

AAPSP
Australian Animal Pathology
Standards Program

**Veterinary Pathology Roadshow
2026**



Davis-Thompson
Foundation



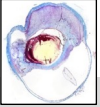
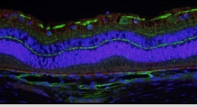
THE UNIVERSITY
WISCONSIN
MADISON

Pathology of the Cornea and Sclera

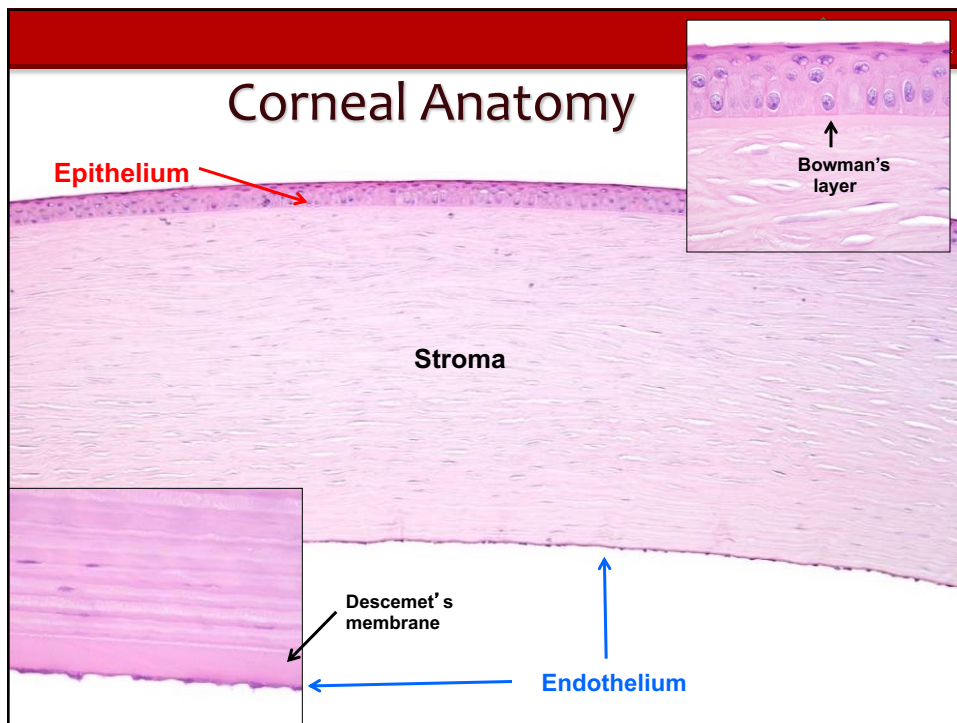
Leandro Teixeira DVM, MSc, DACVP

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Director of the Comparative Ocular Pathology Laboratory of Wisconsin - COPLOW
University of Wisconsin-Madison School of Veterinary Medicine




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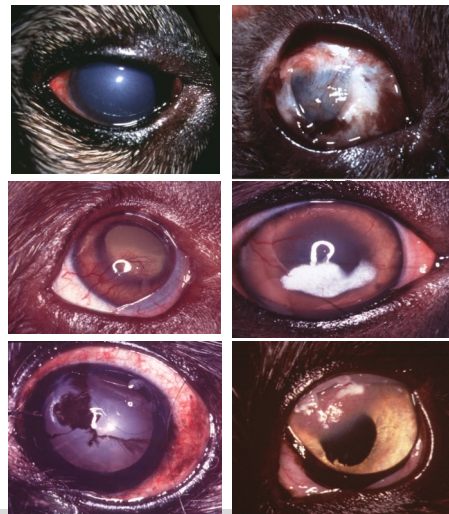
Corneal Optical Clarity

1. AVASCULAR - nutrition provided by:
 - Precorneal tear film
 - Aqueous humor
2. DEHYDRATED - maintained by:
 - Hydrophobic corneal epithelium
 - Corneal endothelial cation pump (Na/K ATPase)
3. Regular array of collagen lamellae and keratocytes

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Corneal Opacifications

- **Edema**
- **Scarring**
- **Blood vessels**
 - Neovascularization
- **Deposits**
 - Mineral, lipids
- **Pigment**
 - Melanin
- **Cellular infiltrates**
 - Inflammatory, neoplastic
- **Foreign bodies**

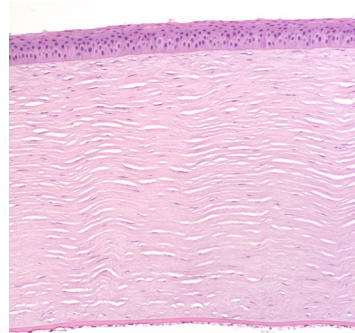


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Tissue response to injury

General Considerations

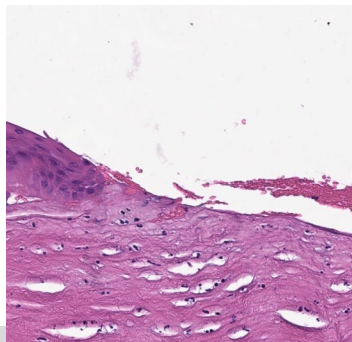
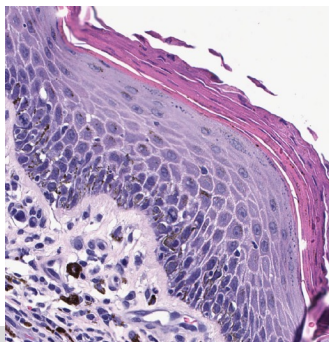
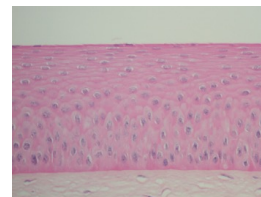
- Cornea has limited ways it responds to injury
- Cornea has limited healing capacity
 - Balance between tissue reaction and maintenance of optical clarity



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Response to injury - Corneal epithelium

- Hyperplasia
- Keratinization
- Necrosis (Erosion / ulceration)
- Atrophy



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Response to injury - Corneal Stroma

Stromal Neovascularization

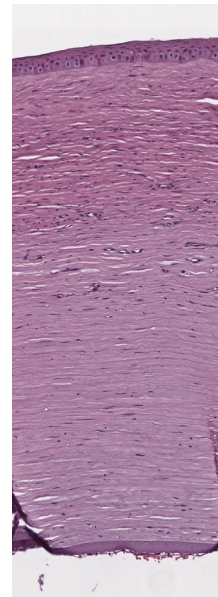
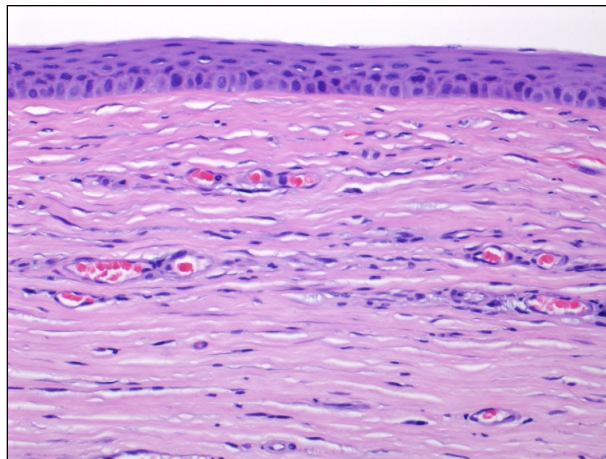
- Begins 48-72 hours after injury
- Progresses up to 1mm/24h
 - *Approx. 1 corneal thickness / day*
- May be superficial, midstromal or deep, depending on the cause
- Midstromal neovascularization can be secondary to uveitis



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Response to injury - Corneal Stroma

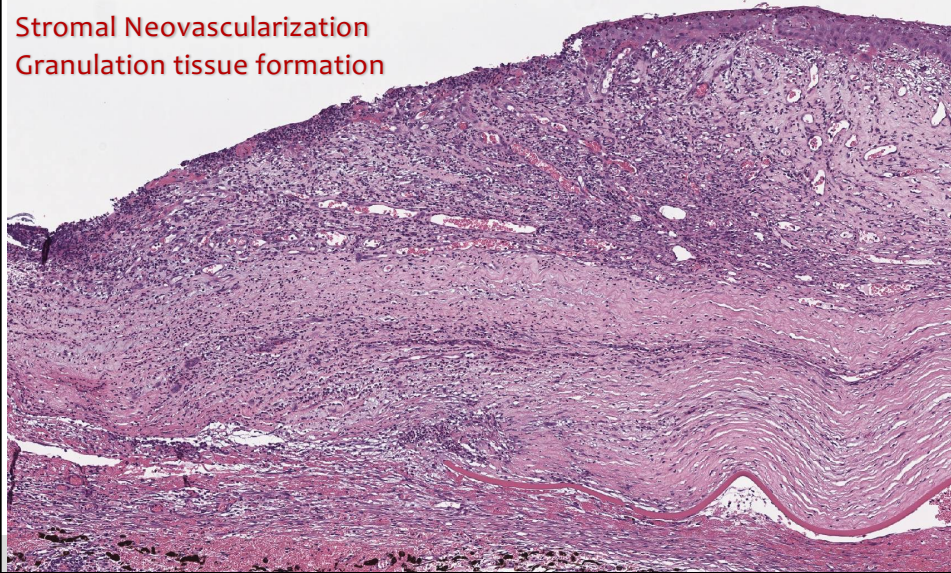
Stromal Neovascularization



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Response to injury - Corneal Stroma

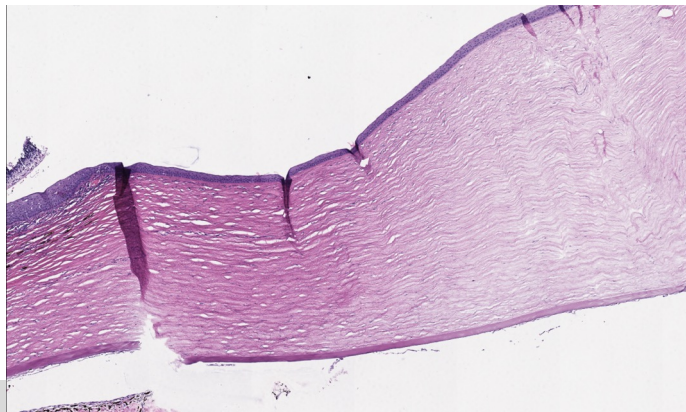
Stromal Neovascularization
Granulation tissue formation



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Response to injury - Corneal Edema

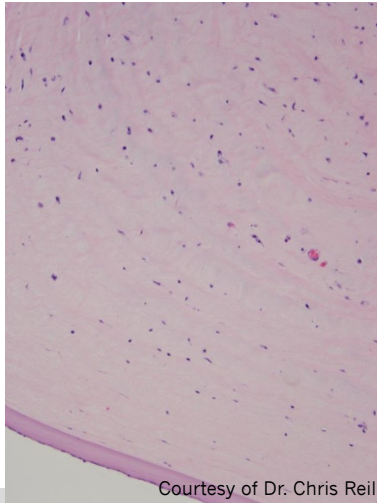
- Loss of normal lamellar arrangement of the stroma
- Must be differentiated from fixation artifact causing separation of lamellae



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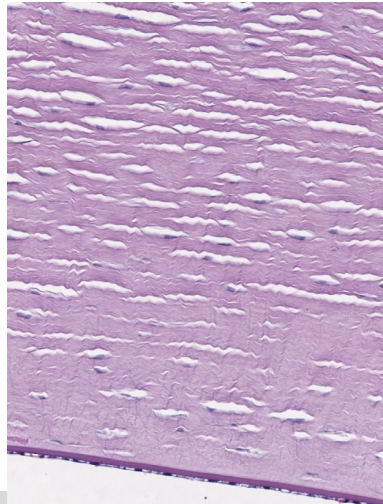
Response to injury - Corneal Edema

Edema



Courtesy of Dr. Chris Reilly

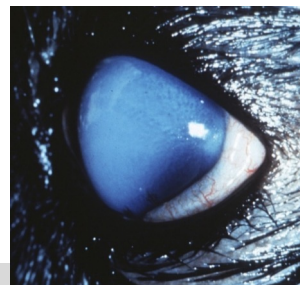
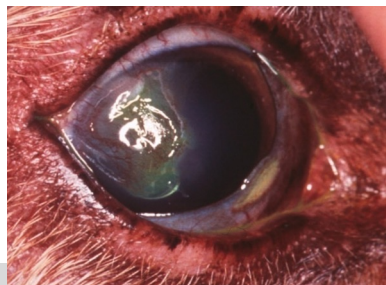
Artifact



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Response to injury - Corneal Edema

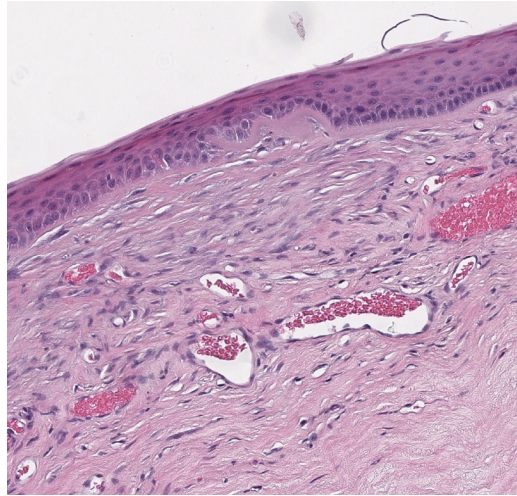
- Epithelial defects (ulcers): superficial stromal edema
- Stromal vascularization - leaky blood vessels
- Endothelial defects - deep stromal edema
 - Uveitis
 - Mechanical trauma - lens luxation
 - Glaucoma



