

Salvage surgical procedures for the blind glaucomatous globe include enucleation, intraocular evisceration-implantation, and pharmacologic ciliary body ablation using intravitreal gentamicin. Not all of these options are indicated, however, in eyes that are blind and painful due to secondary glaucoma. Pharmacologic ciliary body ablation is only appropriate for blind eyes affected with primary glaucoma. It should be used with caution in eyes that have any active inflammation because it can exacerbate uveitis. It should *never* be used in eyes with intraocular tumors or eyes with glaucoma of an undetermined cause (often the case with secondary glaucoma). Intraocular evisceration-implantation offers a high success rate and results in a relatively cosmetic and very comfortable globe that usually requires no further therapy. The implant procedure produces a high rate of client satisfaction, and complications are rare. It should not be used in eyes with a known intraocular tumor. When the procedure is performed in a blind glaucomatous eye of undetermined cause, it is essential for the uveal tract and lens to be submitted for histopathologic examination because neoplasia cannot always be definitively diagnosed preoperatively. When blind painful eyes with secondary glaucoma are removed, it is always important to have the globe examined histopathologically by a veterinary pathologist because these findings can often have systemic implications and implications for the fellow eye (see Chapter 17).

BIBLIOGRAPHY

1. Gelatt KN, Brooks DE: The canine glaucomas. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Baltimore, Lippincott Williams & Wilkins, Baltimore, 1999, pp 701–754.

15. MEDICAL TREATMENT OF GLAUCOMA

James E. Gaarder, D.V.M.

1. What are the major considerations when evaluating an eye affected with glaucoma?

Choosing the proper therapy depends on accurate and thorough diagnostic evaluation. It must first be determined whether the eye is affected with primary or secondary glaucoma because primary glaucoma is, by definition, ultimately bilateral and the normal fellow eye is at risk. Primary glaucoma is also an incurable disorder that, at best, can be effectively managed only for variable periods of time. Secondary glaucoma is usually a unilateral disease and can sometimes be treated and even cured with preservation of vision if the underlying cause can be identified and corrected. Secondary glaucoma is associated with concurrent ocular disease such as inflammation, neoplasia, hemorrhage, and lens disorders. **Vision or potential for vision** of the affected eye must be assessed before appropriate therapy can be employed. Eyes afflicted with chronic glaucoma are usually irreversibly blind and uncomfortable. Blind eyes with acute glaucoma may still have potential for vision provided the intraocular pressure (IOP) can be normalized in a timely manner and the disease is still in its early stages. Because greatly elevated IOP can cause irreversible damage to the visual potential of the eye within hours, acute glaucoma is an ocular emergency. By the time the signs of chronic glaucoma are evident, the vision potential of the eye is usually lost.

2. What is a reasonable therapeutic goal for the treatment of primary glaucoma?

It must be communicated to the clients that primary glaucoma in dogs and cats (although the disease is much more common in dogs) is not a curable disorder. The goals of therapy are to maintain vision and ocular comfort for as long as possible using medical or surgical therapy and, if unilateral, to prevent or delay occurrence in the fellow eye. Multiple drug therapy is often required. One should be aware that most antiglaucoma drugs lose their efficacy over time. When the pressure begins to rise despite medical therapy, surgical intervention is indicated. When the eye becomes irreversibly blind and painful, a salvage procedure (enucleation, intraocular evisceration-implantation, or pharmacologic ciliary body ablation) is indicated.

3. What is the therapeutic goal for treating secondary glaucoma?

The underlying cause must first be identified and corrected if possible. For glaucoma secondary to uveitis, aggressive anti-inflammatory therapy (topical, systemic or both) is critical and should be combined with antiglaucoma therapy. The various etiologies of uveitis in dogs and cats should also be investigated. When glaucoma is secondary to a primary intraocular tumor, medical therapy is usually ineffective. Eyes affected with glaucoma secondary to metastatic neoplasia can sometimes be managed in conjunction with treatment of the systemic disease (lymphosarcoma is a common example). Surgical lensectomy is usually required for managing glaucoma secondary to anterior lens luxation. Therefore, the therapeutic goal for treating secondary glaucoma depends on the primary cause and the ability to treat it.

4. What are the initial therapeutic goals for treating sighted or potentially sighted eyes?

The goal of medical therapy for primary or secondary glaucoma is to decrease intraocular pressure by shrinking the intraocular volume, decrease aqueous production, or increase aqueous outflow.

Osmotic agents are useful in the emergency treatment of acute glaucoma because they rapidly dehydrate the vitreous and decrease intraocular volume. Carbonic anhydrase inhibitors, β-blockers, and sympathomimetic agents decrease aqueous production. Miotics, sympathomimetic agents, and prostaglandin analogues increase aqueous outflow.

5. How do osmotic agents work and when should they be used?

Hyperosmotic agents include intravenous mannitol and oral glycerol and are used in acute severe elevations of IOP in sighted or potentially sighted eyes. Hyperosmotic agents increase plasma osmolality, producing an osmotic gradient between the ocular vasculature and intraocular fluids (primarily the vitreous). Hyperosmotics are the most potent medical therapy available in terms of reducing severe IOP elevations, and they usually produce ocular hypotension lasting $\geq$ 5 hours within 30 minutes of administration. They are useful in emergency situations but lose their effectiveness after the second or third administration making osmotherapy ineffective for chronic therapy. Mannitol should be administered intravenously at a dosage of 1–2 gm/kg over 20 minutes. High concentrations of mannitol (over 20%) may crystallize at room temperature, so warming the solution in a water bath to dissolve the crystals and administering the solution through a blood filtration set are indicated. Mannitol is never the sole agent used for treating glaucoma. An oral carbonic anhydrase inhibitor should be given during or before mannitol administration along with one or more topical agents. Glycerol (50%) is an oral osmotic diuretic and also produces ocular hypotension. It is not as potent as mannitol and often produces vomiting. Glycerol should not be used in diabetics because it can cause hyperglycemia. Water should be withheld for a minimum of 4 hours after hyperosmotic administration to maintain intraocular dehydration.

Hyperosmotic Agents

USP OR NF NAME	TRADE NAME	PREPARATION	DOSE	ROUTE	ONSET/DURATION OF ACTION	COMMENTS
Mannitol	Osmitrol	25%	0.5–2 g/kg	IV	30–60 min/6 hr	Useful in emergency therapy of acute glaucoma in potentially visible eyes
Glycerol	—	50%	1–2 gm/Kg	PO		May cause vomiting Do not use in diabetic dogs

For acute glaucoma, after the IOP is normalized and maintained, referral to a veterinary ophthalmologist should be discussed with the client. If IOP does not normalize within 6–8 hours after instituting therapy, emergency referral to a veterinary ophthalmologist should more strongly be considered.

6. How do carbonic anhydrase inhibitors lower IOP?

Oral carbonic anhydrase inhibitors (CAIs) are the mainstay of veterinary medical therapy for glaucoma and are the only systemic agents used in long-term management. Carbonic anhydrase catalyzes the combination of carbon dioxide and water to form carbonic acid. The CAIs decrease the production of aqueous by blocking this process. Because CAIs reduce the production of aqueous, they are useful in managing all forms of glaucoma. Therapeutic effect of orally administered CAIs begins 2–3 hours after administration, the maximum effect occurs within 4–8 hours, and IOP is usually reduced by 20–30%. Although oral CAIs are the most potent medical agent for long-term control of IOP and are the foundation for the medical management of glaucoma, they also have the greatest incidence of side effects.

7. Why do oral CAIs have so many side effects?

The carbonic anhydrase enzyme is present in many nonocular tissues, including the kidney, pancreas, central nervous system, red blood cells, and lungs. Because of the ubiquitous nature

of carbonic anhydrase, side effects of CAIs are expected and include polyuria/polydipsia, metabolic acidosis, depression, confusion, anorexia, vomiting, diarrhea, and rarely blood dyscrasias. In humans, these side effects are severe enough in 40–50% of patients to require the discontinuation of therapy. Potassium excretion is increased by oral administration of CAIs, and hypokalemia is a potential sequela of chronic use. Supplementation with oral potassium is recommended. Although dogs appear more tolerant than humans to systemic CAI therapy, side effects are not uncommon in the canine patient. Similar to the pain of glaucoma, these side effects may be subtle and not easily appreciated by the owner or veterinarian until discontinuation of therapy produces notable change in the animal's attitude, activity level, and appetite. When severe side effects are noted, reducing the dosage, substituting another oral CAI, or discontinuing oral CAI therapy is recommended. Most dogs appear to tolerate dichlorphenamide and methazolamide better than acetazolamide. Currently, only methazolamide and acetazolamide are readily available, because the production of dichlorphenamide has been discontinued. If the side effects are mild and the animal remains sighted, continued CAI therapy is warranted. If the side effects are severe or the animal is permanently blind and in pain, other options are available. In contrast to dogs, cats appear to poorly tolerate systemically administered CAIs. When warranted, methazolamide is the CAI of choice in cats because it is available in 25-mg tablets for more accurate dosing.

Carbonic Anhydrase Inhibitors

USP OR NF NAME	TRADE NAME	PREPARATION	DOSE	ONSET/DURATION OF ACTION
Acetazolamide	Diamox	125-, 250-mg tablets 500-mg (timed-release) capsules	2.2 mg/kg q 12 hr	2 h4/4–6 hr
	Available generically	125-, 250-mg tablets		
Acetazolamide sodium	Diamox Parenteral	500 mg		5–10 min/2 hr
Brinzolamide	Azopt	1% ophthalmic suspension	1–2 times/day	—
Dichlorphenamide	Daranide	50-mg tablets	2.2 mg/kg q 8–12 hr PO	30 min/6 hr
Dorzolamide HCl	Trusopt	2% ophthalmic solution	2–3 times/day	—
Methazolamide	Glauctabs	25, 50 mg tablets	2–4 mg/kg (maximum dose: 4–6 mg/kg)	2 hr/4–6 hr
	MZM	25, 50 mg tablets	q8–12h PO	
	Neptazane	25, 50 mg tablets		
	Available generically	25, 50 mg tablets		

8. How do topical CAIs compare to oral CAIs?

Topical CAIs are relatively new additions to the ophthalmologist's armamentarium. Currently, three are available: dorzolamide (Trusopt, Merck), brinzolamide (Azopt, Alcon), and a combination of dorzolamide and timolol (Cosopt, Merck). Preliminary clinical results have indicated that these agents may be effective and beneficial in some cases of canine and feline glaucoma. Although these agents are not as effective in reducing IOP as oral CAIs, the side effects appear to be minimal. Because of a similar mechanism of action, there is generally little benefit from using a topical CAI in conjunction with an oral CAI. The main disadvantage of topical CAIs is that they, like oral CAIs, are expensive. Topical CAIs do not have as many systemic side effects as oral CAIs.

*Internet Antiglaucoma Medication Price Comparison**

	DRUGSTORE.COM	PLANETRX.COM	DRUGEMPORIUM.COM	AMERICARX.COM
Timolol (5%)				
5 ml	$11.24	$11.85†	$16.15	N/A
15 ml	$17.36	$17.63†	$34.15	$13.87
Trusopt (2%)				
5 ml	$24.10	$22.53	N/A	$23.50
10 ml	$45.10	$45.95	N/A	$43.75
Cosopt 2 (0.5%)				
5 ml	$40.12	$41.60	N/A	$38.25
10 ml	$77.07	$78.69	N/A	$76.50
Neptazane†				
25 mg	$39.72/60	$13.39/60	$26.95/60†	$15.00/60
50 mg	$58.85/60	$18.57/60	$38.95/60†	$21.00/60
Xalatan (0.005%)				
2.5 ml	$42.10	$44.01	$50.95	$40.05

*Price as of 2000.
†Generic drug.

9. What are the indications and contraindications for using a miotic agent as part of the treatment for glaucoma?

Topical miotic agents produce pupillary constriction, contraction of the ciliary musculature, and increased outflow of aqueous through a configurational change in the trabecular meshwork. Pilocarpine is a direct-acting cholinergic miotic available in several concentrations; 2% appears most effective in the dog. Theoretically, pilocarpine is most effective in treating primary open-angle glaucoma (POAG), the least common form found in dogs. Most forms of canine glaucoma are due to narrowing or closure of the iridocorneal angle, not the trabecular meshwork, making the effectiveness of pilocarpine questionable for closed-angle glaucoma (CAG), the more common form found in dogs. Advantages of pilocarpine include its effectiveness for some forms of glaucoma and its relatively inexpensive cost. Disadvantages include its topically irritating qualities and the frequency of administration (3–4 times daily). A 4% pilocarpine gel (Pilopine HS, Alcon) is available and has the advantage of once-daily administration. Because it can potentiate breakdown of the blood aqueous barrier, pilocarpine should not be used when uveitis is present or when treating secondary glaucoma. Indirect-acting miotics include echothiophate iodide (Phospholine Iodide, Wyeth-Ayerst) and demecarium bromide (Humorsol, Merck) and act by inhibiting cholinesterase, thus increasing endogenous acetylcholine. These agents are less irritating and longer-acting than pilocarpine but are more expensive. As with pilocarpine, they can activate latent uveitis and intensify concurrent uveitis. Thus, they are most useful in primary glaucoma. They are especially useful in primary glaucoma with early lens luxation or subluxation because they produce miosis and discourage a luxated lens from gaining access to the anterior chamber, resulting in acute pupillary block glaucoma, which necessitates surgical intervention.

10. Which of the β-adrenergic blocking agents are commonly used in veterinary ophthalmology and when are they useful?

Although topical β-blockers are the most frequently prescribed agents for treating glaucoma in man, their efficacy in dogs and cats is controversial. β-blockers reduce IOP by decreasing aqueous production. The most commonly used drug is 0.5% timolol maleate (Timoptic, Merck). Timolol is useful in both primary and secondary glaucoma and unlike topical miotic agents, does not potentiate uveitis. Because β-blockers decrease aqueous production by a mechanism other than CAIs, their ocular hypotensive effect when used together with CAIs is additive. Timolol is most commonly used as an adjunctive therapy and combined with oral CAIs. Although it is not adequate as the sole agent when treating a glaucomatous eye, it may be useful in prophylactic therapy for the fellow eye in cases of primary glaucoma. Timolol is also available in an ophthalmic gel forming solution (Timoptic-XE, Merck) that allows for once daily dosing. Be careful to dis-

pense or prescribe timolol in the 0.5% concentration as the 0.25% concentration that is also available is ineffective in dogs and cats. A common side effect of timolol (a nonselective β-blocker) in humans is bronchoconstriction and bronchospasm (predominantly in patients with preexisting bronchospastic disease). Although this side effect is uncommon in animals, betaxolol (Betoptic, Alcon), a selective β-blocker has fewer side effects and can be used as an alternative. Betaxolol does not appear to be as potent as timolol in reducing IOP.

β-Adrenergic Blocking Agents

GENERIC NAME	TRADE NAME	CONCENTRATION	DOSE	SIZE(S) (ML)
Betaxolol hydrochloride	Betoptic-S	0.25%	2 times/day	2.5, 5, 15
	Betoptic	0.5%		2.5, 5, 10, 15
Carteolol hydrochloride	Ocupress	1%	1–2 times/day	5, 10
Levobunolol hydrochloride	Akbeta	0.25%, 0.5%	1–2 times/day	5, 10, 15
	Betagan	0.25%, 0.5%	1–2 times/day	2, 5, 10, 15
	Available generically	0.25%, 0.5%	1–2 times/day	5, 10, 15
Metipranolol	OptiPranolol	0.3%	1–2 times/day	5, 10
Timolol hemihydrate	Betimol	0.25%, 0.5%	1–2 times/day	2.5, 5, 10, 15
Timolol maleate	Timoptic	0.25%, 0.5%	1–2 times/day	2.5, 5, 10, 15
	Available generically	0.25%, 0.5%		5, 10, 15
Timolol maleate (gel)	Timoptic—XE	0.25%, 0.5%	1 times/day	2.5, 5

11. How do sympathomimetic agents reduce IOP?

Adrenergic compounds decrease IOP by stimulating a-receptors and increasing aqueous outflow, and by stimulating β-receptors and decreasing production. As with β-blockers, they are minimally effective when used as sole agents but can be useful adjuncts when combined with other classes of drugs. Topical epinephrine and epinephrine-pilocarpine combinations are available. Dipivefrin hydrochloride (Propine, Allergan) is an epinephrine prodrug that is converted to epinephrine in the anterior chamber. Dipivefrin hydrochloride is the drug of choice in this group because it is less irritating, has better intraocular penetration into ocular tissues, and has more potency and less toxicity. However, it is more expensive than either epinephrine or epinephrine-pilocarpine combinations.

Sympathomimetics

GENERIC NAME	TRADE NAME	CONCENTRATION (%)	DOSE	SIZE(S) (ML)
Dipivefrin hydrochloride	Akpro	0.1	1–2 times/day	5, 10, 15
	Propine	0.1	1–2 times/day	5, 10, 15
	Available generically	0.1		5, 10, 15
Epinephryl borate	Epinal	0.5, 1	1–2 times/day	7.5
	Eppy/N	1		7.5
Epinephrine hydrochloride	Epifrin	0.5, 1, 2	1–2 times/day	5, 10, 15
	Glaucon	1, 2		10

12. What are prostaglandin analogues?

Prostaglandin analogues (prostanoids) are a new class of topical glaucoma medications developed for once-daily usage in humans. The prototype in this class is latanaprost 0.005% (Xalatan, Pharmacia and Upjohn). Several similar drugs currently are becoming available. Prostaglandin analogues reduce IOP by increasing aqueous outflow by the unconventional or uveoscleral route. The mechanism of action is different from that of other antiglaucoma medications. In dogs and cats, the uveoscleral outflow has been considered a less important avenue for normal aqueous loss than the conventional outflow pathway through the iridocorneal angle. However, latanaprost has been very useful in treating some cases of acute primary glaucoma in dogs (used alone or in combination with conventional hyperosmotic and oral CAI therapy). Although this particular prostaglandin analogue has not been extensively evaluated for efficacy in animals, topical appli-

cation of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) and similar drugs was shown to cause significant IOP reduction in rabbits, cats, dogs, and monkeys. The recommended dosage in humans is once daily at bedtime, and the most common side effect is an iris color change with long-term use. The iris color change has not yet been noted in animals. Latanaprost, in addition to its antiglaucoma effects, is also a very potent miotic and often produces profound pupillary constriction in cats and dogs. It is usually administered once or twice daily in animals. It is expensive but can be very useful in selected cases.

α_2-Selective Agonists and Prostaglandin Analogues

GENERIC NAME	TRADE NAME	CONCENTRATION	DOSE	SIZE(S) (ML)
Aprachlonidinne	Iopidine	0.5%	2–3 times/day	5
		1.0%		Single use bottle
Brimonidine	Alphagan	0.2%	2 times/day	5, 10, 15
Latanoprost	Xalatan	0.005%	1 times/day	2.5
Travoprost	Travatan	0.004%	1 time/day	5

13. What is acute glaucoma?

Acute glaucoma results from a rapid increase in IOP over a course of several hours. Clinical signs include acute **blindness,** ocular **pain,** conjunctival and **episcleral** vascular congestion, and **diffuse corneal edema**. The pupil is usually **dilated** and unresponsive or sluggishly responsive to bright light stimulation. The combination of these clinical signs is very suggestive of acute glaucoma but they are not pathognomonic. Because any or all of these signs can be seen in other ocular disorders, **tonometry** is essential for accurate diagnosis. When in doubt about the visual potential of the eye, institute emergency therapy to reduce IOP. If the eye is irreversibly blind, this will become apparent soon (see Figure 1).

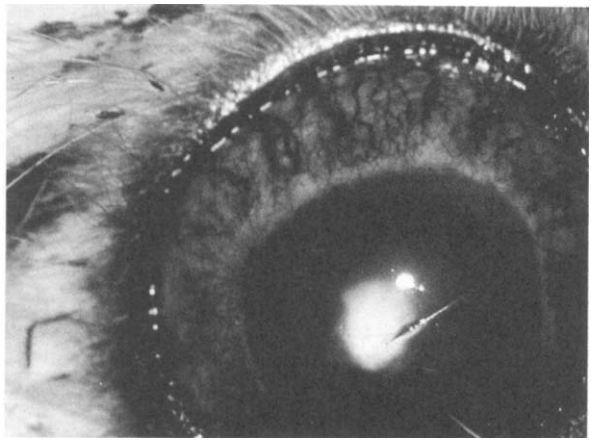


Figure 1. Acute glaucoma in an American cocker spaniel. The intraocular pressure was 60 mmHg. Also note the cataract, which is insignificant to the glaucoma.

14. How should emergency treatment of acute glaucoma be approached?

A complete ophthalmic examination including tonometry is the first step. The clinician should look closely for any sign of underlying intraocular disease such as uveitis, hemorrhage, or intraocular tumor. If primary glaucoma is diagnosed (no underlying abnormalities) or if a cause of secondary glaucoma is addressed, the focus of therapy should be on reducing IOP as rapidly as possible. Permanent ganglion cell and optic nerve damage can occur within hours following marked elevations in IOP. Therefore, rapid intervention is critical. Emergency medical treatment should consist of the administration of a hyperosmotic agent such as intravenous mannitol or oral glycerol. Mannitol is preferred because it is more potent and has fewer side effects. Hyperosmotic agents are the most potent medications available for the acute reduction of IOP. In addition, an

oral carbonic anhydrase inhibitor such as methazolamide or dichlorphenamide should be administered. These oral CAIs begin to reduce IOP 2–3 hours after administration. IOP should be measured every hour until it normalizes. Mannitol can be repeated in 4–6 hours if necessary. Methazolamide or dichlorphenamide are continued at a dose of 2–4 mg/kg every 8–12 hours. Referral to a veterinary ophthalmologist should be considered.

15. Which topical drugs are useful for acute glaucoma?

There is a wide variety of topical medications. Topical β-blockers such as timolol or Betaxolol are useful becauase they can be used in all forms of glaucoma and provide an additive effect to hyperosmotic agents and oral CAIs. They are not useful as sole agents for acute glaucoma because they only reduce IOP by 5–10 mmHg. Pilocarpine is useful for primary open-angle glaucoma and in some cases of primary closed-angle glaucoma, but it should not be used in cases of secondary glaucoma because it can worsen uveitis. A sympathomimetic agent such as dipivefrin can be used in conjunction with a topical β-blocker if necessary. The prostaglandin analogue latanoprost is also very useful in breaking high-pressure attacks of primary glaucoma in affected dogs when used alone or in conjunction with intravenous mannitol and an oral CAI.

16. If immediate referral to an ophthalmologist is impossible, what are the best medications for treating acute glaucoma?

For acute primary glaucoma, administer topical latanoprost and oral methazolamide and recheck IOP in 30–60 minutes. If IOP is not significantly reduced (to less than 30 mmHg), begin intravenous mannitol. Add 0.5% timolol (b.i.d.), dipivefrin (b.i.d.), and/or 2% pilocarpine if necessary. If latanoprost is unavailable, begin mannitol administration immediately. For acute secondary glaucoma, avoid latanoprost and pilocarpine and use topical and/or systemic anti-inflammatory agents as necessary for any underlying uveitis. Topical drugs causing miosis (latanoprost and pilocarpine) should not be used in cases of glaucoma due to anterior lens luxation.

17. Which medications are most useful after IOP has normalized?

There is not a single correct method for long-term medical management of the visual but glaucomatous eye. In general, the clinician should try to find the one medication or combination of medications that will control IOP and result in the fewest side effects. In some cases, topical administration of one agent is sufficient. In others, multiple medications are required. If IOP remains controlled for several weeks, the drug dosages or frequency of administration can be gradually reduced. Long-term medical management is challenging and requires frequent and careful monitoring, dosage adjustments, and drug changes. Most patients are best managed with an oral CAI and one or more topical agents of different classes. Remember that most antiglaucoma medications lose their efficacy over time and eventually surgical intervention becomes necessary. If the eye is irreversibly blind and painful, a surgical salvage procedure is indicated. Glaucomatous eyes require frequent monitoring, and tonometry should be performed at least every 3 months.

18. What is the prognosis for acute glaucoma?

Although many cases of acute glaucoma can be successfully managed for a period of time, the long-term prognosis for preserving vision in most cases is guarded to poor. Initial response to therapy can be a useful indicator of future success. With aggressive medical or surgical intervention, many animals regain or retain vision for several months or longer. However, even with successful management of the IOP, glaucoma is almost always progressive and incurable. Fortunately, there are many surgical options available for the blind painful eye that provide comfort and alleviate the need for chronic medication.

19. When is surgery indicated for glaucoma?

There is considerable controversy within the veterinary ophthalmology community regarding when surgical intervention is appropriate. Some ophthalmologists prefer to manage glaucoma in the visual eye medically until medical management begins to fail. Others advocate early sur-

gical intervention in hopes of alleviating the need for chronic medical management and prolonging vision in the affected eye. It remains to be seen which method works best. The surgical modalities employed all have potential complications, are expensive, and have risks. As with medical management, they can prolong vision in an affected eye but do not cure the disease.

20. Can primary glaucoma be prevented from developing in the fellow eye?

Primary glaucoma always has bilateral potential. In at least 50% of cases, the initially normotensive fellow eye becomes overtly glaucomatous within 6–12 months after the onset of disease in the affected eye. In dogs with primary glaucoma, it appears that prophylactic therapy using a topical β-blocker, sympathomimetic, or miotic is effective in prolonging the period of time until the fellow eye becomes affected, but does not necessarily prevent glaucoma. In addition, prior prophylactic therapy may make glaucoma—if it occurs—easier to manage.

BIBLIOGRAPHY

Gelatt KN, Brooks DE: The canine glaucomas. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Baltimore, Lippincott Williams & Wilkins, 1999, pp 701–754.

16. GONIOIMPLANTS

Dennis E. Brooks D.V.M., Ph.D.

1. Is there an optimal way to medically and surgically manage cases of canine glaucoma?

The optimal clinical management to aid preservation of vision has not been developed for each of the different types of primary glaucomas in dogs. Medical treatment usually provides a few months of effective control of intraocular pressure (IOP). Traditional surgical therapies for canine glaucomas may also provide short-term IOP control.

2. What is the cause of elevation of intraocular pressure?

The basic mechanism for the elevation in IOP found in the primary canine glaucomas involves progressive accumulation of biochemical substances in the aqueous outflow pathways such that aqueous humor is unable to exit the globe and the IOP levels become harmful to the intraocular structures. This outflow obstruction may also be associated with inherent microcirculatory disturbances to the retina and optic nerve. As this progressive iridocorneal angle closure occurs, the choice of medical, surgical, or most frequently a combination of both therapeutic modalities to maintain IOP at "safe" levels in canine glaucomas must change.

3. Why is surgical therapy important in glaucoma?

Eyes with glaucoma eventually become refractory to medical therapies to reduce IOP. Surgical treatment is thus important in maintaining IOP at physiologic levels in glaucomatous dogs with iridocorneal angles that are narrow or closed. Unfortunately older surgical treatments of primary glaucomas in the dog such as iridencleisis, corneoscleral trephination, cyclodialysis, combined iridencleisis and cyclodialysis, and posterior sclerectomy have not been very successful at lowering IOP for long periods. Anterior chamber shunts (gonioimplants) appear to be the most physiologically appropriate means to provide longer periods of successful control of IOP because they increase outflow rather than reduce production of aqueous humor.

4. What are gonioimplants?

Anterior chamber shunts or gonioimplants are surgical filtration devices that provide an alternate pathway of aqueous humor drainage around the obstructed, nonfunctioning iridocorneal angle. Aqueous humor is redirected by a tube in the anterior chamber that is connected to a plate sitting on the sclera. This scleral plate or explant induces formation of a fibrous capsule permeable to the aqueous humor. Aqueous humor thus moves through the tube to the scleral explant to be absorbed beneath the conjunctiva. A subconjunctival swelling or "bleb" is noted to form over the scleral explant when the gonioimplant is functional.

5. Which eyes are the best candidates for gonioimplantation?

The optimal canine candidates for the antiglaucoma surgeries are visual patients with early glaucoma, no iridocyclitis or lens subluxation, and normal-appearing optic discs. Patients with vision and IOP that is increasing despite maximum levels of medical therapy are also good candidates. Surgical treatments for blind eyes with advanced glaucomas not under adequate medical control are probably going to be less successful and require different strategies. In the author's practice, the anterior chamber shunts thus are reserved for glaucomatous eyes that are visual or have the potential to regain vision.

6. When are gonioimplantation surgeries most successful?

Higher success rates may result when the filtering techniques and the gonioimplants for the canine glaucomas are employed early in the glaucomatous disease process. The reasons for the apparently higher success rate include: (1) there is still some remaining aqueous humor outflow; (2)

damage to the retina and optic nerve head is not advanced and vision is present; (3) the likelihood of lens subluxation, buphthalmia, peripheral anterior synechiae, and ciliary cleft collapse is reduced; and (4) the complications of concurrent iridocyclitis, preiridal rubeosis, and vitreous within the posterior or anterior chamber are reduced. In addition, the aqueous humor of humans with primary glaucomas, as well as with uveitic glaucomas, seems to stimulate proliferation of the subconjunctival fibroblasts more than normal aqueous humor, and this may be related to previous glaucoma drug administration and higher levels of growth factors in chronically affected eyes.

7. What preoperative treatment is needed for gonioimplantation?

Preoperative considerations in the treatment of primary glaucoma include: (1) preoperative control of IOP to near normal; (2) suppression of any concurrent iridocyclitis with topical corticosteroids and nonsteroidals; (3) maintenance of the desired pupil size; and (4) dehydration and reduction in the size of the vitreous with osmotic agents. IOP must be reduced to 15–20 mmHg with medical therapy. A sterile Schiotz tonometer can be used to estimate IOP immediately before entry into the anterior chamber. If IOP is 30 mmHg or higher, paracentesis is recommended to prevent anterior vitreous presentation, retinal detachment, and expulsive choroidal hemorrhage. Many types of canine glaucoma also exhibit concurrent iridocyclitis. Topical and systemic corticosteroids and nonsteroidal anti-inflammatory agents are indicated to suppress inflammation and reduce inflammatory cells and proteins in the aqueous humor. These exudates can compromise short-term and long-term aqueous humor outflow through the new surgical filtration site. IOP lowering medications are continued till bleb patency is assured.

8. Are there different types of gonioimplants?

Gonioimplants are divided into those with unidirectional valved systems designed to permit aqueous humor passage at about 10–12 mmHg and those with bidirectional nonvalved systems that have no pressure regulatory devices, except for the limited resistance in the shunt's tubing. In the early 1980s the silastic Krupin-Denver valve was evaluated in the beagle dog with inherited glaucoma. This small implant consisted of a small tube placed in the anterior chamber, a valve mechanism to prevent hypotony, and a short tube that extended a few millimeters into the subconjunctival spaces. Without a broad area for the reabsorption of aqueous humor to occur, the exit opening of this implant became scarred and occluded in 50% of the dogs by 6 months. A modified (nonvalved) silicone Joseph implant was evaluated in 15 dogs (21 eyes) with primary glaucoma with encouraging results. Additional reports have evaluated silicone Ahmed, Baerveldt, and other anterior chamber shunts in dogs. Without effective antifibrosis therapy, IOP rises about 3–6 weeks postoperatively from the fibrous capsule that forms around the extrascleral implant. The presence or absence of the valve mechanism in the anterior chamber shunt influences the immediate postoperative management because IOP below 5 mmHg is injurious to the eye and long-term function of the implant. The Ahmed valve has been evaluated in an in vitro system at flow rates that approximate the rate of aqueous turnover in the dog (Fig. 1).

9. Why do some gonioimplants have valves?

Clinical utilization of a valved or nonvalved system affects the immediate postoperative clinical management. Valved or unidirectional systems maintain a minimal IOP, which prevents ocular hypotony and collapse of the anterior chamber immediately after surgery. The nonvalved or bidirectional flow-systems in the immediate postoperative period may result in ocular hypotony ($\leq$ 5 mmHg), but rarely a shallow anterior chamber and disruption of the blood-aqueous barrier. After the fibrous capsule forms around all extrascleral implants several weeks postoperatively, resistance develops to increase IOP. In the long term, there is no difference in IOP control between valved and nonvalved implants.

10. What is the surgical procedure for installation of anterior chamber shunts?

A120–140° fornix-based dorsal bulbar conjunctival flap is prepared using mainly tenotomy scissors and alternating sharp and blunt dissection. This is continued posteriorly between Tenon's

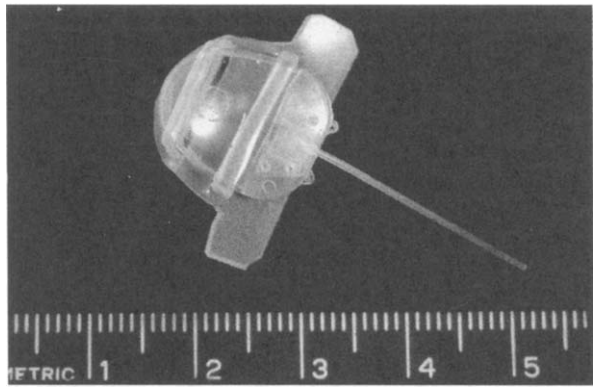


Figure 1. Ahmed gonioimplant with scleral strap attached to increase the surface area of the subconjunctival bleb.

capsule and sclera and between the dorsal and lateral or dorsal and medial rectus muscle insertions. The implant is usually positioned at or just posterior to the equator, its rostral end about 10–12 mm from the limbus. The anterior border of the implant should be posterior of the dorsal rectus muscle insertion. The episcleral or main portion of the anterior chamber shunt is placed between the dorsal rectus and medial rectus muscles or the space between the dorsal rectus muscle and the lateral rectus muscle. Once the surgical site has been adequately dissected and excessive epibulbar fascia excised, the area may be treated with a sterile surgical cellulose spear soaked with mitomycin-C (0.25–0.5 mg/ml) to impede the fibrosis that develops about this base. After exposure of the tissues to the intraoperative mitomycin-C for 5 minutes, the area is flushed profusely for an additional 5 minutes with lactated Ringer's solution. Mitomycin-C should not have access to the anterior chamber or to the leading edges of the conjunctival wound. All anterior chamber shunts are checked prior to placement for function and patency. A 25–27-gauge hypodermic needle is cannulated into the end of the anterior chamber tubing, and sterile lactated Ringer's solution is injected. With the shunt system filled with fluid, it is "primed" and ready for implantation. The device is carefully positioned into the sub-Tenon's capsule space, making certain that the implant borders are in contact with the sclera. Once the device is properly positioned, it is secured to the sclera and Tenon's capsule by 2–4 nonabsorbable 7–0 sutures, usually placed at the anterior border and near the extraocular muscle insertions (Fig. 2). The overall length of the anterior chamber silicone tubing is carefully measured. If cut too long, it may contact the posterior surface of the cornea and produce focal edema. However, if cut too short, the tubing lumen can become obstructed by the base of the iris or preiridal inflammatory membranes. Once in the anterior chamber, the tubing should not touch either the iris or cornea and should avoid crossing the center of the pupillary axis. The tip of the tubing is usually cut in a slightly beveled position to facilitate insertion into the anterior chamber. A limbal-based partial-thickness 5 × 8 mm scleral hinge is prepared by a scalpel to prevent tube erosion through the conjunctiva due to upper lid pressure. Entry into the canine anterior chamber is usually at about the 12 o'clock with a 20–22-gauge hypodermic needle (Fig. 3). The hypodermic needle is quickly removed and the beveled silicone tubing inserted. Manipulation of the tubing with special silicone tubing thumb forceps is recommended to prevent damage to the soft silicone tubing. Aqueous humor will generally be noted flowing through the device. Provided little aqueous humor has escaped through the anterior chamber needle track, IOP should be about 10 mmHg. The corners of the scleral hinge are apposed to the underlying host sclera with four simple interrupted 6–0 to 7–0 absorbable sutures. The conjunctival flap wound is apposed using several simple interrupted or a continuous 6–0 to 7–0 absorbable suture. To minimize development of fibrin in the aqueous humor and within the implant postoperatively, 25 μg of tissue plasminogen activator (tPA) is usually injected into the anterior chamber at the limbus.

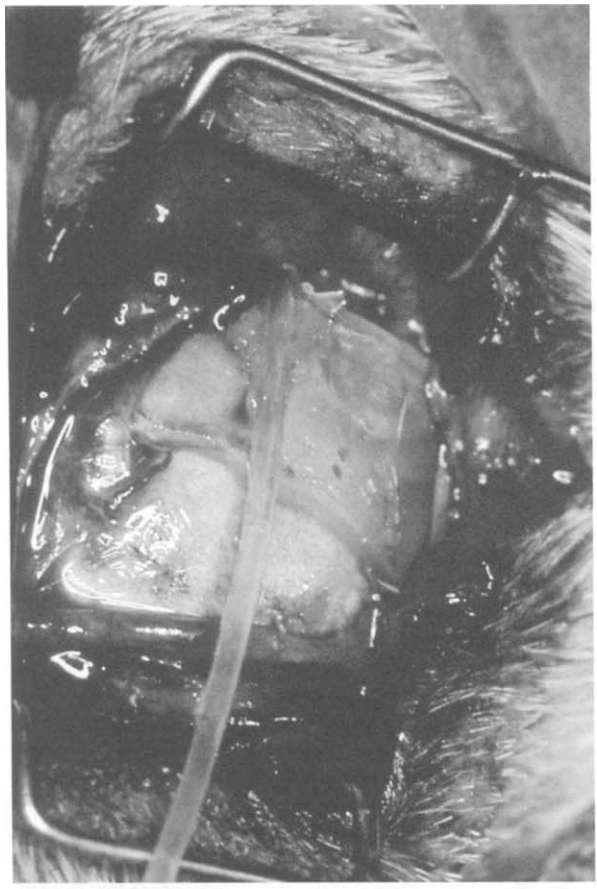


Figure 2. Implant being attached to the sclera intraoperatively.

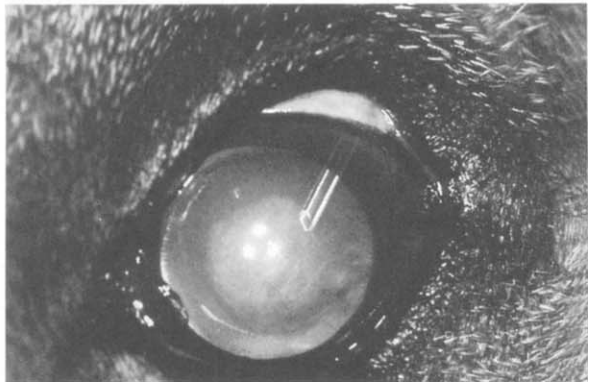


Figure 3. Tube present in anterior chamber of a dog.

11. What is needed for postoperative management?

The general postoperative management includes:

- Control and resolution of the iridocyclitis with topical and systemic corticosteroids and nonsteroidal anti-inflammatory agents
- Moderate pupillary dilatation and encouraging pupil movement with careful use of mydriatics, such as 1% tropicamide

- Prevention of infection with topical and systemic antibiotics
- Maintenance of normal levels of IOP with carbonic anhydrase inhibitors and, if necessary, β-blocker adrenergics; and
- Maintenance of a patent anterior chamber tubing (intracameral injections of 25 μg tissue plasminogen activator). Digital massage may be performed daily.

12. What IOP is expected postoperatively?

Successful anterior chamber shunts will provide IOP, immediately after surgery, of about 5 mmHg with the nonvalved shunts and 8–12 mmHg with the valved shunts. Occasional spikes of 10 mmHg or higher may develop in the first few weeks as the shunt tube is temporarily plugged with fibrin. With development of the capsule about the base of the scleral shunt explant in 3–6 weeks, IOP will gradually increase to 12–20 mmHg several weeks postoperatively.

13. What if tube occlusion occurs?

Anterior chamber shunt tubing may occasionally become occluded to cause an elevation in IOP, and yet examination of the anterior chamber portion of the system may appear normal. Ultrasonography through the upper eyelid over the area of the shunt will demonstrate no surrounding aqueous humor "pool" or bleb if the tube is occluded. In these patients, either digital massage or the intracameral injection of TPA will often cause in a rapid decrease in IOP and re-establishment of patency.[10] Presumably, a fibrin clot within the tubing has produced a temporary occlusion of the system (Fig. 4).

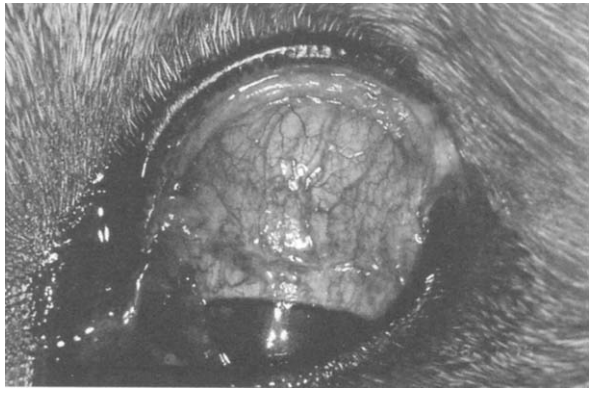


Figure 4. Subconjunctival bleb present over the scleral implant 3 months postoperatively.

14. What if a loss of bleb patency occurs?

Long-term failure of anterior chamber shunts is usually associated with development of an impermeable capsule about the episcleral base of the device. Aqueous humor may contain a number of cellular stimulants that promote continued capsule formation. With time, the capsule becomes thicker or less permeable, and IOP gradually increases over weeks or several months. Surgical removal of the capsule on the top and sides of the implant, which is not disturbed, will immediately restore normal levels of IOP. As the capsule is stripped from the implant, aqueous humor will immediately flow into the incision, and IOP will decrease to about 10 mmHg with the valved systems. A loss of explant bleb patency may also occur with time to prevent filtration of aqueous and thus result in increased IOP. Topical corticosteroids, such as 1% prednisolone, are instilled postoperatively for several months to impede capsule formation about the anterior chamber shunt base.

15. Are there complications of using anterior chamber shunts?

There is a learning curve with anterior chamber shunts as with any new surgical procedure. Every attempt should be made to control uveitis before surgical entry into the anterior chamber because some iridocyclitis is present postoperatively in the dog due to the hypodermic needle pen-

etration into the anterior chamber, further stimulation of a preexisting iridocyclitis, or the initiation of a new iridocyclitis by the presence of the tube. Any fibrin or blood in the anterior chamber may occlude the anterior chamber tubing either temporarily or permanently. If fibrin is detected in the tip of the tubing, injection of tPA will usually digest the clot, but higher levels of corticosteroids and nonsteroidal anti-inflammatory agents are also indicated to resolve the iridocyclitis for the long term. Infectious or sterile endophthalmitis is also an unusual but possible complication of gonioimplants. Use of mitomycin-C may predispose to endophthalmitis, which may occur months after the surgery and require enucleation.

16. What are the surgical results of gonioimplantation?

Strategy for placement of anterior chamber shunts in dogs is still evolving, but some guidelines have emerged. Optimal canine candidates for gonioimplants are visual patients with early glaucoma, no iridocyclitis or lens subluxation, and normal-appearing optic discs. An implant with a valve mechanism may be optimal for these patients. Anterior chamber shunts for canine patients with advanced glaucoma that is not under adequate medical control are probably going to be less successful. Anterior chamber shunts without valved systems and perhaps with a fairly large diameter anterior chamber tubing and episcleral implant may be the choice for these patients.

At this time, the success for anterior chamber shunts is encouraging, but additional improvements are necessary. In a report of 21 eyes of 15 dogs with primary glaucomas that received the modified Joseph shunt, 20 eyes were normotensive at 4 weeks, and 17 eyes were still normotensive at 9–15 months.[2] About 50% of these eyes were also receiving oral dichlorphenamide daily (1.6–2.5 mg/lb). Of the 9 eyes with vision preoperatively, 8 were still visual at 9 months. A larger study involving 83 eyes and 65 dogs compared four different Ahmed anterior chamber shunts for treatment of the primary glaucomas.[5] The criteria for success were maintenance of vision and levels of IOP $\leq$20 mmHg. The median time that IOP began to increase postoperatively depended on the shunt and ranged from 4 to 15 months. The median time for vision loss to develop postoperatively again varied by shunt and ranged from 4 to 9 months. Fifteen of the 22 eyes with $\leq$ 20 mmHg IOP were still visual 1 year postoperatively. The most promising shunt was the large Ahmed shunt attached to a silicone band. Only 18% of all of the operated eyes were still visual 1 year postoperatively.

BIBLIOGRAPHY

1. Bedford PGC: Use of a one-piece drainage system in the treatment of a closed angle glaucoma in a dog. J Small Anim Pract 29:231–237, 1988.
2. Bedford PGC: A clinical evaluation of a one-piece drainage system in the treatment of canine glaucoma. J Small Anim Pract 30:68–75, 1989.
3. Bentley E, Nasisse MP, Glover T, et al: Implantation of filtering devices in dogs with glaucoma: Preliminary results in 13 eyes. Vet Comp Ophthalmol 6(4):243–246, 1996.
4. Cook CS: Surgery for glaucoma. Vet Clin N Am Small Anim Pract 27:1109–1130, 1997.
5. Garcia-Sanchez GA, Brooks DE, Gelatt KN, et al: Evaluation of valved and nonvalved gonioimplants in 83 eyes of 65 dogs with glaucoma. Anim Eye Res 17(1–2):9–16, 1998.
6. Gelatt KN, Brooks DE: Canine glaucomas. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Philadelphia, Lippincott, Williams & Wilkins, 1999, pp 701–754.
7. Gelatt KN, Brooks DE, Miller TR, et al: Issues in ophthalmic therapy: The development of anterior chamber shunts for the clinical management of the canine glaucomas. Prog Vet Comp Ophthalmol 2(2):59–64, 1992.
8. Herrera HD: Glaucoma surgery in dogs with a simplified implant [abstract]. Proc Annu Meet Am Coll Vet Ophthalmol 26:16, 1995.
9. Sherwood MD: Complications of silicone tube drainage devices. In Sherwood MD, Spaeth GL (eds): Complications of Glaucoma Surgery. Thorofare, NJ, Slack, 1990, pp 307–326.
10. Sidoti PA, Morinelli EN, Heuer DK, et al: Tissue plasminogen activator and glaucoma drainage implants. J Glaucoma 4:258, 1995.
11. Strubbe DT, Gelatt KN, Mackay EO: In vitro flow characteristics of the Ahmed and self-constructed anterior chamber shunts. Am J Vet Res 58(11):1332–1337, 1997.
12. Tinsley DM, Betts DM: Clinical experience with a glaucoma drainage device in dogs. Vet Comp Ophthalmol 4(2):77–84, 1994.

17. THE BLIND BUPHTHALMIC EYE OF GLAUCOMA

Kenneth L. Abrams, D.V.M.

1. How do you differentiate the buphthalmic eye of glaucoma from a retrobulbar disease causing protrusion of the globe?

Is the eye actually larger (i.e., buphthalmic) or is it exophthalmic from a retrobulbar mass—that is the question. This question can be difficult to answer in subtle cases. Two techniques can help answer this question.

1. The corneal diameter can be measured and compared to the opposite eye; if it is larger, the globe is probably larger.

2. Digital pressure applied directly posteriorly through a closed upper eyelid can help determine if there is a retrobulbar mass causing protrusion of the globe. Simultaneously compare each eye by using the index fingers to retropulse the globes.

2. How do you determine if the patient is blind from glaucoma?

Several findings during the eye exam can indicate whether the patient has lost vision in the problem eye. Certainly, when the eye is severely buphthalmic with severe corneal pathology, we know that the eye is blind. Abnormalities associated with chronic glaucoma include buphthalmos, luxated lens, Haab's striae (corneal endothelial stretch lines), optic nerve cupping and atrophy, and retinal degeneration. Some shar-pei, chow chow, and beagle dogs seem to maintain vision longer even with severe buphthalmos and associated chronic changes. The reason for this clinical observation is unknown.

3. Is the menace response helpful in determining whether the patient is blind in the glaucomatous eye?

Careful evaluation of the menace response comparing your findings to the sighted eye can help determine whether vision is still present. The response involves a threat gesture made by the examiner's hand to the test eye while covering the non-test eye, a positive response involves a blink and possibly head motion away from the threatening gesture. An intact menace reflex requires clear cornea and ocular media, optic nerve function cranial nerve II [CN2], cortical function, and facial nerve (CN7). Young patients may not be mature enough to understand the threat gesture, and therefore the age of patient is important when performing this test. Also, patients with facial nerve palsy will have a negative response unless they retract the globe causing third eyelid protrusion. Facial nerve palsy can be evaluated separately with the palpebral response by touching the eyelids to elicit a blink.

4. What specific changes are associated with optic nerve disease and retinal degeneration in glaucoma?

Indirect or direct ophthalmoscopy techniques are used to view the posterior segment of the eye; the cornea, lens, and fluid media have to be clear in order to see the fundus. Glaucoma causes optic nerve damage sooner than retinal degeneration, but by the time the globe is buphthalmic many abnormalities can be found on the fundus. Optic nerve cupping is a depression of the nerve head behind the level of the sclera and classically was thought to be caused by simple mechanical damage from the elevated intraocular pressure. However, more current information about the pathogenesis of glaucoma indicates possible chemical or vascular alterations may be responsible for the optic nerve damage. The diseased optic nerve head will be less vascularized when compared to the normal eye and will first appear more pale, then finally very dark in the end stages of the disease. Often times there is a halo of hyperreflectivity around the nerve head early in the dis-

ease process. Retinal degeneration changes associated with the buphthalmic eye include tapetal hyperreflectivity, vascular attenuation, and depigmentation of the non-tapetum.

5. Could a tumor cause the problem?

Intraocular tumors such as lymphoma, iris and ciliary body adenomas and carcinomas, melanomas, and metastatic carcinomas often cause secondary glaucoma. Two issues should be considered in these patients. First, if the glaucoma is thought to be caused by a tumor evidenced by direct viewing of the intraocular mass or other clinical indications of neoplasia, a complete medical work-up should be performed to help make an overall treatment plan package. Second, if a tumor has caused the glaucoma, emphasis should be placed on enucleation rather than medical management or evisceration. Evisceration and prosthesis may be considered risky in an eye with a tumor since some tumor cells may be left behind with this procedure.

6. Is a buphthalmic eye painful, even if the patient seems to have normal behavior at home?

It is often difficult to determine the degree of discomfort in patients with a chronically large globe. However, once the eye is surgically removed, clients report that the patient becomes much more active, and they admit that they had no indication that the pet was previously uncomfortable with the large eye. We can, therefore, assume that the buphthalmic globe is a painful condition.

7. Can you treat a blind or glaucomatous patient with medication?

Often times clients are surprised to learn that their pet is blind in the affected eye since the patient usually functions well with the remaining sighted eye. Initiating treatment with glaucoma medications is reasonable to attempt reduction of the intraocular pressure and to give the client time to accept the blindness in their pet's glaucomatous eye. It is best to use medications as a temporary measure unless there are specific reasons not to proceed surgically such as financial and patient age or health issues. Most of the topical glaucoma medications approved for humans reduce the intraocular pressure around 5–7 mmHg, which may be crucial for early detected glaucoma in people, but the dog or cat with a buphthalmic globe often has an intraocular pressure in the 50–70 mmHg range and these medications are not very useful. There are many new topical glaucoma medications including topical carbonic anhydrase inhibitors and latanoprost, but these drugs are very expensive and are probably a waste of the client's money for the blind or buphthalmic eye. Systemic carbonic anhydrase inhibitors such as methazolamide (Neptazane, Glauctabs) and dichlorphenamide (Daranide) are more effective at reducing the IOP but can have short- and long-term side effects such as vomiting, diarrhea, anorexia, panting, neurologic signs, and hypokalemia.

8. If medical treatment is chosen, does it have to be given for life?

Something is better than nothing. Some clients will never consider a surgical option for the big, blind eye, and in these patients medical treatment may have to be given for the life of the patient. Periodic rechecks with intraocular pressure evaluation should be performed to monitor progress, and some chronic buphthalmic globes eventually degenerate and become smaller (phthisis bulbi) over a long period of time. If the globe becomes phthisical, medications can be weaned, and rechecks can become less frequent than every few months.

9. What are the surgical options for managing the buphthalmic eye?

Some clients immediately accept the concept that the eye will never be useful to the pet and could develop secondary complications such as corneal ulcers from exposure, whereas other clients may need time to get used to the idea that the buphthalmic eye will never be useful to the patient. Once the client understands that the patient will never see out of the eye, some type of removal of the globe should be discussed with the owner. There are three ways to remove an eye: enucleation, evisceration, and exenteration. Exenteration is removal of the globe and all surrounding soft tissue structures as would be performed with an orbital tumor and is usually not nec-

essary with a buphthalmic globe. Enucleation is removal of the eye with preservation of orbital structures by incising extraocular muscles near their insertions at the globe and leaving behind most of the normal orbital tissue. Evisceration is removal of intraocular structures with placement of an intrascleral silicone prosthesis for maximal cosmetic outcome. Enucleation and evisceration are the techniques performed for glaucoma. Enucleation can be performed either as a transpalpebral or subconjunctival approach depending strictly on surgeon preference. Some surgeons will place a silicone prosthesis into the orbit before closing so that the skin over the orbit does not sink in, but closure of the orbital septum arising from the orbital rim usually prevents "sinking" without having to place a space-occupying sphere.

Management of the Buphthalmic Globe

TREATMENT METHOD	ADVANTAGES	DISADVANTAGES
Enucleation	No need for further concerns Pain-free patient immediately Less costly long-term	Emotion for client Initial cost Requires surgical expertise Cosmetic concerns
Evisceration/prosthesis	Cosmetic outcome Pain-free patient Less costly long-term	May be contraindicated—size? Initial cost Requires surgical expertise Corneal concerns long-term
Medical management	Lower short-term costs Time for client to consider other options Avoids anesthesia	High long-term costs Patient may remain painful
Laser or cryotherapy	Short procedure Possibly discontinue the medications Alternative option to medications and removal options	Potential side effects May not be effective Postoperative concerns

10. Do you leave the orbit open with enucleation?

No! After removal of the buphthalmic globe, the superior and inferior orbital septa arising from the orbital rims are sutured together. The septum is isolated by placing forceps over the inner and outer aspects of the orbital rim and then "dragging" them to the edge to grab the tissue. You'll know you have the septum and not just conjunctiva if you can start to lift the patient's head off the surgery table after taking a bite with suture. Finally, the eyelid margins are removed and the remaining skin sutured together.

11. Are all glaucoma patients candidates for cosmetic evisceration and prosthesis?

No, again! In fact, in order for this procedure to be successful with a good cosmetic outcome, the cornea, sclera, and globe should be relatively normal. Buphthalmic globes with exposure keratitis, corneal ulcers, and other corneal pathology are contraindications for performing this procedure. In this procedure, a prosthesis approximately the size of the patient's globe must be placed, and the cornea is preserved. Therefore, any lagophthalmos-related exposure problems, corneal pathology, and dry eye syndrome will persist after surgery. Having said that, if the globe is only mildly to moderately enlarged without corneal pathology, the prosthesis surgery can be performed using a slightly smaller prosthesis than the globe size so that over time the sclera and cornea decrease in size to meet the prosthesis. Measure the limbal diameter of the normal cornea and add 2 mm for the correct size prosthesis to be placed intrasclerally into the buphthalmic globe.

12. With a cosmetic prosthesis, does the owner have to take it out and clean it? Will it fall out?

The evisceration procedure involves a scleral incision, removal of all intraocular contents (aqueous, vitreous, lens, and retina), followed by placement of the silicone sphere to fit inside the scleral shell. The scleral and conjunctival incisions are sutured closed, and the prosthesis remains inside the globe for life. The prosthesis is never touched again and should never be found on the

client's dining room floor. This type of prosthesis differs from a painted prosthetic shell that fits under the eyelids in humans after enucleation.

13. Are there any other surgical options besides removing the globe?

Removal of the buphthalmic globe is the most logical way to deal with such a blind eye. However, some clients emotionally or financially may need more time to consider removal, or the patient may have medical issues that need to be considered for general anesthesia. Other surgical options include laser cyclophotocoagulation or cryotherapy to reduce intraocular pressure by decreasing aqueous humor production, drainage procedures using various types of aqueous humor shunts, and pharmacologic ablation of the ciliary body (gentamicin injection). These procedures still require general anesthesia but since most of them are generally quicker and less invasive than removal methods, certain patients with buphthalmic globes may benefit from one of these procedures (Figs. 1 and 2).

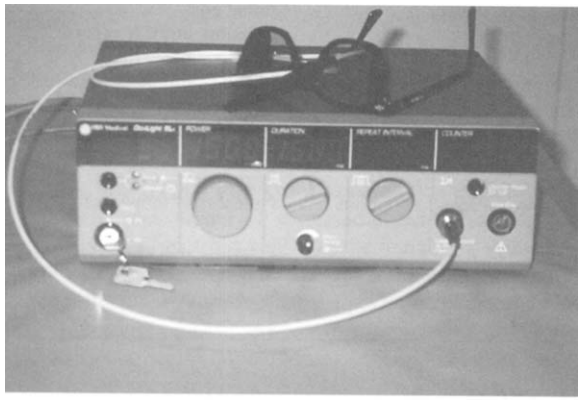


Figure 1. Diode laser instrumentation by Iris Medical Instruments used for cyclophotocoagulation of the ciliary area.

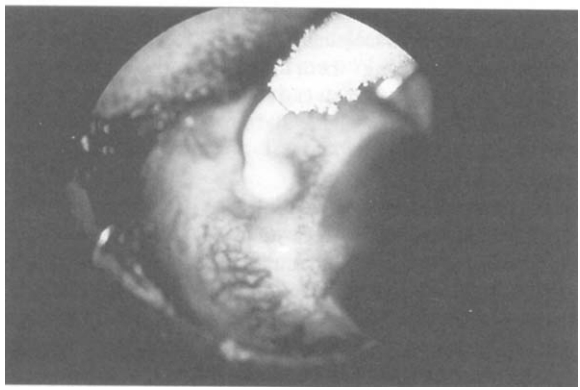


Figure 2. Cryotherapy on a blind buphthalmic globe. Multiple sites are frozen dorsally and ventrally to destroy aqueous production and stimulate uveitis.

14. Will the eye rupture if it gets too large?

It is amazing how large the globe can stretch without rupturing! As the globe enlarges, the sclera and cornea become thinner, and the black uveal tract will begin to show through the thin sclera just posterior to the limbus. However, it is fairly unusual for the globe to rupture unless central exposure corneal ulcers develop causing eventual rupture. Although it is not amusing to the patient, it is also amazing to see a number of cases in which both eyes have become buphthalmic with obvious blindness and the owner, totally unaware of medical anecdotal humor, relates, "Doc, it just started 2 days ago . . .."

15. Will the glaucoma spread to the other eye?

There are many causes of glaucoma including primary, breed-related glaucoma, and secondary glaucomas such as inflammatory, neoplasia, and trauma. Primary glaucoma in purebred dogs such as the cocker spaniel, basset hound, poodle, beagle, Samoyed, and several other breeds is a concern for glaucoma to happen in the second eye. The disease does not spread to the other eye, but those patients are at risk of developing the disease in the second eye. Recent information shows that protection of the second eye with a topical beta blocker or parasympathomimetic prolongs the interval before the second eye develops the disease from an average of 8–30 months.

16. If treatment had been started sooner, could vision have been saved?

The bottom line is that glaucoma causes blindness in millions of human and veterinary patients each year. It is simply a bad disease that needs more questions answered before we really know how to best deal with this problem. The disease is often detected much earlier in humans than in domestic animal species; therefore, the disease is often undetected for a longer period of time in dogs and cats. By the time the disease is noticed, the eye is blind and buphthalmic. Even when glaucoma is detected earlier, as is often the case for the remaining eye, the disease results in a blind and buphthalmic eye.

17. If the second eye becomes blind and buphthalmic, does the owner have to consider euthanasia?

Patients adjust extremely well to complete blindness, probably by fine tuning their already keen senses of smell and hearing. Acute blindness can result in some anxiety and confusion in the patient, but by the time a patient develops bilateral buphthalmos they have had time to get accustomed to their handicap and perform very well. Many owners will readily agree to remove a single buphthalmic globe when the other eye is normal but have difficulty in considering bilateral removal even though the patient will only feel better after surgery (Fig. 3).

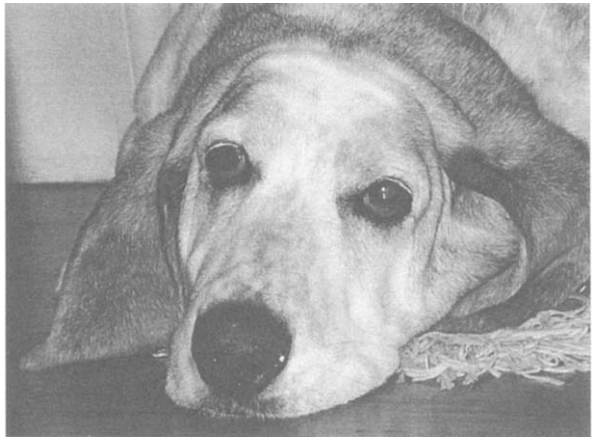


Figure 3. The cosmetic appearance of a 10-year-old basset following a bilateral evisceration/ intrascleral silicone prosthesis.

A second pet in the house is often helpful in guiding the blind patient around its environment. The sighted pet seems to understand the blind pet's handicap and takes on the role of leader of the pack. At least two books have recently been written to help owners handle a blind patient.

BIBLIOGRAPHY

1. Brooks DE: Comparative optic nerve physiology: Implications for glaucoma, neuroprotection, and neuroregeneration. Vet Ophthalmol 2:13–25, 1999.

2. Cook C, Davidson M, et al: Diode laser transscleral cyclophotocoagulation for the treatment of glaucoma in dogs: Results of 6 and 12 month follow-up. Vet Comp Ophthalmol 7:148–154, 1997.
3. Levin C: Living with Blind Dogs. Oregon City, OR, Lantern Publications, 1998.
4. Levin C: Blind Dog Stories: Tales of Triumph, Humor, and Heroism. Oregon City, OR, Lantern Publications, 1999.
5. Miller PE, Schmidt GM, Vainisi SJ, et al: The efficacy of topical prophylactic therapy in canine primary glaucoma: A multicenter clinical trial. Proc Am Coll of Vet Ophthalmol 29:15, 1998.

18. OCULAR MELANOSIS IN CAIRN TERRIERS

Simon M. Petersen-Jones, DVetMed, Ph.D.

1. Is ocular melanosis an inherited disease?

Undoubtedly, ocular melanosis is a hereditary condition. However, the pedigree information to conclusively prove a mode of inheritance has yet to be assembled.

2. At what age can ocular melanosis be detected?

The age at which signs typical of ocular melanosis develop varies considerably. Some dogs develop changes that are typical for ocular melanosis at 4 or 5 years of age while others can present with the early changes as late as 12 or 13 years of age. The occurrence of dogs with a late onset of signs complicates attempts to screen potential breeding dogs prior to their use, and it also means that dogs cannot be considered to be free of ocular melanosis unless they remain ophthalmoscopically normal until they are over 12 or 13 years of age.

3. What are the early changes to look for?

The early stages of the disease are characterized by the presence of a bilateral hyperpigmentation of the irides with a marked circumferential thickening of the iris root (Fig. 1). This thickening causes the peripheral one-third of the iris to protrude into the anterior chamber. Sometimes at this early stage, careful slit-lamp examination reveals the presence of a few pigmented cells floating in the aqueous. At this stage, pigmentation of the sclera or episclera may not necessarily have developed. As the condition progresses, this thickening of the iris becomes less apparent.

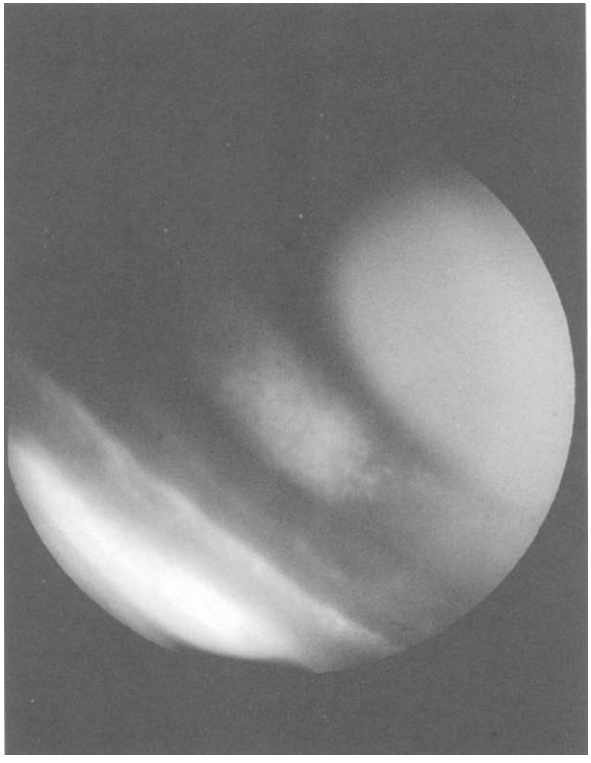


Figure 1. Early stages of ocular melanosis. Photograph taken through goniolens showing a circumferential thickening of the iris root, which protrudes into the anterior chamber.

4. What will gonioscopy show in ocular melanosis–affected eyes?

In the early stages, the pronounced thickening of the peripheral iris may partly obscure visualization of the iridocorneal drainage angle (see Figure 1). The drainage angle is darkly pigmented, and as the condition progresses, deposited pigment cells appear as a dusting on the pectinate fibers and also deeper within the ciliary cleft obscuring visualization of the trabecular meshwork (Fig. 2). Eventually the ventral drainage angle is completely obscured by deposited pigment (Fig. 3), which partly fills the ventral anterior chamber and can be seen externally as a pigment band lining the peripheral ventral cornea. The dorsal parts of the drainage angle are less severely affected. Once glaucoma becomes established the resulting corneal changes makes examination of the drainage angle more difficult.

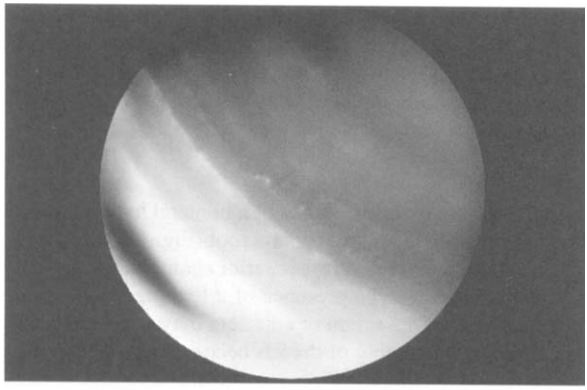


Figure 2. Goniophotograph of early-stage ocular melanosis. Pigment is deposited within the trabecular meshwork and on the pectinate fibers. Individual pectinate fibers are still clearly visible.

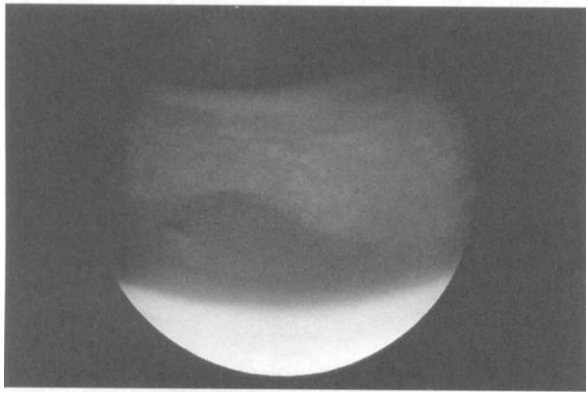


Figure 3. Goniophotograph of the ventral drainage angle of a preglaucomatous eye. A mass of deposited pigmented cells is obscuring the opening into the ciliary cleft and the pectinate fibers.

5. When do the characteristic scleral/episcleral pigmented patches develop?

Although they are not the first indicators of the condition, pigment deposits within the sclera and episclera develop during the early stages. They first appear as small spicule-shaped, black-colored patches 3–5 mm posterior to the limbus (Fig. 4). These patches are readily differentiated from conjunctival pigmentation, which is more superficial, not so dark in color, and typically more diffuse in extent. The scleral/episcleral pigment patches can appear at any point around the circumference of the sclera overlying the ciliary body region. As the condition progresses, the lesions become larger (Figs. 5 and 6) and may eventually appear to bulge from the surface of the globe (Fig. 7). The more ventrally positioned lesions tend to be larger in size.

6. How long does it take for secondary glaucoma to develop?

The time taken for sufficient blockage of the aqueous drainage pathways to cause secondary

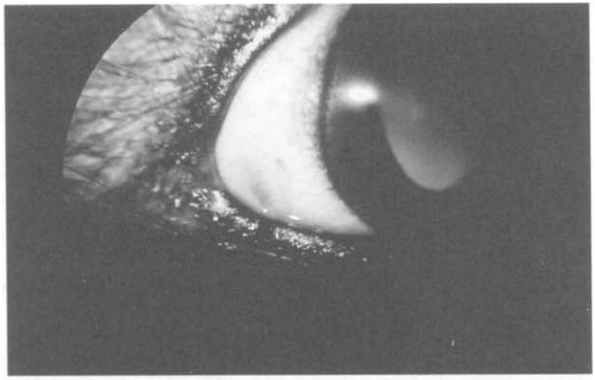


Figure 4. A small patch of scleral pigment in a cairn terrier with early stage disease.

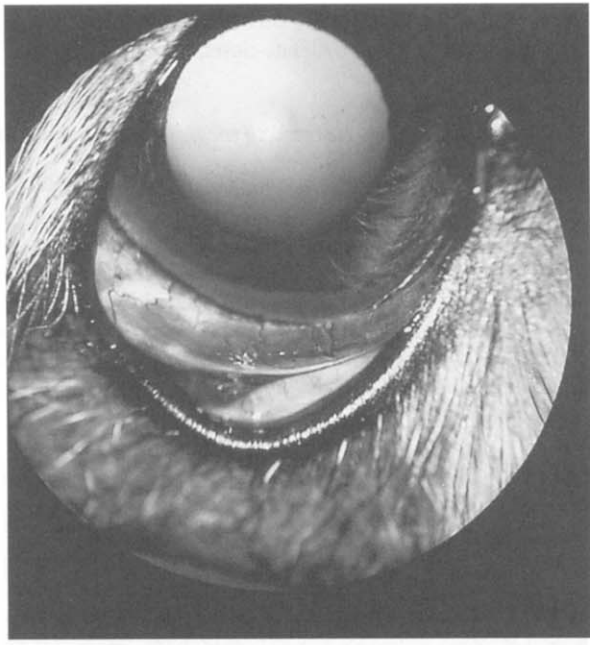


Figure 5. A preglaucomatous eye with ocular melanosis. There are large scleral/episcleral pigment patches and pigment lines the ventral corneal endothelial surface sufficiently to show from under the scleral overhang. Pigmented particles can be seen suspended in the aqueous.

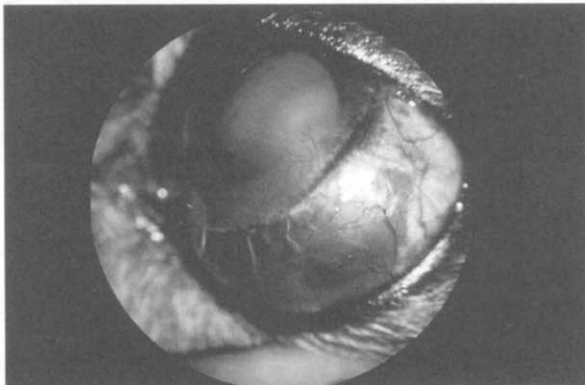


Figure 6. An eye with ocular melanosis and secondary glaucoma. There is a very large pigmented patch in the ventral sclera/episclera. A wide band of pigment deposited on the ventral corneal endothelial surface can be seen.

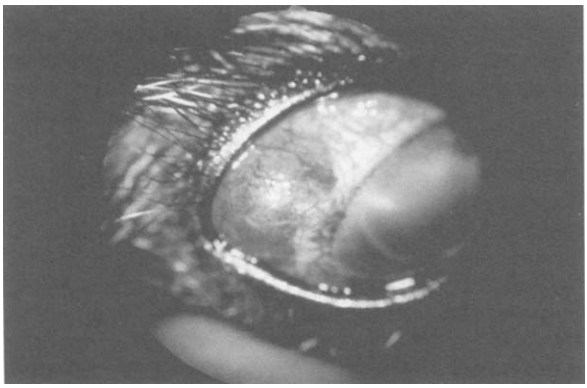


Figure 7. An eye with ocular melanosis and secondary glaucoma. The pigmented patch shown is raised from the surface of the globe. The pigmented sclera is thinned and is therefore bulging as a result of the raised intraocular pressure.

glaucoma varies considerably between affected dogs. Some dogs will develop glaucoma as early as 7 years of age. Dogs with late-onset, slowly progressive ocular melanosis may never develop glaucoma.

7. Ocular melanosis can lead to secondary glaucoma, but are there any other problems associated with it?

Glaucoma with a slow insidious onset is the major problem secondary to ocular melanosis. Some affected dogs do develop attacks of acute anterior uveitis associated with release of large amounts of pigment into the aqueous. This may result in depigmentation of patches of the anterior iris surface. The anterior uveitis usually responds well to topical steroid therapy. Iris atrophy may become a feature prior to a sustained elevation in intraocular pressure. A progressive pigment deposition also affects the fundus and, some dogs develop superficial pigment deposits on the surface of the optic nerve head (Fig. 8). Following sustained glaucoma, complications typical of chronic glaucoma may develop, including severe buphthalmos, exposure keratitis, and phthisis bulbi.

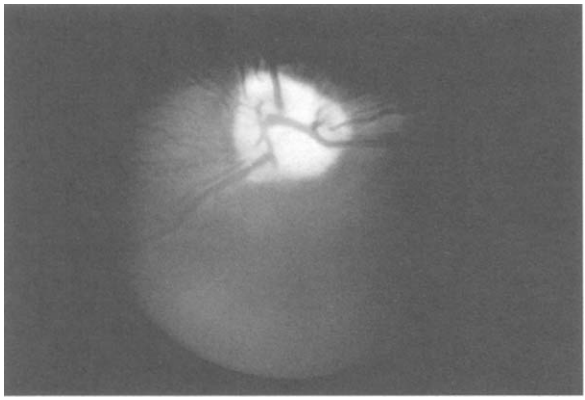


Figure 8. A spicule-shaped pigment deposit is present on the optic nerve head of this cairn terrier with ocular melanosis.

8. How should I manage the condition?

We have not yet identified a method of slowing down or preventing the proliferation of pigment that characterizes this condition. Affected dogs should have their intraocular pressure monitored on a regular basis, particularly as the pigmentation progresses. Conventional antiglaucoma medication may slow down the development of irreversible glaucomatous damage of the optic nerve head and retina. However, the development of an intractable glaucoma is inevitable in the dogs that develop ocular melanosis at a younger age. Only dogs with later onset and slow progres-

sion may maintain useful eyesight up until death. Laser cyclophotocoagulation is not recommended because the sclera of affected dogs is already thinned and weakened considerably; therefore, staphylomas can develop following this method of glaucoma management. Glaucoma drainage shunts have been used with moderate success in the short term.

9. Can I do anything to help the research into the etiopathogenesis of ocular melanosis?

The author has an active research program supported by the Cairn Terrier Club of America aimed at eventually identifying the gene mutation responsible for this condition. Sending a blood sample for DNA extraction, a pedigree, clinical descriptions, and any enucleated eyes will help forward this research.

10. Are other breeds affected with ocular melanosis?

There are anecdotal reports of a condition of similar appearance in other breeds. Ocular pathologists report receiving globes from golden retrievers with a similar melanosis. However, conclusive evidence that the conditions reported in other breeds are identical to ocular melanosis in cairn terriers is lacking.

BIBLIOGRAPHY

1. Covitz D, Barthold S, Diter R, et al: Pigmentary glaucoma in the cairn terrier. Proc Am Coll of Vet Ophthalmol 115:246–250, 1984.
2. Petersen-Jones SM: Abnormal ocular pigment deposition associated with glaucoma in the cairn terrier. J Small Anim Pract 32:19–22, 1991.
3. Petersen-Jones SM, Mould JRB: Pigment deposition resulting in secondary glaucoma in the cairn terrier. Invest Ophthalmol Vis Sci 34(supplement):2354, 1992.

IV. Cataracts

19. OVERVIEW OF CATARACTS

Jane O. *Cho*, D.V.M.

1. What is a cataract?

A cataract is defined as a lens opacity. It may be small and focal, taking up only a small part of the lens, or it may take up the whole lens completely. An object that is **opaque,** by definition, does not allow light to pass through it. (This is distinguished from **translucent,** where light rays do pass through but are bent at different angles such that objects on one side are visible from the other, but not clearly [e.g., frosted glass].) The opacity that comprises a cataract represents an area of disarray of the lens fibers, which normally have a very regular arrangement within the lens to maintain clarity. Other cellular (fibroblastic cells) or noncellular (collagen, lens proteins) elements may be involved in lens opacity as well.

2. How are cataracts classified?

Cataracts may be classified in various ways: by stage of maturity, etiology, location/shape, or time of onset. These categories may overlap.

The classic stages of cataract maturation include:

- **Incipient** (small, incomplete, and not affecting vision)
- **Immature** (more developed than incipient, reducing vision, but still incomplete)
- **Mature** (complete and opaque white)
- **Intumescent** (lens fibers are swollen, the lens itself may be enlarged and "clefts" are often present at the sutures)
- **Hypermature** (undergoing resorption or dissolution of lens proteins, with a subsequent reduction in lens size)
- **Morgagnian** (a stage of hypermaturity where the entire lens cortex is resorbed and the nucleus has settled to the bottom of the lens capsule)

Not all cataracts will progress through all stages, although cataracts at later stages have likely gone through the preceding stages. Some types are more typical of certain etiologies. For exampel, cataracts due to diabetes mellitus are often mature and intumescent (Figs. 1–10).

A cataract may be metabolic, senile, inflammatory, or traumatic (e.g., lens puncture) in origin, or it may be a primary breed-related condition. Other less likely causes of cataracts include nutritional deficiencies, electric shock, and periocular radiation therapy. It is important to test for diabetes mellitus in dogs with a sudden onset of bilateral cataracts.

Cataracts may be at any location in the lens and can be described as being nuclear, cortical (anterior and/or posterior), equatorial, subcapsular, perinuclear, suture-tip, axial (along the central visual axis), paraxial (off-center), peripheral, or any combination of the above. Shape descriptions that have been used to characterize cataracts include lamellar (flat and sheet-like), (multi)focal, pulverulent ("candy floss"), wedge-shaped, triangular or pyramidal (typically at the posterior pole), and coronary (peripheral cortical). A "brunescent" cataract is commonly seen in humans and has a diffuse pale brown coloration due to the presence of urochromes.

Cataracts may be congenital (developing before birth), juvenile (developing in young to middle-aged animals), or senile (developing in aged animals, concurrent with nuclear sclerosis). The

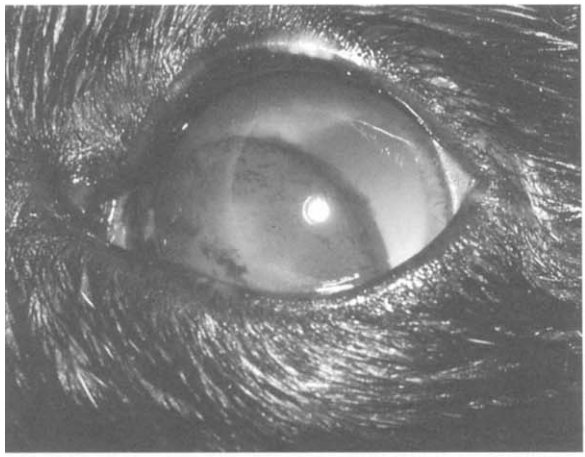


Figure 1. An immature cataract luxated anteriorly and medially. An aphakic crescent allows a good view of the posterior segment dorsally and laterally.

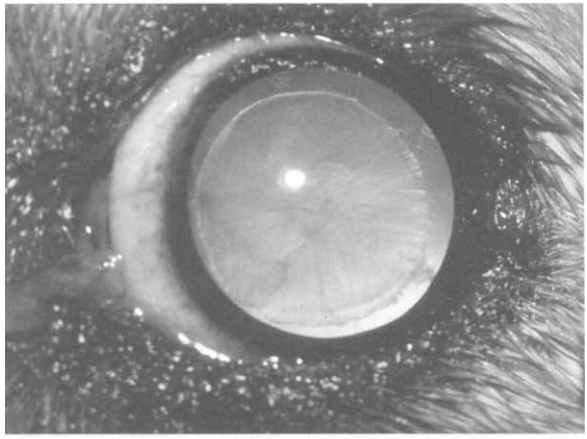


Figure 2. An immature cortical cataract.

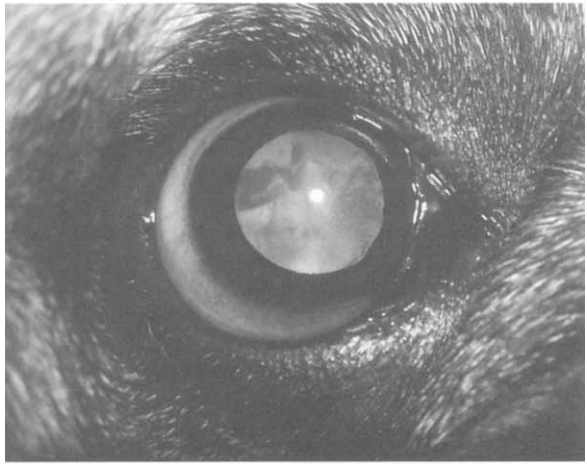


Figure 3. A congenital-inherited cortical cataract in an 8-month-old pug.

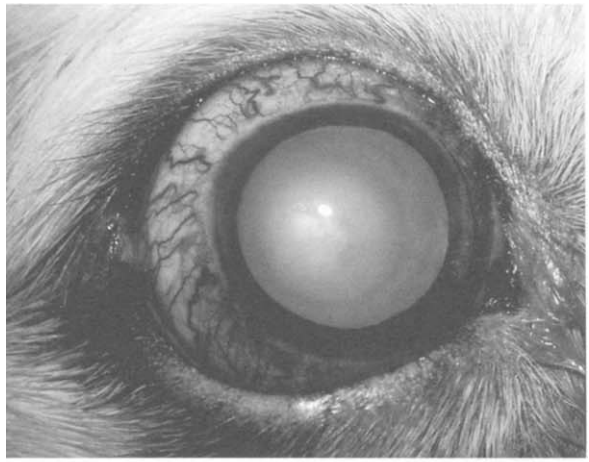


Figure 4. A perinuclear cataract in a 9-year-old American cocker spaniel.

