Clinical Approach to Canine Eyelid Disease:

BLEPHARITIS

Brian L. White, DVM, and Ellen B. Belknap, DVM, MS, Diplomate ACVO & ACVIM (Large Animal) Metropolitan Veterinary Hospital, Akron, Ohio

Eyelid disease is a common clinical challenge for general practitioners. Erythema, alopecia, edema, and conjunctival hyperemia are hallmark signs that occur due to pronounced vascularity of the eyelids. Inflammation may be focal or diffuse, affecting one or both eyes, with variable involvement of all 4 eyelids.

This article reviews common clinical presentations of canine blepharitis, and provides a systematic approach to eyelid disease for the general practitioner.

ANATOMY: REVIEW OF EYELIDS & TEAR FILM

Eyelids

The eyelids primarily:^{1,2}

• Protect and exclude light from the eye

- Produce a portion of liquid tears
- Provide a mechanism to spread preocular tear film across the cornea and bulbar conjunctiva.

Eyelids are upper and lower folds of skin continuous with the planes of the facial skin.¹ The edges of the upper and lower eyelids meet to form the *lateral* and *medial canthi* (**Figure 1**). The eyelids rest on the globe, and while the upper eyelid contains 2 to 4 rows of *cilia* (eyelashes), the lower eyelid does not contain cilia.¹ The modified sweat glands, referred to as the *glands of Moll*, open onto the eyelid margin near the base of the cilia. The *glands of Zeis* are sebaceous glands that are found in the tarsal plate and open onto the eyelid margin posterior to the cilia.

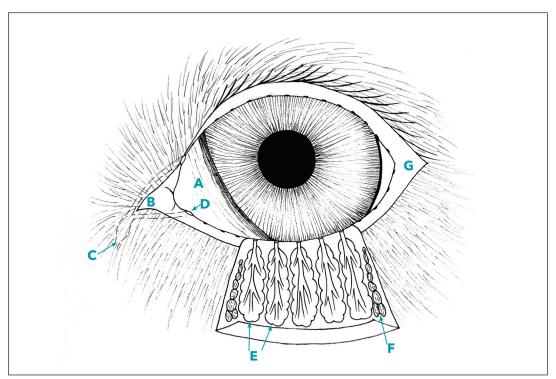


FIGURE 1. Anatomy of the eye: Third eyelid (A), medial canthus (B), nasolacrimal duct (C), inferior lacrimal punctum (D), meibomian glands (E), orbicularis oculi muscle (F), lateral canthus (G). Courtesy Dr. Lisa Wirth



The eyelids can be divided into 4 histologic layers (**Figure 2**):¹

- 1. Outermost layer contiguous with the skin
- 2. Orbicularis oculi muscle layer
- 3. Tarsal plate with stromal layer
- 4. Innermost palpebral conjunctival layer. Near the margins of both eyelids are *meibomian glands*, which form parallel rows of lobules containing duct openings that are visible at the eyelid margin. These ducts—*gland orifices*—are lined by keratinized stratified squamous epithelium. The *levator palpebrae superioris muscle*, innervated by the *oculomotor nerve*, is the main muscle responsible for elevation of the superior eyelid.

Tear Film

The precorneal tear film is classically depicted with 3 layers:1-3

- 1. Outer lipid layer: An oily substance (polar and nonpolar lipids) produced by the meibomian glands that prevents evaporation of aqueous tears; the meibomian glands are arranged linearly within the eyelid and secrete compounds (esters, hydrocarbons, free esterols, and fatty acids) that are fluid at body temperature.
- 2. Middle aqueous layer: Produced by the lacrimal gland and gland of the nictitans, and functions as lubrication and nutrition for the avascular cornea; it also provides a flushing mechanism for the corneal surface and has antibacterial properties, containing substances such as secretory IgA, lysozymes, lactoferrin, lipocalin, and interleukins, that are necessary for ocular immunity.
- 3. Inner mucin layer: Produced by conjunctival goblet cells (Figure 3), which are apocrine secretory cells found in highest density at the level of the conjunctival fornices, and composed of immunoglobulins, glycoproteins, salts, enzymes, and leukocytes; helps provide a smooth refractive surface over the cornea and anchors the aqueous tear film to the corneal epithelium to prevent desiccation.

