OCULAR DISEASE IN THE EXOTIC COMPANION MAMMAL: SEEING BEYOND THE EYES

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GENERAL ADAPTATIONS AND CONSIDERATIONS

Ophthalmic examinations in exotic companion mammals can be performed as in other species but may be more challenging due to the small patient size. Indirect ophthalmoscopy can be beneficial as it enlarges the view for the examiner. Normal values are reported for Schirmer tear test, but the strips are often too large to be used in most species, although they can be cut in half lengthwise for smaller patients. A phenol red thread test is preferred for these small patients.

Most of the patients discussed here are prey species and have adaptations that may affect ocular evaluation. Many of these animals will not have a menace response. Some have greater corneal thickness or decreased cor-neal sensitivity than humans or other mammals and so will not blink in response to small fibers or fur on the corneal surface. Others, such as rabbits, produce a thicker lipid component in their tears, which reduces their blink frequency. Still others, such as rats, produce por-phyrin, so the production of red tears is a normal finding. Understanding these differences is essential to correct interpretation of the ophthalmic examination.

When choosing medications for the exotic companion mammal, it is important to consider potential drug sensitivity. Ophthalmic preparations can be absorbed systemically in the diseased eye, and they also can be groomed from the eye and ingested. Rabbits and rodents can suffer severe dysbiosis, so antibiotics such as penicillins, cephalosporins, erythromycin, lincomycin, tetracyclines, and macrolides should be avoided. Most of these animals are also highly sensitive to the adverse effects of steroids, which should be avoided in almost all cases unless absolutely necessary. Ferrets are the ex-ception, in which steroids are well tolerated in topical and systemic form.

Most surgical procedures performed on dogs and cats can also be performed on exotic companion mammals. The most common procedures performed are tarsor-rhapy and enucleation. Tarsorrhapy can be modified to use small pieces of red rubber tubing as stents, or in some animals stents can be avoided completely if the eyelids can be opposed without tension. In most of these animals a single suture will suffice for tarsorrhaphy.

Enucleation, which is removal of the eye leaving the surrounding structures intact, can be performed via either a transpalpebral or transconjunctival approach. Regardless of the technique used, it is essential to remove the globe, conjunctiva, and any glands that are present in order to prevent dehiscence or drainage. Exenteration—removal of eye and all surrounding structures such as the lids, fat, glands, and muscles—is gen-erally reserved for cases of neoplasia or abscessation in which there is involvement (or potential involvement) of the surrounding tissues. Miscosurgical instruments are recommended for small rodents. Rabbits and some rodents have a venous sinus behind the orbit that may hemorrhage during enucleation. Staying as close to the globe as possible minimizes this risk. It is not necessary to clamp or clip the optic nerve and surrounding vessels, although this may be performed if the nerve is acces-sible. Use caution, however, and do not apply traction on the globe because excessive traction can damage the nerve to the contralateral eye. Pressure is generally ap-propriate to stop hemorrhage and can be applied via sterile cotton applicator, or a small piece of cellulose sponge can be placed in the orbit before closing the lids.

Rabbit

The eyes of the rabbit are laterally positioned, enabling almost 360 degrees of vision. The large cornea occupies almost 30% of the globe. The lens is spherical. The retina is atapetal, and the fundus is merangiotic, where vessels are confined to a broad horizontal band (the larger of these vessels are readily visible macroscopically) coincident with the area of dispersion of the myelinated nerve fibers, which is unique among mammals. Pupils are round, irises are heavily pigmented, and eyes are very prominent and relatively unprotected by the bony orbit. Rabbits have a prominent functional nic-titans and 4 orbital glands: the Harderian, orbital, lacri-mal, and gland of the nictitans. The lacrimal gland pro-duces clear secretions, and the gland of the third eyelid produces milky secretions. Photoreceptors are 95% rods and 5% cones. The prominence of the eyes makes them more susceptible to injury and trauma. The rabbit cornea is less sensitive than that of humans, and their tear film has a high lipid component so they blink infrequently. However, the intraocular inflammatory cascade is rapid and there is greater aqueous fibrin production than in humans following injury or perforation. There is a retro-bulbar venous plexus, which is important when consider-ing enucleation in rabbits. The nasolacrimal duct has only 1 ventral punctum, which is located approximately 3 to 4 mm medial to the eyelid. The duct has two bends prior to exiting the nasal ostium; this increases potential for blockage by debris or exudate.

The lateral location of the eyes, along with the merangiotic fundus, is believed to provide the ability to visualize the horizon; vision is monocular laterally but binocular directly in front of the face and probably above and behind. One study suggested that rabbits are near-sighted when using binocular vision directly forward but farsighted when looking laterally. The majority of cones are green/blue sensitive, which is believed to enable them to detect predator movement in grass and sky.