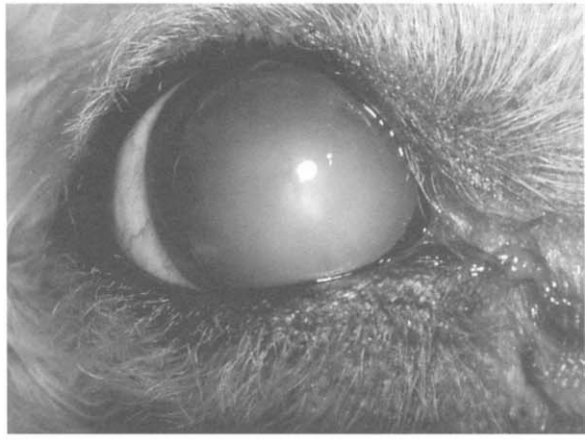


Figure 5. A mature cataract in a 16-year-old bichon frise.

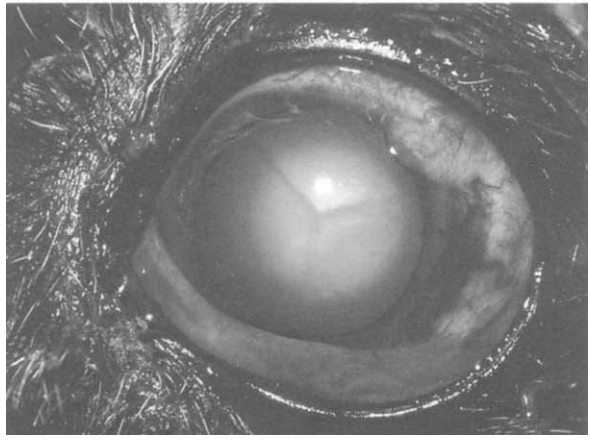


Figure 6. An 8-year-old mixed breed dog with diabetes mellitus. Note the suture "clefts." This is an intumescent cataract.

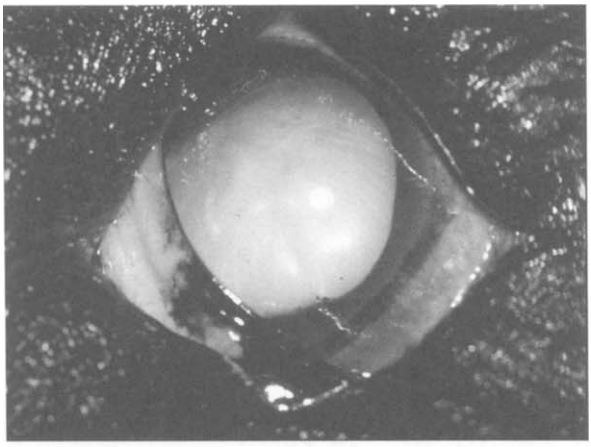


Figure 7. This mature cataract is luxated into the anterior chamber.

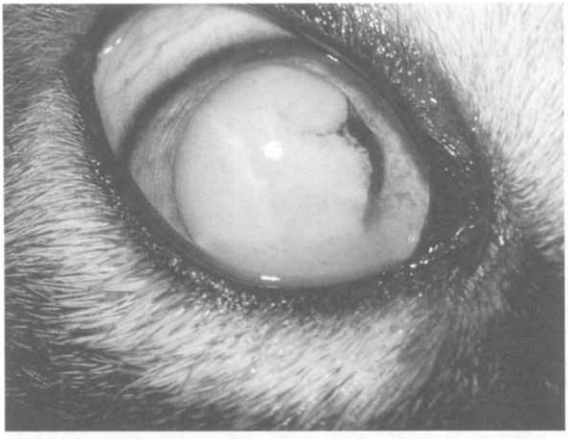


Figure 8. This cataract is hypermature with resultant uveitis. The medial aspect of the cataract is anteriorly subluxated.

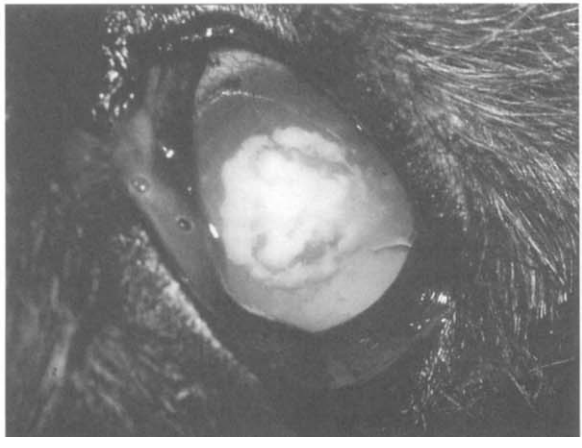


Figure 9. This nuclear cataract is what remains of this hypermature lens. It is termed a **morgagnian** cataract. This was an 11-year-old poodle.

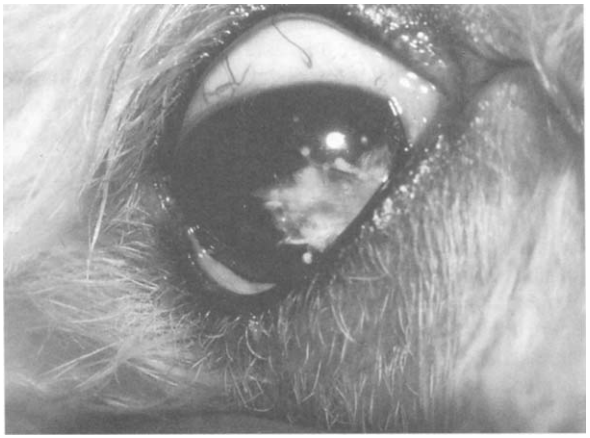


Figure 10. The opacity noted is mineralization on a wrinkled lens capsule, all that remains of a hypermature cataract following dissolution.

classification "juvenile" is not commonly used among veterinary ophthalmologists, probably because it contributes little in specifying the etiology of the cataract.

3. What is the difference between primary and secondary cataracts?

As with other conditions, **primary** cataracts are seen in the absence of other ocular or systemic abnormalities (such as microphthalmia, persistent hyaloid artery [PHA], retinal dysplasia, or diabetes mellitus). Primary cataracts in purebred dogs are often a heritable, autosomal recessive, breed-related condition, although the exact pattern of heritability in most cases is unknown. Mixed-breed dogs may also develop primary cataracts.

Secondary cataracts are those caused by other ocular or systemic abnormalities. Other than those listed above, ocular conditions that may lead to the development of secondary cataracts include uveitis (of any origin) and retinal disease (notably end-stage progressive retinal atrophy [PRA]). Cataracts occur with these conditions because of the presence of an abnormal intraocular metabolic environment. Put simply, the lens depends on the physiologic stability of its milieu to maintain clarity; when these strict conditions are altered, lens opacity may develop.

It can be difficult to differentiate a secondary cataract from a primary cataract with sequelae to the cataract. A full ophthalmologic examination and physical examination are necessary to rule out other causes.

4. What is nuclear sclerosis?

Nuclear sclerosis, also called **(senile) nuclear sclerosis** or **lenticular sclerosis,** is a normal aging change of the lens. It is characterized by a hardening (sclerosis) of the nucleus of the lens at about 7 years of age. This hardening represents the compression of lens epithelial cells (lens fibers) into the center of the lens as the mitotic activity of the peripheral lens epithelial cells progresses throughout life. Grossly, it is seen as a uniform pearly grey translucency (the nucleus) within the pupil, and if the pupil is dilated, the round border of the lens nucleus within the lens cortex may be distinctly visible, particularly when the eye is viewed in retroillumination. This condition is always bilateral, and the fundus should be visible through such nuclei via ophthalmoscopy. Nuclear sclerosis alone does not cause visual impairment that is readily discernable in animals. In humans, presbyopia (the farsightedness of age) accompanies nuclear sclerosis, but such fine changes in visual ability are not commonly observed in the behavior of animals with nuclear sclerosis.

5. How can nuclear sclerosis be differentiated from cataracts?

To distinguish cataracts from nuclear sclerosis, the technique of retroillumination can be used. This technique allows visualization of nuclear sclerosis and other subtle optical irregularities. The pupils are dilated (in nonglaucomatous animals, use 1 drop of 1% tropicamide OU and

wait 10–15 minutes for dilation), and the animal is examined in a darkened room with focal illumination. Nuclear sclerosis will reveal a visible nuclear border with a clearer periphery. The fundus should be visible using direct or indirect ophthalmoscopy; the dense nuclei should not block the path of light to the back of the eye.

Keep in mind that cataracts may exist in addition to nuclear sclerosis.

6. Is the location of focal cataracts significant?

Information regarding progression can sometimes be gained by properly identifying the location of a cataract within the lens. Without the aid of a slit-lamp biomicroscope, lens opacities can be distinguished from vitreal opacities, and the location of cataracts can be ascertained by examination in a darkened room with the patient's pupil dilated (see above). The patient and examiner should be positioned so that the patient's tapetal reflection is shining brightly back at the examiner. The light source is moved slowly from side to side into the patient's eye from about 6–12" while the observer remains stationary; the location of the opacities as they are silhouetted by the tapetal reflection (retroilluminated) are then observed carefully as they appear to move from side to side. Focal opacities in the lens will appear to move in the same direction as the light source; those in the vitreous will appear to move in the opposite direction. Opacities in the anterior half of the lens will move further and more rapidly than those in the posterior half. This technique utilizes the concept of Purkinje-Sansom images, and is based on the principles of parallax and the fact that the nodal point of the eye is located at the posterior pole of the lens.

Cataracts that are strictly nuclear are more likely to be developmental, congenital, and nonprogressive; those in the cortex of the lens are acquired and typically progressive and may eventually include the whole lens. Posterior polar cataracts, particularly if associated with blood, may be due to PHA. In some retriever breeds (golden, Labrador), triangular posterior polar cataracts are often very slowly progressive. Small, triangular, suture-tip opacities seen in the lenses of some puppies may resolve with time. Bilateral, small, pinpoint, diffusely scattered opacities may be due to hypocalcemia.

7. What are the consequences of having a cataract?

Of course, some vision loss is to be expected with cataracts that are large enough or axial enough to obstruct the passage of light to the retina. However, the degree of vision loss may be highly variable, and it can be very difficult to correlate degrees of behavioral vision loss with ophthalmic examination findings. It may also be difficult to compare degrees of vision loss between individual animals.

An important sequela to hypermature cataracts is uveitis. Lens-induced uveitis is caused by the leakage of antigenic lens material from the lens into the anterior chamber. Hypermature cataracts are the most likely type of cataract to incite anterior uveitis due to the dissolution of lens material. Anterior uveitis is characterized by blepharospasm, conjunctival hyperemia, miosis, aqueous flare, ciliary spasm and hypotony (low intraocular pressure [IOP]). More chronic or severe cases of lens-induced uveitis may have keratic precipitates, clots of fibrin, or, rarely, sterile hypopyon in the anterior chamber. Secondary glaucoma, retinal detachment, or phthisis bulbi may also result from chronic, severe, untreated lens-induced uveitis, leading to permanent blindness. Because some of the signs of uveitis are similar to those of glaucoma, it is essential that the IOP be measured when either uveitis or glaucoma is suspected.

Eyes with lens-induced uveitis should be treated for uveitis until the cataracts can be surgically removed. If no corneal epithelial defects are present, topical steroids and atropine are often effective at stabilizing the blood-aqueous barrier, reducing uveitis, and increasing ocular comfort. If the IOP is elevated, topical or systemic antiglaucoma drugs are also necessary (see Chapter 16), and mydriatics should not be used.

8. What are common dog breeds that develop primary cataracts?

As mentioned above, primary cataracts may be seen in both purebred and mixed-breed dogs. Examples of purebred dogs that develop primary cataracts include beagles, Boston terriers,

Chesapeake Bay retrievers, cocker spaniels, Doberman pinschers, dachshunds, English springer spaniels, German shepherds, golden retrievers, Irish setters, Labrador retrievers, Lhasa apsos, Norwegian elkhounds, Old English sheepdogs, poodles (toy, miniature, and standard), rottweilers, shih tzus, schnauzers (miniature and standard), Siberian huskies, and Yorkshire terriers.

New breed predispositions for cataracts are noted every year by veterinary ophthalmologists in the United States and throughout the world. Lists of these predispositions (for both cataracts and other ocular conditions) are printed in a publication by the American College of Veterinary Ophthalmologists entitled *Ocular Disorders Presumed to be Inherited in Purebred Dogs.*

9. Are there any specific breeding recommendations for dogs with cataracts?

The genetics of primary cataracts in most dog breeds have not been fully characterized or tested. In a number of breeds, primary cataracts have been found to be autosomal recessive in inheritance; in a few they are known to be autosomal dominant. Unknown degrees of penetrance make the elucidation of the genetics of canine cataracts even more difficult. However, familial tendencies and the possibility of a heritable component to primary cataracts often cannot be ruled out in an individual case. Consequently, breeding of any dog with even suspected primary cataracts is generally not recommended.

Conditions that can lead to secondary cataracts may or may not be heritable. Breeding recommendations in these cases should be made on a case-by-case basis depending on the cause.

10. Can cats develop cataracts?

Both domestic shorthair and various breeds of purebred cats have occasionally been seen with primary cataracts. Previously reported cases of primary cataracts in cats have been congenital in origin, sometimes associated with multiple ocular abnormalities. This author has seen several cases of what appeared to be primary, bilateral, acquired feline cataracts in domestic shorthair breed cats and kittens.

Lens diseases in adult cats are more commonly secondary to other ocular disease and are often due to long-standing anterior uveitis of any origin. Thus they may be accompanied by clinical signs of acute or chronic uveitis. Diagnostics and treatment for uveitis should be initiated if these are suspected.

11. What treatments are available for cataracts?

Although medical therapies have been attempted to treat and prevent cataracts throughout history, none have been proven to be widely successful.

Cataracts are most appropriately treated with surgical removal. However, not all eyes with cataracts are acceptable surgical candidates (see Chapter 20). Eyes that have cataracts secondary to retinal disease (e.g., PRA) are not considered appropriate cataract surgery candidates. If metabolic disease, trauma, or inflammation is the cause of cataracts, these conditions should be assessed, treated, and stabilized before cataract surgery.

In some cases, vision loss due to focal axial cataracts may be treated temporarily with pharmacologic mydriasis. If a cataract is small and in the axial lens, it may reduce vision, especially under bright lighting conditions when the pupil is small. Mydriasis may provide extra pathways for light to reach the retina if the peripheral lens is still clear. The entire lens should be examined (after pupillary dilation), and the IOP should be measured as normal before recommending this treatment. Pharmacologic mydriasis will not prevent progression of an established cataract. It is a symptomatic treatment that only allows for additional pathways for light to reach the retina. In addition, recall that parasympatholytic mydriatics (such as atropine) are also cycloplegics, which prevent ciliary muscle activity and accommodation of the lens. Thus, visual acuity may theoretically be reduced by parasympatholytic therapy due to the loss of accommodation. This is particularly true in eyes in which accommodation plays a significant role in vision (e.g., humans) and may not be clinically important in dogs and cats. Sympathomimetic therapy may be more appropriate for this type of therapy.

20. CATARACT SURGERY

Jane O. Cho, D.V.M.

1. When is cataract surgery indicated?

Cataract surgery is generally indicated when cataractous lenses obstruct the path of light to the retina; the goal of surgery is to improve vision by removing this optical obstruction. To this end, successful cataract surgery requires that other intraocular structures (most importantly the retina) be functional. Cataractous lenses may also be removed when they are the cause of other problems, including chronic lens-induced uveitis (e.g., when cataracts are hypermature or when lens rupture has occurred), phacomorphic glaucoma (glaucoma due to the presence of an enlarged, intumescent lens, which pushes the iris root forward, narrowing the iridocorneal drainage angle, and reducing outflow of aqueous), and cataractous anterior lens luxation (potentially causing acute pupillary block glaucoma). However, the most common indication for cataract extraction is vision loss due to the obstruction of light.

2. Are all eyes with cataracts candidates for cataract surgery?

No. Cataract surgery is an elective procedure, and preoperative conditions should be made as close to ideal as possible for the best success.

Eyes with active uveitis or any of its sequelae generally make poorer candidates for cataract surgery than those without uveitis. Uveitis should be medically controlled before cataract surgery can be considered. If a cause of uveitis other than a lens-induced etiology is suspected (such as a systemic infectious disease or ocular neoplasia), this possibility must be explored first.

Certain types of cataracts, such as those due to retinal disease, are not appropriate cataract surgery candidates. Many breeds of dogs that are predisposed to cataracts are also predisposed to progressive retinal atrophy (PRA). Because cataracts that develop due to PRA may be clinically indistinguishable from primary cataracts, additional diagnostics (electroretinogram [ERG] and ultrasound) must be used to rule out retinal disease.

Cataracts due to a persistent hyaloid artery (PHA) or persistent hyperplastic tunica vasculosa lentis/persistent hyperplastic primary vitreous (PHTVL/PHPV) may be associated with a patent hyaloid artery. The hyaloid artery is an embryonic vessel that is associated with the primary vitreous and travels from the optic disc to the posterior pole of the lens, supplying blood to the otherwise avascular developing lens. This vessel may feed a network of vessels (the tunica vasculosa lentis) that surrounds the lens. These vascular structures are present in the normally developing eye, but should be almost fully atrophied by 14 days of age. Persistence of a hyperplastic hyaloid artery or tunica vasculosa lentis may cause lens opacity, particularly at the posterior pole of the lens. Cataract surgery may be particularly difficult in cases of patent lens vasculature because of to the risk of intraocular bleeding. Waiting for regression of these structures may permit less complicated surgery.

3. How should one decide when cataract surgery should be performed?

Because the goal of cataract surgery is improvement of vision, the degree to which a cataract is currently causing visual deficits is important when considering the timing of surgery. There is much debate among ophthalmologists over how visually compromised an animal "should" be before the surgery can be considered necessary or helpful. Whereas some feel that a significant visual deficit due to the cataract should be present (e.g., completely ophthalmoscopically obscured fundus, absent menace response, bumping into objects in unfamiliar surroundings), others would consider a dog with a focal cataract and little visual deficit (e.g., mostly visible fundus, intact menace response, little or no hesitation in navigating unfamiliar surroundings) to be acceptable as long as a detectable, potentially progressive cataract was present. (Note that even an eye with a mature, blinding cataract will usually have an intact pupillary light response as long as the retina is functional.) The owners

should be involved in the decision to proceed with cataract surgery and be made aware of the advantages and disadvantages of each option. The visual status of the dog before surgery will have an impact on the impression of degree of visual improvement after surgery (Fig. 1).

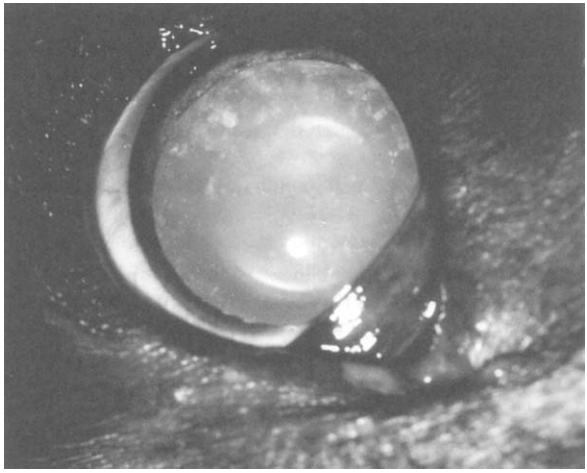


Figure 1. A 12-year-old chocolate Labrador retriever with nuclear sclerosis and multifocal cortical opacities. This Labrador is visual, and cataract surgery at this stage may not result in clinically evident visual improvement.

4. When a dog has a complete cataract in one eye and a small or no cataract in the other eye, should cataract surgery be performed?

In addition to the discussion above regarding the degree of preoperative visual deficit in a single eye, when considering the whole animal, regard must also be given to the degree of visual compensation that the fellow eye provides when considering surgery. As described above, much debate exists as to when cataract surgery is indicated in cases of asymmetrical cataract formation.

Before phacoemulsification techniques for cataract removal (see question 6) became widespread, older lens extraction techniques (extracapsular lens removal) required cataracts to be almost fully mature. This is the origin of the concept of waiting for a cataract to "ripen" before surgery. Now that newer lens removal techniques are widely available, cataracts of any degree of maturity (and even normal lenses) can be removed with similar degrees of success.

Arguments for the early bilateral removal of such asymmetrical cataracts include a potential reduction in pre- and postoperative complications and avoidance of a preoperative period of visual impairment. However, the early removal of a mostly normal lens would result in the loss of any accommodative ability that the normal parts of the lens might still be able to provide. The optical effects of aphakia may be reduced by the implantation of an intraocular lens (see question 10). Arguments that might support a plan to delay surgery (and monitor cataract progression, with possible lens removal later) include a greater improvement in post versus preoperative vision and the possibility of avoiding surgery altogether in the less affected eye.

Unilateral cataract surgery has been performed in dogs with a significant unilateral cataract and no or a small nonprogressive cataract in the fellow eye. Issues to be considered in unilateral versus bilateral cataract surgery include cost (often bilateral surgery is less than twice the cost of unilateral surgery), number of anesthetic episodes, number of postoperative/recuperation periods, the potential need to do surgery in the second eye at a later date, and the potential risks to the cataractous eye (lens-induced uveitis, glaucoma, or retinal detachment) while monitoring progression in the fellow eye.

As mentioned above, these issues should be discussed with the owner so that an informed decision can be made.

If monitoring for progression of the fellow eye is the chosen plan, the owner should be informed to watch for signs that might indicate that complications are developing. These include redness (conjunctival or scleral hyperemia), pain (blepharospasm, rubbing of the eye, depression),

generalized whiteness to the cornea obscuring the iris (corneal edema), and globe enlargement (buphthalmos due to chronic glaucoma).

In any case, early referral for individualized discussion with a specialist is never inappropriate.

5. What type of patient is the ideal cataract surgery candidate?

With the above caveats in mind, the ideal cataract surgery patient:

- Has vision loss solely due to the presence of cataracts
- Has lenses that are in place (nonluxated)
- Has no other ocular disease such as uveitis, keratoconjunctivitis sicca, glaucoma, or corneal opacities of any type
- Is tractable and will tolerate topical medication
- Is systemically as normal as possible (well-controlled diabetes, well-controlled hyperlipidemia) and can tolerate general anesthesia
- Has an owner or caretaker who is willing to administer multiple topical medications, potentially for long periods of time
- Has an owner or caretaker available to present the animal for recheck examinations
- Has an owner or caretaker who understands the risks and financial responsibilities required

While some of these characteristics are more important than others, it should be emphasized that cataract surgery is an elective procedure.

6. What are the techniques used for cataract surgery?

Currently in both animals and humans, cataracts can generally be removed using three techniques: intra- and extracapsular extraction and phacoemulsification. Laser technology for initial cataract extraction is experimental at this time and is not routinely used in animals.

Intracapsular cataract extraction (ICCE) or intracapsular lens extraction (ICLE) involves removal of the entire lens intact. The zonules holding the lens in place are broken down or dissolved before the lens can be removed using this technique. This is accomplished by the use of enzymatic zonulolysis (such as with a-chymotrypsin) or mechanical zonular rupture. Because the entire lens is extracted whole, a relatively large corneal incision must be made to accommodate the lens. This technique often disrupts the anterior vitreous face and may potentially dislocate the rest of the vitreous body and retina. The resulting aphakic eye ideally has vitreous behind the pupil, and the vitreous body is held in place by its peripheral attachments to the posterior ciliary body and retina, which are relatively weak.

Extracapsular cataract extraction (ECCE) or extracapsular lens extraction (ECLE) requires an initial removal of the central portion of the anterior lens capsule. This anterior capsulotomy is ideally a continuous curvilinear capsulorrhexis (CCC), formed by tearing ("-rhexis") of the capsule. A corneal incision is made large enough to accommodate the lens nucleus. The hard lens nucleus is then delivered using a broad instrument outside the eye to push the nucleus onto a second spatula-type instrument. Fibers of the lens cortex (which are adherent to the interior of the lens capsule) are then irrigated and aspirated out of the capsule. This technique ideally preserves the posterior capsule within the eye, leaving the vitreous undisturbed.

Phacoemulsification (PE) utilizes ultrasound energy delivered directly to the lens through a hollow needle-like probe. This probe is inserted into the lens through relatively small incisions in the cornea and lens capsule. Ultrasound energy is used to liquefy (or emulsify) the lens fibers, and the resulting liquified material is aspirated. A CCC is performed before or after phacoemulsification. After emulsification of the hard nucleus, removal of the adherent cortical lens fibers is performed using an automated irrigation/aspiration (I/A) handpiece. The posterior lens capsule is usually preserved with this technique, and the posterior segment of the eye remains untouched. Phacoemulsification is made possible by a machine that supplies electrical power to generate ultrasound energy, creates a vacuum enabling aspiration, and controls flow of irrigation fluids. This is currently the preferred technique for removal of most cataracts in both humans and animals.

"Phaco-" is the prefix denoting "lens" (from the Greek *phakos,* meaning "lentil" or "lentil-shaped object").

7. What is viscoelastic material?

Viscoelastic (often referred to as "visco") is a clear, gel-like material used for many purposes in intraocular surgery. It is used to maintain depth and normal anatomy of the anterior chamber, to provide a protective coating for intraocular structures, to atraumatically manipulate structures such as the iris and lens capsule, to hydrodissect the lens capsule away from the cortical lens fibers, and to tamponade hemorrhage. Its specific rheologic properties (viscosity, elasticity, pseudoplasticity, surface tension) make it ideal for these purposes. Various materials are used for visco, including hyaluronic acid, chondroitin sulfate, and hydroxypropylmethylcellulose. Different combinations of these substances in different concentrations provides a variety of visco products with a range or rheologic properties.

Visco is typically supplied in syringes and is injected through a blunt-tipped cannula.

8. Why is the anterior lens capsule removed in cataract surgery?

The interior surface of the anterior lens capsule is lined with a monolayer of viable lens epithelial cells. The lens epithelial cells located in the periphery (at the *lens bow*) normally undergo mitosis throughout the animal's life, with individual cells elongating and migrating centrally within the lens with maturation. Lens epithelial cells retain mitotic capability even after phacoemulsification. If left behind, they can proliferate and form clumps of lens-like material (called *lentoid*). This lentoid can both optically obstruct the pupil, mimicking a cataract, and serve as a continuing source of lens-induced uveitis. By removing a large area of anterior lens capsule, most lens epithelial cells will be removed, reducing the possibility of the postoperative lentoid production.

Removal of the anterior lens capsule will also allow the placement of an intracapsular intraocular lens (IOL). In this case, the anterior capsulotomy should be large enough to enable passage of the IOL into the capsule, but small enough to keep it there. The circular shape of an anterior CCC allows for maximal flexibility and stretch of the opening without tearing of the capsule.

9. Why is the posterior capsule left in place in cataract surgery?

Following routine extracapsular cataract procedures, the posterior capsule is left in place as a physical barrier between anterior and posterior segments. The presence of this capsular "diaphragm" can provide stability to the posterior segment of the eye, specifically the vitreous and the retina. An opening in the posterior capsule may allow vitreous to herniate into the anterior chamber, especially if the vitreous is degenerate and liquified. Anterior vitreal displacement may facilitate retinal detachment due to traction on the anatomic adhesions between the vitreous and retina. An intact posterior capsule also helps keep an intracapsular IOL in place.

Despite these advantages, in some cases an opening in the axial posterior lens capsule is made on purpose at the end of cataract surgery. This is generally done to treat or prevent axial posterior capsular opacities (PCOs), or opaque plaque-like areas in the center of the posterior lens capsule. These PCOs, if dense enough, can effectively mimic a cataract. They may be present at the time of cataract surgery or develop at any time after surgery. If severe enough at the time of primary surgery, removal of PCOs is performed at that time in order to improve optical clarity of the eye.

10. Why are IOLs used?

Prosthetic IOLs are used to improve the optics of an aphakic eye. An eye without a lens is severely hyperopic, or farsighted, since the lens is not present to focus incoming rays of light onto the retina. The image formed in an aphakic eye is focused at a plane behind the retina. In general, aphakic canine eyes are approximately +14 diopters (D) hyperopic. When an intraocular lens is used, incoming light rays are refracted such that this focal point is at the retinal plane (a condition called *emmetropia*), producing sharper images and a corresponding improvement in vision. In humans, preoperative measurements are made of the globe and cornea, and the proper optical strength required for an IOL for that particular eye is computed. Refractive studies have shown that most dogs require an IOL of approximately 41 D to establish emmetropia or near-

emmetropia. Emmetropia may be particularly important for a working dog that requires excellent vision for its job.

Another advantage to using IOLs is that they may reduce the degree of postoperative PCO formation. By directly contacting the axial posterior capsule, IOLs can reduce the amount of axial fibrous pseudometaplasia from migrating residual lens epithelial cells, thereby decreasing subsequent capsular folding and opacification.

Eyes with implanted IOLs are termed **pseudophakic.**

11. Are there any disadvantages to using IOLs?

Despite their great theoretical benefits, IOL use may be associated with some drawbacks. Implanting IOLs increases the cost and duration of cataract surgery. If an IOL eventually becomes displaced (decentrated) within the eye or remains mobile within the eye, any optical advantage the IOL once provided may be considerably reduced because the IOL may then produce distorted images on the retina. Current IOL technology in dogs requires that the initial corneal incision be significantly enlarged to place an IOL; a wider corneal incision can increase risk of both intra- and postoperative complications. Intraocular lenses that are placed in the anterior chamber (used sometimes in humans) or those that luxate from the posterior into the anterior chamber directly contact the anterior iris face, potentially leading to irritation and mechanical chafing of the iris. In addition, some ophthalmologists believe that the use of IOLs may lead to chronic postoperative uveitis. This uveitis may be so severe as to negate any benefit from the original cataract surgery. As a foreign body implanted within the eye, IOLs may induce chronic inflammation that may only be partially responsive to medical therapy (Fig. 2). Occasionally, explantation of IOLs are necessary when the IOLs become either excessively irritating or displaced.

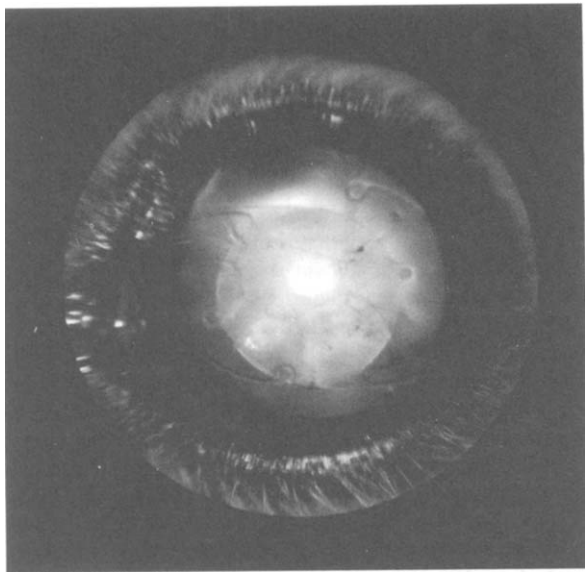


Figure 2. An IOL with a cloudy appearance. Cloudiness may be due to the presence of cells, proteins, and minerals on the IOL surface and opacity and wrinkling of the lens capsule. In this case, the fundus can still be visualized despite the opacity.

12. What do IOLs look like and what are they made of?

The basic design of IOLs includes a central optic, or lens, and peripheral supporting devices called **haptics.** The optic is a lens- or lentil-shaped clear structure that is to be placed in the pupillary path of light. This is held in place with any of a variety of supporting haptics, from curved (J- or C-shaped) arms to angled (V-shaped) arms to flat trapezoidal plates. Both haptics and optics often have small circles or loops cut into them to aid in proper IOL placement. The eventual location of the IOL (anterior chamber, intracapsular or "in-the-bag," "ciliary sulcus" or posterior chamber) and fixation method (sutured or sutureless) all determine the haptic shape and orientation (Fig. 3).

Various clear synthetic materials have been used to make IOLs, including polymethylmethacrylate (PMMA), acrylic and silicone. Lenses made of PMMA are rigid. Only thin structures made of PMMA (e.g., thin J-shaped haptics) can bend to any degree, but these will break if they are excessively stressed. Acrylic and silicone lenses are softer and potentially bendable. Some IOLs are made of two different materials (the optic of one material and the haptics of another) to take advantage the benefits of each.

Intraocular lenses with optics made of PMMA require corneal incisions large enough to accommodate them, usually 5–7 mm, about twice the size of the incision required to do phacoemulsification. Both silicone and acrylic are flexible, allowing bending or folding of the optic. These increasingly popular foldable lenses allow for smaller (3–4 mm) corneal incisions to be used in cataract surgery. The technology for such lenses is widely used in humans but is in an early stage of development in veterinary ophthalmology, and may gain more widespread use as techniques for their use advance.

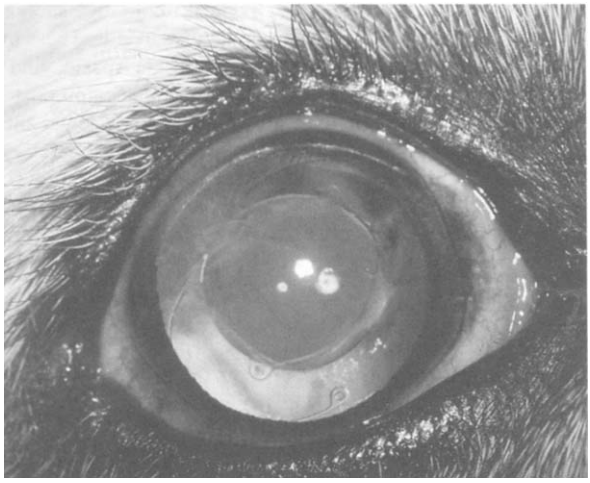


Figure 3. An IOL 19 months after surgery. The IOL is nicely centered in the lens capsule. There is no reaction to the IOL, and the owners claim that the dog has very good vision.

13. Do all eyes that have cataract surgery have an IOL placed?

Not necessarily. All the considerations discussed above should be weighed for the individual case. Surgeon preference is also very important. In addition, the question of which eyes are mechanically able to properly hold an IOL must be addressed.

The majority of IOLs placed in animals are intracapsular IOLs, so conditions of the lens capsule must be appropriate for ideal IOL placement. Secure and proper placement of intracapsular IOLs requires that the anterior capsular opening is the correct size and shape to both allow insertion of an IOL and retain the IOL after surgery. Because the haptics hold the lens in the capsule and keep the optic in the center of the capsule, the integrity of the lens **zonules** is important for keeping the capsule and IOL in an axial location. If an IOL is placed in a subluxated lens capsule (i.e, lens zonules are torn), the IOL will be correspondingly subluxated as well. The posterior lens capsule should be clear (or removed axially) to derive the full visual benefit of the IOL.

Removal of a lens via ICLE results in an eye with no lens capsule. In this case, a **sutured ciliary sulcus** IOL may be placed. This type of IOL is secured with haptics that are sutured to the sclera in two sites 180° apart just behind the iris and in front of the ciliary body. Risks of this procedure include hemorrhage, shifting/nonaxial optic positioning, and retinal detachment. Other methods of improving visual acuity in aphakic dogs (e.g., laser in situ keratomileusis [LASIK]) have been used only experimentally in dogs and are not in widespread use.

14. What is the typical postoperative medical regimen following cataract surgery?

The specific medical regimens used after cataract surgery are as varied as the surgeons doing the procedure.

- **Anti-inflammatories,** usually topical steroids, and less frequently topical nonsteroidal anti-inflammatory drugs (NSAIDs), are given after cataract surgery. These can be supplemented with systemic or subconjunctival anti-inflammatories. Anti-inflammatory drugs are given to counteract the anterior uveitis that invariably results from canine cataract surgery. Sutured surgical corneal wounds generally appear to heal well in the face of topical or systemic anti-inflammatory drug administration. However, these drugs should be temporarily discontinued if a corneal ulcer develops postoperatively and resumed as soon as possible after the ulcer heals.
- **Antibiotics.** Broad-spectrum topical or systemic antibiotics are usually given routinely during and after cataract surgery because of the invasive nature of cataract surgery. Though the risk of postoperative infection is remote, antibiotics may help to further reduce this risk.
- **Mydriatics/cycloplegics.** Topical mydriatics such as atropine or tropicamide are sometimes prescribed to treat postoperative uveitis. These may help to stabilize the blood-aqueous barrier, relieve painful ciliary muscle spasm, and reduce the possibility of posterior synechia development, particularly small-pupil posterior synechiae.
- **Antiglaucoma medications.** Topical or systemic antiglaucoma medications are occasionally prescribed to relieve an elevated postoperative IOP that results from postsurgical uveitis. If IOP elevation is not a primary condition (i.e., the animal does not have primary glaucoma), antiglaucoma medications may not need to be administered indefinitely. However, the decision as to when to discontinue antiglaucoma medications after cataract surgery should be left to the surgeon.

15. How soon after cataract surgery can an improvement in vision be expected?

Many dogs have a rapid improvement in vision after surgery (2–5 days). The degree of perceived improvement often depends on the degree of preoperative visual impairment, whether the dog is aphakic or pseudophakic, the individual dog's personality, activities, and lifestyle, and the dog's use of other senses. Then ability to judge a dog's vision is (by necessity) subjective at best and can be strongly influenced by external circumstances.

BIBLIOGRAPHY

1. Glover TD, Constantinescu GM: Surgery for cataracts. Vet Clin North Am Small An Pract 27:1143–1173, 1997.
2. Jaffe NS, Jaffe MS, Jaffe GF: Cataract Surgery and Its Complications, 5th ed. St. Louis, Mosby, 1990.
3. Miller TR, Whitley RD, Meek LA, et al: Phacofragmentation and aspiration for cataract extraction in dogs: 56 cases (1980–1984). J Am Vet Med Assoc 190:1577–1580, 1987.
4. Nasisse MP, Davidson MG, Jamieson VE: Phacoemulsification and intraocular lens implantation: A study of technique in 182 dogs. Prog Vet Comp Ophthalmol 1:225–232, 1991.

21. COMPLICATIONS OF CATARACT SURGERY

Jane O. Cho, D.V.M.

1. What intraoperative complications might be seen with cataract surgery?

Complications that occur during cataract surgery (phacoemulsification, extracapsular lens extraction) may be classified as minor or major.

Minor types of intraoperative complications include conditions that might make surgery difficult but not impossible, minimally change the postoperative results, and may be treatable in surgery. These include intraoperative miosis, lens subluxation, inappropriate lens capsular tears, minor bleeding, minor iris prolapse through the corneal incision, and vitreous expansion. **Major** complications include those that may substantially and adversely affect visual prognosis and possibly the prognosis for keeping the eye. These include lens fragment loss into the vitreous and expulsive choroidal hemorrhage.

2. Describe the different types of minor intraoperative complications and some ways to treat them.

Minor intraoperative complications, which are often responsive to treatment, include the following:

- **Miosis** limits the surgeon's visibility of the lens fibers and capsule. This makes lens removal more difficult and increases the risk of damaging the posterior capsule and iris. Intraoperative application of mydriatics (e.g., 0.1 ml of 1:10,000 epinephrine) into the anterior chamber may alleviate this.
- **Lens subluxation** can complicate surgery if the one-handed method of phacoemulsification is being used, because this technique relies on the physical immobility of the lens in the globe. Conversion to a two-handed technique or extracapsular lens extraction (ECLE) may be necessary if the mobility is severe.
- **Inappropriate lens capsular tears** can make the lens capsule unsuitable for proper intraocular lens (IOL) prosthesis insertion or may predispose to lens fragment loss or anterior herniation of vitreous. Anterior herniation of vitreous can make phacoemulsification much more difficult, and can eventually lead to pupillary block glaucoma, retinal detachment, or corneal edema.
- **Minor bleeding,** such as that which occurs when a conjunctival vessel is pierced in the process of suturing an incision at the limbus, usually causes minor hyphema that resolves spontaneously with time. Rarely, this bleeding may be more marked and require the use of wet-field cautery or intracameral (i.e., injection into the anterior chamber) vasoconstrictor drugs.
- **Iris prolapse** occurs when the surgical incision is excessively large, causing a portion of the iris to herniate out the wound. This can be controlled by shortening the incision length, applying intracameral miotic agents (e.g., carbachol), or utilizing viscoelastic material in a strategic manner.
- **Vitreous expansion** is a phenomenon in which the volume of the vitreous presumably increases and causes a forward pressure on the lens and lens capsules from behind the lens. This pressure tends to displace the intraocular structures in the direction of the incision and, again, make surgery hazardous. Some have advocated the intraoperative use of intravenous mannitol or highly viscous viscoelastic material for this problem. This condition usually resolves when the wound is closed.

3. What are the major surgical complications that can occur during cataract surgery?

Lens fragment loss is one potential complication of cataract surgery. If the lens is unstable, or if a break develops in the posterior capsule, the lens or fragments of lens material may escape

into the vitreous. Most cataract surgeons operate with the patient in dorsal recumbency, with the iris plane approximately parallel to the floor. Thus, if the vitreous is liquefied, these fragments may settle to the dependent position at the posterior-most aspect of the globe, on the retina. Such fragments can be very difficult or impossible to remove safely through the typical approaches used for cataract surgery and with standard cataract surgery instruments. When this occurs in humans, referral is made to a vitreoretinal subspecialist for vitrectomy and fragment removal. Unfortunately, few in veterinary ophthalmology are equipped or experienced in performing such procedures. Large fragments that are left in the vitreous may be a source of chronic, refractory inflammation and may lead to retinal detachment and other sequelae of posterior uveitis. Sometimes, small lens fragments isolated in formed vitreous remain inactive and uninflamed for long periods of time.

Expulsive choroidal hemorrhage is a very rare, but for obvious reasons, very serious intraoperative complication. This sudden, unpredictable, massive bleeding from the posterior segment makes further surgery on the lens impossible and may lead to blindness.

Fortunately, serious intraoperative complications are very unusual in routine cataract surgery.

4. How can the incidence of intraoperative complications be minimized?

Proper choice of surgical candidates can reduce the incidence of surgical complications. Dogs without active uveitis, luxated lenses, or corneal disease are better candidates than those with these conditions (see Chapter 21); these animals should be treated for these complicating conditions first. Adequate pre- and intraoperative treatment with anti-inflammatories and mydriatic agents can help control against excessive intraoperative inflammation and miosis.

Control of **patient positioning** can also reduce the incidence of surgical complications. Proper positioning of the patient under the operating microscope is critical to a good outcome. Position of the head must be changed as surgery is performed on each eye, and an experienced surgical nursing staff can facilitate this intraoperative adjustment. Adequate skeletal muscle paralysis (with assisted ventilation) is also very important to positioning. Ideal globe position, with no external pressure on the opened eye, is most easily achieved with full paralysis (using agents such as intravenous atracurium or pancuronium). Canthotomy, stay sutures, and other globe immobilization techniques may also be helpful.

Proper surgical equipment and an experienced surgeon and staff can make a considerable difference in the prevention and management of complications. Adequate lighting, an operating microscope with excellent optics that can be adjusted by the surgeon, high-quality instrumentation (including the ability to perform vitrectomy), appropriate viscoelastic materials, and most of all meticulous surgical technique will help to reduce problems.

As with any surgery, preparation for the most likely complications is prudent. Items such as injectable epinephrine, mannitol, and cautery are useful to keep in stock in case of emergency.

5. What are the most common immediate postoperative complications of cataract surgery? How are they treated?

Some of the more common problems seen in the first 12–72 hours following cataract surgery include uveitis, corneal edema, postoperative hypertension, corneal erosions or ulcers, hyphema, and hypotony or surgical wound leakage.

Virtually every dog that undergoes intraocular surgery experiences some degree of **postoperative anterior uveitis.** This develops for several reasons. One of the most commonly cited is the predisposition of the canine anterior segment to irritability, particularly when compared with the human anterior segment. Very little intraocular disturbance is required to incite anterior uveitis in dogs. In fact, one model of experimentally induced canine uveitis involves only the simple paracentesis of a small amount (0.1 ml) of aqueous. In addition to the dog's tendency for uveitis, the mechanical trauma of surgery—the insertion and removal of instruments into and out of the eye, the application of ultrasound, and the large amount of fluid circulated into the eye by the phacoemulsification handpiece (when this technique is used)—is a considerable stimulus for

uveitis. Good surgical technique minimizes uveitis. Postoperative uveitis is treated routinely by the use of topical, subconjunctival, and systemic anti-inflammatory drugs.

Corneal edema may develop around the surgical wound as fluid is imbibed by the stromal lamellae that have been exposed by incision. Mild diffuse corneal edema may also develop due to the generalized mechanical trauma of cataract surgery to the corneal endothelium. These forms of corneal edema are common following cataract surgery. They are typically transient and require no specific treatment.

Postoperative hypertension (acutely increased intraocular pressure [IOP] after surgery) is theorized to develop secondary to (1) a temporary alteration in the anatomy of the drainage angle due to surgery and (2) postoperative inflammatory products or viscoelastic material that "clogs" the angle. Depending on the IOP, this condition may or may not be treated. Topical and systemic antiglaucoma medications, intracameral tissue plasminogen activator to break up fibrin that may be blocking aqueous drainage, intracameral miotics to increase aqueous outflow, and sometimes the mechanical removal of fluid from the anterior chamber have been used to treat extreme postoperative pressure spikes. Judicious monitoring of IOP after surgery is always warranted.

Corneal erosions or ulcers may develop as an unwanted result of general anesthesia and exposure, the effects of which are exacerbated by the use of muscle paralytics. Self-trauma and the use of presurgical topical medications (which may be locally irritating or inhibit corneal healing) may also contribute. Surgeons must be mindful of this possibility and take preventative action wherever practical. Fortunately, these erosions tend to heal relatively quickly when treated appropriately (i.e., avoidance of topical steroids).

Hyphema (bleeding into the anterior chamber) may result from excessive activity, barking, self-trauma (rubbing, head shaking), neck trauma, uveitis, or retinal detachment. Postoperatively, cataract surgery patients should wear Elizabethan collars that are fitted appropriately, and should be kept quiet.

Hypotony (excessively low IOP) may be due to surgical wound leakage. This situation is best prevented by proper wound closure, but occasionally it is difficult to avoid. Flattening of the anterior chamber, a visibly leaking wound, or a positive Seidel test are telltale signs of wound leakage. Identification of wound leakage is facilitated by the use of dry cellulose sponges placed at the sutured wound edge. If leakage is detected, another attempt at suture placement or a conjunctival flap placed is necessary to remedy the problem. These procedures may require a second anesthetic episode. Alternatively, some have advocated the injection of a very small amount of saline or other fluid into the corneal stroma at the wound site in an effort to create enough swelling and corneal edema to seal the wound.

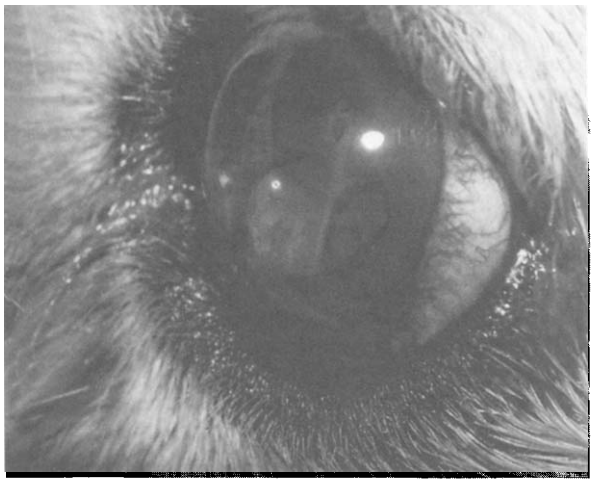


Figure 1. American cocker spaniel presenting several months after phacoemulsification and IOL placement surgery. Apparently uveitis resulted in fibrin formation, which luxated the IOL (lateral view).

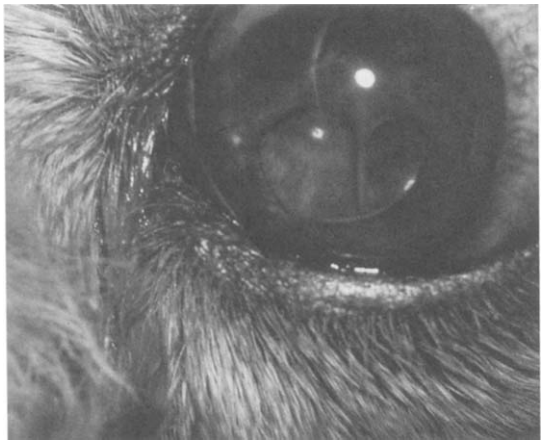


Figure 2. Same case as Figure 1 showing the frontal view.

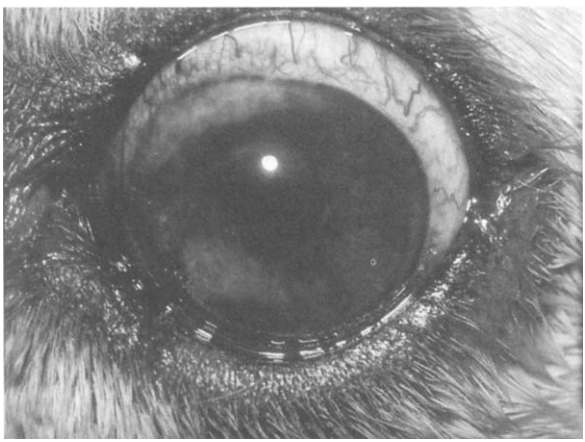


Figure 3. The IOL was extracted and the pupillary adhesions severed, giving an improved aphakic vision.

6. How is a Seidel test performed?

A Seidel test is performed by applying concentrated fluorescein dye to the cornea without irrigation, then observing the area in question with a blue light for fluorescein streaming. Visualization of a fluorescent apple-green stream of fluid from the pool of orange dye on the corneal surface indicates leakage.

7. How common is infection following cataract surgery?

Fortunately, the catastrophic complication of iatrogenic endophthalmitis (infection within the globe) as a result of cataract surgery is very rare in both dogs and humans. Despite the routine use of steroids before and after surgery and the high incidence of diabetic and geriatric cataract patients, there are very few cases of documented iatrogenic infection. This has been attributed to perioperative antibiotic use, effective local immunity, small potential inoculum size, low virulence of infectious organisms likely to enter the eye during surgery, and integrity of the posterior capsule (preventing posterior segment contamination).

8. What are the major long-term postoperative complications of cataract surgery?

The more common long-term complications ($\geq$ 3–6 months) after surgery include uveitis, posterior capsular opacity, secondary glaucoma, and retinal detachment. Uveitis may manifest in

a wide variety of ways. Corneal edema, keratic precipitates, anterior or posterior synechiae, uveal pigment dispersion in the anterior chamber, optically significant pupillary membranes and capsular opacities, pupillary seclusion, iris bombé, IOL luxation, and vitreal degeneration may result from chronic anterior or posterior uveitis (Figs. 1–3). Both retinal detachment and especially secondary glaucoma can develop due to chronic uveitis. Postoperative retinal detachment may also be a result of small preexisting retinal tears, which can be difficult to identify before surgery, as well as instability of the posterior segment (vitreous + retina) in the aphakic or pseudophakic eye. Removal of the lens contributes to this instability.

Overall, the short-term success rate for cataract surgery as performed by phacoemulsification has been quoted as 90–95% successful (favorable visual outcome at 4–5 weeks). This percentage of success tends to decrease with length of postoperative time considered.

9. Do cataracts ever grow back or re-form?

Once cataract surgery has been performed, a cataract does not regrow to form an entire new lens per se. However, lens remnants may proliferate and form an opacity that ultimately has the same optical effect as a cataract. Posterior capsular opacities (PCOs) may form when residual lens epithelial cells undergo fibrous pseudometaplasia, accumulate, or cause wrinkling of the capsule. These cells and the wrinkled capsule together can grossly appear to be translucent to opaque white, obstructing the path of light in the visual axis. Lens capsular opacification ("aftercataract") is the most common complication following cataract surgery in humans, often requiring surgical intervention.

Lens epithelial cells may also proliferate and accumulate to form a gray, globular material called **lentoid.** This material may also block the visual axis. Lentoid accumulation is more likely to occur in younger animals and in cases where the lens epithelial cells have not been completely aspirated from the lens capsule. Lentoid may build up in the periphery between the anterior and posterior lens capsules, forming either clumps ("Elschnig's pearls") or a doughnut shape ("Söemmering's ring"). If exposed to the intraocular environment, it may be a source of chronic uveitis that will only be resolved by its removal. However, if it eventually becomes sealed off to the intraocular environment in the contracting anterior and posterior lens capsule, it is less likely to incite lens-induced uveitis or obstruct the visual axis.

10. What can be done about PCOs and lentoid?

Significant PCOs that cause noticeable visual impairment have been treated with both laser and surgical capsulotomy. The goal of these procedures is to create an optical clearing in the visual axis. Laser capsulotomy is commonly performed using an Nd:YAG laser as a noninvasive procedure. Laser energy is directed through the clear ocular media to any point in three-dimensional space. Each application of energy causes a focal dissolution of tissue, and laser spots can be made to form a continuous curvilinear, cruciate, or spot pattern depending on the PCO shape and orientation. Surgical capsulotomy is performed by using an intraocular needle or scissors to cut the capsule and move the PCO away from the axis. The PCO may then be fully excised and removed from the eye. If lentoid is causing uveitis or visual impairment, it is often readily removable with irrigation/aspiration. Thorough lentoid removal is simplified if the lentoid is not sealed off by lens capsule or blocked from surgical access by an IOL.

11. Does IOL implantation change the rate of complications?

The complication rate of cataract surgery in dogs without IOLs was not noted to be significantly different from that with IOLs in one study, but detailed comparison in large-scale, long-term studies have not been performed.

Potential complications specifically associated with IOL use include IOL decentration, iris capture, and uveitis. Decentration, or a shift of the IOL's position from the visual axis, is not uncommon in humans. The IOL may tilt, luxate or subluxate, or come out of the capsular "bag," or a haptic or the optic may get caught in the pupil (iris capture). Decentration may be exacerbated by changes in the lens capsule that occur after surgery. Sutured-in IOLs (that have been placed in

the ciliary sulcus after intracapsular lens extraction) are less likely to luxate, but may tilt or rotate in place since they are secured at only two sites. Such alterations in the IOL position can be visually distorting in humans, but seem to be rarely behaviorally significant in animals. Chronic uveitis may arise when an IOL is used, regardless of how unreactive the IOL material or surface is (see Chapter 20). Deposits of pigmented and unpigmented cells on the IOL surface, fibrinous or fibrous membranes on the IOL, and posterior synechiae are some of the more common potential sequelae to such uveitis. As noted in the prior chapter, IOL use may also reduce the incidence of some complications; IOLs may decrease the amount of PCO formation, because the IOL contacts the lens capsule and thus reduces the migration of lens epithelial cells (see Chapter 20, question 11).

BIBLIOGRAPHY

1. Glover TD, Constantinescu GM: Surgery for cataracts. Vet Clin North Am Small An Pract 27:1143–1173, 1997.
2. Jaffe NS, Jaffe MS, Jaffe GF: Cataract Surgery and Its Complications, 5th ed. St. Louis, Mosby, 1990.
3. Miller TR, Whitley RD, Meek LA, et al: Phacofragmentation and aspiration for cataract extraction in dogs: 56 cases (1980–1984). J Am Vet Med Assoc 190:1577–1580, 1987.
4. Nasisse MP, Davidson MG, Jamieson VE, et al: Phacoemulsification and intraocular lens implantation: A study of technique in 182 dogs. Prog Vet Comp Ophthalmol 1:225–232, 1991.
5. Nasisse MP, Davidson MG, Jamieson VE, et al: Phacoemulsification and intraocular lens implantation: A study of surgical results in 182 dogs. Prog Vet Comp Ophthalmol 1:233–238, 1991.
6. Smith PJ, Brooks DE, Lazarus JA, et al: Ocular hypertension following cataract surgery in dogs: 139 cases. J Am Vet Med Assoc 209:105–111, 1996.

V. Neuro-ophthalmology

22. NYSTAGMUS

Alexander deLahunta, D.V.M, Ph.D.

1. What is nystagmus?

Nystagmus is an involuntary movement of the eyes associated with vestibular or visual stimuli. The oscillations can be horizontal, rotatory, or vertical. The excursions can be equal in extent, which is called **pendular nystagmus,** or they can consist of a fast and slow phase, which is a **jerk nystagmus.** The latter is the most common.

2. What does a right nystagmus mean?

Nystagmus is defined by the direction of the fast phase of the jerk nystagmus.

3. Is nystagmus always abnormal?

No. Normal vestibular nystagmus occurs when you move your head in any direction. When the head is moved in a horizontal plane to the right, the eyes will stay focused on an object in their visual field, and as the head moves out of that field, the eyes will suddenly jerk in the direction of the head movement. This is referred to as **physiologic** or **vestibulo-ocular nystagmus.**

4. Will this vestibulo-ocular nystagmus occur in a blind dog?

Yes. The anatomic pathways involved do not include the visual pathways.

5. What is the anatomic pathway involved?

The vestibular portion of the eighth cranial nerve carries impulses generated in the hair cells of the maculae and cristae ampullaris of the membranous labyrinth of the inner ear that constantly monitor the position and movement of the head. Vestibular neurons responsible for eye movements synapse in the vestibular nuclei of the pons and medulla. Neurons in these vestibular nuclei project rostrally in the medial longitudinal fasciculi of each side to synapse on the extraocular somatic efferent neurons in the abducent, trochlear, and oculomotor nuclei. Testing this normal nystagmus serves to evaluate both this vestibular pathway and the somatic efferent neurons. In the horizontal nystagmus that results, the ocular abduction is a function of the medial rectus (oculomotor nerve), and the abduction is a function of the lateral rectus (abducent nerve).

6. Are there any other ways to stimulate normal nystagmus?

Yes. Nystagmus can be generated by the convection currents in the endolymph that results from the irrigation of the external ear canal with cold or warm water. This is called **caloric nystagmus. Postrotatory nystagmus** is the brief nystagmus that occurs after an animal has been spun rapidly in a circle and then stopped. When the spinning stops the endolymph continues to flow for a brief period, and this stimulates a jerk nystagmus directed to the side opposite to the direction of the spin. **Optokinetic nystagmus** can be generated by the visual stimulus on observing a rotating striped drum. Caloric and optokinetic nystagmus are impractical in veterinary medicine as is the postrotatory in a patient that is too large to be picked up.

7. What is an abnormal nystagmus?

The presence of a continual jerk nystagmus with the head motionless in any position. This is a spontaneous or resting nystagmus. Positional nystagmus is that which occurs with the head placed in positions other than the normal resting posture. It may be brief or continuous in these positions. Positional nystagmus is usually looked for with the head held with the neck flexed to either side and in extension or with the animal held in dorsal recumbency. The extent of these observations will be limited by the size and tolerance of the patient.

8. What is the cause of this nystagmus?

There is a constant transmission of impulses from the epithelial receptors to the vestibular nuclei responsible for keeping the eyes in normal position with the head. Any interruption that results in an imbalance in the transmission of these impulses can result in abnormal nystagmus. This interruption can be at the level of the vestibular nerve or the nuclei in the brain stem or the cerebellar structures that function with the vestibular system.

9. Students agonize over trying to remember what the direction of the nystagmus means. How can this be simplified?

The only constant is that when the disorder involves the peripheral portion of the vestibular system, the nystagmus will always be directed to the side opposite to the lesion. In other words, with a left head tilt and loss of balance to the left, the nystagmus will be horizontal or rotatory to the right.

10. How do I tell the direction when it is rotatory and especially with the round pupil of the dog?

Estimate the 12 o'clock position of the iris and determine the direction of the fast movement from there.

11. If the lesion is on one side of the brain stem or cerebellum what will the direction be?

Any direction! Often it will be opposite of the side of the lesion, and therefore you must look for other reasons to implicate the central components of the vestibular system in your anatomic diagnosis.

If the nystagmus is directed toward the side of the lesion, is vertical, or changes direction with different positions of the head, the lesion is in the central components of the vestibular system.

12. Does the abnormal nystagmus always affect both eyes?

Usually. It is very rare to see only one eye affected, but sometimes the nystagmus is less in one eye.

13. When does a pendular nystagmus occur?

Most often this is a congenital disorder that is idiopathic or is related to an abnormal development of the visual pathways. Many Siamese cats have more than the normal number of optic nerve fibers that cross in the chiasm and therefore have a different architecture of the lateral geniculate nuclei. These cats sporadically exhibit a fine pendular nystagmus. An inherited failure of crossing of the optic nerves occurs in Belgian sheepdogs. These achiasmatic dogs have a severe constant pendular nystagmus.

14. Is pendular nystagmus ever acquired?

Only as part of a diffuse whole body tremor such as occurs with numerous poisonings or in the severe form of the canine " shaker syndrome," which is an immune-mediated central nervous system disorder that responds to immunosuppressant therapy.

15. Is there ever a situation when no nystagmus (normal or abnormal) can occur?

Yes. When the vestibular receptors in both inner ears do not form, undergo abiotrophy early in life, or are destroyed by a progressive lesion such as bilateral otitis interna.

BIBLIOGRAPHY

1. deLahunta A: Veterinary Neuroanatomy and Clinical Neurology, 2nd ed. Philadelphia, W.B. Saunders, 1983.

23. THE PUPIL

Ronald C. Riis, D.V.M., M.S.

1. What is the most obvious pupil clinical sign?

The normal pupil symmetry in all lighting intensities is the characteristic we are all comfortable with. Each species has a pupil conformation appropriate for its evolutionary needs. The abnormal pupils are those showing asymmetrical size in similar lighting intensities or asymmetrical reactions to light challenges.

2. What controls the size of the pupil?

Animal pupils are influenced by smooth muscle to either dilate or constrict the pupil. The iris dilator muscle causes pupillary dilation and is innervated by the sympathetic nervous system. The iris sphincter muscle causes pupillary constriction and is innervated by the parasympathetic nervous system. These muscles can balance one another or override one another. When sympathetic tone is increased, the pupil is larger. When parasympathetic tone is increased, the pupil is smaller. Avian and reptile pupils are influenced by skeletal muscle.

3. What is the light reflex pathway for the positive pupillary reflex?

The pupillary light response begins with the rods and cones of the retina. Afferent pupillomotor fibers travel through the optic nerves and optic tracts and exit before the lateral geniculate body to enter the brain stem. Pupillomotor fibers synapse in the pretectal nuclei, which then project to the ipsilateral and contralateral Edinger-Westphal nuclei. The pupillary fibers travel with the third cranial nerve (CN III) into the orbit where they synapse at the ciliary ganglion. Postganglionic fibers innervate the iris sphincter and cause pupillary constriction when stimulated.

4. What is the pathway for dilation or sympathetic pupillary reflex?

The first-order neurons began in the hypothalamus. The fibers travel caudally to terminate in the intermedial lateral cell column of the cervical and thoracic spinal cord. Pupillomotor fibers exit from the spinal cord at T1–T3 and ascend the sympathetic chain to synapse in the superior cervical ganglion, constituting the second-order neuron. The third-order neuron begins with postganglionic fibers of the superior cervical ganglion. These fibers ultimately reach the orbit's ciliary body and dilator muscle via the ciliary nerves.

5. What is an afferent pupillary defect and how should you examine for it?

In animals, use the swinging flashlight test to elicit a relative afferent pupillary defect (rAPD). If you shine a light into one eye of a normal animal, both pupils constrict to the same amount. If you swing the light over the other eye, the pupils stay the same size or constrict minimally. In animals with an rAPD, the affected eye behaves as if it perceives a dimmer light than the normal eye; therefore, both pupils constrict to a lesser degree when the light is shone in the affected eye. For example, if you shine the light in the right eye of a patient with left rAPD, both pupils constrict. If you swing the light to the left eye, it is perceived as dimmer and the pupils dilate. Note, however, that if both eyes are equally abnormal, there may be no rAPD.

6. Can the swinging flashlight test differentiate lesion locations for causes of anisocoria?

A positive swinging flashlight test is pathognomonic for unilateral retinal disease, unilateral prechiasmal optic nerve disease, or both. Sometimes during the swinging flashlight test, a normal pupil will dilate slightly during direct light stimulation but only after the initial contraction from the stimulus. This **pupillary escape** is a normal response resulting from adaptation of the stimulated retina, and it should not be confused with the pathologic dilation resulting in a "positive"

swinging flashlight test when direct light is shifted from the good eye to the bad eye. Nor should pupillary escape be confused with hippus.

7. If an animal presents with an afferent pupillary defect, where is the lesion?

The lesion could be anywhere in the afferent pupillary pathway to cause a rAPD. You must rule out retina, optic nerve, optic chiasm, and optic tract (pupillary fibers exit the optic tract prior to the lateral geniculate body; therefore, lesions posterior to the lateral geniculate body don't cause rAPD). A large retina lesion causes rAPD. An optic nerve lesion causes rAPD in the ipsilateral eye. A lesion in the optic chiasm may cause an rAPD if one optic nerve is affected more than the other. A large lesion of the chiasm affects both pupils. An optic tract lesion causes an rAPD in the eye with the most visual field loss. A mass lesion of the optic tract produces rAPD in the ipsilateral eye, but an ischemic lesion causes rAPD in the contralateral eye. A lesion in the brain stem in the area of the pretectal nuclei may cause rAPD without visual defects.

8. What is the diagnosis of an animal with unequal pupils or asymmetrical pupils?

Anisocoria, which is a difference in size between the two pupils. The question is, which pupil is normal?

9. How should anisocoria be explored?

Examine the pupil size in both bright and dim light. If the anisocoria is greater in bright light, the larger pupil is abnormal and constricts poorly—usually because of a defect in parasympathetic innervation. If the anisocoria is greater in dim light, the smaller pupil is abnormal because it dilates poorly—usually because of a defect in sympathetic innervation. If the difference in size remains the same in both bright and dim light, the anisocoria is physiologic or anatomic and not pathologic. In cats, don't forget the spastic pupil syndrome as a differential. These cats may have pupils alternating in size between their eyes, with or without intervals of normal pupils with equal appearance. This syndrome results from a viral neuritis and has been reported associated with feline leukemia complex.

10. What are some rule-outs for a unilateral dilated, poorly reactive pupil?

- CN III lesion
- Pharmacologic paralysis (anticholinergic block from medications such as atropine or tropicamide)
- Adie's pupil
- Anatomic lesion (adhesions—anterior or posterior synechiae secondary to trauma or inflammation; senile iris atrophy; congenital anomalies such as colobomas)
- Retinal detachment—partial or incomplete
- Glaucoma
- Anteriorly luxated lens

11. What is an Adie's pupil?

Adie's pupil is a postganglionic defect in the parasympathetic innervation to the pupil. These animals present with a dilated pupil that may have a slightly irregular shape that shows segmental iris constriction with a slit lamp. These pupils also may show slow and tonic constriction and redilation phases. This condition is generally benign and thought to be a denervation.

12. How do you test for an Adie's pupil?

An Adie's pupil constricts with dilute pilocarpine (0.125%), whereas a normal pupil does not. This confirms a denervation hypersensitivity.

13. How do you treat an Adie's pupil?

Usually, the chronic condition requires no treatment because tolerance seems develop. The acute conditions may present with photophobia and tearing especially in bright lighting circumstances. Miotic medication will overcome these symptoms (i.e., pilocarpine, phospholine iodide, neostigmine). Keep in mind that miosis may have as many discomfort signs, if not more, than an Adie's pupil.

14. What are some causes of a unilateral, constricted, poorly reactive pupil?

- Horner's syndrome
- Pharmacologic stimulation
- Corneal lesion
- Neoplasia
- Synechia
- Persistent pupillary membranes
- Uveitis
- Brain stem lesion

15. What is included in the differential diagnosis for bilateral, widely, dilated unresponsive pupils?

- Optic neuritis
- Central nervous system lesion
- Sudden acquired retinal degeneration (SARD)
- Detached retinas
- Progressive retinal atrophy (PRA)
- Luxated lenses
- Glaucoma
- Mydriatics
- Dysautonomia

16. Is there a pupillary abnormality in poorly pigmented animals?

In the dog and cat, white hair coat, blue iris, and deafness have been studied. A white hair coat in the cat and other species results from a dominant gene *W*. Cats with unilateral blue irides and albinotic fundus have larger pupillary apertures in that eye. In a group of 185 white cats, 125 (68%) had blue irides, and 101 (55%) were deaf, whereas 68 (32%) had yellow irides and just 13 (2%) were deaf. Electroretinograms from these cats were normal, suggesting the anisocoria was an anatomic difference. Dogs with blue irides do not have anisocoria unless accompanied by iris colobomas, persistent pupillary membranes, iris cysts, dyscorias, or corectopia (Figs. 1–3). Blue

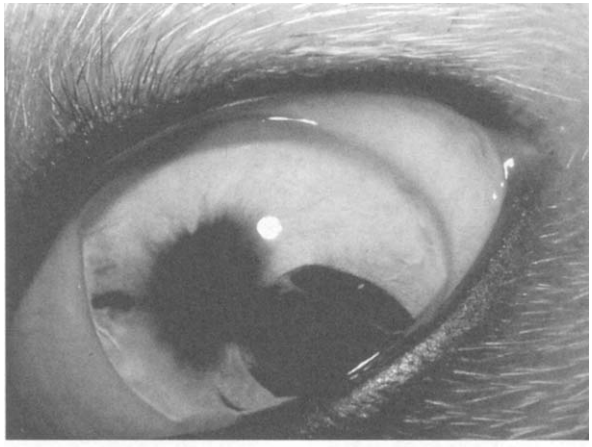


Figure 1. Great Dane showing an iris colobma that must be differentiated from polycoria (two or more pupils in one iris).

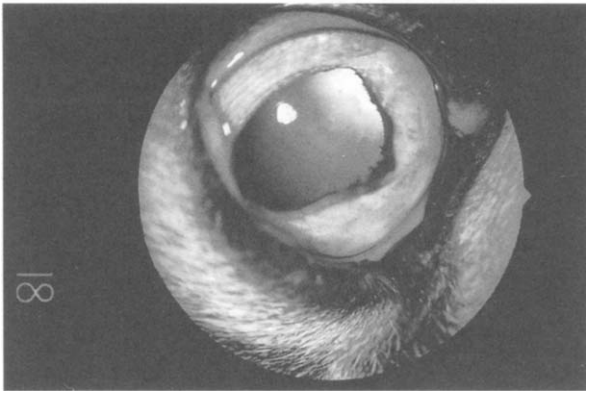


Figure 2. Dog iris dyscoria (an abnormality in the shape of the pupil) caused by a ciliary and iris mass.

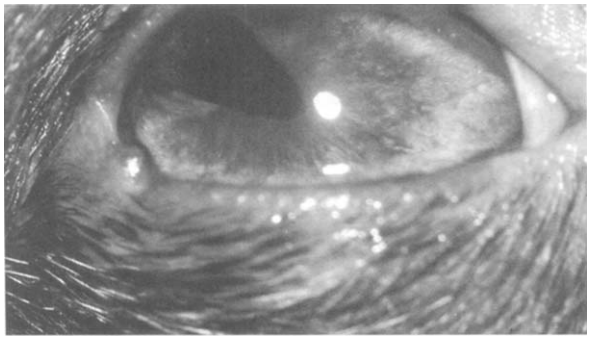


Figure 3. Toy fox terrier with corectopia (an eccentric location of the pupil).

irides associated with partial or complete albinism or merle hair coat have been attributed to an incomplete dominant gene or a recessive trait with incomplete penetrance, respectively.

17. How and where can the most brisk pupillary reflex be elicited from a dog or cat?

Use a focal bright light source directed into the temporal fundus from the medial canthal area of each eye.

18. What is the consensual or indirect pupillary light reflex?

The consensual or indirect reflex is the constriction of the pupil not stimulated by light but generated by the opposite illuminated eye.

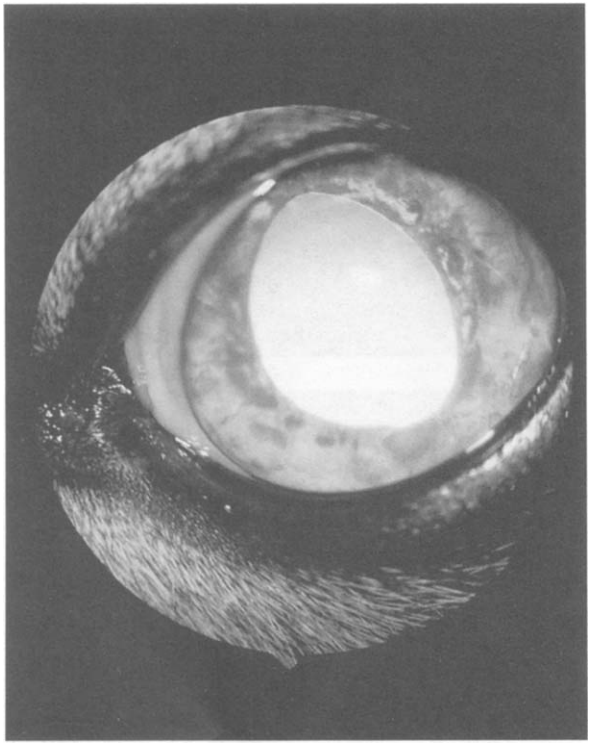


Figure 4. Cat pupil with dyscoria caused by an anterior uveitis. Note the nodular discolorations within the iris stroma. Toxoplasmosis was the etiology.

19. Does a positive direct or indirect pupillary reflex imply normal vision?

No. Only a few functioning photoreceptors are necessary to activate the pupillary light reflex.

20. Does that mean the pupillary light reflex in bilateral cataract cases is not a reliable way to predict normal retinal function?

Retinal function should be evaluated with electroretinograms, especially when the retinas cannot be ophthalmoscopically examined and the animal is blind. This is a mandatory preoperative evaluation for all cataract patients (Figs. 4–8).

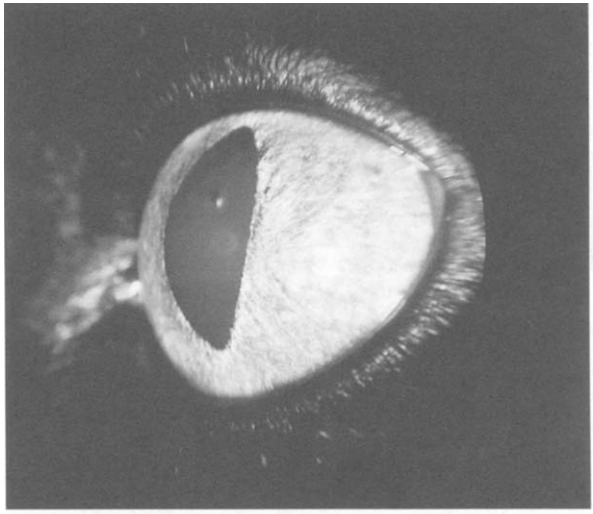


Figure 5. Cat pupil with dyscoria secondary to a luxated lens with forward displacement of lens and vitreous causing an extremely narrow anterior chamber.

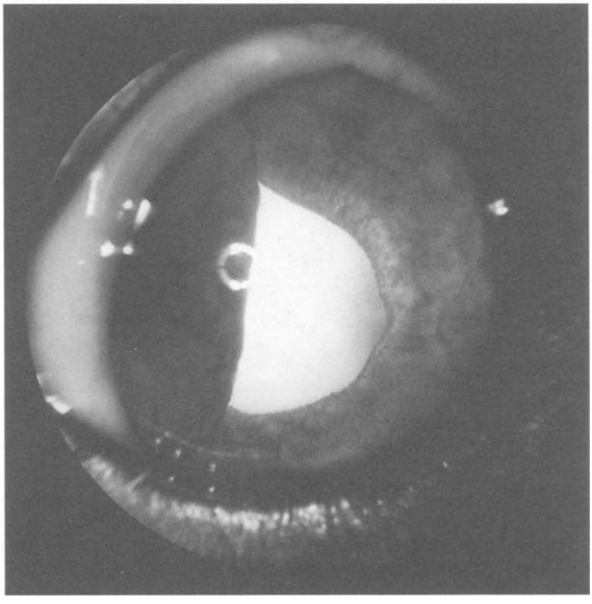


Figure 6. Dog with D-shaped pupil caused by infiltrating lymphosarcoma cells.

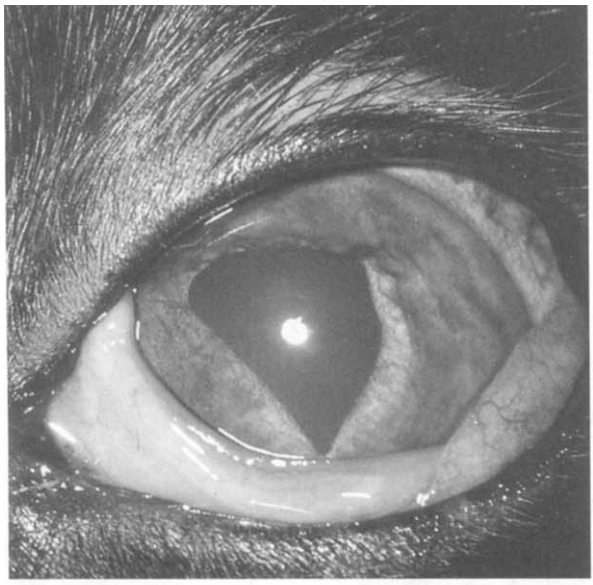


Figure 7. Cat dyscoria caused by a melanoma proliferation of the iris.

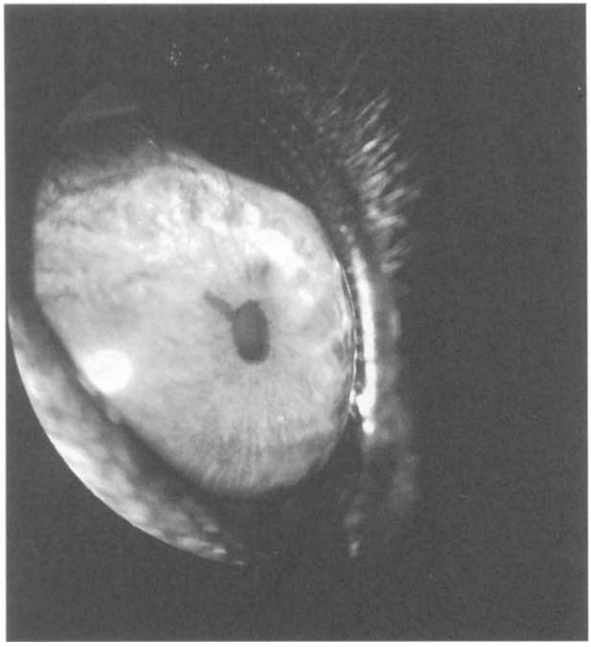


Figure 8. Dog miosis secondary to a uveal melanoma.

BIBLIOGRAPHY

1. Canton DD, Sharp NJH, Aguirre GC: Dysautonomia in a cat. J Am Vet Med Assoc 192:1293–1296, 1988.
2. Coulter DB, Martin CL, Alrarado TP: A cat with white fur and one blue eye. Calif Vet 9:11, 1980.
3. Scagliotti RH: Comparative neuro-ophthalmology. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Philadelphia, Lea & Febiger, 1999, pp 1307–1400.
4. Turner P, Robinson R, Dyte CE: Blue-eyed albino: A new albino allele in the domestic cat. Genetica 56:71,1981.

24. OPTIC NEUROPATHIES

Jeffrey S. *Smith*, BVSc, FACVS

1. What does a blink response to the menacing gesture test indicate?

There is more to this test than a crude assessment of vision.

The response is initiated by the animal visualizing the gesture and interpreting it as threatening. This requires afferent input from the retina, the optic nerve, and its radiations to the visual cortex. Fibers from the cerebral cortex travel via the cerebellum to the nucleus of the seventh cranial nerve (CN VII). The efferent facial nerve travels through the petrous temporal bone to innervate muscles of facial expression, such as the orbicularis muscle closing the eyelids together.

Remember, the animal must regard the gesture as menacing. Very young animals will not blink because they have little negative experience associated with this challenge. Similarly, depressed or trusting animals may not blink, giving a misleading interpretation.

Disturbing tactile hairs around the eyes by touch or air movement when performing the gesture will initiate a blink response (CNV and VII).

2. Upon assessment of an animal with a hypermetric gait and other signs of cerebellar disease, you judge the animal visual and able to blink but not in response to a menacing gesture. How do you explain these findings?

As previously mentioned, the cerebellum is a conduit for messages from visual cortices to facial nuclei. Cerebellar diseases such as neoplasia or cerebellar hypoplasia are possibilities (Fig. 1).

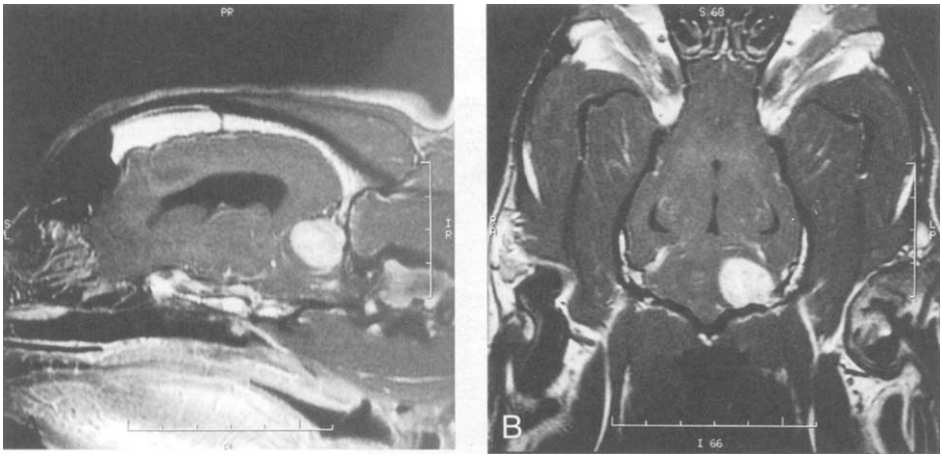


Figure 1. MRI demonstrating a unilateral cerebellar mass lesion right side. The dog did not blink in response to a menacing gesture to the right eye despite having normal vision. (Courtesy Sydney University Veterinary Clinic.)