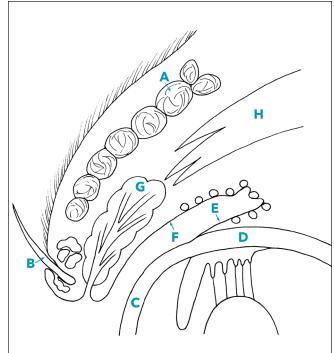


FIGURE 2. Anatomy of the eye: Orbicularis oculi muscle (A), cilium (B), cornea (C), sclera (D), bulbar conjunctiva (E), palpebral conjunctiva (F), meibomian gland (G), levator palpebral tendon (H). Courtesy Dr. Lisa Wirth

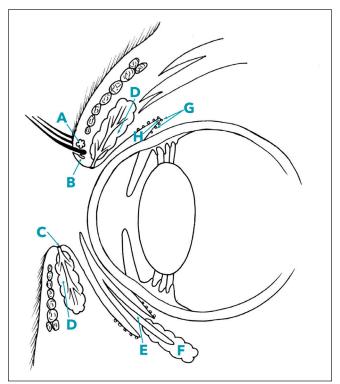


FIGURE 3. Anatomy of the eye: Gland of Moll (A), gland of Zeiss (B), orifice of meibomian gland (C), meibomian gland (D), cartilage of third eyelid (E), gland of third eyelid (F), goblet cells (G), conjunctival fornix (H). Courtesy Dr. Lisa Wirth



FIGURE 4. Ten-year-old castrated male mixed breed dog with a chalazion. Note the firm, nonpainful, and nonneoplastic swelling of the meibomian gland and focal blepharitis. Surgical treatment with a chalazion clamp and curettage was curative. A topical antibiotic preparation with a steroid was also administered due to marked inflammation after curettage. Courtesy Dr. Ellen B. Belknap



purulent discharge from one of the meibomian glands yielded Streptococcus species. A combination of oral antimicrobials, a tapering dose of steroids, and topical antibiotics with a steroid preparation was curative. Courtesy Dr. Ellen B. Belknap

BLEPHARITIS: CLINICAL REVIEW OF DISEASES

Chalazion

Description. A chalazion (Figure 4) is a firm, nonneoplastic, nonpainful swelling of the meibomian gland caused by accumulation of secretions. It results in chronic inflammation and a granulomatous reaction. Chalazia are commonly seen in older animals and may be associated with meibomian gland adenomas because they usually obstruct the duct, leading to glandular rupture.4

Diagnosis. Diagnosis is based on appearance of a focal, nonpainful swelling, with nodule formation at the level of the meibomian gland through the palpebral conjunctiva.

Treatment. Therapy is provided by:

- 1. Under local anesthesia with light sedation, attaching a chalazion clamp to affected region of the eyelid
- 2. Making an incision through the palpebral conjunctiva across granuloma with curettage
- 3. Applying a topical antibiotic/steroid ointment after curettage
- 4. Allowing the incision to heal by second intention
- 5. Using cryosurgery as adjunctive therapy to reduce the incidence of recurrence.

Bacterial Blepharitis (Staphylococcus & Streptococcus Species)

Description. Bacterial blepharitis (**Figure 5**) is characterized by:

• Pyogranulomas of the lid, which may involve

deeper parts of the eyelid and subcutaneous tissues; diffuse lid inflammation; and meibomianitis

- With chronic bacterial blepharitis, ulceration of eyelid skin margins, alopecia, and fibrosis
- In some cases, abscessation and impaction of the meibomian glands.

The condition is commonly bilateral but may have a unilateral presentation.3

Staphylococcus and Streptococcus species are the isolates most commonly involved in bacterial blepharitis of adult dogs.3 In puppies, bacterial blepharitis occurs as part of a juvenile pyoderma in which the entire skin of the head may be involved, with multiple abscesses caused by Staphylococcus species.3,5

The pathogenic mechanism is related to bacterial presence and the immune-mediated reaction induced by their toxins.^{3,5,6} There is no defined breed or sex predilection.

Diagnosis. Diagnosis includes:

- Biopsy with histopathologic examination to reveal microabscesses and associated cocci3
- Impression smears of skin lesions affecting eyelids, which demonstrate large numbers of cocci with presence of neutrophilic inflammation^{3,6}
- · Culture and susceptibility testing of expressed material.

