



THE UNIVERSITY
WISCONSIN
MADISON

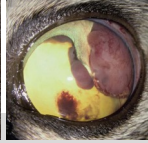


Neoplasia of the Ocular surface

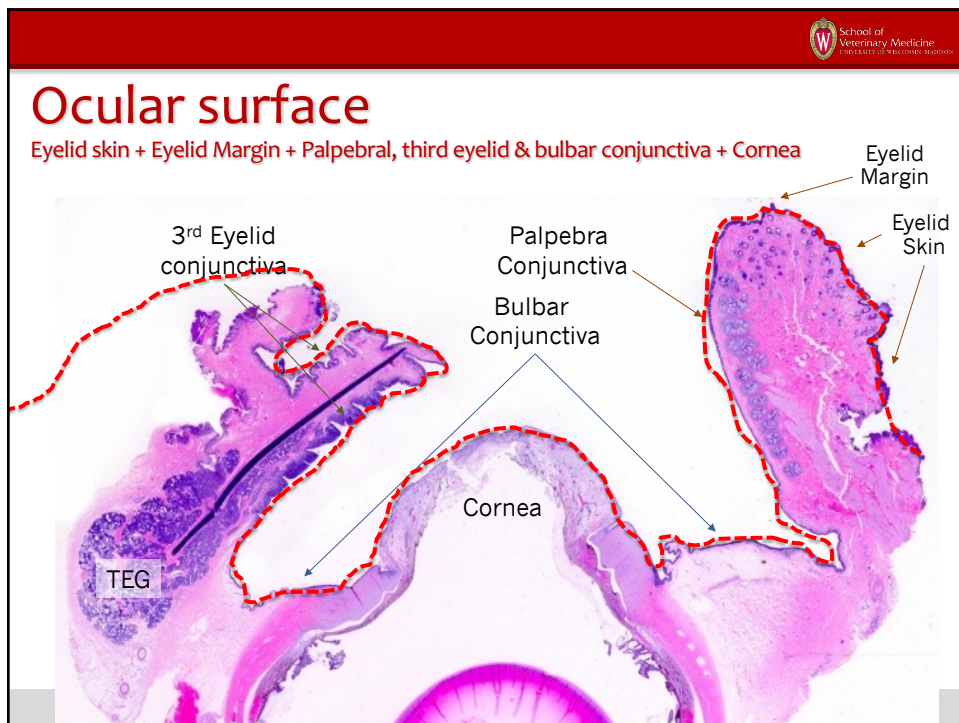
Leandro Teixeira DVM, MSc, DACVP

Associate Professor, Richard R. Dubielzig Professor of Comparative Ocular Pathology and
Director of the Comparative Ocular Pathology Laboratory of Wisconsin - COPLOW
University of Wisconsin-Madison School of Veterinary Medicine




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Ocular Surface Squamous Cell Carcinoma (OS-SCC)

- General discussion
- Dogs
 - Corneal SCC
- Cats
 - Eyelid and conjunctival SCC
 - Bowenoid SCC
- Horses
 - Corneal invasive SCC
- Bovine
 - Eyelid and conjunctival SCC

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Ocular Surface Squamous Cell Carcinoma (OS-SCC)

- SCC common epithelial neoplasm in veterinary species
- SCC one of most common tumors in or around the eye
- Cattle > Horses > Cats > Dogs
- Develops through precancerous stages (plaques > papilloma) before malignant transformation (→ SCC *in situ* → SCC) over months or years
- Can be associated with viral infections: papilloma
- Associated with excessive UV light exposure (actinic keratosis)
- Histo relatively consistent between species → **It's a SCC!**

We will discuss the ocular surface specific features

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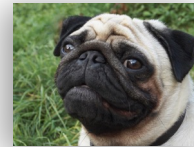
Corneal SCC in dogs with chronic keratitis and topical immunosuppressive treatment

Veterinary Ophthalmology (2011) 14, 3, 161–168

Superficial corneal squamous cell carcinoma occurring in dogs with chronic keratitis

Jennifer Dreyfus, Charles S. Schobert and Richard R. Dubielzig

Comparative Ocular Pathology Laboratory of Wisconsin, Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, 2015 Linden Drive, Madison, WI 53706-1102, USA