3. Which cranial nerves are involved in the eye preservation blink reflex following tactile stimulus?

Air puffer (syringe) or touch will stimulate CN-V afferents, which communicate with the facial nuclei in the medulla. CN-VII responds by inducing lid closure (as well as reflex tearing).

4. Your patient is an elderly Pekingese dog with bilateral corneal pigmentation and scarring. Touching the cornea with a cotton swab fails to elicit a blink response. Is this likely a problem in the afferent or efferent arm of the reflex?

Brachycephalics have fewer afferent CN-V sensory nerve endings in the cornea than dolichocephalics. This results in reduced frequency of blinking, reduced tear film spread, and chronic keratitis. These complications lessen the compromised corneal sensitivity to compound the problem (i.e., both arms of the reflex are involved).

5. A persistent superficial corneal ulcer in a middle-aged dog will resolve only partially with your treatment for indolent ulceration. Blepharospasm, an indication of corneal pain, is surprisingly absent. Have you checked the response to tactile stimulation?

The dog blinks when under observation but not in response to touching the cornea. Similarly, eyeball retraction is not initiated by touch. Conclude a sensory CN-V lesion. The corneal epithelium is dependent on normal CN-V innervation. Denervation can result in a nonhealing ulcer. It is important to provide added lubrication to the cornea until the problem resolves or the cause of the deficit is determined. Tarsorrhaphy is also an option. Determine sensory function of the other divisions of CN-V (e.g., the lateral canthus and nares, testing the maxillary branch). Look for evidence of other neuropathies such as facial palsy or cerebellar signs, which point to central verses peripheral disease.

6. Can the lesions responsible for failure of the efferent arm of the blink reflex (i.e., lesions of CN-VII, the facial nerve) be localized?

In these cases, sensation (afferent CN-V) is normal. The animal will retract the eye (CN-VI) and perhaps withdraw its head, but it will fail to blink. The extent of the facial paralysis must be determined. Check for ear and lip droop (Fig. 2). Check for taste sensation with atropine applied to the rostral part of the tongue on the affected side. Taste buds are innervated by special branches of the facial nerve. Check for normal tear production and nostril wetting (see Chapter 10). Concomitant hypalgesia indicating CN-V involvement points to a central (brain) location of lesions.

Figure 2. Lamb with ear and lip droop because of facial palsy.

7. How important is the petrous temporal bone and the inner ear in cases of facial paralysis in the dog?

The facial nerve courses through the petrous temporal bone giving off branches to the lacrimal gland and salivary glands en route to the stylomastoid foramen from where it exits the skull to innervate muscles of facial expression. Inner or middle ear disease such as infections and petrous osteitis can impair CN-VII function. Many cases of otitis media-interna are low-grade, chronic infections that may not carry obvious clinical signs, and facial paralysis is written off as idiopathic. Otitis externa may not be present. All cases of facial paralysis (and Horner's syndrome) should be given a careful evaluation of the middle ear; this includes radiography of the petrous temporal bone. Increased yawning may be an added sign exhibited. Vestibular signs (e.g.,

nystagmus) may be present as a result either of inner ear involvement or of a lesion in the brain stem (central vestibular signs).

8. Can retinal and optic nerve function be assessed despite the presence of dense cataracts?

This problem confronts the ophthalmologist frequently. The definitive test of retinal function is the electroretinogram (ERG). No matter how dense the cataract, light will pass through the lens, albeit scattered light, to stimulate the retina. The summed electrical potential (in millivolts) generated by a normal retina can be recorded. The ERG may be normal despite optic nerve disease.

9. How should a brisk eyelid closure in response to a very bright light be interpreted?

In this test, called the dazzle response, a very bright light elicits an aversion response seen as a blink of varying speed and intensity in dogs. Humans will avert their gaze, turn away, and even sneeze. This test is not sensitive enough to detect early retinal degenerative disease. The reflex is subcortical. It can be elicited through a cataract. A brisk response is an encouraging sign.

10. Which cranial nerve supplies parasympathetic visceral efferents to the lacrimal gland?

Abranch of the facial nerve (CN-VII).

11. What causes neurogenic keratoconjunctivitis sicca (KCS)?

One of the many pathogeneses of KCS is denervation of the gland by a lesion of the facial nerve. Depending on the location of the lesion, other branches of CN-VII and sometimes CN-V may be involved, with clinical signs consistent with these.

12. How do you interpret the finding of a dry nostril in conjunction with KCS?

Nasal moisture arises primarily from the lateral nasal gland, a serous secreting gland located in the lateral nasal mucosa. Like the lacrimal gland, the nasal gland receives its innervation from a branch of the facial nerve. This branch separates from that to the lacrimal gland at the level of the pterygopalatine ganglion, ventrolateral to the orbital cone and dorsal to the pterygoid muscles. KCS together with a dry nostril (xeromycteria) suggests a preorbital nerve lesion most likely in the petrous temporal bone.

13. Why is it necessary to assess sensation in the lateral canthus area in cases of KCS?

The branches of CN-VII that leave the pterygopalatine ganglion as postganglionic efferents to the lacrimal gland travel to the gland with branches of CN-V, not with CN-VII. These CN-V conduits are sensory to the lateral canthus area. Hypalgesia or anesthesia in the lateral canthal skin, in combination with KCS, enables location of a neuropathy to a peripheral site susceptible to injuries. Remember not all cases of KCS are neurogenic. However, the finding of a CN-VII neuropathy in association with KCS confirms neurogenic KCS.

14. What are the ocular signs of sympathetic denervation (Horner's syndrome)?

Assuming that the Horner's syndrome is unilateral, as it is in most cases (Fig. 3), signs include:

- **Miosis in the affected eye.** The pupil constriction is relative to the normal eye and is relatively less marked in bright light.
- **Enophthalmos.** The affected eye recedes into the orbit when the smooth muscle tone of the periorbita is reduced (i.e., "squeeze" on the eyeball is reduced). This sign is the most variable one that is seen.
- **Narrowing of the palpebral fissure with loss of tone of upper and lower eyelid smooth muscle.** This sign will exaggerate the appearance of enophthalmos
- **Third eyelid protrusion.** This is mainly passive or secondary to enophthalmos in the dog; it is a direct effect of loss of smooth muscle tone in the cat

Figure 3. Left-sided Horner's syndrome in a cat. Miosis and a narrowed palpebral fissure are the obvious signs in this photograph.

15. What is meant by pre- versus postganglionic sympathetic denervation?

The term refers to the site of a lesion in relation to the cranial cervical ganglion, an important structure in the understanding of Horner's syndrome.

- The cranial cervical ganglion is the location of the cell bodies from which postganglionic sympathetic axons stream forth to innervate all smooth muscle in the head area.
- The cranial cervical ganglion is located deep to the tympanic bulla.
- Preganglionic fibers arise in the hypothalamus and descend in the cervical spinal cord to levels T1, T2, and T3. After synapsing at this level, the second-order neuron enters the thorax, joins the vagal trunk, and ascends the neck in the jugular groove to synapse in the cranial cervical ganglion.
- Postganglionic fibers travel to the eye and periorbita via the middle ear, go through the cavernous sinus, and then utilize the ramifying fibers of CN-V as a conduit.

16. What are some of the better documented lesions of the first- and second-order neuron (i.e., preganglionic lesions) accounting for Horner's syndrome?

- Hypothalamic neoplasia
- Cervical cord compression
- Brachial plexus avulsion or neoplasia
- Anterior mediastinal space occupying lesions
- Trauma to the jugular groove area including iatrogenic needle stick injuries

17. What are some of the documented post-ganglionic lesions accounting for Horner's syndrome?

Middle ear disease including iatrogenic injury with bulla osteotomy.

- Otitis media should not be overlooked.
- Ear examination, despite the common lack of external signs, should be conducted.
- Orbital lesions affecting the ophthalmic division of CN-V traveling through the orbital cone combined with the sympathetics

18. Define strabismus, enophthalmos, and exophthalmos.

Strabismus refers to a deviation of the eyeball from the normal visual axis. It is caused by abnormal neurologic innervation of extraocular muscles (CN-III, IV, and VI), primary muscle function disturbances, or space-occupying lesions of the orbit. Remember the vestibular apparatus plays an essential role in the control of eyeball position through its input into the nuclei of CN-III, IV, and VI.

Enophthalmos refers to sinking of the eyeball into the orbit. It should not be confused with active retraction. The most common neurologic cause is Horner's syndrome.

Exophthalmos refers to abnormal protrusion of the eye. This may be passive, as with shallow orbits, or active, as with a space-occupying lesion in the orbit. Apparent exophthalmos oc-

curs in the dog where the animal is blind with widely dilated pupils. A combination of apprehension-increased sympathetic tone in the orbital fascia plus the "staring" attitude of a blind dog contributes to the exophthalmic appearance.

19. How would you expect the eye to deviate with a unilateral lesion of the oculomotor nerve (CN-III)?

One should expect lateral strabismus with an inability to fix the gaze medially, dorsally, or ventrally. Bilateral strabismus of this nature is called **exotropia.** Ptosis (drooping) of the upper eyelid owing to levator palpebrae denervation may or may not accompany the strabismus of oculomotor nerve dysfunction. Similarly involvement of the pupils would depend on the location and extent of the CN-III lesion.

20. What are the neurologic implications for a dog with a unilateral inability to retract the eyeball?

Eyeball retraction can be induced as a preservation response to noxious stimuli of the eye (afferent CN-V). Usually manual or chemical restriction of simultaneous eyelid closure is necessary. The withdrawal of the eye occurs via the abducens-innervated retractor muscle bundle. The third eyelid will passively protrude. Loss of the retraction response indicates an afferent CN-V or efferent CN-VI lesion. A CN-VI lesion will be associated with medial strabismus.

21. What advice can be given to the worried owner of a cross-eyed cat?

The Siamese breed is relatively prone to this trait although domestic shorthairs are affected as well. The eyes are deviated inward. This is called a convergent strabismus or esotropia. Nystagmus may be seen also. Vision is not normal but adequate. The basis of the syndrome relates to abnormal retinal pathways and projections to visual cortices. The eyes deviate to maximize spatial binocular vision.

22. What is the oculocardiac reflex?

Tension on extraocular muscles or retropulsion of the eye will result in slowing of the heart in the normal animal. Orbital space-occupying lesions or manipulation (e.g., during eye removal) can initiate the reflex.

23. Which cranial nerves comprise the oculocardiac reflex?

Afferent impulses are carried by the ophthalmic branch of CN-V to the sensory nucleus in the medulla. The efferent arm belongs to the vagus nerve (CN-X). Vagal stimulation induces bradycardia and can induce cardiac arrest.

Review of cranial nerves involved in eye reflexes

REFLEX	AFFERENT CRANIAL NERVE	EFFERENT CRANIAL NERVE
Menace	II	VII
Tactile blink	V	VII
Tactile retraction	V	VI
Dazzle	II	VII

24. What is the differential diagnosis for an eye that is blind since birth despite appearing normal with routine examination?

The problem most likely involves the retina or optic nerve and may be unilateral or bilateral.

Retinal dysplasia including detachment. This is seen as an inherited trait in some breeds (e.g., rough collie (see Chapter 38). Retinal dysplasia may also be the result of an intrauterine insult to the developing eye (e.g., viral infections, teratogenic drugs). The detached retina looks like a gray veil behind the lens

Optic nerve hypoplasia. The optic disc is very small, usually indicating an hypoplastic optic nerve (Fig. 4).

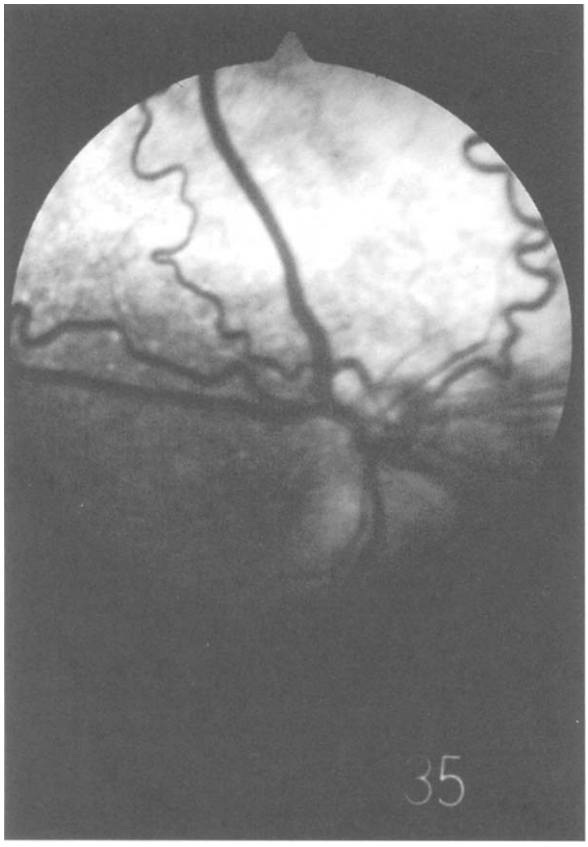


Figure 4. Fundus photograph depicting a very small optic disc in a blind puppy.

25. What is the differential diagnosis for sudden blindness in the dog?

Sudden acquired retinal degeneration (SARD). Vision loss is dramatic and bilateral. Pupillary light reflexes are reduced but seldom absent in the early-presenting case. Retinal examination may be normal or show subtle abnormalities in early stages, progressing to tapetal hyperreflectivity with time. The dog often exhibits polydipsia and polyphagia. Blood cortisol levels are elevated. The dog, however, is not a long-term hyperadrenocorticoid case and does not require therapy for hyperadrenocorticism. Pathogenesis of SARD is not known. Electroretinography (ERG) indicates generalized retinal dysfunction.

Optic neuritis (papilledema). Vision loss is dramatic although not necessarily equal in each eye. Pupils are widely dilated and very poorly or not responsive. The presentation is similar to SARD in that regard. On fundus examination, however, the optic disc is often swollen with retinal vessels climbing up over the protruding disc. The retina may detach and "tent up" around the disc. These features may not always be present and depend on etiology. ERG indicates normal retinal function unless the dog has a concomitant retinitis, in which case the ERG may be suppressed.

26. List the causes of optic neuritis in the dog.

Granulomatous meningoencephalomyelitis (GME) is the most common cause. This multifocal central nervous system disease has a high likelihood of optic nerve involvement (Fig. 5). GME may present initially with signs referable to optic nerve disease only (i.e., sudden blindness with no other neurologic deficit).

- Distemper
- Cryptococcosis and more rarely other mycoses

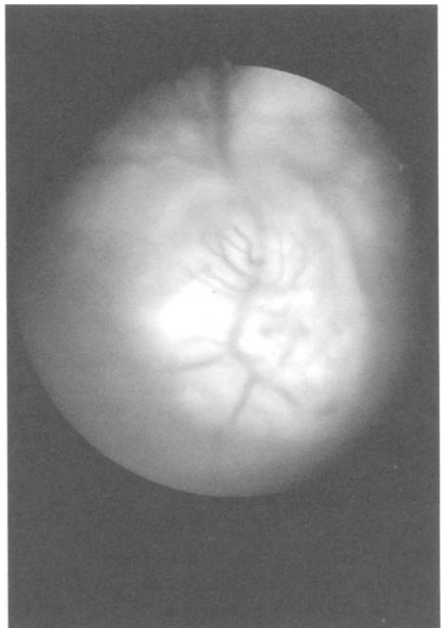
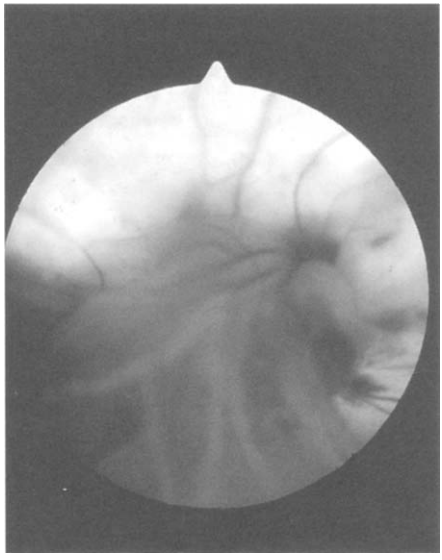


Figure 5. Fundus photograph of a swollen optic disc consistent with optic neuritis.

- Toxoplasmosis
- Neoplasia in the orbit, chiasm, or base of brain (e.g., pituitary gland)
- Trauma. Consider skull fractures around the basisphenoid, foreign bodies, and iatrogenic trauma following orbital abscess drainage procedures

27. Sudden blindness is encountered with increasing frequency in old cats. Why?

Hypertensive retinopathy with retinal detachments and retinal hemorrhage is seen in the old cat with blood pressure levels usually exceeding 200 mmHg (Figs. 6 and 7). Funduscopic examination reveals vascular explosions and a billowing retina. The retinopathy is not always bilaterally sym-



Figures 6. Retinal detachment with hemorrhages in a cat with blood pressure recorded at 300 mmHg.

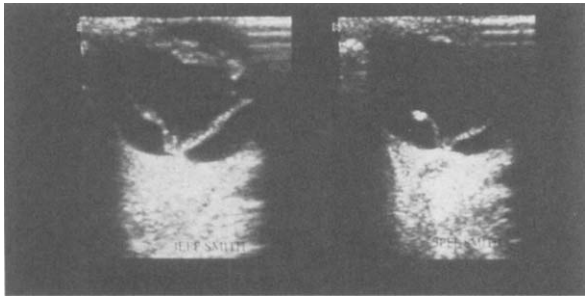


Figure 7. Ultrasound appearance of the retinal detachment with the typical "bird-wing" feature.

metrical. Affected cats may remain relatively more visual in one eye. Therapy directed at blood pressure reduction may preserve vision or even restore vision at times.

28. What are some of the causes of optic neuropathy in cats?

- Cryptococcosis
- Toxoplasmosis
- FIP
- Lymphoma

One should expect signs of retinitis and uveitis with these diseases.

GME does *not* occur in the cat. *Note:* Optic disc edema is not a common sign of optic neuropathy in the cat.

BIBLIOGRAPHY

1. Acheson GH: The topographical anatomy of the smooth muscle of the cat's nictitating membrane. Anat Rec 71:297–311, 1938.
2. Acland GM, Irby NL, Aguirre GD, et al: Sudden acquired retinal degeneration in the dog: Clinical and morphologic characterization of the "silent retina" syndrome. Trans Am Coll Vet Ophthalmol 15:86, 1984.
3. DeHaas EBH: Dessication of cornea and conjunctiva after sensory denervation. Arch Ophthalmol 67:79–92, 1962.
4. de Lahunta A: Veterinary Neuroanatomy and Clinical Neurology. Philadelphia, W.B. Saunders, 1963.
5. Kalil RE, Jhaveri SR, Richards W: Anomalous retinal pathways in the Siamese cat: An inadequate substrate for normal binocular vision. Science 747:302, 1971.
6. Miller ME: Anatomy of the Dog. Philadelphia, W.B. Saunders, 1964.
7. Scagliotti RH: Comparative neuro-ophthalmology. In Gelatt KN (ed): Veterinary Ophthalmology. Philadelphia, Lippincott Williams & Wilkins, 1999, p 1346.
8. Whitehead JE: Oscillation of feline eyes. Mod Vet Pract 40:56, 1959.

VI. Oculoplasties

25. EPIPHORA

Dennis K. Olivero, D.V.M.

1. Define epiphora.

Epiphora is a generic term used to indicate tear overflow onto the face or cheek without reference to a specific cause.

2. Where are tears produced in dogs and cats?

The tear film is composed of three layers. An inner layer of mucus produced by goblet cells of the conjunctiva provides adherence of the tears to the epithelial cells of the cornea. An outer layer of oil is produced by the meibomian glands, and this prevents rapid tear film evaporation. Between the inner mucus and outer oil layer is the aqueous or watery tears.

The aqueous tear layer is produced by two glands. The orbital gland lies in the periorbita of the dorsolateral orbit and empties tear fluid into the adjacent conjunctival fornix. The third eyelid tear gland, located at the base of the T cartilage of the nictitans, secretes tears into the ventral conjunctival fornix. The orbital gland produces approximately 65% of the total tear volume with the other 35% provided by gland of the nictitating membrane.

3. What function do tears provide for the eye?

The tears provide lubrication and protection to the surface cells of the eye. Mechanically, the tears cleanse the ocular surface, removing environmental debris. Nutrient and waste exchange occurs between the tear film and the corneal epithelial cells. The tear film can also provide a limited immune response with surface antibodies, complement, lactoferrin, and other proteins.

4. After lubricating and cleansing the ocular surface, where do the tears drain?

The nasolacrimal system drains tears to the nostril or mouth. Along the eyelid margin and 2–5 mm lateral from the medial canthus, the nasolacrimal puncta open. The puncta provide drainage into the upper and lower canaliculi, respectively, which later converge in the lacrimal fossa of the lacrimal bone as the lacrimal sac. A single duct drains the tears from the lacrimal sac to the nostril. Fifty percent of dogs and cats have an accessory opening of the nasolacrimal duct in the oropharynx. Orbicularis oculi muscle movements alter pressure gradients in the canaliculi, actively pumping tears into the drainage system.

Sixty percent or more of the tear volume drains through the inferior branch to the lacrimal sac, making this segment of the system most important in terms of tear outflow.

5. What is the clinical approach to epiphora?

It is helpful to categorize patients that present with tearing into three groups. One group of patients have epiphora because they are producing tears at an excessive level, overwhelming the capacity of the nasolacrimal system. A second group of patients demonstrate epiphora due to developmental or acquired conditions causing partial or complete closure of the drainage system (Fig. 1). The final group of patients shows epiphora despite relatively normal tear production and a seemingly patent and functional nasolacrimal system. These patients are often referred to as having "idiopathic epiphora" (Fig. 2).

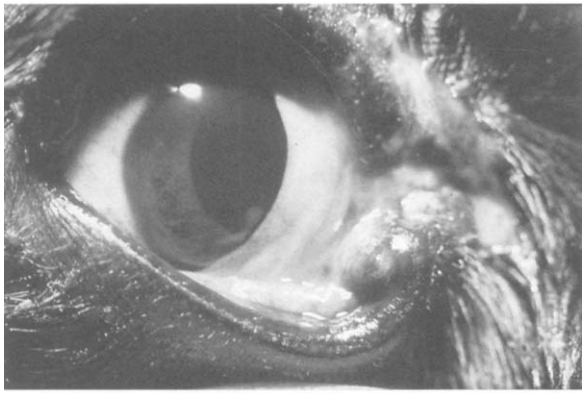


Figure 1. A 3-year-old American cocker spaniel dog presents for epiphora. Note the imperforate lower puncta with marked distention of the lower canaliculi.

Figure 2. A 6-month-old female toy poodle presents for epiphora. The typical appearance of "idiopathic epiphora" and marked tear staining are evident.

6. What are the clinical features of patients that overproduce tears?

These patients show obvious signs of ocular discomfort with conjunctival hyperemia and squinting. High Schirmer tear tests with saturation of the tear strip in less then 1 minute confirms lacrimation. Fluorescein dye passage is confirmed at the nostril or in the mouth in 2–3 minutes, indicating patency and function of the nasolacrimal system. The cause for lacrimation can be identified with evaluation of the ocular adnexa and cornea. Common causes for epiphora include entropion, ectropion, distichiasis, trichiasis, ectopic cilia, conjunctivitis, and ulcerative keratitis.

7. How is epiphora managed in patients with lacrimation?

Epiphora resolves when the primary problem is treated. This can include plastic surgical procedures to correct eyelid conformational problems, removal of irritating hairs in contact with the cornea, and medical or surgical treatments for conjunctivitis and ulcerative keratitis.

8. What are the clinical features of patients with nasolacrimal system closure?

- Normal Schirmer tear tests
- No obvious signs of ocular irritation
- Fluorescein dye passage tests are negative after 5 minutes on the affected side
- Nasolacrimal drainage failure is confirmed with attempted flushing of the system

9. What does a negative fluorescein dye test indicate with respect to nasolacrimal patency?

If fluorescein dye is noted at the nostril after 5 minutes or less in animals, patency and function of the nasolacrimal system are confirmed (positive test). Lack of dye presence (negative test) means nothing with respect to function or patency of the system. Fifty percent of normal animals

will have a negative fluorescein dye test to the nostril, many of these having an accessory duct that drains into the oropharynx. A negative fluorescein dye test necessitates nasolacrimal flushing for further evaluation of the system.

10. Describe the technique used for flushing the nasolacrimal system.

Nasolacrimal system flushing usually can be performed in the absence of general anesthesia or sedation. Topical anesthetic (0.5–1.0 % proparacaine HCl) drops are placed on the ocular surface repeatedly for 2 minutes prior to flushing. Topical anesthetic can then be placed on a cotton swab and held on the superior puncta to further reduce sensation. The superior puncta is cannulated with a 23- to 25-gauge cannula and initially flushed with saline to confirm patency of both canaliculi through the nasolacrimal sac. As soon as saline is noted exiting the lower puncta, the examiner applies gentle pressure over the inferior puncta, and flushing is continued until saline drains from the nostril or swallowing is noted. The ease of flushing and character of initial material exiting the inferior puncta or nostril should be noted.

11. What conditions can result in nasolacrimal system failure?

Imperforate puncta is the most common condition that results in drainage failure. This condition can affect the upper or lower puncta. Often imperforate superior puncta goes undetected because gravity promotes drainage predominantly through the inferior puncta. Imperforate puncta is noted most frequently in American cocker spaniels, Bedlington terriers, golden retrievers, poodles, and Samoyeds. Improved drainage is noted after a thin veil of conjunctiva is removed overlying the most proximal aspect of the upper or lower canaliculi on the eyelid margin.

Aplasia or displacement of the canaliculi or duct is rarely reported in animals. In this situation, primary surgical correction is not available unless clients elect to have an alternative tear drainage pathway into the nasal or oral cavity established.

Trauma or scarring in the medial canthal region can result in cicatricial injury to the proximal drainage system. Fractures of the nasal bone with excessive callus formation or aggressive nasal tumors or infections (fungal) can result in loss of function of the lower aspect of the nasolacrimal system.

Foreign body retention in the nasolacrimal system with chronic secondary bacterial infection (dacryocystitis) occurs occasionally and is most commonly noted in hunting dogs. Foreign bodies frequently are trapped in the nasolacrimal sac, and thorough flushing from the superior puncta often will produce the foreign material at the dilated inferior puncta. Chronic secondary infection of the nasolacrimal system can subsequently be treated with cannulation of the system with silicone or plastic tubing. Topical and systemic antibiotics are administered for several weeks while the tube is in place.

12. What ancillary tests are available to further define nasolacrimal system failure?

When nasolacrimal system flushing is unsuccessful and the system cannot be cannulated, the extent to which the cannula can be advanced indicates the point of blockage. Contrast material can be injected into the nasolacrimal system, and radiographs or fluoroscopy can be performed to identify the exact location of the blockage (dacryocystorhinography). Advanced imaging techniques (Computed Tomography or Magnetic Resonance Imaging) can be used to determine the level and cause of nasolacrimal system blockage when necessary.

13. What are the clinical features of patients with idiopathic epiphora?

These patients show no obvious signs of ocular discomfort or irritation and normal or high normal Schirmer tear tests. Despite overflow of tears onto the face, the fluorescein dye passage test is frequently positive, and, when it is not, the system can be readily cannulated and flushed to confirm patency. Poorly understood anatomic features of these patients provide less resistance to drainage of tears onto the face than through the nasolacrimal system.

14. Is any breed predisposition known for idiopathic epiphora?

Toy breeds of dogs including the poodle, bichon frise, Maltese, and Yorkshire terrier frequently present with the complaint of tearing. Brachycephalic breeds of cats often demonstrate overflow of tears onto the skin of the medial canthus. The vast majority of patients that present

for clinical evaluation have white or lightly colored hair coat. Dogs with darker hair coats can tear excessively, but the associated brown stain of epiphora is not obvious to their owners.

15. What causes the brown stain associated with epiphora in dogs and cats?

Many theories have been advanced explaining the brown color associated with tearing including the presence of porphyrins in the tears or that the brown stain represents a by-product of bacterial digestion of tear constituents on the skin. The exact nature of the brown stain associated with epiphora in animals, however, is not known.

16. Are there any simple remedies for idiopathic epiphora?

A number of treatments have been advanced, but unfortunately a uniformly successful treatment has not yet been developed. Some "treatments" are considered highly controversial, and those that are not are variably successful. Veterinarians spend considerable time convincing owners that tear staining is not harmful or vision threatening and that it represents predominantly a cosmetic problem. Some clients will be satisfied with this explanation and will learn to clean the medial canthal area daily. With time, the brown stains are eventually considered "normal" for their dog or cat. Other clients will continue to seek remedies for epiphora staining in their pets. Both medical and surgical options have been described.

17. What are the medical options for treatment of dogs with idiopathic epiphora?

Dogs with epiphora staining have been successfully treated with tetracycline and metronidazole. By unknown mechanisms, both of these drugs, when given daily at low levels, result in resolution of brown staining on the hair coat. Tear production is not altered, and the skin in the medial canthal region remains wet. These agents may affect porphyrin production by the tear glands or alter local bacterial flora on the skin. As soon as the antibiotic agents are withdrawn, brown staining reappears.

Oral antihistamines decrease saliva and tear production in people and animals. Variable responses have been noted in dogs with epiphora after treatment with topical or oral antihistamine drugs.

18. What are the surgical options for idiopathic epiphora?

When the goal is to improve tear drainage, there are two options. One approach involves improving drainage through the existing nasolacrimal system, and the other approach involves creating alternative pathways for tear drainage away from the skin.

19. Describe procedures used to improve drainage through the existing nasolacrimal drainage system.

Several seemingly minor anatomic features promote tear drainage onto the skin of the medial canthus in animals with epiphora. These include an excessively tight lower eyelid, which limits the lacrimal lake volume and may excessively bend or kink the inferior canaliculus, medial lower eyelid entropion, or nasal folds that tend to roll the lid margin toward the globe with marginal tissue folding over the inferior punctal opening, and hairs growing on the caruncle gland in the medial canthus that provide a "wick" for tear movement onto the skin of the face. Dogs with epiphora often show a "crease" in the skin in the medial canthus, which may act like a trough, siphoning tears onto the skin with each blink. This crease results from attachment of the medial canthal skin to the medial canthal tendon on the nasal bone and mild lower eyelid medial entropion. Micropuncta may contribute to epiphora additionally.

Patients variably show improved nasolacrimal tear drainage with removal of the caruncle gland and associated hairs, enlargement of the nasolacrimal puncta, and partial or complete elevation of the medial canthal tendon to reduce tension on the lower eyelid, which relieves compression on the inferior canaliculi. Entropion corrections can be used alone or in addition to nasal fold reduction or resection to improve drainage via the inferior puncta. In certain cases, medial canthoplastic procedures can be employed to elevate the upper and lower eyelid from the nasal bone and recreate the medial canthus in the absence of a crease created by the medial canthal tendon.

20. What percent of dogs with epiphora are improved with the above procedures?

Approximately 50% of patients show marked improvement in tear staining after the above combination of surgical corrections. The other half of patients are only partly improved or show no change.

21. Describe procedures used to create alternative drainage of tears?

Several procedures have been described to redirect tears from the medial canthal skin in dogs with epiphora. One procedure involves creating a conjunctival-lined fistula from the ventral conjunctival fornix into the nasal passage (conjunctival rhinostomy) or maxillary sinus (conjunctival-maxillary sinusotomy). A second procedure involves rerouting tears via a conjunctival or mucosal-lined fistula under the facial skin from the ventrolateral conjunctival fornix to the mouth (conjunctival buccostomy). These procedures can also be considered in patients with irreversible damage to the nasolacrimal system secondary to trauma, neoplasia, or retained foreign body.

22. Can tear production be decreased surgically in dogs with idiopathic epiphora?

Surgical reduction or removal of the third eyelid tear gland has been advocated by some for the treatment of idiopathic tearing in toy breeds of dogs. This form of treatment is considered controversial.

CONTROVERSIES

23. Should chronic administration of low dosages of tetracycline by mouth be used to alleviate tear staining in dogs?

For chronic oral antibiotic therapy: Veterinary clients who are sufficiently concerned about tear staining to seek professional advice may not be satisfied when told to ignore the unsightly dark stains. These clients appreciate the improved appearance of their animals when treatment with oral tetracycline is instituted. Low dose chronic antibiotic treatment with tetracycline is not frequently associated with complications. The treatment is conservative, does not involve surgical procedures, and is reversible. Tetracycline is not ordinarily used to treat life-threatening bacterial diseases in dogs or cats.

Against chronic oral antibiotic therapy: Chronic antibiotic treatment always carries risk of adverse reactions. Allergic reactions or idiosyncratic reactions have been reported with most common antibiotics. Development of resistant strains of resident bacteria could later threaten the health of the patient.

24. Should alternative tear drainage to the nasal cavity be considered in patients with a nonfunctional nasolacrimal system?

For establishment of drainage into the nasal passage: Tears normally drain to the nostril or oropharynx. Creating a conjunctival-lined passage from the medial canthus to the nasal passage will rapidly alleviate tearing and tear staining.

Against establishment of drainage into the nasal passage: The nostril and oropharynx as well as the ocular surface are not sterile. The nasal passage employs hairs and a system of turbinates to clean debris from air as it progressively passes from the upper to the lower airway. Drainage of tears and mucus material from the ocular surface into the more distal nasal passages may result in bacterial rhinitis.

25. Should toy breeds of dogs with epiphora have the third eyelid tear gland removed?

Yes. Patients with idiopathic tear staining syndrome frequently show high normal tear production. Although the nasolacrimal system is intact and functional it cannot accommodate the volume of tears and staining develops. Removal of the tear gland of the third eyelid, reduces tear production by up to 35%, thereby alleviating excessive drainage of tears onto the skin.

No. Third eyelid gland removal has been studied thoroughly in dogs with prolapsed gland of the nictitans or "cherry eye." One study shows a 37 times increased incidence of keratoconjunc-

tivitis sicca in dogs that have the gland removed versus those in which the tear gland is surgically replaced. Although epiphora is bothersome to clients and unsightly, it is not vision threatening. Dry eye, on the other hand, can be vision threatening particularly in cases unresponsive to topical cyclosporine. Third eyelid gland removal is irreversible.

Classification of Patients with Epiphora

GROUP	GENERAL MECHANISM	CAUSES	TREATMENT
I	Overproduction of tears (lacrimation)	Conjunctivitis Entropion/ectropion Distichia/trichiasis Ectopic cilia Ulcerative keratitis Foreign body	Treat primary problem
II	Nasolacrimal system closed (drainage failure)	Congenital defects Trauma Retained foreign body Tumor Infection	Establish patency when possible Establish alternative drainage if desired
III	Imperfect nasolacrimal system drainage ("idiopathic epiphora")	Medial canthal entropion Nasal folds Tight lower eyelid with shallow lacrimal lake, medial canthal crease Caruncle hairs "wick" tears Micropuncta High normal tear production (?)	Correct predisposing anatomic features or establish alternative drainage if desired

BIBLIOGRAPHY

1. Barnett KC: Imperforate and microlacrimal puncta in the dog. J Small Anim Pract 20:482–490, 1979.
2. Covitz D, Hunziker J, Koch SA: Conjunctivorhinostomy: A surgical method for the control of epiphora in the dog and cat. J Am Vet Med Assoc 171:251–255, 1977.
3. Filipek ME, Rubin LF: Effect of metronidazole on lacrimation in the dog: A negative report. J Am Anim Hosp Assoc 13:339–341, 1977.
4. Gale VG: Use of metronidazole in treating tear staining in the dog. Vet Rec 14:98, 1976.
5. Gelatt KN, Cure TH, Guffy MM, et al: Dacryocystorhinography in the dog and cat. J Small Anim Pract 13:381–392, 1972.
6. Goldberg RA, Heinz GW, Chiu L: Gadolinuim magnetic resonance imaging dacrocystography. Am J Ophthalmol 115:738–741, 1993.
7. Grahn BH: Diseases and surgery of the canine nasolacrimal system. In Gelatt K (ed): Veterinary Ophthalmology, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 1999, pp 569–581.
8. Kerspack RW, Kerspack WR: The orbital gland and tear staining in the dog. Vet Med Surg Small Anim Clin 61:121–124, 1966.
9. Lavach JD, Severin GA, Roberts SM: Dacryocystitis in dogs: A review of 22 cases. J Am Anim Hosp Assoc 20:463–467, 1984.
10. Loftus WK, Kew J, Metreiweli C: Nasolacrimal duct opacity on CT. Br J Radiol 69: 630–631, 1996.
11. Long RD: The relief of epiphora by conjunctivorhinostomy. J Small Anim Pract 16:381–386, 1975.
12. Morgan RV, Dudd JM, McClurg K: Prolapse of the gland of the third eyelid in dogs: A retrospective study of 89 cases (1980–1990). J Am Anim Hosp Assoc 29:56–61, 1993.
13. Murphy JM, Severin GA, Lavach JD: Nasolacrimal catheterization for treating chronic dacryocystitis. Vet Med Small Anim Clin 72:883–887, 1977.
14. Peiffer RL, Gwin RM, Gelatt KN: Correction of inferior medial entropion as a cause of epiphora. Canine Pract 5:27–31, 1978.
15. Seo KM, Nam TC: Tear formation, the patency and angle of bend of nasolacrimal duct in poodle dogs with tear staining syndrome. Korean J Vet Res 35: 383–390, 1995.
16. Thun R, Abraham RS, Helper LC: Effect of tetracycline on tear production in the dog. J Am Anim Hosp Assoc 11:802–804, 1975.
17. Yakely WL, Alexandra JE: Dacryocystorhinography in the dog. J Am Vet Med Assoc 159:1417–1421, 1971.

26. BLEPHAROPLASTIC PROCEDURES

Robert J. Munger, D.V.M.

1. Is a blepharoplastic procedure permitted on a show animal?

The question of performing a blepharoplastic procedure on a show animal revolves around two issues. The first is the cause of the defect or problem that warrants the procedure, and the second is the intended use of the animal after the surgery. Certainly, it is appropriate to perform whatever surgery needs to be done to preserve structure, health, and function of the eye. If the patient is to be used for show and the defect to be corrected is unrelated to inherited causes (e.g., it is associated with trauma, neoplasia, or other disease), no conflict exists and the procedure may be performed without reservations or conditions. However, if the surgery would disguise or resolve an inherited condition, the agency regulating the showing of animals of that breed should be consulted and the owner should be advised when such surgery would disqualify the animal from showing. Above all, the welfare of the animal must not be compromised, and surgery should be performed to alleviate pain or potential loss of vision even when such disqualification would occur.

2. What breeds of dogs are predisposed to entropion?

Chow chow	English bulldog
Norwegian elkhound	Rottweiler
Chinese shar-pei	Labrador retriever
St. Bernard	Golden retriever
English springer spaniel	Toy and miniature poodles
English and American cocker spaniels	Mastiffs

3. What breeds of dogs are predisposed to ectropion?

The bloodhound, St. Bernard, Great Dane, Newfoundland, mastiff, basset hound, and many of the spaniel breeds are predisposed to ectropion. The common denominator in these breeds is the excessive amounts of facial skin and large palpebral fissures, so any dog with such features regardless of breed should be regarded as being at risk of having or developing some degree of ectropion. Such dogs may also have areas where the lids are entropic as well, especially those with the diamond or pagoda-shaped palpebral fissures. These dogs may well require combined or multiple procedures for correction.

4. At what age should entropion or ectropion surgery be performed on a puppy?

Generally, when only the corrective surgery is considered, it is ideal to wait until a patient has achieved full growth and the conformation of the face and lids has reached its mature appearance. Many clinicians arbitrarily set 4–6 months as the age at which surgery should be considered. However, no rule is hard and fast, and the most compelling things to consider are whether the condition is causing harm or pain and whether delaying the surgery will result in undue risk to vision or function. Whenever such delay would be harmful, surgery is indicated. When performing procedures on young animals, the owner should be advised there is greater probability that subsequent surgery may be required in the future. In very young puppies with severe entropion, such as in the Chinese shar-pei, lid tacking with vertical mattress sutures or other such temporary procedures may be performed to see if the puppy will outgrow the condition. If the condition persists or worsens, a modified Hotz-Celsus procedure or other permanent correction may be considered superior to repeated temporary measures.

5. What are the causes of entropion and ectropion and how can they be evaluated?

Although it is easy to say that entropion and ectropion are genetically related, many factors contribute to eyelid position. The relationships between the orbit, eyelids, and globe affect the po-

sition of the lids, and the complexity of these relationships is at best difficult to define genetically. Certainly, conformation is broadly defined as genetic, but other factors can affect the position of the lids. For example, atrophy of orbital fat or musculature can result in enophthalmos that predisposes to entropion. Injuries, either acute or chronic, can result in scarring or blepharospasm that also can cause defects in lid position. Therefore, the clinician must approach each case with careful evaluation of both conformation of the lids, eye, and orbit and any other factors that are present. When blepharospasm is present in association with ocular pain, topical local anesthesia can be applied to evaluate the true degree of entropion when pain is not present. In some cases, the discomfort may be so severe that blepharospasm in not eliminated by topical anesthesia. When that occurs, local anesthetic can be injected to perform a palpebral nerve block to eliminate the blepharospasm. In the large and giant breeds, excessive amounts of skin and lid coupled with a lack of skin tone predispose such animals to ectropion. It may be further compounded by the presence of entropion, especially when the palpebral fissure is large and the lid margins are redundant. Manipulation of the lids usually allows the clinician to judge the amount of correction needed to eliminate excessive skin and lid margins.

6. When performing lid surgeries what are the most critical anatomic considerations with respect to lid function and position?

The eyelids may be divided into two basic layers; the skin and muscle layer and the tarsoconjunctival layer. Dissection and apposition of these layers must be carefully attended during reconstructive surgery. The tarsal plate is thin in dogs and cats so the shape and support of their lids is greatly dependent on the lid margins. Preservation of the lid margins is, therefore, of great importance for proper lid shape, mobility, and retention of tears in the lacrimal sac. The blood supply arises mainly from the medial and lateral canthal areas. Therefore, dissections must strive to preserve this blood supply. When flaps are fashioned from the lids, the medial or lateral pedicle should be 4–6 mm in width (with larger flaps requiring wider pedicles) to preserve good blood supply. The upper lid covers the majority of the cornea during blinking and is more important than the lower lid for protection of the globe. The lower lid is more important for prevention of tear overflow onto the face. The medial and lateral canthi must remain well anchored and stable to allow the best approximation and function of the upper and lower lids with respect to their position and joint function. Whenever possible it is important to preserve the upper and lower puncta in the medial aspect of the lids, but the lower punctum functions to drain the majority of the tears because they are moved medially by blinking. Thus, its preservation should take precedence over the upper.

7. Which surgical instruments should be included in a basic surgical pack for lid surgery?

General soft tissue instruments are appropriate for handling the periocular skin, but a pack should also include certain essential ophthalmic instruments.

- Strabismus or tenotomy scissors should be included for cutting tissues and suture.
- Delicate serrated and toothed forceps such as Bishop-Harmon forceps or 0.3 mm 1 × 2 Castroviejo scissors are excellent for handling the eyelids.
- Smaller toothed forceps such as Colibri or 0.12 mm Castroviejo forceps are excellent for handling the conjunctiva.
- Scalpel blades should be small (Bard-Parker nos. 11 and 15 or Beaver nos. 64 and 65), and suitable handles for these blades should be included.
- Eyelid specula of appropriate size and rigidity are useful and are a matter of surgeon's preference.
- A Barraquer wire eyelid speculum is appropriate for smaller delicate eyelids, but larger more rigid specula are usually needed for larger palpebral fissures.
- An ophthalmic needle holder such as a Derf or large Castroviejo needle holder is essential for handling the delicate needles and suture used in eyelid surgery.
- A Jaeger lid plate is useful as a backing for making lid incisions, although a sterile tongue depressor may be used if this instrument is not available.
- Specialized forceps such as entropion forceps and chalazion forceps are useful in immobilizing and stabilizing the lids during procedures.

8. Which sutures should be kept on hand for blepharoplastic procedures?

Suture preference varies widely among surgeons. In general, the suture and needle that should be chosen is that which causes minimal trauma on passage with minimal tissue reaction and scarring. Closure of the tarsoconjunctiva and subcutaneous tissues is best performed with 4–0 to 6–0 absorbable sutures such as chromic gut, polyglycolic or polyglactic acid, and polydioxanone. When placed in the tarsoconjunctiva, the knots should be well buried to avoid irritation, and smaller suture size is preferable because migration or erosion of larger knots through the conjunctiva may cause corneal irritation and ulceration. Closure of the skin should be performed with 4–0 to 6–0 nonabsorbable suture, depending on the skin thickness and the required placement of sutures. Smaller sutures are generally used in thinner skin and around the lid margins. In the past silk sutures have been the norm, but modern monofilament materials such as polypropylene and nylon are less reactive and are more commonly used in today's surgeries. The monofilament sutures are more likely to be irritating if they contact the cornea, so extreme care must be observed with their placement. Silk sutures are better tolerated in the event of corneal contact, and the disadvantage of their tissue reactivity and potential for wicking, which allows bacterial invasion, can be decreased when suture removal is performed 7–10 days after surgery. Obviously early removal of sutures requires protection of the incision to prevent dehiscence.

9. How can notch defects of the lid margin be prevented when closing defects that involve the margin?

Because of the mobility of the lids, stabilization of the lid margin presents a special challenge to the surgeon. If a suture is not placed across the margin, a notch in the margin can develop, but a knot tied at the margin is likely to irritate the cornea even when the suture ends are left long and tied to other sutures. A cruciate or figure-8 suture allows stabilization of the margin with the knot tied away from the margin. The figure below shows the passage of the suture to achieve the desired results. Initially the needle passes through the skin adjacent to the margin then across the defect to the subcutaneous tissue at the lid margin. From there it passes outward, exiting the lid margin at the level of the duct openings of the meibomian glands (the "gray line"). Next the suture passes across the defect to enter the margin at the gray line pass to the opposite side of the incision through the subcutaneous tissue and out through the skin opposite the initial entry point. Thus, when the suture is tied, the knot is in the upper loop of the figure 8 while the lower loop of the 8 stabilizes the lid margin (see Figure 6).

10. What is the best way to control hemorrhage during blepharoplastic surgery?

Hemorrhage in lid procedures can usually be controlled with fine-point cautery whenever simple pressure proves insufficient. Temporary clamping with a hemostat may be used to assist such cautery, but ligatures are rarely needed except possibly with construction of flaps in some of the more extensive blepharoplastic procedures.

11. Why does entropion occur in an older animal when it has been fine all its life and no injury or other problems occur?

Because the lids of dogs and cats lack a tarsal plate, contact with the globe is extremely important for support of the lids. As animals age, atrophy of the orbital fat or other contents can result in significant enophthalmos, which allows the lids to angle posteriorly. When that occurs, frank entropion may develop and can be difficult to manage because persistent loss of support from the globe can allow for enough tissue shift to allow later recurrence of the entropion. Any orbital disease that results in atrophy or scarring of orbital structures can result in enophthalmos mimicking that is age related.

12. How is the Hotz-Celsus procedure performed and when is it used?

The Hotz-Celsus procedure is the simplest, most versatile, and most often used blepharoplastic procedure. It or one of its modifications may be used to treat congenital, developmental, cicatricial, or senile entropion where the palpebral fissure is of normal size and the lid lengths are normal. The procedure may also be applied in the management of distichiasis in order to evert the

lid margin enough to shift the extra lashes away from the cornea. This latter application works best in patients without excessive amounts of skin that predisposes to postoperative shifting that can negate the eversion of the margin (shar-peis and the exophthalmic breeds with excessive nasal fold skin). Eversion of the medial lid margin may also be used to evert the medial lower lid margin to rotate the lower lacrimal punctum up and out to improve tear drainage in cases of epiphora. The basic technique relies on the removal of a crescent-shaped strip of skin and underlying orbicularis oculi muscle adjacent to the lid margin. The initial incision is usually made parallel to and within 1–2 mm of the lid margin. The second incision is made distal to the first and connects the medial and lateral aspects of the first incision (Fig. 1A). The width of the incision is determined by the degree of entropion that exists (determined prior to anesthesia) and should allow for 0.5–1 mm of additional eversion that can occur during postoperative healing. Suturing of the defect may be performed with simple interrupted sutures or with an inverse running pattern to ensure there is no shifting of the incision edges. The positions of the incisions on the lid depend on which parts of the lid are entropic. Two crescents may be removed when the lateral and medial aspects are entropic but the central lid margin is in normal position (Fig. 1B). In the event the lateral canthus is affected, the procedure can be modified with the crescent centered at the canthus and its arms extending over the upper and lower lids (Fig. 1C). When the lateral aspects of the upper and lower lids are primarily involved with minimal entropion of the canthus itself, the procedure may be further modified to create an arrowhead shaped defect (Fig. 1D). The apex of the defect is closed primarily with and interrupted suture followed by closure of the upper and lower arms of the arrowhead. This modification allows correction of the entropion with minimal lengthening of the palpebral incision. In patients with atonic or excessively long or redundant lids, other procedures must be used either alone or in combination with the modified Hotz-Celsus procedure to achieve optimal correction and lid position.

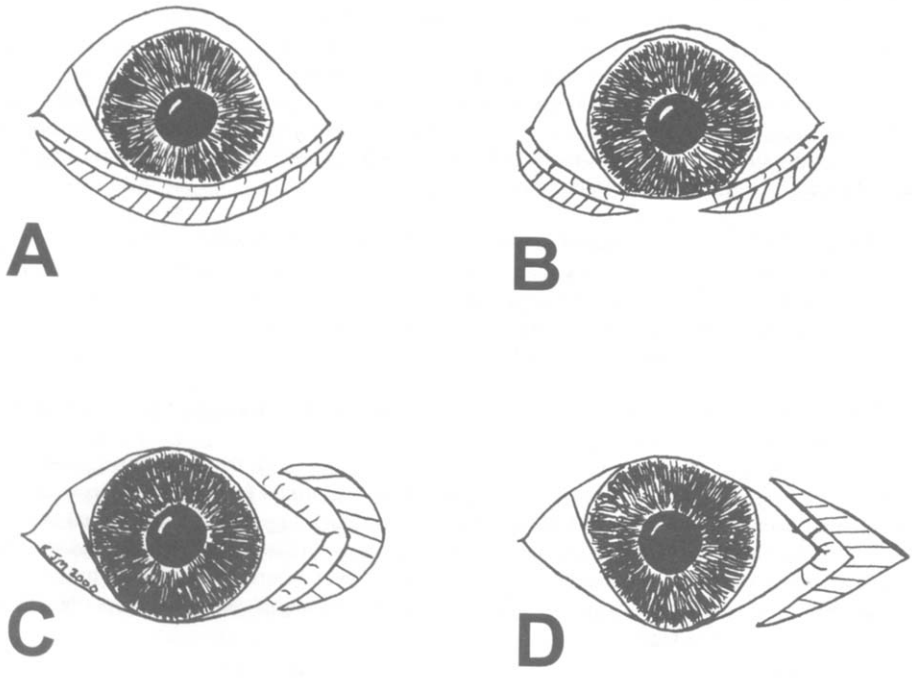


Figure 1. Variations in the modified Hotz-Celsus procedure. *A*, Classic procedure. *B*, Modification of Hotz-Celsus procedure for correction of medial and lateral entropion. *C*, Application of Hotz-Celsus procedure for lateral canthal entropion. *D*, Arrowhead modification for correction of lateral entropion of upper and lower lids with minimal canthal involvement.

13. When only mild entropion of the central lid exists, is there an alternative to the modified Hotz-Celsus procedure?

The Y-to-V blepharoplasty may be used for correcting mild central lid entropion. The arms of the Y are place within 1 mm of the lid margin and their span should encompass and be centered on the entropic portion of the lid margin. The incisions extend through the skin to the depth of the orbicularis oculi muscle and the vertical stem of the Y is of sufficient length to correct the entropion. The triangular flap of skin and muscle is elevated and separated from the underlying tarsoconjunctiva by blunt-sharp dissection using a tenotomy scissor. The apex of the triangle is then sutured to the bottom of the Y with a simple interrupted nonabsorbable suture. The sides of the flap are then closed with similar interrupted sutures to produce the characteristic V closure (Fig. 2).

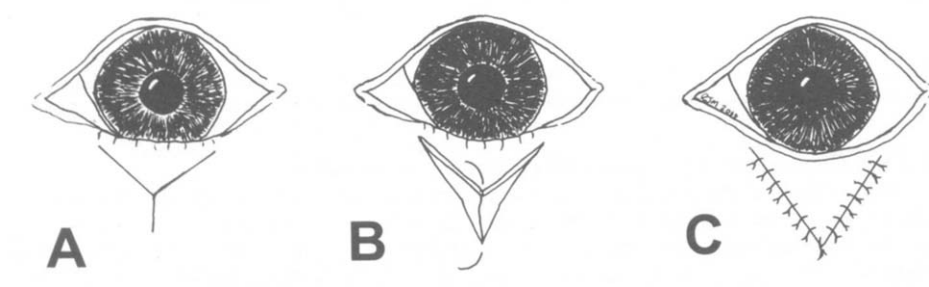


Figure 2. Y-to-V blepharoplasty. *A*, Preparation of initial Y incision adjacent to entropic lid margin. *B*, Skin-muscle flap elevated for shift and closure. *C*, Resultant V incision closed.

14. What is the best way of dealing with the severe entropion and excessive facial folds in the Chinese shar-pei?

The correction of this severe entropion in the shar-pei may be accomplished either by combined modified Hotz-Celsus procedures and removal of the excessive folds of skin around the eyes or by the "brow-sling" technique. The brow-sling technique is a modification of a brow or frontalis suspension surgery used in humans with severe blepharoptosis. It has the advantages that it is less invasive, involves less suturing, and preserves the skin folds that are typical for the conformation of the Chinese shar-pei. The procedure was first described in modern veterinary medicine by Dr. Susan Kirschner, and a series of cases was later reported by Dr. A. Michelle Willis et al. It is well suited for dealing with the redundant brow and forehead skin folds that are common in the shar-pei, chow chow, bloodhound, basset hound, bulldog, and St. Bernard. The technique involves the use of buried braided polyester mesh or suture (such as Mersilene) to tense and support the lids. After surgical preparation of the forehead and brows, two to three rows of incisions are made over each eye. The first row of incisions is located at least 5 cm dorsal to the orbital rim, and the second is performed over the orbital rim itself. A third incision may be performed 2–3 mm dorsal to the upper eyelid margin (Willis modification) to aid in further elevation and eversion of the upper lid margin. The frontalis muscle (and the underlying periosteum of the frontal bone when possible) is engaged, and the strip or suture is passed inferiorly to the other incisions. At its closest approach to the lid margin, the needle traverses horizontally parallel to the eyelid margin and is then redirected subcutaneously to the original incision. Once correct tension has been achieved to create the needed suspension, the strip or suture is tied in place. The skin incisions are closed with interrupted 5–0 to 6–0 nonabsorbable sutures. Usually two slings are placed per eyelid, one medially and one laterally. When only two incisions are used (omitting the incisions adjacent to the lid margins), a modified Hotz-Celsus procedure or other entropion surgery may be used if needed to evert the lid margin and lashes (Fig. 3).

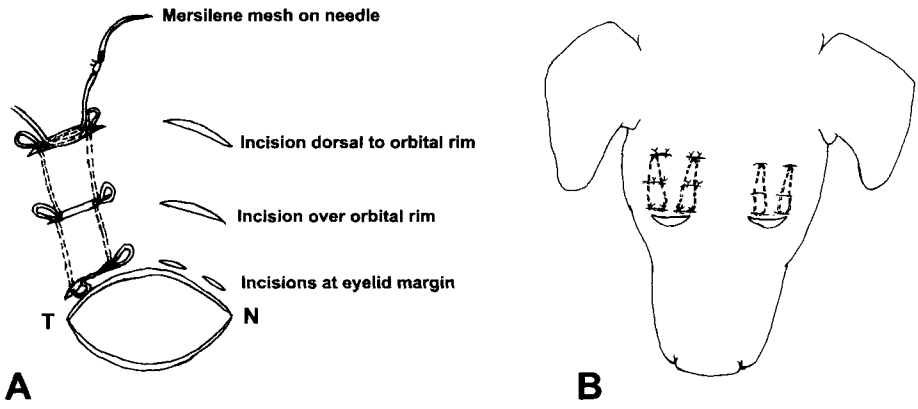


Figure 3. Brow-sling procedure. *A*, Passage of Mersilene mesh or suture from dorsal brow incision subcutaneously to eyelid margin and back with anchoring to the frontalis muscle. *B*, Two slings are used for each upper lid.

15. Describe the best way to cope with recurrence of entropion.

When simple undercorrection causes the recurrence, repeating the surgery to remove more skin may be all that is required. However, when the entropion is severe and unassociated with other lid deformities (macroblepharon, etc.), a central tarsal pedicle can be constructed using the technique of Wyman and Wilkie to compliment and reinforce an additional Hotz-Celsus procedure. The initial incision is performed adjacent and parallel to the lid margin but does not penetrate as deep as the orbicularis oculi muscle. At the level of the most extensive entropion, two parallel incisions perpendicular to the lid margin are made in the orbicularis oculi muscle and the tarsus with a scalpel. The sharp dissection is continued to free the pedicle from the skin and the deeper palpebral conjunctiva, leaving its base attached to the lid margin. Next, a tunnel as wide as the pedicle and long enough to correct the entropion is prepared with tenotomy scissors under the distal skin edge. Using a double-armed 5–0 nonabsorbable suture, a cruciate stitch is passed through the pedicle and then extended through the tunnel. The stitch is passed through the skin and tied through a stent, thus correcting the entropion. The redundant skin can now be excised creating the typical crescent of the Hotz-Celsus procedure, and the skin is closed with an interrupted or inverse running pattern of 4–0 to 6–0 nonabsorbable suture. Multiple tarsal pedicles can be created when large or multiple areas of the lid are affected (Fig. 4).

16. When the lateral canthus is unstable, is there a simple way to correct the attendant lateral canthal entropion?

When the size of the palpebral fissure is normal, Wyman's technique remains among the best for correcting lateral canthal instability and entropion. It may also correct ectropion of the central aspect of the lids when that is present in combination with the lateral canthal entropion. A crescent-shaped portion of tissue is removed as described for the modified Hotz-Celsus procedure around the lateral canthus. The width of the crescent created by the two elliptical skin incisions is determined by the amount of the correction for the lateral canthal entropion. The orbicularis oculi is exposed and sharply dissected to create upper and lower pedicles attached at their base to the lateral canthus. The two pedicles are united with a cruciate 5–0 nonabsorbable suture that is then passed laterally through the periosteum of the lateral orbital rim or the zygomatic arch. As the suture is tied, the tension is adjusted to achieve the desired amount of lateral retraction and eversion of the lateral canthus. The skin incisions are closed with interrupted nonabsorbable sutures. One or two nonabsorbable 2–0 sutures may be used instead of the dissected orbicularis oculi muscle pedicles to create lateral tension to evert the lateral canthus. In this variation the suture is passed through the lateral canthus and the periosteum of the zygomatic arch, and tension is tightened as the knot is tied prior to the closure of the skin (Fig. 5).

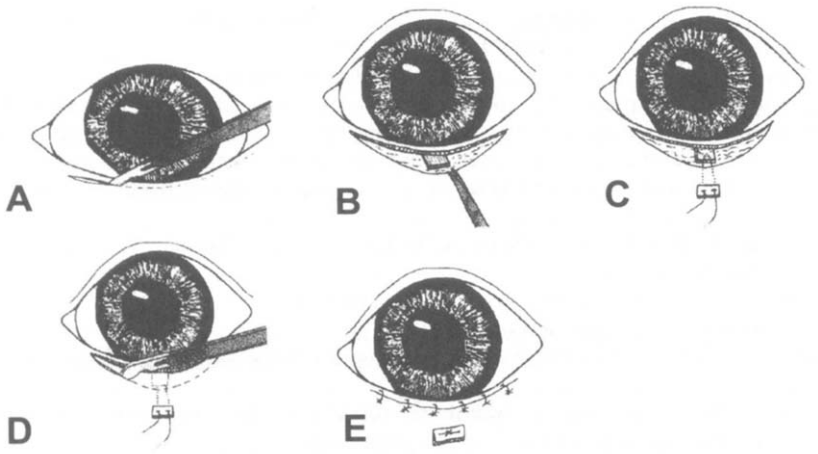


Figure 4. For the central tarsal pedicle for entropion, a tarsal pedicle anchored at the eyelid margin is combined with the Hotz-Celsus procedure. *A,* The initial skin incision is about 1–2 mm from the eyelid margin. *B,* A tarsal pedicle is constructed by scalpel with its base at the eyelid margin at the site of most extensive entropion. *C,* Through a subcutaneous tunnel made by scissors, a 5–0 nonabsorbable cruciate suture attached to the tarsal pedicle is secured with a stent below the surgical wound. *D,* The second skin incision of the Hotz-Celsus method is performed, and the crescent of skin is removed with tenotomy scissors. The width of the crescent depends on the extent of the entropion. *E,* The skin wound is closed with 5–0 nonabsorbable simple interrupted sutures. (From Gelatt K (ed): Handbook of Small Animal Ophthalmic Surgery. Tarrytown, NY, Elsevier, 1994, with permission.)

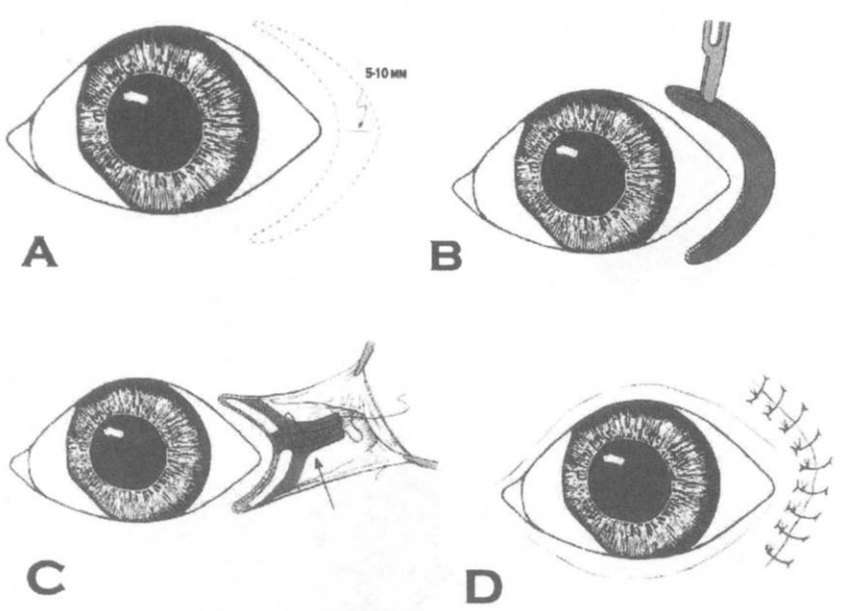


Figure 5. Wyman's lateral canthoplasty and construction of lateral canthal ligament. *A,* Two elliptical incisions are performed with the width of the crescent of tissue to be removed sufficiently to correct the entropion present. *B,* Two orbicularis oculi myotomies are performed to create two strips of muscle with their bases at the lateral canthus that will act as the new lateral canthal ligament. *C,* After subcutaneous dissection with tenotomy scissors, a cruciate 5–0 nonabsorbable suture is used to anchor the orbicularis pedicle (*arrow*) to the periosteum of the zygomatic arch. *D,* The skin is closed with 4–0 to 5–0 interrupted nonabsorbable sutures. (From Gelatt K (ed): Handbook of Small Animal Ophthalmic Surgery. Tarrytown, NY, Elsevier, 1994, with permission.)

17. If immediately after entropion surgery the lids appear to be ectropic, should further surgery be performed to roll the lid inward again?

At the end of surgery it is not uncommon for swelling to result in mild to moderate ectropion (the more reactive the lid skin and conjunctiva, the more ectropion may be apparent). Commonly, the lid will return to the appropriate position as the swelling subsides as long as the amount of correction performed is consistent with that measured prior to the surgery. Therefore, resist any temptation to modify the results, and wait for several weeks after suture removal to evaluate the final results.

18. What techniques are most often used for the correction of ectropion?

Simple wedge resection
Modifications of the Kuhnt-Szymanowski procedure
Kuhnt-Helmbold procedure

The V-Y or Wharton-Jones blepharoplasty is indicated for the correction of cicatricial ectropion.

19. When is the wedge resection technique indicated for the correction of ectropion and what factors are critical in performing this procedure?

The wedge excision procedure is a full-thickness resection usually performed adjacent to the lateral canthus in order to avoid the lacrimal punctae and third eyelid present at the more heavily anchored medial canthus. The surgeon should usually undercorrect the ectropion because postoperative contraction of the tissues may account for an additional 0.5–1 mm of correction. Closure occurs in two layers, using 5–0 or 6–0 absorbable sutures in a continuous pattern to close the tarsoconjunctiva and 5–0 to 6–0 nonabsorbable sutures in an interrupted pattern to close the skin. A nonabsorbable cruciate suture at the lid margin ensures there is no postoperative notching of the lid margin. A modified Hotz-Celsus procedure may be performed concurrently if needed to correct any entropion adjacent to the wedge resection. With lids that are excessively long, the wedge resection can be performed on both the upper and lower lid, but a rhomboid canthoplasty may be superior, especially in cases complicated by lateral canthal entropion. Knots placed in the tarsoconjunctiva should be well buried to prevent irritation of the cornea, and the eye should be monitored closely after surgery for irritation associated with knot migration as the sutures are absorbed in the tissues (Fig. 6).

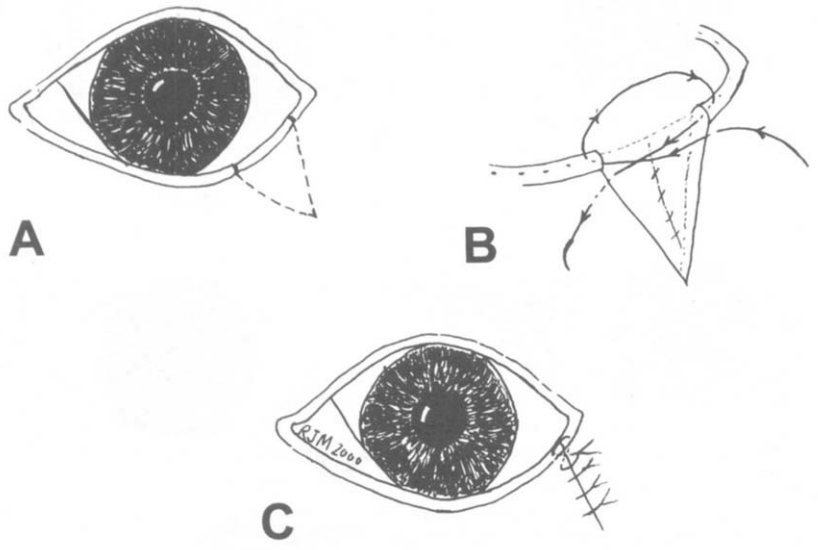


Figure 6. Stable suturing of a lid margin defect. *A*, Removal of a lateral wedge of lid. *B*, Enlarged view of placement of a cruciate suture at the lid margin after initial closure of the palpebral conjunctiva with an absorbable continuous suture. *C*, Closure completed. The knot of the cruciate suture is away from the lid margin and cannot irritate the cornea.

20. What is the difference between a V-shaped resection and a pentagonal or four-sided full-thickness resection of the lid?

The pentagonal or four-sided full-thickness resection is superior to the V-shaped resection for larger resections because it provides a larger surface area for distribution of tension and thus provides for better apposition and cosmesis.

21. When is the V-to-Y technique indicated in the correction of ectropion?

This technique should be reserved for correction of cicatricial entropion. It is basically a reverse of the Y-to-V technique described above for entropion, and, unless the lid margin is resected, it does not result in any shortening of the eyelid.

22. What is the difference between the Kuhnt-Szymanowski and Kuhnt-Helmbold procedures and what advantages and disadvantages do they pose?

Both procedures involve an extensive splitting of the lid margin to create an outer triangular skin-muscle flap and an inner tarsoconjunctival flap. The lid shortening with both techniques is achieved by a central wedge resection of the tarsoconjunctiva and a more lateral wedge resection of the skin-muscle flap. The difference is that the Kuhnt-Szymanowski (K-S) procedure carries the triangular flap dorsally and beyond the lateral canthus and the wedge of skin-muscle is removed from the lateral aspect. With the Kuhnt-Helmbold (K-H) procedure, the wedge removed from the skin-muscle is medial to the lateral canthus. The advantage of both procedures over the simple full-thickness wedge resection technique is that the resected portions are separated and thus less susceptible to dehiscence. The advantage of the K-S procedure over the K-H procedure applies to lids that lack tone and are in need of the greater support. Carrying the triangular skin-muscle flap beyond the lateral canthus creates a sling effect that supports the lid and restores tone to the lid. The disadvantage of both procedures is that they split a significant portion of the lid margin along the gray line introducing a significant potential for complications associated with scarring of the margin and its structures (Figs. 7 and 8).

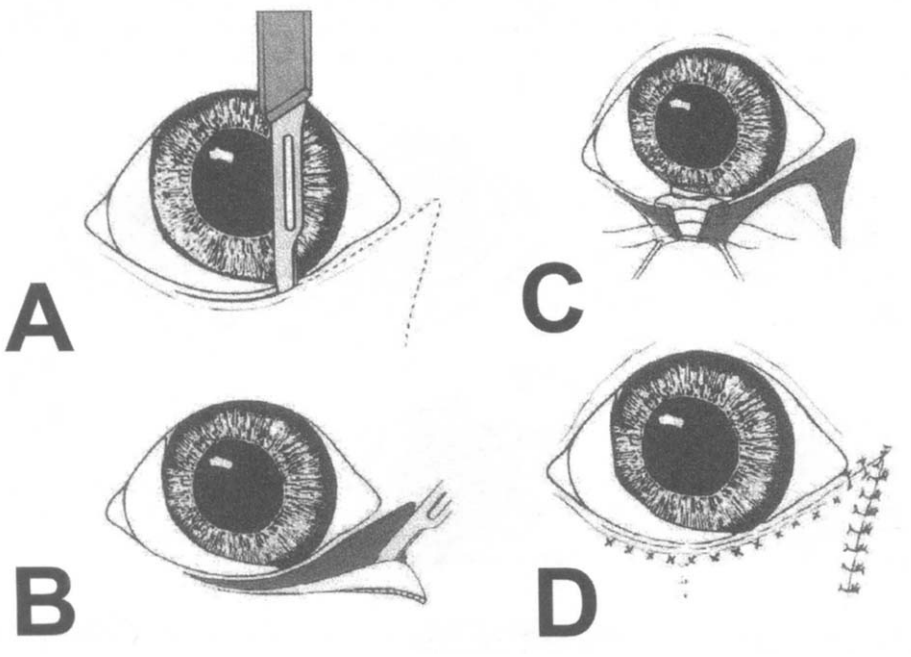


Figure 7. The Kuhnt-Szymanowski procedure supports the lid and improves tone. (From Gelatt K (ed): Handbook of Small Animal Ophthalmic Surgery. Tarrytown, NY, Elsevier, 1994, with permission.)

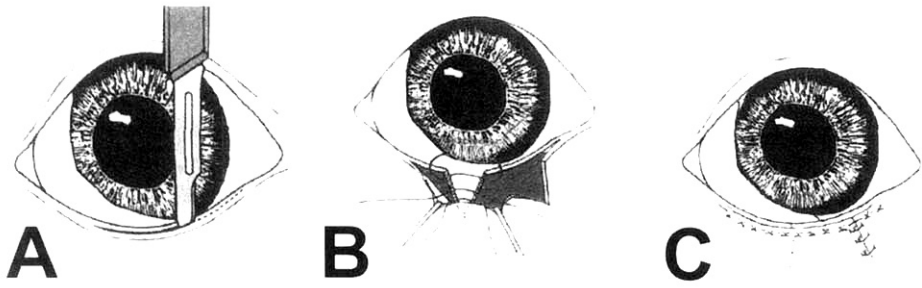


Figure 8. The Kuhnt-Humbold procedure. *A*, Splitting of the lid margin. *B*, Dissection of the skin-muscle flap and wedge resections. Note that the skin-muscle flap does not extend beyond the lateral canthus. *C*, Closure of the incisions is complete. (From Gelatt K (ed): Handbook of Small Animal Ophthalmic Surgery. Tarrytown, NY, Elsevier, 1994, with permission.)

23. What sutures are used and how are they placed with these procedures?

The wedge resection in the tarsoconjunctival layer should be closed with a continuous pattern of 5–0 or 6–0 absorbable suture. A few absorbable interrupted sutures may be placed between the flap and the tarsoconjunctiva to eliminate dead space. The skin flap should be closed with simple interrupted sutures of 4–0 to 6–0 nonabsorbable sutures.

24. How is the Munger-Carter modification different from the K-S procedure and what is its advantage?

The Munger-Carter modification has the advantage of not splitting the lid margin since the incision to create the skin-muscle flap is 1–2 mm distal to the lid margin. This preserves the lid margin and allows for combination of the procedure with the modified Hotz-Celsus procedure when concomitant entropion is present. In that event, a crescent of skin can also be removed from the edge of skin-muscle flap adjacent to the margin to evert the margin and correct the entropion. The defect in the lid margin created by the wedge resection is closed with a cruciate nonabsorbable suture. Knots in the skin sutures along the margin are less likely to irritate the cornea than those with the K-S and K-H procedures (Fig. 9).

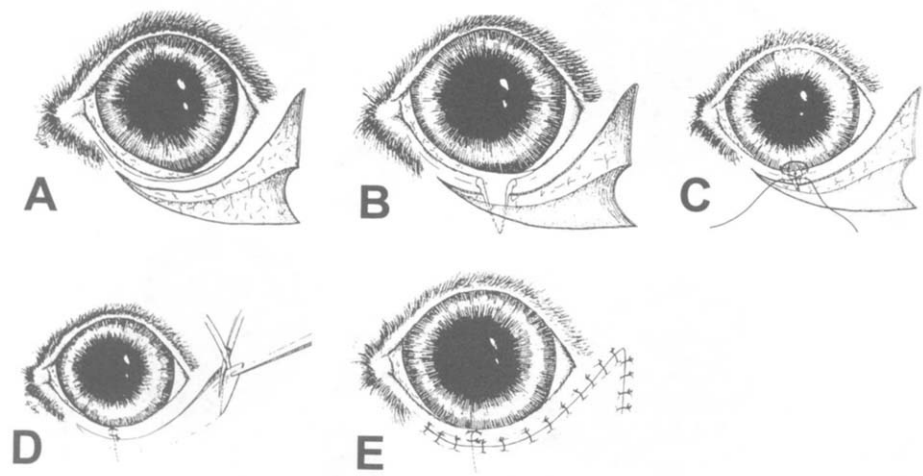


Figure 9. Munger-Carter modification of the K-S procedure. *A*, Initial skin incision and skin-muscle flap. *B*, Wedge resection of the lid margin and tarsoconjunctiva. *C*, Closure of the lid margin and tarsoconjunctiva. *D*, Removal of a triangular wedge equal in width to the tarsoconjunctival wedge from lateral aspect of the skin-muscle flap. *E*, Final closure. Note that the lid margin is not disturbed and the suture knots are not adjacent to the cornea.

25. Describe how to correct a diamond- or pagoda-shaped palpebral fissure with significant lateral canthal entropion when shortening of the palpebral fissure is desired.

A rhomboid or diamond lateral canthoplasty may be used to concurrently evert the lateral canthus and shorten the palpebral fissure (Fig. 10). The lid margin to be removed is measured from the lateral canthus to the point on the margin appropriate to achieve the desired shortening of the palpebral fissure. Both the upper and lower lids are incised perpendicular to their margins and the incisions extended dorsolaterally (for the upper lid) and ventrolaterally (for the lower lid). The length of each incision is approximately 1–2 times the width of the margin to be excised depending on the desired degree of entropion correction. These two incisions form the medial arms of the rhombus or diamond. From the ends of these incisions, two more incisions are made perpendicular to the first to intersect in a right angle lateral to the lateral canthus. The incisions define the diamond-shaped area of skin and tarsoconjunctiva excised to create the typical rhomboid defect. The cut end of the upper and lower lid margins are then joined with a 5–0 to 6–0 nonabsorbable suture using a cruciate pattern to recreate the lateral canthus. The conjunctiva is next closed with a continuous pattern of 5–0 to 6–0 absorbable suture. The lateral canthus is then apposed to the lateral corner of the diamond with an interrupted subcutaneous absorbable suture. The subcutaneous tissue is closed with a continuous pattern of absorbable suture, and the skin is closed with interrupted nonabsorbable sutures. The result is a curved sutured incision that tenses the lateral canthus laterally, and the procedure has shortened the palpebral fissure.

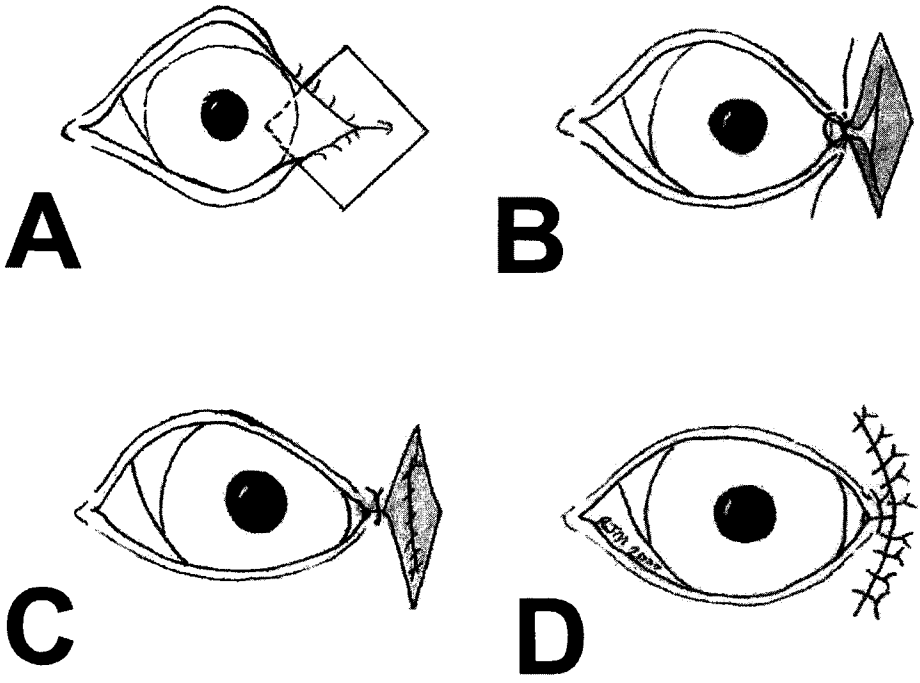


Figure 10. Rhomboid canthoplasty. *A*, Delineation of the tissue to be excised in the rhomboid canthoplasty. *B*, Initial closure of the lateral lid edges to reform the lateral canthus. *C*, Closure of the conjunctiva and subcutaneous tissues with continuous absorbable suture. *D*, Final curvilinear skin closure resulting in narrowed palpebral fissure and resolution of the lateral canthal entropion and ectropion.

26. What techniques can be used to deal with lagophthalmos?

Lagophthalmos associated with transient ocular or orbital swelling may be countered by a temporary tarsorrhaphy using 1–3 nonabsorbable mattress sutures passed though the lid margins at the level of the gray line. When there is little tension on the lids, the sutures may be placed with-

out stents. When lagophthalmos is associated with a permanent condition (e.g., macropalpebral fissure, conformational exophthalmos, lid paralysis), permanent canthoplasty may be performed either laterally or medially depending on the area of the globe and cornea most exposed and which placement will best preserve lid function.

27. In brachycephalic breeds with exophthalmos and lagophthalmos or pigmentary keratitis, what options are available to protect the globe?

Because the eyes of the brachycephalic breeds are usually somewhat exotropic, the medial sclera is often more exposed than the lateral. Therefore, a partial medial tarsorrhaphy or so-called medial canthal closure not only protects the eye and reduces exposure, it also is superior cosmetically because the pupil is then better centered in the palpebral fissure than with a lateral canthal closure. In addition, the medial canthal closure allows removal of hairs associated with the lacrimal caruncle and eliminates contact between the cornea and hairs of the medial lower lid and nasal folds. Medial canthoplasty or canthal closure is usually performed by one of two techniques. The simplest involves the removal of the medial lid margin and adjacent skin while avoiding the lacrimal punctae. The skin can then be closed in two layers. The tarsoconjunctiva is closed with a continuous pattern of 5–0 to 6–0 absorbable suture, and the skin is closed with 4–0 to 6–0 nonabsorbable interrupted sutures. This procedure allows preservation of both lacrimal punctae, but the closure is thinner and more subject to stretching than the pocket-flap technique described by Jensen. With the pocket-flap procedure, the medial upper and lower lids can be split along the gray line to create pockets 10 mm deep. The split in the lower lid passes anterior to the lower lacrimal punctum thus preserving its function. A triangular tarsoconjunctival flap from the upper lid is sutured into the pocket in the lower lid using a 4–0 nonabsorbable suture. The suture is passed through the skin into the ventral aspect of the lower lid pocket, up though the pocket, and then through the tip of the triangular flap. It is then passed back down into the pocket, out through the skin, tightened to pull the flap into the pocket, and tied. The outer margins of the split lids are removed and the skin closed with 4–0 to 5–0 interrupted nonabsorbable sutures. While the superior punctum is sacrificed, the resulting closure results in superior support of the medial canthus. Figures 11 and 12 illustrate the technique and cosmetic appearance that can result.