Treatment. Culture and susceptibility testing reveals directed antimicrobial therapy, and systemic treatment with cephalexin for at least 3 weeks is most common. If inflammation and ulceration are



FIGURE 6. Three-year-old spayed female mixed breed dog with parasitic blepharitis (*Demodex* species). Note the circumferential alopecia, crusting, discharge, and erythema. A secondary bacterial colonization of the eyelids is present. Skin scraping and trichogram yielded numerous *Demodex* mites. Oral antimicrobial therapy combined with oral and injectable ivermectin was curative. *Courtesy Dr. Kevin Shanley*

severe, a short tapering course of corticosteroids can be initiated. Since staphylococcal toxins may have a necrotizing effect, topical corticosteroids may be beneficial. With therapy, improvement is usually observed within 7 to 10 days.

Parasitic Blepharitis (*Demodex, Sarcoptes*, & *Cuterebra* Species)

Description. Parasitic blepharitis is most often caused by infestation with *Demodex* and *Sarcoptes* species,⁵ with *D canis* (**Figure 6**) most commonly isolated.

Localized demodicosis occurs in animals younger than 10 months of age, with lesions characterized by circumscribed alopecia, mild erythema, and scaling, which may be unilateral.⁵ Lesions can often be complicated by secondary bacterial infections that lead to marked periocular swelling and moist erythematous lesions.⁵ In

older animals, demodicosis tends to be more generalized.

Sarcoptes scabei infection affecting the eyelids is characterized by adherent crusts, thickening, and partial alopecia, but it more commonly affects the elbows, ears, and hocks, with erythematous papules, crusts, intense pruritus, and alopecia. ^{5,7} Eyelid disease is unlikely to be seen alone with Sarcoptes infection. ⁵

Infestation with *Cuterebra* species has been reported in

the conjunctiva of a puppy.^{7,8} The larva enters the conjunctiva or eyelid surface and leaves a thick-walled identifying entry hole.^{7,8} *Cuterebra* larvae cause a focal parasitic blepharitis, with presence of a draining tract.

Diagnosis. Diagnostic approach is determined by suspected parasite species:

- *Demodex* species: Trichography with or without skin scraping and microscopic observation of mites
- Sarcoptes species: Clinical signs, skin scraping, or biopsy with microscopic observation of mites, or response to therapy
- *Cuterebra* species: Clinical signs and presence of a draining tract.

Treatment. Similar to diagnosis, therapeutic approach is specific to parasite species identified:

- Demodex species: Spontaneous regression of localized disease occurs, with treatment seldom required; systemic antibiotic therapy indicated if a secondary bacterial infection is present.
 Amitraz can be used if systemic disease is present.
 Ivermectin and moxidectin can also be used for treatment of systemic disease.
- Sarcoptes species: Sulfur dips or amitraz can be used with systemic disease without eyelid involvement.
 With eyelid involvement, consider using moxidectin or selamectin as approved therapies.
- Cuterebra species: Larva removal, topical antibiotic therapy for visible draining tract, and systemic antibiotic therapy.

Pyogranulomatous Blepharitis

Description. Pyogranulomatous lesions (**Figure 7**) are well circumscribed and contain predominantly macrophages and neutrophils. The disease can occur as part of a dermatologic condition, particularly in response to rupture of a hair follicle



FIGURE 7. Six-year-old spayed female Irish setter with pyogranulomatous blepharitis. Note the well-circumscribed pyogranulomas, diffuse eyelid swelling, erythema, and edema of eyelid margins. Biopsy of one of the well-circumscribed lesions revealed granulomas with macrophages, neutrophils, and evidence of folliculitis. A combination of oral doxycycline, oral and topical steroids, and topical cyclosporine was used for initial management. Long-term management included azathioprine for additional immune suppression. Courtesy Dr. Ellen B. Belknap

or subsequent to meibomianitis. Rupture of the meibomian gland leads to release of sebaceous material into the palpebral tissue that causes an inflammatory response.

Pyogranulomatous blepharitis may be bilateral or unilateral, and clinical signs include exudative and ulcerative eyelid lesions, focal or diffuse eyelid swellings, conjunctival hyperemia, edema of the eyelid margins, and mucopurulent ocular discharge. ^{3,5,7,9} There is no well-defined breed predilection, but clinical reports indicate that dalmatians and miniature schnauzers may be overrepresented.⁹

Diagnosis. Diagnosis includes:

- Biopsy with histopathologic examination that demonstrates granulomas with macrophages and neutrophils, folliculitis, and meibomianitis;⁶ cocci may also be observed
- Impression smears of skin lesions that demonstrate marked numbers of neutrophils and macrophages, with or without cocci.