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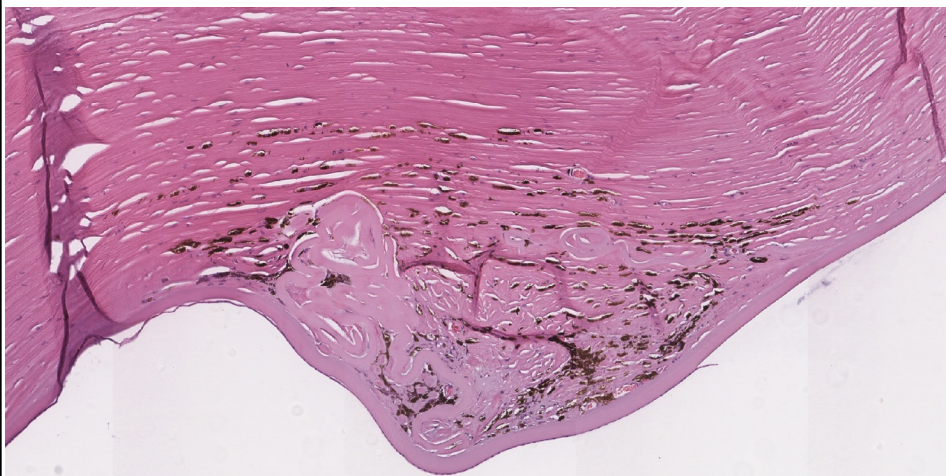
Corneal Healing and Repair

- Healed corneal epithelium may be irregular
- Basement membrane may be thickened
- Stromal heals mostly with fibrosis +/- neovascularization
- Descemet's membrane can be doubled



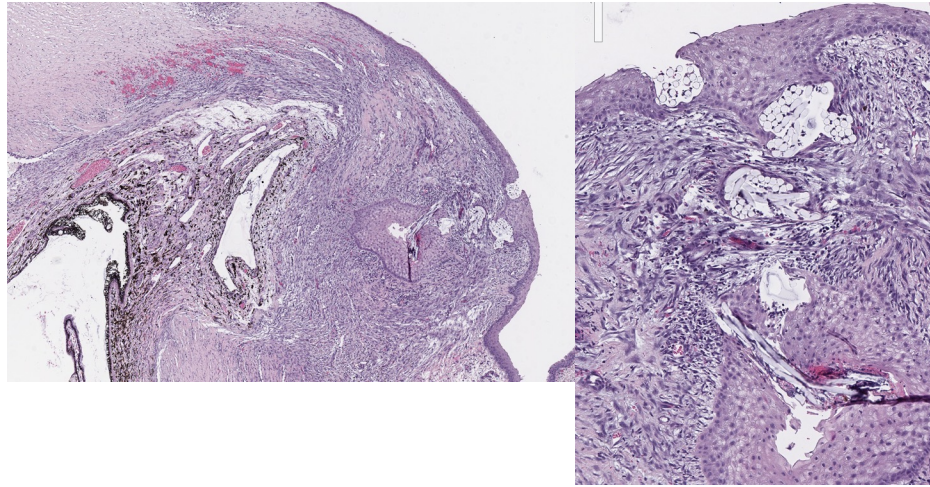
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Corneal Healing and Repair



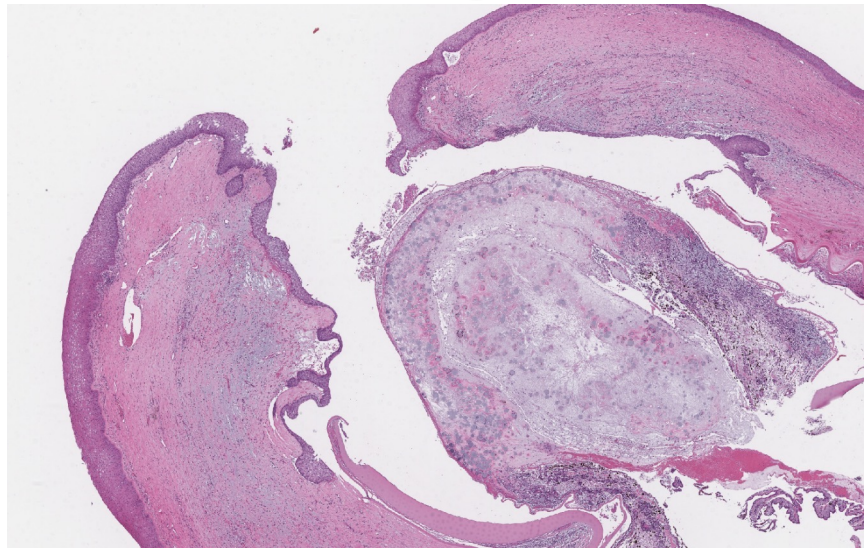
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Corneal Healing and Repair



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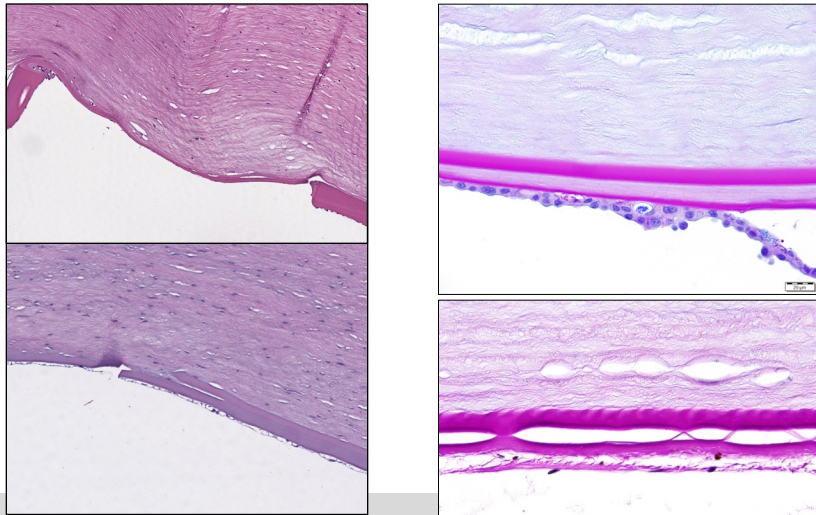
Corneal Healing and Repair



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Response to injury – Descemet's Membrane

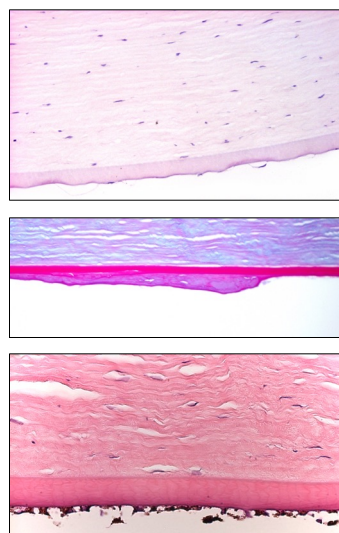
Doubling and breaks in DCMTs



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Response to injury - Corneal endothelium

- Corneal endothelium – poor regenerative capacity
- Atrophy → Stretching migration
- Melanin pigmentation
 - Secondary to release of uveal pigment
 - Neoplasia, inflammation, anterior synechia, ruptured uveal cyst, iris-cornea PPM
 - Does not appear to affect function (not associated with corneal edema)



Sanchez RF et al, VO 2020.

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Congenital abnormalities

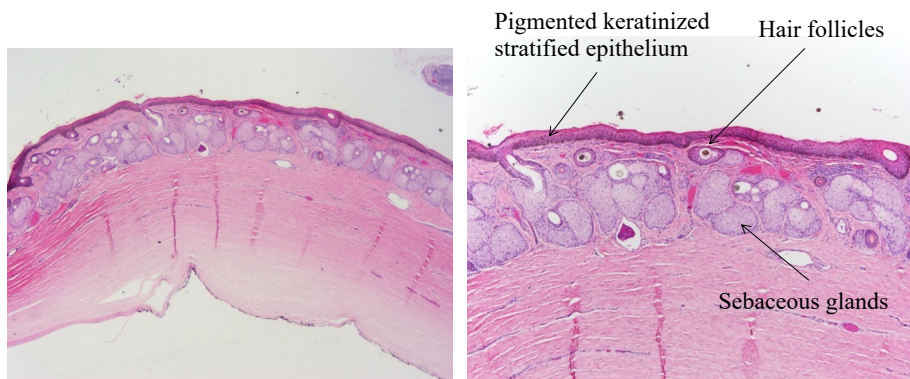
Corneal (conjunctival) Dermoid

- Ectopic island of skin on cornea (or conjunctiva)
- Congenital choristoma
- Has many or all features of normal skin
- “Cutaneous metaplasia” is not analogous to a dermoid
- Common in all species



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Corneal Dermoid



Horse, Courtesy of Dr. Chris Reilly

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Corneal Dystrophy and Degeneration

- Epithelial, stromal or endothelial
- True dystrophy is bilateral and symmetric
 - Not associated with inflammatory or metabolic disease
 - Often breed-related/heritable
- Degeneration: Lesions secondary to other diseases, not true dystrophies
 - Much more common

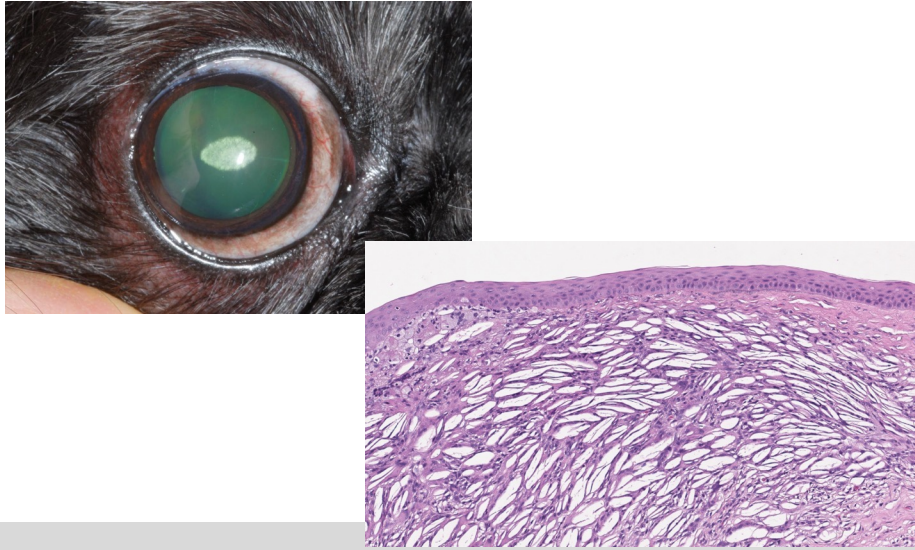
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Stromal Lipid Dystrophy / Lipid keratopathy

- “Corneal lipid dystrophy”
 - Bilateral and symmetrical with no association to metabolic disease
- Lipid keratopathy
 - Acquired - can be associated with corneal or adjacent disease, or metabolic disease;
- Accumulation of lipids within the stroma
- Macrophages may border these foci

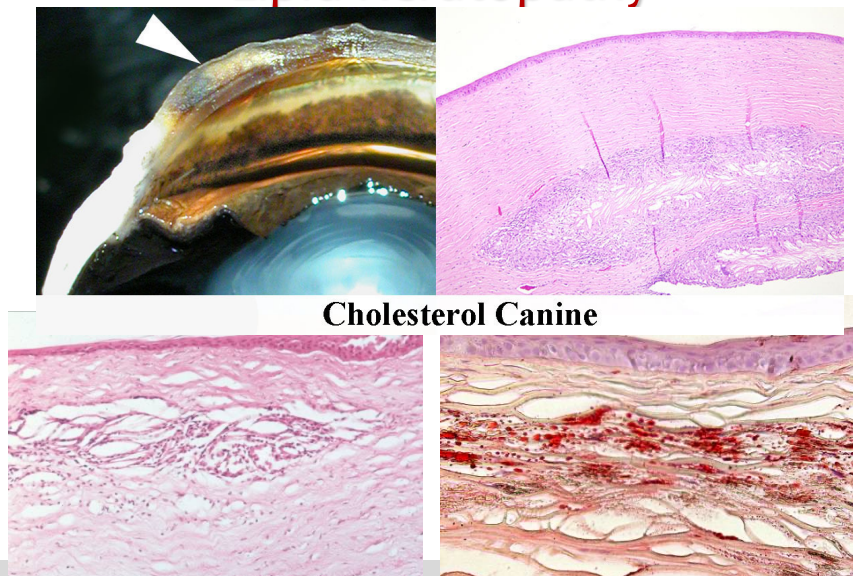
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Lipid/Cholesterol Dystrophy