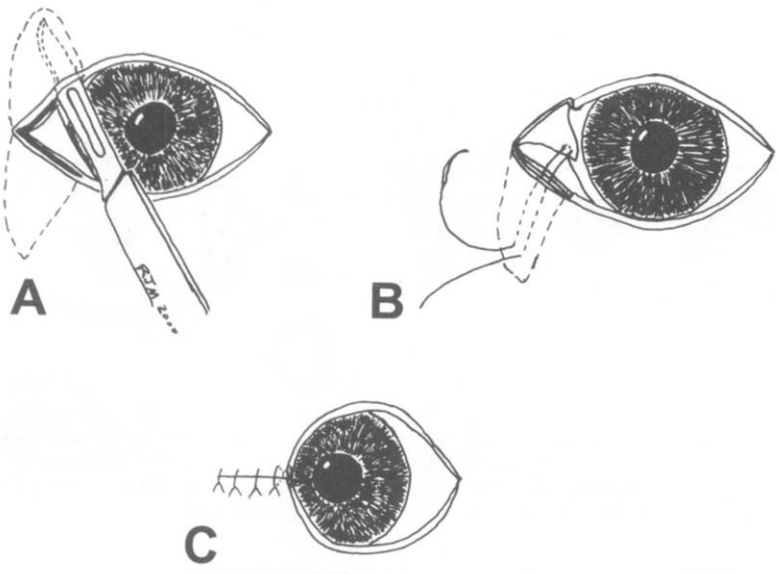


Figure 11. The Jensen technique for medial canthal closure to narrow the palpebral fissure. *A*, Splitting of the medial upper and lower lids to create the pocket and tarsoconjunctival flap for closure. *B*, Passage of the suture from the pocket to draw and anchor the flap into the pocket. *C*, Final closure narrowing the palpebral fissure.

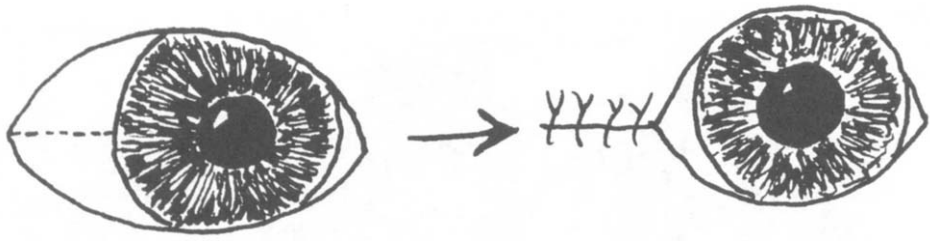


Figure 12. Medial canthal closure protects the globe while narrowing the palpebral fissure and masking the medial sclera. Most brachycephalic breeds show more sclera medially resulting in an exotropic appearance. Medial canthal closure to narrow the palpebral fissure (extent indicated by the dashed line) not only protects the globe but also improves the cosmetic appearance.

28. Is there a simple way of dealing with medial canthal trichiasis?

The simplest and perhaps most effective way to resolve medial canthal trichiasis is to use cryoablation of the offending hairs. The tissue from which the hairs arise can be frozen with a liquid nitrogen spray (being careful to ensure the adjacent structures are protected from freezing). The tissue should be frozen twice, separating each freeze by a slow thaw. In patients with lagophthalmos in which a partial medial tarsorrhaphy is contemplated, the lacrimal caruncle and other structures from which the hairs arise may be removed prior to closure.

29. When confronted with removal of large lid tumors, how much of the lid may be removed and still allow simple apposition and closure?

The rule of thumb is that up to one-fourth of the lid may be removed by a simple wedge resection without requiring more than simple closure. However, all rules have exceptions, and more lid may be removed in dogs with more expansive or elastic periocular skin and lids. Figure 13 presents a good example from a cocker spaniel with a large sebaceous adenoma on the upper lid. A pentagonal, full-thickness resection is used to remove the tumor, and because the upper lid is long, primary closure can be achieved. While the resultant upper lid shortening narrows the palpebral fissure, the elasticity of the tissue has allowed closure, and gradual stretching allows the palpebrae to assume a more normal and quite acceptable appearance by the time of suture removal. Further remodeling and reshaping will continue with time.

30. What is an H blepharoplasty and how is it performed?

H-plasty uses a sliding skin flap to move adjacent skin vertically into a lid defect. The tissue removed at the lid margin represents the first section of the H, and the flap of skin to be mobilized represents the second. Once the full-thickness resection of the lid lesion has been performed, two slightly diverging incisions are extended away from the defect. These incisions should be twice the height of the lid defect, and two triangles of equal size (Burow's triangles) are removed from the skin adjacent to the distal extent of the sliding flap. The flap is then dissected free from the subcutaneous tissue and advanced, closing the triangles. The deep surface of the flap may be covered by adjacent palpebral and fornix conjunctiva, conjunctiva from the opposite lid, or a free graft from the buccal mucosal. The skin flap is advanced to 0.5–1.0 mm beyond the adjacent lid margins to compensate for postoperative contraction of the graft. The sides of the skin flap are apposed with 4–0 to 6–0 simple interrupted nonabsorbable sutures. The conjunctiva or mucosal graft is attached to the flap with continuous 5–0 to 6–0 absorbable sutures using either a continuous pattern or interrupted sutures with knots carefully buried or positioned away from the edge of the flap to avoid contact with the cornea (Fig. 14).

31. Describe how larger upper eyelid defects (those that cannot be closed by primary apposition of the edges) can be repaired to preserve optimal lid function.

Because the upper lid covers the majority of the cornea during blinking, preservation of its function is extremely important for optimal lid function. Preservation of upper lid mobility and

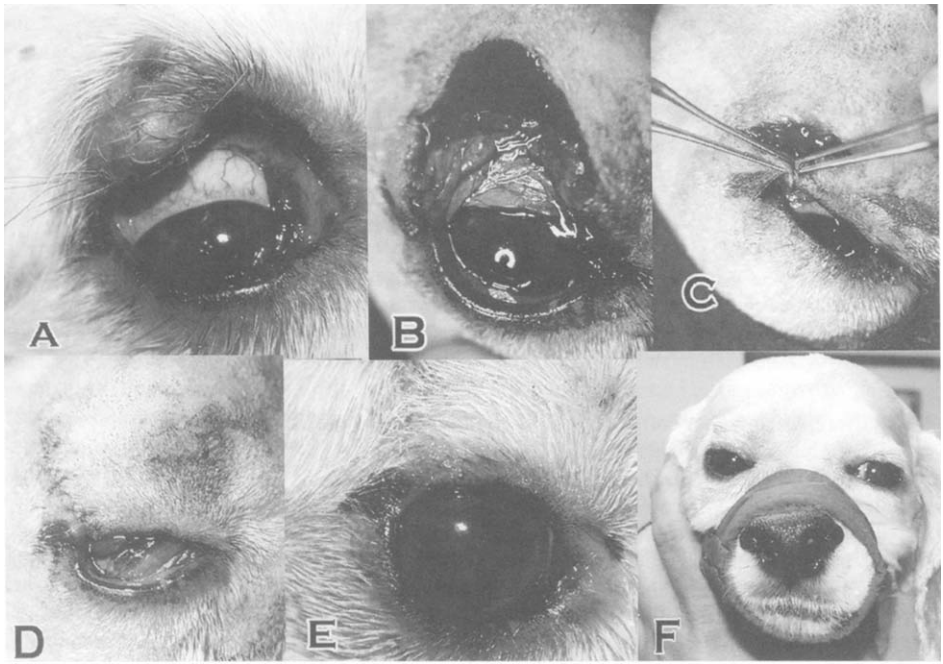


Figure 13. Simple closure of a large eyelid defect. *A*, Preoperative appearance of large sebaceous adenoma. *B*, Pentagonal defect at time of resection. *C*, Checking apposition. *D*, Immediately after closure. *E*, Close-up appearance at 11 days postoperatively after suture removal. *F*, Comparison with fellow eye 11 days postoperatively.

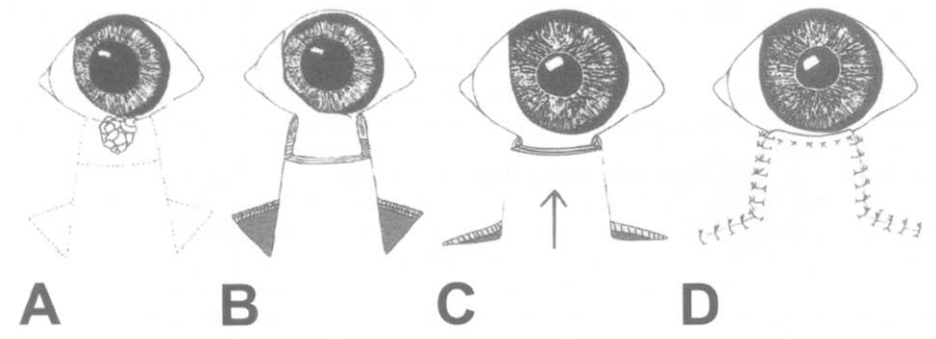


Figure 14. H-plasty. *A*, Initial incisions for removal of mass and formation of sliding skin-muscle flap. *B*, Lid defect and Burow's triangles performed in preparation of sliding of the flap. *C*, Skin-muscle flap sliding into position with collapse of the Burow's triangles. *D*, Final closure with flap advanced 0.5–1.0 mm beyond lid margins to allow for postoperative contraction of the skin. (From Gelatt K (ed): Handbook of Small Animal Ophthalmic Surgery. Tarrytown, NY, Elsevier, 1994, with permission.)

provision for a good lid margin are critical factors that cannot be achieved with advancement and rotational flaps. Munger and Gourley describe a cross lid flap that uses a lower lid flap to reconstruct the upper lid, thus providing for both a lid margin and mobility for the upper lid. The width of the flap from the lower lid is 3/4 of the width of the defect in the upper lid because the adjacent upper lid tissue can be stretched to fill 1/4 of the defect. The pedicle of the flap must be at least 4 mm wide to preserve blood supply to the flap. The pedicle may be either medial or lat-

eral, but the lower lacrimal punctum must be preserved in either case. The flap is rotated 180° into the upper eyelid defect, and closure is accomplished in two layers using 5–0 to 6–0 interrupted absorbable sutures for the conjunctiva and subcutaneous tissues and 5–0 to 6–0 interrupted nonabsorbable sutures in the skin. A cruciate suture is used to appose the margins. After 14–21 days, when vascularization of the flap is ensured, the pedicle is resected, rotated up, and sutured to reform the lid margin. The lower lid defect is then closed either by primary closure (when sufficient lower lid remains) or by advancement skin flap from the infraorbital skin tissue (Fig. 15).

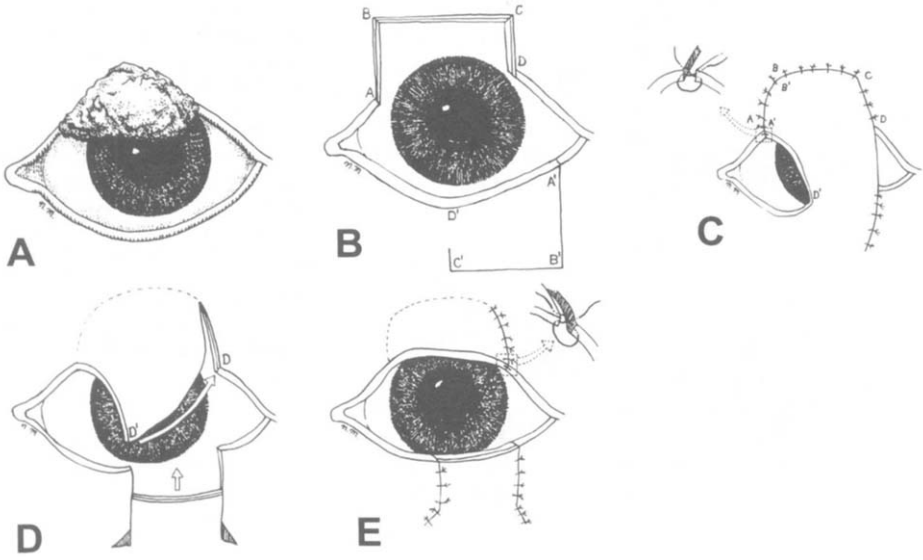


Figure 15. Cross lid flap for repair of large upper eyelid defects. *A*, Diagram of a large upper eyelid tumor. *B*, Full-thickness pedicle flap is constructed from the lower lid with the margin. It is the full depth and three-fourths of the width of the upper eyelid defect. The pedicle (*d'*) is directly opposite the center of the upper eyelid defect. *C*, The cross lid flap has been rotated across the palpebral fissure and sutured in place. Point c in the flap would be somewhere in the vicinity of point d. *D*, After 14–21 days, the second stage is performed severing the pedicle and rotating the pedicle into position with d' apposed to point d. An H-plasty has been performed here to close the lower lid defect and can be lined with conjunctiva or mucosal from the nasal or oral cavity. *E*, Final closure illustrating the reconstructed upper lid margin from the lower lid margin.

32. When reconstructing lid lacerations that involve the lacrimal canaliculi, how can the canaliculus be identified and restored?

A pigtail probe is an excellent instrument for use in reconstructing the lacrimal canaliculus. The probe is passed through the lacrimal punctum and canaliculus of the opposite lid and rotated out through the medial aspect of the severed canaliculus. A 3–0 to 4–0 monofilament nonabsorbable suture is passed through the "eye" in its tip so that when the probe is withdrawn it pulls the suture through the canaliculi and out the punctum. The probe can next be passed through the lacrimal punctum on the injured lid and out through the lateral severed end of the canaliculus. The suture is then reengaged and pulled back through the punctum. Silastic tubing is passed over the end of the suture that is then clamped inside the tubing with a hemostat. By gentle traction on the suture, the silastic tubing can then be pulled through the lacrimal canaliculi and left in place until healing of the laceration is complete. The silastic tubing may be sutured in place after passing it through or over each lid or it may be tied in place in the medial canthus (Fig. 16).

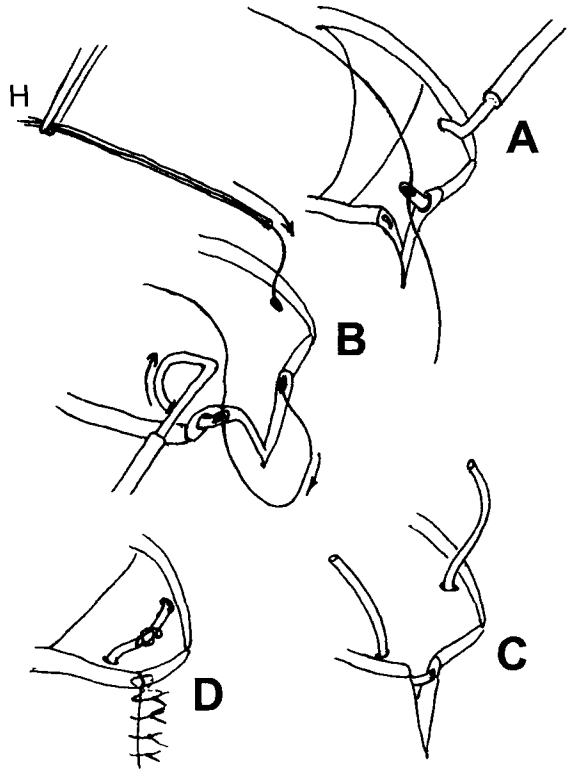


Figure 16. Repair of laceration of lacrimal canaliculus using a pigtail probe. *A*, Pigtail probe passed from the superior punctum into medial lower canaliculus. Note suture passed through eye of probe that will be retracted out through superior punctum. *B*, In the next stage, the probe is passed through the lower punctum and out through the lacerated canaliculus. The suture is then passed through the eye and retracted out through the lower punctum. Silastic tubing passed over the suture and clamped to the suture with a hemostat (*H*) can then be pulled through the system. *C*, Silastic tubing in place. *D*, Closure complete with silastic tube tied in the medial canthus.

BIBLIOGRAPHY

1. Gelatt KN, Gelatt JP: Surgery of the eyelids. In Handbook of Small Animal Ophthalmic Surgery. Vol 1: Extraocular Procedures. Tarrytown, Elsevier Science, 1994, pp 69–124.
2. Jensen JE: Canthus closure. Comp Cont Educ 1:735–741, 1979.
3. Munger RJ, Cater JD: A further modification of the Kuhnt-Szymanowski procedure for correction of atonic ectropion in dogs. J Am Anim Hosp Assoc 20:651–656, 1984.
4. Munger RJ, Gourley IM: Cross lid flap for repair of large upper eyelid defects. J Am Vet Med Assoc 178:45–48, 1981.
5. Wyman M: Lateral canthoplasty. J Am Anim Hosp Assoc 7:196–201, 1971.
6. Wyman M: Ophthalmic surgery for the practitioner. Vet Clin North Am Small Anim Pract 9:311–348, 1979.
7. Wyman M, Wilkie DA: New surgical procedure for entropion correction: Tarsal pedicle technique. J Am Anim Hosp Assoc 24:345–349, 1988.

27. EYELID NEOPLASMS

Annajane B. *Marlar*, D.V.M.

1. How common are lid tumors in dogs and cats?

Lid tumors are quite common in dogs. By contrast, in cats, lid tumors are rare and make up only 2% of neoplasias. In one study of ocular neoplasia, tumors of the lid and conjunctiva combined comprised 25%, but in reality the figure is probably even lower.

2. When do most lid tumors arise and in what location?

The average age of onset for lid tumors in dogs is 9 years. Malignant neoplasms tend to develop in dogs older than average, whereas benign tumors such as histiocytomas have a tendency to develop in younger patients. The central portion of the upper and lower lids is the usual location for tumors with the upper lid being slightly more common than the lower. Canthal involvement is uncommon. In cats, the age of onset is greater, and the medial canthus is a more common location than in the dog.

3. What are the most common types of tumors in dogs?

Most lid tumors encountered in the dog will be benign. The most frequent types encountered include sebaceous adenomas, papillomas, and melanomas. If the lesion is pigmented and smooth, it is likely a melanoma. Benign behavior is typical of eyelid melanomas, although sometimes these tumors can be more aggressive. When malignancies occur, the lid lesion is usually the primary site, and metastasis from the eyelid is generally slow. Of the malignancies that can develop in this area, sebaceous adenocarcinoma, mast cell tumor, squamous cell carcinoma, and basal cell carcinoma seem to be most common. Mesenchymal tumors of the eyelid are uncommon. Generally, if one thinks about the tissue types in this area, then a list of possible tumor types can be constructed: skin, sebaceous glands, conjunctiva, etc. (Figs. 1–3).

4. How does this differ in the cat?

Although benign lid tumors can occur in the cat, malignant types are more frequent and comprise 75% of eyelid neoplasms. The most common type of lid tumor is squamous cell carcinoma, particularly in patients with light coat color or with white fur around the face. One benign process described is xanthoma, which presents as a focal or multifocal, yellowish mass within the lid and

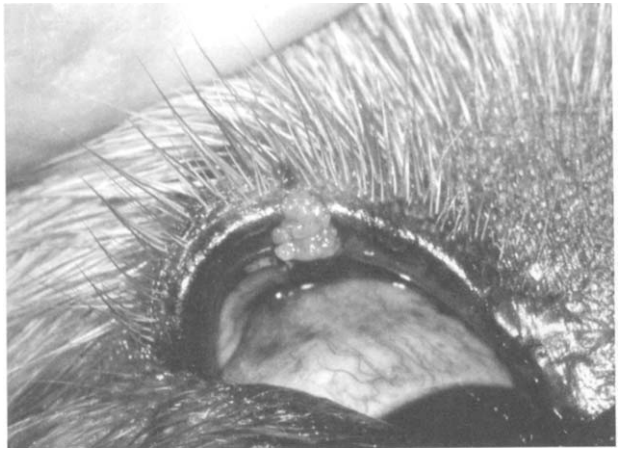


Figure 1. A typical sebaceous adenoma of the lid margin. Note the involvement of the conjunctival surface.

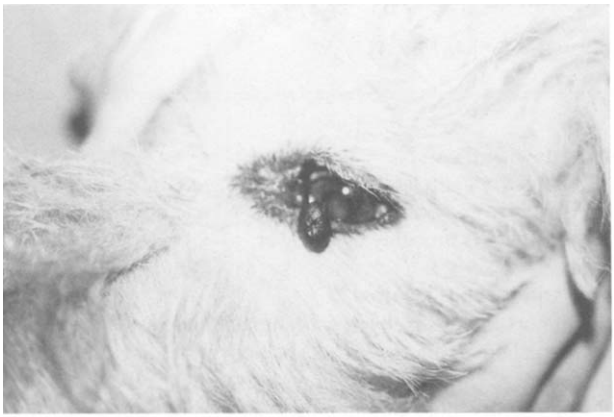


Figure 2. A melanoma on the upper lid. These are locally invasive but usually do not metastasize.

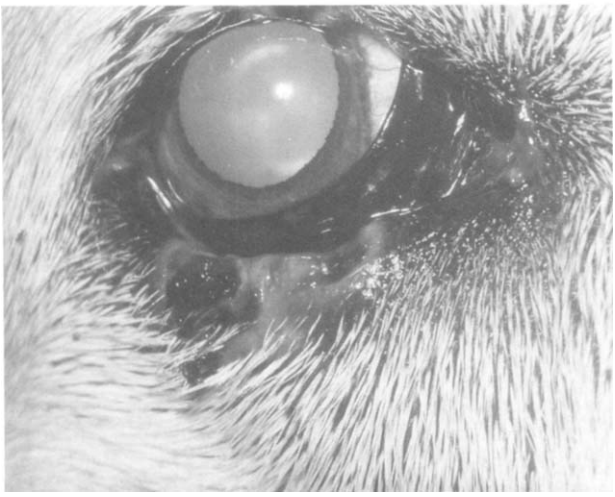


Figure 3. A squamous cell carcinoma of the lower lid. These can be a challenge (see Chapter 27).

conjunctiva. Other tumor types that have been reported include meibomian gland adenoma and adenocarcinoma, basal cell tumor, melanoma, mast cell tumor, and fibroma/fibrosarcoma (Figs. 4 and 5).

5. Are all mass lesions neoplastic?

Some conditions of the eyelid may be difficult to distinguish from neoplasms (e.g., granuloma, chalazion, and even some acute lesions such as marginal inflammatory conditions). Patient history can be helpful in the identification because most lid tumors tend to grow gradually rather than rapidly. A lesion that is bilateral and symmetric is unlikely to be neoplastic. Eyelid lesions that are associated with pruritus are less likely to be neoplastic (mast cell tumor may be the exception). If all lids are affected with nodules, consider immune-mediated blepharitis or sterile pyogranulomas as a possible etiology. The diagnosis is best made with histopathology of an area of affected lid margin.

6. How can I tell if a tumor is benign or malignant?

Histopathology is recommended for all lid tumors. Without it, you cannot be 100% sure whether you are dealing with a benign or malignant process. However, several characteristics point to malignant neoplasms and may prove useful tools during examination of the eyelids.

MALIGNANT	BENIGN
Destruction of hair follicles	Hair follicles intact
Lesion is ulcerative	Lesion is not ulcerative
Rapidly growing	Lesion is slow growing

7. If the mass is not irritating to the cornea, why remove it?

As discussed earlier, although many lid tumors will be benign, it is not always possible to differentiate their behavior based on examination only, and many benign lid tumors will still cause extensive local destruction of tissue if left untreated. For many patients requiring extensive reconstruction, early intervention may have prevented procedures that prove to be more uncomfortable for the patient and more costly to the client. Therefore, it is becoming widely accepted

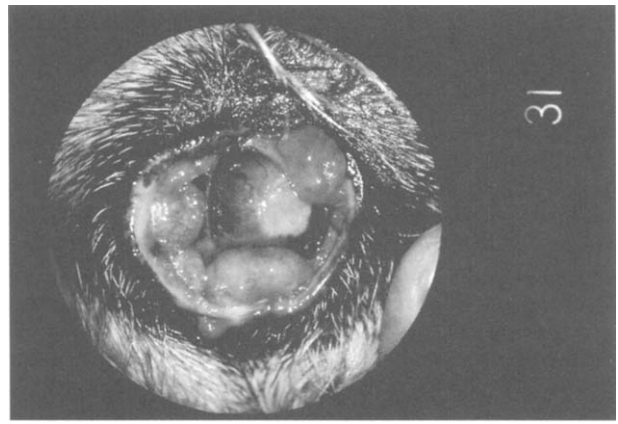


Figure 4. Multiple conjunctival tumors which were diagnosed as melanosarcomas

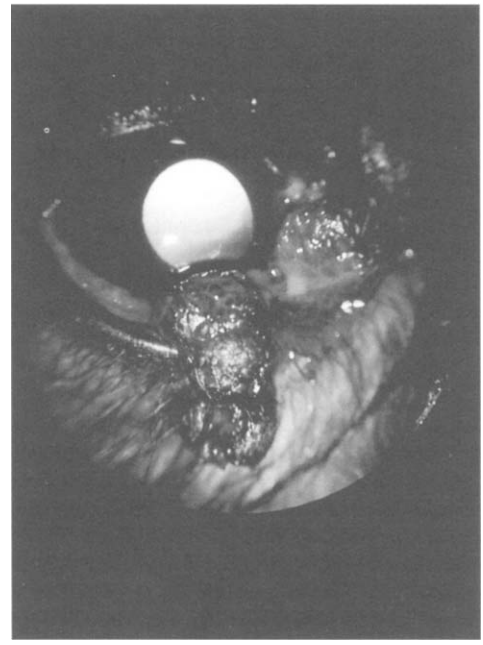


Figure 5. A large lower lid papilloma.

that lid masses should be removed or treated prior to onset of clinical symptoms. At the earlier stage, it may be possible to retain both functional and cosmetic lid margin.

8. When is it appropriate to biopsy a mass before excision?

If the mass is extremely ulcerated and extending away from the lid margin, consider biopsy prior to definitive surgery. The diagnosis may alter the treatment options. An example of this is a large squamous cell carcinoma that may be amenable to therapies other than surgery. If the lesion is less than one-third the length of the eyelid, it is more appropriate to perform an excisional biopsy or biopsy and cryotherapy.

9. How should the tissue be processed?

Tissue that is removed should be placed in an appropriate container with 10% formalin as fixative. If the mass is small, microcassettes can be used to better preserve the tissue and make it easier to process. This is very helpful when tissue specimens are small, and it avoids calls from the laboratory that tissue was misplaced! Even with a treatment modality other than surgical excision, submitting a sample for pathology is still recommended.

10. What are the anatomic considerations when choosing a treatment plan?

There are two main goals to consider when considering treatment alternatives. The first is to preserve mechanical lid function and normal glandular function. Maintaining the lid margin as a mucocutaneous junction is key. The second is the preservation of a cosmetic eyelid. The location of the mass also may be important with regard to the lacrimal puncta. The superior punctum is less important to normal lacrimal flow than the inferior punctum. The latter should be preserved if at all possible to prevent chronic epiphora.

11. What is the most common method of mass removal?

For lesions that constitute less than 25–30% of the lid length, a full-thickness, four-sided (wedge) resection is the standard technique and provides a functional and cosmetic result by preserving the lid margin completely. The incision is closed in two layers. The subconjunctiva should be closed with an absorbable suture such as 6–0 Vicryl with knots buried. The skin can be closed with a number of suture patterns of 5–0 or 6–0 nonabsorbable suture; generally, an interrupted pattern provides the best results. In darkly pigmented patients, a colored suture such as Prolene is a good choice because it is easy to see. It is important that the lid margins are aligned correctly during this closure and that the suture ends and knots cannot contact the cornea to prevent irritation. An Elizabethan collar is suggested to prevent self-trauma, and suture removal is performed after 2 weeks.

12. What instrumentation do you need for this type of surgery?

A basic set of ophthalmic instruments are ideal for lid surgeries.

- Mosquito hemostats × 2
- Castroviejo needle holder
- Steven's tenotomy scissors
- Tissue forceps or Bishop Harmon forceps
- Magnification (either head loop or glasses)
- Optional: Jaeger lid plate, chalazion clamp

13. How do I choose a reconstructive technique if I need one?

In human reconstructive techniques, planning involves consideration of relaxed skin tension lines (RSTL) and lines of maximum extensibility (LME). In veterinary ophthalmology, attention is paid to skin biomechanics, but there is another factor to consider: the direction of hair growth. Particularly when using flap techniques, it is important to plan with attention to normal hair direction. For inferior lid defects, the primary techniques that have been described include H-plasty

and several rotational flaps. For superior lid defects, there is an increased likelihood of corneal irritation from lid margin, and, therefore, marginal reconstruction becomes more important. Many of the flap techniques that have been described originate in the human literature and have been modified for veterinary ophthalmology. The Table lists some common techniques and areas of lid in which they may be helpful.

TECHNIQUE	SUPERIOR LID	INFERIOR LID
Wedge resection	+	+
H-plasty	±	+
Sliding rotational	+	+
Transposition	+	+
Lip to lid	−	+
Cross-lid flap	+	−
Bucket handle	+	−
Z-plasty (canthal)	+	+

14. What other surgical modalities are available for eyelid neoplasms?

For many years, the only other surgical modality used in the treatment of eyelid neoplasia was cryosurgery, which is the use of a freezing agent, typically liquid nitrogen or nitrous oxide, to ablate both normal and abnormal tissue. Recently, however, more and more clinicians are using laser technology to treat lid conditions including neoplasia. The carbon dioxide laser has increased in availability and is now used on a routine basis. The carbon dioxide laser provides not only sharp dissection capability but also generalized ablative function.

15. How does cryosurgery work?

The freezing of tissue causes events at a cellular level that occur in three phases: immediate, delayed, and late. During the immediate phase, cells are destroyed because of dehydration with concentration of toxic solutes, formation of both intracellular and extracellular ice crystals, denaturation of proteins, and direct thermal shock. In the delayed phase, cellular destruction occurs because of vascular stasis resulting in thrombosis, ischemia, and cell death. Finally, in the late phase, there may be an immunologic, response to freezing with formation of antibodies to the altered tumor cells. Normal cells tend to show increased resistance to the above effects, and, therefore, there is a sparing effect of normal tissue. Isolation of the local blood supply will increase the effectiveness of this technique particularly in highly vascular tissues such as the eyelid.

16. How is cryosurgery performed?

The most common cryogen used in veterinary medicine is liquid nitrogen which has a temperature of −195.8°C. The most common delivery device is a hand-held unit such as the Cryogun (Brymill Corporation), but others are also available. There are a variety of probes available. Both spray and solid probe tips can be used, although spray tips will often result in more rapid freezing of tissue. If solid tips are used, the size should be approximately the size of the lesion to ensure a rapid freeze. In general, the goal is to freeze the tissue to −80°C or below for a duration of 1 minute or more to induce cryonecrosis. A rapid freeze and slow thaw are optimal. If possible, the lesion should be debulked (often tissue for biopsy is removed during this process). The lesion should be treated for two to three freeze/thaw cycles. Thermocouples are ideal to measure tissue temperature. One can also use the size of the ice ball to gauge the depth of freeze. The visual advancing of the ice ball only represents 0°C, and therefore only 75% of the visible ice ball is likely to be at optimal temperature. In general, an area of 5–10 mm of normal tissue would be desirable for most malignancies. Remember that the ice ball formation is three dimensional and the depth of freeze should be monitored closely in order to prevent freezing the tissue too much or too little. Probe freezing is less lethal but easier for persons inexperienced with these techniques. The probe can be applied directly to the tumor for contact freezing. If the lesion is circu-

lar, a biopsy can be taken from the center of the mass with the probe introduced into the lesion to achieve a circular freezing pattern.

Another commonly used cryogen is nitrous oxide. Spray tips of this cryogen are not very effective. However, gas supercooling a probe is very effective. Probe tip temperatures of −89°C can be achieved. Its use is usually restricted to masses smaller than 2–3 cm. After care includes topical antibiotics, Elizabethan collar, and sometimes the use of systemic antibiotics and anti-inflammatory drugs (Figs. 6 and 7).

17. How is laser technology utilized?

In recent years, laser technology has become more available to the veterinary profession. The carbon dioxide laser is receiving some attention as a useful tool in ophthalmic adnexal surgery. The carbon dioxide laser operates at wavelengths of 10,600 nm, which is in the far-infrared portion of the light spectrum. It is invisible to the naked eye, and therefore, a coaxial red helium or neon aiming beam is used. The tissue absorption of this laser is independent of tissue pigmentation. The carbon dioxide laser has higher water absorption, which minimizes the depth of penetration making it a precise cutting tool. It can be used in both cutting and ablative modalities. With regard to eyelid neoplasia, some clinicians use it to remove small lesions by sharp dissection and also to ablate larger lesions in a similar fashion to cryosurgery. Adequate documentation is still lacking in the veterinary ophthalmic literature as to the advantages and disadvantages of one surgical modality over the other and of specific protocols.

18. What about chemotherapy?

Systemic chemotherapy is of little value in treating most eyelid neoplasias unless the lid tumor is not a primary lesion. Intralesional chemotherapy has been used primarily for squamous

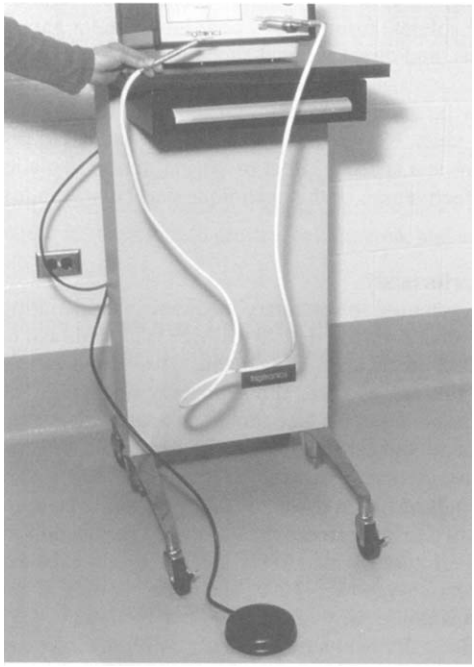


Figure 6. A cryosurgical unit made by Frigitronics, a product of Cooper Surgical. The stand houses two nitrogen gas cylinders for the cooling source of the hand piece.

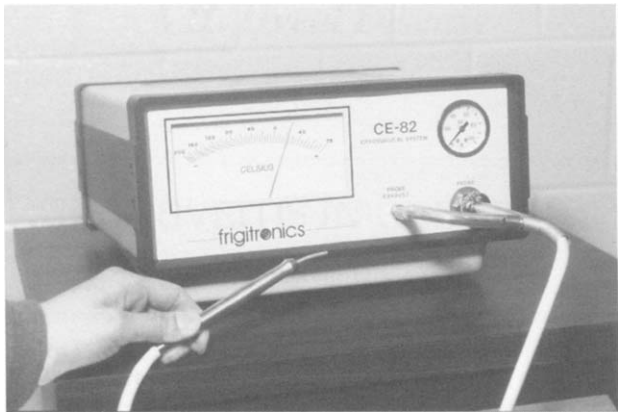


Figure 7. A close-up of a hand piece containing sensors for temperature. The monitor in the background shows temperature in celsius and cylinder pressure.

cell carcinoma. Cisplatin, carboplatin, and 5-fluorouracil (5Fu) have been used mostly in feline patients, but the technique may also be applicable to canine patients with varying success. In addition, some anecdotal reports exist of using intralesional injection of distilled water as a treatment modality of mast cell tumor.

19. Are there any other treatment modalities available?

Yes. Radiation therapy, brachytherapy, and radiofrequency hyperthermia are all acceptable treatment modalities, although their use has declined in recent years, most likely because of earlier diagnosis and treatment of eyelid neoplasms. Radiation therapy, in particular, can cause severe ocular damage; its use should be considered carefully, and it is indicated only in the event of aggressive neoplasms that are difficult to treat with other modalities (e.g., fibrosarcoma). Photodynamic therapy is a relatively new technique where a photosensitizing chemical is administered systemically and preferentially retained by the tumor. The site is then irradiated with wavelengths absorbed by the chemical. This technique can be used only in superficial tumors and is still in early stages of clinical use.

20. Should enucleation ever be considered when treating eyelid neoplasia?

The goal of any treatment should be to preserve the function and cosmesis of the eye whenever possible. However, if a tumor is malignant and too large in size to allow for sparing of ocular function, then enucleation should be considered in an attempt to prevent systemic disease. Such a decision should not be made without a diagnosis of the mass and possibly evaluation by a specialist, particularly if the patient is monocular. The most common tumor requiring enucleation that this author has seen is eyelid fibrosarcoma because often radiation therapy will be required.

BIBLIOGRAPHY

1. Gelatt KN: Veterinary Ophthalmology, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 1998, pp 558–567.
2. Hamilton HL, Whitley RD, McLaughlin SA, et al: Basic blepharoplasty techniques. Comp Cont Educ Pract Vet 21:946–952, 1999.
3. Roberts SM, Severin GA, Lavach JD: Prevalence and treatment of palpebral neoplasms in the dog: 200 cases (1975–1983). J Am Vet Med Assoc 189:1355–1359, 1986.
4. Ruslander D, Kaser-Hotz B, Sardines JC: Cutaneous squamous cell carcinoma in cats. Comp Cont Educ Pract Vet 19:1119–1129, 1997.

VII. Uveal Disease

28. UVEITIS IN GENERAL

Cynthia C. *Powell*, D.V.M., M.S.

1. What is the uvea or uveal tract?

The structure of the eye consists of an outer wall (cornea and sclera), inner retinal layer, and the uvea, a highly pigmented, vascular layer sandwiched between the sclera and retina. The uvea consists of the iris, ciliary body, and choroid. The iris and ciliary body are collectively referred to as the **anterior uvea.** The **posterior uvea** is the choroid. Although the anatomic regions have different names, the tissues are basically continuous with each other.

2. How is the uvea different from the uvula?

In contrast to the ocular uvea, the term *uvula* stems from a Latin word that means "little grape." The palatine uvula is a small, pendulous, fleshy mass hanging from the posterior soft palate edge above the root of the tongue in humans. Other structures associated with the term *uvula* include the bladder (uvula vesicae, a rounded elevation at the bladder neck) and cerebellum (uvula vermis, part of the cerebellum vermis between the pyramis and nodulus).

3. What is uveitis?

Uveitis is inflammation of one or more of the uveal tissues. Inflammation that involves a single tissue is termed iritis, cyclitis, or choroiditis if the iris, ciliary body, or choroid is inflamed, respectively (Fig. 1).

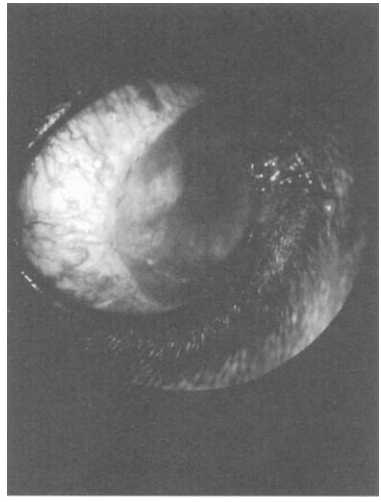


Figure 1. Dog with uveitis. Note the congested conjunctival vasculature and the swollen iris with miotic pupil.

4. What is anterior uveitis?
Inflammation of both the iris and ciliary body.

5. What is posterior uveitis?
Choroidal inflammation.

6. Can inflammation involve the anterior and posterior uvea simultaneously?
The division of the uvea into anterior and posterior does not imply a physical barrier between the two regions. Inflammation often involves both anterior and posterior portions. The terms *uveitis, endophthalmitis,* and *panophthalmitis* are used to describe diffuse uveal inflammation.

7. What is endophthalmitis?
Inflammation of the entire uveal tract is called endophthalmitis. Because of the close apposition of the choroid and retina, choroidal inflammation rarely occurs without retinal involvement (i.e., chorioretinitis). Thus, the prognosis for vision with endophthalmitis is poor (Figs. 2 and 3).

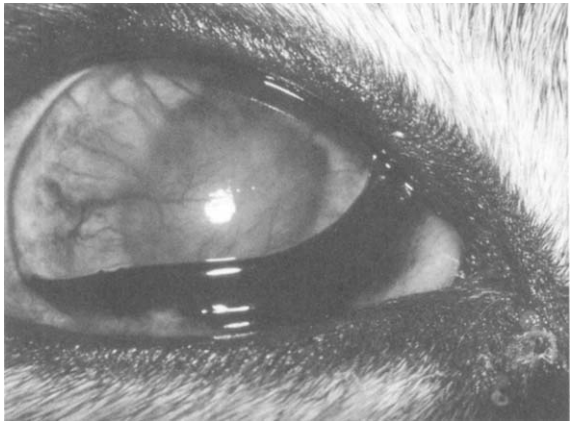


Figure 2. Cat with endophthalmitis. Note the vascular response with hemorrhage and fibrin.

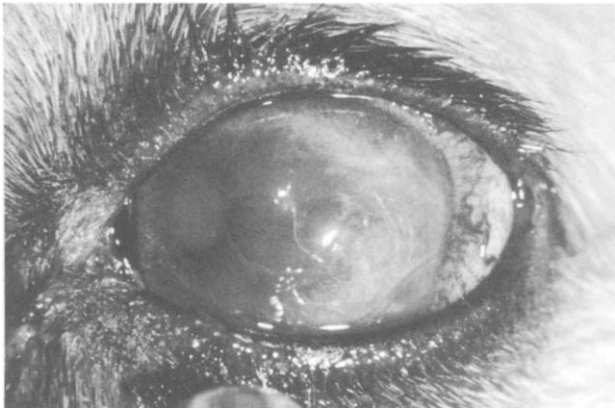


Figure 3. Dog with endophthalmitis. This is a very painful disease.

8. What is panophthalmitis?

Uveal tract inflammation coupled with scleral and corneal inflammation is termed panophthalmitis. It is difficult to maintain a normal-appearing globe with inflammation of this severity and distribution. Preserving vision is hopeless (Fig. 4).

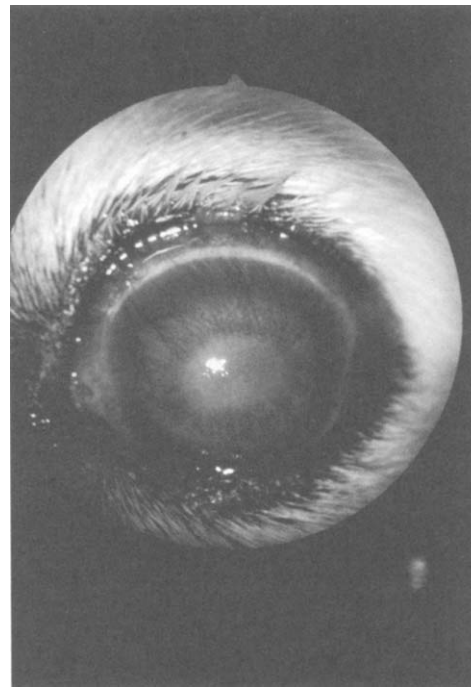


Figure 4. Chronic panophthlamitis in a dog. Note the severe neovascularization of the cornea and the periocular inflammation.

9. What are the major clinical signs of uveitis?

Anterior uveitis typically causes a painful eye with conjunctival and episcleral hyperemia, miosis, aqueous flare and cell accumulation, corneal edema, iris swelling and hyperemia, and reduced intraocular pressure (hypotony). Vision is impaired but rarely lost with simple anterior uveitis. Vision loss indicates more extensive ocular tissue damage and usually occurs with increased severity or duration of inflammation. An ophthalmoscope is required for assessment of posterior uveitis. Ophthalmoscopic signs include loss of the normal tapetal color, retinal detachment, subretinal transudation or exudation, and loss of retinal pigment epithelial cell and choroidal pigmentation. Posterior uveitis almost always also involves the retina (chorioretinitis) and may cause blindness.

10. Can the clinical signs be used as an indication of chronicity, severity, or prognosis?

The spectrum and magnitude of signs depend on the severity of insult. The Table differentiates acute versus chronic anterior uveitis based on clinical signs. If trauma, vasculitis, or bleeding disorders are underlying causes of uveitis, hyphema and anterior chamber fibrin clots are common. Septic or neoplastic disorders also can induce the above changes and are often bilateral with varying degrees of hypopyon (white blood cells within the aqueous humor) or keratic precipitates (white blood cells and fibrin adherent to the corneal endothelial surface). Posterior uveitis warrants a guarded prognosis for vision. Acute signs include retinal edema, retinal hemorrhage, loss of normal tapetal color, subretinal fluid accumulation, and decreased vision. Chronic signs consist of hyperreflective areas in the tapetal fundus (caused by retinal atrophy and thinning), abrupt color changes of the tapetum, and pigment proliferation or loss (Figs. 5–7).

ACUTE ANTERIOR UVEITIS	CHRONIC ANTERIOR UVEITIS
Mild conjunctival hyperemia	Deep corneal vascularization
Iris swelling	Iris hyperpigmentation
Aqueous flare	Iris neovascularization
Mild episcleral hyperemia	Synechia formation
Miosis	Cataract
Photophobia	Secondary glaucoma

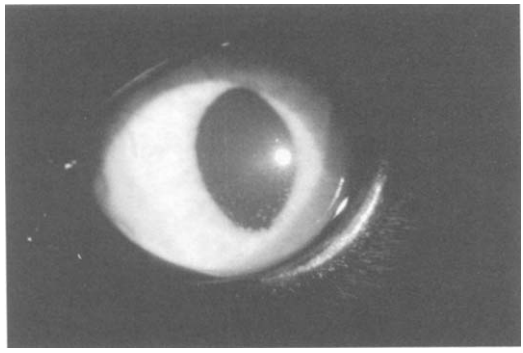


Figure 5. A cat with chronic anterior uveitis. Note the hazy iris and the fine keratic precipitates (KP) on the corneal endothelium.

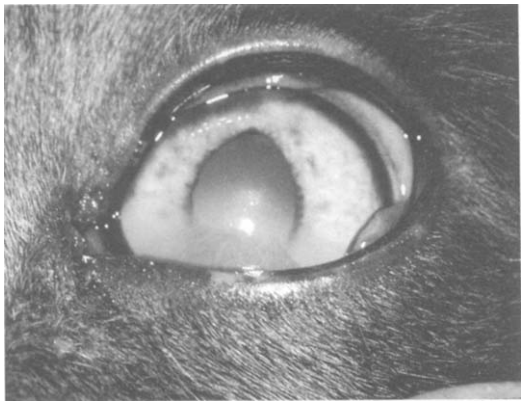


Figure 6. Cat with chronic uveitis. Note the iris color. Multifocal nodules give the surface a mottled appearance. Ventrally the cornea is less clear because of hypopyon (fibrin) in the anterior chamber.

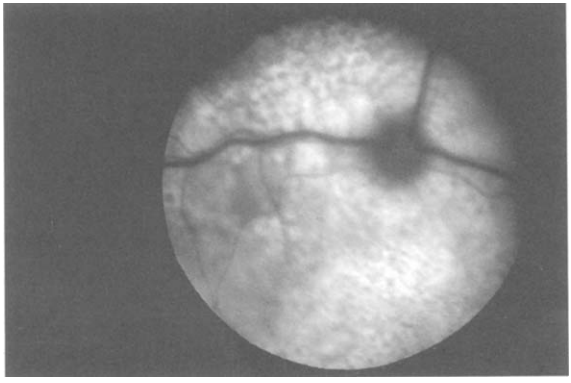


Figure 7. Cat with retinitis showing retinal edema and flat detachment secondary to posterior uveitis.

11. What is the significance of aqueous humor flare and cell accumulation?

The blood-ocular barrier maintains the low total protein content (0.15–0.55 mg/dl in the cat) and cell-free state of the aqueous humor. Uveal inflammation disrupts this barrier, resulting in an increased amount of protein and influx of cells within the aqueous humor. The increased protein causes light directed into the eye to back-scatter, thus imparting a turbid characteristic to the aqueous humor. This phenomenon is termed **flare** and is subjectively graded using a scale ranging from 0 to 4+ (0 = normal and 4+ = fibrin clot formation). The accumulation of cellular material may consist of white blood cells, red blood cells, pigment, or tumor cells as well as pigment granules. The presence of increased amounts of aqueous protein indicates inflammation (with the severity approximating the magnitude of the flare reaction). Likewise, cell accumulation indicates inflammation but suggests a more severe inflammatory response. Flare and cells (including hypopyon) may be the result of sterile inflammation or infection.

12. Which is more common, anterior uveitis or posterior uveitis?

Anterior uveitis is more common, especially considering the propensity for the globe to suffer traumatic injury. The anterior segment (cornea, iris, ciliary body, and lens) is more frequently damaged than the posterior segment (vitreous, retina, optic nerve, and choroid) in ocular trauma. The posterior location of the choroid within the orbit gives the choroid considerable protection, but contrecoup forces may result in choroidal contusion. Anterior and posterior uveal inflammation are both common with other causes of uveitis.

13. What are the common causes of uveitis?

Uveitis is a component of most intraocular disease processes and a frequent result of trauma to the globe. Despite the ease with which uveitis can be recognized clinically, most cases are classified as idiopathic. Many endogenous causes of uveitis have been recognized (see Table). Common causes of uveitis in companion animals presented for emergency care include blunt trauma, corneal ulceration, and perforation of the cornea or globe.

Causes of Endogenous Uveitis in Dogs and Cats

CANINE UVEITIS	FELINE UVEITIS
Algae	Fungal
Prototheca spp.	*Blastomyces dermatitidis*
Bacterial	*Candida albicans*
Brucella canis	*Coccidioides immitis*
Borrelia burgdorferi	*Cryptococcus neoformans*
Fungal	*Histoplasma capsulatum*
Blastomyces dermatitidis	Parasite
Coccidioides immitis	*Cuterebra* larva
Cryptococcus neoformans	*Dirofilaria immitis*
Histoplasma capsulatum	Metastrongylidae nematodes
Parasitic	Protozoan
Dirofilaria immitis	*Toxoplasma gondii*
Diptera spp. (fly larvae)	Viral
Ocular larva migrans (*Toxocara* and *Baylisascaris* spp.)	Feline immunodeficiency virus
Protozoan	Feline infectious peritonitis
Leishmania donovani	Feline leukemia virus (tumor formation)
Toxoplasma gondii	Idiopathic
Rickettsial	Trauma
Ehrlichia canis or *platys*	Neoplastic disorders
Rickettsia rickettsii	Fibrosarcoma
Viral	Primary tumor (melanoma)
Adenovirus	Secondary tumor
Distemper (lymphosarcoma)	
Herpesvirus	

(*Table continued on next page.*)

Causes of Endogenous Uveitis in Dogs and Cats (cont'd)

CANINE UVEITIS	FELINE UVEITIS
Idiopathic	
Trauma	
Toxemia (e.g., pyometra, pancreatitis)	
Ulcerative keratitis	
Neoplastic and paraneoplastic disorders	
Hyperviscosity syndrome	
Granulomatous meningoencephalitis	
Primary neoplasia (ocular melanoma, adenocarcinoma)	
Secondary neoplasia (lymphosarcoma most common)	
Metabolic disorders	
Diabetic cataract (lens-induced uveitis)	
Miscellaneous causes	
Coagulopathy	
Immune-mediated disorders	
Immune-mediated vasculitis	
Lens trauma (phacoclastic uveitis)	
Cataract (lens-induced uveitis)	
Uveodermatologic syndrome	

14. What significance can be attributed to anterior uveitis?

Anterior uveitis indicates injury to the anterior uveal tissue resulting from either an exogenous cause, such as trauma or surgery, or an endogenous cause, such as systemic infection. Bilateral uveitis is more likely to result from systemic disease. Although the presence of uveitis is not necessarily an indication of infection, infectious causes should be considered. However, any pathophysiologic mechanism that results in uveal damage will trigger an inflammatory response. Because many intraocular tissue antigens are not recognized by the host as self, immune responses to antigenic material, released as a result of the inflammation, can propagate the inflammatory process and contribute to the development of chronic uveitis. Chronic anterior uveitis often leads to development of synechia. When extensive, synechia can obstruct aqueous humor outflow, causing secondary glaucoma.

15. Can a prognosis be determined in emergency cases with uveitis?

Obviously, the prognosis depends on the actual condition or injury. However, the prognosis for vision in cases with mild-to-moderate degrees of uveitis is favorable. Severe cases have a guarded prognosis. Within 24–48 hours of treatment initiation, the prognosis needs to be reevaluated and possibly upgraded or downgraded. In cases of endophthalmitis or panophthalmitis, the prognosis for vision is poor, and the prognosis for globe salvage is guarded to poor. If secondary conditions develop as a result of uveitis (e.g., hyphema, glaucoma, intensified pain), a guarded-to-poor prognosis is warranted.

16. How should anterior uveitis be treated in an emergency setting?

If not contraindicated by the patient's overall condition, nonspecific anti-inflammatory therapy with topical or systemic corticosteroids is optimal. Although not as effective, nonsteroidal anti-inflammatory drugs (NSAIDs) can be used as an alternative to corticosteroids when necessary. NSAIDs should be avoided in cases associated with coagulopathies or intraocular hemorrhage. Topical preparations should be used with caution in cases of globe perforation, because the drug, vehicle, or preservatives may damage intraocular tissues. If an infectious cause is suspected, topical or systemic antimicrobial agents can be used. If antibiotics are indicated, use of a topical triple antibiotic ophthalmic solution and systemic first-generation cephalosporin is appropriate.

Initial Therapy for Uveitis by Grade of Severity

INFLAMMATION GRADE	DESCRIPTION	TREATMENT	DOSE
Mild	Subtle to pronounced miosis, subtle flare, photophobia	Topical corticosteroids	3 times/day
		Topica NSAIDs	3 times/day
		Topical cycloplegics (e.g., atropine)	Every 24 hr
Moderate	Aqueous flare and cells, iris swelling, blepharospasm, corneal edema	Systemic corticosteroids (e.g., prednisone)	1 mg/kg/day
		Topical corticosteroids (e.g., 1% prednisolone or 0.1% dexamethasone)	4 times/day
		Topical NSAIDs	4 times/day
		Cycloplegics	2 times/day until mydriasis occurs
Severe	Hyphema, hypopyon, aqueous fibrin, irregular pupil shape and iris swelling	Systemic corticosteroid pulse-therapy initially (e.g., methylprednisolone sodium succinate)	30 mg/kg IV over 20–30 min
		or	
		Systemic corticosteroids (e.g., prednisone)	2 mg/kg/day in place of or 6–12 hours after pulse-therapy
		Topical corticosteroids (e.g., 1% prednisolone or 0.1% dexamethasone)	Every 1–2 hr until improved, then 4 times/day
		Topical NSAIDs	4 times/day

BIBLIOGRAPHY

1. Aguirre GL, Gross SL: Ocular manifestations of selected systemic diseases. In The Compendium Collection: Ophthalmology in Small Animal Practice. Trenton, NJ, Veterinary Learning Systems, 1996, pp 89–98.
2. Bistner S, Shaw D, Riis RC: Diseases of the uveal tract (part I, part II, and part III). In The Compendium Collection: Ophthalmology in Small Animal Practice. Trenton, NJ, Veterinary Learning Systems, 1996, pp 161–185.
3. Bistner SI: Recent developments in comparative ophthalmology. Comp Cont Educ 14:1304–1323, 1992.
4. Davidson MG, Nasisse MD, Jamieson VE, et al: Traumatic anterior lens capsule disruption. J Am An Hosp Assoc 27:410–414, 1991.
5. Hakanson N, Forrester SD: Uveitis in the dog and cat. Vet Clin North Am Small An Pract 20:715–735, 1990.
6. Kural E, Lindley D, Krohne S: Canine glaucoma: Medical and surgical therapy. In The Compendium Collection: Ophthalmology in Small Animal Practice. Trenton, NJ, Veterinary Learning Systems, 1996, pp 226–233.
7. Rathbone-Gionfriddo J: The causes, diagnosis, and treatment of uveitis. Vet Med 90:278–284, 1995.
8. Roberts SM: Assessment and management of the ophthalmic emergency in cats and dogs. In The Compendium Collection: Ophthalmology in Small Animal Practice. Trenton, NJ, Veterinary Learning Systems, 1996, pp 252–267.
9. Schmeitzel LP: Recognizing the cutaneous signs of immune-mediated diseases. Vet Med 86:138–163, 1991.
10. Serevin GA: Anti-inflammatory drugs. In Serevin's Veterinary Ophthalmology Notes, 4th ed. Fort Collins, Co, University of Colorado, 2001, pp 91–97.
11. van der Woerdt A: Lens-induced uveitis. Vet Ophthalmol 3:227–234, 2000.

29. UVEITIS: OCULAR MANIFESTATIONS OF SYSTEMIC DISEASE IN DOGS

Craig A. Fischer, D.V.M., and Thomas Evans, D.V.M.

1. Can one look into an eye and diagnose a systemic disease?

Not usually. As with most things in medicine, pathologic changes within the eye such as uveitis often contribute to a piece of the diagnostic pie that can ultimately lead to a definitive diagnosis. It is best for the clinician to have a thorough grasp of the patient's history and clinical and diagnostic findings before expecting the ocular changes to significantly help in completing a definitive clinical and etiologic diagnosis (Table). There are some systemic disorders in which uveitis is expected (e.g., systemic mycoses) and others where it occurs only occasionally (e.g., ocular filariasis–canine heartworm disease).

Clinical Signs of Uveitis in Dogs

ANTERIOR UVEITIS (IRIS AND CILIARY BODY)	INTERMEDIATE UVEITIS (PARS CILIARIS RETINAE AND PERIPHERAL CHOROID)	POSTERIOR UVEITIS (CHOROID)	PANUVEITIS
Aqueous flare Cataract Conjunctival/episcleral hyperemia Corneal edema Corneal neovascularization (deep) Eye pain Hyphema Hypopyon Intraocular pressure decrease Iris color change (usually darker) Iris swelling Keratic precipitates Miosis Phthisis bulbi Rubeosis iridis (or preiridal fibrovascular membrane formation) Secluded pupil and iris bombé Secondary glaucoma Vision decrease	Cataract (posterior capsular) Intraocular pressure decrease Vitreal opacification-anterior (accumulation of inflammatory components in anterior vitreous and onto posterior lens capsule)	Fundic hyperpigmentation (tapetal region) Fundic hypopigmentation (nontapetal region) Granuloma(s) (focal or multifocal) Optic neuritis Retinal detachment (usually exudative) Retinal hemorrhage Vision decrease Vitreal opacification (preretinal)	One or more of the signs of anterior, immediate, and posterior uveitis are present

2. What is uveitis and its significance in relation to systemic disease?

Uveitis in a complex inflammatory process characterized clinically by altered vascular permeability and cellular infiltration of the uveal tract and intraocular spaces (anterior chamber, posterior chamber, vitreous, and subretinal space). In most cases the basic pathophysiologic characteristics of the systemic disease process are present in the uveal tract as well as in other tissues.

3. What specific characteristics of uveitis can a clinician use to match it with a specific systemic disease?

The location within the uvea (anterior, intermediate, posterior) where the inflammation occurs is often specific to certain systemic diseases (e.g., anterior uveitis with canine adenovirus 1, posterior uveitis and retinitis with canine distemper virus). The presence or absence of blood within the eye is important. Other characteristics includes whether the inflammation is unilateral or bilateral, sudden or insidious, self-limiting or chronic, recurrent or continuous, and nongranulomatous or granulomatous. In addition, complications such as cataracts and glaucoma are helpful in differentiating one systemic disease from another.

Basic Characteristics and Incidence of Uveitis in Selected Systemic Diseases in Dogs

DISEASE	BASIC CHARACTERISTICS OF UVEITIS	INCIDENCE OF UVEITIS
Infectious		
Borreliosis	Anterior, intermediate, and/or posterior uveitis, blood common	Uncommon
Brucellosis	Anterior and intermediate uveitis, blood common	Uncommon
Leptospirosis	Anterior, intermediate, and/or posterior uveitis, blood common	Uncommon
Endogenous gram-negative bacterial infections, endotoxin-associated (e.g., *E. coli* in pyometra)	Anterior, intermediate, and/or posterior uveitis	Uncommon
Septicemia	Anterior, intermediate, and/or posterior uveitis, blood common	Common
Canine adenovirus I	Anterior uveitis, corneal edema	Common
Canine distemper	Posterior uveitis, retinochoroiditis, optic neuritis	Common
Toxoplasmosis	Anterior, intermediate, and/or posterior uveitis, retinochoroiditis, optic neuritis	Common
Leishmaniaisis	Anterior and intermediate uveitis	Uncommon
Ehrlichiosis	Anterior, intermediate, and/or posterior uveitis, blood common	Common
Rocky Mountain spotted fever	Anterior, intermediate, and/or posterior uveitis, blood common	Common
Blastomycosis	Panuveitis, exudative retinal detachment	Common
Coccidioidomycosis	Panuveitis, exudative retinal detachment	Common
Histoplasmosis	Panuveitis, exudative retinal detachment	Uncommon
Cryptococcosis	Panuveitis, exudative retinal detachment, optic neuritis	Common
Noninfectious		
Diabetes mellitus	Anterior uveitis, cataract induced	Common
Granulomatous meningoencephalitis	Posterior uveitis, optic neuritis	Common
Neoplasia-infiltrative (e.g., lymphosarcoma)	Anterior, intermediate, and/or posterior uveitis, blood common	Common
Systemic hypertension	Posterior uveitis, serous retinal detachment, blood common	Common
Uveodermatological syndrome (similar to Vogt-Koyanagi-Harada syndrome in humans)	Panuveitis	Common

4. What are the pathophysiological mechanisms in which systemic infections can lead to uveitis?

Direct destruction of the uveal tissues by infectious agents is one mechanism (e.g., toxoplasmosis). Immune-mediated events associated with infectious agents, including all four of the classical hypersensitivity responses (I, II, III, and IV), have been proven to occur within the uveal tract of the eye. Where immune-mediated uveitis is present in systemic infections the organism is often not located in the eye but in a distant tissue(s). Also cytokine-induced inflammation within the uveal tract has been associated with endotoxemia related to gram-negative infections such as seen with *E. coli* in canine pyometra patients. Other possible foci of gram-negative bacterial infections that may lead to uveitis include the heart, kidneys, prostate, and gingival or dental regions.

5. What is the significance of the presence of blood in the eye along with uveitis in relation to systemic diseases?

Blood in the eye is often associated with uveitis, and its presence can be suggestive of some systemic diseases (e.g., tick-borne rickettsial diseases, brucellosis, systemic hypertension). Uveitis leads to compromise of the blood-ocular barrier, which can lead to leakage of red blood cells particularly if other hemostatic-inhibiting mechanisms are associated with the systemic disease process. These include vasculitis, thrombocytopenia, thrombocytopathy, coagulopathy, systemic hypertension, hyperviscosity, anemia, intraocular neoplasia, and intraocular neovascularization. Also red blood cells and their breakdown products further promote uveitis and, when present in the vitreous, have been found to be retinotoxic.

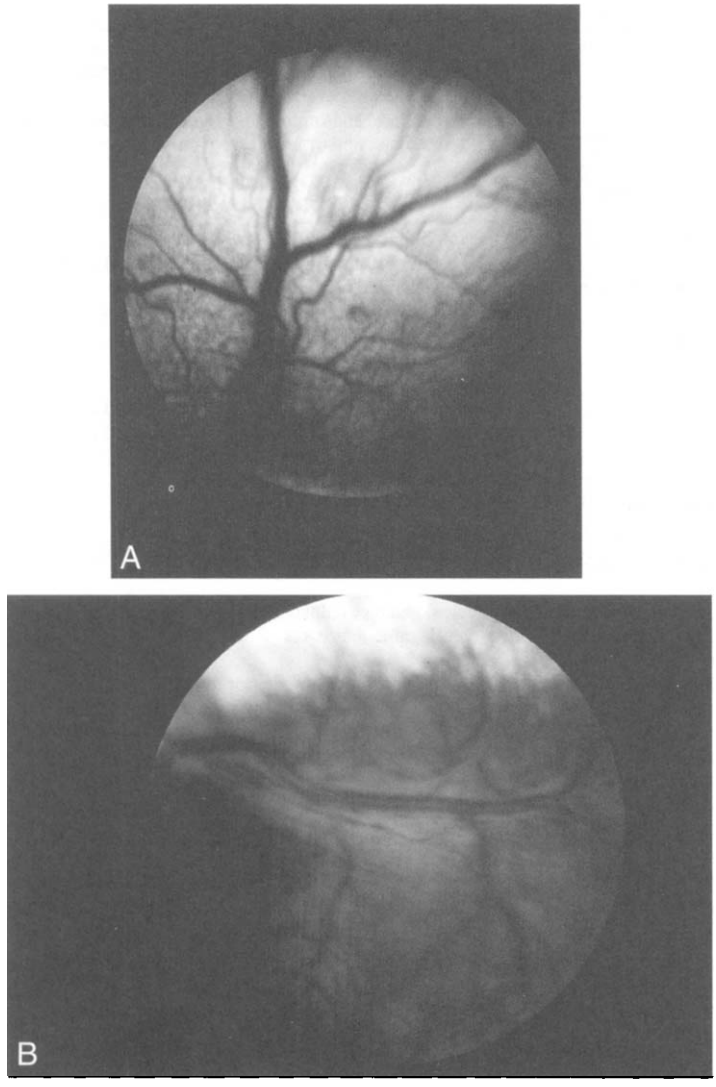


Figure 1. Retinochoroidal lesions in the tapetal (*A*) and nontapetal (*B*) regions in the fundus of a young dog with concurrent acute neurologic signs associated with canine distemper.

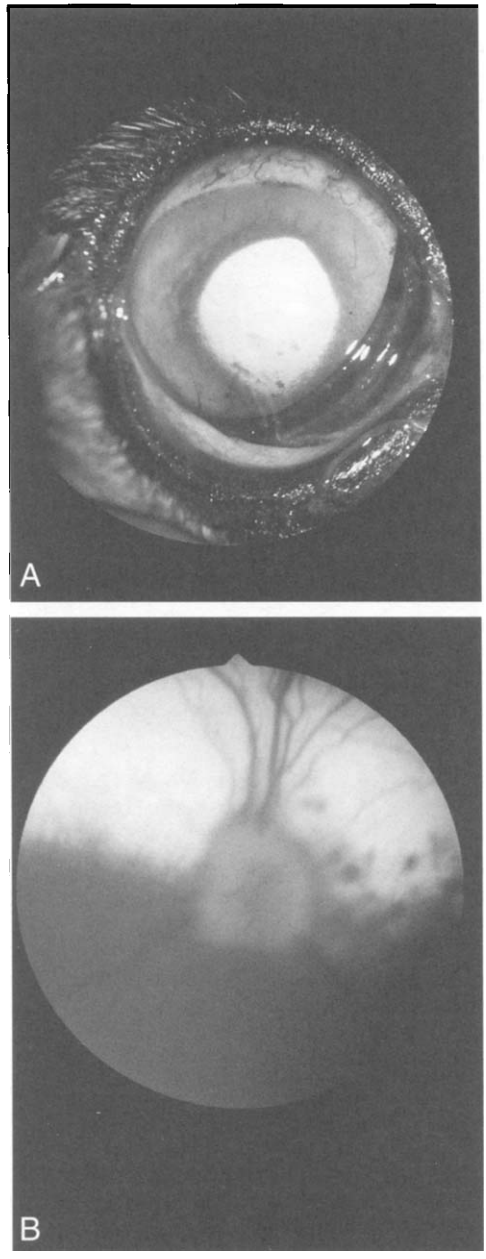


Figure 2. Subacute anterior uveitis with mild hyphema (*A*) in the right eye and multifocal peripapillary retinal hemorrhages (*B*) in the left eye in a dog with ehrlichiosis.

6. Besides the usual diagnostic tests used to differentiate one systemic disease from another, what ocular diagnostic modalities can be used in patients with uveitis to further bring about a definitive diagnosis?

Ocular ultrasonography is often helpful to discern changes in the posterior segment of the eye, particularly if the ocular fluid is cloudy or if there is a significant cataract present. Changes such as detached retina, posterior segment granulomas, accumulation of intravitreal blood, and intraocular neoplasia can be evaluated using ultrasonography. In addition, anterior chamber paracentesis can be done to determine cytologic features, serologic testing, and microbial culture. In cases of posterior uveitis with exudative retinal detachment, vitreocentesis or subretinal aspiration can be particularly helpful for cytologic study and microbial culture.

7. What infectious systemic diseases that cause uveitis have geographic predilections?

The systemic fungal diseases tend to be geographically endemic. Blastomycosis is seen more in the midwest regions of the United States than any other location. Coccidioidomycosis is mainly seen in Mexico, the southwest United States, and California, particularly in the San Joaquin valley region. Histoplasmosis is classically seen in the Ohio and Mississippi river valley regions of the U.S. Cryptococcosis appears to be more geographically ubiquitous. The filamentous fungal diseases, such as aspergillosis, are more concentrated in the deep south of the U.S. Borreliosis is more likely diagnosed in the northeast United States. However, its incidence is increasingly seen in other parts of the United States as well as the tick-borne rickettsial diseases. Old World leishmaniaisis (*Leishmania donovani*) is seen in the Mediterranean area, Africa, and Asia. New World leishmaniaisis (*Leishmania donovani chagasi*) is found in certain parts of the United States and Central and South America.

Because of these geographic predilections, the clinician should always question the owners about previous travel and living locations of the affected patient. In addition, it should also be kept in mind that some infectious agents might be harbored in a subclinical form. When these patients are exposed to immunosuppressive events (e.g., corticosteroids or other immunosuppressive drugs, debilitating disease, old age), the hidden infection may have become clinically evident.

8. What is the treatment for uveitis in a patient with systemic disease?

The basic treatment is to maintain the functional visual capacity of the eye. Therefore, drugs that control inflammation are fundamental. Of course, specific therapy is also instituted for the systemic disease process if it is identified initially.

Corticosteroids are the most common group of drugs used to control uveitis. Even in cases of infectious systemic diseases where the uveitis is mainly initiated and promoted by immune-mediated events, corticosteroids are used along with appropriate antimicrobial drugs. The exceptions for their use would be in cases such as systemic mycoses and septic endophthalmitis in which the eye pathology is caused principally by the direct destructive presence of the organisms and immunosuppression by corticosteroids is to be avoided. Also, corticosteroids may be withheld initially in cases where an infectious systemic disease is suspected but the definitive diagnosis can only be based on serologic, cytologic, or microbial findings that are not initially available. In these cases other forms of systemic anti-inflammatory therapy may be initiated until the definitive diagnosis is established.

In general, in marked cases of anterior uveitis and especially in intermediate and posterior uveitis, corticosteroids, usually prednisone, are delivered orally at an initial dose of 1 mg/kg/day (anti-inflammatory dose) to 2 mg/kg/day (immunosuppressive dose). To achieve rapid blood levels of corticosteroids, an initial injection of dexamethasone sodium phosphate at 1 mg/kg may be given intravenously. In addition, flunixin meglumine (although not labeled for use in dogs) may be given at 0.2 mg/kg IV. Depending on the initial response of the uveitis to corticosteroids and the chronicity of the disease process, the oral corticosteroids may be tapered from 1 to 2 mg/kg per day for 3–5 days to 1 to 2 mg/kg every other day for 10 days and then 0.5 to 1.0 mg/kg every other day for another 10 days, and so on.

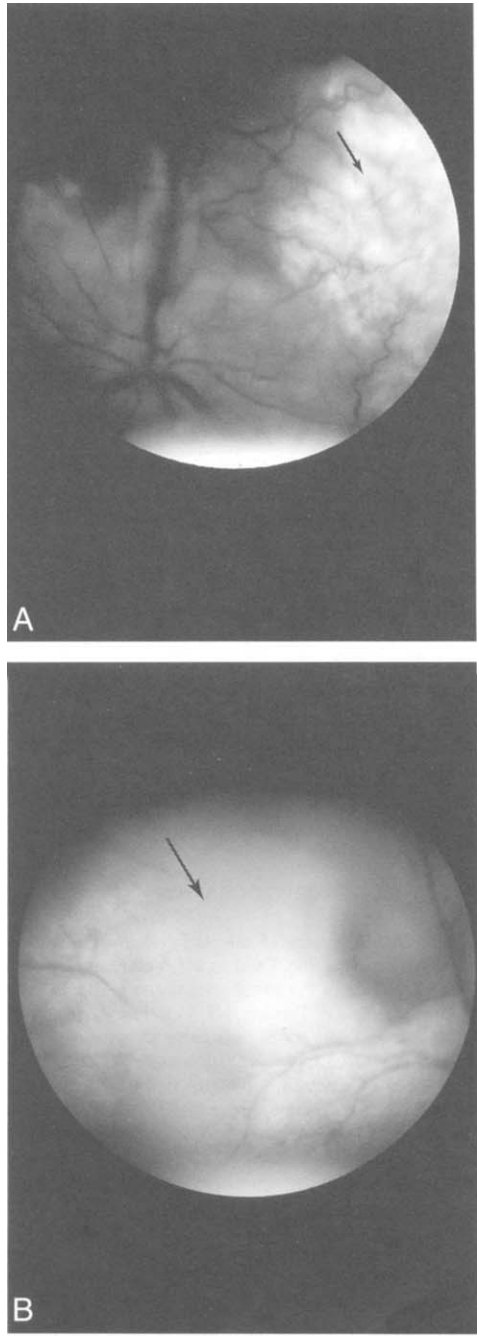


Figure 3. Exudative retinal detachment (*A*) and a subretinal granuloma (*B*) associated with diffuse choroiditis in a dog with blastomycosis (*arrows*).

In those noninfectious immune-mediated systemic diseases that are characterized by their prolonged nature, such as uveodermatologic syndrome (similar to Vogt-Koyanagi-Harada disease in humans), anti-inflammatory or immunosuppressive drugs such as azathioprine are often used. The usual dosage is 2 mg/kg/day for 5 days, then 1 mg/kg/day for 10 days, then 0.5 mg/kg/day thereafter for maintenance. Oral cyclosporine (5 mg/kg/day) is beginning to be used more frequently as well. For whatever reason, if systemic corticosteroids cannot be used to control uveitis, oral nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin may be used at an anti-inflammatory dosage rate of 15 mg/kg three times daily.

Most cases of uveitis associated with systemic diseases include the iris and ciliary body (anterior uveitis). Topical ophthalmic medications are formulated in such a way that they enter, to some extent, the anterior and posterior chamber structures. Therefore, topical anti-inflammatories, particularly dexamethasone 0.1% and prednisolone acetate 1%, are usually used. Depending on the intensity of the anterior uveitis they may be used as frequently as 4 times daily. In the case of preexisting corneal ulceration, direct intraocular invasion by systemic mycotic agents, or other situation where topical corticosteroids are contraindicated, topical NSAIDs may be used. Available topical NSAIDs include diclofenac 0.1%, flurbiprofen 0.03%, ketorolac 0.5%, indomethacin 1%, and suprofen 1%. In addition, in cases of marked anterior uveitis, a combination of both topical corticosteroids and topical NSAIDs may be used.

Mydriatics, such as atropine sulfate 1%, have often been advocated to treat anterior uveitis to prevent posterior synechiae formation and to inhibit eye pain. The use of mydriatics, however, must be weighed against the possibility of iridocorneal angle compromise including obstruction because mydriatics may actually promote increases in intraocular pressure (glaucoma). Glaucoma secondary to anterior uveitis is particularly common in certain breeds that have an inherited predisposition for glaucoma such as the American cocker spaniel. In cases where glaucoma is present or presumed to be likely, topical antiglaucoma therapy such as carbonic anhydrase inhibitor drugs (dorzolamide 2%, brinzolamide 1%) may be used to suppress aqueous humor production at a dosage of 1 drop three times daily.

Topical antimicrobials notoriously have poor anterior chamber penetration capabilities. Usually systemic antimicrobials have a greater ability to enter the intraocular structures through a compromised blood-ocular barrier that occurs with uveitis. Subconjunctival administration of certain antimicrobials such as gentamicin (10–20 mg) and cefazolin sodium (100 mg) may be given. Also, intracameral (into the anterior chamber) delivery of certain antimicrobial drugs, such as fluconazole in the case of systemic mycotic infections, have also been used.

BIBLIOGRAPHY

1. Aquirre GL, Gross SL: Ocular manifestations of selected systemic diseases. In Compendium Collection: Ophthalmology in Small Animal Practice. Trenton, NJ, Veterinary Learning Systems, 1996, pp 89–98.
2. Bistner S, Shaw D, Riis RC: Diseases of the uveal tract (Parts I–III). In Compendium Collection: Ophthalmology in Small Animal Practice. Trenton, NJ, Veterinary Learning Systems, 1996, pp 161–185.
3. Collins BK, Moore CP: Diseases and surgery of the canine anterior uvea. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Baltimore, Lippincott Williams & Wilkins, 1999, pp 755–795.
4. Gilger BC: Ocular manifestations of systemic infectious diseases. In Bonagura JD (ed): Kirk's Current Veterinary Therapy: Small Animal Practice, 13th ed. Philadelphia, W.B. Saunders, 2000, pp 276–279.
5. Hakanson N, Forrester SD: Uveitis in the dog and cat. Vet Clin North Am Small Anim Pract 20:715–735, 1990.
6. Johnson BC, Miller WW: Recognizing ocular signs of systemic diseases in dogs. Vet Med 85:1076–1090, 1990.
7. Kern TJ: Canine uveitis. In Bonagura JD (ed): Kirk's Current Veterinary Therapy: Small Animal Practice, 12th ed. Philadelphia, W.B. Saunders, 1995, pp 1248–1253.
8. Komaromy AM, Brooks DE, Kallberg ME, et al: Hyphema. Part I. Pathophysiological considerations. Comp Cont Educ 21:1064–1069, 1999.
9. Khrone SD, Vestre WA: Ocular use of anti-inflammatory drugs in companion animals. In Compendium Collection: Ophthalmology in Small Animal Practice. Trenton, NJ, Veterinary Learning Systems, 1996, pp 252–278.

10. Martin CL: Ocular manifestations of systemic disease. Part I. The dog. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Baltimore, Lippincott Williams & Wilkins, 1999, pp 1401–1448.
11. Martin CL, Stiles J: Ocular infections. In Greene CE (ed): Infectious Diseases of the Dog and Cat, 2nd ed. Philadelphia, W.B. Saunders, 1998, pp 658–672.
12. Rathbone-Gionfriddo J: The causes, diagnosis and treatment of uveitis. Vet Med 90:278–284, 1995.
13. Stiles J: Canine rickettsial infections: Infectious diseases of the eye. Vet Clin North Am Small Anim Pract 30:1135–1149, 2000.
14. Ward DA: Oculomycosis. In Bonagura JD (ed): Kirk's Current Veterinary Therapy: Small Animal Practice, 12th ed. Philadelphia, W.B. Saunders, 1995, pp 1257–1261.
15. Willis AM: Canine viral infections: Infectious diseases of the eye. Vet Clin North Am Small Anim Pract 30:1119–1133, 2000.

30. UVEODERMATOLOGIC SYNDROME

Ronald C. Riis, D.V.M., M.S.

1. What is unique about uveodermatologic syndrome?

This syndrome combines eye, hair, and skin involvement. Although not necessarily all in unison, the three symptoms change not only how the animal sees, but how it appears (Fig. 1). This syndrome has a human counterpart known as Vogt-Koyanagi-Harada (VKH) syndrome, named for the authors who first described it.

Figure 1. Three-year-old black Labrador retriever with predominant eye and facial skin and hair involvement.

2. Is there any sex or age predilection?

The mean age is 2.8 years, and there is no sex predilection.

3. Is there a breed predilection?

Yes, the northern Asian breeds lead the list, but others have been reported. These include the Akita, chow chow, Samoyed, and Siberian husky. Less frequently, the Australian shepherd, golden retriever, Irish setter, Labrador retriever, Old English sheepdog, St. Bernard, and Shetland sheepdog.

4. How do these dogs usually present?

The ocular manifestations are usually the chief concern. These include bilateral anterior uveitis or panuveitis; both showing aqueous flare and depigmentation of the iris and nontapetal fundus. Secondary glaucoma is frequently a part of the syndrome as is retinal detachment—both causes of blindness. Recurrent episodes of the uveitis generally damage the lens with synechiae and cataract sequelae (Figs. 2–5).

5. What dermatologic manifestations accompany the ocular signs?

Poliosis and vitiligo ranging from mild to severe. Depigmentation of the lid and lip margins or any of the mucocutaneous junctions. Remarkable hair color loss is possible. Pigmentation loss of the nose, footpads, and scrotum. The loss or return of skin and hair pigment is frequently the easiest clinical sign for the owners to monitor. They become the barometric gauge of when the medications are controlling the syndrome (Figs. 6–8).

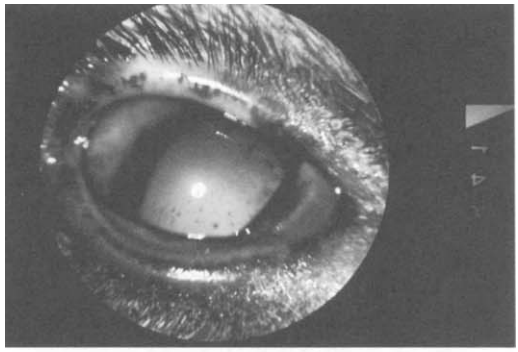


Figure 2. Three-year-old Shetland sheepdog with typical uveitis and lid margin depigmentation.

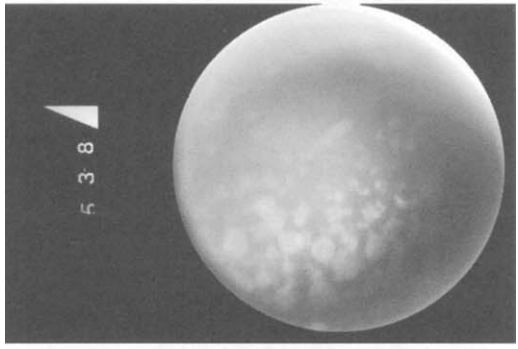


Figure 3. Three-year-old Shetland sheepdog with acute uveodermatologic syndrome showing the multifocal nontapetal depigmentation.

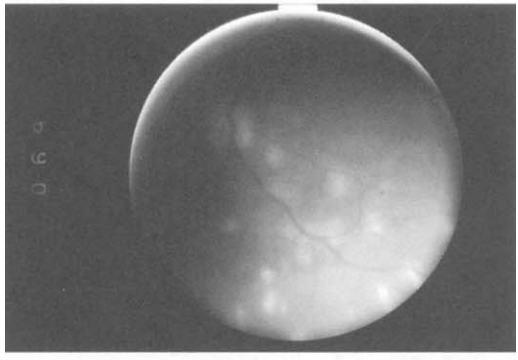


Figure 4. Siberian husky at 2 1/2-years-old with acute uveodermatologic syndrome. Note the hazy fundus view through a flare but still able to make out the multifocal depigmentations.

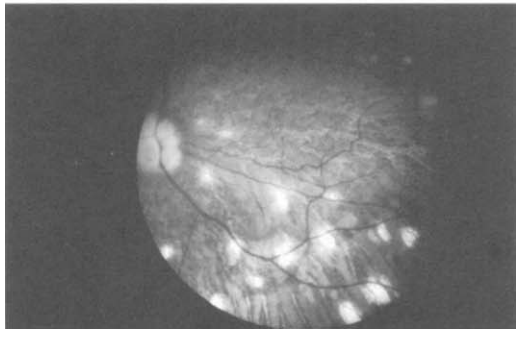


Figure 5. Same Siberian husky as Figure 4 after 2 weeks on immunotherapy.