Normal rabbit intraocular pressure (IOP) is 15 to 25 mm Hg. Normal Schirmer tear test values are 5.30 +/- 2.96 mm/min (range, 0–11.22 mm/min). Phenol red

thread test values are 20.88 mm/15 sec (range, 15–17 +/- 2.90 mm/15 sec).

Atropinesterase is present in about 40% of rabbits, so atropine may be ineffective at pupil dilation. Tropicamide can be used in these cases.

Guinea Pig

Guinea pigs have small eyes with rudimentary nictitans and a round pupil. The guinea pig eye has an atapetal retina with a paurangiotic fundus in which the retinal blood vessels are minute and restricted to the direct neighborhood of the optic disk. Normal Schirmer tear test values for guinea pigs are 3 mm/min (range, 0–12 mm/min). Normal phenol red thread values are 21 +/-4.2 mm/15 sec. Guinea pigs have a large intraorbital lacrimal gland and a prominent zygomatic salivary gland. They are a precocious species and eyelids are opened at birth. Corneas are less sensitive than in other species.

Chinchilla

The fundus of chinchillas is anangiotic (lacks blood vessels). The pupil is a vertical slit, and the nictitans is rudimentary. Chinchillas are precocious and have eyelids open at birth. IOP is 17.71 +/- 4.17 mm Hg for applanation tonometry, although values may be much lower using a Tonopen or rebound tonometry.

Rat/Mouse/Hamster/Gerbil

Rats and mice have small eyes, round pupils, and thin corneas. Hamsters and gerbils have larger eyes relative to body size, and hamsters have shallower orbits among the small rodents (and thus are more predisposed to proptosis). The fundus of all these rodents is holangiotic, with vessels radiating from the center, and lacks a tapetum lucidum. There are three orbital glands in rats: intraorbital, extraorbital, and Harderian. The Harderian gland is associated with the third eyelid and produces porphyrin, resulting in porphyrin-stained tears. Porphyrin production by the Harderian gland is controlled by parasympathetic innervation, so factors such as disease or stress may increase porphyrin production as well as the appearance of red tears. Rats have a retro-orbital venous plexus, whereas mice and hamsters have an orbital venous plexus.

Rats and mice have predominantly rods, and they have mainly ultraviolet green and blue vision, which is believed to be beneficial during dawn and dusk. They have very poor visual acuity but a wide field of view. Schirmer tear test values for the rat are 10.2 +/- 1.6 mm/min. IOP in rats is 15 to 30 mm Hg when measured via TonoPen and 13.0 +/- 1.2 mm Hg using rebound tonometry. IOP in mice is 10 to 20 mm Hg.

Ferrets

Ferrets have a small globe and laterally located, prominent eyes with a large spherical lens. The nictitans is prominent. The pupillary opening is elliptical along the horizontal axis. They have a holangiotic fundus in which the retina contains a compact plexus of blood vessels located in the major part of the light-sensitive portion of the retina and a tapetum lucidum. Rods are the predominant characteristic of the retina and also have an area centralis (area of increased photoreceptor density). The ferret has less visual acuity than the cat or human but has a lower light threshold, enabling improved vision at lower light. IOP via rebound tonometry is 14.07 +/- 0.35 mm Hg, similar to values obtained by applanation tonometry (14.5 +/- 3.27 mm Hg). Normal Schirmer tear test values are 5.31 +/- 1.32 mm/min.

Hedgehog

Hedgehogs have very small but prominent eyes that are unprotected by the bony orbit. Normal hedgehog eyes are mildly exophthalmic with strabismus. Visual acuity is fair, although other senses are primarily used for navigation. Hedgehogs have monochromatic vision and lack cones, although some of the rods contain cone-type nuclei. Mean Schirmer tear test values are 1.7 +/- 1.2 mm/min (range, 0–4 mm/min), and IOP is 20.1 +/- 4 mm Hg (range, 11.5–26.5 mm Hg).

Sugar Glider

Sugar gliders are nocturnal and have large prominent eyes with round pupils. They have a lacrimal gland, and the retina is avascular. A tapetum lucidum is present, and the predominant photoreceptors are rods.