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Lipid Keratopathy

**Cholesterol Canine**

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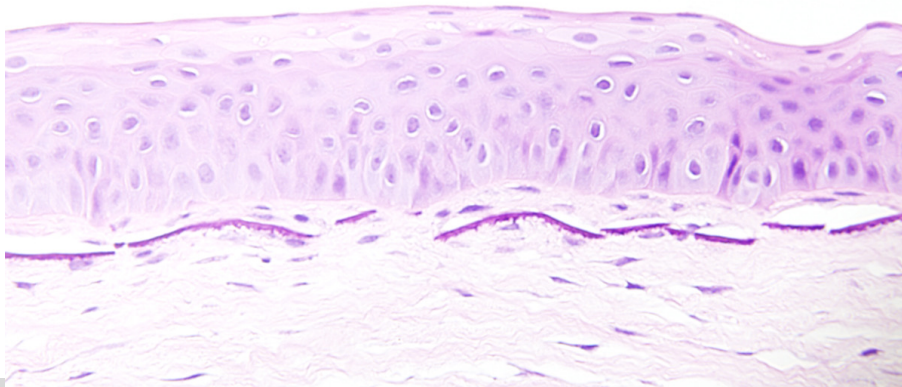
Mineral/Band Keratopathy

- Deposition of mineral in the basement membrane of the corneal epithelium and/or superficial stroma
- Usually secondary (not a true dystrophy)
- Inflammation and hypercalcemia are potential causes of secondary mineral deposition.
- Horses (uveitis/ steroid and phosphate containing topical solutions)

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Stromal Deposits - Mineral

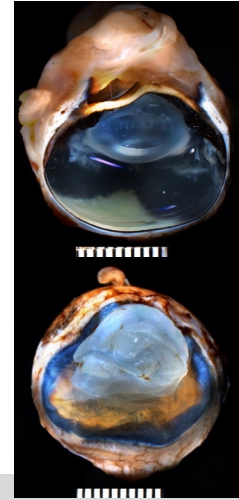
Band keratopathy



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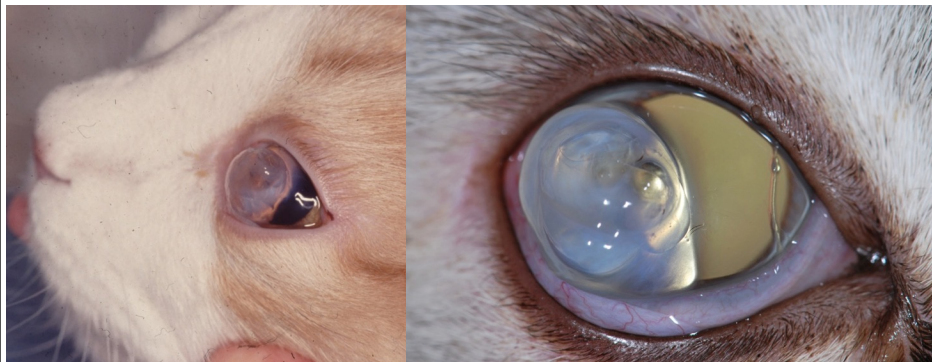
Severe corneal edema (corneal hydrops) Acute Bullous Keratopathy

- Cats and horses
- Severe rapidly developing, dense, well-circumscribed corneal edema
- Rupture of Descemet's membrane
- The cause is not known
- Pronounced conical forward protrusion of the cornea



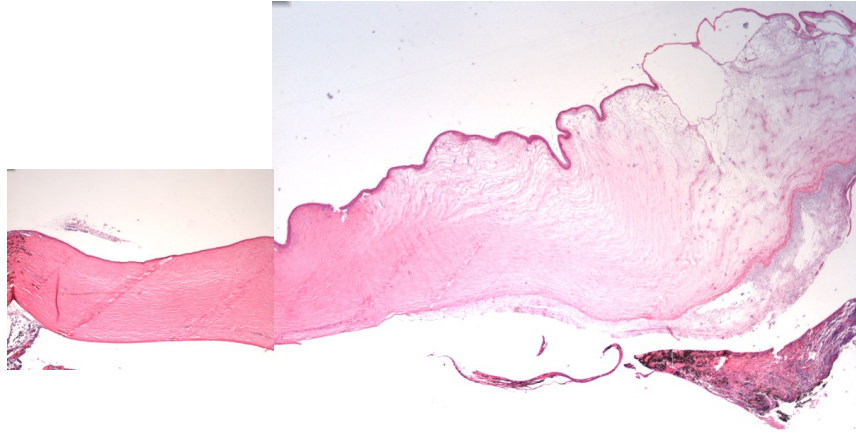
29

Severe corneal edema (corneal hydrops) Acute Bullous Keratopathy



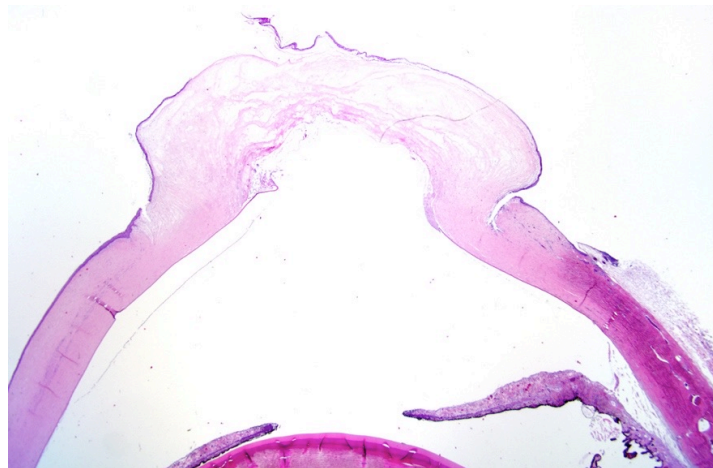
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Severe corneal edema (corneal hydrops) Acute Bullous Keratopathy



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Severe corneal edema (corneal hydrops) Acute Bullous Keratopathy



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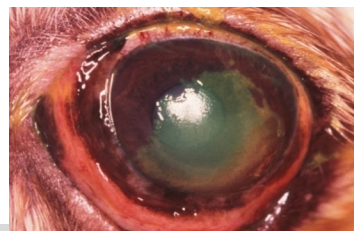
Keratitis, General Considerations

- Ulcerative vs non-ulcerative
- Inflammatory cellular infiltrate
- Acute = neutrophils
- Chronic = lymphoplasmacytic
- Corneal edema
- Stromal neovascularization

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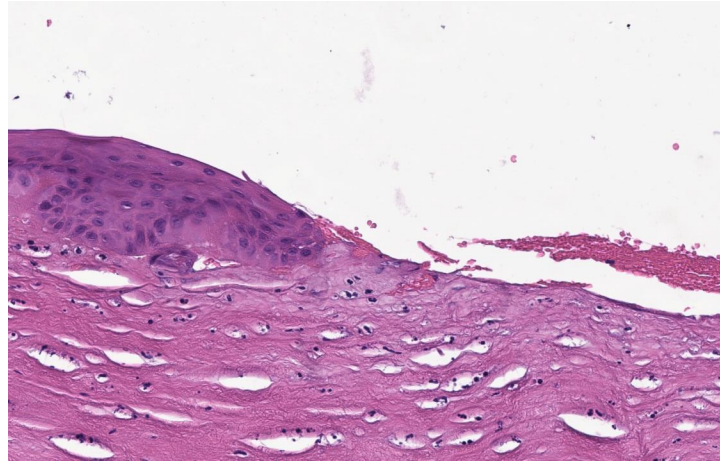
Ulcerative Keratitis

- Corneal erosion
- Corneal ulceration = full-thickness epithelial defect +/- stromal loss (varying depths)
- Descemetocoele - ulceration with full stromal thickness defect leaving only Descemet's membrane and endothelium
- Corneal perforation (+ iris prolapse)



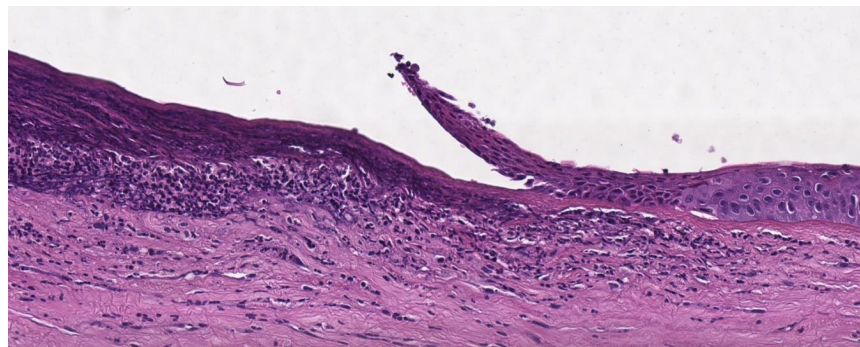
34

Ulcerative keratitis



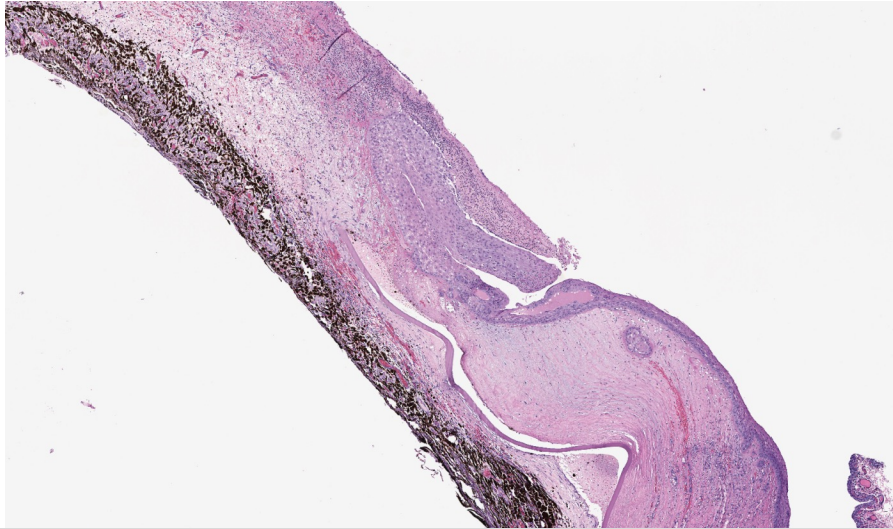
35

Ulcerative keratitis



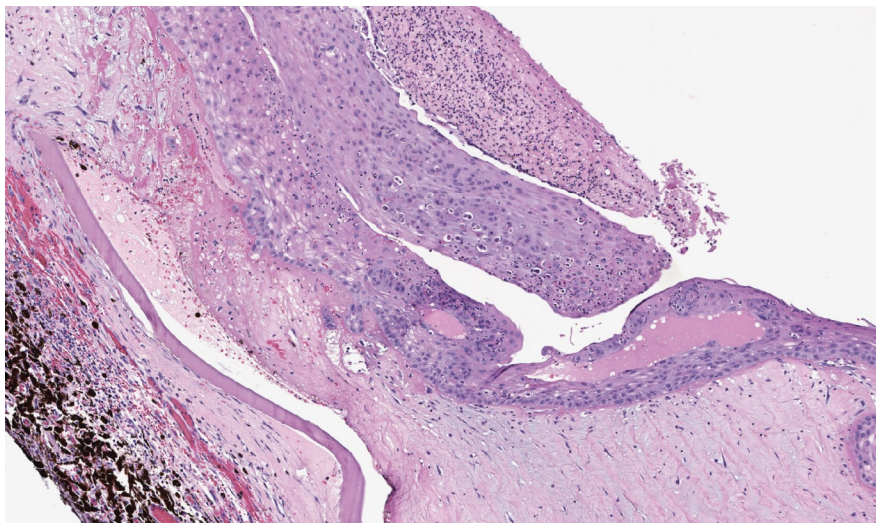
36

Ulcerative keratitis



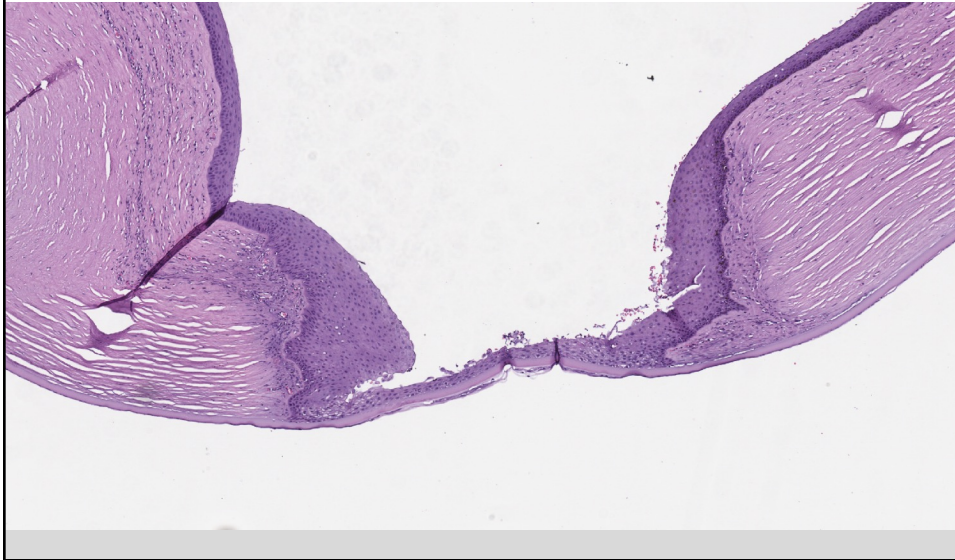
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Ulcerative keratitis