Treatment. Therapy includes:

- Initial management with doxycycline, oral corticosteroids, topical steroids, and topical cyclosporine⁹
- Long-term management with azathioprine for additional immune suppression.

Immune-Mediated Blepharitis Pemphigus Complex

Description. The pemphigus complex is a group of uncommon immune-mediated diseases with 5 described variants: vulgaris, foliaceous,

erythematosus, vegetans, and bullous. Vulgaris, foliaceous, and erythematosus are the most well-documented variants, with foliaceous most commonly seen in small animal patients. In all types of pemphigus, autoantibodies against the intercellular matrix of the epidermis lead to a type II hypersensitivity reaction, resulting in skin lesions. ^{6,7,10}

The pemphigus group can involve the mucocutaneous junctions, with inflammation and ulceration of the eyelids commonly seen.⁷ Facial lesions involving the eyelids (pemphigus foliaceous and pemphigus erythematosus) are characterized by pustules or vesicles that eventually rupture, leaving erosions, ulcers, crusting, scaling, and hypopigmentation.⁵ Pemphigus vulgaris (**Figure 8**) is the most severe type of pemphigus, in which the oral cavity, nail beds, skin, eyelids, lips, and nares are affected.⁶

Pemphigus foliaceous and pemphigus vulgaris can be fatal, while pemphigus erythematosus is a more benign condition that rarely produces systemic signs and responds well to treatment.³

Diagnosis. Biopsy with histopathologic examination is important for differentiation between variants:

- Pemphigus foliaceous: Neutrophils or eosinophils present within vesicle or pustule, intragranular and subcorneal acantholysis with cleft and vesicle formation, and acantholytic epidermal cells found at surface of erosions
- Pemphigus erythematosus: Lichenoid infiltrate of plasma cells, mononuclear cells, and eosinophils





FIGURE 8. Seven-year-old castrated male mixed breed dog with immune-mediated blepharitis (pemphigus vulgaris). Note the diffuse crusting, ulceration, discharge, and scales affecting both eyes and all 4 eyelids, and extending to the nasal planum and mucocutaneous junctions (**A**). Biopsy of an affected area on the nasal planum revealed vesicle formation, with basal epidermal cells arranged in a row of "tombstones." The inflammatory reaction was interstitial. Topical and systemic corticosteroids were used initially to control the disease, and long-term therapy may consist of immunosuppressive drugs, such as cyclophosphamide or azathioprine, and a consultation with a veterinary dermatologist. Close-up view of the left eye (**B**); note the diffuse crusting, ulceration, discharge, and scaling affecting the eye circumferentially. Courtesy Dr. David Wilkie

• Pemphigus vulgaris: Cleft and vesicle formation with suprabasilar acantholysis, basal epidermal cells arranged in row of "tombstones," and, sometimes, inflammatory reaction that is interstitial to lichenoid.

Treatment. Effective treatment depends on diagnosis of the particular pemphigus variant. General long-term treatment includes topical and systemic corticosteroids, combined with additional immune suppression through the use of cyclophosphamide, azathioprine, or cyclosporine for refractory cases. Blepharoplasty may be indicated for correction of cicatricial entropion.

Discoid Lupus Erythematosus

Description. Canine discoid lupus erythematosus (DLE) is a relatively benign skin disease that lacks systemic involvement.^{6,11} Pathogenesis is unclear, but photosensitivity may exacerbate the disease.⁵

DLE (Figure 9) has been associated with facial dermatitis consisting of crusts, depigmentation, erosions, and ulcers, which typically affect the nasal planum and muzzle, but eyelids and oral lesions are also documented.5,6,12

Diagnosis. Diagnosis includes:

History and physical examination with thorough



FIGURE 9. Three-year-old spayed female Akita with immune-mediated blepharitis (discoid lupus erythematosus). Note the crusts, depigmentation, and ulceration of the nasal planum with ocular involvement. Biopsy of the nasal planum revealed mononuclear cells and plasma cells around skin vessels, with pigmentary incontinence of the basal epidermis. Topical dexamethasone and cyclosporine were implemented for the ocular disease, while oral corticosteroids were administered long term to control the disease. Courtesy Dr. Brian L. White

evaluation of eyelids, facial skin, and muzzle

• Biopsy with histopathologic examination to identify focal thickening of basement membrane zone, marked accumulations of mononuclear cells and plasma cells around skin vessels, and focal hydropic degeneration of basal epidermal cells with pigmentary incontinence, where melanin granules are free in the dermis and macrophages, that is associated with damage to the stratum basale and basement membrane of the epidermis. Antinuclear antibody test results are not reliable.