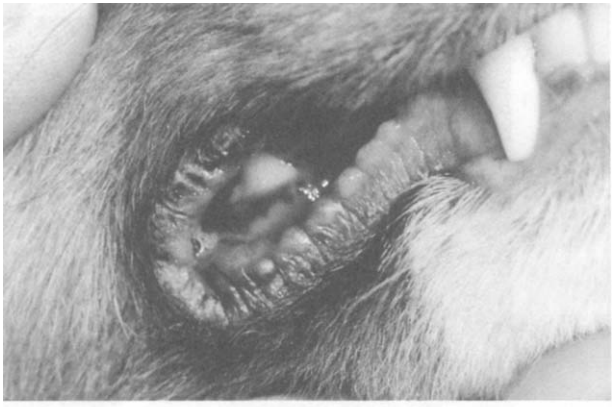


Figure 6. Same Shetland sheepdog as Figure 2 showing lip depigmentation

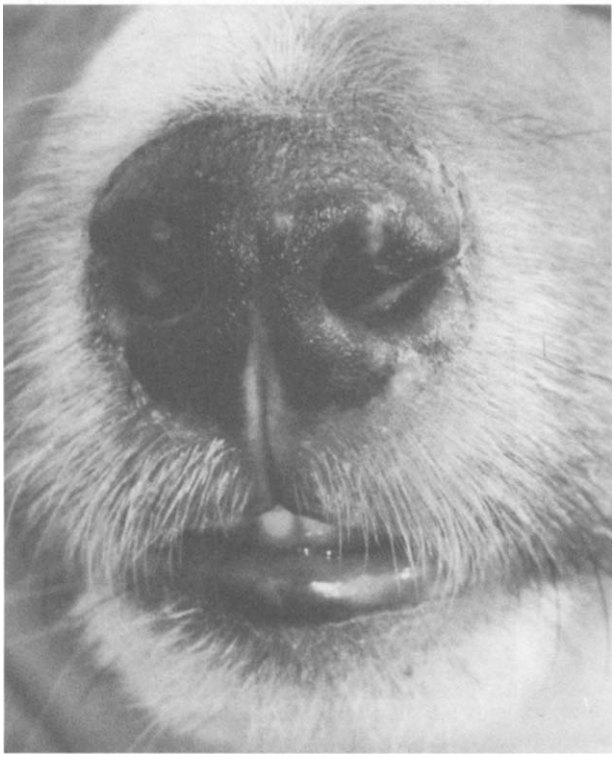


Figure 7. Same Shetland sheepdog as Figure 2 showing early nasal planum depigmentation.

6. Is there a known etiology for the syndrome?

No, but melanin is highly suspected as being a part of this syndrome, both in humans and dogs. Antimelanin antibodies have been demonstrated, and the syndrome is responsive to immune suppression therapy.

7. What is the treatment for this syndrome?

Both topical and systemic corticosteroids are recommended, but long-term use has typical undesirable side effects. Initially, use prednisolone (1 mg/kg twice a day), but taper the dose systemically while adding azathioprine (2 mg/kg/day) for 1 week and reduce the daily frequency to every other day; over the course of weeks reduce even further to every third day. Every 2 weeks, monitor

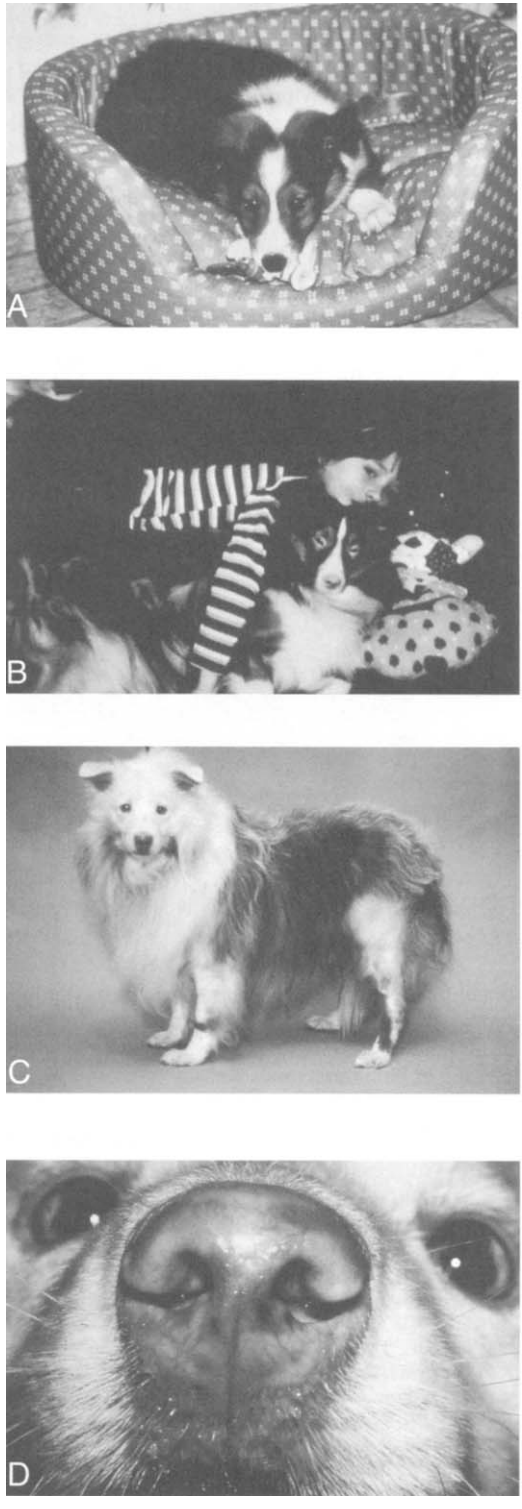


Figure 8. Shetland sheepdog as a puppy (*A*), as a 2-year-old (*B*), as a 3-year-old (*C*), and at 3 years showing complete loss of nasal, iris, and nontapetal pigment but still visual (*D*). (Courtesy of Dr. D. Walton.)

the white blood cell count while on azathioprine (Imuran). If the count falls to ≤ 2000, discontinue until it regains normal levels, then return to an every other or every third day administration. The owners will monitor lid or lip pigmentation and eye comfort signs. If the uveitis is severe, give 0.1 ml of 40 mg/ml methylprednisolone (Depo-Medrol) subconjunctivally. After topical anesthesia, the injection is given into the dorsolateral fornix. The subconjunctival injection may be repeated in 2–3 weeks, if necessary. Topical antibiotic-corticosteroids are also used as is cyclosporine.

8. How successful is treatment?

Resolution of most signs are possible, but just when things look good a recurrence may happen. The prognosis for long-term control is poor. Many patients can be maintained on Imuran every third day for years. Aggressive treatment is vital initially for saving the vision; once that has been achieved, the long-term control depends on owner compliance and observational skills.

9. What are the histopathologic findings in eyes lost to this syndrome?

These eyes show severe granulomatous panuveitis. Within the iris and choroid are infiltrates of chronic inflammatory cells, histiocytes, and macrophages containing melanin granules consistent with antimelanocytic autoimmunity. Destruction of the vascular choroid by these infiltrates leads to retinal detachment as well as retinal infiltrates. A breakdown in the blood-retinal barrier and exposure to retinal-specific antigens leading to antiretinal antibodies compounds the uveitis complex.

10. Does the skin histopathology aid the diagnosis?

Yes, biopsies of the lips at the mucocutaneous junctions show lichenoid pathology with histiocytic cells, plasma cells, and chronic inflammatory cells.

11. Are other species known to develop this syndrome?

Yes, including Arabian, Camergue, Lippezan, and Percheron horses, Sinclair minipigs, and Dam chickens.

12. What are the current etiology hypotheses?

Autocytotoxic
Immune or autoimmune
Neurochemical

13. Have any other therapies been tried besides immunosuppression?

Yes. Immunomodulators have been tried when the patient has become intolerant to conventional therapy. The most success has been with tetracycline and niacinamide given orally three times a day over extended time periods (6–9 months). The dosing is rather broad for dogs: (dogs ≤ 50 pounds, 250 mg of tetracycline and niacinamide three times per day; dogs > 50 pounds, 500 mg of both three times per day).

BIBLIOGRAPHY

1. Asakukra I: Vogt-Koyanagi-Harada syndrome (uveitis diffusa acuta) in the dog. Jpn J Vet Med 673:445–455, 1977.
2. Gwin RW, Wyman M, Ketring K, et al: Idiopathic uveitis and exudative retinal detachment in the dog. J Am Anim Hosp Assoc 16:153–170, 1980.
3. Inomata H, Rao NA: Depigmented atrophic lesions in sunset glow fundi of Vogt-Koyanagi-Harada disease. Am J Ophthalmol 131:607–614, 2001.
4. Kern TJ, Walton D, Riis RC, et al: Uveitis associated with poliosis and vitiligo in 6 dogs. J Am Anim Hosp Assoc 187:408–414, 1985.
5. Murphy CJ, Bellhorn RW, Thirkill C: Antiretinal antibodies associated with Vogt-Koyanagi-Harada-like syndrome in a dog. J Am Anim Hosp Assoc 27:399–402, 1991.
6. Read RW, Rechodouni A, Butani N, et al: Complications and prognostic factors in Vogt-Koyanagi-Harada disease. Am J Ophthalmol 131:599–606, 2001.
7. Read RW, Holland GN, Rao NA, et al: Revised diagnostic criteria for Vogt-Koyanagi-Harada disease: Report of an international committee on nomenclature. Am J Ophthalmol 131:647–652, 2001.

31. THOUGHTS ABOUT PIGMENTARY UVEITIS IN GOLDEN RETRIEVERS

Ronald C. Riis, D.V.M., M.S.

1. How does pigmentary uveitis in golden retrievers generally present?

Usually without the knowledge of the owner. On routine ocular evaluations, one iris color may be darker brown than the opposite. This heterochromic characteristic may be noticed by the owner. Depending on the chronicity, the pupil may be adhered to the lens capsule, so pupillary reflexes can be asymmetrical.

2. What does the term "pigmentary uveitis" imply?

The uveitis components fit most of the applied uveitis signs of hypotonia, flare, photophobia, tearing, and conjunctival hyperemia. However, an additional sign of "pigmentary" applies to the deposits of pigment on the lens capsule and corneal endothelium. The pigment is within macrophages that most probably arose from the anterior uveal tract (Fig. 1).

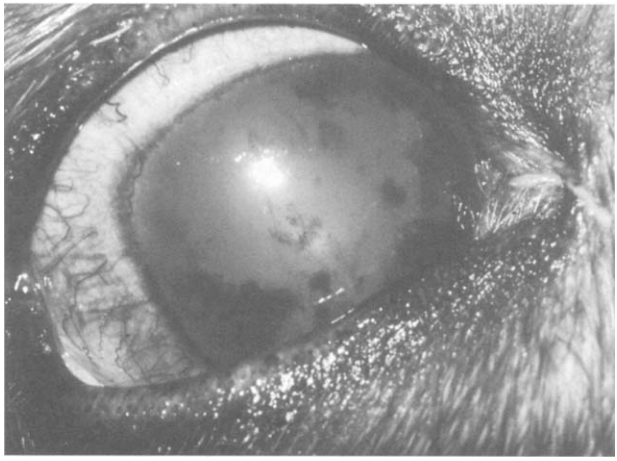


Figure 1. This golden retriever developed uveitis followed by glaucoma. Pigment adhesions and deposits are located predominantly on the anterior lens capsule.

3. Other than the pigment and uveitis, what other signs have been noticed?

The smoldering uveitis many times encourages a good deal of fibrin to accumulate in the anterior chamber. Plasmoid aqueous from dilated iris vasculature is rich in fibrinogen. Clotting puts clumps of fibrin onto iris, lens capsule, and cornea.

4. What can be done to clear the fibrin accumulation?

Treat the uveitis with corticosteroids or nonsteroidal anti-inflammatories. In addition, if the clot appears fresh (within 2 weeks old), tissue plasminogen activator (tPA) can be injected into the anterior chamber to dissolve the clot (tPA dose: 25–40 μg injection with a 30-gauge needle).

5. Is this disease associated with any other systemic abnormalities?

So far it has not been associated with other abnormalities. Usually the pursuit of an etiology results in no significant findings. Blood values generally are completely normal, anterior pericentesis for culture are negative, and cytology may yield mononuclear inflammation (ANA titers, *Brucella* and *Leptospira* titers negative). The hunt for a neoplastic antigen (i.e., radiographic and/or ultrasound evaluation of the chest and abdomen) is usually nonproductive. Because so

much money has been spent trying to find an etiology to no avail, this disease has become recognized as a possible immune-mediated uveitis unique to the breed.

6. So the disease can self-destruct the eyes?

Yes. The uveitis may be unilateral at first, but usually becomes bilateral. The chronic uveitis creates posterior synechiae, postinflammatory cataracts, and ultimately glaucoma. The glaucomatous globes usually end up enucleated or eviscerated.

7. What would the outcome be if the eyes were prophylactively treated for glaucoma in the initial uveitis stages?

Adding an intraocular pressure–reducing medication to an eye that is hypotonic does not help prevent the occlusion of the drainage angles. If the medication is directed at the aqueous production, a balance of outflow versus production may be maintained for a while. Unfortunately, the outcome is always the same in the long run despite anti-inflammatory and antiglaucoma medication.

8. To what extent has the treatment of the uveitis been explored?

The use of topical medication has been extended to parental immunosuppressive doses of prednisolone, azathioprine, and cyclosporine. These medications each have positive effects but also their own adverse effects. Usually because of the latter, the dose frequency is tapered off, and that is when a recurrence of the uveitis causes more damage. To avoid this, start with prednisolone orally and subconjunctivally, and later add azathioprine for long-term maintenance while decreasing the prednisolone. Topically, the frequency of dexamethasone and cyclosporine administration should depend on the need and comfort.

9. Iris cysts are commonly seen in golden retrievers; are they related to this disease?

Iridociliary cysts are often seen along with pigmentary uveitis. They are also seen frequently in golden retriever glaucoma (13 out of 18 cases in one study), leading to the conclusion that they may be important in the pathogenesis of glaucoma. Although glaucoma and pigmentary uveitis have cysts in common and most pigmentary uveitis cases end up with glaucoma, a direct relationship between cysts and uveitis in unproven (Fig. 2).

10. Has histopathology given any clues to this syndrome?

No. The role of histopathology should be to permit a diagnosis that clinical examinations were unable to make. However, most eyes sectioned are those that have end-stage glaucoma. These eyes have usually been treated with antiglaucoma and immunosuppressive medications both topically and systemically. Recently, this author evaluated the uveal tract from a golden retriever with this history. The uveal tract showed few cellular infiltrates (lymphocytes and plasma cells), indicating that the medications were doing their job. Special stains of IgA, IgG, IgM, CD_{79a}, BLA_{36}, and CD_3 were essentially unhelpful. A review of other patient files for cases of pigmentary uveitis and glaucoma untreated with immunosuppressive medication revealed similar cellular responses.

11. Explain the theory behind use of these special stains.

Immunophenotypic analysis uses antibodies that specifically bind to marker molecules on the cell surface membrane, cytoplasm, or nucleus. The major application of this type of analysis has been to classify lymphomas based on the cell origin (i.e., B-cells or T-cells). Veterinary researchers attempt to use the markers to diagnose and stage tumors and monitor the response. CD_{79} stains membrane markers of B-cell differentiation. CD_3 and CD_4 stain membrane markers of T-cell differentiation.

An immune theory is presumed for the etiology of pigmentary uveitis in golden retrievers mainly because some relief is obtained by the symptomatic treatment results. Because lymphocytes and plasma cells are involved with immunoregulation, cell-mediated immunity, antibody production, suppression of other T-cells, tolerance, cytotoxicity, and probably many unknown immune activities, their presence is expected in pigmentary uveitis.

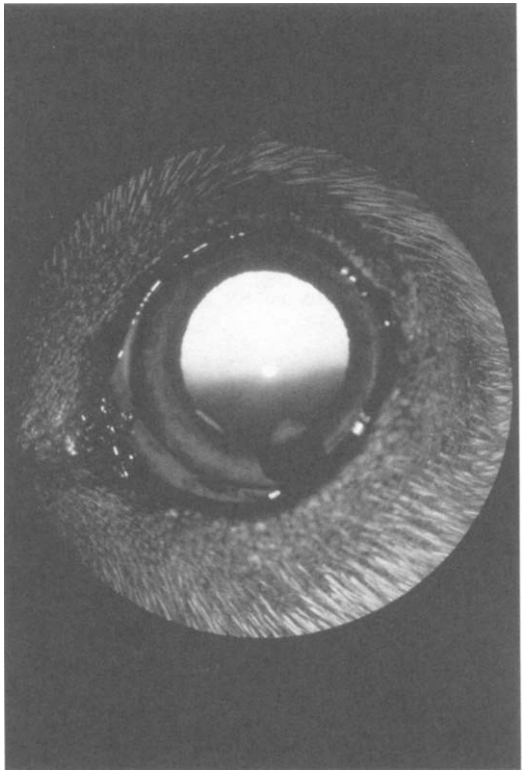


Figure 2. A typical finding in a golden retriever: a free-floating iris cyst in the anterior chamber as well as several attached cysts in the posterior chamber.

12. What is the best way to classify this uveitis?

The etiology of pigmentary uveitis in golden retrievers is unknown. Histopathology does not bring us more precision on the etiology, at least not yet. Therefore, the preferred classification based on the clinical signs rather than the pathologic signs prevails.

BIBLIOGRAPHY

1. Deehr AJ, Dubielzig RR: Glaucoma in golden retrievers. Trans Am Coll Vet Ophthalmol 28:105, 1997.
2. Ocular Disorders Presumed to be Inherited in Purebred Dogs, 2nd ed. West Lafayette, IN, Genetics Committee of the American College of Veterinary Ophthalmology, 1996.
3. Sapienza JS, Simó-Domenech FJ, Prades-Sapienza A: Golden retriever uveitis: 75 cases (1994–1999). Vet Ophthalmol 3:241–246, 2000.

32. FELINE TOXOPLASMOSIS

Cynthia C. Powell, D.V.M., M.S.

1. How are cats infected by *Toxoplasma gondii*?

Cats are infected most commonly by ingestion of tissue cysts in prey species, but they may also be infected in utero or lactationally from an infected queen or by ingestion of sporulated oocysts that have been shed in the feces.

2. How do humans usually get toxoplasmosis?

Humans can be infected with *T. gondii* by ingesting sporulated oocysts or tissue cysts or transplacentally. Cats only shed oocysts in the feces 1–3 weeks after they become infected. The oocysts are unsporulated when shed and require 1–3 days in the environment to sporulate; however, the oocysts can live in the environment for months to years. Tissue cysts are usually ingested in undercooked meats, especially pork. Transplacental infection is the result of primary exposure of the mother during pregnancy.

3. What are the clinical signs of generalized toxoplasmosis in cats?

The clinical signs of toxoplasmosis depend on the organ system involved. Fever, anorexia, and lethargy are common findings. Dyspnea is frequent in cats with pneumonia, abdominal pain and jaundice are common in cats with hepatitis, and various neurologic signs are reported with central nervous system (CNS) involvement. However, in cats, most infections with *T. gondii* are subclinical.

4. What are the clinical signs of ocular *T. gondii* infection?

Histopathology from eyes of cats with generalized toxoplasmosis shows that the organism invades the uveal tract, retina, and optic nerve. Thus, the clinical signs of ocular toxoplasmosis include anterior uveitis, posterior uveitis, and optic neuritis. Aqueous flare, keratic precipitates, iritis, hyphema, retinal hemorrhages, focal or diffuse chorioretinitis, decreased pupillary light reflexes, and blindness are common findings (Figs. 1–9).

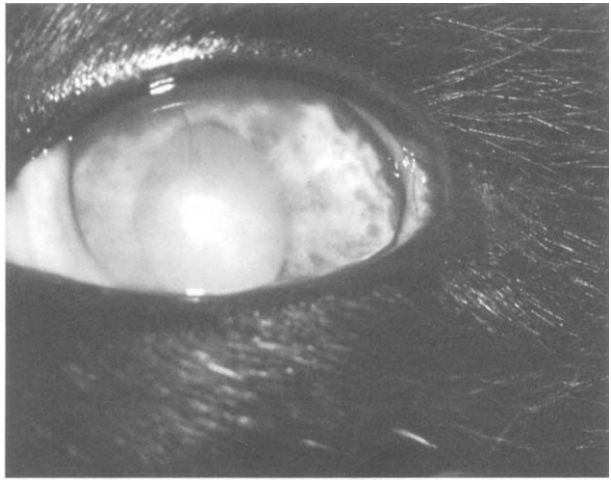


Figure 1. An 11-year-old domestic shorthair presenting with uveitis and glaucoma. Aqueous flare, irregular iris surface, and hazy, velvety-appearing keratic precipitates were among the clinical signs of ocular toxoplasmosis.

Figure 2. Right eye of a 7-year-old domestic shorthair with a fibrinous clot in the anterior chamber. Uveitis compromised the blood-eye barrier, allowing the formation of plasmoid aqueous and an organizing fibrin clot.

Figure 3. Left eye of the cat with ocular toxoplasmosis in Figure 2 showing a slightly more chronic nature to the uveitis. The clots are darker and adhere to the lens capsule.

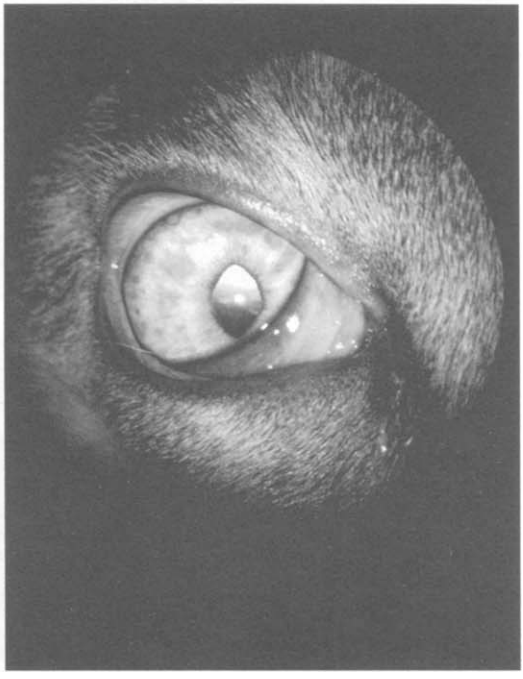


Figure 4. Note the nodular appearance of the iris. This was clinically diagnosed as nodular iritis, which was biopsied to show granulomatous lesions with toxoplasmic cysts.

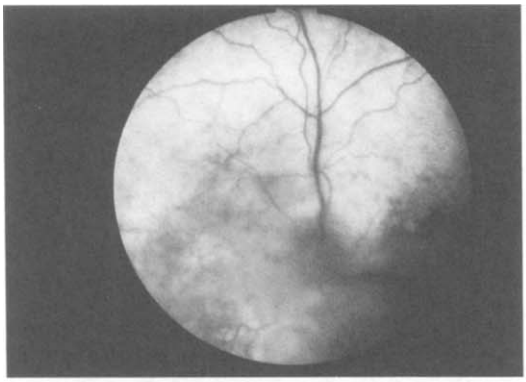


Figure 5. Fundus view of retinitis caused by toxoplasmosis.

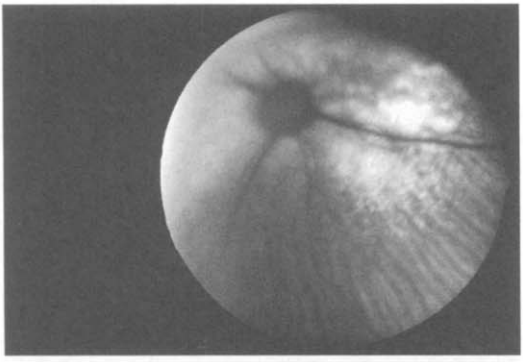


Figure 6. A subalbinotic fundus with retinal edema and flat retinal detachment secondary to toxoplasmosis.

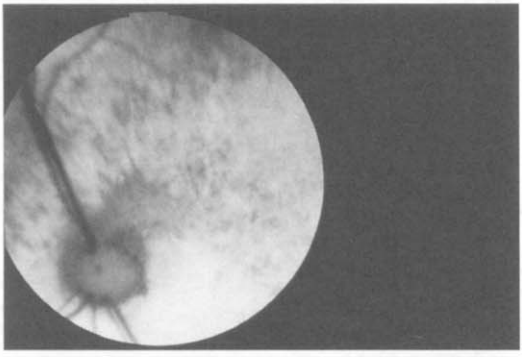


Figure 7. A domestic shorthair showing CNS signs and a color change to the tapetal fundus. Edema and multifocal chorioretinitis are present.

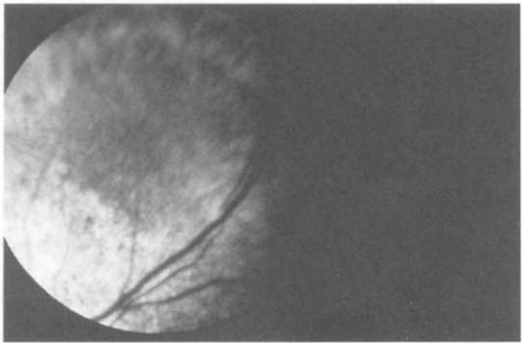


Figure 8. The periphery of the eye in Figure 7. A large area of inflammation within the retina secondary to toxoplasmosis.

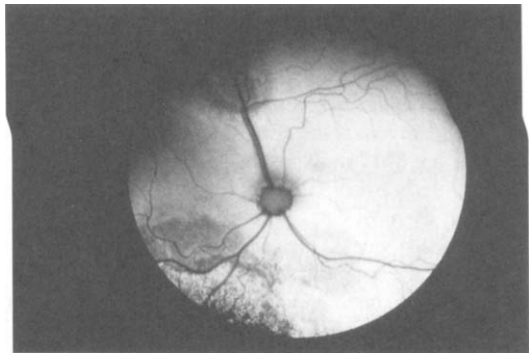


Figure 9. Chorioretinal scars, most likely secondary to toxoplasmosis.

5. Is it possible for cats to have ocular toxoplasmosis without having generalized disease?

The role that *T. gondii* plays in causing ocular disease in cats that show no evidence of other organ involvement is controversial. Ocular histopathology from cats with uveitis and that are seropositive for *T. gondii* rarely identifies the *Toxoplasma* organism. This has led some to believe that ocular toxoplasmosis is rare or does not occur in cats that are infected with the organism but are otherwise healthy. However, some studies have shown that uveitis is more prevalent in systemically healthy cats that are seropositive for *T. gondii* than in healthy cats from the general population. Thus, it is likely that *T. gondii* does cause uveitis in some cats that show no other clinical signs of toxoplasmosis. Also, there is evidence that different strains of the organism vary in their ability to cause ocular disease. This helps to explain why there are so many cats with positive serology for *T. gondii* but so few with ocular disease.

6. How do you determine if ocular disease is caused by *T. gondii* infection?

A definitive diagnosis of ocular toxoplasmosis is difficult to make. Serum IgG antibodies develop approximately 2 weeks postinfection and may remain elevated for years, even in healthy animals. Although positive titers for *T. gondii* have been detected in as many as 74% of cats with uveitis, depending on the region the seroprevalence of *T. gondii* can be as high as 50% in the general cat population. A positive IgG titer is supportive but does not confirm the diagnosis of ocular toxoplasmosis.

7. Are there any other tests that will help confirm the diagnosis?

An increasing IgG titer (four-fold increase over 2–3 weeks) indicates recent or active infection and correlates better with disease than a stable titer. Serum IgM against *T. gondii* also can be used as an indication of recent infection, because this antibody class is usually not detectable after 9 weeks postinfection. Detection of *T. gondii* IgM is also superior to IgG for correlation with clinical illness because it is rarely detected in the background population of healthy cats (1.2%). Detection of *T. gondii* antibody production in the aqueous humor is also used to support the diagnosis of ocular toxoplasmosis in cats.

8. How does the aqueous humor antibody test work?

This test uses an enzyme-linked immunosorbent assay (ELISA) to detect antibodies to *T. gondii* in both serum and aqueous humor. The Goldman-Witmer coefficient (C-value) is calculated to adjust for antibody leakage from the serum. A C-value greater than 1 indicates *T. gondii*–specific antibody is being produced in the eye. Because IgM production has only been detected in the aqueous humor of cats with uveitis, detection of IgM might indicate disease due to the organism.

9. If the diagnosis of ocular toxoplasmosis is so difficult to make, when should a specific anti-*Toxoplasma* drug be used?

Systemically ill, *T. gondii*–seropositive cats should always be treated with an anti-*Toxoplasma* drug. In cats with uveitis alone, treatment with an anti-*Toxoplasma* drug can be jus-

tified in *T. gondii*–seropositive cats when other causes of uveitis have been ruled out, particularly if there has been a failure to respond to glucocorticoid therapy.

10. What drugs are commonly used to treat *T. gondii* infection?

Clindamycin is the drug of choice for treating clinical toxoplasmosis in cats. Recommended dosages are 8–17 mg/kg orally or intramuscularly every 8 hours or 10–12.5 mg/kg orally or intramuscularly every 12 hours for 4 weeks. Liquid oral clindamycin, administered cold (4°C), is tolerated by most cats. Trimethoprim-sulfonamide combination therapy (15 mg/kg PO every 2 hours for 2–4 weeks) also can be used for treatment of toxoplasmosis, although it is less suitable because of the potential side effects of folic acid deficiency in cats. Frequent monitoring for mental depression, anemia, leukopenia, and thrombocytopenia are required especially if treatment is longer than 2 weeks. Azithromycin is a potential alternate choice for cats intolerant of clindamycin or sulfa drugs; however, the most appropriate dose has not been determined.

11. How should the eyes be treated when *T. gondii* infection is suspected?

Anterior uveitis should be treated with a topical glucocorticoid, such as 1% prednisolone acetate, to control inflammation, and a parasympatholytic, such as 1% atropine sulfate, to relieve ciliary and iris muscle spasm and to avoid formation of posterior synechia. Chorioretinitis is best treated by systemic administration of clindamycin hydrochloride.

BIBLIOGRAPHY

1. Burney DP, Lappin MR, Cooper C, et al: Detection of *Toxoplasma gondii*-specific IgA in the serum of cats. Am J Vet Res 56:769–773, 1995.
2. Chavkin MJ, Lappin MR, Powell CC, et al: *Toxoplasma gondii*-specific antibodies in the aqueous humor of cats with toxoplasmosis. Am J Vet Res 55:1244–1249, 1994.
3. Lappin MR, Roberts SM, Davidson MG, et al: Enzyme-linked immunosorbent assays for the detection of *Toxoplasma gondii*-specific antibodies and antigens in the aqueous humor of cats. J Am Vet Med Assoc 201:1010–1016, 1992.
4. Lappin MP, Cayatte S, Powell CC, et al: Detection of *Toxoplasma gondii* antigen-containing immune complexes in the serum of cats. Am J Vet Res 54:415–419, 1993.
5. Powell CC, Lappin MR: Clinical ocular toxoplasmosis in neonatal kittens. Vet Ophthalmol 4:87–92, 2001.

33. PHACOLYTIC UVEITIS

Bruce H. Grahn, D.V.M.

1. What is phacolytic uveitis?

Phacolytic uveitis is one of two forms of uveitis induced by the lens. The other form is phacoclastic uveitis. Phacolytic uveitis is a mild uveitis, and it develops secondary to progressive cataract development. This is a common syndrome, and most advanced cataracts in the dog are associated with some degree of phacolytic uveitis. Phacolytic uveitis is presumed to develop secondary to leaching of soluble lens proteins through an intact lens capsule. Exposure of the uvea to minimal concentrations of lenticular proteins induces an immune tolerance; however, increased exposure to soluble crystalline and insoluble albumen induces a breakdown of the anterior uveal blood-ocular barrier (i.e., the tight junctions of the iridal endothelium, and the ciliary epithelium). This allows plasma proteins to seep into the aqueous and vitreous humor and lymphocytes and plasma cells to accumulate in the anterior uvea (Fig. 1).

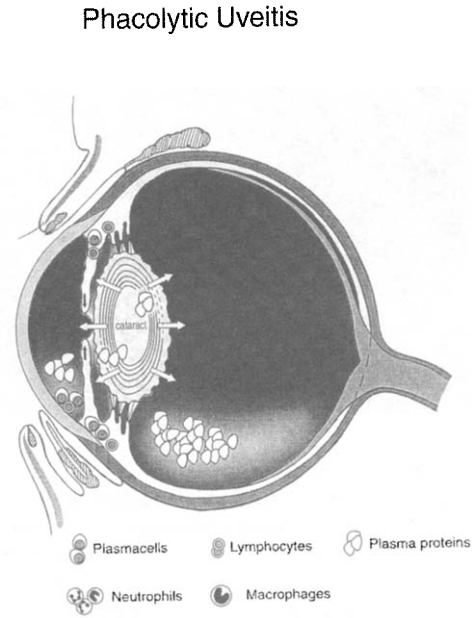


Figure 1. The release of lenticular proteins from a hypermature cataract and pathogenesis of phacolytic uveitis. The soluble proteins pass through the lens capsule, and the increased concentration of these proteins induces a breakdown in the anterior uveal blood-ocular barrier. This allows plasma proteins to leak into the aqueous and vitreous humor and lymphocytes and plasma cells to collect in the iris and ciliary body.

2. What are the clinical manifestations of phacolytic uveitis?

Phacolytic uveitis has two clinical presentations, a mild and severe form. The mild form, which is subtle, is the most common. It presents as mild miosis, subtle aqueous flare, increased iridal pigmentation, and resistance to pharmacologically induced mydriasis (Fig. 2); when the condition is long-standing, hypotony, posterior synechia, and vitreous degeneration may develop. The severe form of phacolytic uveitis is less common and manifests as marked uveitis, hypopyon, keratic precipitates, miosis, marked aqueous flare, posterior synechia, hypotony, and hyalitis (Fig. 3).

3. How is phacolytic uveitis diagnosed?

The clinical diagnosis of phacolytic uveitis is a diagnosis of exclusion. It is an anterior uveitis that is always associated with a cataract. Most commonly, the cataract will be hypermature (shrunken, wrinkled lens capsule, liquefied cortex); however, immature, mature, and intumescent

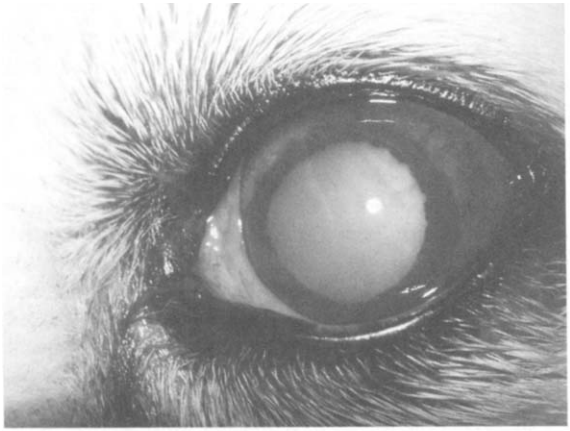


Figure 2. Note the hazy hemorrhagic iris surface secondary to a reaction to a cataract that was intumescent.

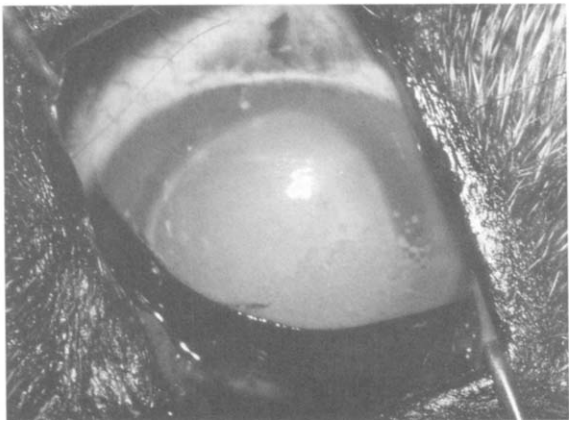


Figure 3. A miniature schnauzer with diabetes showing severe lens-induced uveitis. The plaques on the inside of the cornea are keratic precipitates made up of inflammatory cells.

cataracts may be accompanied by phacolytic uveitis as well. Phacolytic uveitis is common, and it is prudent to assume that it is present with most mature and hypermature cataracts or even immature cataracts when the ophthalmic examination reveals subtle miosis and loss of the three distinct color bands in the iris, hypotony, mild aqueous flare, and a resistance to papillary dilatation with a mydriatic. Unfortunately, there is no definitive way to confirm the diagnosis, and several differential diagnoses need to be ruled out.

4. What is the differential diagnosis for phacolytic uveitis? How are the other diagnoses excluded?

The clinical manifestations of phacolytic uveitis are not specific. A cataract will always accompany phacolytic uveitis, and usually only the anterior uvea is affected. The differential diagnoses include only those disorders that include a cataract and uveitis. However, cataracts and uveitis also develop secondary to a ruptured lens capsule, which is present in **phacoclastic uveitis** (Fig. 4). Phacoclastic uveitis is usually a fulminant uveal disease in the dog, and the confirming manifestation is a ruptured lens capsule.

Nonseptic or septic endophthalmitis may develop from primary ocular disorders or develop secondary to systemic diseases. It is prudent to consider **systemic diseases** as a cause for bilateral uveitis that is accompanied by incipient subcapsular cataracts, especially when a choroiditis is present. Posterior uveitis (choroiditis) is an infrequent accompaniment to phacolytic uveitis and warrants a careful examination for systemic diseases. Bilateral panuveitis should always be accompanied with a thorough physical examination with assessment of a complete blood count, serum biochemical profile, urinalysis, and serum for evaluation of titers to common infective

agents based on the geographic location of the animal. Chest and abdominal radiographs, ultrasonography, or other advanced imaging may be required to rule out systemic diseases.

Traumatic uveitis may be accompanied with a history of the accident and evidence of physical trauma. Hyphema is a frequent manifestation with traumatic uveitis, and this is rarely seen with phacolytic uveitis.

Uveitis frequently develops secondary to **ulcerative keratitis.** Corneal ulcers are confirmed with fluorescein staining.

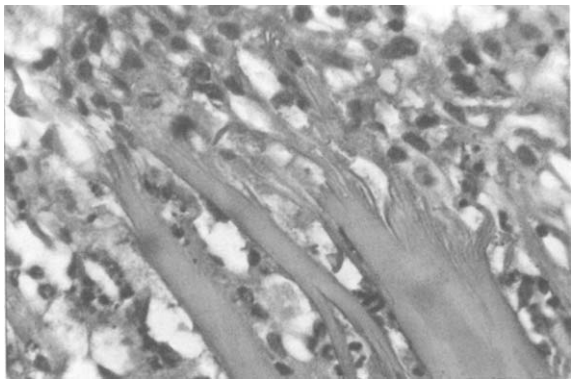


Figure 4. Histopathology of phacophagocytosis with lens fibers infiltrated following a capsule break. Uveitis and glaucoma developed as a result of this reactive process (40×).

5. Why does phacolytic uveitis require therapy?

Although phacolytic uveitis is usually subtle and may not be accompanied by overt manifestations of discomfort (blepharospasm, severe miosis, marked aqueous flare), it is a progressive disease with ongoing mononuclear cell infiltration of the uvea. These inflammatory cells are very long lived, and the inflammation requires life-long medical management to prevent further infiltration of mononuclear infiltrates, synechiae, preiridal or lenticular fibrovascular membranes, vitreous degeneration, and retinal detachment. If cataract surgery is completed to restore vision, the phacolytic uveitis should be controlled prior to the surgery, and postoperative uveitis may require long-term topical anti-inflammatory therapy.

6. How is phacolytic uveitis treated?

Because phacolytic uveitis is usually mild and predominately involves the anterior segment of the eye, topical ocular therapy with steroids or nonsteroidal anti-inflammatory drus (NSAIDs) is usually adequate. The anterior segment inflammation responds to topical steroids (1% prednisolone acetate or 0.1% dexamethasone) or NSAIDs (ketorolac, dichlorofenalac, or flurbuprofen) applied every 8–12 hours for a few days to weeks. Once the clinical manifestations are suppressed, prophylactic maintenance therapy on a once-a-day, alternate-day basis is usually required as long as the cataract is present.

7. What is the prognosis for an eye with phacolytic uveitis?

With appropriate medical management, phacolytic uveitis usually has a good prognosis. However, life-long medication is required, and referral for cataract assessment and removal is recommended (Fig. 4).

BIBLIOGRAPHY

1. Fischer C: Lens-induced uveitis in dogs. J Am Anim Hosp Assoc 8:39, 1972.
2. Paulson M, Lavach J, Severin G, et al: The effect of lens-induced uveitis on the success of extracapsular cataract extraction: A retrospective study of 65 lens removals in the dog. J Am Anim Hosp Assoc 22:49, 1986.
3. van der Woerdt A: Lens-induced uveitis. Vet Ophthalmol 3:227–234, 2000.
4. Wilcock B, Peiffer RL: Pathology of lens-induced uveitis in dogs. Vet Pathol 24:549, 1987.

34. ACUTE OCULAR TRAUMA

Cynthia C. Powell, D.V.M., M.S.

1. What are the major considerations in evaluating acute ocular injury?

Overall patient condition is the first consideration with acute trauma. Once the patient is stable, attention then should be focused on the eye. Prognosis and therapeutic options vary depending on cause and duration of injury and ocular structures involved. If other injuries preclude immediate evaluation and attention to the injured eye, it should be protected from further damage with lubricants and a protective collar if necessary. In cases of chemical injury, the globe should be examined to determine its integrity, and lavage should be instituted immediately.

2. Are certain injuries more threatening to vision or the integrity of the globe?

Ocular proptosis and injuries that rupture or perforate the globe often result in vision loss or require enucleation and carry a guarded prognosis. In general, blunt traumatic injury carries a worse prognosis than sharp penetrating injury because of the increased incidence of retinal detachment and broader scope of uveal damage. Alkali chemical burns, such as those due to ammonia, lye, lime, and magnesium hydroxide, are more likely to cause globe or sight-threatening injury than acid chemical burns.

3. Why are alkali injuries worse than acid injuries?

Most acids coagulate corneal epithelial and stromal proteins, forming a barrier and limiting corneal penetration. Alkalis, however, saponify plasma membrane lipids, denature collagen, and readily penetrate the cornea, increasing possibility of anterior segment damage.

4. How are chemical burns of the eye treated?

Copious irrigation to decrease contact time and concentration should be instituted immediately if a chemical burn is suspected or confirmed. Continuous lavage with a sterile solution of lactated Ringer's and 5% dextrose in water or saline can be delivered through a standard IV set. During irrigation, the conjunctival and corneal surfaces should be inspected and cleaned of chemical residue. Lavage should be continued for 30 minutes or until the pH of the ocular surface returns to normal range (7.3–7.7). After irrigation, the eye should be treated for corneal ulceration, uveitis, and glaucoma, if present.

5. Do any specific therapies for alkali burns help treatment and improve prognosis?

Alkali corneal burns decrease aqueous and corneal ascorbic acid levels and may result in impaired collagen synthesis in the injured cornea. Evidence suggests that topical 10% sodium ascorbate applied every 1–2 hours and high doses of oral ascorbate, 30 mg/kg 4 times/day, may decrease the incidence (but not progression) of sterile stromal ulceration after alkali chemical injury. Treatment is continued at this level for 1 week at which time the topical medication is decreased to 4 times/day. Both topical and systemic medications are continued until the cornea is reepithelialized. Topical sodium citrate 10% inhibits neutrophil activity and decreases sterile ulceration and should be used every 2 hours for the first 10 days after injury. Tetracycline derivatives inhibit neutrophil and collagenase activity and can be administered both topically and systemically.

6. What are some of the long-term sequelae of chemical burn?

Long-term complications of chemical burns include corneal scarring, uveitis, glaucoma, keratoconjunctivitis sicca, symblepharon, and entropion. If uveitis is severe, synechia and cataract formation are also possible.

7. What causes proptosis of the eye?

Trauma to the head either from a car accident or from a dog fight is the most common injury associated with globe proptosis (refer to Chapter 11).

8. What clinical signs indicate the extent of ocular injury?

Physical ocular trauma may be blunt or sharp, perforating or nonperforating. The degree of injury depends on the force of the injury, depth of penetration, and involvement of intraocular structures. Blunt injury causing globe rupture almost always carries a poor prognosis because it often is accompanied by severe uveal herniation, hemorrhage, and retinal detachment. Penetrating wounds by sharp objects and nonperforating blunt trauma vary greatly in the amount of damage. Clinical signs indicating a guarded or poor prognosis include large or deep corneal laceration, collapsed anterior chamber, severe hyphema (more than one-third of the anterior chamber full of blood), inability to visualize the iris due to corneal edema or anterior chamber opacity, uveal prolapse, lens luxation, vitreous hemorrhage, and retinal detachment.

9. How can you tell if the eye has been perforated?

Large perforating scleral wounds result in severe hypotony and often marked subconjunctival and intraocular hemorrhage. Small perforating scleral wounds are harder to detect because chemotic conjunctiva obscures the point of entry and intraocular pressure may be affected only mildly. Large, full-thickness corneal lacerations result in anterior chamber collapse and iris incarceration in the wound. Small, full-thickness lacerations may self-seal as a result of swelling of the stroma when aqueous and tears enter the cornea. The Seidel test helps to detect small perforating corneal injuries.

10. What is the procedure for the Seidel test?

A sterile fluorescein strip is moistened with sterile saline or eye wash, and a drop is administered to the wound area. As aqueous fluid mixes with fluorescein, a bright green stream of fluid will form. If the animal is under general anesthesia, gentle digital pressure can be applied to the cornea to check for wound leakage.

11. What is the significance of a perforating wound if it has already sealed?

Eyes with full-thickness lacerations or perforations are at risk for endophthalmitis and should be treated aggressively with a broad-spectrum, systemic antibiotic. In addition, perforating injuries may involve intraocular damage not easily detected, such as lens rupture or retinal tear. If the cause of the injury is not known, radiography or ultrasonography to look for a metallic foreign body (BB or pellet) is warranted.

12. What treatment should be provided by the emergency care clinician?

The primary goals of emergency therapy are to prevent or treat infection, to protect and support the wound, and to prevent sequelae by controlling intraocular inflammation. If perforation of the eye is suspected, a broad-spectrum systemic antibiotic, such as a first-generation cephalosporin, should be started as soon as possible. Trauma to the globe almost always results in some degree of anterior uveitis and should be treated with topical or systemic nonsteroidal anti-inflammatory drugs (NSAIDs) and topical cycloplegics (see Chapter 28). Topical corticosteroids should be avoided in the presence of ulcerative keratitis, and ophthalmic ointments should not be used if the globe is perforated.

1. To control or prevent infection:
   - If not perforated, topical antibiotic ointment or solution
   - If perforated, systemic antibiotic (e.g., cefazolin) with or without topical antibiotic solution
2. To protect and support wound:
   - Suture, if > half-thickness laceration of cornea
   - With or without conjunctival graft

3. To control intraocular inflammation:
   - Corticosteroids: systemic (e.g., prednisolone, dexamethasone)
   - NSAIDs: topical (e.g., diclofenac [Voltaren], suprofen [Profenal], flurbiprofen [Ocufen])
   - Cycloplegic: topical (e.g., atropine, tropicamide)

13. What kinds of protection and support should be used?

Partial tarsorrhaphy decreases the palpebral fissure size and thus helps to protect the cornea and maintain an adequate tear film. This is especially important in exophthalmic or lagophthalmic animals. A nictitans flap should be used with caution because it interferes with topical medication of the cornea and prevents observation of the wound. If self-trauma is a consideration, a protective collar should be used. Other methods of support include a conjunctival graft or flap, tissue adhesive, and collagen shields.

14. When should a corneal laceration be sutured?

Small corneal lacerations (< 3–4 mm) of less than half thickness may be treated as a corneal ulcer with topical antibiotics and mechanical support (see Chapter 7). Larger or deeper lacerations should be closed with 7–0 to 9–0 suture. If the iris is incarcerated in the wound, it should be amputated or replaced into the anterior chamber before closure. A conjunctival graft placed over the sutured wound may be used for added support if necessary. Before suturing a laceration that has perforated the cornea, the integrity of the lens should be evaluated. Lens capsule perforation necessitates lens removal, preferably at the time of corneal repair. If this is not possible, referral for lens removal should be made as soon as possible to avoid severe uveitis associated with lens rupture (Fig. 1).

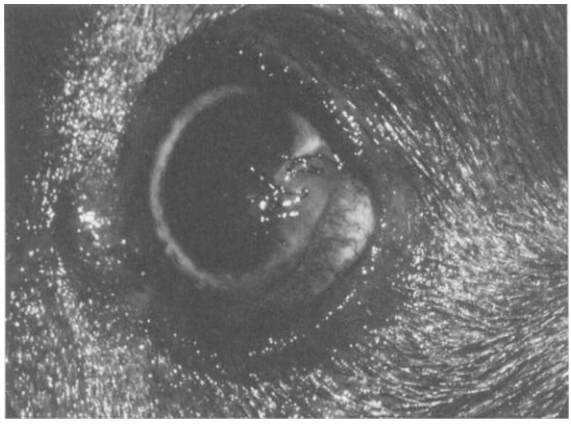


Figure 1. Lacerated cornea sutured with 6–0 Vicryl. The sutures are not full thickness but rather two-thirds thickness. They will be rejected in approximately 3–4 weeks.

15. When should a conjunctival graft or flap be used?

Conjunctival flaps not only provide mechanical support and surface protection to the cornea but also furnish blood supply. Leukocytes, antibodies, anticollagenases, antiproteases, and nutrients for healing and wound repair are thus brought directly to the injury. Lacerations with loss of deep stromal tissue that prevent adequate primary closure and lacerations in which the viability of the sutured tissue is in question should be supported with a conjunctival flap (Figs. 2, 3, 4, and 5).

16. How can the collapsed anterior chamber be reformed?

In a healthy eye, the aqueous humor reforms at a rate of 2.5 μl/min in dogs and 15 μl/min in and cats. If the eye is not severely damaged, the aqueous production rate may be sufficient to reform the anterior chamber within several minutes after the eye has been sealed. Usually, however, the anterior chamber is reformed with lactated Ringer's or balanced salt solution. A 25- or 27-

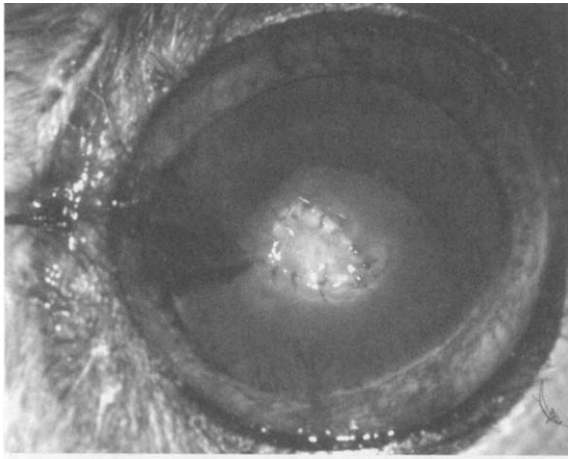


Figure 2. A free graft of Tenon's tissue taken from the dorsal area of the globe.

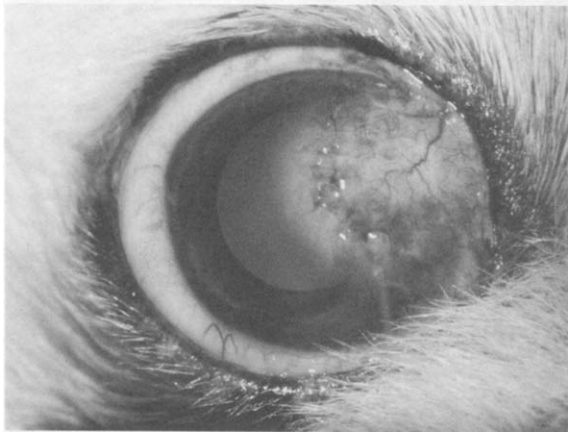


Figure 3. A pedicle graft covering a large ulcerative wound.

gauge needle is inserted at the limbus, parallel to the iris plane, and enough fluid is injected to restore the anterior chamber to its normal depth without creating high intraocular pressure (IOP). The IOP should be in the low-normal range (10–15 mmHg).

17. How and when should the entrapped iris be amputated or replaced?

When a prolapsed iris should be excised rather than repositioned is controversial. Recommendations are based on the time it takes for the exposed iris to become sufficiently contaminated to cause infection if replaced. Recommended times range from 1 to 24 hours. It is safe to assume that smaller prolapses take longer to pose a threat of infection. Magnification is essential if iris amputation or replacement is attempted. Tissue to be excised should be grasped gently with fine forceps and cut flush with the cornea. A dilute solution of epinephrine (1:10,000 in lactated Ringer's or balanced salt solution) aids hemostasis. To replace the iris, it is carefully freed from fibrinous corneal attachments with an iris spatula or irrigating cannula or dissected with viscoelastic material. After the iris is freed from the cornea, the anterior chamber is reformed with viscoelastic material (1% sodium hyaluronate or 2% hydroxypropylmethylcellulose). Care must be taken to avoid trauma to the corneal endothelium, iris, and lens. Just before placing the last suture, the viscoelastic material can be gently flushed from the anterior chamber or left in place. This procedure is difficult for inexperienced practitioners and preferably should be performed by a trained ophthalmologist.

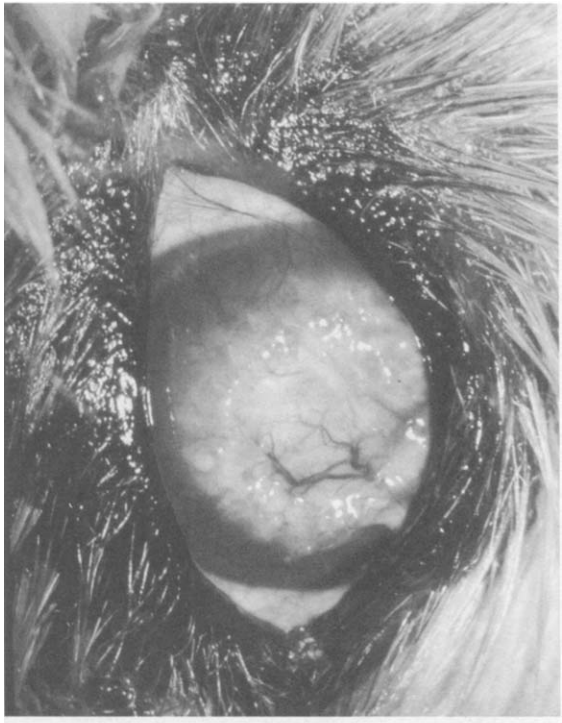


Figure 4. A healing corneal perforation covered with a conjunctival flap.

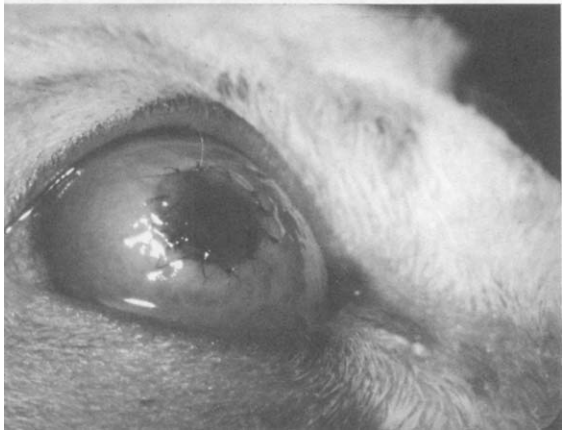


Figure 5. Corneal transplant into a degenerative cornea.

18. What type of suture pattern should be used in the cornea?

Simple interrupted sutures are the easiest to place correctly. If you experience a lot of tension, horizontal mattress sutures may be placed first, followed by interrupted sutures. Correct suture placement is important to avoid internal wound gape (too shallow), wound override (sutures of unequal depth and length on each side of the wound), and intraocular contamination (too deep). Sutures should be approximately 75–90% of corneal depth, 1.5–2 mm in length, of equal depth on each side of the wound, and 1–1.5 mm apart.

19. What are the common types of foreign body–related injuries?

Corneal and conjunctival foreign bodies from plant material and sand are frequently encountered in dogs, especially those used for hunting or field trials. Patients often present with an acutely red and painful eye. Linear abrasions of the cornea are an indication for eversion of the lid to examine for foreign material lodged in the upper palpebral conjunctiva. Superficial corneal foreign bodies may present with variable amounts of discomfort and usually can be detected with simple magnification (e.g., loupe or diagnostic otoscope head). Deeper corneal foreign bodies may have the appearance of a puncture wound and are harder to detect without the use of a slit lamp. Foreign body penetration into deeper ocular structures is often associated with BB-pellet, bird shot, and glass. Involvement of orbital structures, iris, lens, retina, or vitreous humor is possible, and the prognosis is affected accordingly.

20. How should foreign bodies involving the ocular surface be treated?

Superficial foreign bodies can be removed with topical anesthesia in many cases, but some animals may require sedation or general anesthesia. A spatula, corneal forceps, or hypodermic needle (25- or 27-gauge) is used to elevate the foreign body from the ocular surface. If loosened foreign material remains on the eye, it can be picked up with a moistened cotton-tipped swab. Hypodermic needles should be held at a shallow angle to the cornea to avoid perforation. After removal, treat topically with a broad-spectrum antibiotic drop or ointment 3 times/day for 5–7 days. A single application of 1% atropine sulfate is given if the pupil is miotic.

21. What should be done to manage an intraocular foreign body?

Management of intraocular foreign bodies depends on how long the foreign body has been in the eye, its location, and what it is made of. The potential for damage during removal should be compared with the potential for damage if it is left in the eye. Organic material leads to sepsis if not removed soon after penetration. Some metals and glass, however, may cause little reaction if left alone and eventually become anchored by fibrin or scar tissue. If the foreign body is recent and located in the anterior chamber, it should be removed through a limbal incision. Surgery to remove a foreign body from the posterior segment often results in complications leading to a blind eye and carries a poor prognosis. Broad-spectrum topical and systemic antibiotics should be used to control infection. Topical corticosteroids, cycloplegics, and oral corticosteroids (anti-inflammatory dosages) or NSAIDs may be used to treat uveitis. Corticosteroids should be used with caution because of the potential for sepsis.

TYPE OF FOREIGN BODY	POTENTIAL FOR DAMAGE	REMOVAL NECESSARY?
Organic	Reactive; sepsis possible	Early removal essential
Nonferrous metal, glass, or plastic	Minimal; becomes walled off by fibrin and fibrous tissue	Removal not necessary
Ferrous metal	Highly reactive; toxic to intraocular tissue	Early removal recommended

BIBLIOGRAPHY

1. Featherstone HJ, Sansom J, Heinrich CL: The use of porcine small intestinal submucosa in 10 cases of feline corneal disease. Vet Ophthalmol 4:147–153, 2001.
2. Morgan RV: Ocular emergencies. Comp Cont Educ Vet 4:37–45, 1982.
3. Roberts SR: Assessment and management of the ophthalmic emergency in cats and dogs. In The Compendium Collection: Ophthalmology in Small Animal Practice. Trenton, NJ, Veterinary Learning Systems, 1996, pp 252–267.
4. Wilkie DA, Whittaker C: Surgery of the cornea. Vet Clin North Am Small Anim Pract 27:1067–1107, 1997.

35. OCULAR HEMORRHAGE

Cynthia C. Powell, D.V.M., M.S.

1. Name the common causes of ocular hemorrhage.

Trauma, coagulopathies, thrombocytopenia, vasculitis, and neoplasia are potential causes for ocular hemorrhage. Trauma-related hemorrhage is probably the most common cause of ocular hemorrhage presented as an emergency.

2. What forms of ocular hemorrhage have emergency significance?

All forms of ocular hemorrhage have the potential to be associated with life-threatening systemic disease. If the cause of hemorrhage is not known, patients should be evaluated for systemic diseases, especially those causing clotting abnormalities and vasculitis. Although the ocular hemorrhage may not require emergency treatment, the disease associated with hemorrhage might. Intraocular hemorrhage alone or related to other diseases (e.g., uveitis or hypertension) can quickly become sight-threatening, and prompt medical management is important. Complications of intraocular hemorrhage that cause vision loss include glaucoma, cataract, retinal detachment, retinal degeneration, and phthisis bulbi.

3. Why is blunt trauma so potentially damaging to intraocular tissues?

Tremendous tissue distortion results from blunt ocular trauma. The four phases of blunt injury that induce tissue damage are:

1. Compression
2. Overshooting
3. Decompression
4. Oscillation

The initial anteroposterior globe compression at the cornea causes equatorial expansion and shortening of the globe along the anteroposterior axis so that the cornea may touch the iris and lens. As the momentary force of deformation is removed, the anteroposterior globe diameter increases, whereas the equatorial diameter decreases. The tissues overshoot so that the anteroposterior diameter becomes momentarily greater than normal and the equatorial diameter less than normal. The globe subsequently oscillates between these maximums and minimums with decreasing amplitude for a brief time. This extreme stretching of the ocular tissues causes injury to the choroid, lens, optic nerve, retina, and vitreous gel (Fig. 1).

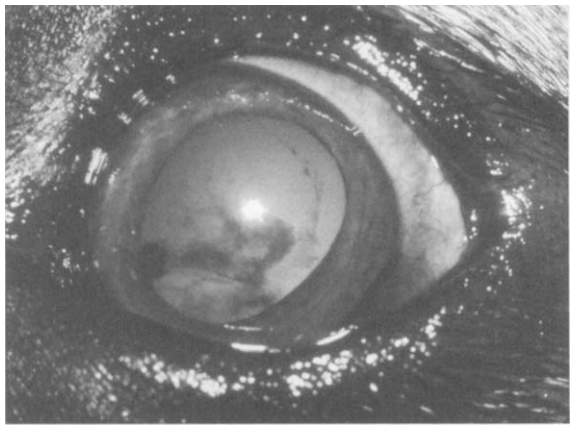


Figure 1. Five days after blunt trauma to the eye of a German shepherd police dog. Clotting and resorption underway, but mild uveitis needs to be treated.

4. Describe the implications of hyphema.

Hyphema is the presence of blood within the anterior chamber. Blunt or sharp trauma to the globe is the most common cause. However, hyphema may be due to thrombocytopenia, coagulopathies, iritis, intraocular neoplasia, congenital ocular anomalies, chronic glaucoma, and hypertension. Initial examination should determine whether the globe has been penetrated. Hyphema often causes little damage to the eye itself but may result in glaucoma, anterior uveitis, iris adhesions secondary to clot contraction, and capsular cataract formation. Anterior chamber bleeding may not clot completely because the iris produces fibrinolysin. Maximal clot integrity requires 4–7 days. Hyphema should be treated as a clinical sign, and its cause should be determined as soon as possible (Figs. 2 and 3).

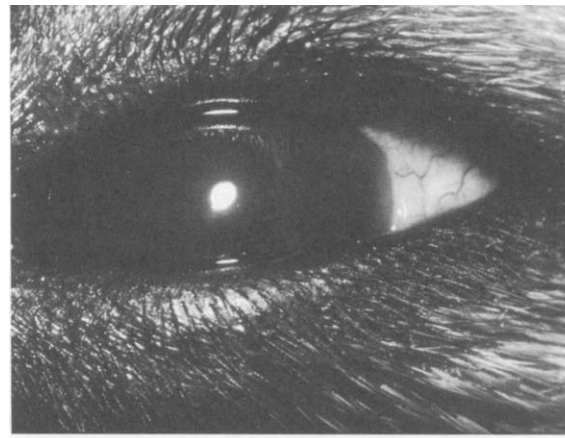


Figure 2. Unclotted hyphema fills the anterior chamber in this dog with a clotting factor deficiency.

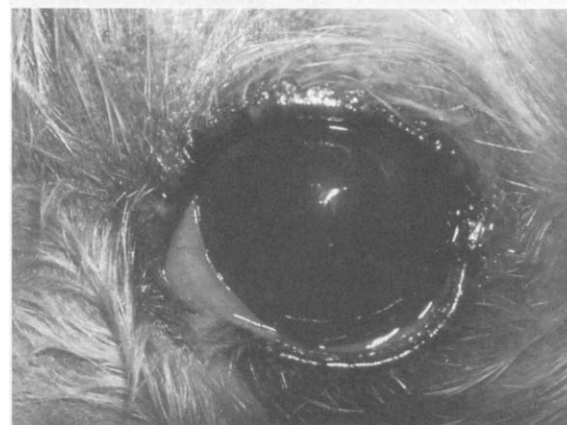


Figure 3. Recurring hyphema from constant barking following this dog's cataract extraction.

5. What clinical parameters should be evaluated in cases of hyphema?

A complete eye examination should be performed, and the entire animal must be evaluated to assess concomitant injury or disease. In particular, globe rupture should be ruled out. Vision should be estimated based on the degree of menace when bright light is suddenly directed into the eye. Assuming that the examination light penetrates to the posterior part of the globe, the consensual pupillary light reflex indicates whether the retina and optic nerve are functional. If a globe rupture is not present, intraocular pressure should be measured. Finally, the hyphema should be graded by the anterior chamber volume occupied by the blood. The grading system is helpful prognostically because it indicates the severity of hemorrhage and the degree of intraocular tis-

sue damage in trauma cases. Hyphema of grade 1 severity generally clears in less than 1 week. Grades 2 and 3 take several weeks or longer to resolve. Grade 4 hyphema often is associated with globe atrophy (phthisis bulbi).

GRADE	AMOUNT OF BLOOD IN ANTERIOR CHAMBER
1	Less than one-third
2	One-third to one-half
3	One-half to nearly total
4	Total

6. How should hyphema be treated?

If a primary cause other than trauma is determined, initial treatment must address the underlying problem. All animals with hyphema should be kept quiet and subdued, possibly by use of sedation. Many medical treatments have been proposed, but no studies have evaluated their effectiveness. Interest in some treatments continues, whereas others remain controversial. Basically the treatments can be separated into the following categories:

Cycloplegics
Antifibrinolytic agents
Miotics
Fibrinolytic agents
Adrenergic agonists
Surgical intervention
Corticosteroids

7. What cycloplegics may be useful and why?

Cycloplegics are parasympatholytic drugs that cause paralysis of ciliary body and iris sphincter smooth muscles. Thus, the ocular accommodation by the ciliary body is prevented, and the pupil dilates. Prevention of smooth muscle spasm may enhance patient comfort and facilitate fundus examination. Topical atropine, 1% solution once or twice daily, is sufficient. Once mydriasis (pupil dilation) occurs, the frequency of treatment may be reduced and the drug used to effect.

8. What miotics are useful and why?

Parasympathomimetic agents are miotics that induce spasm of the ciliary body and iris sphincter smooth muscles. In theory, use of a miotic such as pilocarpine 1% should open the filtration angle. However, miotics also tend to increase intraocular inflammation, so when pupil size is decreased, the chance of pupil obstruction by fibrin is increased. No scientific evidence suggests that they enhance the clearance of blood from the anterior chamber. In the author's opinion, miotics should not be used to treat hyphema.

9. What adrenergic agonists have been advocated and why?

Sympathomimetic agents such as topical epinephrine 1% and phenylephrine 2.5% have been advocated to decrease anterior chamber hemorrhage by way of vasoconstriction. Such treatment may be helpful with evidence of ongoing hemorrhage but usually provides little effect. It is rarely considered an option in the treatment of hyphema in humans.

10. Which corticosteroids are best to use?

Invariably, traumatic hyphema is associated with anterior uveitis ranging from mild to severe. Thus, topical steroids such as prednisolone acetate, prednisolone sodium phosphate, and dexamethasone ophthalmic drops are used 4 times/day. Their efficacy in improving outcome is unproved. Systemic steroids are more controversial but commonly used. Certainly any concurrent anterior uveitis will be lessened, and theoretical evidence suggests that steroids may enhance clot stabilization. Controlled studies, however, are lacking.

11. When is antifibrinolytic treatment indicated?

Agents such as aminocaproic acid have been proposed as a means of reducing rebleeding in cases of traumatic hyphema. Rebleeding may result from premature clot lysis mediated by the fibrinolytic system. The theoretical rationale is that the reduced rate of clot lysis allows more time for the damaged blood vessels to heal. In humans, the current recommended dosage is 50 mg/kg orally every 4 hours for 5 days. Antifibrinolytic drugs are contraindicated in cases of intravascular clotting disorders, pregnancy, and cardiac, hepatic, or renal disease.

12. What is the purpose of fibrinolytic treatment?

Hyphema typically progresses from free blood to varying degrees of blood clot formation 1–7 days after injury. Once fibrin formation has occurred, clot lysis may be induced with fibrinolytic agents such as tissue plasminogen activator (tPA). Clinically, tPA is used by injecting 25 μg in a 100 μl volume into the anterior chamber. Clot lysis typically occurs within 30–60 minutes of injection. As clot lysis occurs, red blood cell clearance is facilitated. Topical application of tPA is also promising.

13. What surgical interventions are used for hyphema?

If hyphema persists beyond 5–10 days or intraocular pressure increases, surgical removal may be necessary. An anterior chamber wash-out is the simplest and safest surgical procedure to clear free blood from the anterior chamber. Removal of the clotted blood is not required, only evacuation of loose blood cells and debris. A 30-gauge needle or cannula is used to irrigate a balanced salt solution into the anterior chamber, and a second 2-mm incision is made to allow fluid egress. Removal of the entire clot is possible but may result in lens, iris, and corneal endothelial trauma. Other surgical procedures are available but should be performed by someone experienced and equipped for intraocular surgery.

14. What drugs may be contraindicated in cases of hyphema?

Based on the antiplatelet effect of the cyclooxygenase inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, flunixin megulamine, and topical ocular NSAIDs should be avoided. Although cycloplegics such as atropine are advocated for medical management of hyphema, a small percentage of patients develop glaucoma associated with use of atropine.

15. How can vitreous hemorrhage be recognized?

Disorders of the posterior segment (ocular tissues posterior to the lens) are more difficult to detect and characterize because direct examination must be performed through the pupil, or indirect imaging techniques such as ultrasound must be used. Direct examination is impaired with disease of the anterior segment and cornea. Dilation of the pupil, if possible, greatly facilitates evaluation of the posterior globe. If vitreous hemorrhage is near the lens, it may be visible with a penlight or transilluminator. Otherwise, an indirect ophthalmoscopic examination is the best way to evaluate the vitreous cavity. Vitreous hemorrhage appears as strands, sheets, or diffuse areas of blood accumulation. If the hemorrhage is preretinal (between the vitreous and retina), it may resemble a "boat keel" because of gravitational settling of the erythrocytes (Figs. 4 and 5).

16. Does vitreous hemorrhage have special implications?

The most common cause of vitreous hemorrhage is trauma-induced rupture of uveal or retinal blood vessels. The animal should be evaluated closely for rupture of the cornea or sclera. Causes of vitreous hemorrhage may be grouped as follows (Fig. 6):

- Tearing of a blood vessel in a congenital or acquired retinal detachment
- Retention of the fetal hyaloid artery system
- Widespread ocular disease (inflammation of the choroid and retina, optic neuritis, chronic glaucoma, and intraocular neoplasia)
- Systemic disease (hypertension, coagulopathies, and thrombocytopenia)

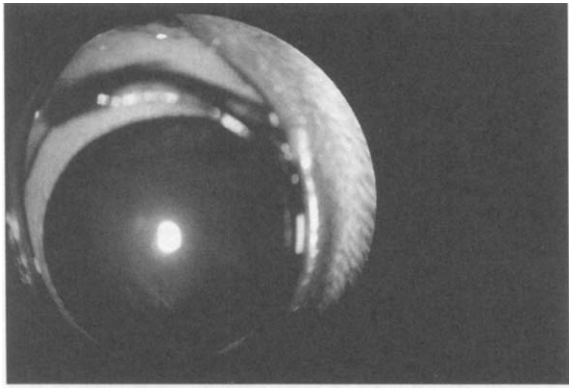


Figure 4. Vitreal hemorrhage from retinal vessels in the this domestic shorthair cat with a monoclonal gammopathy

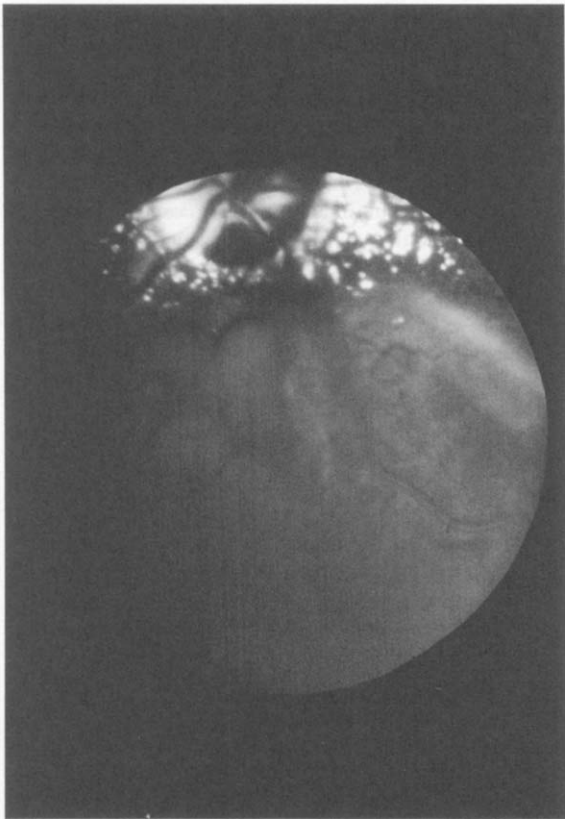


Figure 5. Preretinal hemorrhage and focal retinal detachment in a dog following an automobile accident.

17. How is vitreous hemorrhage treated?

Other than dealing with the underlying ocular or systemic disorder associated with vitreous hemorrhage, no simple treatment is available. If hemorrhage occurs into the solid vitreous gel, clotting is rapidly activated because the gel matrix serves as a collagen framework for platelet adhesion. Infiltration of neutrophils and macrophages hasten clot removal but cause further vitreous gel breakdown and inflammation. Preretinal hemorrhage clots poorly. Concurrent use of topical and systemic corticosteroids is appropriate and may ameliorate the inflammatory reaction. If an-

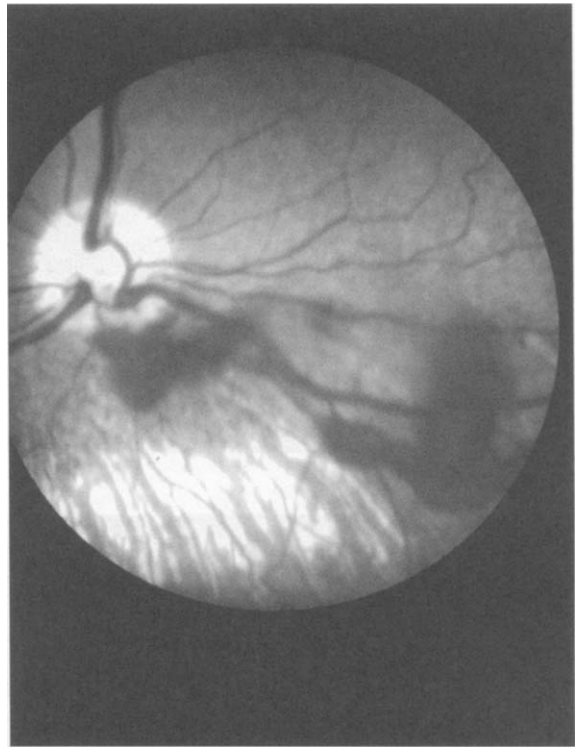


Figure 6. Retinal hemorrhage in a dog with thrombocytopenia.

terior uveitis is present, the use of topical atropine as a cycloplegic is appropriate. Depending on the hemorrhage area and density, resolution may take many months.

18. What does retinal hemorrhage look like?

The appearance of retinal hemorrhage depends on the retinal layer involved. Because of the relatively loose attachment between the retina and vitreous gel and the retina and retinal pigment epithelium, hemorrhage of large size may develop in either space. Preretinal hemorrhage (between the retina and vitreous) frequently has a boat keel shape because of gravitational settling of the erythrocytes. Intraretinal hemorrhages primarily are aligned vertically; their end on appearance is round, and the hemorrhages are small. Nerve fiber layer hemorrhages are typically feathered or striated and flat, because the hemorrhage follows the path of the nerve fibers. The retinal depth of a focal hemorrhage may be estimated based on which structures are positioned beneath and thus obscured or positioned above and thus visible (Fig. 7).

19. Explain the significance of retinal hemorrhage.

Retinal hemorrhage indicates disruption or inflammation of the vasculature. If there is no clear history or physical evidence of trauma, systemic disorders must be considered. Infectious diseases capable of causing vasculitis or retinitis must be considered. Disorders that may be immediately life-threatening are coagulopathies, severe anemias, and blood dyscrasias. Chronic disorders such as hypertension, hyperviscosity syndromes, and neoplasia may cause retinal hemorrhage. Although not immediately life-threatening, such conditions may cause ocular signs that can be confused with a more acute process. The clinician should consider performing a complete blood count, serum chemistry profile, and clotting profile if retinal hemorrhage is noted. A portion of the serum should be saved for potential serologic testing (see Figures 2 and 3).

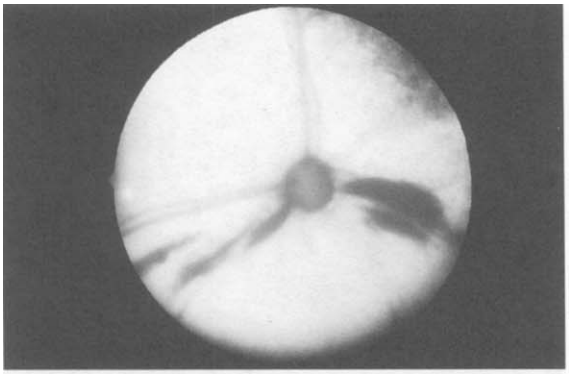


Figure 7. Retinal hemorrhage in the nerve fiber layer of a cat.

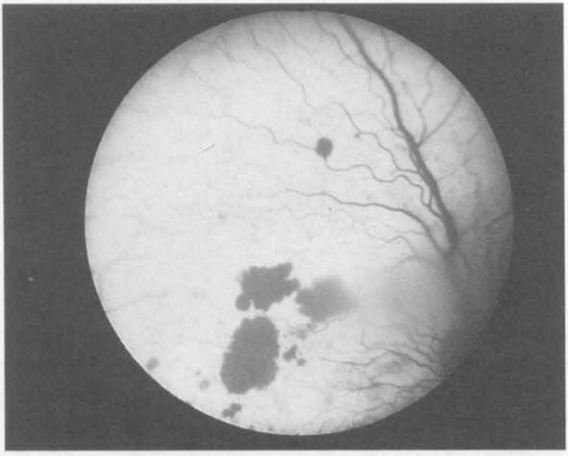


Figure 8. A 10-year-old basset hound with intraretinal hemorrhages secondary to hypertension. These hemorrhages are located within the layers of the photoreceptors, outer nuclear, outer plexiform, inner nuclear, or inner plexiform.

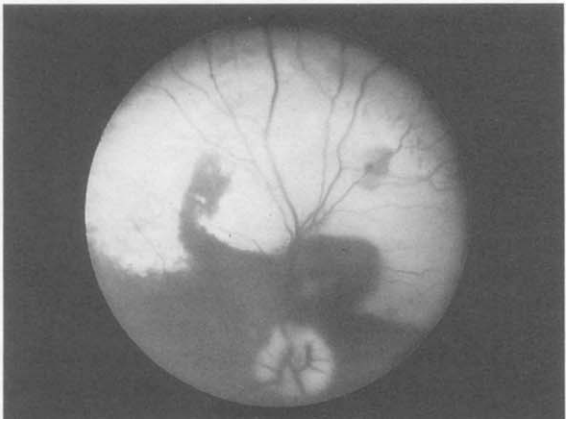


Figure 9. A 7-year-old Norwegian elkhound with retinal hemorrhage and detachment secondary to renal disease. These hemorrhages are both preretinal and intraretinal.

20. Is there any specific treatment for retinal hemorrhage?

No. If an underlying systemic disorder is identified or suspected, appropriate treatment is indicated. Severe subretinal or preretinal hemorrhage can be surgically removed or lysed with intracameral injection of tPA, but these procedures must be performed by someone well-versed in intraocular and posterior segment surgery.

BIBLIOGRAPHY

1. Aguirre GL, Gross SL: Ocular manifestations of selected systemic diseases. In The Compendium Collection: Ophthalmology in Small Animal Practice. Trenton, NJ, Veterinary Learning Systems, 1996, pp 89–98.
2. Collins BK, Moore C: Diseases and surgery of the canine anterior uvea. In Gelatt KN (ed). Veterinary Ophthalmology. Philadelphia, Lippincott Williams & Wilkins, 1999, pp 755–795.
3. Lane IF, Roberts SM, Lappin MR: Ocular manifestations of vascular disease: Hypertension, hyperviscosity, and hyperlipidemia. J Am Animal Hosp Assoc 29:28–36, 1993.
4. Roberts SM: Assessment and management of the ophthalmic emergency in cats and dogs. In The Compendium Collection: Ophthalmology in Small Animal Practice. Trenton, NJ, Veterinary Learning Systems, 1996, pp 252–267.

36. ENDOPHTHALMITIS

Bruce H. Grahn, D.V.M.

1. What is endophthalmitis?

Endophthalmitis is an inflammation of the contents of the globe. Extension of the inflammation through the sclera and into the orbit is panophthalmitis. Endophthalmitis develops when there is disruption of the corneal, conjunctival, scleral, and blood-ocular barriers. Endophthalmitis affects both the anterior and posterior ocular segments. The etiology of endophthalmitis is diverse and may be septic and involve infectious agents that arrive from outside the eye. These agents may enter the eye through the ocular blood supply, through the central nervous system via the central spinal fluid and optic nerve, or by perforation of the cornea or conjunctiva and sclera. Nonseptic endophthalmitis may develop secondary to blunt trauma, cataracts, ruptured lens capsules, or other varied disruptions of the blood-ocular barriers.