DISEASES AND CLINICAL PRESENTATION

Rabbit

Bacterial **conjunctivitis** in rabbits has commonly been associated with *Staphylococcus* spp and *Pasteurella multocida*, but other infectious agents may be involved. Epiphora and reddened eyelid margins are the most common clinical signs, and infected rabbits often present with a clear to milky aqueous discharge that causes matting and crusting of the facial fur near the medial canthus. Initial treatment involves topical antibiotic ophthalmics such as ciprofloxacin. If the patient does not respond, then **dacryocystitis** (inflammation of the lac-rimal sac) or **dacryosolenitis** (inflammation of the naso-lacrimal duct) should be considered. With disease pro-gression, white threads of mucus or pus appear at the medial canthus or in the ventral conjunctival sac. The nasolacrimal drainage system provides a conduit for tears from the lacrimal lake to the nasal cavity. In rab-bits, a single ventral lacrimal punctum can be found 3 to 4 mm from the medial canthus lid margin. Facial derma-titis as a result of **chronic epiphora** secondary to dacryocystitis is not uncommon in rabbits and may result from thick inflammatory discharge or in association with an elongated incisor or third or fourth upper cheek tooth reserve crown, both of which may result in blockage of the nasolacrimal system. If lacrimation is excessive and nasolacrimal obstruction is suspected, fluorescein stain can be used to assess nasolacrimal duct patency. If obstruction is suspected, a topical ophthalmic anesthetic can be applied and in the sedated patient using a 23-gauge (0.64-mm) lacrimal cannula, or an appropriately sized IV catheter (with the stylet removed) can be used as an irrigating cannula to enter and flush (with 0.9% saline or eyewash solution) the proximal nasolacrimal duct via the punctum lacrimale, which is

located in the ventral lid margin several millimeters from the medial canthus. This will help remove purulent debris and pos-sibly relieve any blockage. Samples can be collected for cytology and culture. A retrospective study looking at the results of bacterial culture and sensitivity from naso-lacrimal duct flushes in rabbits with ocular and/or nasal discharge showed a prevalence of *P. multocida, Entero-bacter cloacae*, *Bordetella bronchiseptica, Moraxella* spp, *Pseudomona*s spp, and *Staphylococcus* spp.[1] The cannulation technique can be used to infuse iodine-based contrast medium in order to perform a contrast study to confirm more severe and permanent blockage, possibly the result of underlying dental disease, and aids in prognosis and long-term management.

Viral conjunctivitis resulting from herpes simplex virus has been reported in rabbits in association with close contact between affected rabbits and humans with herpes labialis.[2] In addition to bilateral conjunctivitis, infected rabbits show hypersalivation and severe signs of central nervous system dysfunction, including incoor-dination, intermittent myoclonic seizures, and opistho-tonos resulting from herpesvirus-associated nonsup-purative meningoencephalitis of cerebral grey matter.

Pseudopterygium or **corneal occlusion syndrome** is a rare condition in rabbits in which the conjunctiva grows over, but does not adhere to, the cornea, eventually leaving a small opening in the center before progression stops. The condition is acquired but the exact cause is unknown; however, this sudden growth of tissue could reflect an acquired inflammatory reaction or a hyperplastic response to changes in corneal sensiti-vity.[3] Veterinarians have reported treating any underlying pathology and leaving the corneal membrane undis-turbed. The rabbits are pain free and remain unchanged on annual physical examinations. Surgical removal of the precorneal membrane has also been documented, but a high rate of recurrence is reported. Postoperative application of topical cyclosporine may be effective in preventing recurrence.

Ulcerative keratitis is relatively common in pet rabbits, with the normal lateral positioning of the rabbit eye predisposing to traumatic injury. Typical clinical signs include epiphora, conjunctivitis, blepharospasm, and corneal edema. A defect in the corneal epithelium and stroma may be observed, and application of fluorescein dye is recommended to visualize the extent and depth. Signs of anterior uveitis such as miosis and aqueous flare may also be present. Eyelid diseases such as **entropion** and **distichiasis** have been reported as causes of corneal trauma and ulceration and may be more common in giant breeds. Chronic dacryocystitis, keratoconjunctivitis sicca, and orbital disease resulting in exophthalmos and exposure keratitis are also possible underlying causes. Treatment involves determining and treating the underlying cause along with treatment of secondary infection and support of corneal health. Broad-spectrum ophthalmic antibiotic solutions, artificial tears, immune-modulating preps, autologous serum, and anti-inflammatories have all been advocated depending on the underlying cause and severity of disease.