Treatment. Treatment includes:

- Avoidance of exposure to sunlight
- Topical immunosuppressive drugs, such as cyclosporine or dexamethasone
- Systemic corticosteroids for refractory cases. Lifelong treatment is recommended.

Uveodermatologic Syndrome Description. Uveodermatologic syndrome (Figure 10) is an idiopathic condition theorized to have



FIGURE 10. Two-year-old castrated male Siberian husky with uveodermatologic syndrome. Note the ulceration, crusting, and depigmentation of all 4 eyelids and nasal planum. This patient presented for chronic loss of pigmentation around the nose and eyelids concurrent with blindness. Corneal edema, aqueous flare, and bilateral retinal detachments were observed on ophthalmic examination. Topical corticosteroids were initiated for uveitis, along with oral corticosteroids and azathioprine. Disease was severe and ultimately controlled, but blindness was irreversible. Courtesy Dr. Kimberly Coyner

TABLE 1.

Key Ocular Examination Findings: Uveodermatologic Syndrome

- Presence of aqueous flare
- Signs of uveitis, bullous retinal detachments, secondary cataract formation, and glaucoma
- Progressive depigmentation of iris and retinal pigment epithelium
- Development of hyper-reflective tapetal fundus, with vascular attenuation and optic nerve atrophy
- Gradual or rapid development of vitiligo and poliosis (ulcerative) restricted to the face, usually involving the eyelids

resulted from Th-1 lymphocytic cell, immunemediated attack on melanocytes in the uvea and skin.

The syndrome is characterized by bilateral panuveitis accompanied by facial poliosis and vitiligo. ^{13,14} Loss of pigmentation of the nose and eyelids is the primary clinical sign observed, and patients are often presented due to sudden blindness or gradual vision loss.

Dogs are usually affected in young adulthood, and ocular lesions are seen before dermatologic lesions. Dermatologic lesions usually affect the mucocutaneous junctions, with ulceration, crusting, and hypopigmentation of the eyelids. The condition is commonly bilateral, but unilateral disease has been reported.

Arctic breeds are overrepresented for this condition, including the Siberian husky, Alaskan malamute, and Akita, but the condition has been reported in golden retrievers, rottweilers, Shetland sheepdogs, and other breeds. 6,13,14,16

Diagnosis. Key ocular examination findings are listed in **Table 1**. No specific diagnostic test is available; findings on routine laboratory tests, including blood work, are typically unremarkable. The best information is provided by:

- · Clinical signs and breed predisposition
- Histopathologic examination of skin biopsy, which reveals lichenoid dermatitis, histiocytes, and giant cell infiltration, as well as decreased levels of melanin in the epidermis and hair follicles.

Treatment. Initial therapy involves immunosuppressive doses of oral prednisone with or without azathioprine and/or cyclophosphamide. Cyclosporine can also be used as adjunctive therapy, but the patient's size is a limiting factor in its use. The oral steroid dose should be tapered after 5 weeks of therapy (once azathioprine completes the lag period). Topical corticosteroids can be used for anterior segment lesions. Therapy is lifelong.

Eyelid Neoplasia

Description. Many different neoplasms affect the canine eyelids; most are locally invasive lesions that respond fairly well to conservative surgical procedures. Eyelid neoplasms can produce focal or diffuse blepharitis, depending on the location on the eyelid and behavior of the neoplasm.

Benign neoplasms are more common than malignant neoplasms, and epithelial neoplasms are more frequent than mesenchymal neoplasms. Most eyelid neoplasms occur in dogs older than 10 years of age, with the superior lid affected more often than the inferior lid. Common eyelid neoplasms are described in **Table 2** (page 78); however, mast cell tumors, histiocytomas, and hemangiomas/hemangiosarcomas also occur frequently.

Diagnosis. Diagnosis is based on appearance of eyelid neoplasm and invasiveness, while histopathologic examination of neoplasm after resection allows definitive diagnosis.