- 176 cases in the COPLOW Database
- All history of chronic keratitis
 - 77% Brachycephalic breed
 - 30% Pugs
- Potential local recurrence with compromised margins
- No invasion beyond ocular tissues or metastasis
- 20/21 cases with follow-up:
 - **Long standing treatment with topical ciclosporine or tacrolimus!!!**

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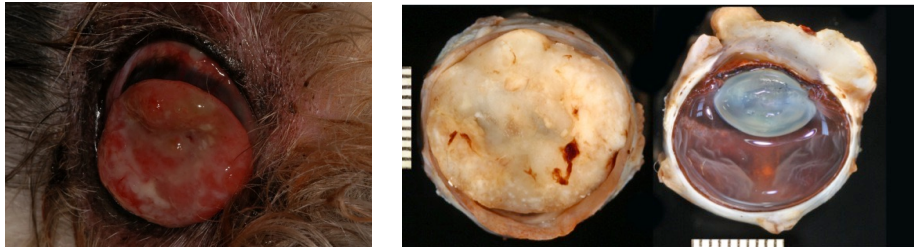
Corneal Squamous Cell Carcinoma



Dreyfus J, Schobert CS, Dubielzig RR. (2011) Superficial corneal squamous cell carcinoma occurring in dogs with chronic keratitis. *Vet Ophthalm.* 14: 161-168.

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Corneal Squamous Cell Carcinoma



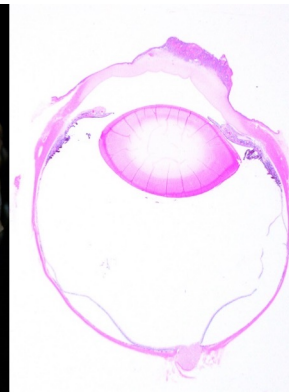
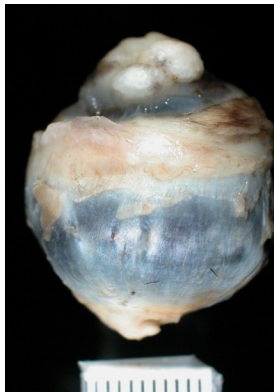
- Strong association between chronic keratitis and topical immunosuppressive treatment with corneal SCC development
- Chronic inflammation can induce neoplastic transformation
- Immunosuppressive treatment can be implicated in some instances, but we cannot be certain
 - Cyclosporine can cause alteration in cell apoptosis

Dreyfus J, Schobert CS, Dubielzig RR. (2011) Superficial corneal squamous cell carcinoma occurring in dogs with chronic keratitis. *Vet Ophthalm.* 14: 161-168.

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Corneal Squamous Cell Carcinoma

- 9 y/o Male Pug dog
 - Chronic pigmentary keratitis
 - Cyclosporin treatment for last 2 years
 - Corneal mass 6 months prior
 - Suspicion of SCC
 - Owner elected enucleation



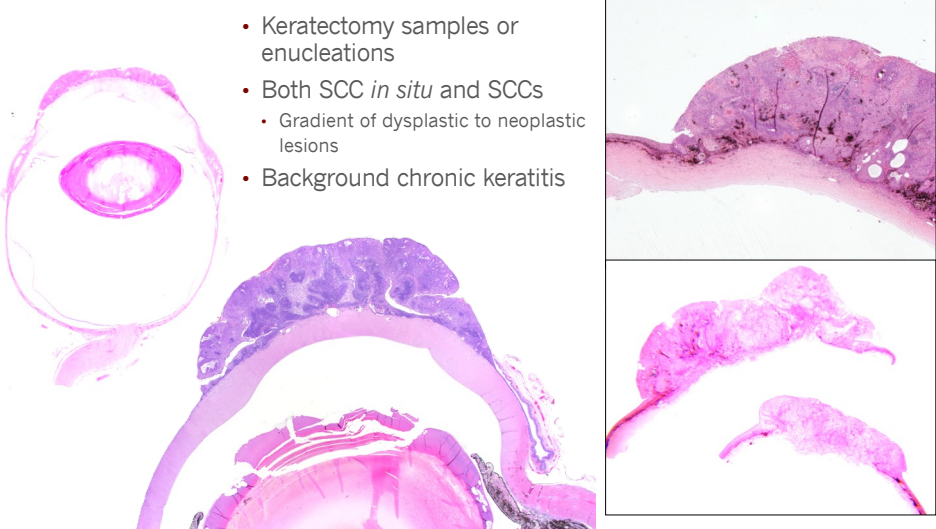
Dreyfus J, Schobert CS, Dubielzig RR. (2011) Superficial corneal squamous cell carcinoma occurring in dogs with chronic keratitis. *Vet Ophthalm.* 14: 161-168.