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Ulcerative keratitis



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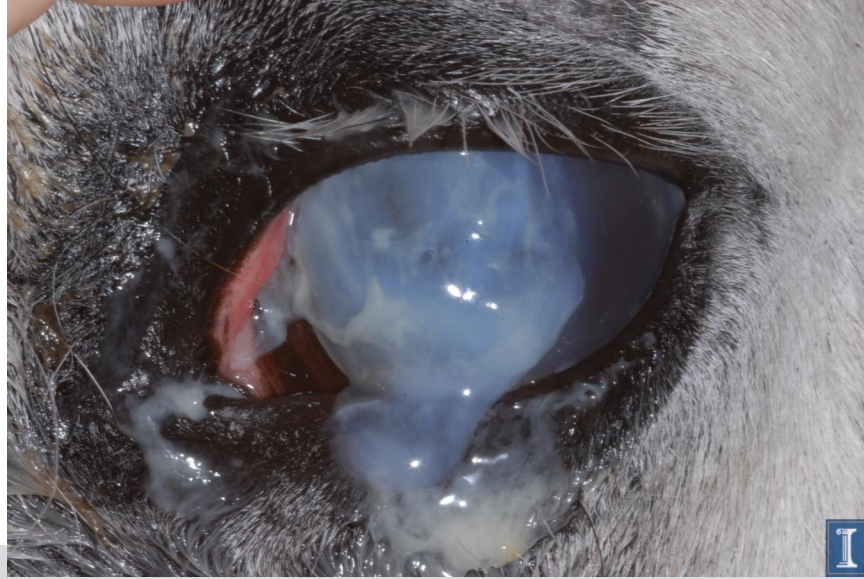
Ulcerative Keratitis with Keratomalacia Collagenolytic Keratitis

- Melting ulcer
- Horses, dogs (brachycephalic) +/- cats
- Degeneration of stromal collagen
- Metalloproteinases, serine proteases
- Endogenous (inflammation/neutrophils)
- Exogenous (some bacteria and fungi produce proteases)



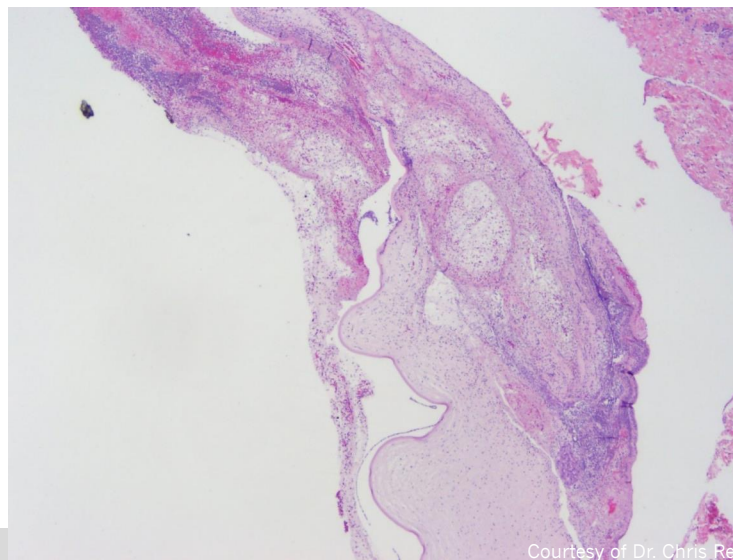
40

Ulcerative Keratitis with Keratomalacia



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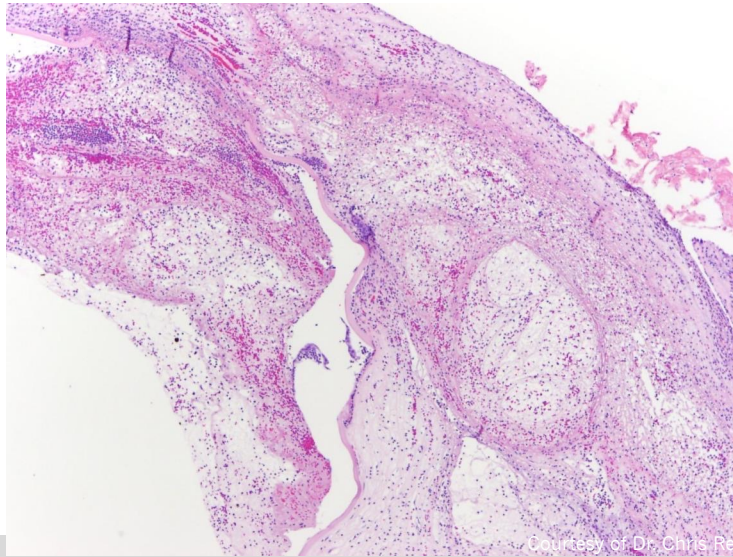
Ulcerative Keratitis with Keratomalacia



Courtesy of Dr. Chris Reilly

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Ulcerative Keratitis with Keratomalacia

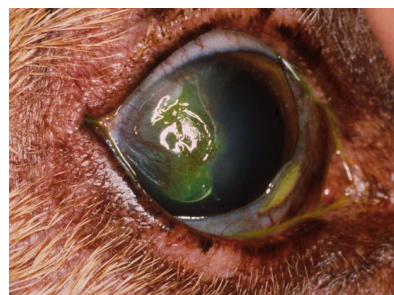


Courtesy of Dr. Chris Reilly

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Indolent Ulcer (Dog, Cat, horses) *Superficial Chronic Corneal Epithelial Defects -SCCEDs*

- Globes are seldom removed with this condition as a primary diagnosis
- Morphologic criteria
 - Separation of the epithelium from the stroma
 - Loss of epithelial polarity and loss of basal cells
 - Cell-free zone in the superficial stroma
- Indolent ulcer can exist in the cornea alone or as part of other severe changes



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Chronic Keratitis (Nonspecific)

- “Chronic keratitis, superficial”
- End result of a variety of corneal insults
- It is not a disease, but a response pattern
- Frequent in enucleated globes
- Severe cases may mimic Chronic Superficial Keratitis/Pannus

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Chronic keratitis

Potential causes

- Physical irritation - contact with hair
- Inflammatory or neoplastic masses
- Airborne particulate material
- Desiccation caused by:
 - Exophthalmos or buphthalmos
 - Inability to blink related → neurologic lesions
 - Loss of corneal sensitivity
- KCS – Dry eye

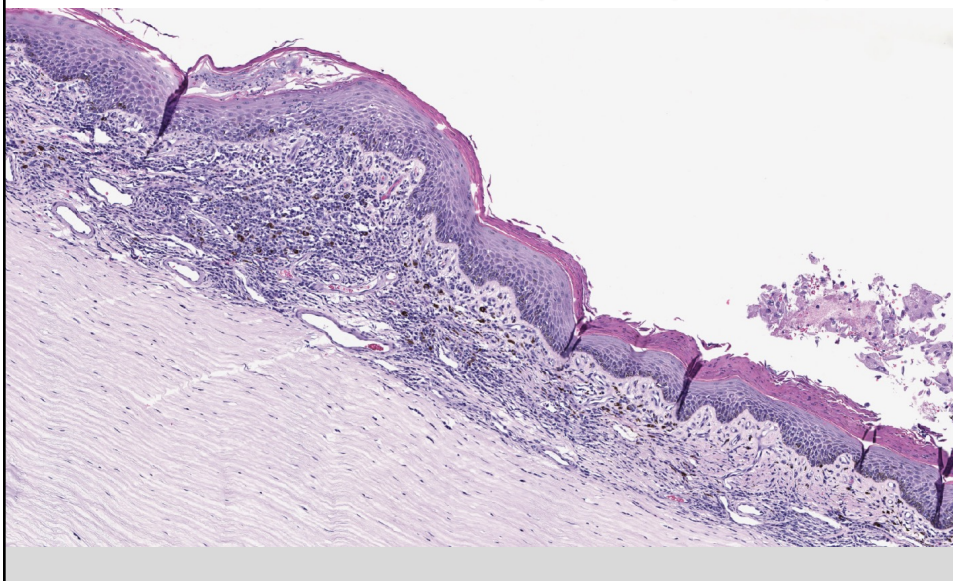
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Chronic Keratitis (Nonspecific)

- Morphologic changes
 - Epithelial lesions (hyperplasia, pigmentation +\-keratinization)
 - Lymphoplasmacytic inflammation
 - Pigmentary incontinence (leakage of melanin)
 - Stromal fibrosis and neovascularization
 - Pigmentary keratitis/keratopathy

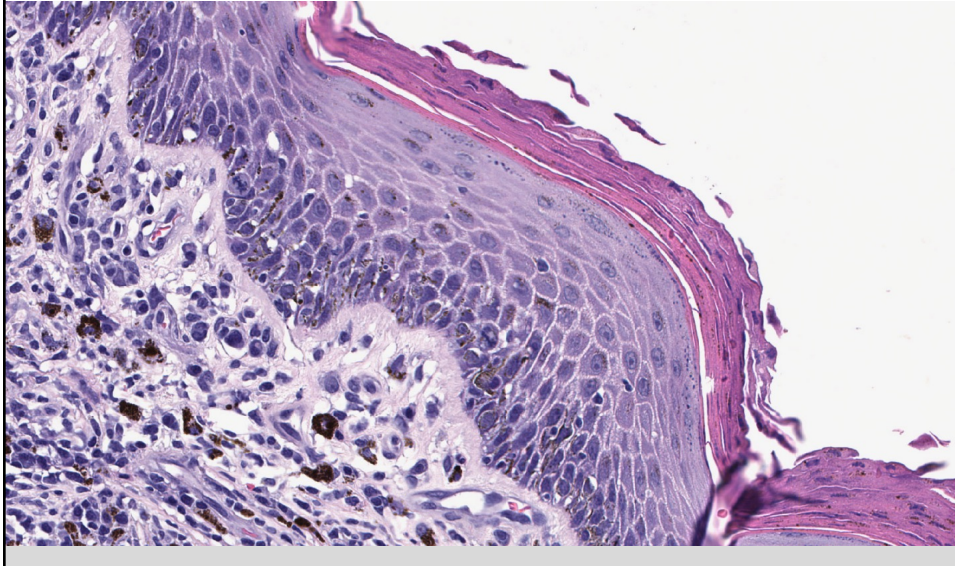
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Chronic Keratitis (Nonspecific)



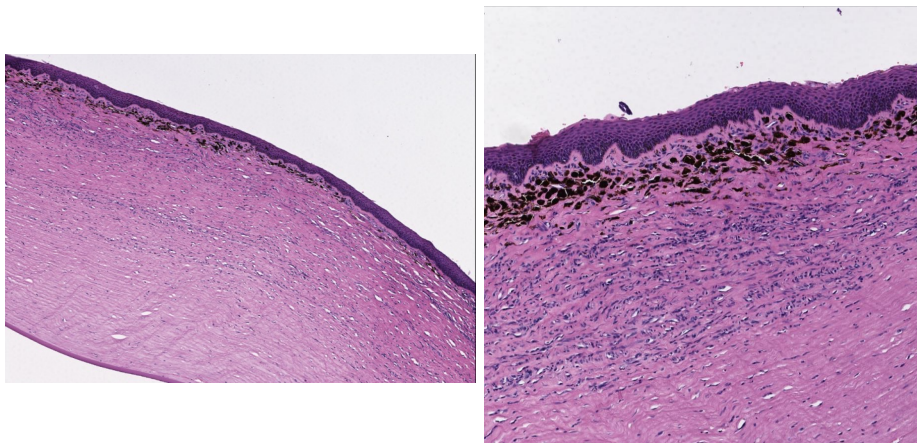
51

Chronic Keratitis (Nonspecific)



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Chronic Keratitis (Nonspecific)

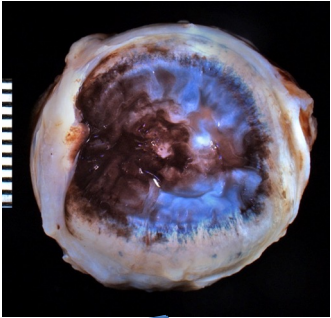
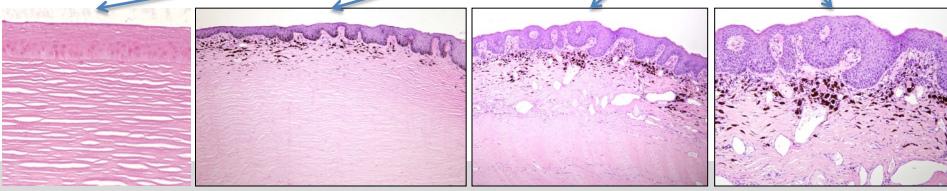


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Chronic Keratitis

- Epidermalization of the cornea
- Epithelial thickening with keratinization
- Rete ridge formation
- Pigmentation of the epithelium and superficial stroma
- Superficial neovascularization
- Superficial inflammation
- Goblet cell hyperplasia (conjunctiva)

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Keratoconjunctivitis sicca (KCS)

- Common disease of dogs
- Cavalier King Charles Spaniel, English Bulldog, Lhasa Apso, Shih Tzu, West Highland Terrier, Pug, Bloodhound, Cocker Spaniel, Pekingese, Boston Terrier
- Decreased production of aqueous portion of tear film
- Causes:
 - Autoimmune (breeds)
 - Drug related (sulfonamide)
 - Removal of third eyelid gland
 - Neurologic disease
 - CN V or VII defects
 - Infectious (CDV, Leishmania)
 - Senile



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Eosinophilic Keratitis in Cats & Horses