Spontaneous chronic corneal epithelial defects (SCCED), also known as indolent ulcers, have been well described in dogs.[4,5] However, these chronic, superficial, nonhealing corneal ulcers have not been well described in rabbits. The authors have seen several cases in rabbits that present with blepharospasm, conjunctival hyperemia, corneal edema and neovascularization, and ocular pain associated with these nonhealing ulcers. In dogs, classic histopathologic features include nonad-herent, dysplastic epithelium adjacent to the ulcerated region, loss of basement membrane, the presence of a hyalinized, acellular zone in the superficial stroma, and an abnormal nerve plexus in the anterior stroma surrounding the erosion. Reported surgical therapies include debridement, anterior stromal puncture techniques (grid keratotomy, multiple punctate keratotomy), third eyelid flaps, temporary tarsorrhaphy, application of cyanoacrylate tissue adhesives, thermal cautery, and superficial keratectomy. More recently, the use of a handheld device (Algerbrush) for diamond burr mecha-nized debridement of the cornea in cases of SCCED has been described.[5] The burr is passed over the corneal ulcer bed in multiple circular or wave-like passes, removing nonadherent epithelial tissue until stable epithelium is encountered. This technique has been used by the author (PGF) for successful resolution of a rabbit SCCED. Ophthalmologists have suggested that the diamond burr creates micro-erosions of the base-ment membrane that contribute to an alteration of corneal topography, which aids in the adhesion of new epithelial cells, and that the technique may contribute to fibrosis and improved epithelial adhesion strength.

Cataracts may be seen in mature rabbits as part of the lens aging process, but they have also been associated with *Encephalitzoon cuniculi*, a microsporidial obligate intracellular parasite. As the lens has no independent blood supply, it is theorized that *E. cuniculi* infection of the lens occurs in utero. The granulomatous inflammation associated with *E. cuniculi* may result in lens rupture leading to **phacoclastic uveitis**. Topical ophthalmic corticosteroids may be indicated, along with benzimadazole therapy if phacoclastic uveitis is suspect-ed. However, other authors dispute the use of steroids in any case and prefer flurbiprofen.

Exophthalmos can occur in rabbits due to ocular, periocular, or systemic disease. Ocular and periocular disease results in unilateral exophthalmos, with the differential diagnosis including retrobulbar abscess (most often secondary to dental infection), neoplasia, salivary mucocele, and trauma. Bilateral exophthalmos can occur secondary to engorgement of the orbital sinus (retro-bulbar venous plexus located behind the globe), which is most often the result of cranial thoracic disease (eg, thymoma, lymphoma, abscess) causing pressure on the vena cava.

Glaucoma can also occur in rabbits, usually associated with buphthalmos. This is reported in rabbits and it is important to differentiate from exophthalmos. In many rabbits glaucoma is attributed to a recessive gene

known as the *bu* gene (for buphthalmos), which may be more prevalent in New Zealand white rabbits but may occur in any breed. Diagnosis is via measurement of IOP; the unaffected eye can be used for comparison. Manage-ment is similar to other species.

Guinea Pig

Chlamydial conjunctivitis associated with *Chlamydo-phila caviae* is the most common cause of infectious conjunctivitis in guinea pigs. Spread is via direct contact or aerosol. Common in guinea pigs 4 to 8 weeks old, clinical disease most often results in inflammatory con-junctivitis (mild to severe) along with signs of rhinitis (sneezing, clear to mucopurulent nasal discharge). Polymerase chain reaction testing is the most reliable method of diagnosis. Antichlamydial therapy with sys-temic tetracyclines and ophthalmic ciprofloxacin are the treatments of choice, although tetracyclines can cause bacterial gastrointestinal dysbiosis. Concurrent bacterial infections may worsen clinical signs and can lead to development of uveitis or a **corneal stromal abscess** characterized by a focal corneal stromal infiltrate (yellow or white) that varies in size and can affect any stromal to endothelial level of the cornea. Samples for cytology and culture and sensitivity can be obtained by scraping the lesion. Aggressive systemic and topical antibiotic therapy is indicated. Keratectomy and conjunctival graft placement should be considered with corneal abscesses that do not respond to medical therapy.

Pea eye, a permanent protrusion of the conjunctival sac, is considered an inherited trait in guinea pigs and may be associated with fat deposition. In general, affected guinea pigs do not seem uncomfortable and can thrive without treatment. Alternatively, surgery may be performed to remove these conjunctival protrusions. **Prolapse of the infraorbital gland of the third eyelid** (cherry eye) can look similar to pea eye and is treated surgically by returning the prolapsed gland to a deeper position with suture techniques employed as for the same condition in the dog.

Heterotropic bone formation (formerly **osseus choristoma**), an ossification of tissue at the iridocorneal angle, may appear as a ring of irregular opaque material. The ciliary body is the most common site of choristoma development and is often an incidental finding in clini-cally normal guinea pigs. The exact cause is unknown, but the concentration of plasma ascorbic acid into the aqueous humor and its promotion of ciliary body ossifi-cation has been proposed. No treatment is indicated, but monitoring for signs of glaucoma is recommended.