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Corneal Squamous Cell Carcinoma

- Keratectomy samples or enucleations
- Both SCC *in situ* and SCCs
 - Gradient of dysplastic to neoplastic lesions
- Background chronic keratitis

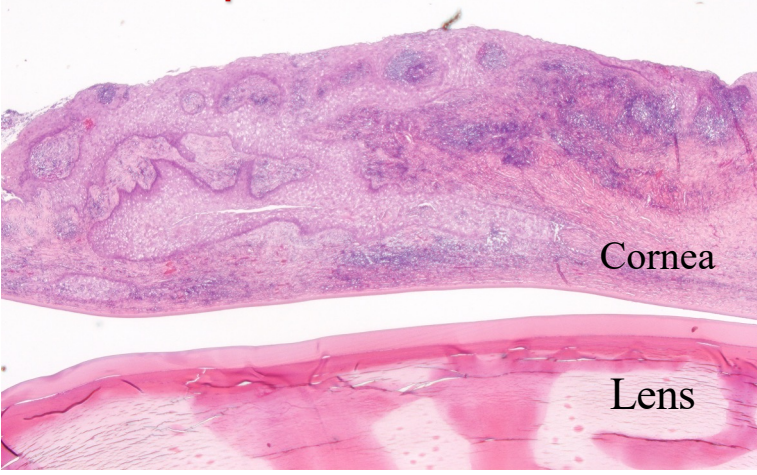


Dreyfus J, Schobert CS, Dubielzig RR. (2011) Superficial corneal squamous cell carcinoma occurring in dogs with chronic keratitis. *Vet Ophthalm.* 14: 161-168.

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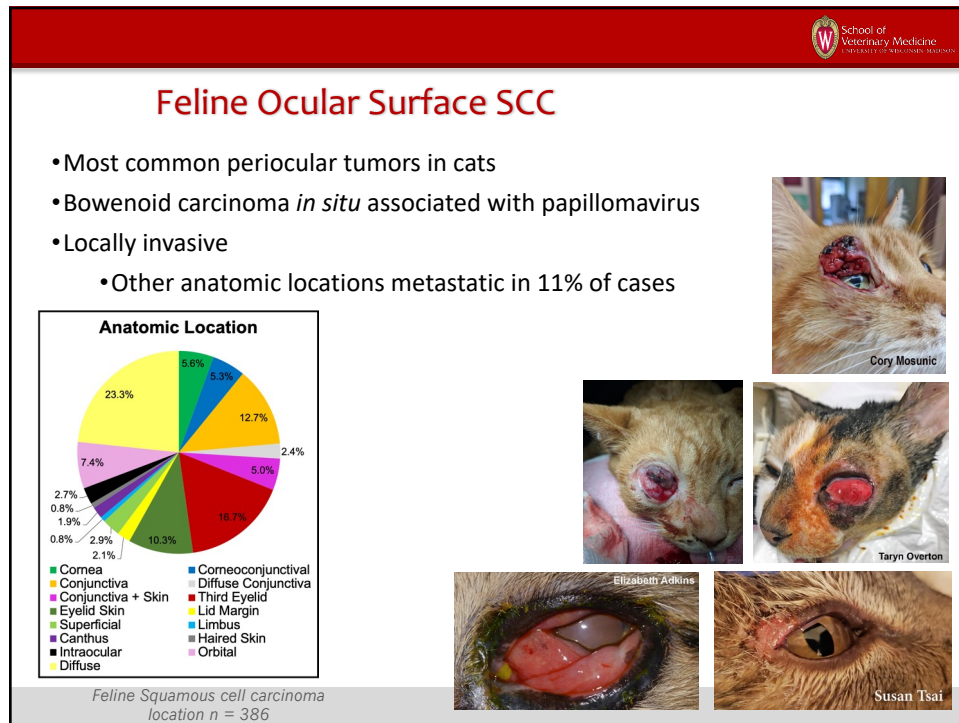
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Corneal Squamous Cell Carcinoma