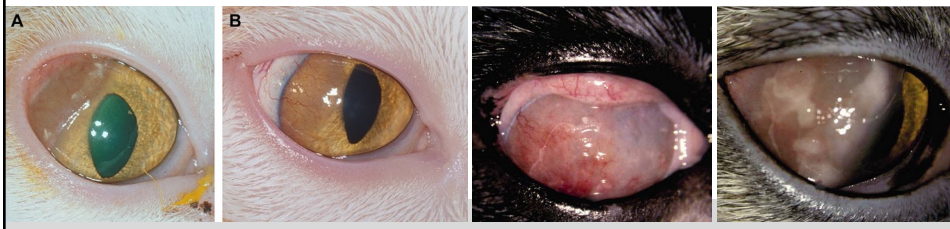
- Relatively common disease in cats and uncommon in horses.
- Unknown etiology and pathogenesis
- Based on the cell types present in the lesion:
 - Type I hypersensitivity (IgE, degranulating mast cells, tissue injury)
 - Type IV hypersensitivity (T cells, IL-5, eosinophil, tissue injury)
- **Cats:**
 - FHV-1 might play a role - direct cytolysis and/or an immune response mediated by T cells
- **Horses:**
 - Potential parasite infection (habronema, onchocerca etc.)
 - Environmental allergens

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Feline eosinophilic keratitis

Clinical presentation

- An association with Feline herpesvirus-1
- Mycoplasma and chlamydiae felis?
- Dramatic response to topical immunosuppressive therapy

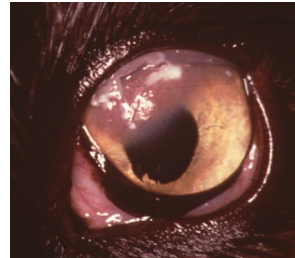


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Feline eosinophilic keratitis (proliferative keratitis)

Gross lesions

- Keratoconjunctivitis - extends across the limbus (bulbar conj.+ 3rd eyelid)
- Eyelid margin erosive lesions
- Most often unilateral (bilateral involvement does occur)
- Peri-limbal vascularized, raised and proliferative lesions
- Irregular surface
- Superficial plaques of white material

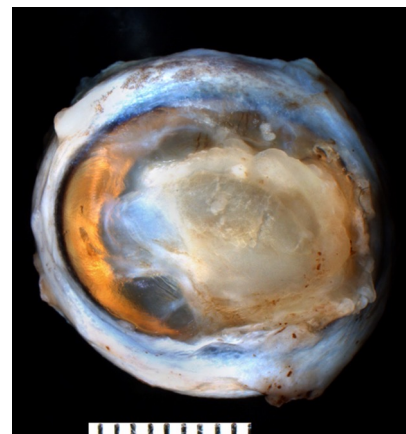


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Feline eosinophilic keratitis

Microscopic lesions

- Mostly lymphoplasmacytic inflammation variable numbers of eosinophils and mast cells
- The epithelium is usually intact
- Ulcerated surface may be lined by granular protein released by eos and/or mast cel
 - Eosinophilic basic protein
- Loss of lamellar corneal stroma
- Neovascularization

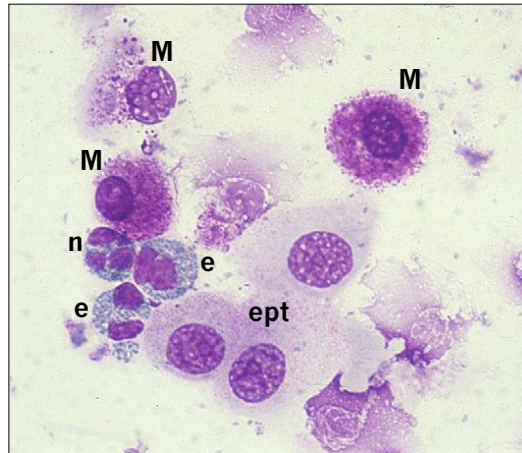


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Feline eosinophilic keratitis

Cytologic Diagnosis

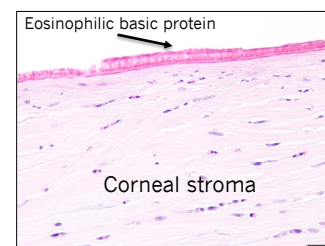
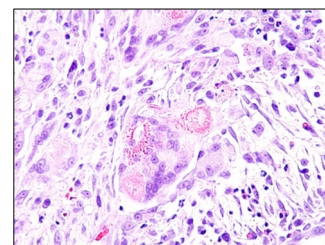
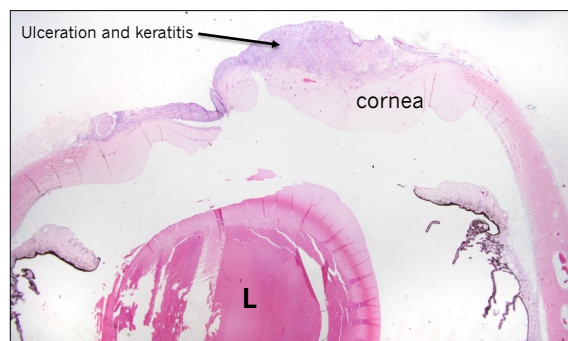
Not routinely biopsied!



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Feline eosinophilic keratitis

Gross and microscopic lesions



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Eosinophilic keratitis/ “Sequestrum” in horses

- Seasonal disease (summer months)
 - Potential parasite infection (habronema, onchocerca etc.)
 - Environmental allergens
 - Insects (fly)
 - Comorbidity with allergic dermatitis – systemic eosinophilic disease?
- Most often bilateral disease (70% cases)



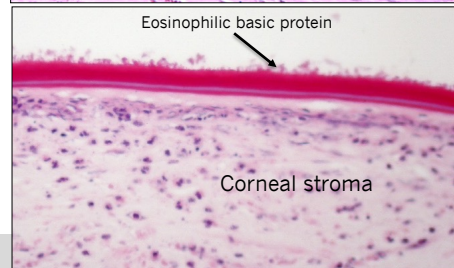
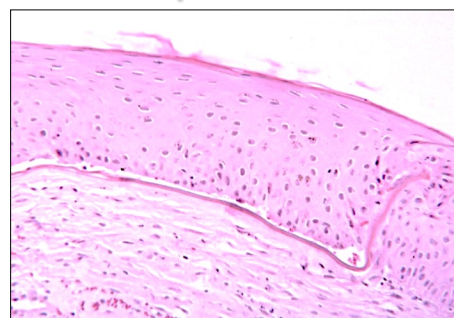
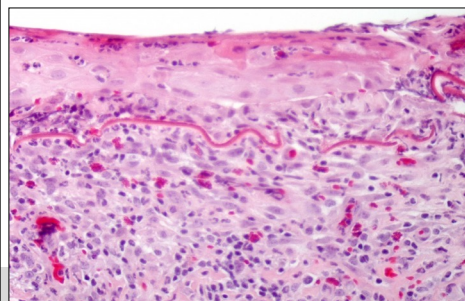
Hakanson NE, Dubielzig RR. (1994) Chronic superficial corneal erosions with anterior stromal sequestration in three horses. *Vet & Comp Ophthalmol.* 4: 179-183

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Eosinophilic keratitis / “Sequestrum”

Microscopic lesions

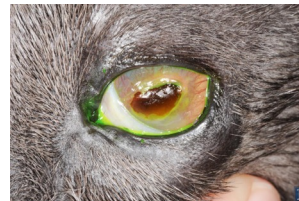
- Cytology also very useful for diagnostic
- Often receive keratectomy from non-responsive case
- Mostly lymphoplasmacytic inflammation variable numbers of eosinophils and mast cells



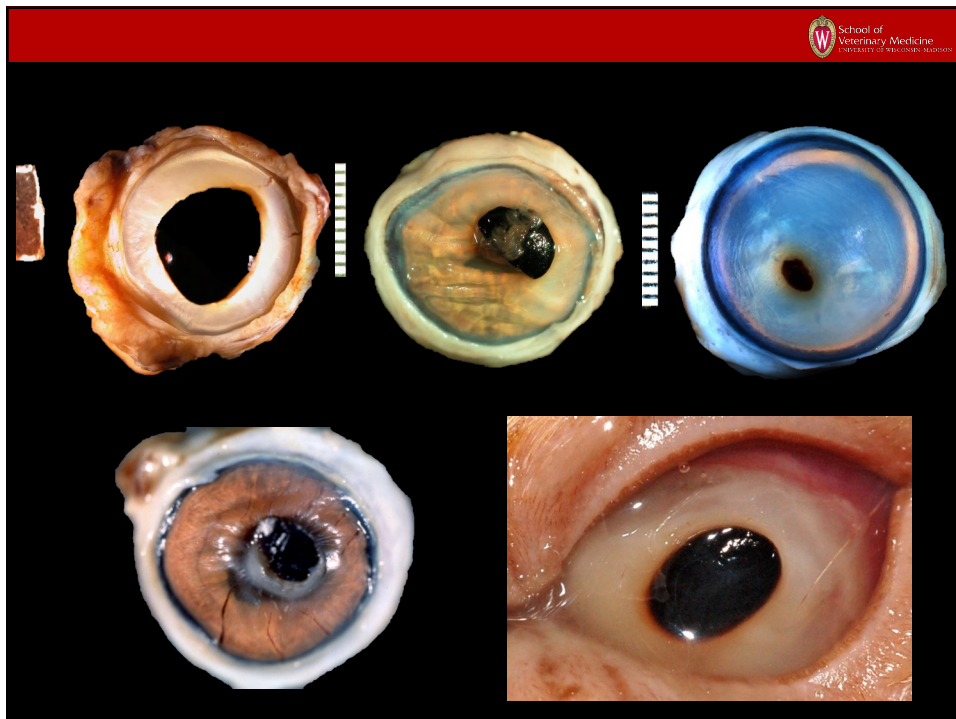
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Corneal Sequestrum

- Cats (Persians) +\- horses, dogs
- Well-circumscribed area of devitalized stroma often with pigmentation
 - Acellular/devitalized/necrotic stroma
- Some are not overtly pigmented
- Inflammation and neovascularization only at the periphery
- Ulceration
- Iron? Porphyrins? Melanin?



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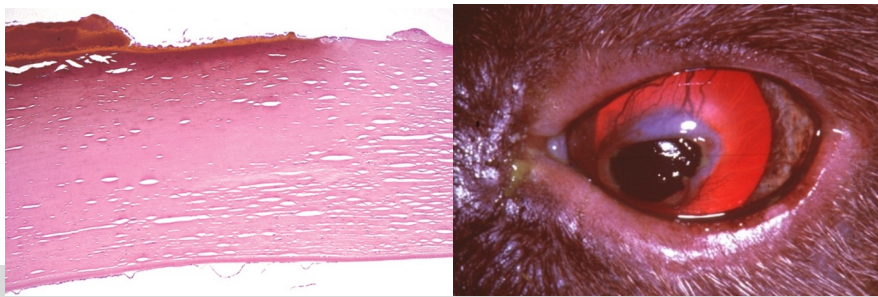


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Corneal Sequestrum

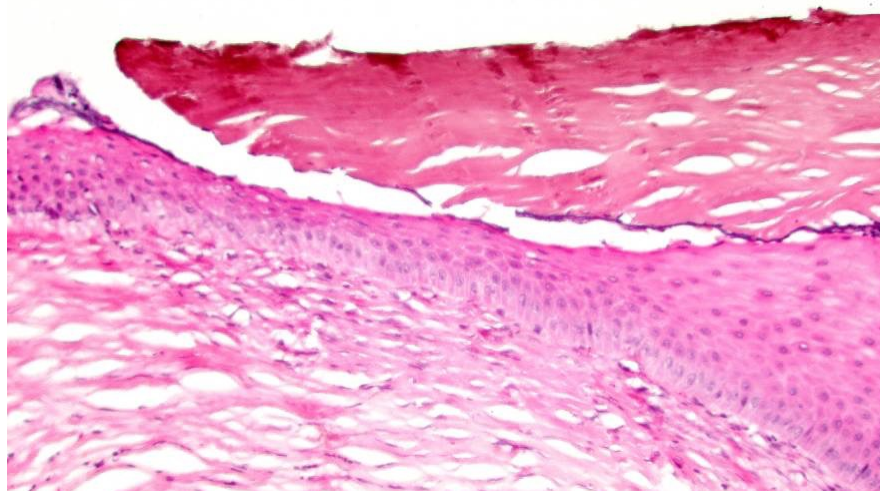
Microscopic lesions

- Degenerate collagen and a brown pigment
- Typically involves the anterior to mid-stroma, rarely extending to Descemet's membrane
- Chronicity: surrounded and eventually undermined by a rim of neovascularization and mixed inflammatory cells
- May slough



66

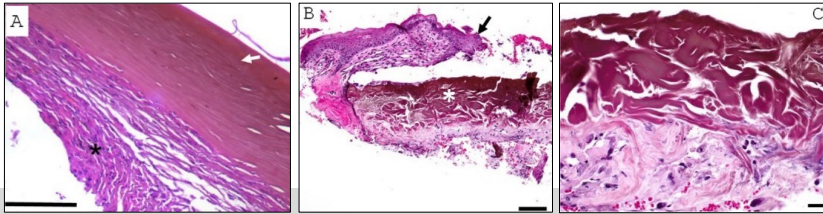
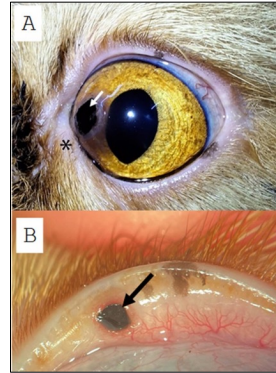
Corneal Sequestrum