Treatment. Surgical excision (most common) and/or cryotherapy are performed. Consider debulking neoplasm if full surgical removal is not indicated. Surgical procedures depend on neoplasm size and involvement of lid margin:^{7,17}

 Eyelid masses involving up to 25% of the lid: Four-sided defect wedge (house shape) and V wedge are the best surgical procedures, which are performed by scissors and/or scalpel and should extend at least one meibomian gland beyond the



FIGURE 11. Thirteen-year-old spayed female Labrador retriever with a meibomian gland adenoma. Note the mass arising from the superior eyelid, erupting through the eyelid margin to the palpebral conjunctiva. The mass is causing local irritation characterized by conjunctival hyperemia and epiphora. Surgical correction, which was curative, with a 4-sided defect wedge was performed with careful consideration of the dorsal nasolacrimal puncta. Courtesy Dr. Ellen B. Belknap

TABLE 2. Common Eyelid Neoplasms⁷

NEOPLASM	NOTES
Meibomian gland neoplasms (Figure 11 , page 77)	 Include adenomas and adenocarcinomas Commonly erupt behind the eyelid margin through the palpebral conjunctiva Usually cause local irritation, resulting in epiphora, conjunctival hyperemia, pigmentation, and blepharospasm
Eyelid melanomas (Figure 12)	 Two forms: 1. Eyelid skin tumor with single or multiple pigmented neoplasms 2. Pigmented eyelid margin tumor with expansion in both directions More locally aggressive than meibomian gland neoplasms Significantly more benign behavior than melanomas that appear elsewhere (eg, mouth or other parts of skin)
Papillomas	 Represent approximately 10% to 20% of eyelid neoplasms Most commonly affect young dogs Viral origin and typically regress with time Intervention necessary only when corneal involvement with direct irritation present
Squamous cell carcinomas (Figure 13)	Do not routinely affect the canine eyelid Can be seen as proliferative ulceration
Fibromas or fibrosarcomas	Uncommon Primarily seen as subcutaneous masses affecting the eyelids

FIGURE 12. Ten-year-old spayed female mixed breed dog with melanoma. Note the large pigmented mass with ulceration. discharge, and hemorrhage causing local invasion of the inferior evelid and associated adnexal structures. Surgical correction with a reconstructive blepharoplasty



using an H-figure plasty technique was curative. Histopathologic examination was consistent with melanoma. No additional disease was found systemically. Courtesy Dr. Ellen B. Belknap



FIGURE 13. Eleven-year-old spayed female Labrador retriever with squamous cell carcinoma. Note the extensive ulceration and hemorrhage of the mass, which is affecting surrounding eyelids and invading the medial canthus and superior and inferior eyelid. Surgical correction with reconstructive blepharoplasty using a whole-lid graft technique was performed. Referral to an oncologist was recommended for further treatment. Courtesy Dr. Ellen B. Belknap

- neoplasm margins. The eyelid margin is apposed with a figure-of-8 suture pattern using 5-0 or 6-0 monofilament nylon. The 4-sided wedge technique is more advantageous because it provides equal tension across the defect and prevents an obvious notch defect, while the V wedge technique leaves a small notch after surgery.
- Eyelid masses involving 25% to 50% of the lid: A split or full-thickness graft is advised and H-figure plasty is preferred.
- Eyelid masses exceeding 50% of the lid: A semicircular skin flap is advised and permits medial movement of the eyelid to increase the size of the palpebral fissure.
- Eyelid masses involving between 60% and 90% of the lid: Reconstructive blepharoplasty is recommended with use of an H-figure plasty technique, sliding skin graft, sliding Z plasty, or whole-lid graft to successfully remove the eyelid neoplasm and preserve the portion of

the eyelid affected.

Eyelid neoplasms should be submitted for histopathologic examination to further characterize the neoplasm and provide information on surgical margins.

IN SUMMARY

Eyelid disease can be a painful condition in small animal species. Biopsy and clinical description can help differentiate among infectious, immune-mediated, and neoplastic eyelid disease. Many conditions can be treated effectively with medical therapy, and response to treatment can be an important diagnostic tool.

DLE = discoid lupus erythematosus

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BRIAN L. WHITE

Brian L. White, DVM, is an ophthalmology specialty intern at Metropolitan Veterinary Hospital in Akron, Ohio. His clinical interests include ocular manifestations of systemic disease and retinal disease. He received his DVM from Michigan State University and has a background in private practice emergency/critical care medicine.



ELLEN B. BELKNAP

Ellen B. Belknap, DVM, MS, Diplomate ACVIM (Large Animal) & ACVO, is an ophthalmologist at Metropolitan Veterinary Hospital in Akron, Ohio. She received her DVM from University of Georgia and completed a large animal medicine residency at Michigan State University before pursuing ophthalmology residencies at Auburn University and Ohio State University.