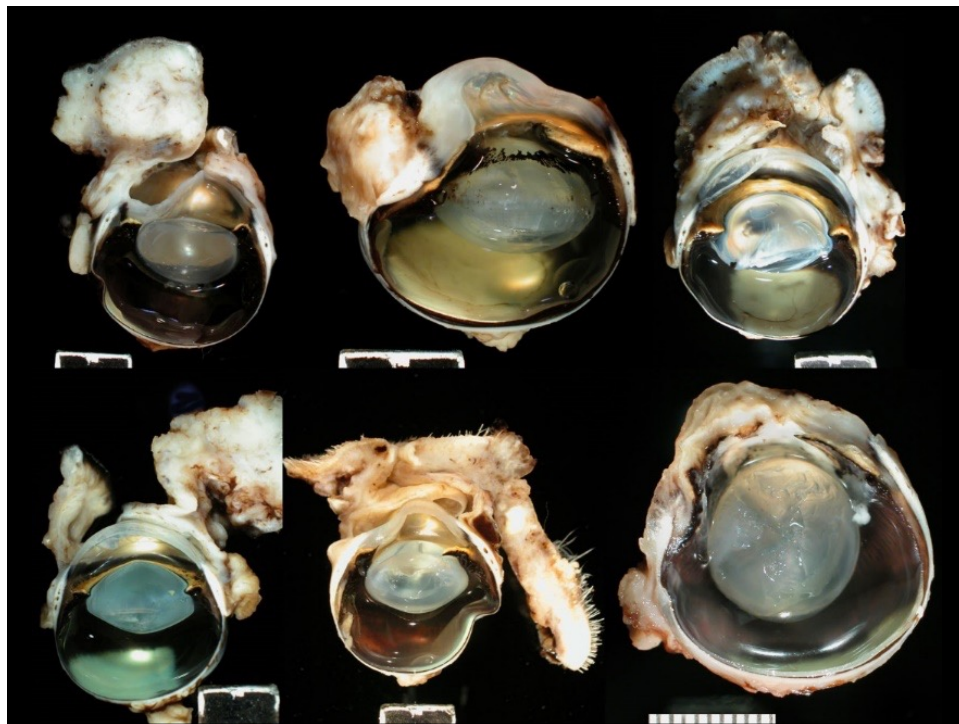


Multiple recurrences extending deep into the corneal stroma requiring enucleation in this case

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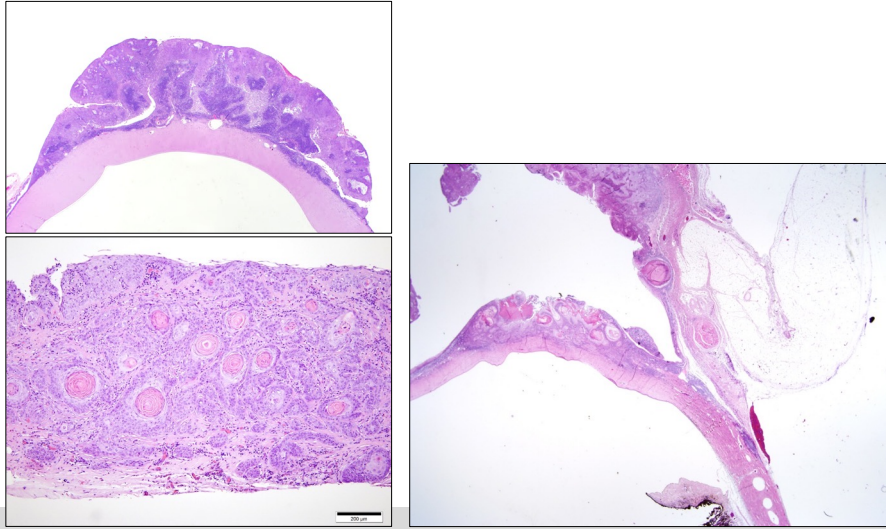