67

Conjunctival Sequestrum

- Cats
- Often with corneal sequestra
- Unknown pathogenesis
- Well-circumscribed area of devitalization, often with pigmentation
- Acellular/devitalized/necrosis
- Ulceration



68

Carbonic anhydrase inhibitors (CAI) (Dorzolamide / Brinzolamide) keratitis in dogs

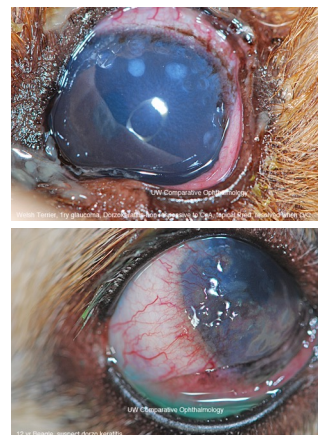
JAVMA, Vol 247, No. 12, December 15, 2015

SMALL ANIMALS

Keratitis in six dogs after topical treatment with carbonic anhydrase inhibitors for glaucoma

Billie Beckwith-Cohen, DVM, MBA; Ellison Bentley, DVM; David J. Gasper, DVM, PhD;
Gillian J. McLellan, BVMS, PhD; Richard R. Dubielzig, DVM

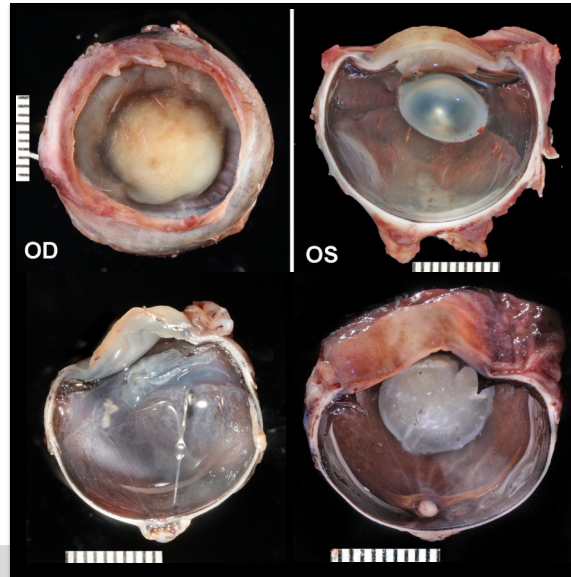
- Topical administration of CAIs (brinzolamide and dorzolamide) first-line treatment for glaucoma in dogs
- Immune-mediated drug hypersensitivity manifested as punctate keratitis
- Uncommon disease that does not respond to corticosteroid treatment
- Affected patients improved rapidly after discontinuation of CAI



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CAI keratitis

- Not many enucleated globes
 - Keratectomy specimens more common
- Glaucoma related alterations
- Diffuse corneal infiltration, opacity and vascularization



70

CAI keratitis

- Severe lymphoplasmacytic and lichenoid superficial keratitis
- Extensive intraepithelial lymphocytic infiltration

10-year-old FS Australian Shepherd-crossbred dog

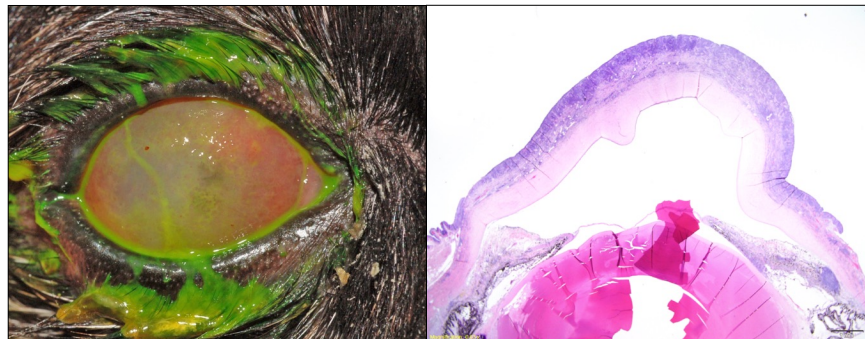
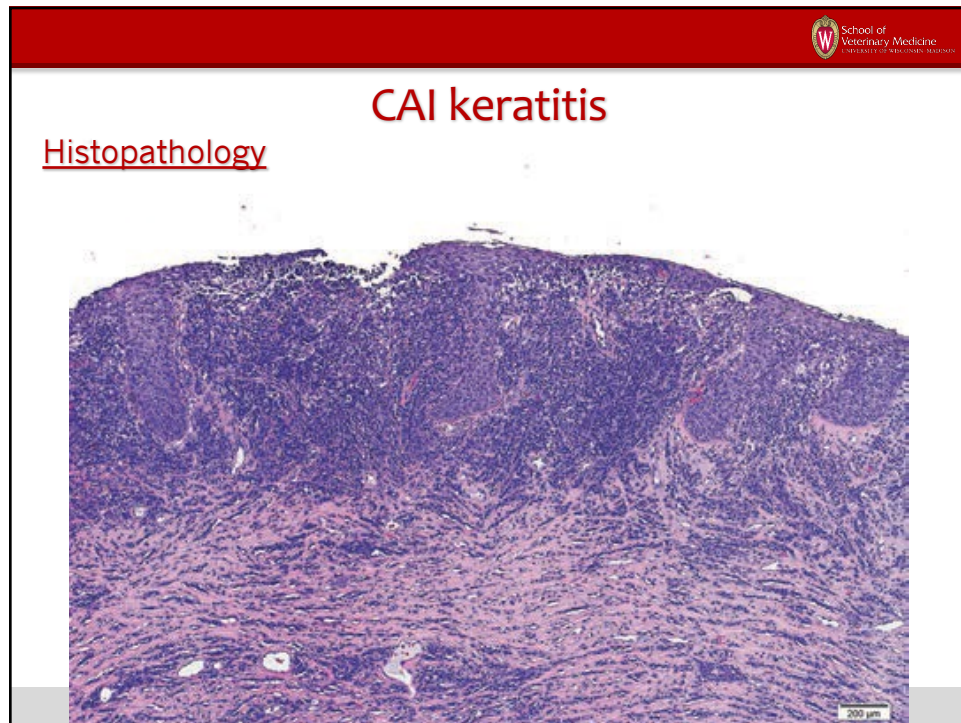
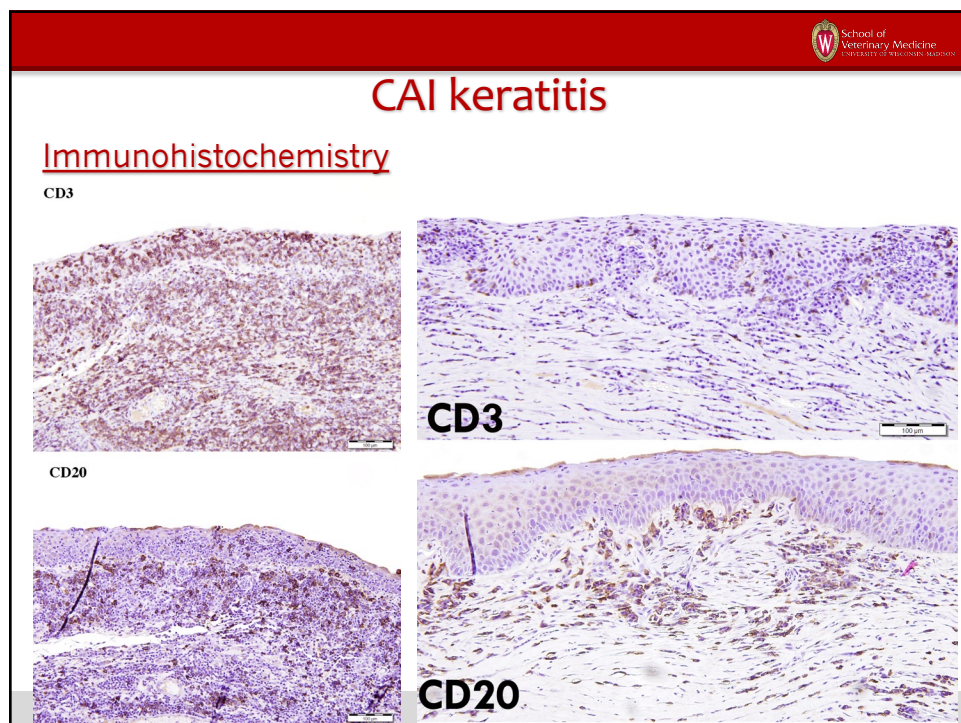


Image from Elizabeth Adkins

71



72



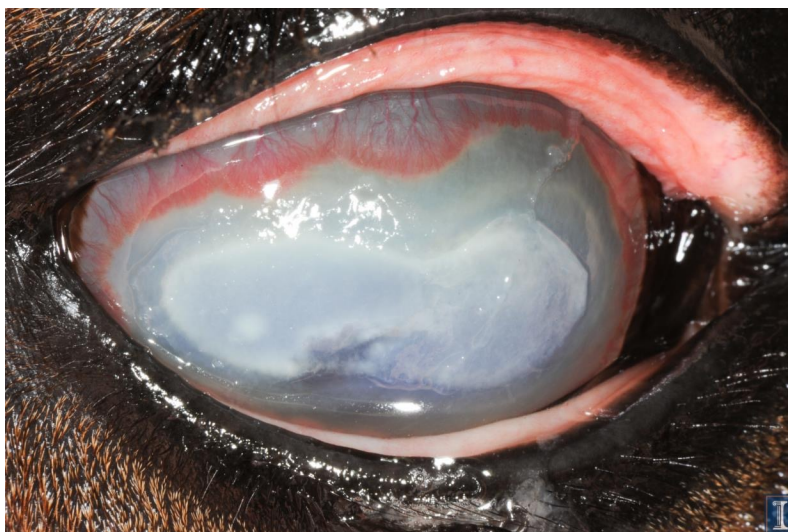
73

Fungal Keratitis

- Horses +\- dogs, rarely cats
- Neutrophils +\- keratomalacia +\- stromal abscess
- Ulceration
- Fungal hyphae may be numerous or rare
- Fungal hyphae are mostly in the deep stroma
- Fungal hyphae may invade Descemet's membrane
- *Aspergillus spp*, *Fusarium spp*.
- Opportunistic fungal colonization of injured corneas can be only superficial

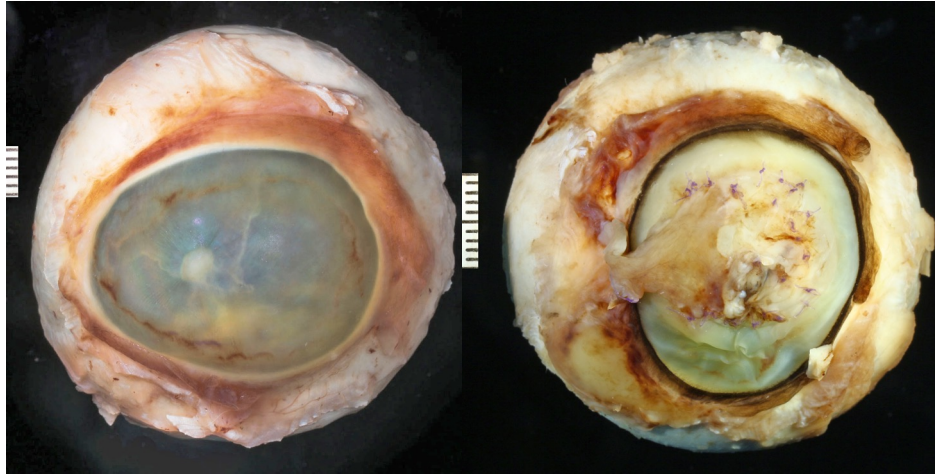
74

Fungal Keratitis



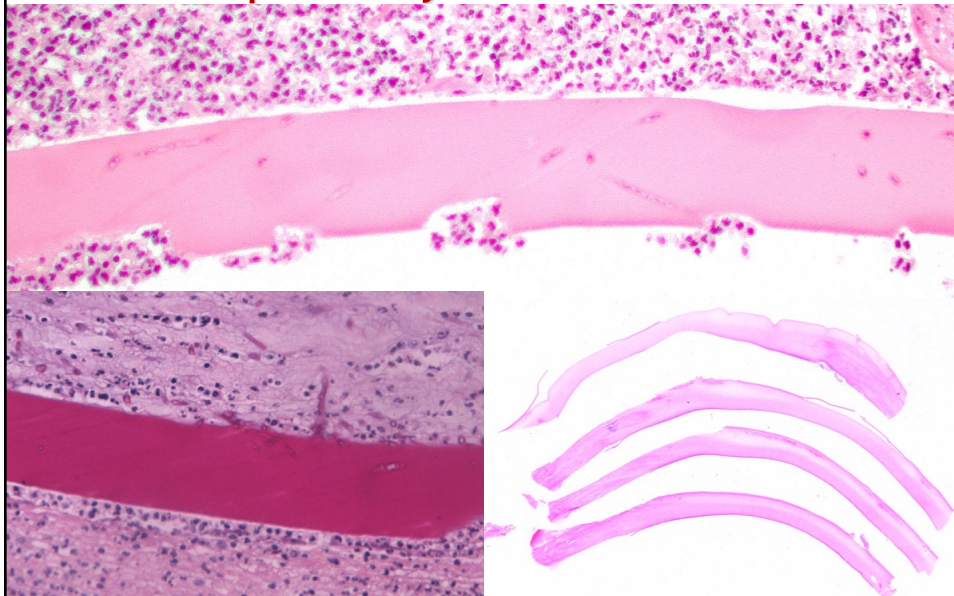
75

Equine Mycotic Keratitis



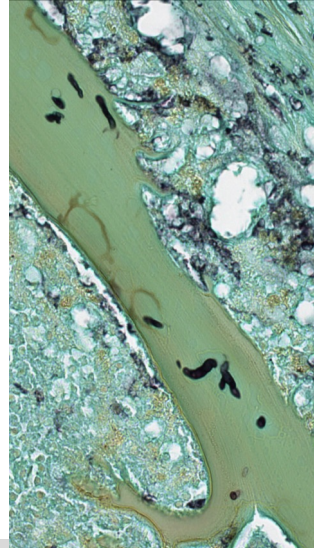
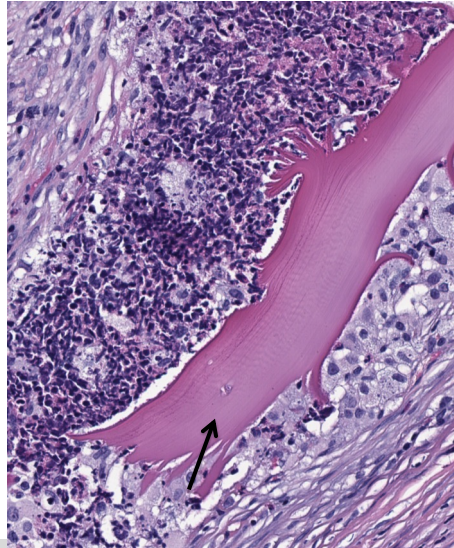
76