2. What are the clinical manifestations of endophthalmitis?

Endophthalmitis is manifested by a variety of nonspecific signs of uveitis including miosis, aqueous flare, hyphema, hypopyon, hypotony, synechiae, exudative retinal detachments, and hyalitis (Fig. 1). Cataracts, ruptured lens capsules, and corneal or scleral perforations also may be present. When endophthalmitis arises from a systemic disease, there is often an accompanying general malaise, hyperthermia, altered respiration, vomiting, and diarrhea.

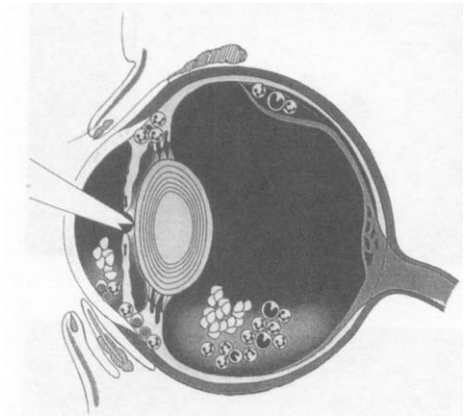


Figure 1. Septic endophthalmitis that is developing secondary to corneal perforation. Note the neutrophil-rich inflammatory infiltrates throughout the inside of the eye.

3. What are the two types of endophthalmitis?

Septic and nonseptic.

4. How is septic endophthalmitis diagnosed?

The classic clinical manifestations for this acute progressive uveitis include hypopyon, hyphema, hyalitis, and exudative retinal detachments. Once the vitreous becomes infected, the fundus usually cannot be visualized because of cellular and protein infiltrates. Detection of the

exudative retinal detachments may require ultrasonography or other advanced imaging techniques. The diagnosis of septic endophthalmitis is confirmed by oculocentesis and cytologic examination of a vitreous and aqueous humor aspirate. Cytology or bacterial cultures will reveal a marked neutrophilic inflammatory infiltrate and may reveal infectious agents. Fortunately septic endophthalmitis is an uncommon diagnosis.

5. What is the treatment for septic endophthalmitis?

This is a fulminant disease, and the prognosis for saving the eye is poor even when the diagnosis is established within hours of onset. Septic endophthalmitis requires aggressive therapy including surgery (vitrectomy or enucleation) combined with systemic and topical medical therapy. This condition is an emergency and requires immediate systemic therapy with antibiotics chosen on the basis of cytologic identification of the infectious agent. If vision salvage is attempted, a surgical vitrectomy is required to reduce contamination of the vitreous and allow reattachment of the detached retina. Intrathecal antibiotics are indicated to eliminate the remaining infectious agents, and nonsteroidal anti-inflammatory drugs (NSAIDs) should be implemented to stabilize the blood-aqueous barrier. When chronic endophthalmitis has destroyed the globe or financial conditions preclude a vitrectomy, an enucleation should be completed immediately to prevent extension of the septic process into the central nervous system through the optic nerve and meninges. Postsurgical medical management with appropriate antibiotics and NSAIDs are indicated for several days (Fig. 2).

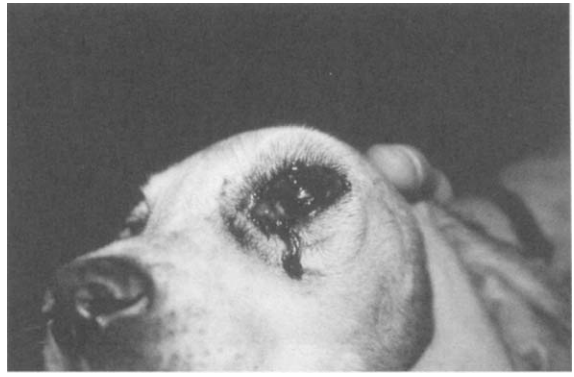


Figure 2. Endophthalmitis and orbital cellulitis. Usually these animals are in severe pain.

6. How is nonseptic endophthalmitis diagnosed?

Nonseptic endophthalmitis is usually not as fulminant as septic endophthalmitis. The diagnosis is also confirmed with fine-needle aspiration of aqueous and vitreous humor. Cytologic examination of the aspirates will reveal a neutrophil-rich infiltrate; however, microbiologic culture will fail to reveal infective agents. Many etiologies need to be considered in the case of nonseptic endophthalmitis including trauma, phacoclastic or phacolytic uveitis, lens luxations, retinal detachments, and immune-mediated uveitis. The etiology may be confirmed with a thorough physical and ocular examination, and appropriate data collection (complete blood count serology, urinalysis, ultrasonography) is required.

7. What is the treatment for nonseptic endophthalmitis?

Nonseptic endophthalmitis is usually treated medically with systemic and topical nonsteroidals, steroids, and cycloplegics. Topical and systemic antibiotics are given prophylactically while the microbial cultures from the aqueous and vitreous humor aspirates are completed. When the cornea, sclera, or lens capsule is perforated or the lens is luxated, surgical management is also indicated to repair the cornea and sclera and remove the lens. Postoperative management is recommended with NSAIDs, steroids, and cycloplegics until the endophthalmitis is controlled.

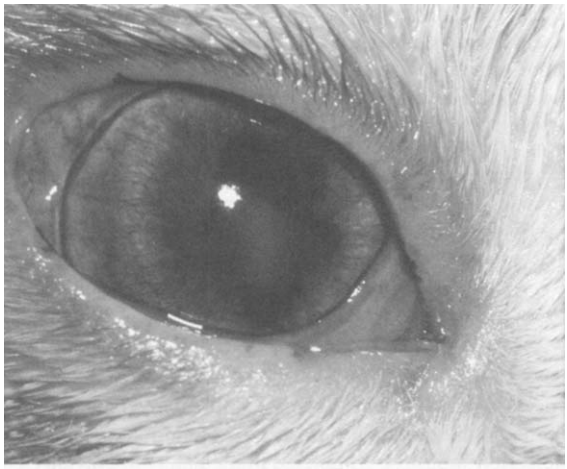


Figure 3. Feline domestic shorthair with septic endophthalmitis showing iris bombé, fibrin, and hypopyon.

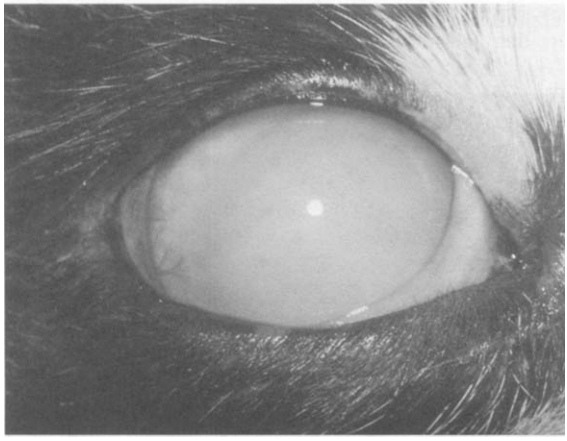


Figure 4. Feline domestic shorthair with septic endophthalmitis secondary to a cat claw perforation.

8. What is the prognosis for septic and nonseptic endophthalmitis?

The prognosis for an eye diagnosed septic endophthalmitis is poor even with aggressive medical and surgical management. The eye with nonseptic endophthalmitis has a slightly better prognosis, provided that the diagnosis is established early and appropriate therapy is instituted for an appropriate length of time (Figs. 3 and 4).

BIBLIOGRAPHY

1. Smith PJ: Surgery of the canine posterior segment. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 1999, pp 935–980.

VIII. Retina

37. ACQUIRED DISEASES OF THE FUNDUS

Michael G. *Davidson*, D.V.M.

1. What is a fundus?

The term *fundus* literally means the internal surface of an organ, farthest away from its opening. The fundus of the eye is therefore the internal, posterior section of the eye that is seen with an ophthalmoscope. In small animals, the fundus is a composite of several different tissues including the optic nerve, sensory retina (and retinal blood vessels), choroid, tapetum (which is part of the choroid), and sclera.

2. What is the best way to examine the fundus?

The fundus is examined by a technique known as ophthalmoscopy, which can be performed with either a **direct** method or an **indirect** method after the pupil is dilated with tropicamide. The direct method uses a direct ophthalmoscope headpiece and gives the examiner a highly magnified view but only of a very small portion of the fundus (< 2% of the surface area). The indirect method uses a light source and an indirect ophthalmoscopy lens that is held in front of the eye, which gives the examiner a less magnified, but much larger field of view.

3. Which method of ophthalmoscopy is the best?

Although the direct method is technically easier, it is not possible to examine the fundus adequately with the direct method because of the small field of view, so the indirect method is preferred. However, the indirect method is technically more difficult to perform because the image viewed, called a "virtual image," is upside down and reversed. Thus, a lot of practice is required to become proficient at the indirect method.

4. When should I examine the fundus of my patients?

Ophthalmoscopy should be a part of a complete eye exam in patients with ocular disease of any type, pupillary light reflex deficits, or vision loss. It should also be routinely performed in animals with undefined systemic illness or those with infectious, vascular, or neoplastic diseases, because many times these conditions affect the tissues of the fundus.

5. When I look at the fundus of a dog or a cat, how can I tell if it is normal or if a lesion is present?

Interpreting the appearance of the fundus can be challenging and requires a basic understanding of the layers of the fundus (see question 1) and the normal variations (Fig. 1). The most common variations of normal are those relating to the amount of pigment in the tissues of the fundus, the size and shape of the optic nerve, and the size and color of the tapetum. A good ophthalmology atlas helps in recognizing these normal variants, but mostly it requires experience and looking at a lot of normal animals.

6. What are the most common types of funduscopic lesions?

In the tapetal area of the fundus (which is usually the dorsal one-third to one-half), lesions are characterized as being either **hyporeflective** if they are darker or grayer than the surrounding,

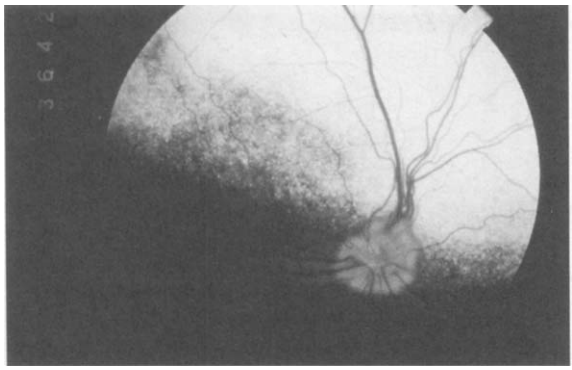


Figure 1. Normal canine fundus. Note well-developed tapetum, pigmented nontapetal area, myelinated optic nerve head, and retinal vasculature.

normal tapetum or **hyperreflective** if they are brighter. These lesions correspond to either a thickening of the retina (hyporeflective lesion—the thick retina blocks some of the light reflecting from the tapetum) or a thinning or degeneration of the retina (hyperreflective—the thin retina allows more reflected light off the tapetum). These identical lesions appear differently in the nontapetal fundus (ventral two-thirds to one-half) and appear as either a fluffy white lesion with indistinct margins (thickening of the retina) or a white to gray lesions with distinct margins (thinning, which is caused by loss of pigment in one of the retinal layers called the retinal pigment epithelium). Other common lesions include certain pigmented lesions and hemorrhage. Lesions are generally easier to visualize and understand in the tapetal fundus.

7. What is the significance of the hyporeflective lesion in the tapetum or the fluffy white lesion in the nontapetum?

These two lesions are exactly the same; they just appear differently because they are being viewed against a different background (i.e., the tapetum versus pigmented background) and are caused by thickening of the retina (Figs. 2 and 3). The most common mechanisms by which the retina becomes thickened are:

- Congenital thickening (retinal dysplasia)
- Edema or inflammatory cells
- Neoplastic cells

8. What is the significance of the hyperreflective lesions in the tapetum or the depigmented lesions in the nontapetal fundus?

These lesions are also analogous to each other and are caused by a thinning of the retina (Figs. 4 and 5). They are almost exclusively caused by atrophy or degeneration (this is the way the retina

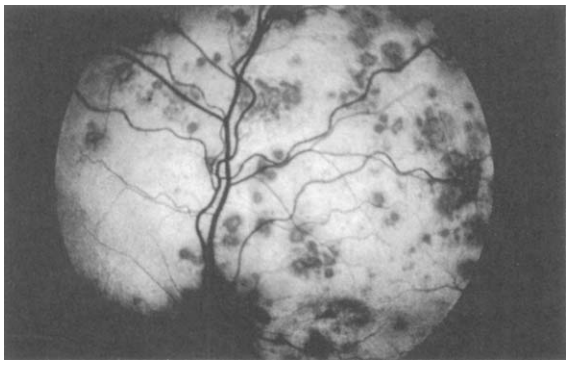


Figure 2. Multifocal areas of tapetal hyporeflectivity in a young domestic shorthair cat. In this case, the lesions are caused by exudate accumulation in the sensory retina caused by coronavirus of feline infectious peritonitis infection.

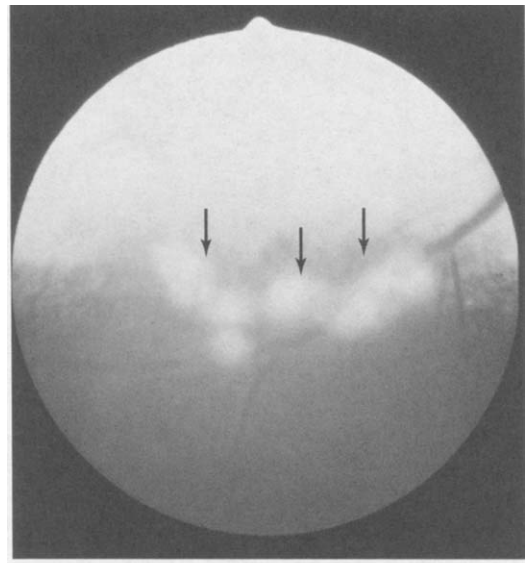


Figure 3. Multifocal areas of exudate adjacent to a retinal blood vessel in the nontapetal fundus of a young domestic shorthair cat with retinitis

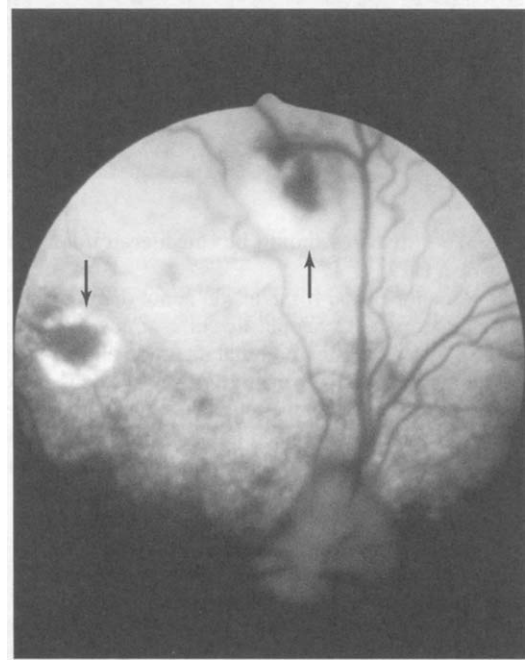


Figure 4. Two large hyperreflective lesions, with pigmented center, in the tapetal fundus of a dog. These lesions are caused by sensory retinal thinning or atrophy, and the pigmented lesion results from tapetal destruction and pigment proliferation.

"scars" or responds to insult, because it can't undergo a regenerative repair like most other tissues). This degeneration may be caused by a number of different diseases with different mechanisms including inflammation, ischemia, malnutrition, or an inherited type of degeneration called progressive retinal atrophy. Focal lesions resulting from inflammation of the retina can be thought of as an inactive lesions.

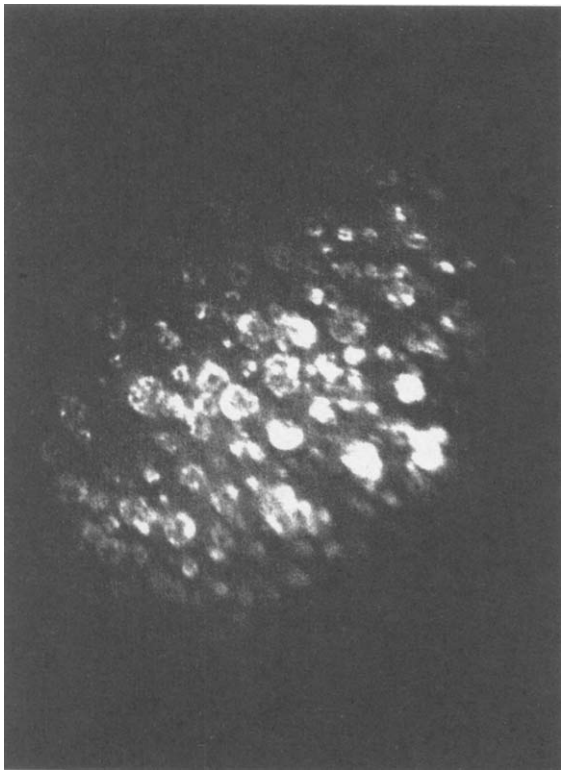


Figure 5. Multifocal depigmented lesions in the nontapetal fundus of a dog with inactive chorioretinitis.

9. What diseases should be considered if a hyporeflective lesion is seen in the fundus of a dog or a cat?

Remember that if the lesion is not due to dysplasia, then thickening of the retina is due to inflammatory cells, neoplastic cells, or edema. Inflammation involving the retina is commonly caused by a systemic microbial infection and less commonly by trauma or an immune-mediated inflammation or hypersensitivity. Any systemic infection has the capability of affecting the fundus in this way. When the retina is the primary tissue affected, this is referred to as a **retinitis** or retinochoroiditis, and when the choroid is the predominate tissue affected, it is called a **chorioretinitis.** It is useful to think about the different microbial agents in broad categories that include:

Bacterial
Fungal
Protozoal
Rickettsial
Viral

These hyporeflective lesions can also be caused by edema alone (with cells). When this occurs, the vascular system of the fundus is pathologically affected and leaks fluid into the retina. This often results from:

- Systemic hypertension
- Disease causing hyperviscosity syndrome (e.g., multiple myeloma or ehrlichiosis)
- Profound anemia and hypoxia of the vessels

Lastly, the hyporeflective lesions can be caused by neoplastic cells. The most common type of neoplasia affecting the fundus in this manner is lymphosarcoma. However, any malignant neoplasia is capable of metastasizing to the tissue of the fundus, and this should also be considered.

10. How can dysplasia be distinguished from these other causes of hyporeflective lesions?

Dysplasia affects certain breeds of dogs. American cocker spaniels, English springer spaniels, King Charles spaniels, Labrador retrievers, and beagles are some of the common breeds, but there are many others. Dysplasia is generally bilateral and does not change in appearance over time. Dysplastic thickening of the retina often produces focal or multifocal linear lesions, whereas inflammation tends to cause multifocal circular lesions. If there is a systemic disease present that might cause inflammation, neoplastic infiltrate, or vascular insult to the retina, the hyporeflective lesion probably is not dysplasia. (See Chapter 40.)

11. If dysplasia is ruled out as the cause of a hyporeflective lesion, what should be done next?

Because there really are very few distinguishing or pathognomonic features of the different diseases that cause these lesions, the diagnosis cannot be made by ophthalmoscopy alone. The ocular exam has simply provided a clue that a systemic disease process is occurring. Therefore, follow the normal diagnostic steps including a thorough physical examination and a differential diagnosis list and perform the appropriate diagnostic tests to confirm or rule out these differentials.

12. What causes hyperreflective lesions (or depigmented lesions in the nontapetal fundus), and what is their significance?

These lesions are caused by atrophy or degeneration of the sensory retina. Characterize the lesions as focal (or multifocal) or more diffuse. Causes of diffuse hyperreflectivity include:

- Progressive retinal atrophy (PRA), an inherited retinal degeneration occurring mostly in pure-bred dogs
- Sudden acquired retinal degeneration (SARD), an idiopathic retinal degeneration affecting mostly older, female, pure-bred dogs. Note that the fundus initially will appear normal with acute SARD; only after several weeks to months will the hyperreflectivity appear.
- Diffuse retinitis or diffuse vascular insult that has resolved
- Rarely, nutritional deficiencies such as chronic taurine deficiency in cats or vitamin E deficiency in dogs

Focal or multifocal hyperreflective lesions are most commonly caused by either an inflammation or a vascular insult that has now resolved, causing a scarring of the retina. As with hyporeflective lesions, there is no pathognomonic appearance to these lesions suggesting one specific type of disease. In fact, these types of multifocal, degenerative lesions are often incidental findings and do not require any diagnostic evaluation (because the insult by which they were caused has already resolved).

13. If a hemorrhage is seen in the fundus, what does this imply?

As with most fundus lesions, there is nothing specific about the presence of a hemorrhage, and both ocular and systemic diseases can cause this (Fig. 6). Examples of ocular disease that cause funduscopic hemorrhage include:

- Inflammation (chorioretinitis)—look for the other lesions of this syndrome
- Trauma
- Retinal detachment
- Developmental disorders such as persistence of the hyaloid artery system

Systemic diseases that cause fundus hemorrhage are the same conditions causing bleeding anywhere else in the body:

- Hypertension
- Coagulopathies such as clotting disorders, disseminated intravascular coagulopathy, thrombocytopenia
- Profound anemia (from hypoxia of the retinal blood vessels)

Thus, once again, the funduscopic findings often characterize the ocular condition or indicate that a systemic bleeding tendency is present. Proceed with the appropriate diagnostic evaluation based on ocular and physical examination findings.

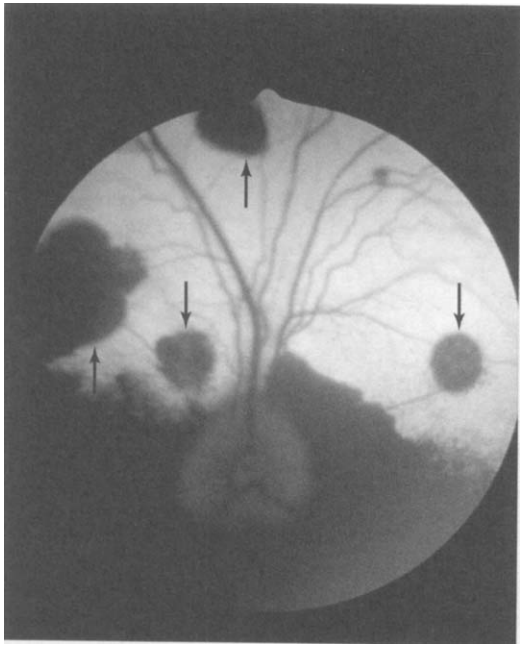


Figure 6. Multifocal intraretinal hemorrhage in a dog with thrombocytopenia.

14. What if, instead of a hyporeflective lesion, a darker lesion that looks like melanin or some other pigment is seen? What can cause this?

Hyporeflective lesions, which generally have a grayish appearance, are distinguished from pigmented lesions, which have a dark brown to black color. There are several mechanisms by which melanin or other types of pigment may become deposited in the tissues of the fundus. Most commonly, this is seen with focal or multifocal retinal and choroidal degeneration or atrophy. This results from damage to the tapetum or proliferation of pigment by the retinal pigment epithelium (RPE) following inflammation or vascular insult. Typically, these lesions would be chronic and "inactive," with no current inflammation. For example, a pigmented center is often seen in hyperreflective lesions from these mechanisms. Also, pigment clumps are often seen in depigmented, inactive lesions in the nontapetal fundus.

Although very rare, melanomas arising from the choroid can cause pigmented, raised lesions in the fundus. These would progress slowly over time and are generally considered benign in dogs.

Remember that patchy clumps of pigment in the tapetal fundus can be a normal finding, caused by focal areas where the tapetum did not develop. Therefore, look for other lesions such as the appearance of hyperreflectivity or depigmentation before considering the pigment abnormal.

Rarely, other types of pigment besides melanin may be deposited in the retina. For example, systemic vitamin E deficiency in dogs may cause an accumulation of lipofuscin, a golden-brown pigment, in the RPE.

15. What is a retinal detachment?

Retinal detachment is actually a separation of two layers of the retina: the sensory retina and the RPE, rather than a separation of the retina from the underlying choroid. Fluid accumulates in the potential space between these two layers of the retina, referred to as the **subretinal space.**

16. What causes a retina to detach?

1. **Exudative** detachment is caused by edema or cells effusing into the subretinal space. This is generally caused by inflammation in the choroid (or a chorioretinitis) or a profound vascular insult to the retinal or choroidal vessels (e.g., severe systemic hypertension).

2. **Rhegmatogenous** detachment results from a tear in the retina, usually peripherally, that allows liquefied vitreous to leak through the tear and into the subretinal space. This tear often is created by pathologic changes in the vitreous. Vitreal changes can occur with aging, from cataracts and other lens diseases, and following intraocular surgery.

3. **Tractional** retinal detachment results from blood or fibrin clots (or rarely from anomalous vessels) in the vitreous that are attached to the retinal surface. As the clot retracts, it pulls the retina, creating a detachment. Often, the traction also creates a tear that causes a rhegmatogenous detachment. Tractional detachments are uncommon in veterinary patients.

17. How does retinal detachment appear on ophthalmoscopic exam?

Because fluid collects in the subretinal space and in front of the tapetum (or the pigmented RPE for the nontapetum), retinal detachments often appear as large areas of hyporeflectivity in the tapetal fundus or as whitish, indistinct areas in the nontapetal fundus (Fig. 7). Hemorrhage in the retina or even in the vitreous also can be seen, and occasionally this hemorrhage will migrate anteriorly into the anterior chamber, producing hyphema. Because the retina is displaced forward into the vitreous, the surface is out of focus to the ophthalmoscopic lens and observer and appears fuzzy and indistinct. If the retina if detached forward to a great extent, the retinal blood vessels may be seen clearly and in focus without the use of an ophthalmoscope, simply by looking through the pupil with a focal light source.

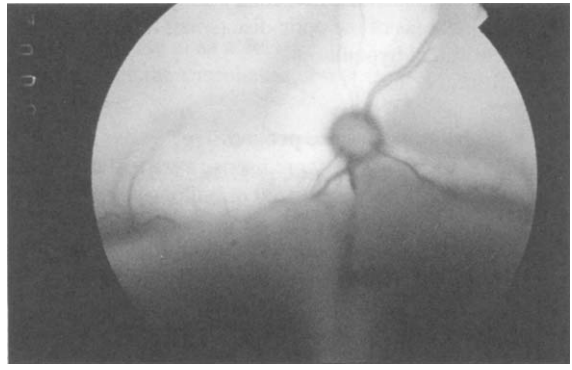


Figure 7. Total, bullous retinal detachment in a cat with systemic hypertension.

18. Is there any treatment for a retinal detachment? Can the eye regain vision?

The specific treatment and prognosis for retinal detachment depend largely on the mechanism (exudative versus rhegmatogenous) and duration of the detachment. Exudative detachments are managed by treating the specific disease process (i.e., antimicrobial agents if infectious inflammation; anti-inflammatory agents if traumatic or immune-mediated inflammation; antihypertensive agents if systemic hypertension is the cause). Rhegmatogenous detachments must be treated surgically by sealing the tear, generally with laser or cryoprobe and various other adjuvant surgical techniques. The eye has an effective mechanism to pump the subretinal fluid out, so if the underlying problem is corrected, retinal reattachment and recovery of some vision are possible. However, because the retina becomes ischemic, retinal detachment of > 1 week duration is unlikely to become functional again. Unfortunately, most retinal detachments in animals are not recognized in a timely fashion, and the visual prognosis is relatively poor (see Chapter 42).

BIBLIOGRAPHY

1. Barnett KC: A Colour Atlas of Veterinary Ophthalmology. London, Wolfe Publishing, 1990.
2. Barnett KC, Crispin SM: Feline Ophthalmology: An Atlas and Text. Philadelphia, W.B. Saunders, 1998.
3. Ketring K, Glaze MB: Atlas of Breed-Related Canine Ocular Disorders. Trenton, NJ, Veterinary Learning Systems, 1998.
4. Rubin LF: Atlas of Veterinary Ophthalmoscopy. Philadelphia, Lea & Febiger, 1974.

38. INHERITED EYE ANOMALIES OF AUSTRALIAN SHEPHERDS, COLLIES, AND SHETLAND SHEEPDOGS

Ronald C. Riis, D.V.M., M.S.

1. At what age should collies, Shetland sheepdogs, and Australian shepherds be examined for eye anomalies?

The eye size and cooperation of the puppy have a lot to do with a successful evaluation of the fundus, regardless of the expertise of the examiner. Ideally, puppies that are 7–8 weeks old should be examined, but 6–9 weeks of age should be a sufficient window of time to accommodate the variables.

2. Are the anomalies progressive?

No, generally, not, but there are exceptions.

3. Which are *not* progressive?

- Colobomas of the iris, ciliary body, and retina (Australian shepherd)
- Colobomas of the optic disc (small to medium)
- Choroidal hypoplasia
- Scleral ectasia

4. Which anomalies are progressive?

Large colobomas may predispose to retinal detachment. Small or incomplete retinal detachment may enlarge to generalized or bullous detachments.

5. Which anomalies cause vision problems?

Large colobomas have related visual impairment, but complete retinal detachment causes blindness.

6. What does the breeder term "go normal" mean?

When puppies are examined at the recommended age and a finding of small or trace choroidal hypoplasia is found, those characteristics may change with maturity, especially in tri- and sable-colored dogs. The maturing migrating pigment of the retinal pigment epithelium disguises the underlying choroid, and the hypoplasia appears to resolve. Although the choroidal hypoplasia remains, breeders say the eyes "go normal."

7. What is the importance of a "go normal" evaluation?

Evaluations done in the 6–9-week window allow minimally affected animals to be classified correctly as phenotypically affected.

8. What breeding recommendations produce the best eye evaluations?

Obviously, the mating between two genotypically normal–eyed dogs is ideal. However, breed standards dictate other qualities that allow for minor anomalies in order to express other physical desirable traits.

9. What is allowable in eye anomalies for a breedable trait?

In order to breed away from undesirable traits, use a mate with extreme minimal traits (i.e., breeding a dog with minor choroidal hypoplasia with a normal-eyed dog).

10. Does this breeding guarantee good eye examinations?

That depends on the breeder's interpretation of "good." Usually, any eye found with a trace, small, or medium amount of choroidal hypoplasia is acceptable or "good." However, even dogs bred with this degree of choroidal hypoplasia may produce offspring with colobomas and retinal detachments if a dog considered "normal" is not genotypically normal.

11. When is breeding not recommended?

Dogs affected with colobomas and retinal detachments should not be bred. Poorly pigmented dogs, such as whites and merles, that are bred together produce offspring with multiple sensory deficits and ocular anomalies.

12. What is a scleral crescent?

A white elliptical characteristic adjacent to the optic disc. This is a patch of sclera without overlying choroid (i.e., a focal choroidal hypoplastic area).

13. What is a staphyloma?

In association with these breeds, it is a protrusion of sclera posteriorly, lined with uveal tissue. It is also called **scleral ectasia.**

14. Is an eye with choroidal hypoplasia blind in the area affected?

No, the overlying retina is normal. Even though the vasculature of the choroid is deficient in these areas, the retina has its own vascular sources.

15. Is retinal dysplasia (folds) a manifestation of choroidal hypoplasia, coloboma, and retinal detachment?

No, retinal dysplasia may be seen along with the other conditions or by itself. It is not thought to be inherited as a manifestation related to the others (see Chapter 40).

16. Is optic nerve hypoplasia a manifestation of choroidal hypoplasia, coloboma, and retinal detachment?

No, optic nerve hypoplasia is thought to be on a separate gene. It, too, can be seen with other anomalies, but rarely.

17. Is microphthalmos a manifestation of coloboma, choroidal hypoplasia, and retinal detachment?

No, microphthalmos is on a separate gene. Although the breed standard for collies and shelties states an almond eye is desirable, a globe that is asymmetrically smaller than the opposite eye or bilaterally small globes with protruding nictitans are undesirable.

18. What other ocular abnormalities are seen in these breeds?

Corneal dystrophies, persistent pupillary membranes, retinal degenerations, lid deficits, granulomatous proliferations, and cataracts.

19. Is the incidence of coloboma, choroidal hypoplasia, and retinal detachment decreasing?

Somewhat. Over the last 30 years, more animals have been examined and certified as free from anomalies, but the percentage of affected collies with choroidal hypoplasia remains high. Other anomalies are relatively low, mainly through the efforts of conscientious breeding.

Incidence of Optic Disc/Nerve Coloboma, Choroidal Hypoplasia, and Retinal Detachment, 1991–1999

	AUSTRALIAN SHEPHERD	COLLIE	SHETLAND SHEEPDOG
Optic disc/nerve coloboma	0.27%	8.75%	0.79%
Choroidal hypoplasia	0.22%	66.7%	0.39%
Retinal detachment	0.13%	1.88%	0.05%

Data from Canine Eye Registration Foundation, West Indianapolis, IN.

20. If a retinal detachment is diagnosed, is there anything that can be done?

Possibly. A partial detachment in an eye with pigment can be treated with laser surgery. Some success at arresting the detachment and even reattaching the flat detachments has been achieved. A subalbinotic or albinotic fundus absorbs the laser energy poorly, and success is less likely. Therefore, cryosurgery may be the treatment of choice.

21. If a nonvisual eye is diagnosed in a puppy, is it necessary to surgically enucleate or eviscerate the globe?

Surgical intervention is necessary only if the globe has other complications causing discomfort to the dog. Generally, an inherited blind eye is well-tolerated by the dog for the duration of its life. Visually, the dog compensates with one eye. Ironically, the expression of severe or extreme colobomas and retinal detachments are rarely bilaterally symmetrical.

22. What other breeds of dogs have excessively white hair coats and inherited ocular and otic defects?

By breeding two merle-coat color patterns together, litters of puppies have been produced with variable degrees of ocular anomalies, microphthalmia, and hearing deficits. These breeds include border collies, dachshunds, fox hounds, Great Danes, and Norwegian dunkerhounds.

23. Because breeding merle-coated animals results in undesired traits, can the fundic examination identify subtly merled dogs such as the sable merle?

Yes, the retinal characteristics can distinguish solid-coat dogs from merle-coat dogs. The solid-coat dogs will have a normal tapetum and fundic pigment, whereas merles will be subalbinotic or albinotic. In the fundus of a merle, there is partial or complete absence of pigment in the uveal tract, so that choroidal vessels can be seen as well as the retinal vasculature. Choroidal vessels are broader, paler red, and parallel, inspiring the name "tigroid fundus" to the describe the striped effect. Thinner retinal vessels run over or on top of the choroidal vessels. The tapetum is faint or absent. Grossly, there is a very red reflex from the merle fundus; this also occurs in other albinotic or subalbinotic animals such as the Siberian husky, Samoyed, white cat, Siamese cat, Appaloosa horse, and albino or partial albino cattle.

24. Should the merle eye anomaly be considered different from the collie eye anomaly?

Yes. The eye anomaly of the homozygous merle has been confused with the collie eye anomaly because the two conditions are similar in some respects. Both are inherited, have variable severity of fundic lesions, and may result in blindness. Both anomalies have been documented in the Australian shepherd, border collie, collie, and Shetland sheepdog. In these breeds, the differential diagnosis is based on a few dissimilarities.

25. What are these dissimilarities?

In nearly all cases, homozygous merles are products of merle-to-merle breeding, and the coat colors are whiter than their littermates. Collie eye anomaly can be found in all coat colors.

The homozygous merle condition is inherited as an autosomal recessive trait linked to the incompletely dominant coat color—merle. The mechanism of linkage involves a transposable

genetic element. Collie eye anomaly has been reported to be inherited through several genes, one or more of which may be dominant. No linkage of collie eye anomaly to other traits has been identified.

Microphthalmia is not associated with collie eye anomaly, although collies frequently appear symmetrically and mildly microphthalmic. Microphthalmia in collies is inherited independently of collie eye anomaly. Severe or asymmetric microphthalmia is a prominent feature of the homozygous merle anomaly.

The lesions of collie eye anomaly involve the sclera, choroid, retina, retinal vessels, and optic disc only. No uveal or lens changes are associated with collie eye anomaly. In the homozygous merle, the lens and iris are frequently involved.

Funduscopically, focal choroid hypoplasia is common in collie eye anomaly. The hypoplastic area has a characteristic location temporal to the optic disc. Choroid hypoplasia in the homozygote merle is multifocal or diffuse.

Colobomas in collie eye anomaly occur most commonly in the optic disc and occasionally in the peripapillary area as scleral ectasia. Colobomas in the homozygous merle are most frequently equatorial (i.e., iris and ciliary body). Ocular examinations of merle puppies should always include a predilation as well as postdilation evaluation of the iris.

26. Has the incidence of merle eye anomaly decreased?

Yes, dramatically over the last 30 years. Occasional inadvertent breeding results in affected puppies, but the word is being spread that merle eye anomaly can be eliminated only by *not* breeding merle to merle.

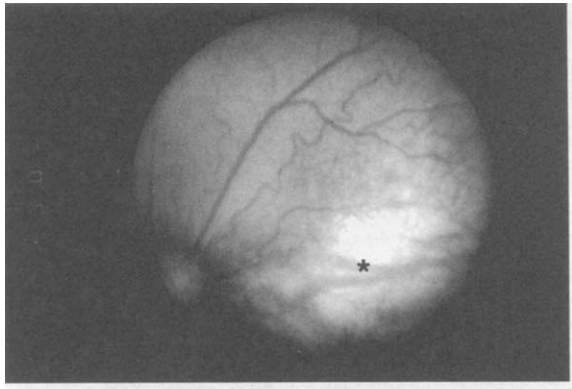


Figure 1. Collie puppy fundus showing white sclera with anomalous choroidal vessels (i.e., choroidal hypoplasia).

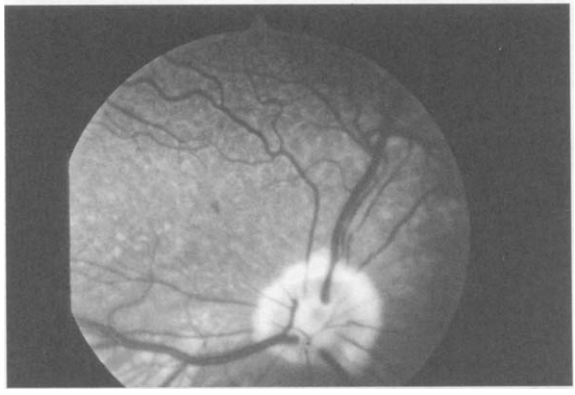


Figure 2. A normal blue merle fundus. This eye was albinotic and displayed the choroidal vascular patterns.

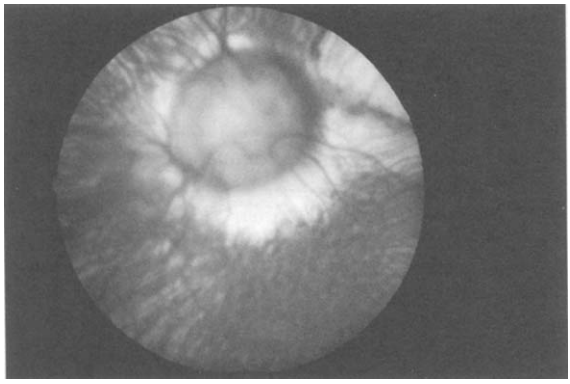


Figure 3. An albinotic fundus with choroidal hypoplasia and slight optic disc depression.

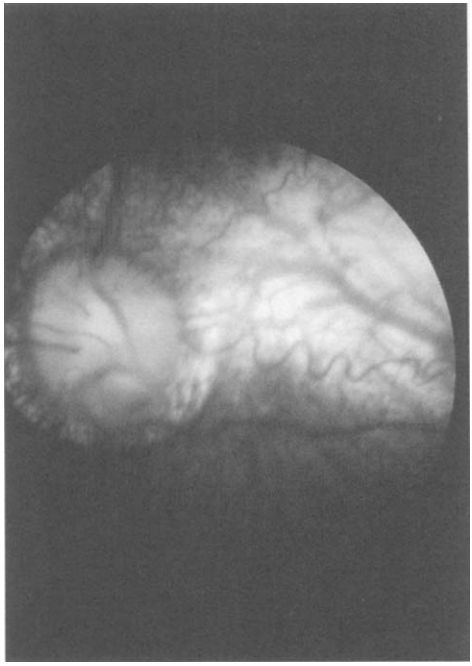


Figure 4. Choroidal hypoplasia, small coloboma at 6 o'clock within the optic disc, and a scleral crescent around the disc from 3 o'clock to 9 o'clock.

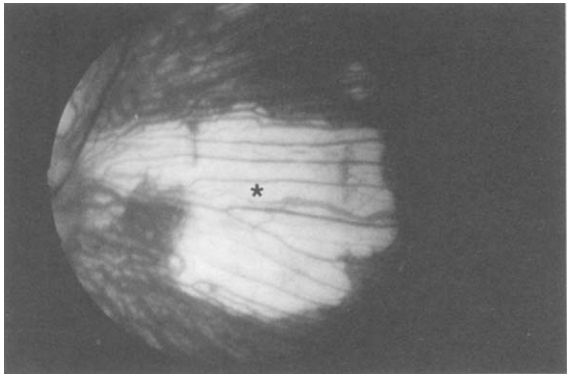


Figure 5. An albinotic fundus with choroidal hypoplasia.

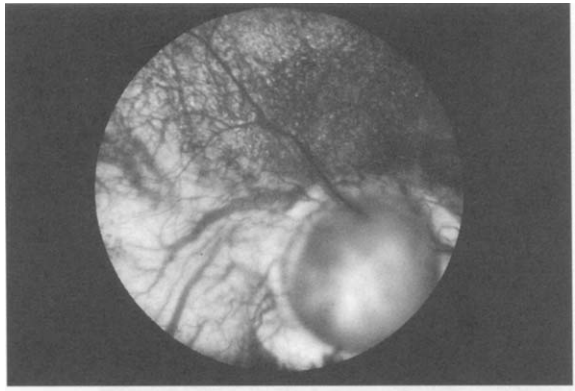


Figure 6. Varying degrees of choroidal hypoplasia and optic disc coloboma involving most of the disc area

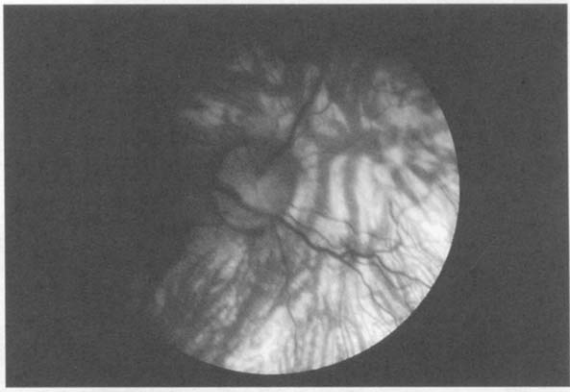


Figure 7. Large choroidal hypoplasia and a small optic disc coloboma at 3 o'clock.

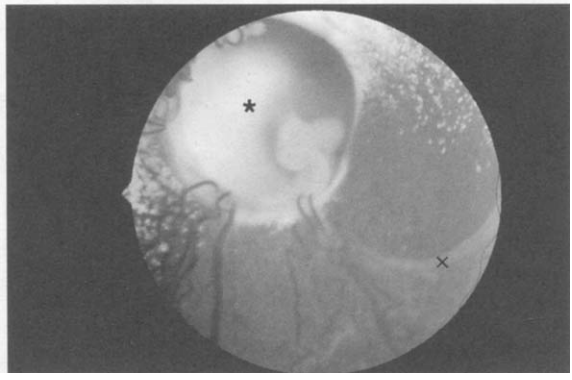


Figure 8. Very large optic disc coloboma (*) and associated retinal elevation (×).

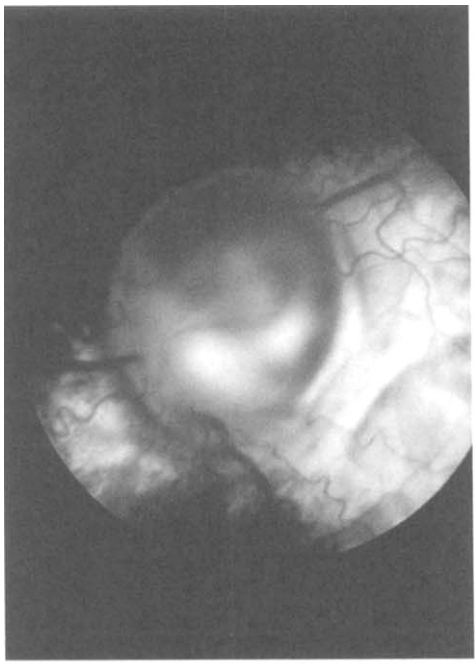


Figure 9. Optic disc coloboma, choroidal hypoplasia, and scleral ectasia in an Australian shepherd dog.

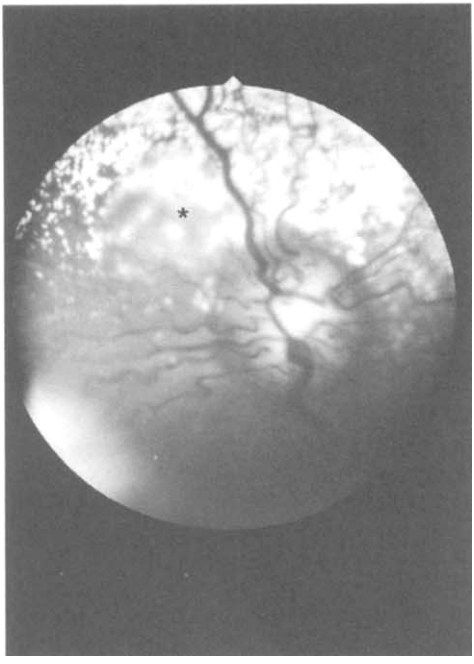


Figure 10. A collie with a focal retinal detachment adjacent to the optic disc at the 10 o'clock to 12 o'clock position (*).

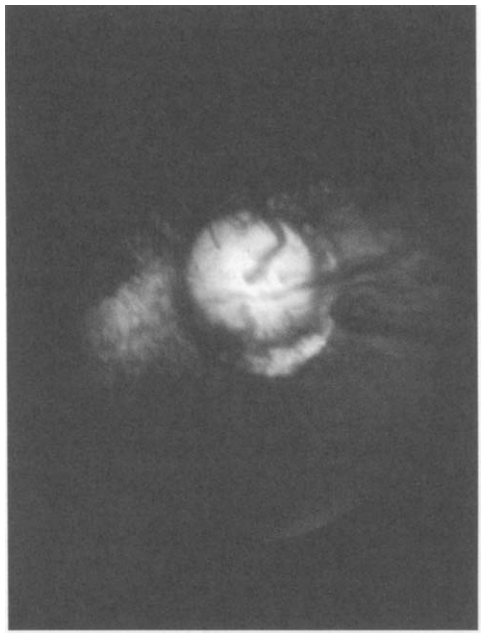


Figure 11. A Shetland sheepdog with unilateral scleral crescent and faint choroidal hypoplasia.

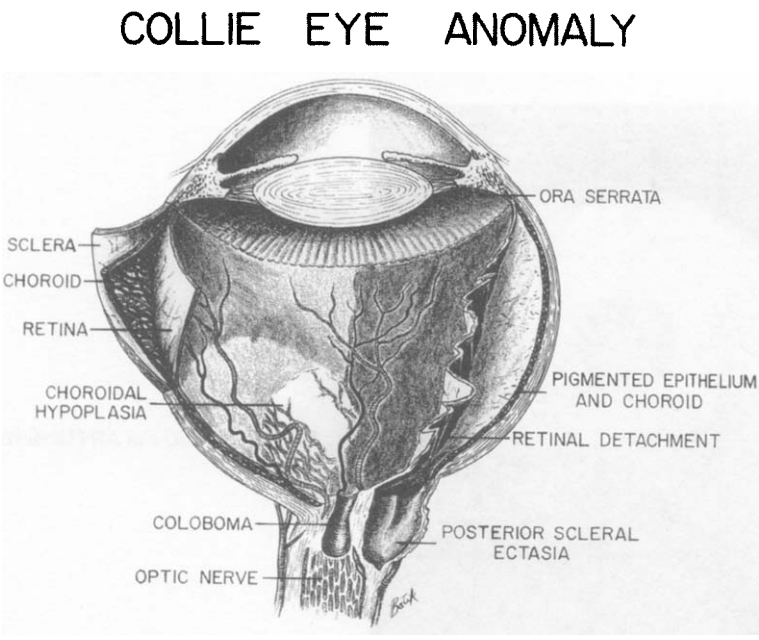


Figure 12. Artist's interpretation of the collie eye anomaly showing anatomic abnormalities as they relate to the normal ocular layers.

BIBLIOGRAPHY

1. Acland G, Aguirre GD, Chader GJ, et al: Canine early onset hereditary retinal degenerations: Genetic and biochemical distinction of 3 diseases. Proc Am Coll Vet Ophthalmol 11:1, 1980.
2. American College of Veterinary Ophthalmologists Genetics Committee: Ocular Disorders Presumed to be Inherited in Dogs, 2nd ed. AVCO, 1999. Available from Canine Eye Registration Foundation, West Indianapolis, IN.
3. Barnett KC, Staades FC: Collie eye anomaly in the Shetland sheepdog in the Netherlands. J Small Anim Pract 20:321, 1979.
4. Freeman HM, Donovan RD, Schepens CL: Retinal detachment, chorioretinal changes, and staphyloma in the collie. I. Ophthalmoscopic findings. Arch Ophthalmol 76:412, 1966.
5. Gelatt KN, Powell NG, Huston K: Inheritance of microphthalmia with coloboma. Am J Vet Res 42:1686, 1981.
6. Roberts SR: The collie eye anomaly. J Am Vet Med Assoc 155:859, 1969.
7. Rubin LF, Nelson EJ, Sharp CA: Collie eye anomaly in Australian shepherd dogs. Prog Vet Comp Ophthalmol 1:105, 1991.
8. Sponenberg DP: Germinal revision of the merle allele in Australian shepherd dogs. J Hered 75:78, 1984.
9. Wallin-Hakanson B, Wallin-Hakanson N, Hedhammar A: Collie eye anomaly in rough collie in Sweden: Genetic transmission and influence on offspring vitality. J Small Anim Pract 41:254–258, 2000.
10. Wallin-Hakanson B, Wallin-Hakanson N, Hedhammar A: Influence of selective breeding on the prevalence of chorioretinal dysplasia and coloboma in the rough collie in Sweden. J Small Anim Pract 41:56–59, 2000.
11. Yakely WL: Collie eye anomaly: Decreased prevalence through selective breeding. J Am Vet Med Assoc 161:1103, 1972.

39. RETINAL DEGENERATIONS

Ronald C. Riis, D.V.M., M.S.

1. Is generalized retinal atrophy always bilateral?

Yes, and usually very symmetrical.

2. Does generalized retinal atrophy lead to blindness?

Yes, but the blindness is varied in its completion depending on the breed. The visual loss is progressive, hence the name progressive retinal atrophy (PRA).

3. What is the earliest complaint from the owners of a PRA dog?

Nyctalopia or impaired vision in reduced lighting. Keep in mind that dogs kept in familiar surroundings do very well despite their diminishing vision. Therefore, their visual deficits may not be noticed until something changes in their environment or their routine.

4. Is PRA painful?

No. Animals show no ocular signs of pain.

5. What are the ophthalmic signs of PRA?

The signs depend on the stage of degeneration. **Advanced PRA** is the easiest to diagnose because the entire tapetum is hyperreflective with attenuated vasculature. The nontapetum is depigmented, sometimes in patterns. The optic disc is darker and smaller (Figs. 1–7).

Moderately advanced PRA will show either a well-demarcated color change or a gradual color change between the normal and degenerated tapetal areas. The vasculature attenuates most

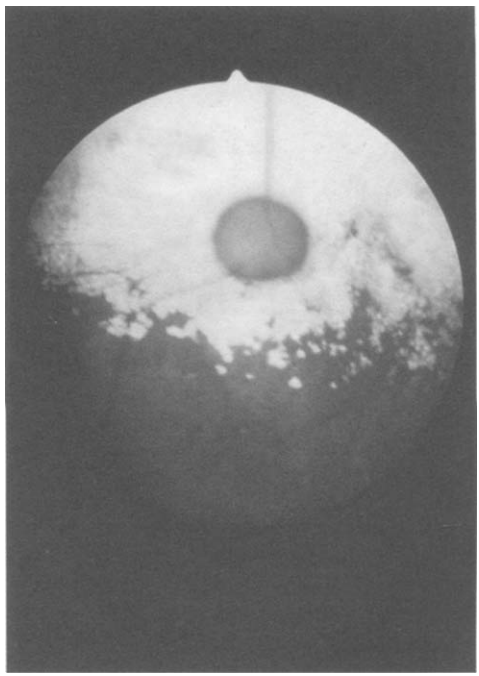


Figure 1. Advanced PRA in a German shepherd.

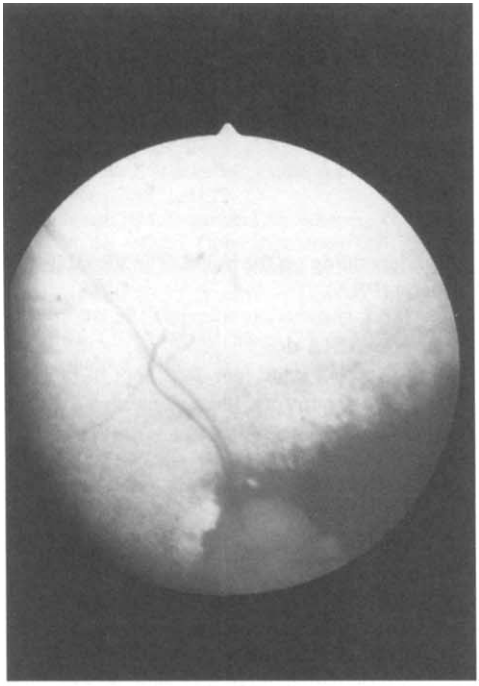


Figure 2. Advanced PRA in a cocker spaniel.

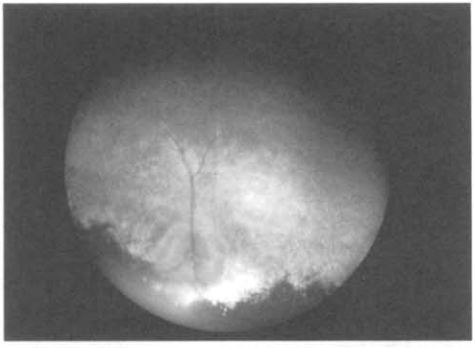


Figure 3. Advanced PRA in an Akita.

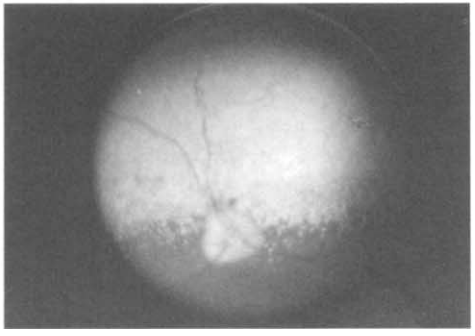


Figure 4. Advanced PRA in an Old English sheepdog.

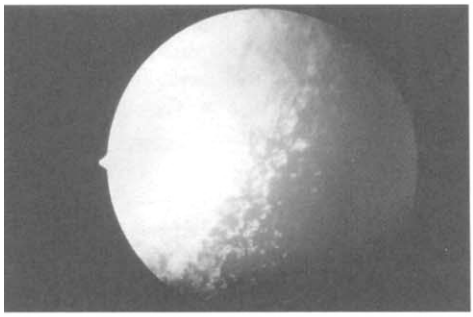


Figure 5. Advanced PRA showing avascularity in the tapetal-nontapetal periphery.

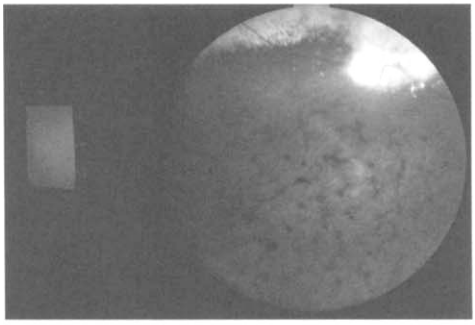


Figure 6. Advanced PRA in the nontapetal fundus of a standard poodle.

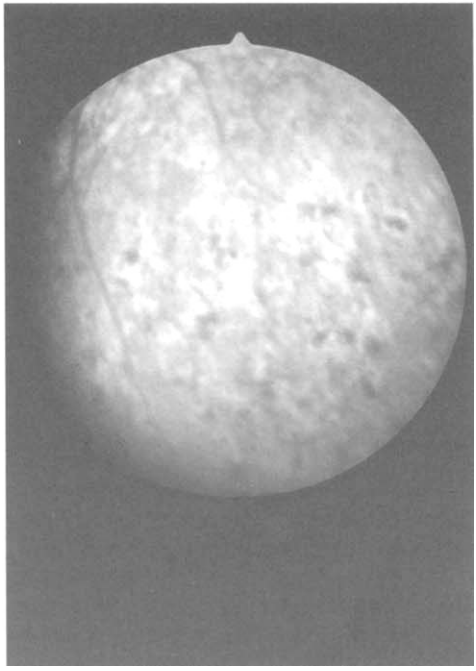


Figure 7. Advanced PRA in the nontapetal fundus of a toy poodle.

significantly within the degenerated zones and especially the periphery. Hyperreflectivity is dependent on the incidence of light so it is variable from being dull to bright with an indirect ophthalmoscopic evaluation. A slight decrease in pigmentation may be noted in the nontapetum. Changes in the optic disc are slight and may be hard to document unless a normal eye is close by to compare (Figs. 8 and 9).

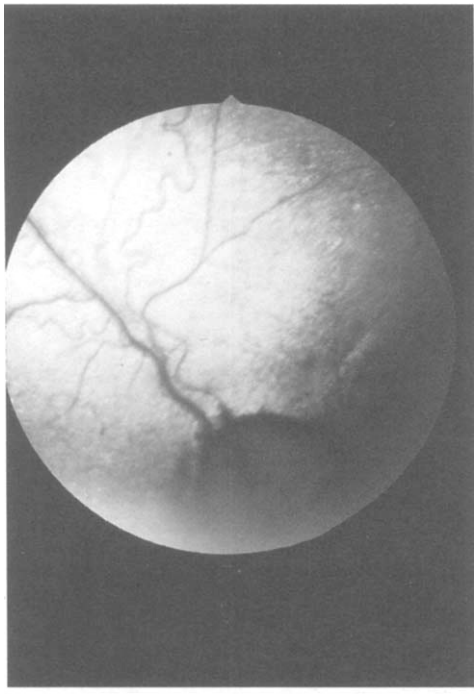


Figure 8. Moderately affected PRA fundus with hyperreflectivity and vascular attenuation

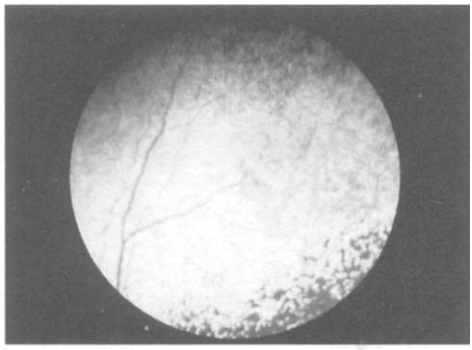


Figure 9. PRA in a miniature poodle. Moderately attenuated peripheral vasculature.

Early PRA is sometimes difficult to diagnose. Slight peripheral tapetal color changes can be misleading, especially if the dog is darkly pigmented where diffusion of pigment into the peripheral tapetum appears gray. If it is PRA, the vasculature will show attenuation of the vessel diameters especially in the periphery and circumciliary vessels. Vessels in the mid periphery may have variable wall diameters (called "boxcarring" or "beading"). Usually, the nontapetal area and optic disc look pretty good (Figs. 10–13).

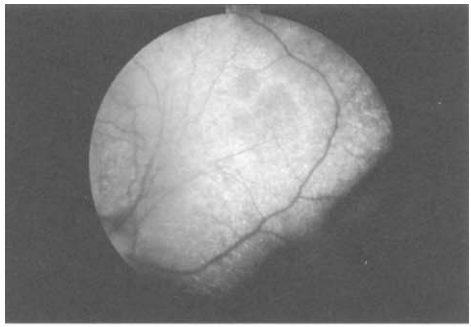


Figure 10. Moderately attenuated peripheral vasculature and thinning of the peripheral retina (note change in reflectivity).

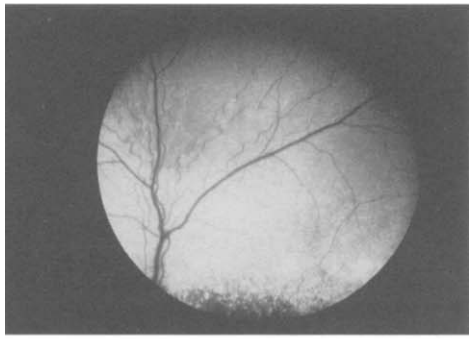


Figure 11. Early PRA in an English cocker spaniel. Changes in reflectivity and tapetal color aid the suspicion of PRA diagnosis.

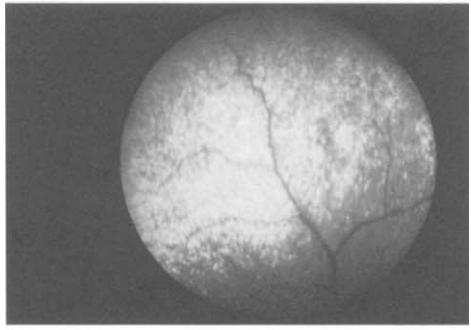


Figure 12. Early PRA showing vascular attenuation.

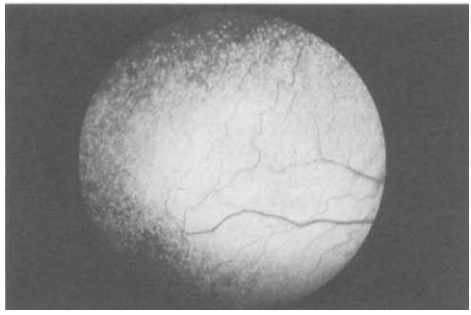


Figure 13. Early PRA fundus changes in the lateral tapetal fundus. Note the vascular changes.

6. How can the diagnosis of PRA be confirmed?

The electroretinogram (ERG) and the DNA blood test are both diagnostic (see Chapters 1 and 41).

7. What if the owner doesn't give consent for those tests?

A simple visual ability test can be performed through a maze in different lighting. Keep in mind that most dogs can see normally far better than we can in the darkness. Schedule future ophthalmoscopic examinations, which may show the progressive character of the degeneration as well as the visual impairment.

8. What should the owners of PRA dogs be advised concerning breeding?

Becauase most PRA is passed as an autosomal recessive trait, definitely advise against breeding.

9. If PRA is in the early-to-midstage of development, should the dog be dietarily supplemented?

Studies have been done in both humans and animals with vitamin A, E, and long-chain fatty acids to bolster the diet with these supplements since it is known that these are vital to the health of the retina. Unfortunately, the course of the degeneration is not altered, and blindness is not curtained. In fact, vitamin A supplements seem to hasten the degeneration (i.e., supplements are not recommended).

10. What other ocular abnormalities occur in PRA?

The pupillary reflex becomes more sluggish as PRA progresses. In advanced PRA, the resting pupil is often wider than in normal-aged matched dogs. In some dogs, the major complaint from the owner may be "large pupils" and "clumsiness." Cataracts are frequently secondary to PRA in some breeds.

11. Why do cataracts develop in some PRA breeds?

The exact etiology has not been proven, but several theories make sense. The preferred theory is that the lens environment is no longer conducive to lens health. The degenerating retina contaminates the fluids of the eye, affecting the lens fibers. The analogy is similar to fish in a pond; polluted water eventually destroys the fish (Fig. 14).

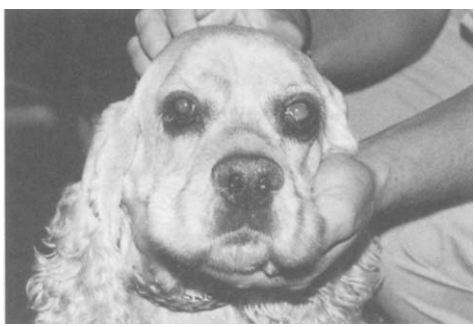


Figure 14. Cataracts secondary to PRA in an American cocker spaniel.

12. Are central progressive retinal atrophy (CPRA) cases different than PRA?

Yes, the degenerated retinas look different. The CPRA retinas have multifocal discolorations throughout the tapetum with hyperreflective areas in between. The vasculature attenuates similar to PRA, and the optic disc undergoes changes similar to PRA in the advanced stages. Histopathologically, the lesions differ predominantly by the accumulation of lipopigment material within the retinal pigment epithelium; hence, the preferred term is now **retinal pigment epithelial dystrophy** (RPED). The lipopigment is responsible for the multifocal discoloration (Figs. 15 and 16).

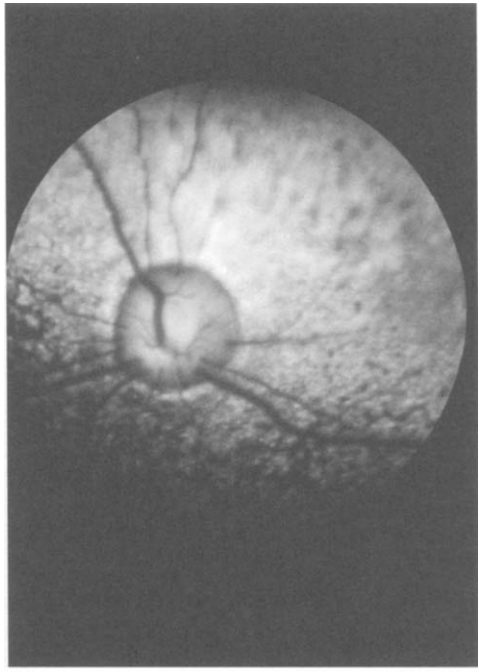


Figure 15. Central fundus of RPED. Note the multifocal dark areas in the tapetum.

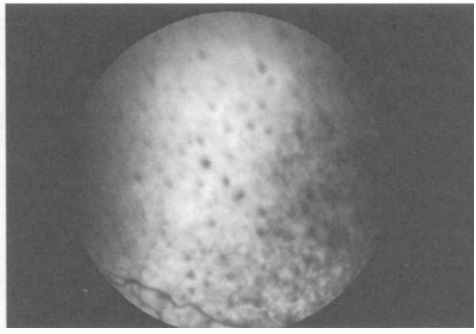


Figure 16. Peripheral tapetal fundus of RPED. Note the vascular absence and the multifocal accumulations throughout.

13. Are there dissimilarities within PRA?

Yes, PRA seems to fall into 2 broad categories: **developmental** or abiotrophy and **degenerative** diseases of the photoreceptors. Within these categories, more unique differences have and will be discovered at the cellular and molecular levels, ultimately identifying each with gene symbols.

14. How can I keep these categories straight in my mind?

The degenerative categories are those retinas that were normal at some earlier point in time and progressed to photoreceptor cell death. The abiotrophy or developmental categories encompass retinas that are structurally or biochemically abnormal before the retinas become mature. Eventually both categories end up in blindness, but the developmental category is usually much sooner.

15. Is there any other way to think about these categories?

Yes, the developmental category has also been given the description of **photoreceptor dysplasias,** because the condition becomes clinically obvious before the first 1–1 1/2 years of life.

Photoreceptor Dysplasias

PRIMARY DYSPLASTIC CELL	BREED	OPHTHALMOSCOPY DIAGNOSIS	INHERITANCE	PHYSIOLOGIC AND HISTOPATHOLOGIC ABNORMALITY
Cone	Alaskan malamute	Small	Autosomal recessive	6weeks: ERG—cone-, rod N
Rod and cone	Belgian shepherd	11 weeks	Unknown	4weeks: ERG—rods and cones
Rod and cone	Collie	16 weeks	Autosomal recessive	6weeks: ERG—cone ↓, rod -
Rod and cone	Irish setter	16 weeks	Autosomal recessive	6weeks: ERG—cone ↓, rod -
Rod and cone	Miniature schnauzer	1.5–5 years	Autosomal recessive	6weeks: ERG—cone ↓, rods ↓
Rod and cone	Norwegian elkhound	1.0–1.5 years	Autosomal recessive	6weeks: ERG—cone N/↓, rod-

16. What are some examples of PRA photoreceptor degeneration?

PRIMARY DYSPLASTIC CELL	BREED	OPHTHALMOSCOPY DIAGNOSIS	INHERITANCE	PHYSIOLOGIC AND HISTOPATHOLOGIC ABNORMALITY
Unpublished	Akita	1–3 years	Autosomal recessive	1.5–2.0 years: ERG—cone ↓, rod ↓↓
Rods then cones	American cocker spaniel	2.5–3 years	Autosomal recessive	9 months: ERG—cone ↓, rods ↓↓
Rods then cones	English cocker spaniel	3–8 years	Autosomal recessive	2–3 years: ERG—cone ↓, rod ↓↓
Rods then cones	Labrador retriever	3–6 years	Autosomal recessive	1.5 years: ERG—cone ↓, rod ↓↓
Rods then cones	Miniature long-haired dachshund	6 months	Autosomal recessive	4 months: ERG—cone ↓, rod ↓↓
Early rods then cones	Norwegian elkhound	9–12 months	Autosomal recessive	5 weeks: ERG—A wave dominate, cone ↓, rod ↓
Unpublished	Papillon	1.5–5 years	Autosomal recessive	9 months-1.5 years: ERG—cone ↓, rod ↓↓
Rods then cones	Portuguese water dog	3–6 years	Autosomal recessive	1.5 years: ERG—cone ↓, rod ↓↓
Unpublished	Siberian husky	2 years	X-linked	1 year: ERG—cone ↓, rod ↓↓
Unpublished	Tibetan spaniel	3–5 years	X-linked	1.5 years: ERG—cone ↓, rod ↓↓
Unpublished	Tibetan terrier	1–1.5 years	X-linked	10 months: ERG—cone ↓, rod ↓↓
Rods then cones	Toy and miniature poodles	3–5 years	X-linked	9 months: ERG—cone ↓, rod ↓↓

17. What does prcd stand for?

Progressive **r**od-**c**one **d**egeneration indicates a PRA that affects the rods primarily and then the cones. It is always bilateral histopathologically. It may vary slightly electrophysiologically and ophthalmoscopically in the early and moderate stages.

18. List the purebred dogs that have been diagnosed with retinal degeneration.

Akita
Alaskan malamute
Australian cattle dog
Irish setter
Italian greyhound
Labrador retriever

Australian shepherd
Basenji
Beagle
Belgian sheepdog
Border collie
Borzoi
Briard
Cardigan Welsh corgi
Chesapeake Bay retrieve
Cocker spaniel (American and English)
Collie
Dachshund
English springer spaniel
German shepherd
German shorthaired pointer
Golden retriever
Gordon setter
Great Dane
Greyhound
Lowchen
Mastiff
Miniature schnauzer
Norwegian elkhound
Nova Scotia ducktolling retriever
Old English sheepdog
Papillon
Pekingese
Poodles
Portuguese water dog
Rottweiler
Samoyed
Shetland sheepdog
Shih tzu
Siberian husky
Tibetan spaniel
Tibetan terrier
Welsh springer spaniel
Yorkshire terrier

19. Does retinal degeneration develop in the cat?

Yes, with a similar classification as found in dogs. Known classifications are abiotrophies, degenerations or atrophies, infections, metabolic, nutritional, and toxic (Figs. 17 and 18).

20. What is known about the retinal abiotrophies in cats?

The most significant reports are in Persian cats that have a photoreceptor dysplasia that is autosomal recessive. Abyssinian cats have been reported to have a rod-cone dysplasia that is auto-

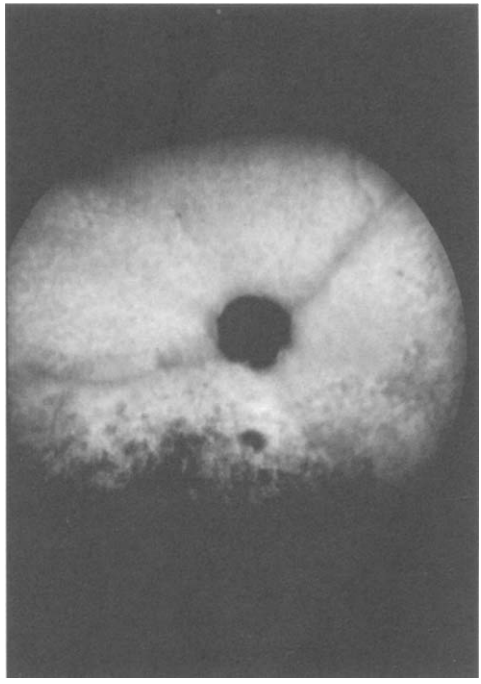


Figure 17. Cat retinal degeneration. Note the vascular attenuation. The hyperreflective character was so intense that a green filter was used to prevent overexposure.

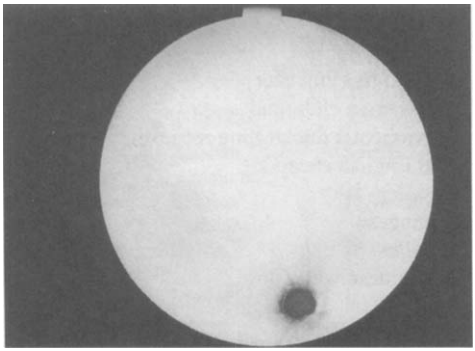


Figure 18. Cat with retinal and optic disc degeneration. Generalized hyperreflective tapetum and a darker than normal optic disc. The retinal vessels are just about absent.

somal dominant. Mixed breed domestic shorthair cats with a rod-cone dysplasia with possible autosomal dominance are also reported. These retinal lesions are diagnostic ophthalmoscopically at an early age.

21. What is known about retinal atrophy as an inherited disease?

The Abyssinian cats have an autosomal recessive rod-cone degeneration that is progressive. Mixed breed domestic shorthair cats with gyrate atrophy have been diagnosed to have an ornithine aminotransferase deficiency that is inherited as autosomal recessive.

22. What are the infectious causes of retinal lesions in cats?

Kittens infected with panleukopenia virus 7 days before birth through 7 days postbirth are known to develop retinal dysplasia or cerebellar hypoplasia. Those kittens are neurologically ataxic and hypermetric. They are usually presented for these signs between the ages of 3 and 4 weeks of age. Funduscopic lesions are not always present but are pathognomonic when found (Fig. 19).

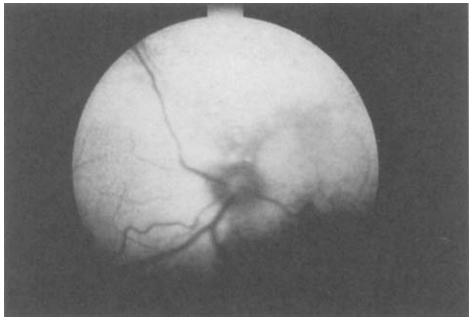


Figure 19. Young kitten with retinal degenerative areas throughout secondary to panleukopenia virus infection.

23. What are the nutritional causes of retinal atrophy in cats?

Any cat breed is likely to develop a degenerative retinopathy if its diet is deficient in taurine. The early stages are classical as the degeneration is zonal within the area centralis progressing horizontally from the central retina toward the periphery. Advanced degenerations look like any other end-stage retinal atrophy. These lesions are known as feline central retinal degeneration (FCRD). Since taurine was discovered as a required amino acid in cat diets, the pet food industry has dramatically reduced the incidence of this retinopathy by taurine supplementation (Fig. 20).

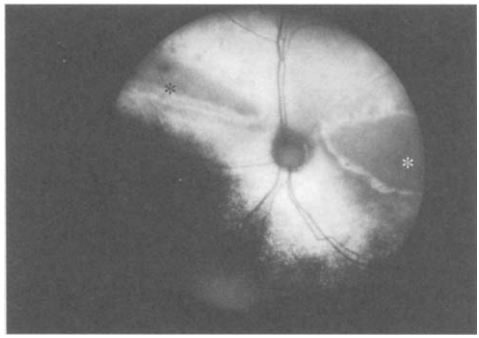


Figure 20. Feline central retinal degeneration secondary to nutritional causes (i.e., taurine deficiency). The well-demarcated zones of hyperreflectivity on either side of the optic disc are areas of degeneration (*). At this stage, the cat is still visual.

24. What are some of the causes of retinal toxic degenerations?

Liver disease and gallbladder stones have an ocular manifestation of retinal degeneration. Recently, Baytril, given at the recommended systemic dose, has been reported to cause retinal degeneration in cats (Fig. 21).

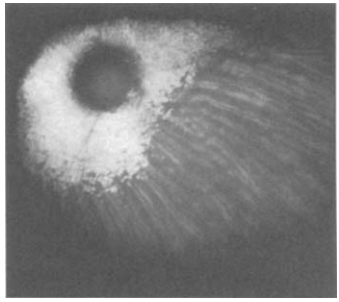


Figure 21. Retinal degeneration thought to be secondary to enrofloxacin (Baytril) administration. (To prevent retinal complications, do not exceed 5 mg/kg/day.)

25. Are there blood tests available for cat retinal degeneration?

No. DNA-based tests are not currently available to identify cats that are affected, are carriers, or are genetically normal for PRA or other inherited retinal diseases.

BIBLIOGRAPHY

1. Acland GM, Aguirre G, Chader GJ, et al. Canine early-onset hereditary retinal degeneration: genetic and biochemical distinction of 3 diseases (abstract). Invest Ophthalmol Vis Sci 119:250, 1980.
2. Acland GM, Blanton SH, Hershfield B, et al: XL-PRA: A canine retinal degeneration inherited as an X-linked trait. Am J Med Genet 52:27–33, 1994.
3. Aguirre GD: Inherited retinal degenerations in the dog. Trans Am Acad Ophthalmol Otolaryngol 81:667–676, 1976.
4. Aguirre GD: Retinal degenerations in the dog. I. Rod dysplasia. Exp Eye Res 26:233–253, 1978.
5. Curtis R, Barnett KC: Progressive retinal atrophy in miniature longhaired dachshund dogs. Br Vet J 149:71–85, 1993.
6. Gelatt KN, Van der Woerdt A, Ketring KL, et al: Enrofloxacin-associated retinal degeneration in cats. Vet Ophthalmol 4:99–106, 2001.
7. Håkansson N, Narfström K: Progressive retinal atrophy in papillon dogs in Sweden. A clinical survey. Vet Comp Ophthalmol 5:83–87, 1995.
8. Narfström K, Ehinger B, Brunn A: Immunohistochemical studies of core photoreceptors and cells of the inner retina in feline rod-cone degeneration. Vet Ophthalmol 4:141–145, 2001.
9. Parshall C, Wyman M, Nitray S, et al: Photoreceptor dysplasia: An inherited progressive retinal atrophy in miniature schnauzer dogs. Prog Vet Comp Ophthalmol 1:187–203, 1991.
10. Ray K, Baldwin V, Acland G, et al: Molecular diagnostic tests for ascertainment of genotype at the rod-cone dysplasia 1 (rcd1) locus in Irish setters. Curr Eye Res 14:243–247, 1995.
11. Sandberg MA, Pawlyk BS, Berson EL: Full-field electroretinograms in miniature poodles with progressive rod-cone degeneration. Invest Ophthalmol Sci. 27:1179–1184, 1986.

40. RETINAL DYSPLASIA

Ronald C. Riis, D.V.M., M.S.

1. What is the definition of retinal dysplasia (RD)?

RD is an abnormal development of the retina.

2. What causes the abnormal development?

RD lesions in puppies have been caused by adenovirus and herpesvirus infections and in kittens by panleukopenia virus. Some RD lesions are associated with genetic traits such as a simple recessive in Bedlington terriers, golden retrievers, and Labrador retrievers and as recessive in American cocker spaniels, beagles, collies, corgis, English springer spaniels, and Sealyham terriers.

In addition to RD, other ocular lesions have been diagnosed, such as cataracts, colobomas, persistent pupillary membranes, retinal detachments, hemorrhage, and microphthalmia.

The most noted breeds with RD and other anomalies include (* = most common):

Akita*	American cocker spaniel*	Australian shepherd*
Beagle	Basset griffon Veudeen (petite)	Bedlington terrier
Belgian Malinois	Border collie	Bull mastiff
Collie*	Cavalier King Charles spaniel	Chow chow
Clumber spaniel	Doberman pinscher	English springer spaniel*
Field spaniel	German shepherd	Golden retriever
Gordon setter	Labrador retriever*	Mastiff
Norwegian elkhound	Old English sheepdog	Pembroke Welsh corgi
Rottweiler	Samoyed*	Sealyham terrier
Yorkshire terrier		

3. Has RD been referred to by other names?

RD was once called "vermiform streaks" because ophthalmoscopically the lesions looked like worms imbedded in the retina. Because the pathology of RD may take on the appearance of retinal rosettes or uplifting folds away from the retinal pigment epithelium, "retinal folds" became a popular term, especially if the dysplasia was linear, with and without branching.

4. Are there degrees of RD?

Yes, the linear dysplastic lesions (folds) are usually the least serious. When the linear lesions become numerous and fuse together, a larger area of retina is scarred. These areas take on various shapes with some appearing like states or countries on a map, thus the name "geographic RD" (Figs. 1–8).

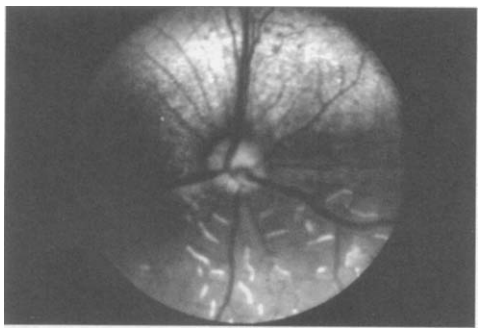


Figure 1. Yellow Labrador puppy with multiple linear retinal folds in the nontapetum and focal scars in the developing tapetum.