Dermoid, a congenital area of normal skin component tissues, may be found involving the cornea or conjunct-tiva in both guinea pigs and rabbits. Keratectomy of the abnormal tissue is the treatment of choice.

Chinchilla

Ocular disease is uncommon in chinchillas, with epi-phora and cataracts being the most commonly reported clinical complaints. **Epiphora** has been associated with environmental irritants (eg, dust bath material); infectious conjunctivitis from *Pseudomonas* spp, *Staphylococcus* spp, and *Corynebacterium*; and dental disease, most commonly elongation of the maxillary molar reserve crowns.

Rat/Mouse/Hamster/Gerbil

In rodents the Harderian gland, a lacrimal structure located posterior to the globe in the orbit, contains por-phyrin, a red-brown pigment. As a result, overflow of tears (epiphora) resulting from ocular irritation, naso-lacrimal duct inflammation, and inflammation of the sali-vary or lacrimal glands is often associated with **red tear staining of the face.**

Dacryoadenitis, inflammation of the lacrimal system and, most importantly, the Harderian gland, is usually associated with **sialodacryoadenitis virus**, a coronavirus that is readily transmitted between rats by direct contact, aerosol, or fomites. Rhinitis resulting in sniffling is usually followed in several days by unilateral or bilateral blepharospasm and photophobia. Interman-dibular swelling resulting from involvement of the sali-vary glands is also frequently seen. Other secondary conditions include keratitis, conjunctivitis, uveitis, exoph-thalmia, and possible multifocal retinal degeneration.

Mycoplasmosis is a primary cause of **conjunctivitis** in rats and mice and may also cause dacryoadenitis. Tetracyclines are the treatment of choice. Other bacteria implicated in rat conjunctivitis include *Pseudomonas* spp, *Salmonella* spp, *Streptococcus* spp, and *Coryne-bacterium.* Treatment is based on results of culture and sensitivity testing.

Microphthalmos is seen periodically as an incidental congenital finding in rats and mice.

Cataracts, both congenital and due to aging, may occur spontaneously in rats.

Corneal dystrophies, characterized by punctate white opacities observed in the interpalpebral fissure, are common in both rats and mice. The opacities are often present shortly after birth and do not tend to progress. Elevated cage ammonia levels resulting from poor en-closure hygiene and its effect on the cornea has been proposed as one potential underlying cause. Treatment is not necessary.

Ferret

Ferret **infectious conjunctivitis** has been reported in association canine distemper virus, human influenza virus, systemic salmonellosis, and mycobacteriosis. With canine distemper, ocular signs are often the first signs of this nearly 100% fatal disease. At 7 to 9 days postex-posure a moderate to severe conjunctivitis with muco-purulent ocular and nasal discharge becomes apparent. As the disease progresses, so do the associated ocular signs, which may include blepharitis, corneal ulceration, keratoconjunctivitis sicca, and ankyloblepharon (partial or complete fusion of the eyelids). Ferrets are suscep-tible to several strains of human influenza virus, and early clinical ocular signs (most commonly conjunctivitis) can mimic early canine distemper. However, with influ-enza the conjunctivitis does not progress and responds to topical antibiotic ophthalmic therapy. *Mycobacterium genavense*

infection has been diagnosed in ferrets, with cases of disseminated mycobacteriosis showing gener-alized peripheral lymph node enlargement along with a proliferative lesion of the conjunctiva and nictitating membranes resulting in serous ocular discharge. Defini-tive diagnosis is based on histopathology and sequence analysis of 16S rRNA amplicons from formalin-fixed, paraffin-embedded tissue. Infected ferrets have been treated successfully using rifampicin.

Spontaneous **cataracts**, of congenital, hereditary, or acquired origin, have been reported in ferrets. Cataracts in ferrets usually involve both the cortex and nucleus of the lens, with the exact cause unknown. Inherited, genetic, and nutritional causes have all been postulated.

Zygomatic salivary gland mucocele and malignant lymphoma involving the orbit have both been reported in ferrets and may lead to **exophthalmos** and subsequent **exposure keratitis**.

Ophthalmia neonatorium is seen in kits aged 3 days to several weeks. Bacterial infection involving the conjunctival mucous membranes results in exudate accumulation behind the closed lids and is clinically recognized by unilateral or bilateral swelling of the sealed eyes. Treatment involves surgically separating the natural suture line between the eyelids and flushing away the purulent debris, followed by application of a broad-spectrum ophthalmic ointment for several days. Warm compresses and gentle manipulation of the lid margins may be used to prevent recurrence.

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