Equine Mycotic Keratitis



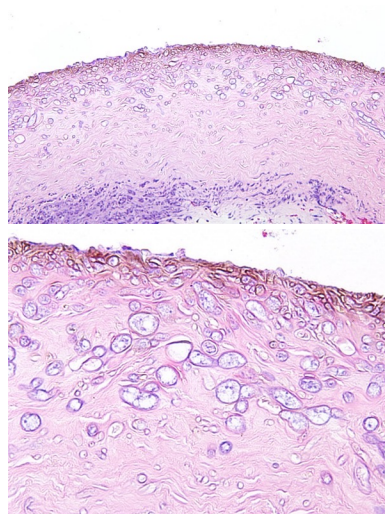
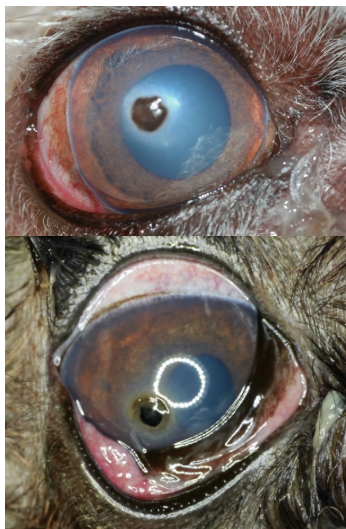
77

Fungal Keratitis



78

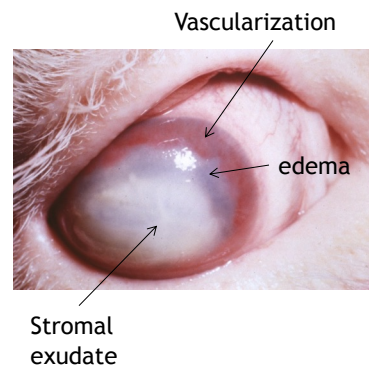
Fungal keratitis Dogs



79

Infectious Bovine Keratoconjunctivitis IBK

- Aka. Pink eye
- *Moraxella bovis*, Gram negative bacillus
- Primary corneal pathogen with cytotoxic effects on:
 - PMNs
 - Corneal epithelial cells



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Infectious Bovine Keratoconjunctivitis IBK

- Highly contagious
- Predisposing factors
 - Summer months
 - Corneal irritation (fly vectors, UV radiation, long grasses)
 - Hereford and Hereford-cross breeds
 - Younger cattle higher morbidity
 - Cattle housed inside have higher infection rate of longer duration but milder clinical disease

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Infectious Bovine Keratoconjunctivitis IBK

- Clinical appearance
 - Unilateral (initially) central corneal ulcer
 - Intense inflammatory cell infiltrates may develop into a stromal abscess
 - Superficial neovascularization
 - Outcomes:
 - Corneal healing with scarring
 - Corneal perforation w/ iris prolapse (blindness)

Stage 1



Stage 2



Stage 3



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Protozoal / Microsporidial Keratitis & Conjunctivitis

- Dogs, rare
- Mass effect in the cornea +/- conjunctiva
- Granulomatous/pyogranulomatous inflammation
- No inflammation with Microsporidia
- Preexisting ocular surface disease, typically KCS
- Immunomodulatory therapy
 - Amoeba, T. gondii, Leishmania; Sarcocystis
(Beckwith-Cohen B et al. VO, 2016; Swinger RL et al. VO 2009)
 - Microsporidia (Nosema)
(Scurr E et al. VO 2020.)

83

Opportunistic Corneal infections chronic topical immunosuppression in dogs

Veterinary Ophthalmology (2016) 19, 3, 206–213

DOI:10.1111/vop.12285

Protozoal infections of the cornea and conjunctiva in dogs associated with chronic ocular surface disease and topical immunosuppression

Billie Beckwith-Cohen,* David J. Gasper,* Ellison Bentley,* Howard Gittelman,† Angela E. Ellis,‡ Karen F. Snowden,§ Barbara C. Shock,¶ Michael J. Yabsley** and Richard R. Dubielzig*

- 8 dogs
- Sex- 3 MN, 5 FS
- Age- Median 10 years (range 5-15 years)
- Breeds
 - 2 Pugs and 1 each: Shih Tzu, Havanese, Cavalier King Charles Spaniel, Yorkshire Terrier, German Shepherd cross, Terrier cross
- Clinically, SCC was on top of the differential list
- All cases received topical tacrolimus 0.03% or cyclosporine 0.2%

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	Eye	Preexisting ocular disease	Clinical presentation	Duration of treatment	Microorganism
1	OU	KCS + Pigmentary keratitis	Pink limbal mass	6 years	Toxoplasma
2	OU	Pigmentary keratitis	Corneal mass	8 months	Neospora? Leishmania
3	OU	Meibomitis	Corneal masses	>2 years	Toxoplasma?
4	OD	KCS	Corneal mass	>2 years	Protozoa
5	OD	KCS	Corneal mass	4 months	Amoeba
6	OS	KCS	Corneal mass	Long-term	Amoeba
7	OD	(Pannus) CSK	Corneal mass	Years	Gram + Bacteria
8	OD	KCS	Devitalized ulcerating cornea	4 months	Candida Parapsilosis

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Case 1

KCS, pigmentary keratitis years of topical immunosuppression

Veterinary Ophthalmology (2009) 12, 1, 56–60

CASE REPORT

Keratoconjunctivitis associated with *Toxoplasma gondii* in a dog

Robert L. Swinger,* Karl A. Schmidt, Jr.* and Richard R. Dubielzig†

*Animal Eye Specialty Clinic, 20290 NW 2nd Avenue, Miami, FL 33169, USA; †Department of Pathobiological Science, University of Madison-Wisconsin, School of Veterinary Medicine, Madison, Wisconsin, USA

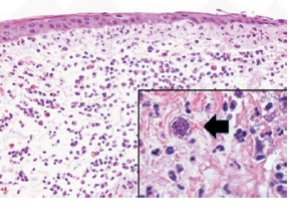
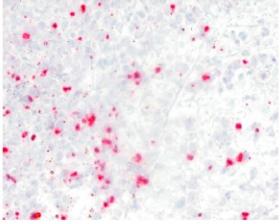




Figure 1. Photograph OD 7 weeks following superficial keratectomy and cryosurgery for a corneal mass. Note the dorsomedial 10 mm yellow/tan perilimbal bulbar conjunctival mass and associated diffuse conjunctival chemosis and hyperemia. Additionally, dense pigmentary keratitis affects the entire corneal surface.

Figure 2. Photomicrographs of the conjunctival biopsy from the mass shown in Figure 1. There is extensive tissue edema, lymphoplasmacytic and suppurative inflammatory infiltrate, and dilated blood vessels. Clusters of *T. gondii* tachyzoites are noted by the arrow.

Figure 3. Immunohistochemical staining of the conjunctival biopsy in Figure 1. *Toxoplasma gondii* antigens are labeled red.

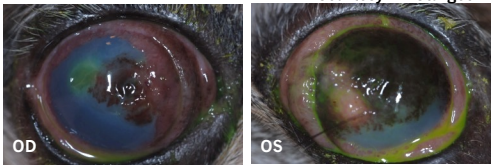
86

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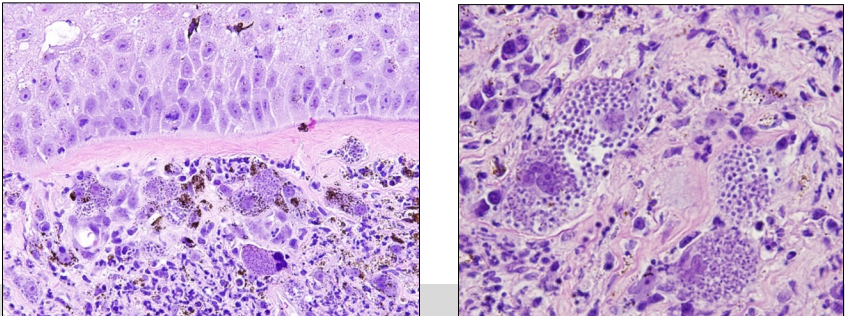
Case 2

Pigmentary Keratitis 8 months of tacrolimus

Courtesy Dr. Sturgeon



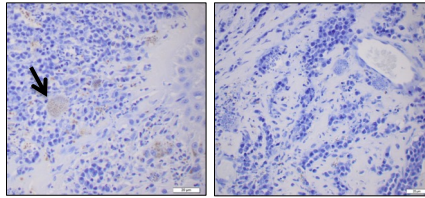
Histology- suspicious of toxoplasma



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Case 2

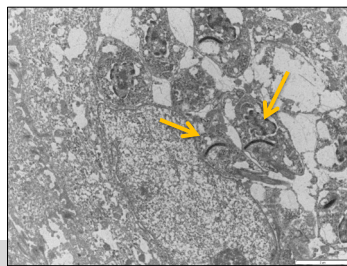
IHC



Neospora +

Toxoplasma -

TEM



- Histology
 - Suspected toxoplasma
- IHC
 - Neospora positive
 - Toxoplasma negative
- TEM
 - Kinetoplast - Leishmania
- PCR
 - Leishmania positive
 - T. Cruzi. negative
- Concurrent infection?
 - Neospora and Leshmania?

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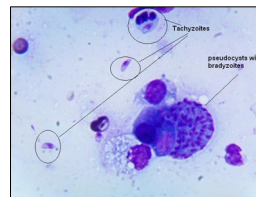
Case 3

Pyogranulomatous meibomitis >2 years systemic and topical immunosuppression

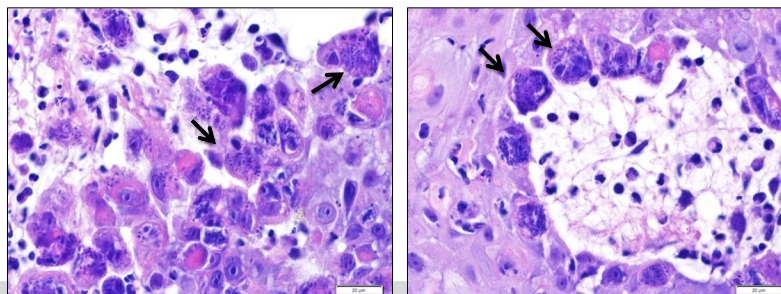
Courtesy Dr. Gittelman



Cytology suspicious neospora, toxoplasma or leishmania



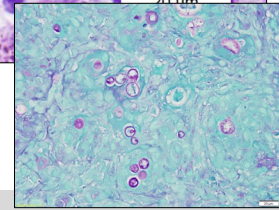
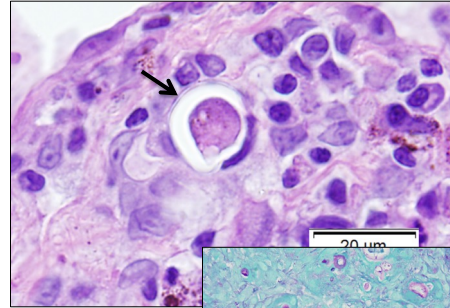
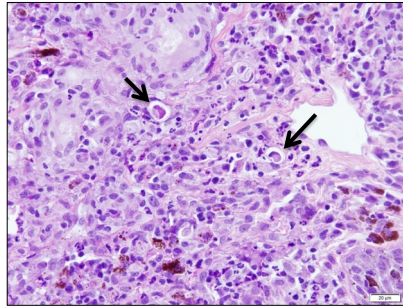
Histology suspicious of toxoplasmosis or neospora



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Case 5**KCS - 4 months tacrolimus****Amoeba keratitis 1**

- Suspected SCC clinically
- Improved after keratectomy and d/c tacrolimus

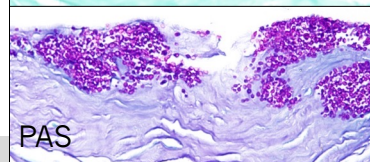
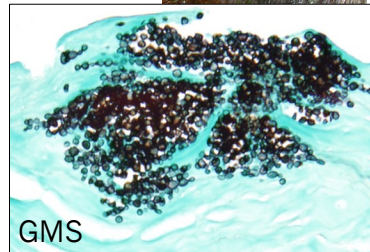
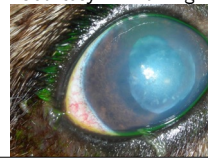