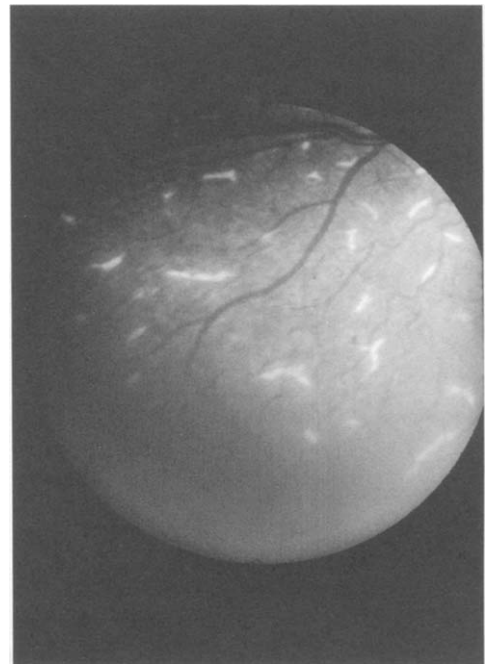


Figure 2. Young American cocker spaniel with retinal folds.

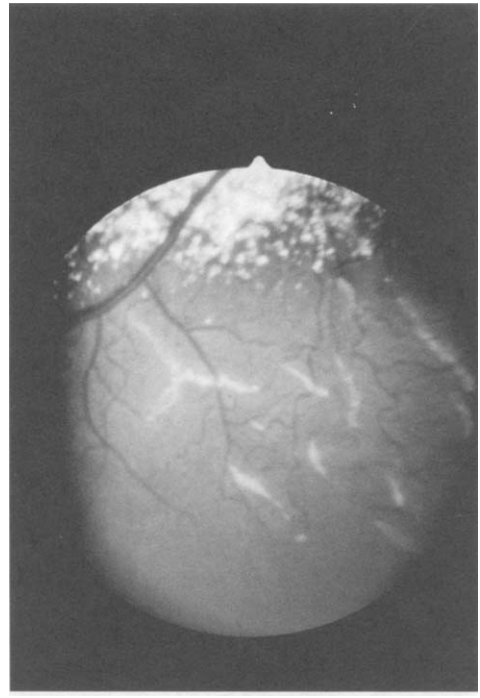


Figure 3. Nontapetal retinal folds. Note venules crossing retinal folds.

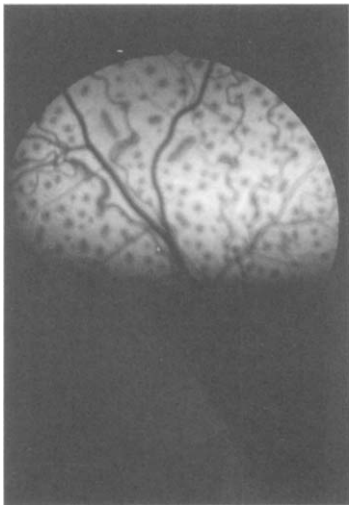


Figure 4. Six-month-old beagle with many nontapetal retinal folds that are fading with pigment from the retinal pigment epithelium.

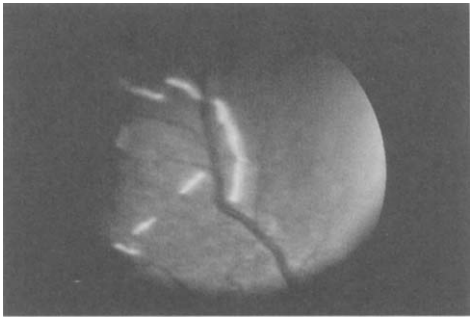


Figure 5. A 6-week-old Australian shepherd puppy with elongated retinal folds.

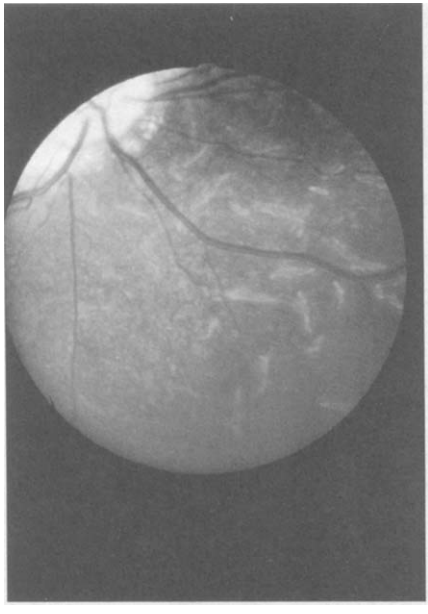


Figure 6. A 4-month-old Akita puppy with focal and linear retinal dysplasia.

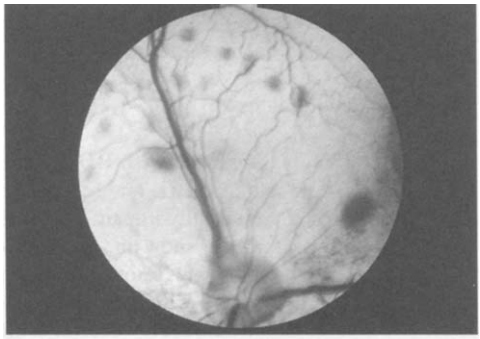


Figure 7. A 6-month-old bull mastiff puppy with multifocal retinal dysplasia.

Figure 8. An adult springer spaniel with multiple tapetal scars dorsal to the disc. Pigmentation has proliferated among the hyperreflective areas.

5. Can RD lesions heal

Yes and no. The first answer is yes because the retina will compensate in various ways. The small linear lesions (folds) take on a gray or hyperreflective appearance within the tapetal fundus, whereas the same type of RD lesion may pigment with melanocytes in the nontapetal fundus. These areas never heal to become functional, but do scar to form pathologic thin areas of the retina. Very large geographic RD lesions may also scar, but the larger lesions might be complicated with detachment.

Some of the infectious RD lesions take on punctuate or circular appearances in both the cat and dog. They may become ophthalmoscopically healed or less numerous over the years. Even though the RD may have been severe and only a few scars remain, the owner may comment about some visual impairment.

6. When should the retinas be examined for RD?

Most conscientious breeders present their puppies for evaluation before they are placed in homes. Between 6 and 9 weeks of age which is a good time to rule out RD in the "fold" category.

However, examination at this age does not guarantee the puppies will be free of all types of RD. Puppies that are free of linear fold RD at 6–9 weeks have later been found to have geographic RD. Therefore, it is recommended to have examinations performed between the ages of 6 and 9 weeks and again at 6–9 months.

7. If an animal is diagnosed with RD, should it be bred?

It depends on the type of RD and breed. The minor linear fold RD lesions are thought to be nonprogressive and not visually impairing. Usually, these lesions are left to the breeder's discretion when rating animals for show and breeding quality.

The larger geographic RD lesions are serious enough that animals with them should not be bred. RD is often associated with infectious or anomalous development and not genetic causes, so these animals could be bred. However, it is difficult to judge etiology in older, scarred retinas, so caution should be taken (Figs. 9–14).

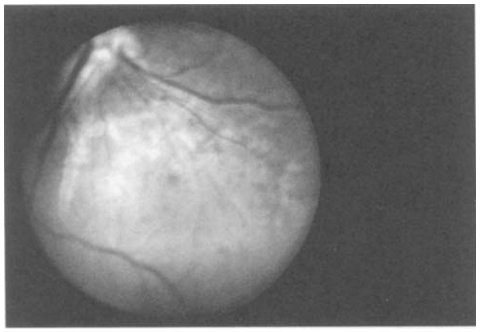


Figure 9. An adult springer spaniel with nontapetal retinal dysplasia and focal detachment.

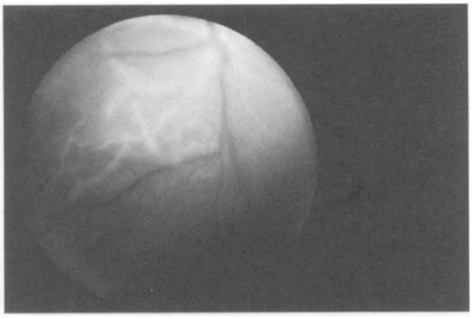


Figure 10. A springer spaniel puppy with retinal detachment and generalized retinal folds over the entire fundus.

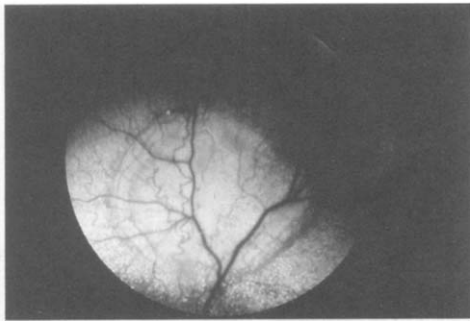


Figure 11. Retinal dysplasia adjacent to the optic disc with associated retinal detachment.

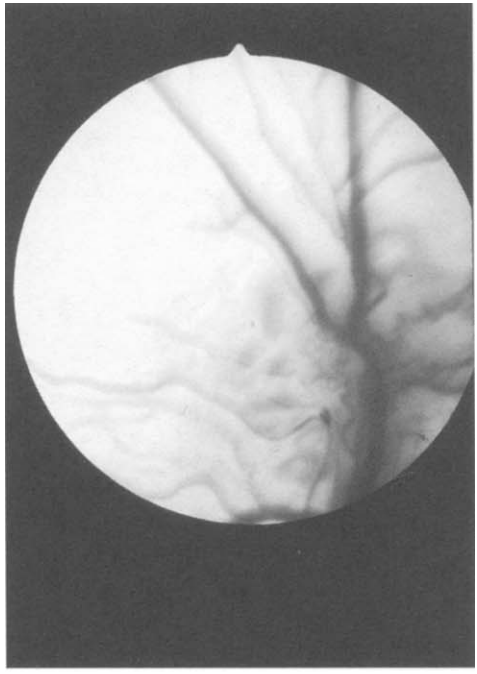


Figure 12. An adult beagle with multifocal coalescent retinal folds causing retinal detachment dorsal to the optic disc.

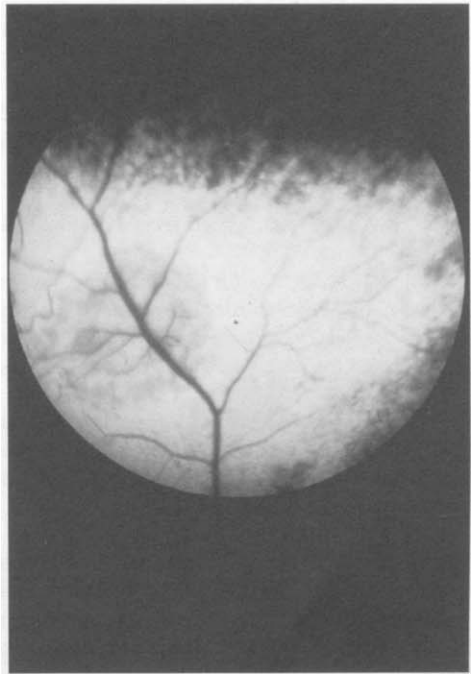


Figure 13. A geographic retinal dysplastic lesion in an American cocker spaniel.

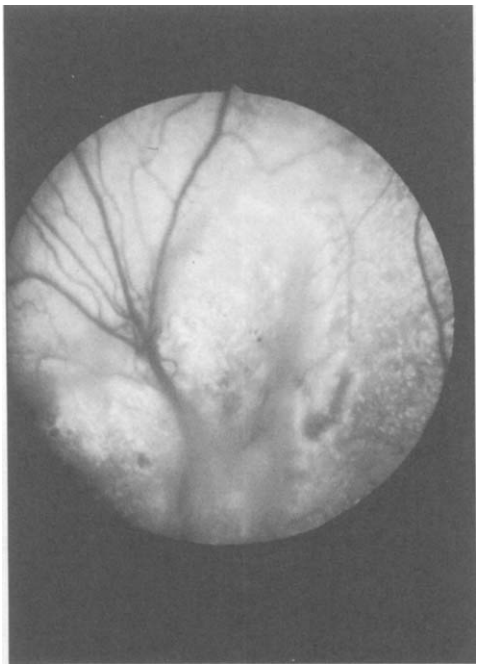


Figure 14. A very large geographic retinal dysplastic lesion.

8. What is the most severe RD presentation?

Blind puppies with retinal detachment secondary to the dysplasia. These puppies usually have a rotary nystagmus. The leukocoria present is the retina dislocated just behind the lens. Some of these puppies also have microphthalmia or intraocular hemorrhage. Ironically, the severe presentation does not always happen bilaterally.

9. What is the least severe RD presentation?

Those eyes that are entirely normal with the exception of a few small linear or dot retinal scars.

10. If the minor RD lesions were reevaluated at an older age, couldn't they be potentially normal?

The RD areas may fill in with pigment, especially if they were noted only in the nontapetal fundus. Evaluation records have documented that animals do go from phenotypic affected to phenotypic normal. However, the earlier evaluation determines whether the animal is geneotypically affected, and the inherited traits will be passed on.

11. Is it difficult to examine eyes for RD lesions?

The early examination (6–9 weeks of age) is the most difficult. This age normally requires good restraint, maximally dilated pupils, expertise with ophthalmoscopic techniques, and persistence for a good view of the fundus periphery.

12. Should all puppies be referred to a diplomate of the American College of Veterinary Ophthalmologists (DACVO) for the early evaluation?

Not necessarily. If a veterinarian feels comfortable evaluating the puppies, referral may not be required unless a lesion is questionable or a second opinion is recommended. If the breeder or owner desires certification by the Canine Eye Registration Foundation (CERF), it is necessary to refer to a DACVO member because CERF only accepts their evaluations.

13. Is there a DNA test for RD?

Not yet.

14. Has RD been classified any other way?

RD has been classified histopathologically by the rosette architecture. **Three layer rosettes** indicate a mature retina that has detached and in which folds have developed. **Two layer rosettes** and **one layer rosettes** arise from either the outer or inner retinal layers. These are examples of true dysgenesis (Figs. 15 and 16).

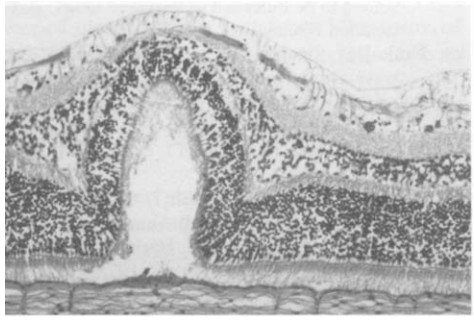


Figure 15. Histopathology of a retinal fold (formalin fixed). Note photoreceptor and outer nuclear layer fold. 10×.

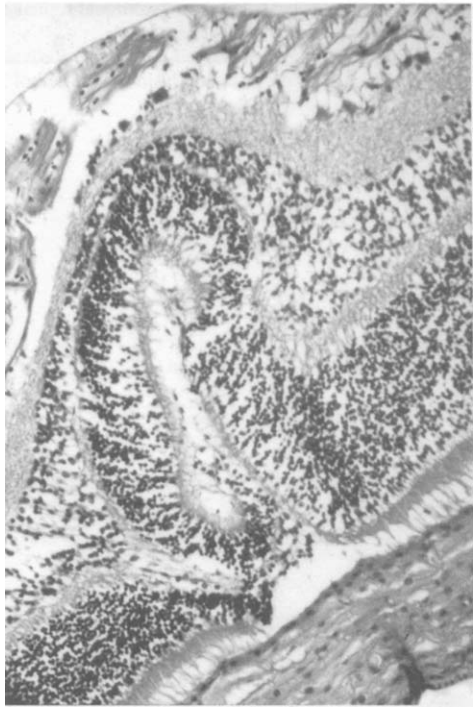


Figure 16. Histopathology of a large retinal fold (formalin fixed). Note rosette of outer nuclear layer. 40×.

CONTROVERSY

15. Should animals with RD fold scars be bred?

For: Many breed organizations have taken a stand on this question. Because RD fold scars are a minor flaw and all other characteristics about the animal may be highly desirable, it is irrational to cull the animal for this trait alone.

Against: Top dogs are especially popular for breeding, and some have had RD. The incidence of RD in several breeds has increased dramatically over the last 25 years. This high incidence would not be a factor today if having RD had been discriminated against when breeding.

BIBLIOGRAPHY

1. Carrig CB, Spouenberg DP, Schmidt GM, et al: Inheritance of associated ocular and skeletal dysplasia in Labrador retrievers. J Am Vet Med Assoc 293:1269, 1988.
2. Genetics Committee of the American College of Veterinary Ophthalmologists: Ocular Disorders Presumed to be Inherited in Purebred Dogs, 2nd ed. West Indianapolis, IN, ACVO and Canine Eye Registration Foundation, 1996.
3. Holle DM, Stankovics ME, Sarna CS, et al: The geographic form of retinal dysplasia in dogs is not always a congenital abnormality. Vet Ophthalmol 2:61, 1999.
4. Lahav M, Albert DM, Wyand S: Clinical and histopathological classification of retinal dysplasia. Am J Ophthalmol 75:648, 1973.
5. Laratta LJ, Riis RC, Kern TJ, et al: Multiple congenital ocular defects in the Akita dog. Cornell Vet 75:381, 1985.
6. Lewis DG, Kelly DF, Sansom J: Congenital microphthalmia and other developmental ocular anomalies in the Doberman. J Small Anim Pract 27:559, 1986.
7. MacMillan AD, Lipton DE: Heritability of multifocal retinal dysplasia in American cocker spaniels. J Am Vet Med Assoc 172:568, 1978.
8. Meyers VN, Jezyk GD, Aquirre G, et al: Short-limbed dwarfism and ocular defects in the Samoyed dog. J Am Vet Med Assoc 183:975, 1983.
9. Nelson DL, MacMillan AD: Multifocal retinal dysplasia in field trial Labrador retrievers. J Am Anim Hosp Assoc 19:388, 1983.
10. Toole DO, Young S, Severin GA, et al: Retinal dysplasia of English springer spaniel dogs: Light microscopy of the postnatal lesions. Vet Pathol 20:298, 1983.

41. GENETIC TESTING FOR PROGRESSIVE RETINAL ATROPHY

Jeanette S. Felix, Ph.D.

1. Are there molecular genetic tests for inherited forms of progressive retinal atrophy (PRA)?

The number of DNA-based tests for canine PRA is growing. Because various forms of PRA are caused by various genetic defects, tests are developed specifically for each form. Most forms of canine PRA are inherited as autosomal recessive conditions, although at least two breeds have an X-linked form. One autosomal dominant form of PRA is known. Several of the mutant genes responsible for PRA are detectable by DNA-based direct mutation tests or by marker/linkage tests. Research on PRA is ongoing, so up-to-date information should be sought whenever you have a need.

2. Which forms of canine PRA can be detected and in which breeds?

At the time of this writing, seven genetic tests are available for retinal degenerative diseases, involving a total of thirteen breeds. Congenital stationary night blindness (CSNB) is included in this list because it is a nonprogressive retinal disease that can be confused with PRA. Because a breed can exhibit more than one type of PRA (inherited or acquired), one needs to be specific about the test used and its results. A dog that is normal by one test could be at risk for another form of PRA.

DISEASE	BREED	GENE	GENETIC TEST
Congenital stationary night blindness (CSNB)	Briard	RPE65	Mutation
Dominant PRA	Mastiff	Unnamed	Mutation
Type A PRA	Miniature schnauzer	Unnamed	Mutation
Progressive rod cone degeneration (prcd)	Chesapeake Bay retriever English cocker spaniel Labrador retriever Poodle Portuguese water dog	Unknown	Marker
Rod cone dysplasia 1 (rcd1)	Irish setter Sloughi	PDE6B	Mutation
Rod cone dysplasia 3 (rcd3)	Cardigan Welsh corgi	PDE6A	Mutation
X-linked PRA	Siberian husky Samoyed	Unnamed	Mutation

3. Are there genetic tests for canine retinal dystrophies or retinal dysplasias?

Not so far, but if a disease is inherited in simple Mendelian fashion, it is just a matter of work and time (and funding for the research) before a test is developed (see Chapter 39).

4. Why is a genetic test done and when?

Reliable identification of "clear" dogs (those not carrying the mutant disease gene) is key to preventing the disease. Through DNA-based genetic tests, this can be achieved with a high degree of reliability not possible with pedigree analysis or clinical examination. Genetically clear (homozygous normal) dogs can be bred to another dog of any genetic status (clear, carrier, or affected) and not produce the disease. Offspring can be tested to identify carriers, and repeated selection for clear animals eventually will decrease the frequency of the mutant gene in the breed.

Genetic testing should be done before the owner uses the dog for breeding and whenever the information is beneficial for diagnosis and decision-making. Testing can be done at any age, as soon as a small blood sample or other useful tissue sample can be obtained.

5. Is a genetic test useful if information from a clinical examination is already available?

A genetic test reveals the dog's genotype for the disease in question, thereby confirming its normal status or revealing the affected status. In many cases, a genetic test provides information not available otherwise. A normal clinical examination cannot always rule out PRA even after the "typical age" of onset for the disease in a specific breed. A normal genetic test result definitely rules out that form of PRA. If the dog appears suspicious for PRA on clinical examination, the dog's genetic status can confirm or negate the tentative diagnosis. Also, a genetic test is useful to confirm a clinical diagnosis of PRA, because many times PRA is incorrectly diagnosed.

6. Is a clinical examination useful if information from a genetic test is already available?

Examination by a certified veterinary ophthalmologist is always useful and is generally recommended for dogs of all ages on an annual basis to look for a variety of inherited and acquired eye conditions in addition to those for which genetic tests are available. In the United States, Canine Eye Registration Foundation (CERF) examinations by a diplomate of the American College of Veterinary Ophthalmologists (ACVO) and, in Europe, examinations by a diplomate of the European College of Veterinary Ophthalmology (ECVO) lead to eye examination certificates used for registration purposes. If a dog is genetically normal or a carrier for a specific form of PRA, an electroretinogram (ERG) will give no additional information about inherited PRA status. However, when there is a possibility of a false-positive result (see question 13), and the dog in question is well beyond the typical age of onset, an ERG can be useful.

7. How many dogs in the pedigree must be tested in order to get a diagnostic result?

Most commercial marker and mutation tests make a diagnosis on an individual dog, without information on other members of the pedigree. Research on a new test could depend on tracing markers and the disease gene through a pedigree. In that case, a linkage test is done on a set of samples including at least the test dog, its dam and sire, and one affected and one unaffected dog from the same parentage.

8. What is the difference between a mutation test and a marker/linkage test?

A mutation test identifies the specific DNA abnormality responsible for the disease. The abnormality might involve an altered DNA sequence, a substitution in the sequence, or a deletion or addition of DNA. A mutation test is possible once the precise DNA defect for a specific disease is known for the breed being tested. For example, the precise mutation in the RPE65 gene that causes CSNB in briards is known and forms the basis of its test. Because different breeds can have different mutations that cause the same clinical disease, the specific cause must be discovered for each breed.

In contrast, when a disease gene and its mutations are not known, it is sometimes possible to develop a genetic test using DNA sequence markers closely linked to the gene. Genetic linkage can be established without knowing the specific gene or mutation causing the disease. Instead, DNA sequences that are always inherited with the disease gene (i.e., linked) are defined. By tracing such markers in a pedigree, conclusions are made about inheritance of the mutant disease gene. Because recombination between these markers and the disease gene can occur, the probability of such recombination must be factored into the value and interpretation of the test. The good news is that some markers are so close to the gene that no recombination between the markers and gene can be detected. Tests using such tightly linked markers allow greater accuracy than tests with markers located farther from the gene. The *prcd*-PRA marker test uses markers that never recombine with the *prcd* gene (see question 13).

9. Is the frequency of PRA disease and the frequency of the mutant gene known for each breed?

Very few thorough studies have been done to establish the frequency of PRA or the frequency of the causal mutation in dog populations, particularly within specific breeds. To do so with some reliability, a direct mutation test applied to a large cross-sectional sampling of the breed is needed.

The best study to date was reported for rcd1-PRA in Irish setters, showing a carrier rate of 7–10% for the *rcd1*-PRA mutant gene in the United States. As more testing is done and the results shared through breed club registries, more information on mutation frequency will accumulate.

10. Are new mutations frequent and do they impact test accuracy?

The probability of a new mutation is much less than 1 chance in several million meioses. Thus, new mutations at any single gene are extremely infrequent, and there is no practical impact on genetic test accuracy. The mutations causing the various forms of PRA are very old, most predating modern dog breeds.

11. Does a normal test result certify that there is no risk for PRA in the tested dog?

It is important to remember that the test result applies *only* to the specific disease gene being tested. Because there are multiple forms of PRA, sometimes more than one form in one breed, the test result must be interpreted only for the gene being tested. For example, a dog determined to be clear by DNA test for the *prcd*-PRA mutation could still be at risk for a different form of PRA known to affect that breed. The genetic tests currently available are for the predominant causes of PRA in the test breeds.

Of course, vision loss can be due to conditions other than PRA. Although PRA is by far the predominant cause of retinal degeneration in those breeds currently being tested, there could be other uncommon types of PRA, or vision could be affected by retinal dysplasias, cataracts, inflammatory conditions, infections, or trauma. Genetic testing allows diagnosis and control of a specific cause of blindness, but not for all possible causes of vision loss.

12. What tissue is sampled for a genetic test and how is the test actually done?

A small (1–3 ml) unclotted blood sample, obtained by a veterinarian or veterinarian technician, is the most reliable source of DNA for testing because the dog's identity can be verified at the time of drawing and contamination from other dogs can be avoided. Although it is easier to take cheek scrapings, these can be contaminated by variables such as contact with other animals and food. DNA can be prepared from other fresh or frozen tissues, such as, semen or liver, but testing of these tissues is not done routinely in a service lab.

DNA is extracted and processed to amplify the targeted gene through the use of specific DNA primers and polymerase chain reaction (PCR) technology. This amplified DNA is run on an electrophoretic gel under conditions that will separate and distinguish the mutant gene (or markers) from the normal. The DNA patterns on the gel are revealed by use of stains and ultraviolet illumination. If the precise sequence of the gene is known, automated sequencing technology can be used to analyze the amplified DNA.

13. How are the results reported to the owner?

For mutation-based tests, results are reported as:

- **Normal**—clear, homozygous for the normal gene; no mutant gene is present
- **Carrier**—carrier of the disease with one normal and one mutant gene copy
- **Affected**—homozygous for the mutant gene; no normal gene is present

With linkage tests, the above results would be qualified further to indicate the probability of a recombination between the linked marker and the disease gene in the tested dog. A recombination event could yield a false-negative or false-positive result. A good linkage test will have a very low probability of recombination.

With marker-based tests, such as the original test for *prcd*-PRA, the markers are so close to the disease gene that no recombination between them and the gene has ever been observed. This test gives a definitive result for **normal/clear** prcd status of a dog. However, **carrier** status (designated pattern B—probably a carrier) and **affected** status (designated pattern C—probably affected) are qualified because of possible presence of a false-positive allele. This complexity will be resolved either with an improved marker test or with a direct mutation-based test.

In each case, the laboratory performing the test should provide sufficient information and explanation to interpret the results.

14. How are the results used?

Reliable identification of clear dogs that do not carry a mutant disease gene is the key to eliminating diseases. Specific breeding recommendations depend on whether the disease gene is autosomal recessive or X-linked. The breeder can use test information to avoid producing affected pups and to control the frequency and occurrence of the mutant gene in their line.

15. Outline the expected results for various breeding strategies with PRA.

Expected Results of Breeding Strategies Using DNA-Based Tests for Autosomal Recessive PRA

	PARENT 2		
PARENT 1	NORMAL	CARRIER	AFFECTED
Normal	All = Normal	1/2 = Normal 1/2 = Carrier	All = Carrier
Carrier	1/2 = Normal 1/2 = Carrier	1/4 = Normal 1/2 = Carrier 1/4 = Affected	1/2 = Carrier 1/2 = Affected
Affected	All = Carrier	1/2 = Carrier 1/2 = Affected	All = Affected

Expected Results of Breeding Strategies Using DNA-Based Tests for Recessive X-Linked PRA

DAM (XX)	SIRE (XY)—NORMAL	SIRE (XY)—AFFECTED
Normal	All = normal	All females = carrier All males = normal
Carrier	1/2 females = normal 1/2 females = carrier 1/2 males = normal 1/2 males = affected	1/2 females = carrier 1/2 females = affected 1/2 males = normal 1/2 males = affected
Affected	All females = carrier All males = affected	All = affected

16. What breeding strategies are recommended based on DNA test results?

This is straightforward for autosomal recessive diseases: the breeder should always select one parent that has tested clear for the disease in question. The other parent can be untested, carrier, or affected, because the offspring can be tested before planning the next generation.

For X-linked diseases, breeding is more restricted. The breeder should select only normal females but can select either normal or affected males because no affected offspring will be produced in these matings. For autosomal dominant diseases, the breeder should select only normal male *and* female dogs, because all dogs with either one or two mutant genes will be affected.

17. Is the goal of canine genetic testing to eliminate the recessive disease or to eliminate the recessive mutant gene?

A reasonable short-term goal for breeders is to avoid producing affected dogs by using one parent that tested clear for the recessive mutant disease gene. With this approach, carrier and even affected dogs of excellent quality for other traits can be kept in breeding schemes, and

there is little risk of unduly restricting the gene pool of the line or breed. The longer term goal of reducing the frequency of the recessive mutant disease gene, or eliminating it from the breed altogether, must be pursued over many generations, making choices to retain the preferred qualities of the breed represented. Using this approach for the longer term goal will avoid coincidentally increasing the frequency of a recessive mutation for a different inherited disease and perhaps even a new disease for the breed.

18. What if a champion dog is diagnosed with autosomal recessive PRA by both clinical and genetic test criteria? Should the owner exclude it and its offspring from further breeding?

No, even though this dog is homozygous for a form of PRA and its offspring will be at least carriers, the DNA test allows it to be bred safely to any dog that does not carry the mutant gene. These clear dogs can be bred to any mate—even to an affected or carrier dog—and no affected pups will be produced. By breeding subsequent generations to clear dogs, not only will affected dogs be prevented, but the mutant gene eventually will be eliminated from the line. And, the fine qualities of this champion dog will be retained.

19. What if a valuable and unaffected dog comes from a pedigree with known PRA carriers or affecteds? Should it be pulled from breeding?

Not if more information can be obtained. Careful analysis of the pedigree might give useful information for a breeding plan. Better yet, if the form of PRA in question can be DNA-tested, this dog should be tested. Even if the dog carries an autosomal-recessive form of PRA, it can be bred to a genetically normal dog with no risk of producing affected offspring. If the PRA is X-linked and the dog is a genetically normal female, it can be bred to either a normal or affected male. If it is male, it can be bred to a normal female. Refer to question 15 for breeding strategies.

20. An 18-month-old Labrador retriever presents with severe PRA-like symptoms, but the DNA test has shown at least one parent is genetically normal for *prcd*-PRA. How can this be explained?

Dogs tentatively diagnosed with PRA, especially with an atypical clinical presentation at a very young age, might have a nongenetic form of retinal disease or might have a genetic form that is not detected by the DNA test used. To date, no false-negative result for the *prcd* gene test has been verified. That is, every dog diagnosed clinically with the form of PRA that fits the standard description of *prcd*-PRA for age of onset, progression, and degree of severity also is homozygous for the mutant *prcd* DNA markers. Each dog would have received one mutant set of markers from each parent. Therefore, for an explanation of this affected dog with a genetically normal parent, several issues must be pursued:

1. Is the clinical diagnosis solid? Is this PRA?
2. If it is PRA, is it *prcd*-PRA or another retinal condition?
3. If it fits the criteria for *prcd*-PRA, genetic testing should be repeated and extended to more family members to determine if there was a technical or procedural error or if this case is due to genetic recombination or false-negative result.
4. Has parentage of the dog been verified? The possibility of mistaken parentage should be ruled out.

21. What if a dog tests normal and clear for the *prcd*-PRA mutant gene or for another PRA gene, but the owner reports the dog has PRA?

Because the *prcd*-PRA test result is completely accurate when it detects the normal, clear genotype, this dog definitely does not have the *prcd* form of PRA. The same is true for the other PRA genetic tests. It must have another form of PRA, retinal dysplasia, retinal dystrophy, or another cause for the retinal disease. Consultation with an expert in canine retinal conditions should be obtained.

22. A 6-year-old-dog has normal CERF and ERG examinations, yet the *prcd*-PRA marker test gives a test result of pattern C—high risk to be affected. Why?

This is difficult to resolve using the *prcd*-PRA marker test (available as of this writing) because of detection of a false allele. As discussed in question 13, some dogs can be homozygous for a set of markers that can segregate either with the *prcd* mutation or the normal gene. This status is designated pattern C with the *prcd* test. It is possible this dog actually is a carrier of *prcd* or is clear of the mutation. Unfortunately at this time, the frequency of the *prcd* false allele is not known.

The likelihood that the dog will not be affected with *prcd* increases with the dog's age. If it is beyond the latest known age of onset for the breed, false alleles probably were detected. Also, if the pedigrees of both parents are clear of *prcd*-PRA for several preceding generations, likelihood of the false allele increases. Finally, one must take into account the variable age of onset among different breeds. Most cases of prcd in Chesapeake Bay retrievers, Labrador retrievers, and Portuguese water dogs are diagnosed by 6 years. In contrast, English cocker spaniels have been diagnosed as late as 11 years of age with the early ophthalmoscopic lesions of PRA.

23. Does coat color of the dog affect the use or interpretation of the test result?

Based on current experience, neither coat color itself nor color lines within a breed impact use or interpretation of test results. The *prcd* test applies to all color varieties of the breeds listed above. The same is true for the *rcd1* test in Irish setters (solid reds and red/white have the same PRA disease gene and mutation) as well as the other PRA genetics types.

24. Will more breeds have genetic tests for PRA in the future?

Some form of PRA is recognized in more than 70 breeds, and usually the genetic type of PRA cannot be predicted based on the clinical picture of the condition. Several of these breeds are being studied to determine whether the marker-based test for *prcd*-PRA will detect their form of PRA. Based on genetic and breeding studies, we know that other breeds have non-*prcd* forms of PRA. Development of tests for these diseases waits for discovery of the responsible genes or useful markers. Examples of breeds for which PRA is a major concern include:

BREED	DISEASE
Alaskan malamute	Cone degeneration (cd)
American cocker spaniel	prcd
Australian cattle dog	PRA (specific form under study)
English springer spaniel	PRA (specific form under study)
Italian greyhound	PRA (specific form under study)
Norwegian elkhound	Early retinal degeneration (erd)
Nova Scotia duck tolling retriever	prcd
Papillon	PRA (specific form under study)
Poodle, toy and miniature	prcd
Rough collie	Rod-cone dysplasia 2 (rcd2)
Tibetan terrier	PRA (specific form under study)

25. Is it surprising that there are so many genes causing PRA?

There are many parallels between canine and human inherited diseases, PRA in particular. Human retinal degenerations, akin to canine PRA, also result from mutation in any one of a growing collection of genes whose functions are important to the retina. Given this experience, the multitude of PRA-causing genes is not unexpected, and in fact, more such genes undoubtedly will be discovered.

26. Are the chromosomal locations of the PRA genes of significance or of interest?

The specific chromosomal location of a gene is irrelevant diagnostically unless the disease is linked to the X chromosome, thereby exhibiting an X-linked pattern of inheritance with breeding consequences outlined above in question 15. For research purposes, knowing the general gene lo-

cation is necessary for eventual cloning and sequencing of the gene. The location also gives clues to candidate disease genes based on parallels with the human genome.

27. Have the American Kennel Club (AKC) and individual breed clubs set standards for genetic testing?

Genetic testing, as a powerful tool for canine breeding strategies and health management, is an emerging field. As more experience is gained, it is expected that health and breeding standards will include certain genetic qualities as goals.

28. Is there a registry for genetic testing results?

In the United States, several AKC parent clubs have established breed-specific genetic registries, either independently or as part of CERF's Canine DNA Registry or Orthopedic Foundation for Animals (OFA) registry. Several European kennel clubs have registries in place. Owners should be encouraged to contact their parent club for information about registries and to participate in developing a better breed based on shared genetic information.

29. How are genetic tests obtained?

Currently, DNA tests are not performed in private veterinary practice or clinic settings because methodology requires use of high-cost instruments and specialized technical expertise. Most of the genetic tests for canine PRA are available exclusively from OptiGen, LLC, a veterinary genetic service laboratory (www.optigen.com). Other companies offer tests for a growing variety of diseases. The AKC–Canine Health Foundation maintains a list of genetic tests on their Web site (www.akcchf.org).

BIBLIOGRAPHY

1. Acland GM, Ray K, Mellersh CS, et al: Linkage analysis and comparative mapping of canine progressive rod-cone degeneration (prcd) establishes potential locus homology with retinitis pigmentosa (RP17) in humans. Proc Natl Acad Sci USA 95:3048–3053, 1998.
2. Aguirre GD: DNA testing for inherited canine diseases. In Bonagura JD (ed): Kirk's Current Veterinary Therapy, 13th ed. Philadelphia, W.B. Saunders, 1999, pp 909–913.
3. Aguirre GD: Mechanism of photoreceptor disease and degeneration. Great Basin Vis Sci Symp II:6–21, 1996.
4. Aguirre GD, Baldwin V, Pearce-Kelling S, et al: Congenital stationary night blindness in the dog: common mutation in the RPE65 gene indicates founder effect. Mol Vis 4:23, 1998.
5. Dekomien G, Runte M, Godde R, et al: Generalized progressive retinal atrophy of Sloughi dogs is due to an 8bp insertion in Exon 21 of the PDE6B gene. Cytogen Cell Gen 90:3–4, 2000.
6. Langston A, Mellersh C, Wiegand N, et al: Towards a framework linkage map of the canine genome. J Hered 90:7–14, 1999.
7. Mellersh CS, Langston AA, Acland GM, et al: A linkage map of the canine genome. Genomics 46:326–336, 1997.
8. OptiGen, LLC: www.optigen.com.
9. Petersen-Jones SM, Entz DD, Sargan DR: cGMP phosphodiesterase-a mutation causes progressive retinal atrophy in the Cardigan Welsh corgi dog. Invest Ophthalmol Vis Sci 40:1637–1644, 1999.
10. Ray K, Tejero MDL, Baldwin VJ, et al: An improved diagnostic test for rod-cone dysplasia 1 (***rcd1***) using allele-specific polymerase chain reaction. Curr Eye Res 15:583–587, 1996.
11. RetNet—Retinal Information Network: www.sph.uth.tmc.edu/RetNet.
12. Werner P, Mellersh C, Raducha M, et al: Anchoring the canine linkage groups with chromosome-specific markers. Mamm Genome 10:814–823, 1999.
13. Zeiss CJ, Ray K, Acland GM, et al: Mapping of X-linked progressive retinal atrophy (XLPRA), the canine homolog of retinitis pigmentosa 3 (RP3). Human Molec Genet 9:531–537, 2000.

42. RETINAL DETACHMENTS

Samuel J. Vainisi, D.V.M.

1. What is a retinal detachment (RD)?

A retinal detachment is the separation of the neurosensory retina (rods, cones, and inner layers) from the retinal pigment epithelium. This results in the accumulation of fluid between the two layers. RD is classified as a **rhegmatogenous** retinal detachment (RRD) if there is a break or tear allowing vitreous to separate the retinal layers. A **traction** RD results if there is a pulling force (band, membrane) in the vitreous, and an **exudative** RD is caused by fluid secondary to damage to the blood barrier (choroiditis, hypertension).

2. What are the factors responsible for rhegmatogenous retinal detachments?

The most common cause is cataract surgery, especially if the RD is complicated by a tear in the posterior lens capsule, vitreous loss, retained lens fragments, intraocular hemorrhage, or prior lens-induced uveitis. Breeds with inherited retinal dysplasia, especially if there is retinal thinning or holes along with vitreous degeneration (Labrador retrievers, English springer spaniels), are predisposed to RRD. Dogs with excessive vitreous degeneration, especially if they are violent head shakers with toys, are prime candidates for RRD (shih tzus, Boston terriers, poodles). Trauma due to penetrating injuries or with associated vitreous hemorrhage is also a cause of RRD.

3. What are the main causes of exudative retinal detachments?

Exudative RDs are due to the accumulation of fluid in the subretinal space. Conditions such as choroiditis or hypertension may result in an exudative or serous RD. Immune-mediated diseases are frequent causes of this type of RD (Vogt-Koyanagi-Harada, sclerouveitis). However, fungal, bacterial, or rickettsial infections that cause panuveitis also can cause this type of RD. Choroidal tumors and optic nerve colobomas also may result in exudative detachments.

4. What does a retinal detachment look like?

For many general practitioners, the diagnosis may be difficult, especially if the RD is associated with panuveitis and there is considerable inflammation. Ultrasound is helpful in the diagnosis. If the media is clear, anterior displacement of the retina may be fairly obvious. With large serous or exudative retinal detachments, the retina may almost be in contact with the posterior lens capsule (Figs. 1). If there is a large tear or retinal dialysis, the retina may appear as a gray curtain floating loosely in the vitreous (Fig. 2), or the detached retina may appear as a blur while the attached retina is in focus (Fig. 3). If the tear or dialysis is approaching 360°, the retina will be attached only at the optic disc and the tapetum lucidum will be extremely hyperreflective (Fig. 4).

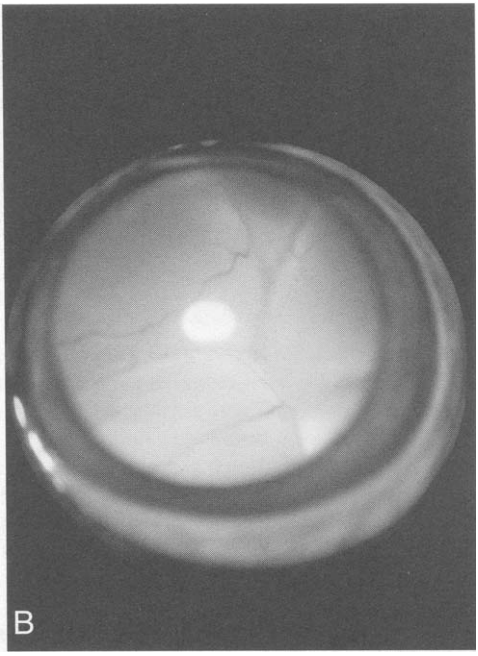
5. What is the treatment for retinal detachments?

Treatment will vary depending on the etiology. Exudative detachments will frequently respond to appropriate drug therapy: immune-mediated diseases to anti-inflammatories and infectious diseases to proper antimicrobials or antifungal drugs. It is usually necessary to use anti-inflammatory therapy along with antimicrobial drugs to expedite retinal reattachment. RDs associated with hypertension usually responds well to antihypertensive drugs unless there is a retinal break. Rhegmatogenous and traction retinal detachments always need some form of surgical intervention to repair or to prevent progression of the RD.

6. Why does lens-induced uveitis (LIU) predispose to a retinal detachment?

When cataracts develop rapidly or become hypermature, there is some leakage of the altered lens protein out of the lens capsule. This altered lens protein elicits an inflammatory reaction in the uvea that manifests clinically as episcleral inflammation and aqueous flare (Fig. 5). Several

Figure 1. Serous retinal detachment. *A*, Note retina against posterior surface of the lens (inferiorly). *B*, Note retina against posterior surface of the lens (circumferentially). This is a bullous retinal detachment.



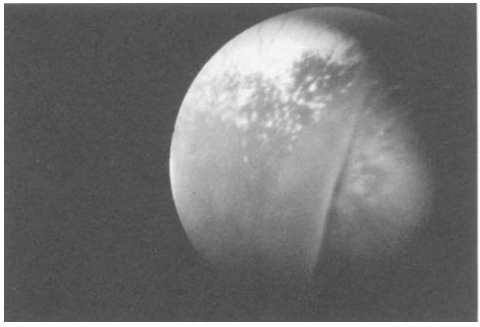


Figure 2. Retinal dialysis. Note edge of retina (gray retinal band) folded on itself.

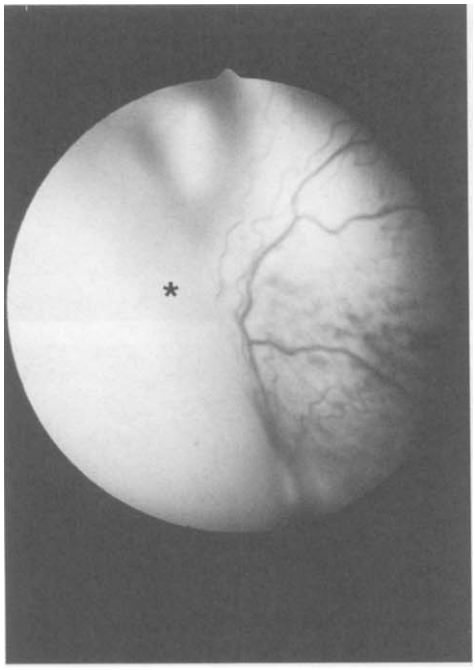


Figure 3. Vertical retinal detachment. Note normal retina in focus, detached retina out of focus (*).

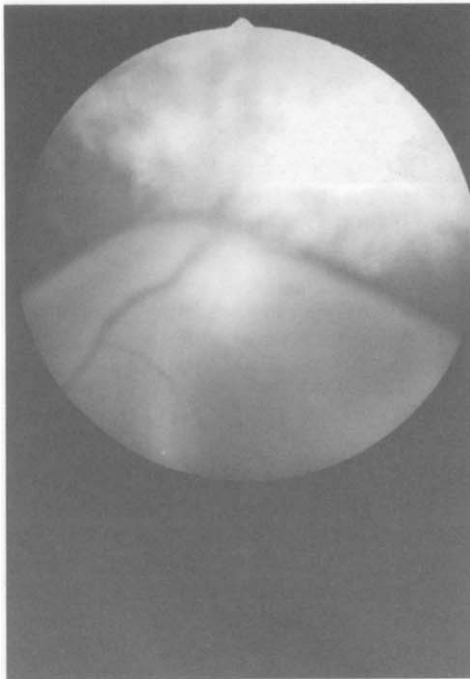


Figure 4. Giant retinal tear (360°). Retina is attached only at optic nerve. Tapetal area is hyperreflective.

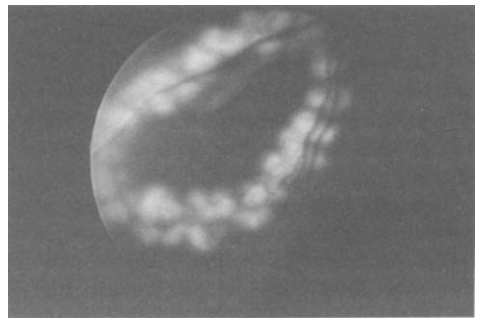


Figure 5. Hypermature cataract with lens-induced uveitis. Note episcleral congestion.

sequelae from this inflammation may produce a RD: (1) vitreous retraction and degeneration, (2) obliteration of peripheral retinal vessels with secondary retinal thinning and weakness, (3) formation of retinal cysts, and (4) transient glaucoma attacks with intermittent stretching of the globe and further insult on the peripheral retina. Certain breeds (bichon frise, Siberian husky, American cocker spaniel) with early onset cataracts are prone to LIU because of the rapid development. The association of LIU and RD with resorbing cataracts or postcataract surgery has been reported to be 10–30%.

7. Is there any prophylactic treatment prior to cataract surgery for cases with LIU?

Because of the common occurrence of RD following cataract surgery where prior LIU has occurred, some form of retinopexy (laser or cryotherapy) prior to surgery is recommended. Randomized studies comparing RDs in eyes with or without prior retinopexy are not available. The procedure can be performed 3 weeks prior to removing the cataract. It is important to do an ultrasound at the time of the retinopexy surgery to be sure a small detachment does not already exist. Retinopexy is also indicated in eyes where the fellow eye has detached either from prior cataract surgery or from severe vitreous degeneration. Retinopexy may benefit certain animals with retinal dysplasia where the dysplastic area is very thin and the vitreous has degenerated (barrier treatment around the dysplastic area). Laser retinopexy can be done either before, if possible, or after luxated lens surgery.

8. What is the treatment for rhegmatogenous retinal detachments?

The surgical procedure depends on the type and extent of the RD. Small localized tears or holes may be treated by barrier laser photocoagulation or cryotherapy (Fig. 6). If the RD is a vertical dialysis and no vitreal traction bands are present, then demarcation laser retinopexy may be helpful. If the RD is a small superior tear, then pneumatic retinopexy (inert gas) may cure the problem. Larger RDs over 3 clock hours (giant tears) or RDs with traction bands require more exten-

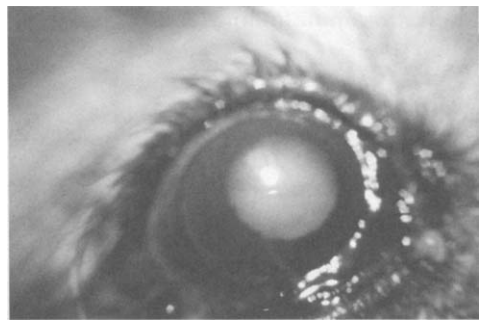


Figure 6. Retinal hole treated by barrier laser retinopexy.

sive surgery such as scleral buckling or pars plana vitrectomy. In the dog, pars plana vitrectomies may be more successful than scleral buckling. In the former, three sclerotomy openings are made at the pars plana: one for the infusion of fluids, one for a vitrector, and one for a fiber-optic light. After removal of the vitreous strands, vitreous, and any other debris, a perfluorocarbon liquid is injected to flatten the retina back to normal position. Then, endolaser coagulation is done to form chorioretinal scars. This fluorocarbon liquid is then replaced with silicone. It is a lengthy procedure, but has given this author the best results to date—approximately 72% success rate (Fig. 7).

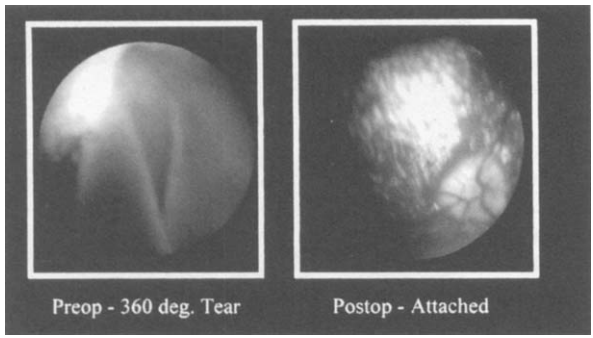


Figure 7. Giant retinal tear repair in the dog. Preoperative and postoperative fundus photograph

9. What is demarcation retinopexy?

This is an attempt to halt a RD in progress. In humans, it has been helpful in stopping temporal rhegmatogenous detachments before the RD extends to the macula. This "salvage retinopexy" in the dog can be used for a vertical dialysis, either nasal or temporal, moving toward the optic disc. If several rows of laser coagulation are made along the leading edge of the RD (Fig. 8), there is a fairly good chance of stopping the detachment. It also has been helpful in horizontal RDs if the break is inferior, but not superior because gravitational forces seem to overcome the adhesions.

10. What is pneumatic retinopexy?

Pneumatic retinopexy involves injecting air or an inert gas into the vitreous cavity in an attempt to have the gas bubble act as a tamponade against the retina, flattening it onto its normal position against the choroid. Because the gas bubble tends to rise to the top of the eye, this procedure has been very helpful for treating small breaks in the superior retina (8–4 o'clock). Prior cryotherapy or postsurgery laser coagulation is done on the detached area. In order for pneumatic retinopexy to work, the bubble must be kept against the detached area. Humans must position their head several hours a day until the retina has reattached. This can be a problem with dogs for obvious reasons. The inert gases sulfur hexafluoride (SF_6) and perfluoropropane (C_3F_8) are the most common used. SF_6 will expand 2–3 times and remain in the eye approximately 2 weeks, whereas C_3F_8 expands 4 times and remains about 4 weeks. Air will last 2–3 days. This author has used C_3F_8 for small superior tears in the dog with a 60% success rate.

11. What are the predisposing factors for tractional retinal detachments?

In the dog, the most frequent cause is a membrane in the vitreous pulling on the retina. Penetrating wounds, vitreous hemorrhage, and vitreous disruption during surgery are common causes of membranes forming in the vitreous and exerting traction on the retina. In dogs that have severe persistent hyperplastic primary vitreous (PHPV), especially with persistent hyaloid vessels, cataract formation with traction detachments is not uncommon. Proliferative vitreoretinopathy (PVR) results in tractional membranes due to the proliferation of retinal pigment epithelial cells,

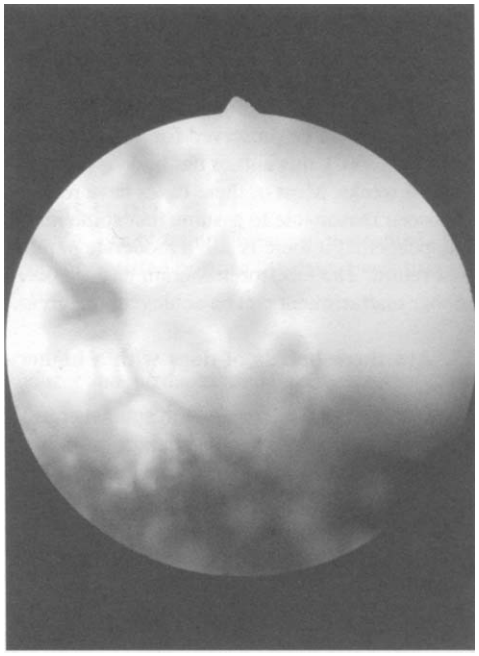


Figure 8. Nasal retinal dialysis treated by three rows of laser photocoagulation along leading edge of detachment. Eye still visual 7 years post-treatment.

fibroblasts, and glial cells on the anterior and posterior surface of the retina. PVR is usually associated with rhegmatogenous retinal detachments and are seen more in man than in dogs. Most cases occur with long-standing retinal detachments, especially in Labrador retrievers and English springer spaniels with retinal dysplasia.

12. What is the treatment for tractional retinal detachments?

Treatment is always surgical and is dependent on releasing the traction. Pars plana vitrectomy with excision of the traction band in some cases is sufficient; however, many cases also require additional laser photocoagulation or cryosurgery to maintain reattchment. Dogs with severe PHPV along with persistent patient hyaloid artery (PHA) will generally require cataract surgery. Usually also required are a posterior capsulorrhexis to relieve traction from the PHA and an anterior vitrectomy and cautery to any patient hyaloid vessels. Laser retinopexy is sometimes needed to firmly attached the retina. Surgery for PVR is much more involved and difficult, requiring complete vitrectomy with stripping, pealing, or cutting of all membranes attached to the retina and the use of fluorocarbon liquid, laser, or cryosurgery and gas or silicone oil tamponades. Although the success rate for surgical reattchment in man varies from 60% to 80%, the visual results are generally poor. This author has not had good surgical results with the dog.

13. Is there a window of time for reattaching a retina with hopes of some vision?

If the retinal detachment is the exudative type, then the nature of the subretinal fluid and the height of the detachment play a factor in the rapidity of photoreceptor death. Exudative detachments with considerable inflammatory debris or hemorrhage give a poorer prognosis than serous types. This is evident clinically because it is more important to resolve more quickly an exudative retinal detachment with inflammatory debris than one with serous fluid if some visual return is the goal. Some serous RDs that have been elevated for as long as 3 months gradually reattach with the return of some vision, whereas some inflammatory type RDs may reattach in 2–3 weeks with no visual recovery.

Regarding rhegmatogenous RDs, several experimental studies in animals including dogs have attempted to determine the rate of degeneration once the retina is detached. Photoreceptor death begins immediately; however, it tends to vary among the different species. In the dog, there is significant degeneration of the inner and outer segments after 2 weeks, but the photoreceptor nuclei appear to be preserved for a much longer period. In clinical cases of dogs with giant retinal tears (360°), this author has had visual return in many patients that have been clinically blind for 6–8 weeks. Most of these cases have required 3–4 weeks before vision is detectable. It would thus seen reasonable to assume that some inner and outer segment regeneration has taken place. It appears that if there is still a moderate pupillary response, then there is some possibility for visual return. The electroretinogram has not been found to be a valuable indicator. Obviously, the sooner reattachment can be achieved, the greater the chance of vision.

13. Are there breeds of dogs with a higher genetic predilection for spontaneous detachments?

In a series of 200 cases with spontaneous RDs, the most frequent patient has been in a breed with significant vitreous degeneration. Shih tzus accounted for almost 40% of surgical cases. Other breeds are toy and miniature poodles, Boston terriers, Lhasa apsos, Yorkshire and silky terriers, and Italian greyhounds. Almost all of these animals were violent head shakers with toys. Labrador retrievers and English springer spaniels with large areas of retinal dysplasia are also at risk for spontaneous retinal detachment.

14. Once the retina has reattached, what are the possibilities for redetachment?

It is not uncommon for exudative RDs to redetach once therapy is decreased or stopped. Thus, it may be necessary to keep these cases on maintenance level of drugs for months or even years.

Retinas that have been surgically reattached should stay attached if there is good retinal adhesion. However, several possibilities will lead to redetachment. Retinal tears or holes that were inadequately sealed may loosen and allow fluid to migrate subretinally. This may also happen with new holes or tears. Proliferative vitreoretinopathy may provide membranes that cause traction of the retina. Incomplete removal of vitreous or vitreous bands, uveitis, glaucoma, postoperative trauma, or hemorrhage are all possible causes of redetachment. Removal of silicone oil before the retina has firmly adhered is also an occasional cause.

BIBLIOGRAPHY

1. Hilton GF, Kelly NE, Salzano TC, et al: Pneumatic retinopexy: A collaborative report of the first 100 cases. Ophthalmology 94:307–314, 1987.
2. Hilton GF, McLean EG, Brinton DA: Retinal Detachment: Principals and Practice. Ophthalmology Monograph Series. San Francisco, American Academy of Ophthalmology, 1995.
3. Michels RG, Wilkinson CP, Rice TA: Retinal Detachment. St. Louis, Mosby, 1990.
4. Ryan SJ: Retina. In Geaser BM (ed): Surgical Retina, 2nd ed. Vol 3. St. Louis, Mosby, 1994.
5. Smith PA: Surgery of the canine posterior segment. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Baltimore, Lippincott Williams & Wilkins, 1999.
6. Vainisi SJ, Packo KH: Management of giant retinal tears in dogs. J Am Vet Med Assoc 206:491–495, 1995.
7. Vrabec TR, Baumal CR: Demarcation laser photocoagulation of selected macular-sparing rhegmatogenous retinal detachment. Ophthalmology 107:1063–1067, 2000.

43. SUDDEN ACQUIRED RETINAL DEGENERATION

Seth A. Koch, V.M.D., M.M.Sc., and John Sykes, D.V.M.

1. What is sudden acquired retinal degeneration (SARD)?

SARD, which was first described in the early 1980s, is a blinding disease in the canine. The disease has not been reported in the cat. SARD probably existed prior to the date it was first reported but had not been recognized as an entity in itself.

2. What breeds of dog are affected?

All breeds in general are affected, but the schnauzer and the dachshund have been cited more than other breeds.

3. Is there an age or gender specificity?

The majority are middle-aged dogs, and more females have been reported affected.

4. Is there a body condition unique to the disease?

Yes. Most of these dogs are pudgy or Rubenesque.

5. What are the clinical signs?

The most profound clinical sign is sudden loss of vision. These dogs are visual one day and blind the next. Some other associated signs are present that generally can be elicited.

6. What are these associated signs?

Most of the dogs will exhibit polyuria and polydipsia. The most striking sign is a tremendous increase in appetite prior to or concurrent with the visual loss. These dogs become "garbage hounds," and their "pudgy" form becomes obese. They will beg incessantly; they will gobble down their food and often even exhibit pica. Drinking often becomes excessive, and urine volume increases concurrently.

7. What are the ophthalmoscopic abnormalities?

None.

8. How can there be no ophthalmoscopic abnormalities?

In the initial stages of the disease, there are no ophthalmoscopic abnormalities. There may be pupillary dilation that may be responsive, but it usually is a diminished response.

9. Is the diagnosis based on history then?

Not entirely. However, the history, the visual loss, and the lack of any ophthalmoscopic findings put the index of suspicion very high.

10. What else is in the differential diagnosis?

The two entities that must immediately come to mind are acute optic neuritis and cortical or optic chiasmal blindness. Other entities that should be considered are glaucoma, progressive retinal atrophy (PRA), retinal detachment, neoplasia, and meningoencephalitis.

11. Why consider optic neuritis?

Optic neuritis is generally characterized by acute visual loss as well. With optic neuritis, there is usually some swelling of one or both of the optic nerves. Optic neuritis is usually responsive to

high levels of systemic corticosteroids with restoration of vision in 3–5 days. It becomes, in simple terms, a diagnosis of exclusion.

12. How about the other diseases in the differential?

PRA is characterized by gradual loss of vision. Glaucoma has many other clinical signs besides visual loss. Retinal detachment does occur suddenly and causes an acute visual loss, but the detachment is observed ophthalmoscopically. Meningoencephalitis usually has other clinical signs as does neoplasia.

13. How do you differentiate SARD from cortical disease?

Because SARD is a disease of the retina, one can distinguish it from cortical disease by means of an electroretinogram (ERG).

14. What is an ERG?

An ERG measures retinal response primarily from the retinal photoreceptors (rods and cones). If there is photoreceptor degeneration (as in SARD) then the ERG will be extinguished. With cortical disease or optic neuritis, where there is no retinal degeneration, the ERG will be normal.

15. Are there any other clinical signs besides the visual loss and polyphagia?

Yes. Polyuria and polydipsia occur on occasion, and laboratory findings often show enzyme abnormalities related to liver pathology that initially resembles Cushing's syndrome.

16. So these dogs have Cushing's disease?

No. They have Cushing's-like signs, but the findings are not consistent. Some of the indicators for Cushing's are the same (e.g., high ALKP activity and polyuria, polydipsia and polyphasia), but they are inconsistent. A full compliment of cortical testing (urine, cortisol/creatinine, ACTH stimulation, low-dose dexamethasone suppression) will usually distinguish SARD patients as not truly cushingoid.

17. What causes SARD?

The etiology remains an unknown. Theories and suppositions abound. Among those bandied about are abnormal fat metabolism, hepatopathy, excitotoxins, autoimmune disease, and the current favorite and pathologic buzz word of the 1990s, apoptosis.

18. What's next on the horizon?

The answer probably will be found in the world of immunocytochemistry or endocrinology if we don't find that great toxin somewhere out there.

BIBLIOGRAPHY

1. Acland G: Differentiation of retinal disease in small animals by electroretinography. Semin Vet Med Surg 3:15–27, 1988.
2. Miller P, Galbreath EJ, Kehren JC, et al: Photoreceptor cell death by apoptosis in dogs with sudden acquired retinal degeneration syndrome. Am J Vet Res 59:149–152, 1998.
3. Millichamp N: Retinal degeneration in the dog and cat. Vet Clin North Am 20:799–831, 1990.
4. Riis RC: EM observations of a SARD case. Proc Am Coll Vet Ophthalmol 21:112–113, 1990.
5. van der Woerdt A, Nasisse M, Davidson M: Sudden acquired retinal degeneration in the dog. Prog Vet Comp Ophthalmol 1:11–18, 1991.

44. FELINE HYPERTENSION CAUSING OCULAR LESIONS

Ronald C. Riis, D.V.M., M.S.

1. **What constitutes a diagnosis of hypertension in cats?**
   Systolic blood pressure > 170 mmHg.

2. **What are the causes of hypertension in cats?**
   Chronic renal failure is the most common cause; however, diabetes mellitus, chronic anemia, hyperthyroidism, and diets high in salt also have been indicated.

3. **How frequently are ocular lesions seen in hypertensive cats?**
   Many studies suggest that 80–100% of hypertensive cats have ocular lesions.

4. **What are these ocular lesions?**
   Retinal detachment (Figs. 1 and 2)
   Hemorrhage
   Intraretinal hemorrhage or edema (Fig. 3)
   Subretinal hemorrhage or edema
   Blindness

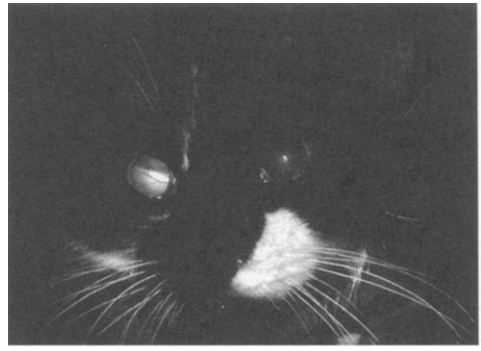


Figure 1. Retinal detachment of the right eye. Note the asymmetry of the retinal reflex.

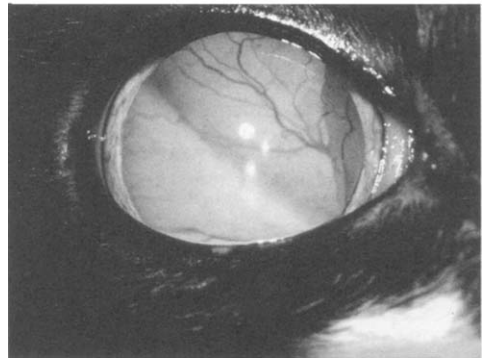


Figure 2. Retinal detachment of the cat shown in Figure 1. The dorsal retinal vasculature is easily focused because of its close proximity to the lens. The cause of this hypertensive cat was mesothelioma.

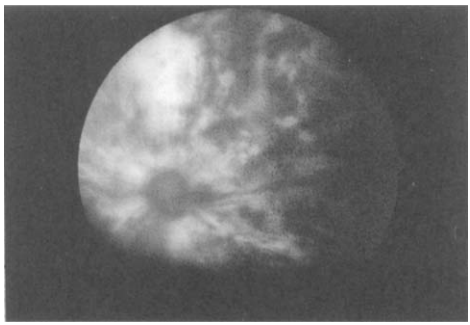


Figure 3. Hypertensive retinopathy with massive intraretinal and subretinal hemorrhages. The blood pressure varied around 250 mmHg.

5. How do hypertensive cats usually present?

In one study, the primary complaint (68%) was sudden blindness or retinal detachment, hyphema, or retinal or vitreous hemorrhage diagnosed by the referring veterinarian. The remaining 22% had a variety of clinical findings including:

Heart murmur
Heterochromia
Neoplasia
Neurologic signs
Renal failure
Recumbency
Weight loss

6. What neurologic signs are associated with hypertension?

Disorientation
Ataxia
Cervical ventroflexion
Paraparesis
Tremors
Vestibular signs

7. What are the cardiac auscultatory abnormalities found in hypertension?

- Systolic heart murmurs
- Cardiac gallop and sinus tachycardia

8. Do diagnostic imaging studies help with the diagnosis of hypertension?

One study used thoracic radiography or echocardiography and found 85% of the hypertensive cats had cardiomegaly. Abdominal radiography or ultrasonography may show hyperechoic small kidneys, renal calculi, or renal cysts. Ocular ultrasound is very helpful in defining retinal detachments in globes with hyphema (Fig. 4).

9. What are the findings for renal function in hypertensive retinopathy cases?

One study found 54 of 69 cats had elevations in blood urea nitrogen (BUN) or creatinine.

10. When is hypertensive retinopathy predictably seen?

Usually when the systolic blood pressures exceed 200 mmHg.

11. When should blood pressure be reevaluated after treatments have been instituted?

Indirect blood pressure measurements should be checked within 5–10 days after treatment has begun. A good response to medication is achieved if the systolic blood pressure decreases 20% or to less than 170 mmHg. The decrease may take 1 month with a response range of 1 week to 6 months. A relapse in hypertension is when the blood pressure increases by 20%.

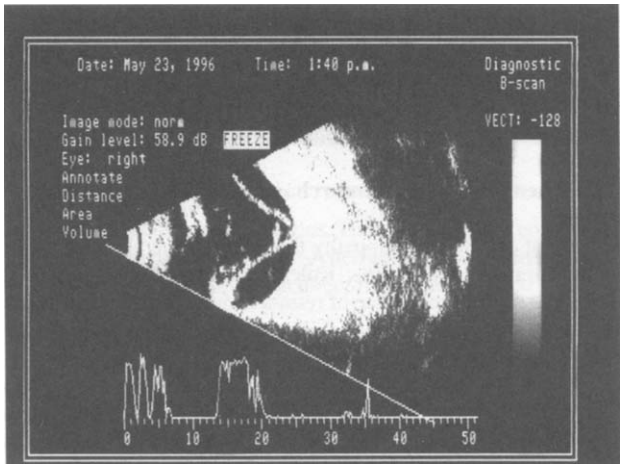


Figure 4. Ocular ultrasound showing a detachment with B-scan. Note the typical "flying sea gull" pattern. In this case, the retina remained attached at the optic disc and ora. With antihypertensive therapy, the entire retina reattached.

12. What antihypertensive drugs are used for cats?

DRUG	DOSE
Atenolol	6.25–12.5 mg every 24 hr
Propranolol	2.5–10 mg ever 8–12 hr
Enalapril	1.25–2.5 mg every 24–48 hr
Captopril	3.125–6.25 mg every 8–12 hr
Furosemide	3.0–012.5 mg every 8–12 hr
Amlodipine besylate	0.625–1.25 mg every 12–24 hr

13. What antihypertensive drug has given the best results?

Amlodipine. Blood pressures fall within a more respectable range and the retinopathy usually resolves. A study using amlodipine had ocular improvement in retinal lesions in one or both eyes in 18 of 26 cats. In this group, 20 of 46 eyes with retinal detachment had less subretinal fluid, partial-to-complete retinal reattchment, or both. Eyes that had retinal edema or hemorrhage without detachment (14 of 26) had partial to complete resolution of retinal lesions. In the amlodipine-treated cats, 30 eyes were blind on initial evaluation, and 4 eyes with complete retinal detachment had reattachment and some visual recovery following treatment.

14. Do cats recover their vision if the blood pressure is controlled?

Not always. Even if the retina reattached, it may be too late and the retina maybe degenerate.

15. Why do ocular lesions develop in hypertension?

It is thought that the retinopathy results from a failure in vascular autoregulation of the retinal arterioles. Increased blood pressure causes the arterioles to vasoconstrict, resulting in a compensatory hypertrophy and hyperplasia of the vascular smooth muscle. Fibrinous changes within the smooth muscle allow for plasma leakage into the vessel wall, causing hyalinization with smooth muscle necrosis. Leakage results causing retinal edema, hemorrhage, and retinal detachment.

16. Is hyperthyroidism contributory to hypertension?

With hyperthyroidism, increased β-adrenergic activity can result in tachycardia, increased myocardial contractility, systemic vasodilation, and activation of the renin-aldosterone-angiotension system, resulting in hypertension. In one study, mild-to-moderate systolic blood pressure increases were detected in 34 of 39 hyperthyroid (87%) cats.

17. Do hyperthyroid cats have ocular manifestations?

Most cats with hyperthyroidism do not develop retinopathy or hypertensive-associated ocular manifestations. In a large group (131) of hyperthyroid cats, obvious ocular manifestations such as blindness were not reported. Another prospective study of hyperthyroid cats found 1 of 13 to have funduscopic retinal lesions.

18. When diagnosing hemorrhagic retinopathy in a cat, what other organs should I worry about?

Most cats with retinopathy that includes hemorrhage and detachment have one or more abnormal renal function tests. Rule out kidney disease first. Although conflicting information is available on the prevalence of retinal lesions in cats with chronic renal failure, a clear association exists between chronic renal failure and systemic hypertension in cats.

19. Is it possible that a cause for hypertension cannot be found?

Once kidney disease and hyperthyroidism are ruled out, other causes such as pheochromocytoma, hyperadrenocorticism, hyperaldosteronism, and renal arterial stenosis must be ruled out. Treatment of the hypertension is advocated despite the etiology. Amlodipine besylate treatment gives satisfactory results without clinically evident adverse effects. After reduction in blood pressure, approximately 70% have improvement in ocular signs.

18. How many treated hypertensive cats with retinopathy recover their visual function?

Recovery of visual function in cats with retinal reattchment is dependent on several factors. The most important factor is duration of detachment prior to diagnosis and treatment. Retinal degeneration is a common finding in cats with retinal reattachment, especially if detached 2–4 weeks. Approximately 50% of the cats with multifocal retinal edema and hemorrhages and controlled hypertension with amlodipine either lack progression of these retinal lesions or have partial resolution of these retinal lesions. Early recognition of hypertensive retinopathy prior to retinal detachment offers the best prognosis for vision once antihypertensive treatment is instituted.

BIBLIOGRAPHY

1. Crispin SM, Mould JRB: Systemic hypertensive disease and the feline fundus. Vet Ophthalmol 4:131–140, 2001.
2. Henik R, Snyder P, Volk L: Treatment of systemic hypertension in cats with amlodipine besylate. J Am Anim Hosp Assoc 33:226–234, 1997.
3. Maggio F, DeFrancesco T, Atkins C, et al: Ocular lesions associated with systemic hypotension in cats: 69 cases (1985–1998). J Am Vet Med Assoc 217:695–702, 2000.
4. Sansom J, Barnett K: Ocular disease associated with hypotension in 16 cats. J Small Anim Pract 35:604–611, 1994.
5. Snyder P: Amlodipine: A randomized, blinded, clinical trial in 9 cats with systemic hypertension. J Vet Intern Med 12:157–162, 1998.
6. Stiles J, Polzin D, Bistner S: The prevalence of retinopathy in cats with systemic hypertension and chronic renal failure or hyperthyroidism. J Am Anim Hosp Assoc 30:564–572, 1994.

45. ASTEROID HYALOSIS AND SYNCHYSIS SCINTILLANS

Ronald C. Riis, D.V.M., M.S.

1. What is asteroid hyalosis?

Asteroid hyalosis appears as "snow ball" opacities in the vitreous. These opacities are complexes of lipid-mineral embedded in an amorphous vitreous framework. Asteroid bodies shimmer as colored balls when illuminated from the side and as white balls with direct illumination (Figs. 1 and 2).

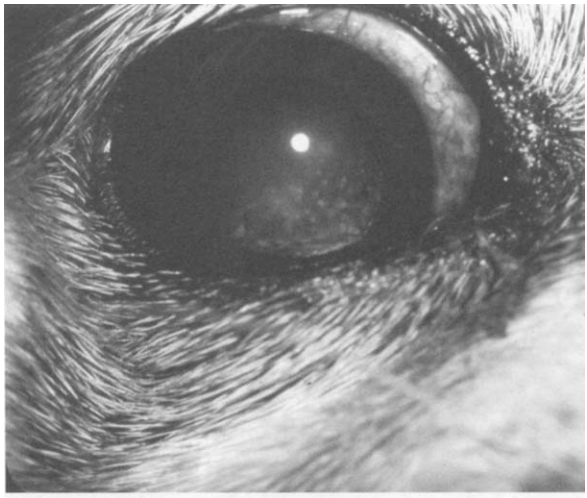


Figure 1. Asteroid hyalosis in an adult dog.

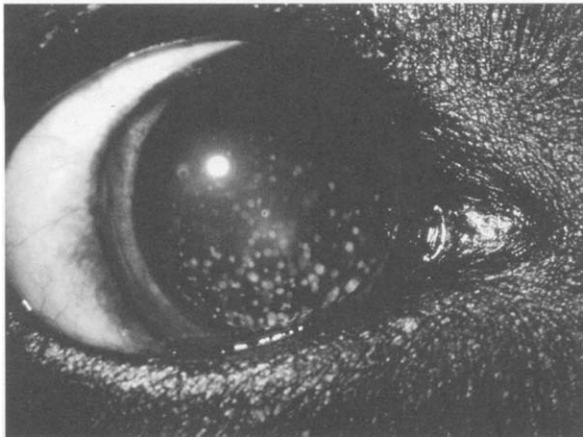


Figure 2. Asteroid hyalosis diagnosed bilaterally in a 10-year-old Labrador retriever. The dilated pupil allows a more complete assessment.

2. What is the mineral component of asteroid hyalosis?

The human literature states the composition of mineral to be predominantly calcium and phosphorus. Analysis of dog asteroid hyalosis found calcium and other minerals such as iron, phosphorus, lead, nickle, copper, and zinc as well (Fig. 3).

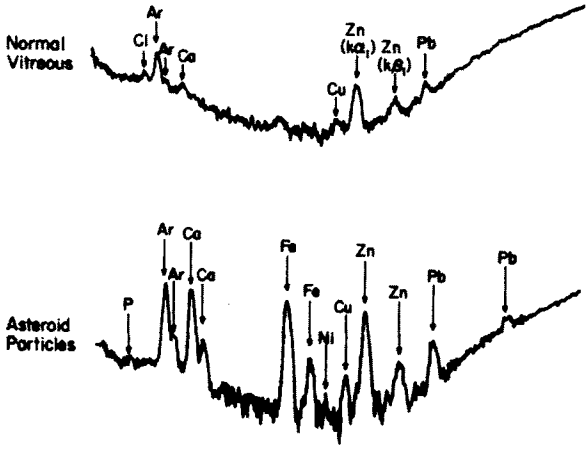


Figure 3. Microanalysis of vitreous mineral content, comparing normal to affected vitreous with asteroid hyalosis. Analysis by radiographic fluorescence spectrophometry.

3. What is synchysis scintillans?

Synchysis scintillans are degenerative bodies unattached to the vitreous framework. These bodies are within the vitreous chamber, but the vitreous is liquified. The bodies are free floating; therefore, when the eye moves, they also move and then settle inferiorly when the eye is stationary. These bodies are reminiscent of snow globe paper weights.

4. What is the analysis of synchysis scintillans?

Synchysis scintillans are predominantly lipid or more specifically cholesterol crystals. Grossly, they appear brownish or golden with direct oblique or retroillumination. Synchysis scintillans is also known as **cholesterolosis bulbi.** This term is preferred because of the known composition, but also it is easier to say and remember.

5. Does the presence of asteroid or synchysis bodies indicate the eye has had other problems?

Asteroid hyalosis is most commonly seen in older dogs and most without a history of ocular inflammation or trauma. Very little visual disturbance seems to be typical. Asteroid hyalosis is rarely diagnosed in cats. Synchysis scintillans frequently follows intravitreal hemorrhage or iridocyclitis. It is rarer than asteroid hyalosis. Insults to the vitreous can result in liquification of the vitreous without development of cholesterolosis bulbi.

6. How are these conditions of the vitreous usually diagnosed?

Usually these are noted on routine eye examinations. Many times they are diagnosed during a precataract evaluation. Preoperative electroretinogram (ERG) and ultrasound examinations should be part of the evaluation. Ultrasound identifies both asteroid hyalosis and cholesterolosis bulbi (see Chapter 4). Their presence should be discussed with the owner presurgically. It is not necessary to make special attempts to remove these bodies unless they are exceptionally dense (Fig. 4).

7. Is there any evidence of asteroid hyalosis being inherited?

There is no published pedigree information, but owner comments suggesting that related dogs also have been diagnosed with asteroid hyalosis suggest that it may be possible.

8. What age is asteroid hyalosis usually seen in the dog?

Asteroid hyalosis is unusual in dogs younger than 8 years of age. Dogs over 12 years of age with dense asteroid hyalosis usually compound their visual impairment with nuclear sclerosis or cataracts. Lens removal aids these dogs despite the presence of vitreal asteroid hyalosis.

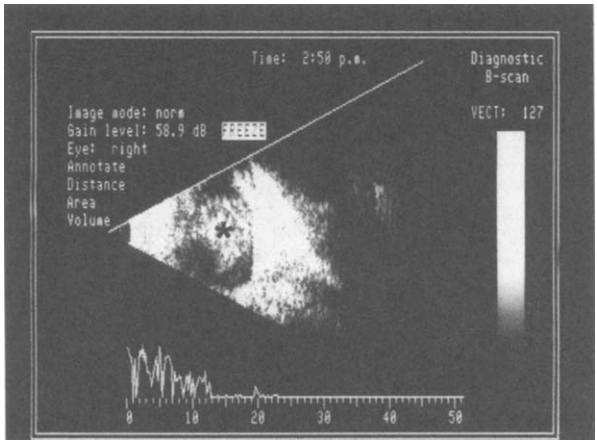


Figure 4. An ultrasound of the globe showing dense asteroid hyalosis in the vitreous cavity. The anterior segment of the eye is at the apex on the left. The hyperechoic area is asteroid hyalosis (*).

9. What are the histologic features of asteroid hyalosis?

Asteroid bodies are easily recognized in the vitreous as spherical bodies of approximately 0.1 mm in diameter. They stain weakly with hematoxylin and eosin, PAS, and acid mucopolysaccharide positive (Fig. 5). All lipid stains are positive. When examined with bright field or polarized light, they appear crystalline (Fig. 6).

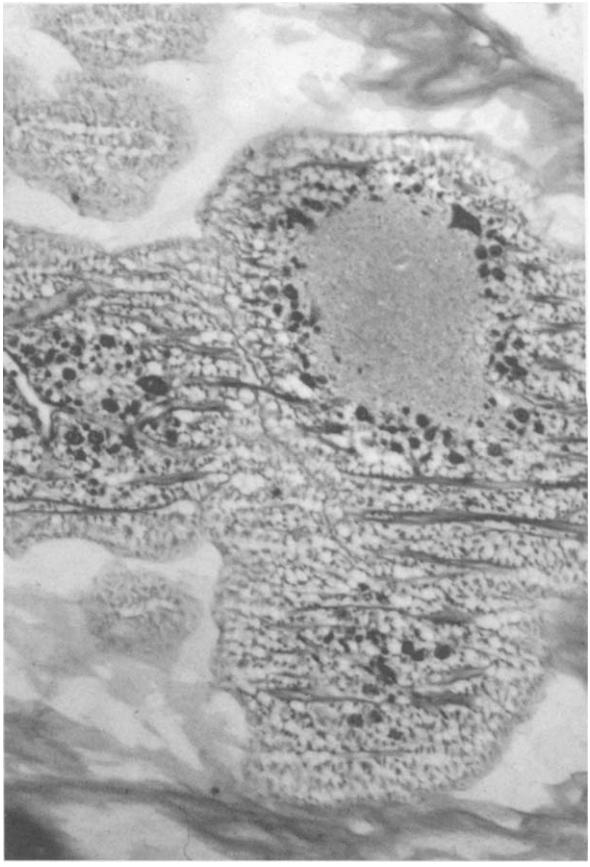


Figure 5. Histosection of vitreous affected with asteroid suspended in a collagen matrix. This section was from an 18-year-old cat (100× H&E stain).

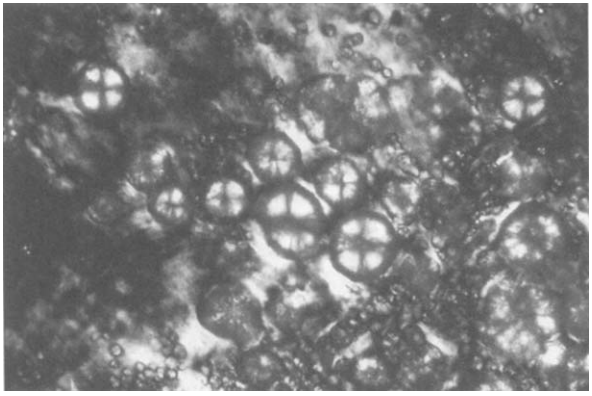


Figure 6. Dog asteroid hyalosis bodies magnified 64×. Slight polarized light, extension one-quarter wavelength out, showing unique crystalline character.

10. What does scanning electron microscopy tell us about asteroid hyalosis?

The scanning electron microscopy of asteroid bodies ironically looks just like miniature meteoroids. The surface is pock-marked and smooth. Each body is held in place by strands of vitreous collagen (Fig. 7).

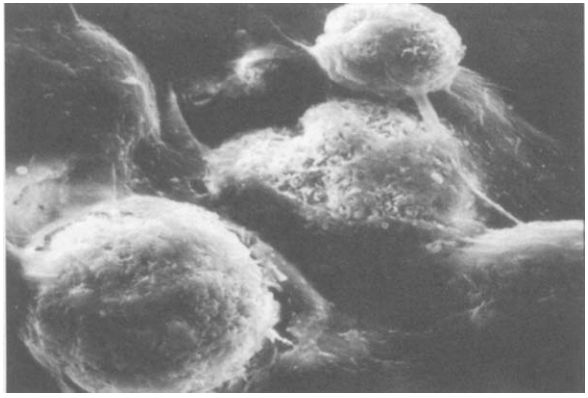


Figure 7. Dog asteroid hyalosis bodies magnified with scanning electron microscopy.

11. What does transmission electron microscopy tell us?

The electron microscopy of asteroid hyalosis shows the bodies to be porous. The matrix is a homogeneous granular texture filled with a stippling of clear holes. Very high magnification shows filamentous structures (Figs. 8 and 9).

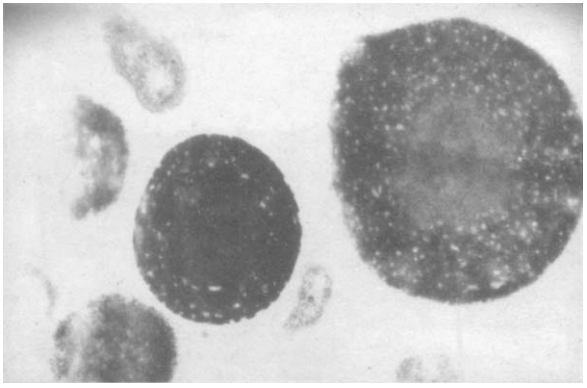


Figure 8. Dog asteroid bodies sectioned for transmission electron microscopy and magnified (62,500×).

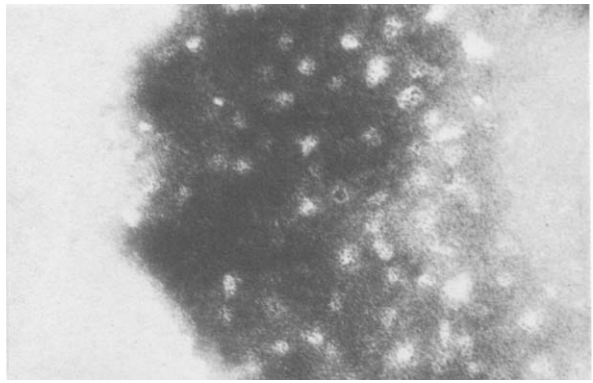


Figure 9. Transmission electron microscopic section of an asteroid body magnified (2,750,000×).

12. Diagnostically, what is the challenge?

Both asteroid hyalosis and cholesterolosis bulbi are findings that require positive location within the vitreous (i.e., differentiating the opacities from lenticular densities or retinal infiltrations or Drusen). By concentrating on their location with good illumination or a slit lamp, note any movement. Slight suspended movement identifies the opacities as asteroid hyalosis. Free-floating movement identifies the opacities as cholesterolosis bulbi (Figs. 10 and 11).

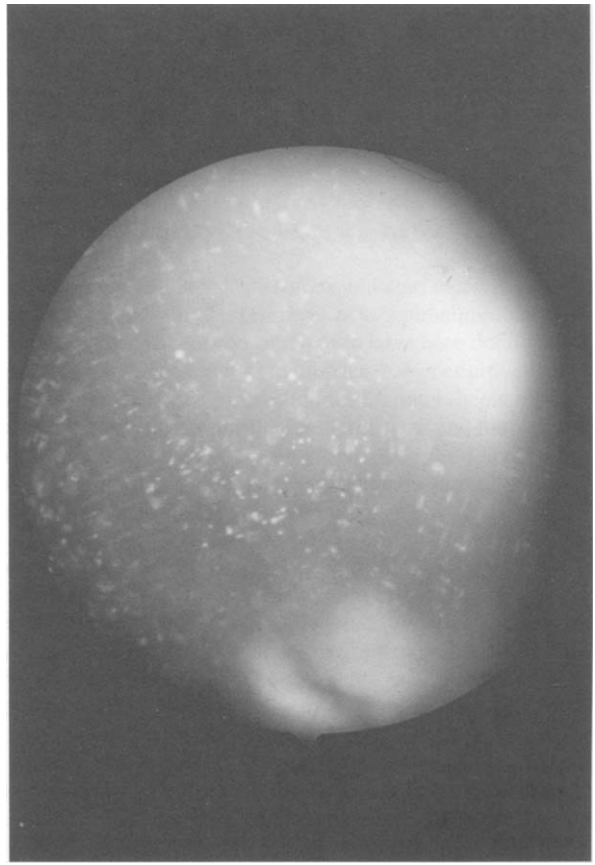


Figure 10. A funduscopic appearance of asteroid hyalosis. Note the optic disc ventrally at 6 o'clock (out of focus).

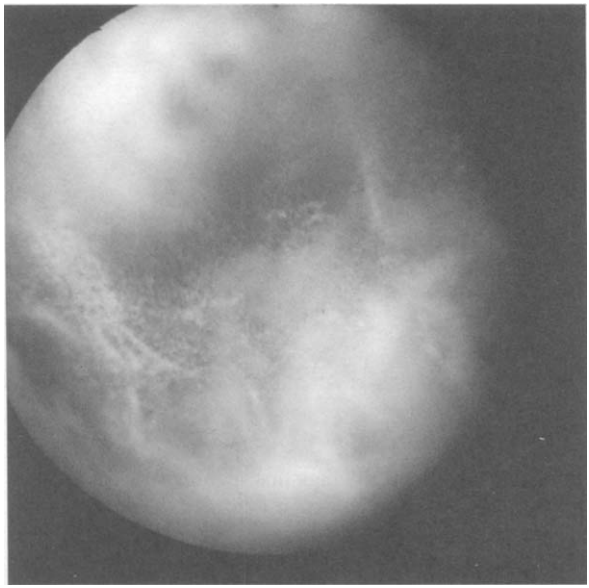


Figure 11. A funduscopic view of concentrated asteroid hyalosis in the ventral vitreous allowing a clear tapetal view dorsally.

BIBLIOGRAPHY

1. Riis RC: What is new with asteroid hyalosis? Proc Am Soc Vet Ophthalmol Intern Soc Vet Ophthalmol pp 153–159, 1982.
2. Rubin LF: Asteroid hyalosis in the dog. Am J Vet Res 24:1256–1262, 1963.

IX. Ocular Tumors

46. INTRAOCULAR TUMORS

Robert L. Peiffer, Jr., D.V.M., Ph.D.

1. What is the epidemiology of ocular tumors in the dog and cat?

There is sparse data regarding the incidence of intraocular tumors in dogs and cats. Although not common, they are not rare and in general tend to be underdiagnosed. Based on observations from a comparative ocular histopathology laboratory of globes enucleated over a 20-year period, primary intraocular tumors are more common than secondary or metastatic tumors in the dog; in the cat, the relatively high incidence of ocular involvement with lymphosarcoma narrows the difference between incidence of primary and secondary ocular neoplasia. The most common intraocular neoplasms in dogs are those of melanocytic origin, occurring two to three times more frequently than those arising from the ciliary body epithelium. In the cat, diffuse iris melanoma is the most common primary intraocular tumor, followed in decreasing frequency by primary ocular sarcomas, nodular melanomas, and ciliary body epithelial neoplasms. Other primary intraocular tumors may occur in either species and theoretically may arise from any of the neural, connective tissue, vascular, or epithelial tissues that are normally encountered within the eye, but they are quite rare.

In both species, lymphosarcoma is the most common secondary intraocular tumor, followed by metastatic carcinoma. The eye itself is devoid of lymphatics; however, rich capillary networks and the anatomic and physiologic features that sequester the eye somewhat from the immune system likely make it a preferential spot for the development of metastatic lesions from primary sites elsewhere in the body.

Ocular neoplasia is most commonly seen in animals of middle or old age; there are exceptions, however. Medulloepitheliomas, which arise from the primitive neuroepithelium, are typically seen in younger animals. In the dog, melanocytic lesions of the uvea have been documented in animals as young as 4 months of age. No breed or sex predisposition has been definitively documented, but there is a suggestion that golden and Labrador retrievers and German shepherds may be at greater risk for the development of melanocytic neoplasia of both the uvea and limbus, and the possibility of an inherited anterior uveal melanoma has been proposed in the Labrador retriever. Diffuse bilateral uveal melanocytosis is seen in older terriers, especially cairns, and cases in German shepherds and boxers have been documented.

2. What are the clinical signs of ocular neoplasia?

The clinical signs of ocular neoplasia are variable and are based on location, extent, and nature of the particular process. With the exception of ocular melanocytosis, primary ocular neoplasia is always unilateral; secondary intraocular neoplasia may involve one or both eyes. In general, rate of progression reflects biologic behavior; benign processes progress over months to years, and malignant primary or metastatic lesions progress much more rapidly.

If located in the anterior segment, the patient may present with a noticeable change in the appearance of the eye. With regard to nodular proliferations, degree of pigmentations and vascularization may provide some insight into the nature of the disease; pigmentation of melanomas tends to be golden-brown to black, although amelanotic variants may misguide clinical diagno-

sis. Ciliary body epithelial tumors tend to be gray, richly vascularized lesions, but those that arise from the pigmented epithelium of the iris or ciliary body may retain features that make it challenging to distinguish from a melanoma on clinical examination. Medulloepitheliomas are white in color and in general not as well vascularized as ciliary body epithelial neoplasms; they may have satellite lesions related to seeding of neoplastic cells. Metastatic lesions tend to be smaller in size (1–3 mm) with variability both in vascular supply and coloration, from white to gray to yellow. Lymphomas tend to be white to gray. Location of directly observable anterior segment lesions may include the anterior chamber, iris, or the ciliary body; those that involve the iris root may represent anterior extension of ciliary body lesions. Nodular ciliary tumors may extend into the posterior chamber, between the posterior surface of the iris and the anterior surface of the lens, or, less commonly, grow into the anterior vitreous to appear as retrolental lesions. Ciliary body adenomas tend to demonstrate this endophytic pattern of growth, whereas adenocarcinomas tend to invade the iris root. Tumor growth can occur along the inner surface of the cornea or through the sclera, generally along the routes of vessels and nerves as they enter the eye, to appear as episcleral nodules. Uveal melanomas or melanocytosis may present with nodular or diffuse intercalary brown pigmentation related to intra- or trans-scleral extension. The nodular lesion of limbal uveal melanocytoma most commonly occurs in the superior quadrants.

3. What complications do intraocular tumors cause?

Tumors of the anterior or posterior segments of the eye may be accompanied by complicating factors of uveitis, spontaneous intraocular hemorrhage, or secondary glaucoma. Not uncommonly, these complicating factors are the presenting cause, and by virtue of their effects on the transparent media of the eye can make clinical diagnosis challenging (Figs. 1 and 2).

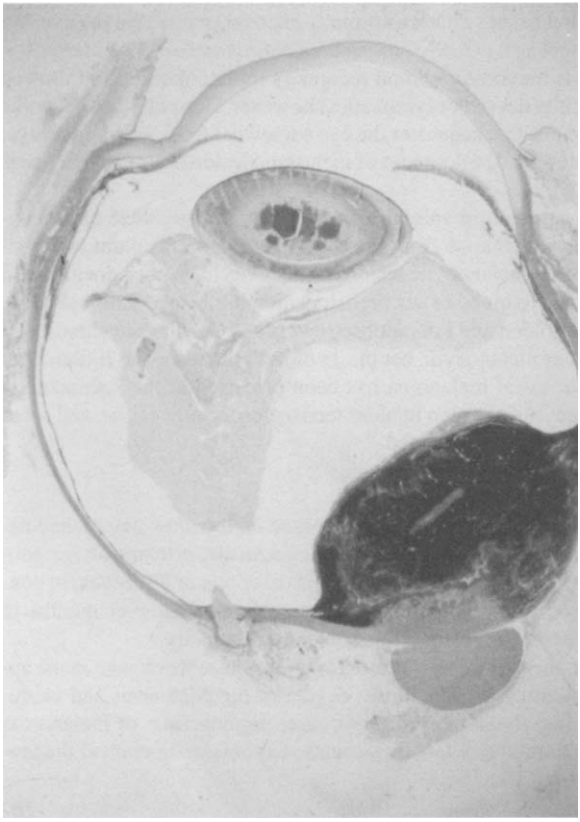


Figure 1. A posterior choroidal melanocytoma in an Australian shepherd is characterized by transscleral extension with a nonpigmented extrascleral nodule. The dog presented with acute intraocular hemorrhage.

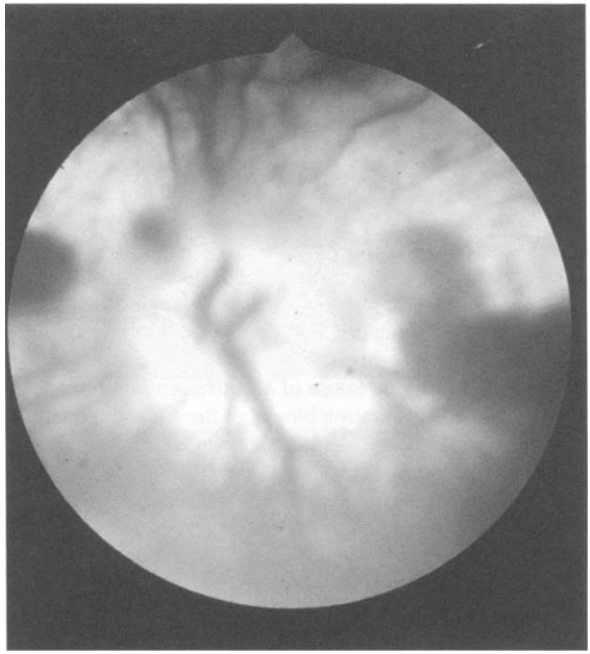


Figure 2. A metastatic transitional cell carcinoma of the bladder detected by careful abdominal palpation was the cause of retinal and preretinal hemorrhages in this canine patient.

Uveitis is usually encountered in neoplasms that have outgrown or have a compromised vascular supply, with resulting tumor necrosis. Ocular lymphoma may demonstrate a uveitis related to cytokine production by the neoplastic cells. Spontaneous intraocular hemorrhage can occur as the result of vascular occlusion and erosion by metastatic emboli or, more commonly, as a consequence of the formation of fragile neovascularization on the anterior surface of the iris. Either benign or malignant neoplasms elaborate vasogenic factors as they grow in order to produce their own blood supply. These soluble factors can diffuse through the aqueous media of the globe to stimulate other vascularized tissues, especially the iris, to produce new blood vessels, which typically elaborate on the anterior iris surface as a preiridal fibrovascular membrane. These vessels lack anatomic fortitude and may bleed spontaneously.

Glaucoma can occur by three mechanisms in association with intraocular neoplasia. The first, and probably most common, is due to the proliferation of preiridal fibrovascular membranes across the pectinate ligament with resultant obstruction of aqueous outflow either by the membrane itself or by associated peripheral anterior synechia. Ciliary body epithelial neoplasms are notorious for their propensity to cause glaucoma by this mechanism. Second, tumor cells may directly invade and obstruct the ciliary cleft and trabecular meshwork; this is the most common pathogenesis of glaucoma seen with diffuse feline malignant melanoma, canine anterior uveal melanoma, and ocular melanocytosis. Lastly, a large space-occupying posterior segment neoplasm can result in anterior displacement of the lens and iris with resultant shallowing of the anterior chamber, closure of the ciliary cleft, and anterior synechia.

4. What additional diagnostics are recommended if an ocular tumor is suspected?

Clinical diagnostics ideally should determine the presence of the neoplastic process; allow determination of whether the neoplasm is primary or secondary; if primary, determine whether the tumor is benign or malignant; and define complicating ocular factors and potential for vision. With this data in hand, the clinician should be able to offer a course of management and prognosticate with reasonable accuracy both for the health of the eye and the general well being of the patient. Few cases are ideal, however, and it is not unusual for definitive diagnosis to be obtained only after enucleation and histopathologic evaluation.

A thorough ophthalmic examination is requisite of both involved and fellow eye, including tonometry, gonioscopy, and dilated examination of the posterior segment. Imaging techniques including ultrasound, CAT scan, or MRI are particularly valuable in determining the presence of a proliferative lesion in the presence of opaque media due to such factors as severe corneal edema or intraocular hemorrhage. Imaging modalities also can be useful in determining if there is involvement of the ciliary body or peripheral choroid, which can be difficult to directly visualize. A thorough physical examination is indicated with emphasis on palpation of the regional nodes (while the eye itself lacks lymphatics, the conjunctiva does and the orbit may possess them) and lymph nodes in general and determination of the presence of a primary lesson elsewhere that might have metastasized to the eye or a potentially malignant primary ocular tumor that has spread beyond the globe. If there is a clinical suspicion of a malignant ocular tumor, chest radiographs and clinical biochemistry to evaluate organ function may be helpful.

5. Can a biopsy be taken of an intraocular tumor?

Fine-needle aspiration biopsy of the aqueous or vitreous cavities or of observable ocular tumor masses has both its critics and its advocates and in general is likely underutilized as a diagnostic tool. Some neoplasms, such as lymphoreticular tumors and melanomas, tend to have noncohesive cells that are shed into the aqueous or vitreous and can be obtained by aqueous or vitreous centesis. Uveal lymphoma is one tumor that is likely to lead to an accurate cytologic diagnosis following a fine-needle aspiration of the mass itself. Other tumors are more likely to provide samples that are low in cellularity and to be problematic for critical interpretation even by experienced cytopathologists. Putting needles into eyes is not an innocuous procedure and can be accompanied by complications such as hemorrhage, rupture of the lens capsule, and potential seeding of neoplastic cells (Figs. 3–5).

Incisional biopsy likewise has the potential for significant intra- and postoperative complications. In some instances, biopsy may provide an indication of tumor morphology at the time of biopsy but is not predictive of future transformation. Diffuse iris melanoma in cats, for example, may undergo a prolonged premalignant stage with relatively bland melanocytic cells confined to the iris surface that at a future point in time can undergo transformation to a malignant invasive neoplasm. A few intraocular tumors, those that are confined to the iris stroma or the ciliary body processes, may lend themselves to excisional biopsy (see question 7).

6. What is the prognosis for ocular neoplasia?

Prognosis depends on the nature of the neoplasm and stage of tumor development. Two questions need to be addressed: what is the prognosis for the globe both in terms of visual potential and cosmesis? and what is the prognosis for the general well-being of the patient? In general, eyes that harbor secondary intraocular tumors should be considered within the perspective of the whole animal. Less aggressive means should be used to control ocular complications; topical and sys-

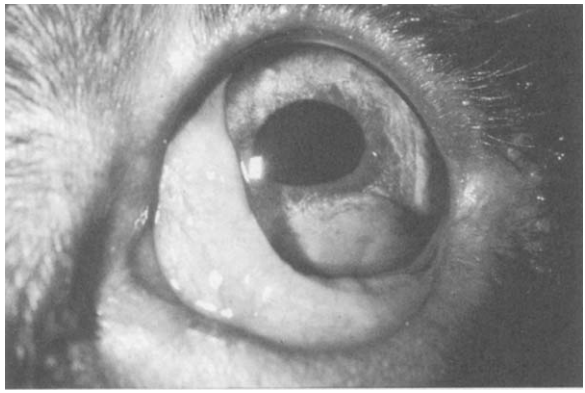


Figure 3. Ocular lymphoma in a canine and feline; the left eye of this dog shows a dyscoria related to a space occupying iridal stromal lesion and diffuse thickening of the bulbar conjunctiva of the third eyelid.

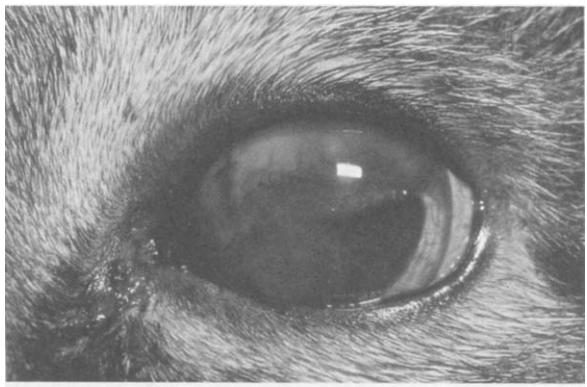


Figure 4. The gray vascularized superior anterior chamber mass demonstrated is shown with a fibrohemorrhagic anterior chamber reaction.

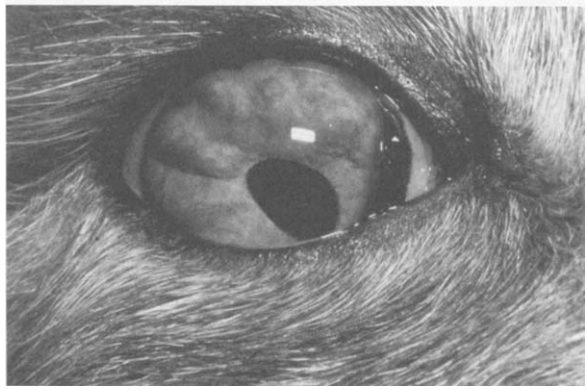


Figure 5. Iris intrastromal thickening seen in the temporal quadrants of the right eye of a feline patient. The diagnosis was malignant melanoma.

temic corticosteroids can control uveitis, and hypotensive agents should be used to treat glaucoma. The majority of canine melanocytic neoplasms—roughly 90%—are benign in terms of their morphology. Of the remaining 10% that have morphologic features of malignancy, probably only about half actually metastasize. Both nodular and diffuse iris melanomas in cats are aggressive, with metastatic rates as high as 50% reported. Whereas metastatic disease tends to manifest within months in canine malignant uveal melanoma (although isolated cases with long latent periods prior to detectable metastasis have been documented), latency up to 2 years following enucleation is characteristic of diffuse iris melanomas in cats. When it occurs, metastatic disease in either species can affect any of the body's organ systems (Figs. 6 and 7).

In the dog, benign and malignant tumors of ciliary body epithelium occur with approximately equal frequency. In the cat, the majority demonstrate worrisome histologic features. However, although malignant tumors of the ciliary body epithelium do possess malignant potential, actual metastasis has been documented rather infrequently in both species (Figs. 8 and 9).

Primary ocular sarcomas in cats are very aggressive neoplasms, with mortality rates approaching 100%. These tumors typically will invade the optic nerve to gain access to the central nervous system, extend through the sclera into the orbit and beyond, and commonly metastasize to distant sites.

Even benign intraocular neoplasias can grow slowly and expansively along the planes of least resistance and result in complications that cause ocular pain or blindness. Preiridal fibrovascular membranes may form associated with benign and malignant neoplasms. Even limbal melanocutomas can extend into the globe if neglected, and an intractable glaucoma invariably develops in dogs with diffuse melanocytosis. Thus, as a rule of thumb, ocular neoplasia, either benign or malignant, carries a guarded prognosis for the involved eye.

Figure 6. Diffuse malignant melanoma of the left iris in a cat.

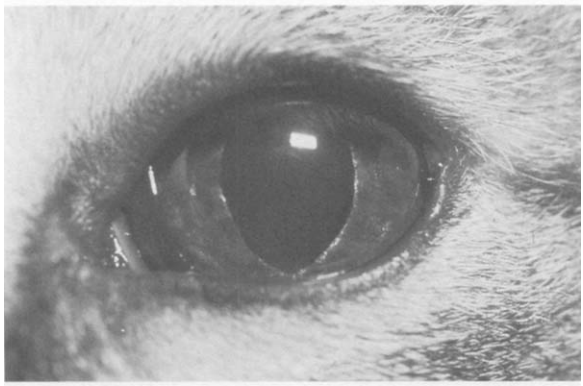


Figure 7. Melanomas most commonly present as a diffuse velvety thickening of the anterior surface of the iris.

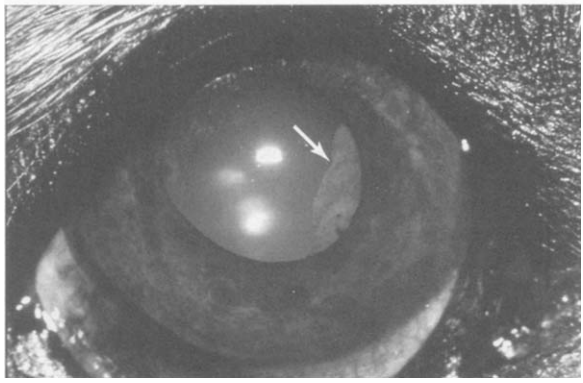


Figure 8. Ciliary body epithelial tumors. Ciliary body adenomas typically present as proliferative lesions extending into the posterior segment or anterior vitreous as evidenced in the nasal quadrant of this patient. (Photograph courtesy of Dr. RIE Smith).

7. What are the management options for ocular neoplasia?

Management options are limited to observation; excisional biopsy, laser ablation, enucleation, and, if the tumor has extended beyond the glove, exenteration. Localized lesions in eyes without tumor-associated complications may be managed by excisional biopsy, if amenable, or by observation over time in order to gain a sense of their biologic behavior. Tumor size should be carefully documented by photography or drawings. Notable increase in size over a relatively short period of time (weeks) suggests more aggressive biological behavior and demands intervention. In addition to excisional biopsy, laser ablation of tumors has been proposed as an effective means

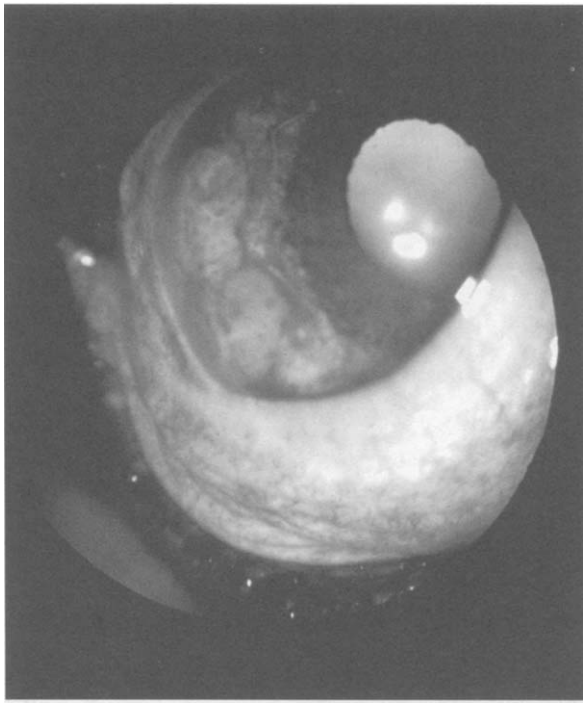


Figure 9. Adenocarcinomas tend to invade the iris root as seen in the temporal quadrants in this Brittany spaniel.

of treatment for these tumors, and some success has been reported using transscleral diode laser application or direct application of diode laser energy using an indirect ophthalmoscope or operating microscope attachment. A disadvantage of laser ablation is the failure to obtain a specific tissue diagnosis, without which it is impossible to unequivocally recommend management options. In addition, some neoplasms, notably diffuse iris melanomas in cats, may "seed" by shedding cells into the aqueous that become entrapped in the trabecular meshwork, beyond the reach of laser energy and excisable only by enucleation. Observation of slow-growing lesions in eyes without tumor-associated complications might also be indicated in an elderly canine patient or a one-eyed canine patient. In this species, the odds are favorable that conservative therapy is not likely to adversely affect general health and well-being. In general, cat eyes with diffuse primary iris hyperpigmentation or nodular pigmented lesions that demonstrate rapid increase in size should be enucleated. Some controversy exists as to whether cats can acquire a benign diffuse primary iris hyperpigmentation that never undergoes malignant transformation; the data that has been collected indicates that, although the premalignant stage may persist for years, malignant transformation is likely inevitable at some point in time. Until proven otherwise, the axiom that early enucleation will minimize the metastatic potential should be adhered to. Canine eyes with rapidly growing lesions or eyes that have experienced tumor-associated complications should be enucleated. Cat eyes with suspected primary ocular sarcoma, based on history of prior trauma, change of appearance in a blind or phthisical, or the observation of a gray to white vascularized tumor mass, should be promptly enucleated or exenterated, although prognosis for general health is bleak. Indeed, the aggressive nature of this tumor and the strong association with ocular trauma provide suggestions for prevention that are likely to be much more effective than treatment. Blind phthisical eyes in cats should be enucleated, and cosmetic globe sparing procedures such as pharmacologic ablation of the ciliary body with intravitreal Cidofovir or gentamicin and evisceration with an intraocular prosthesis are, in the opinion of the author, contraindicated in cats. Once the tumor is characterized by pathology, consult with an oncologist regarding additional treatments available.

8. Are limbal melanomas different?

Limbal melanocytomas in dogs and cats are benign lesions in terms of potential for metastatic disease, even though they may increase in size relatively rapidly and on occasion may extend through the sclera to involve the anterior uvea with a potential for tumor associated complications. Options for treatment include laser or cryoablation with or without debulking of the tumor and full-thickness eye wall resection and subsequent allografting. Unless complications occur, which is an uncommon event, these eyes should not be enucleated (Figs. 10 and 11).

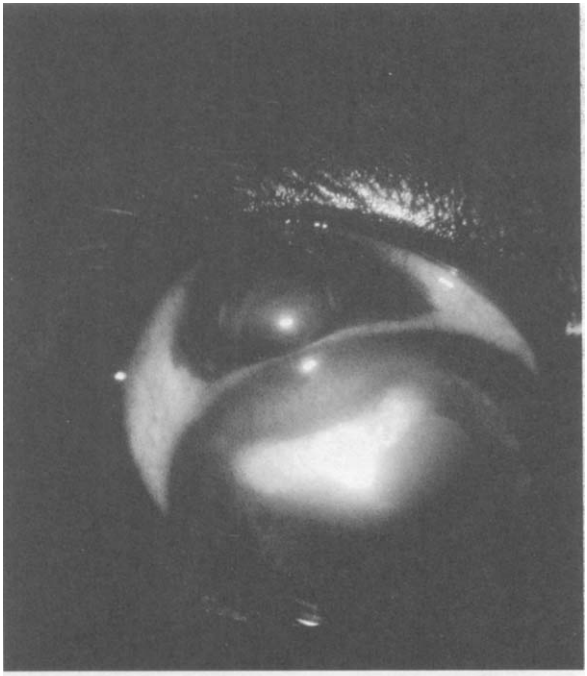


Figure 10. Limbal melanocytoma in the left eye of a golden retriever. There is intracorneal extension with a leading edge of lipid degeneration.

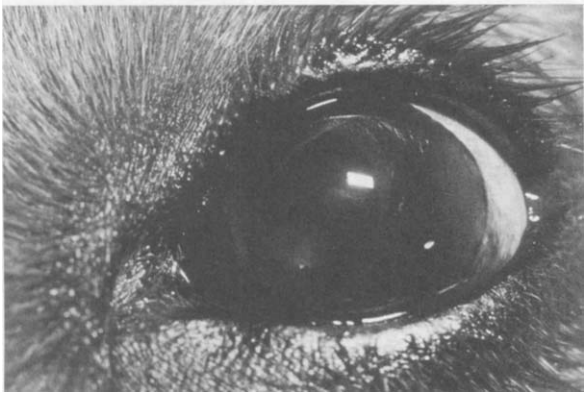


Figure 11. Nodular iris melanocytoma is present in the left eye of this middle-aged German shepherd dog, involving the temporal quadrants and extending to the iris root.

9. Is diffuse melanosis unique?

Diffuse ocular melanocytosis is a particularly challenging disease to manage because of the insidious and relentless nature of the cellular proliferation and the secondary glaucoma that it causes. Tumor involvement of the sclera makes the surgical manipulations used to treat glaucoma, such as gonio implantation, difficult if not impossible to perform. Cycloablative procedures with

either cryo or laser theoretically should be effective but more often than not fall short in terms of controlling intraocular pressure and preserving vision. Topical and systemic hypotensive agents are likewise likely to be unsuccessful in controlling the glaucoma, and visual prognosis in these eyes should be guarded (Figs. 12 and 13).

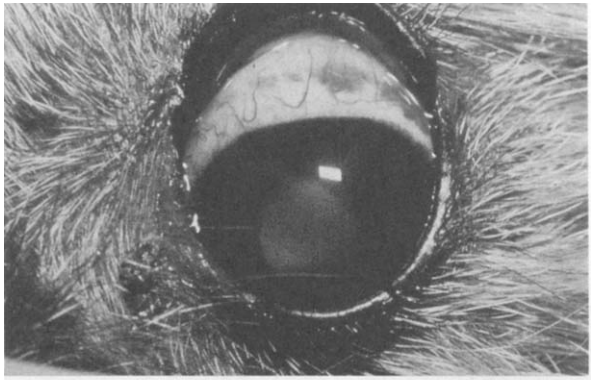


Figure 12. Uveal melanocytosis is a bilateral condition seen in elderly cairn terriers. In this patient, the left eye demonstrates diffuse iris hyperpigmentation, intercalary hyperpigmentation of the sclera, and pigment flecks on the anterior lens capsule.

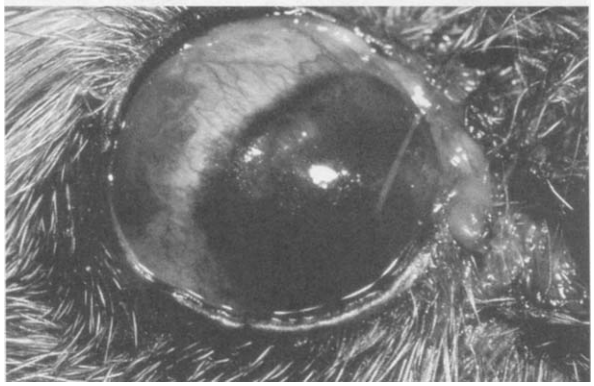


Figure 13. In the fellow eye, chronic secondary glaucoma is present.

10. What type of follow-up is indicated in a patient with an ocular tumor?

All tissues obtained at surgery should be submitted for histologic interpretation, and morphology can provide guidelines for prognostication. Uveal melanocytomas in dogs have an excellent prognosis and have not been demonstrated to recur even if the tumor has extended transsclerally into the orbit. Transscleral extension and involved surgical margins in malignant tumors are ominous harbingers of either locally recurrent or metastatic disease. The tendency for some of these tumors to demonstrate long latency prior to metastasis has been discussed, and regular follow-ups should be conducted over a 2-year period before the animal can be pronounced "cured" of this disease. One-eyed animals function quite well with an excellent quality of life, but enucleation or exenteration places a premium on the remaining fellow eye, and pet owners should be instructed about the sensitivity of the globe to insult and to seek attention promptly at the earliest suspicion of any problems with the remaining eye.

BIBLIOGRAPHY

1. Cello RM, Hutcherson B: Ocular changes in malignant lymphoma of dogs. Cornell Vet 52:492, 1962.
2. Collinson PN, Peiffer RL: Clinical presentation, morphology and behavior of primary choroidal melanomas in 8 dogs. Prog Vet Comp Ophthalmol 3:158, 1993.
3. Corcoran K, Peiffer RL, Koch S: Histopathology of feline ocular lymphosarcoma: 49 cases. Vet Comp Ophthalmol 5:35–41, 1995.

4. Dubielzig RR: Iridociliary epithelial tumors in 100 dogs and 17 cats: A morphological study. Vet Ophthalmol 1:223, 1998.
5. Dubielzig RR, Everitt J, Shadduck JA, et al: Clinical and morphologic features for post-traumatic ocular sarcomas in cats. Vet Pathol 27:62–65, 1990.
6. Peiffer RL: Ciliary body epithelial tumors in the dog and cat: A report of 13 cases. J Small Anim Pract 24:347–370, 1983.
7. Peiffer RL, Monticello T, Bouldin TW: Primary ocular sarcomas in the cat. J Small Anim Pract 29:105–116, 1988.
8. Peiffer RL, Wilcock BP: Morphology and behavior of primary ocular melanomas in 91 dogs. Vet Pathol 23:418, 1986.
9. Peiffer RL, Wilcock BP, Yin H: The pathogenesis and significance of pre-iridal fibrovascular membrane in domestic animals. Vet Pathol 27:41, 1990.

47. IRIS AND CILIARY CYSTS

Ronald C. Riis, D.V.M., M.S.

1. What is the identifying characteristic of an iris cyst?

Iris cysts are in the anterior chamber, attached to the iris, or in the posterior chamber. The cyst may be black or clear depending on whether the origin was from the pigmented or nonpigmented iris epithelium. Cysts are usually round to oblong. Their presence is usually not visually impairing. Owners usually present their pets for consultation when cysts are noted (Figs. 1 and 2).

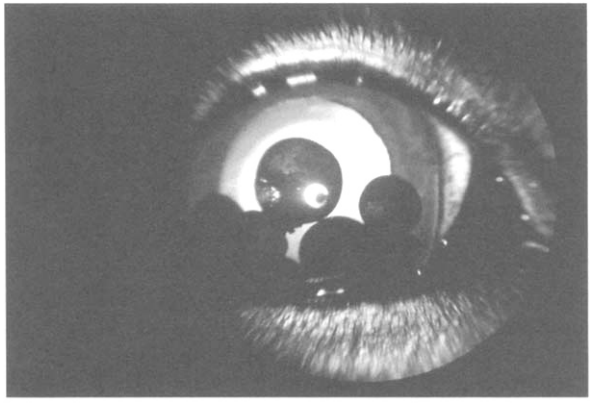


Figure 1. Multiple free-floating iris cysts in the anterior chamber of a dog. The tapetal reflex helps transilluminate the cysts.

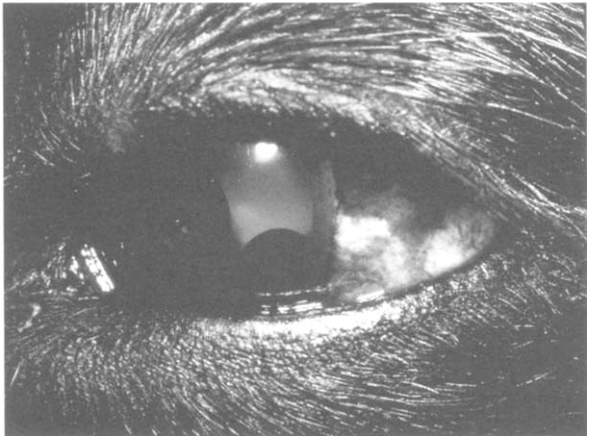


Figure 2. Two large iris cysts stuck between the cornea and lens. These cysts interfered with vision, especially when the pupil was small. Deflation helped this dog's vision.

2. How is a ciliary body cyst different than an iris cyst?

Ciliary body cysts are similar in their appearance, but usually are attached behind the iris. If they should become free floating, they tend to locate into the anterior chamber but occasionally stay in the posterior chamber. Ciliary body cysts go unnoticed by owners if they are in the posterior chamber (Figs. 3 and 4).

3. What is the differential diagnosis for cysts?

Cysts must be differentiated from intraocular tumors. An easy differentiation is possible with a strong focal light source, directed from an oblique angle to illuminate the cyst enough to define

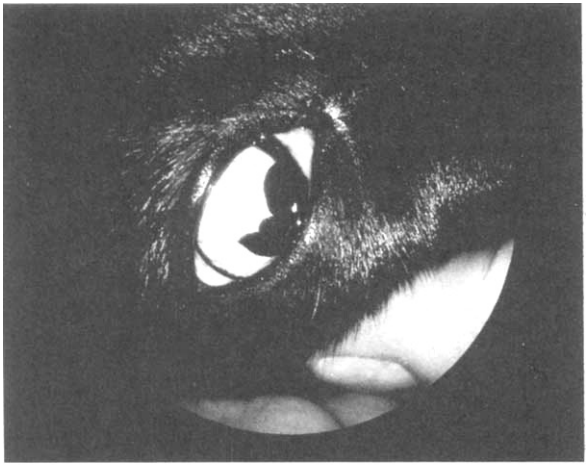


Figure 3. An elongated pigmented ciliary cyst in a cat.

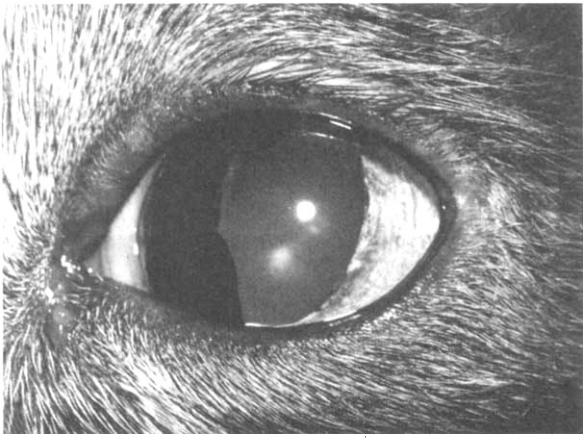


Figure 4. A ciliary cyst protruding into the anterior chamber of a 13-year-old domestic shorthair cat.

its translucency (Fig. 5). Cysts are filled with aqueous fluid. The cyst walls are only one or two layers thick, so they transilluminate nicely. Another differentiating method is with ultrasound using a standoff gel or water in a surgical glove between the probe and cornea. Differentiation is necessary to rule out malignant melanoma.

4. Are cysts diagnosed frequently in dogs and cats?

The dog is much more frequently diagnosed with cysts than the cat.

5. Are cysts inherited?

Cystic characteristics are thought to be inherited in humans. Some dog owners have commented about related dogs having cysts. A documented pedigree identifying cysts has yet to be published, but inheritance probably is a factor in some breeds. A recent publication identified an affected male golden retriever related to many affected offspring.

6. Because most cysts are not vision impairing, is it necessary to remove them?

Small cysts need not be removed. Their presence may concern owners, but your assurance of monitoring their size and location until they become obviously a problem is helpful.

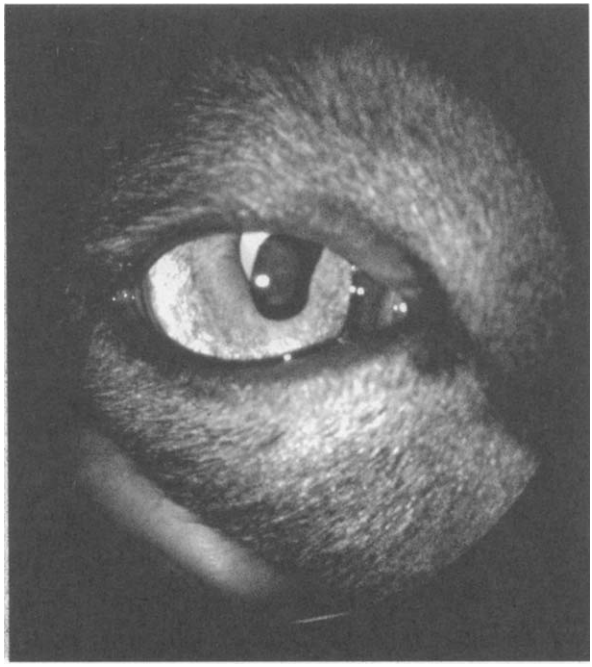


Figure 5. An iris/ciliary cyst adherent at the iris pupillary margin in an adult cat. Note the light passing through the pigmented cyst to rule out melanoma.

7. How are cysts treated?

Before laser treatment, cysts were deflated with a fine needle. The needle technique usually was not as successful as you wished. Successful deflation is always gratifying with the laser. It is like "star wars" to shoot the cyst wall and visualize the results.

8. What laser is used?

The neodymium:yttrium aluminum-garnet (Nd:YAG) laser is ideal. These lasers have a targeting laser of helium and neon allowing you to synchronize the exact site for energy to explode the cyst wall. Low energy of approximately 1 MHz is used.

9. Is the procedure of cyst deflation complex?

No, not at all. Most dogs and cats allow the procedure to be completed without tranquilization. Because most Nd:YAG lasers are designed for human use, the focal length of the laser is closer than many long-nosed dogs are comfortable with, thereby requiring some restraint in unusual positions. Once the position is obtained, the treatment is transcorneal. No topical anesthesia is required; however, topical lubrication is recommended if the lids are retracted for several minutes. Lubrication helps clearly target the cyst wall through the cornea. The target point for deflation should not be directly adjacent to the cornea or lens capsule because these sites allow for the deflated cyst to adhere (Fig. 6). Always dilate the pupil so a misfire will not traumatize the iris for potential breeding.

10. What happens to the deflated cyst?

Once a hole is made, the deflated cyst sinks to the ventral iridocorneal angle.

11. Among dog breeds, are some notorious for cysts?

Yes, the golden retriever outshines the rest of the breeds. Uveal cysts (i.e., those associated with the iris, ciliary body, and ora serrata) occur commonly in golden retrievers.

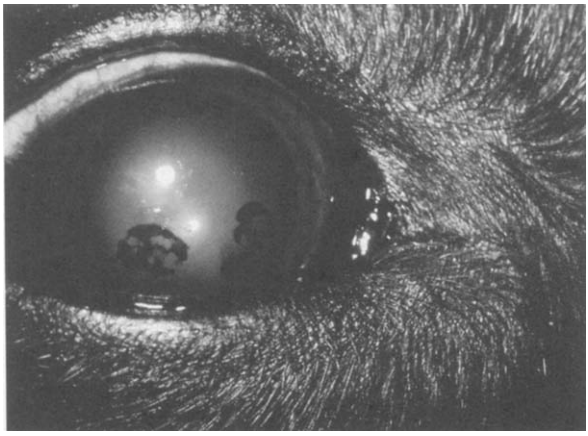


Figure 6. Multiple cysts deflated by Nd:YAG laser in a dog. Note the holes made by the laser as well as the deflated position. The remnants of the cyst will remain in this undesirable site permanently.

12. Are uveal cysts associated with any other ocular abnormality?

Uveal cysts often have been diagnosed in conjunction with pigmentary uveitis in golden retrievers. A pathologic study of 18 glaucomatous eyes from golden retrievers revealed iridociliary cysts in 13.

BIBLIOGRAPHY

1. Deehr AJ, Dubielzig RR: Glaucoma in golden retrievers. Trans Am Coll Vet Ophthalmol 28:105, 1997.
2. Genetics Committee of the American College of Veterinary Ophthalmologists: Ocular Disorders Presumed to be Inherited in Purebred Dogs, 2nd ed. Little Falls, NJ, ACVO, 1996.
3. Sapienza JS, Simó-Domenech FJ, Prades-Sapienza A: Golden retriever uveitis: 75 cases (1994–1999). Vet Ophthalmol 3:241–246, 2000.

48. ORBITAL INFLAMMATIONS AND NEOPLASMS

David T. Ramsey, D.V.M.

1. What are the primary clinical signs of orbital disease?

Clinical signs of orbital disease are divided arbitrarily into primary and secondary categories. Primary signs are referable only to the globe-orbit relationship and denote three-dimensional changes in position, placement, or alignment of the globe within the orbit. There are four primary signs of orbital disease. **Exophthalmos** and **enophthalmos** are terms applied to anterior and posterior displacement of the globe along the orbital axis. **Strabismus** is the term applied to involuntary deviation of the globe from the normal optical axis. **Shift** is the term used to describe displacement of globe position in the horizontal (lateral, medial) or vertical (dorsal, ventral) meridian or a combination thereof (oblique). Oblique shifts in position are designated as a combination of the two directions in which the globe is displaced (e.g., dorsolateral oblique displacement).

2. What are the secondary clinical signs of orbital disease?

Secondary signs of orbital disease occur as a result of exophthalmos, enophthalmos, strabismus, or shift. Secondary signs include changes in anatomy or function of the globe, eyelids, orbital structures, or surrounding tissues. These include alterations in vision, globe, ocular movements, eyelid and nictitating membrane position, pupillomotor function, sensation (pain or numbness), globe indentation, vascular engorgement (conjunctiva, episclera, fundus), corneal or conjunctival exposure, and pain during (or limitation of) mandibular excursion.

3. How do you localize the mass effect within the orbit to a specific location?

Lesion localization within the orbit may be broadly divided into three orbital compartments: **intraconal** (within the endorbital muscle cone), **extraconal** (outside the endorbital muscle cone but within the soft tissue confines of the orbit) and **extraendorbital** (beneath the periosteum). When an orbital mass effect is present, the direction of globe displacement is generally opposite the location of the mass or directly away from the mass lesion and along the path of least tissue resistance. The table below summarizes the direction of globe displacement and localization of the mass.

DIRECTION OF GLOBE DISPLACEMENT	LOCATION OF ORBITAL MASS
Lateral displacement	Medial mass effect
Medial displacement	Lateral mass effect
Dorsal displacement	Ventral mass effect
Ventral displacement	Dorsal mass effect
Dorsolateral displacement	Ventromedial mass effect
Dorsomedial displacement	Ventrolateral mass effect
Ventrolateral displacement	Dorsomedial mass effect
Ventromedial displacement	Dorsolateral mass effect
Axial anterior displacement	Posterior mass effect

Intraconal mass lesions cause axial exophthalmos, minimal or absence of protrusion of the nictitating membrane, and minimal strabismus (unless extensive in volume). Extraconal and extraendorbital mass lesions are characterized by exophthalmos, protrusion of the nictitating membrane, shift in globe position, and strabismus.

4. How are exophthalmos and buphthalmos differentiated?

Buphthalmos is absolute enlargement of the globe secondary to glaucoma. Both buphthalmos and exophthalmos result in a widened palpebral fissure. In most instances, buphthalmos will

not occur as the only clinical sign of glaucoma. When buphthalmos is evident, funduscopic examination may show cupping and atrophy of the optic papilla and peripapillary or diffuse retinal degeneration. Exophthalmos attributable to orbital mass effect may have moderately increased intraocular pressure, but exophthalmos does not occur in glaucoma. Horizontal corneal diameter may be measured and compared between eyes to differentiate buphthalmos from exophthalmos.

5. What are the major considerations when the eye recesses or "sinks" into the orbit?

Axial posterior displacement of the globe is termed **enophthalmos.** Enophthalmos does not occur from a mass effect. Enophthalmos occurs most frequently as an active retraction response to ocular pain. It also may occur with sympathetic denervation to the eye (Horner's syndrome) or when there is loss of orbital mass (soft tissue, bone) in a disease process. Disease processes causing loss of orbital mass include severe dehydration, weight loss, cachexia, orbital neoplasia, severe chronic myopathy (masticatory myopathy), neuropathy (trigeminal), constrictive myopathy (tetanus), or restrictive myopathy (trauma, extraocular polymyositis) of the extraocular muscles (Fig. 1).

Figure 1. Enophthalmos of the right eye with prominent elevation of the nictitating membrane secondary to loss of orbital mass.

6. Does protrusion of the third eyelid signify an orbital mass effect?

The base of the nictitating membrane (third eyelid) lies within the orbit. It has passive movement in the dog but can actively be protruded in the cat. Protrusion of the third eyelid may occur with exophthalmos (orbital mass effect displacing the base of third eyelid) or enophthalmos (globe volume and extraocular muscle contraction displacing the base of the third eyelid). Protrusion of the third eyelid does not invariably signify orbital mass effect as the cause. Sympathetic innervation to the third eyelid is primarily responsible for keeping the third eyelid retracted. Loss of sympathetic innervation to the eye (Horner's syndrome) results in protrusion of the third eyelid. Globe retraction also may occur in response to ocular pain (voluntary contraction of extraocular muscles) or tetanus (involuntary contraction of extraocular muscles).

7. Does the rate of onset of clinical signs correlate with the type of orbital disease?

As a general rule, a history of rapid onset of clinical signs is most likely attributable to an inflammatory orbital disease process. The opposite correlative is that slowly progressive signs of orbital disease are most consistent with orbital neoplasia or cystic orbital disease. However, some neoplastic orbital diseases (lymphoma, mast cell sarcoma) have an associated inflammatory component that can result in rapid onset of clinical signs and pain. Other neoplasms may have rapid periods of growth or volume expansion and enlarge in mass rapidly, thereby exceeding their blood supply and nutritional requirements, and result in necrosis of the neoplasm. When this occurs, an inflammatory component is also common and may result in a rapid progression of clinical signs, and pain may become more conspicuous suddenly.

8. How do you differentiate neoplastic, inflammatory, and cystic classifications of orbital disease?

Orbital neoplasia generally affects older animals (mean age for dogs, 8 years; mean age for cats 8.9 years), resulting in slowly progressive clinical signs over a period of weeks to months, and usually does not cause pain until the neoplasm is of considerable size. Orbital inflammation can affect cats and dogs at any age but most often affects younger animals. Inflammatory orbital disease usually has a history of sudden onset of clinical signs, pain when opening the mouth, and chemosis, and the animal may be febrile. Cystic orbital disease may have a slow or rapid onset of clinical signs, and pain is usually absent or minimal. When history and clinical signs direct your index of suspicion toward a specific classification of orbital disease, diagnostic tests are indicated to confirm or deny your tentative diagnosis and to identify the specific type of inflammatory, neoplastic, or cystic orbital disease (see Chapters 3 and 4) (Figs. 2–5).

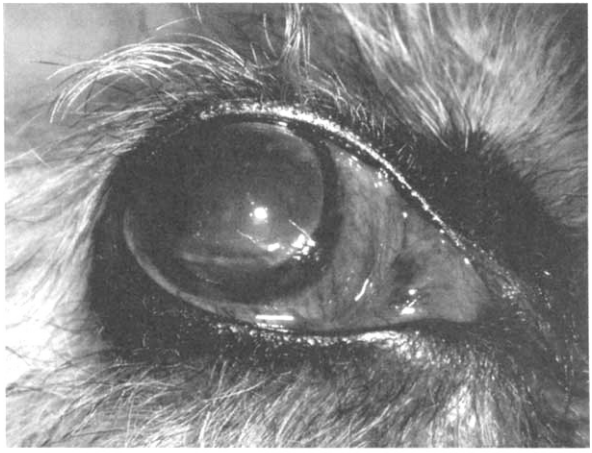


Figure 2. Exophthalmos with dorsolateral displacement indicative of a ventromedial mass that turned out to be an adenocarcinoma.

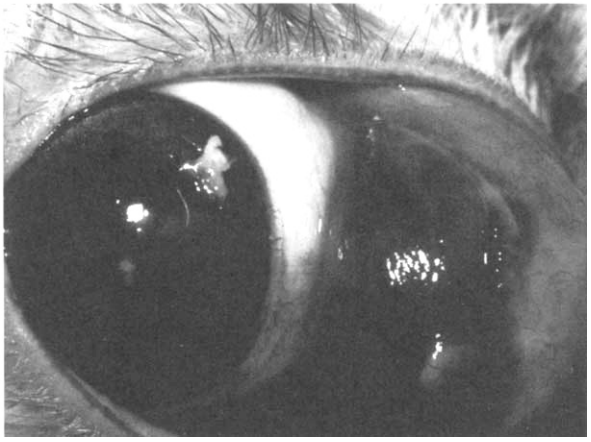


Figure 3. Exophthalmos with lateral displacement indicative of a medial mass that turned out to be a hemangiosarcoma.

9. What is an orbital abscess?

An orbital abscess is a localized septic or nonseptic inflammatory response composed of purulent exudate (primarily dead white blood cells and products of inflammation). Orbital abscess occurs most frequently secondary to periodontal or endodontic disease in the dog and cat. It may also occur from hematogenous, transscleral, or transmucosal (conjunctiva, nasal, oral, sinus) in-

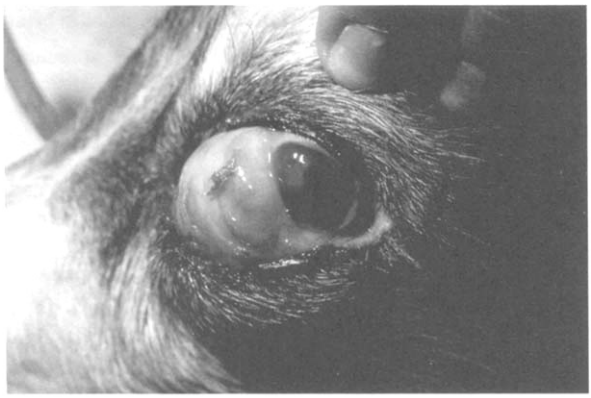


Figure 4. Exophthalmos with dorsolateral displacement secondary to orbital sarcoma.

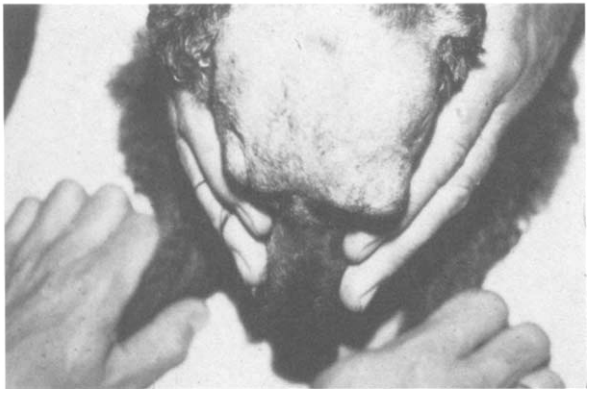


Figure 5. Exophthalmos with axial anterior displacement secondary to a posterior orbital intraconal meningioma.

jury or disease resulting in inoculation of the orbital space with infectious organisms. When an orbital abscess is suspected, orbital ultrasound should be done. When an orbital ultrasound clearly shows an orbital abscess, surgery is indicated. However, the cause of orbital abscess should be pursued. The oral cavity should be examined under general anesthesia. The caudal maxillary teeth should be evaluated using a periodontal probe and dental explorer, and radiographs of the caudal maxillary teeth should be made. The conjunctival fornices and oral cavity should be examined closely for abnormalities (Figs. 6 and 7).

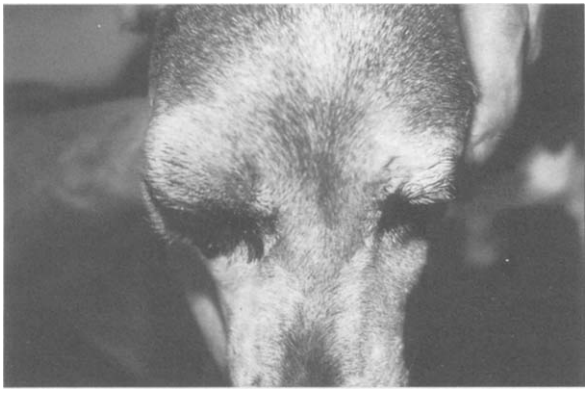


Figure 6. Orbital abscess causing significant swelling. Note the asymmetry.

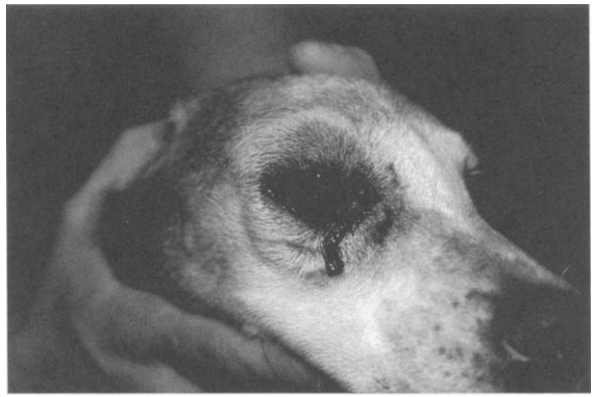


Figure 7. Orbital abscess (same case as Figure 6) shown from a lateral view. Fistulization of the abscess through the ventral conjunctival fornix is sometimes a natural route.

10. How do you treat an orbital abscess?

Surgical drainage must be established. When concurrent dental disease is evident by direct examination or radiographically with orbital abscess, transalveolar drainage of the abscess is indicated. Extraction of the offending tooth to establish transalveolar drainage and treatment with orally administered broad-spectrum antibiotics are indicated after extraction. When dental disease is not evident as the cause of the abscess, transmucosal surgical drainage may be done using ultrasound to select the most appropriate surgical approach. A small incision is made in the oral mucosa caudomedial to the maxillary second molar tooth. A sterile blunt instrument is then introduced into the incision, forced gently through the medial pterygoid muscle using a short finger stop so that damage to the globe does not occur. Purulent exudate should be collected for cytology and culture. The surgical wound should be allowed to drain on its own or with a drain positioned into the orbital space.

11. How do you differentiate an orbital abscess from orbital cellulitis?

Making a distinction between orbital abscess and cellulitis based on clinical signs and physical examination is virtually impossible. Ultrasound of the orbit should be done to differentiate orbital cellulitis from abscess. Diffuse orbital cellulitis produces a generalized loss of definition of the orbital tissues, resulting in the optic nerve and extraocular muscles being difficult to visualize when compared with the opposite eye. Cellulitis also may produce focal mass lesions that may be mistaken for a neoplasm. Abscesses are variable in appearance, but most are recognized as a hypoechoic area within a well-defined hyperechoic wall. The abscess wall may not be seen with ultrasound in all cases. When an orbital abscess is not evident ultrasonographically, broad-spectrum oral antibiotic and nonsteroidal anti-inflammatory drugs should be administered and the animal monitored closely for improvement of clinical signs. Frequent orbital ultrasound is recommended to determine if cellulitis is resolving, unchanged, or transformed into an abscess cavity. If unchanged or transformed to an abscess, or if clinical signs deteriorate, surgical intervention is indicated (see abscess) (Figs. 8 and 9).

12. What causes masticatory myositis?

Masticatory myositis is immune-mediated inflammation and swelling of the muscles of mastication (temporalis, medial pterygoid, and masseter) that has been reported in dogs. Cellular and humoral mediated destruction of type IIM myofibers (common to masticatory muscles) is thought to cause masticatory myositis. Because these muscles define the medial, ventral, and lateral borders of the orbit, inflammation imposes upon and compresses orbital structures, resulting in anterior displacement of orbital contents (exophthalmos and/or protrusion of the third eyelid) (Fig. 10).

13. How is masticatory myositis diagnosed?

Dogs with masticatory myositis may have either the acute or chronic form of the disease. Acute myositis is typified clinically by pain on opening the mouth, difficulty eating, swelling of the mas-

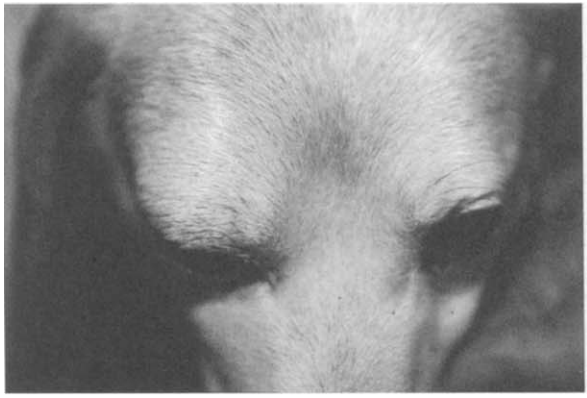


Figure 8. Orbital cellulitis from a dorsal view. Much pain is elicited upon opening the mouth, which stems from impingement of the coronoid process of the mandible on inflamed orbital soft tissue.

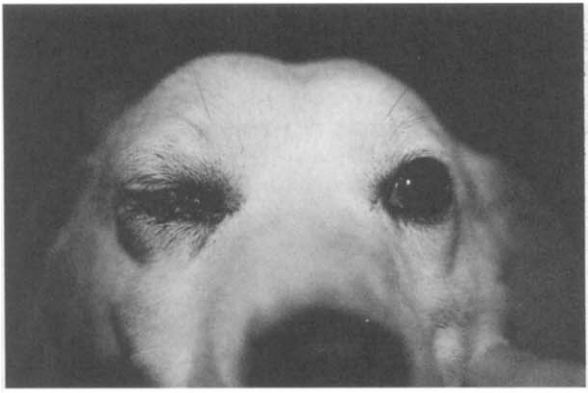


Figure 9. Orbital cellulitis (same case as Figure 8) from a frontal view. Retropulsion of the globe is usually restrictive.

Figure 10. Myositis causing exophthalmos and strabismus with lateral shift.

ticatory muscles, unilateral or bilateral exophthalmos, protrusion of the third eyelids, and conjunctival hyperemia and chemosis. Infrequently, vision may be compromised. Atrophy and loss of masticatory muscle mass, enophthalmos, protrusion of the third eyelid, pain or reluctance to open the jaw, and trismus typify the chronic form. Mean age of affected dog is 3 years; male and female dogs are affected equally. Definitive diagnosis is based on histologic evaluation of frozen muscle biopsies sent to specialized neuromuscular laboratories. Serum from affected dogs may also be submitted to these laboratories to determine if circulating antitype IIM antibodies are present.

14. What is extraocular polymyositis?

Extraocular polymyositis is a rare, immune-mediated inflammatory myopathy that is limited to the extraocular muscles in dogs. Young, female golden retrievers are affected most frequently (median age of 8 months). An antecedent "stressor" (ovariohysterectomy, estrus, castration, boarding at a kennel) occurred within 14 days of the onset of clinical signs in 43% of affected dogs. The mononuclear cell infiltrate of extraocular muscles is composed primarily of CD3+ T lymphocytes and macrophages directed against fine extraocular myofibers. Affected dogs have axial exophthalmos, retraction of the upper eyelid, and absence of third eyelid protrusion, and dogs are not in pain. This disease responds to a prolonged course of topical and oral corticosteroids (Fig. 11).

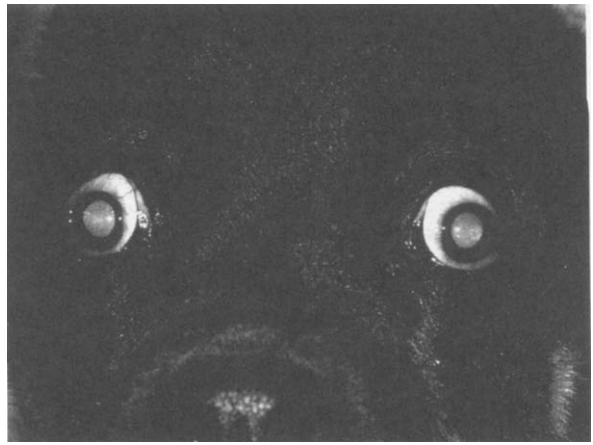


Figure 11. Extraocular polymyositis with the classic "bug eyes." Although this condition is usually seen in golden retrievers, it is also seen in other breeds such as this young rottweiler.

15. Are masticatory myositis and extraocular polymyositis the same disease?

Extraocular muscles do not contain type IIM myofibers. Type IIM myofibers are found only in specific muscles innervated by the mandibular branch of the trigeminal nerve. Although both diseases have similar inflammatory cell infiltrate within affected muscles, cellular and humoral immunity is directed at distinctly different muscle antigens. Age, breed, and gender predilections also exist and are different for both diseases. Therefore, these two diseases are distinctly different immunologically and clinically.

16. How is zygomatic mucocele differentiated from zygomatic sialoadenitis?

The floor of the orbit, in most animals, is formed by the zygomatic salivary gland. A zygomatic mucocele is a collection of saliva outside the salivary ductal system. Zygomatic sialoadenitis is inflammation of the zygomatic salivary gland. Zygomatic mucocele and zygomatic sialoadenitis may or may not have signs of ocular involvement, depending on severity of disease. Mucocele may protrude beneath the lower conjunctival fornix and appear as pale blue-gray when transilluminated. It also may appear as a fluctuant swelling beneath the lower eyelid or as a protrusion beneath the oral mucosa caudal to the maxillary molar teeth. Mucocele is usually nonpainful or minimally painful; however, clinical signs of pain similar to sialoadenitis may be pre-

sent if mucocele has associated inflammation. Fine-needle aspiration of a mucocele will produce a thick, tenacious, clear or rust-colored mucoid substance. Animals with zygomatic sialoadenitis exhibit signs of pain when the mouth is opened and may or may not have swelling along the side of the face ventral to the palpebral fissure. Affected animals frequently have thick, tenacious, mucoid saliva emanating from the zygomatic salivary papillae. Orbital ultrasound is useful to differentiate mucocele (hypoechoic or anechoic cavity) from sialoadenitis (diffuse hyperechogenecity) (Fig. 12).

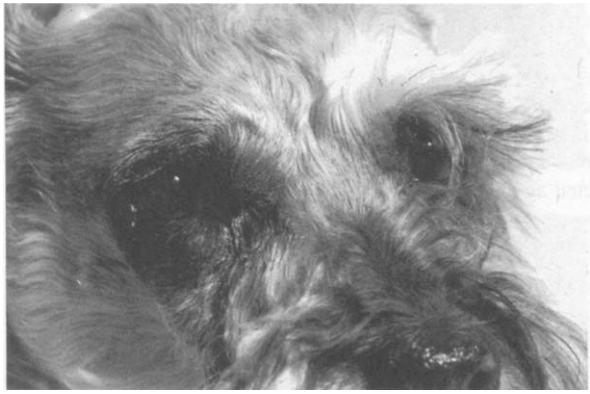


Figure 12. Zygomatic mucocele that was stubbornly recurrent after repeated surgeries.

17. How should zygomatic mucocele and sialoadenitis be treated?

Although surgical removal of zygomatic mucocele by orbitotomy is recommended in standard surgical textbooks, treatment with a broad-spectrum antibiotic resolves zygomatic mucocele in many instances. Culture and susceptibility testing of material collected from mucocele (aspirate) and sialoadenitis (collected from zygomatic papillae) should be done. When clinical signs do not improve within several days of medical treatment, surgical intervention may be necessary for the resolution of mucocele. Zygomatic sialoadenitis also should be treated with a broad-spectrum antibiotic or the antibiotics specified by culture and sensitivity. When exophthalmos is present, the cornea and conjunctiva should be treated topically with an ophthalmic ointment to prevent exposure and desiccation.

BIBLIOGRAPHY

1. Gilmour MA, Morgan RV, Moore FM: Masticatory myopathy in the dog: A retrospective study of 18 cases. J Am Anim Hosp Assoc 28:300–306, 1992.
2. Hendrix DVH, Gelatt KN: Diagnosis, treatment, and outcome of orbital neoplasia in dogs: A retrospective study of 44 cases. J Small Anim Pract 41:105–108, 2000.
3. Ramsey DT: Exophthalmos. In Bonagura JD (ed): Kirk's Current Veterinary Therapy, 13th ed. Small Animal Practice. Philadelphia, W.B. Saunders, 2000, pp 1086–1089.
4. Ramsey DT, Manfra Marretta S, Hamor RE, et al: Ophthalmic manifestations and complications of dental disease in dogs and cats. J Am Anim Hosp Assoc 32:215–224, 1996.
5. Ramsey DT, Fox DB: Surgery of the orbit. Vet Clin North Am Small Anim Pract 27:1215–1264, 1997.

49. THE ULTIMATE OCULAR HISTOPATHOLOGY

Ronald C. Riis, D.V.M., M.S., and Mary Lou Norman, B.S., H.T. (ASCP)

1. From a pathologist's standpoint, is an eye an unfortunate mixture of tissue?

Yes, because the sclera is a dense fibrous tissue through which fixatives permeate slowly. Uveal retinal tissues have high metabolic characteristics which deteriorate rapidly and must be fixed quickly. If these important factors are not addressed, then histopathology of the eye is a study of postmortem artifacts.

2. What is the first secret of meaningful results?

First and foremost, the eye must be removed rapidly after death, at necropsy, or rapidly at surgery. Trim off extraocular adnexa, fat, muscle, and promptly immerse in a fixative.

3. Is there anything special about enucleation techniques?

Although the enucleation must be done quickly, it must be done carefully to minimize the production of artefacts. It is particularly easy to produce an artifactual retinal detachment. Although this can be determined histologically from an antemortem lesion, it is better to view and analyze the photoreceptors intact and not around artifacts.

4. What is the best fixative for a globe?

Zenker's fixative (containing mercury) is the best considering the tissues being evaluated. The fixative requires adding glacial acetic acid just before use, and this can be seen as inconvenient. Bouin's fixative has been used with good results and compliance from necropsy. Davidson's fixative is also among those that penetrate rapidly into the eye for excellent results.

5. What should be the fixative to globe ratio?

This is a very important point. The volume of fixative should be 20 times the volume of the tissue being fixed.

6. Once the globe is rapidly removed, trimmed, and immersed in fixative, what is required next?

The globe will float in Zenker's glacial acetic acid and Bouin's fixatives only until the fixative penetrates equally into the globe chambers. Once the globe sinks to the bottom, it is fixed. However, it is not recommended to leave it in the fixative for more than 24 hours. The globe should be washed in running tap water and stored in 70% alcohol. If Bouin's is used, the picric acid will color the alcohol yellow. Changes of alcohol are recommended until the alcohol remains clear.

7. Can the globe be kept in fixative until processed?

This is not ideal because prolonged exposure to Zenker's or Bouin's fixatives causes the lens to become rock hard, adding another artifactual challenge to the sections. The exception to this is 10% neutral buffered formalin.

8. What about cutting a hole in the globe to allow fixatives to enter or injecting fixative into the globe?

Both the procedures are unnecessary if Bouin's or Zenker's fixatives are used. It is actually harmful to do either one of these because it adds an iatrogenic lesion that may be noted.

9. What fixative can be used if Zenker's or Bouin's are not available?

Ten percent neutral buffered formalin is better than no fixative. Formalin is good for the cornea and lens, but terrible for the retina. If formalin is all that is available, it can be injected into

the vitreous to expedite retinal fixation. Artifactual changes of the retinal architecture limits the retinal evaluation due to formalin.

10. Many times we have no control over the time of death and fixation. What harm has been done?

The histologic examination of eyes from animals that have been dead for several hours is often a useless exercise. Considerable artifact becomes prominent within the lens and retina in a very short time. The only exception may be eyes infiltrated with tumors.

11. Can an eye be sent to any pathology laboratory for processing?

It is recommended sending the globe in 70% alcohol (after being in Bouin's or Zenker's fixative) or 10% formalin to a laboratory of notable ocular experience. The processing, embedding, and sectioning after proper fixation involves considerably more expertise than other tissues. The analysis of the final slide should be completed by an individual trained in veterinary ophthalmic pathology.

12. What time frame should be expected to receive an answer back after submitting a fixed globe?

Generally, a period of 2 weeks is required for globe sections. If tumors are attached to the globe, they can be processed separately to expedite the turnaround time.

13. Can frozen globe sections be done for a quicker diagnosis as is done with other tissues?

No, globe sections cut at frozen thickness are approximately 10–15 μm. These sections are too thick for retinal evaluation. The nature of the globe dictates paraffin infiltration to support the lens and keep the retina in place for sections at approximately 5 μm.

14. What are the formulations of the fixatives discussed for light microscopic histopathology?

FIXATIVE	INGREDIENTS	AMOUNTS	DIRECTIONS
Zenker's stock fixative	Distilled water	1 L	Stir all ingredients until dissolved; add 5 ml of reagent-grade glacial acetic acid to 95 ml of stock solution just before use to prevent turbidity and a dark brown precipitate (due to the toxicity of mercury, zinc chloride can be substituted without compromise).
	Mercuric chloride	50 g	
	Potassium dichromate	25 g	
	Sodium sulfate	10 g	
Bouin's fixative	Saturated picric acid in distilled water (21 g in 1 L)	1500 ml	
	Formalin (37–40%)	500 ml	
	Glacial acetic acid	100 ml	
Neutral buffered formalin (10%)	Formalin (37–40%)	100 ml	
	Distilled water	900 ml	
	Sodium phosphate, monobasic, monohydrate	4.0 g	
	Sodium phosphate, dibasic, anhydrous	6.5 gm	

15. Can the above fixatives be used if the tissue requires transmission electron microscopy?

Transmission electron microscopy fixatives must be made fresh according to the requirements of the laboratory. The above fixatives are not ideal for electron microscopy.

BIBLIOGRAPHY

1. Peiffer RL Jr, Wilcock BP, Dubielzig RR, et al: Fundamentals of veterinary ophthalmic pathology. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd ed. Baltimore, Lippincott Williams & Wilkins, 1999, pp 355–425.
2. Sheehan DC, Hrapchak BB: Theory and Practice of Histotechnology, 2nd ed. Columbus, OH, Battelle Press, 1980.
3. Yanoff M, Fine BS: Ocular Pathology: A Color Atlas. Baltimore, Lippincott Williams & Wilkins, 1988.
4. Yanoff M, Fine BS: Ocular Pathology: A Text and Atlas, 3rd ed. Baltimore, Lippincott Williams & Wilkins, 1989.

50. MYTHS AND MISCONCEPTIONS IN VETERINARY OPHTHALMOLOGY

Gary L. Blanchard, D.V.M., M.S.

To paraphrase Voltaire, veterinarians are people who treat disease of which they know little; with drugs of which they know less; in patients of which they know nothing. The practice of medicine has many times been described as both an art and a science. The result of which has been many anecdotal treatments and interventions from which clients expect to receive benefit for their pet. The client also has developed some curious, amusing, and entertaining misconceptions of medicine. These perceptions are very prominent in veterinary ophthalmology as a result of the mystique of the eye and human's own great dependence on this sensory organ. These perceptions are not only in the mind of the lay person, but also in that of the professionals. The following are some of the classic misconceptions and misguided comments overheard in the clinic:

Old English sheepdogs will go blind if you trim the hair from their eyes.
All cocker spaniels have red eyes.
Both his parents are normal. How can he have progressive retinal atrophy [insert your favorite inherited disease]?
Do you use lasers for cataracts?
My dog has only 90% vision; he only catches 9 out of 10 cookies. [heard after cataract surgery]
Will the vision leak out because of the corneal perforation?
His favorite color is red.
She doesn't like white coats.
He has never bitten anyone except his doctor.
Can you transplant a new eye?
Retinal atrophy is related to light exposure due to his dilated pupils.
Since his eyes are so big [buphthalmia], can he see better?
He's overweight because he can't see.
Brown tears are normal in the Persian [Himalayan, etc.].
The eye medication didn't work, so I stopped using it.
I didn't give him his glaucoma medication today so you can see him without it.
My brother is a doctor [or nurse, EMT, animal technician, fireman, school teacher—add your favorite], and he said it's . . ..
My breeder says his animals never had PRA [cataracts, etc.] in their lines.
Will he have dry eye if you treat him for glaucoma?
My doctor said blue eyes are normal.
Will my PRA dog see better if I leave the lights on?
He can see the neighborhood cat [squirrel, etc.], but he constantly bumps into things.
Shar-peis are supposed to have small eyes.
He doesn't like television anymore; can he still see?
Their eyes [brachycephalics] are prominent, so they'll see better.
She has always had wet eyes [tearing], so I guessed she would have glaucoma.
Dogs with blue irises see better.
Could my cat have caught herpes from me [or vice versa]?
Cats with crooked tails are always cross-eyed.
He's such a good watch dog, he even sleeps with his eyes open.
My diabetic can't see; that's why we can't regulate his insulin.
His mother had cataracts when she was four. We want to breed him before he goes blind.
He'll be able to see with the "new" [prosthetic] eye, won't he?
When she's in the car, my dog sees everything, especially with her head out the window.

"REMEDIES"

The various therapies for ocular and medical conditions add to the mystique of medicine. The Egyptians once distilled sacred bull urine as a treatment for cataracts. Vitamin E and selenium elixirs and beef liver extracts have also been recommended to treat cataracts.

Dr. Louis Dor of Lyons (La Clinique Ophthalmologie, 10 Janvier 1911) published a cure of incipient cataracts in man with an iodine salt, as recommended by Bodal. He based his investigations on the well-established idea that cataract is produced by a ferment that passes into the aqueous humor, when it ought to remain in the blood. The ferment, which is a hydrating one, determines the hydration of the albumin of the lens. With a view to the destruction of this ferment, Dor experimented with many drugs and combinations and proposed the following as the best:

Desiccated sodium iodide—5 gm
Crystallized calcium chloride—5 gm
Distilled water—400 gm

He averred: "With this solution, one can check the progress at least eight cataracts out of ten, can cure one, and can expect failure in the tenth. It is used in the form of an eye bath and should be continued over a long period, dropped, and then recommenced."

In 1914, Gray stated, "the different methods of surgical intervention employed in human cataract practice have all been used in dealing with animals (i.e., discission, reclination or "couching," depression, or displacement and extraction); and it must be admitted that all who have attempted these operations are unanimous in stating that conditions are in every way less favorable to success than in man."

Killed typhoid bacillus was once injected and utilized as "fever" therapy for uveitis. It is now known that this stimulated ACTH release and hence a nonspecific steroidal anti-inflammatory response. Phlebotomy (bleeding) was once popular therapy. Today, this sometimes parallels what is called "diagnostics" by internists. While some therapies and concepts appear quaint, archaic, or obsolete, remember Herbert Spencer, "There is a principle which is a bar against all arguments and which cannot fail to keep man in everlasting ignorance. That principle is contempt prior to investigation."

A TRIBUTE TO DOGS' EYES

"Far more than by his bark a dog communicates through his eyes—from a soulful half-raised eyebrow when denied a special treat to the wide and sparkling 'Yippee! We're going for a walk!'. Perhaps nothing can wrench the heart of a dog lover more than the pitiful, hardly-daring-to-be-hopeful gaze of an abandoned dog waiting to be adopted." *(J.R.E.)*

"One of the saddest sights is to see a Dane ill. Their big eyes are a picture of misery, for make no mistake, a sick Dane puts on everything it can to get all the love and sympathy when it feels ill." *(Barbara Woodhouse, 1910–1988)*

"It is by muteness that a dog becomes for one so utterly beyond value; with him one is at peace, where words play no torturing tricks . . .. Those are the moments that I think are precious to a dog—-when, with his adoring soul coming through his eyes, he feels that you are really thinking of him." *(John Galsworthy)*

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