90

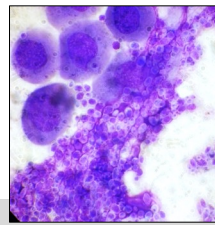
Case 8 KCS – 4 months tacrolimus

- Only case that did not present a mass lesion
- Impossible to differentiate by histology
- Candida was suspected
- Candida parapsilosis identified by culture
- Resolved with keratectomy and conj. graft
- Common in immune compromised patients
- Not reported in veterinary medicine

Courtesy Dr. Burling



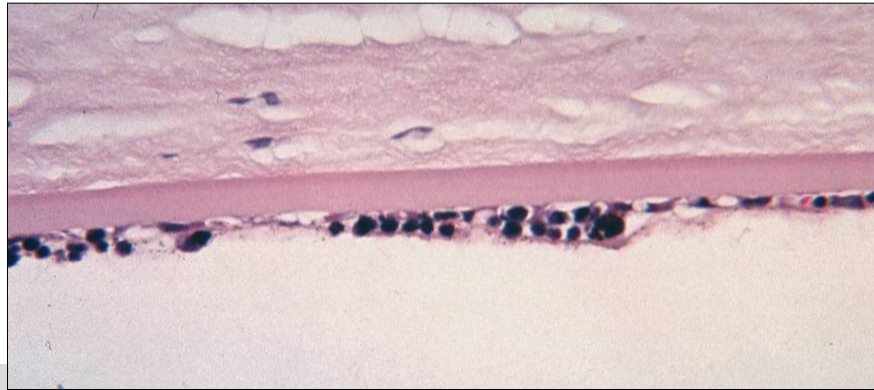
Cytology



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Malignant Catarrhal Fever

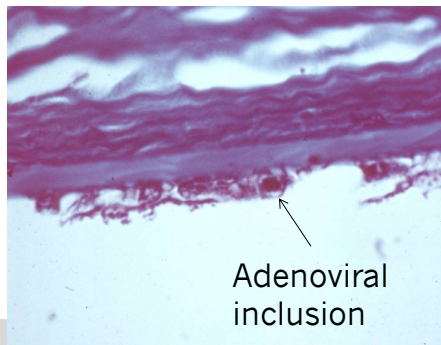
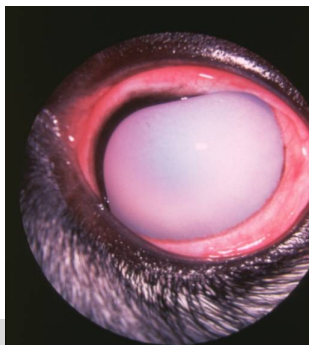
- Bovine
- Alcelaphine herpesvirus 1, ovine herpesvirus 2
- Endotheliitis



92

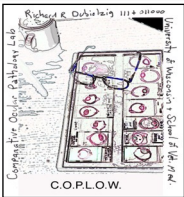
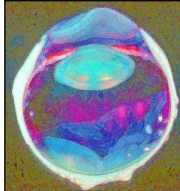
Canine Adenovirus

- Infection or some vaccines
- Adenovirus type 1-2
- Endothelial necrosis +/- inclusions
- Results in severe corneal edema, “blue eye”

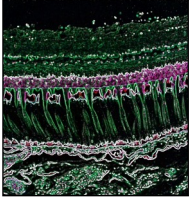
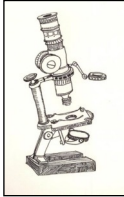


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Disease of the sclera

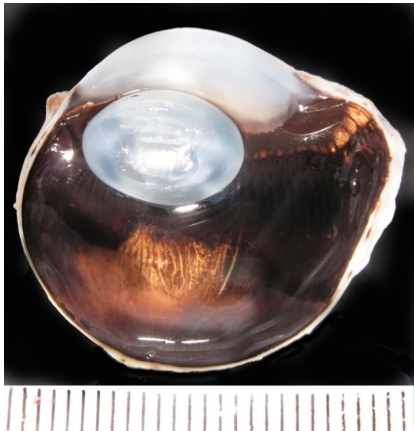



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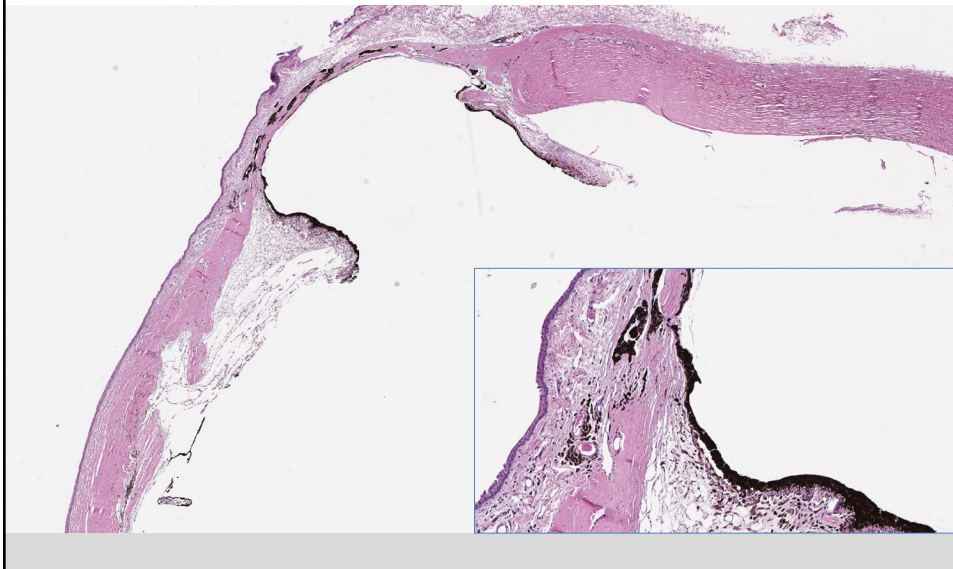
Staphyloma

- Full or partial thickness scleral (or corneal) defect lined by protruding uvea
- Congenital or acquired (glaucoma, ocular melanosis)
- Some cases with staphyloma present as a suspicion of neoplasia (melanocytic neoplasia)



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Staphyloma



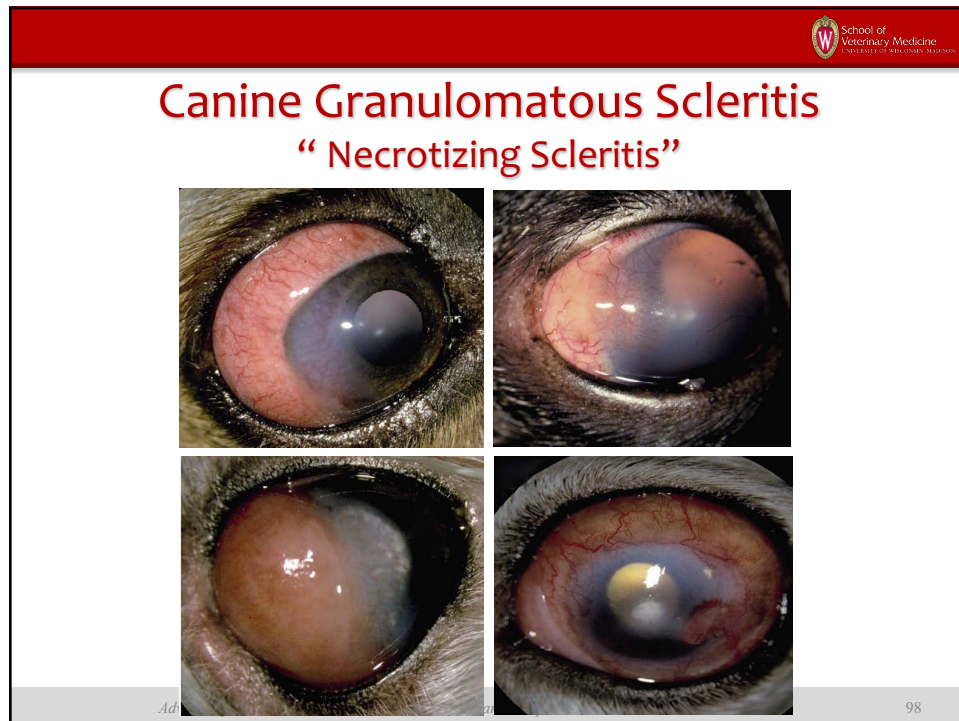
96

Granulomatous Scleritis

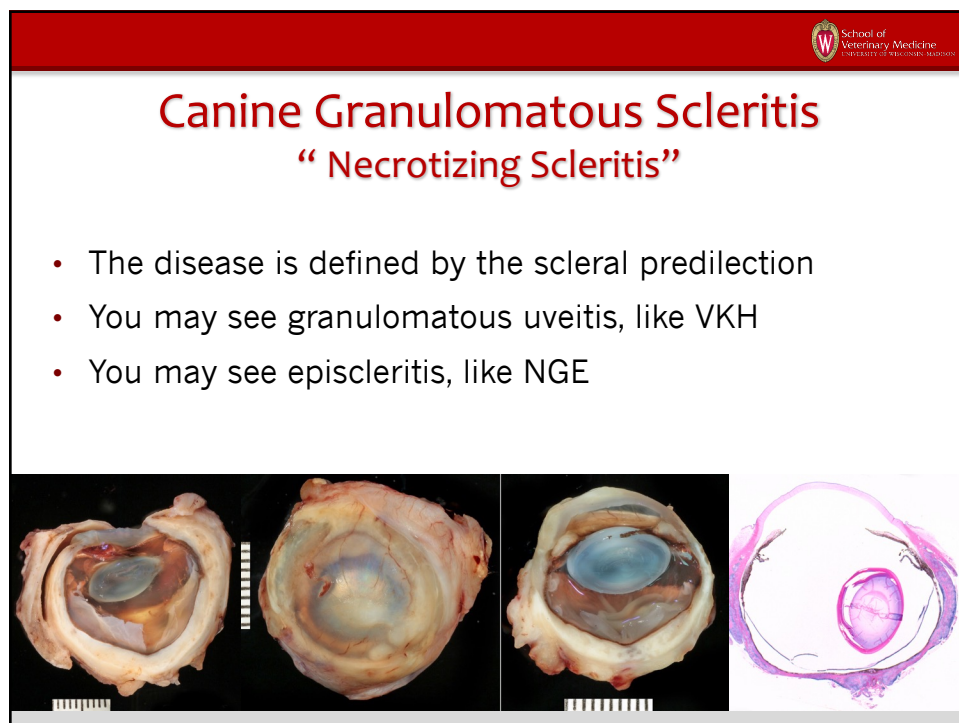
- Severe granulomatous inflammation centered on the sclera
- The term “necrotizing” causes confusion as it has been used in reference to cases with collagen degeneration/lysis or cases with neutrophils
- Can extend in the uveal tract
- No association with immune-mediated diseases affecting other sites (except 1 dog).

Denk et al, VO, 2012; Day et al. VO, 2008.

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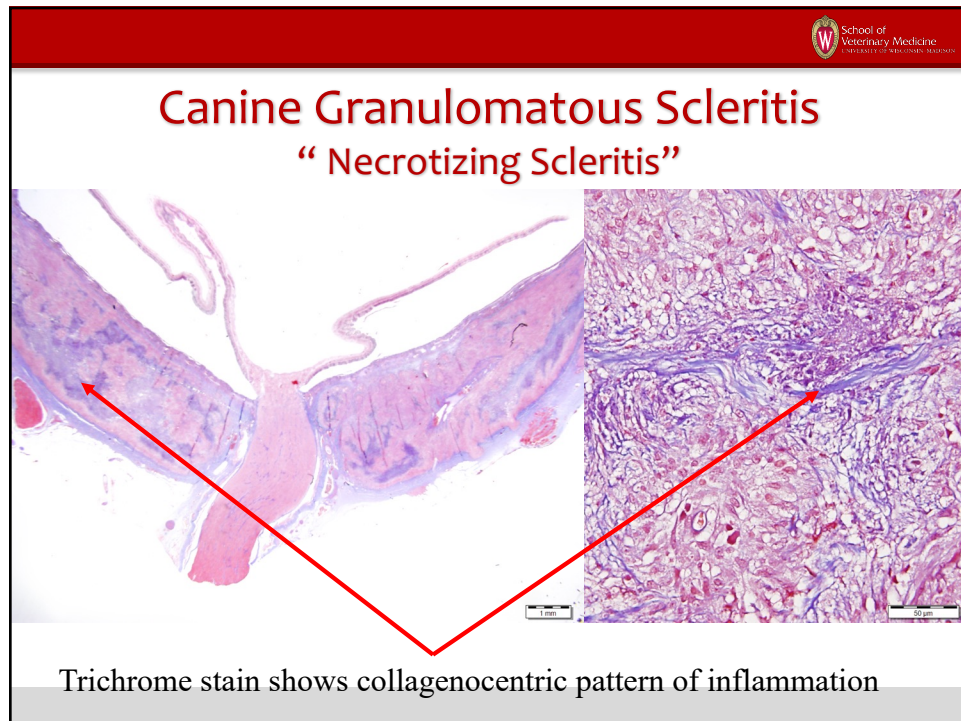
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100



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