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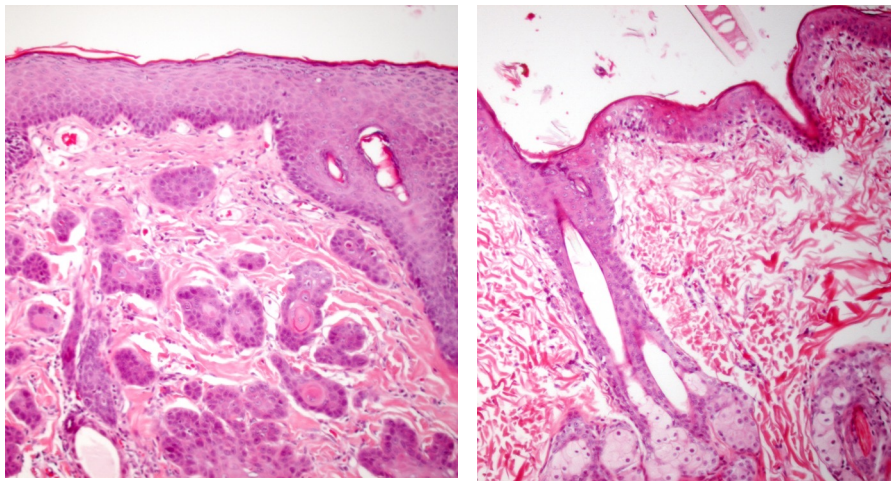
Feline Ocular Surface SCC



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Feline Ocular Surface SCC

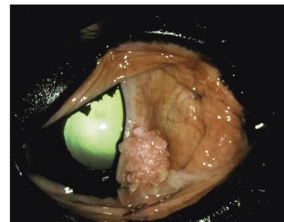
Bowenoid in situ carcinoma (BISC)
(papillomavirus-associated squamous cell carcinoma in situ)



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Equine Ocular Surface SCC

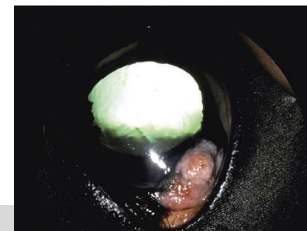
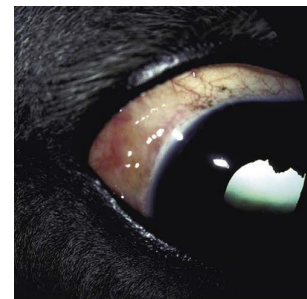
- Similar to other species
- Can be exophytic, plaque-like, or invasive
- Clear spectrum of progression
 - Hyperplasia > dysplasia/SCC *in situ* > overt SCC
- Mets late
- Look for other signs of UV damage



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Equine Ocular Surface SCC

- 186 cases in the COPLOW collection (10% of equine submissions)
- UV light exposure
 - High % of mutant p53 expression
 - Prevalence in geographic regions with high UV light exposure
 - More likely to occur in less pigmented animals
 - Solar elastosis and actinic keratosis common present



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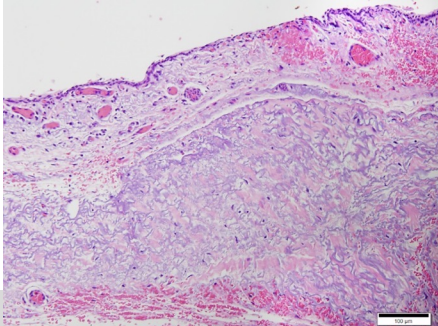
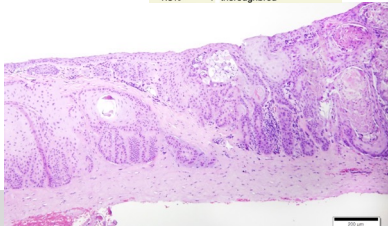
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Equine Ocular Surface SCC

Solar elastosis – 30% cases

Mary Lassaline – UC-Davis

- Associated with a variant in UV damage DNA repair gene
 - Damage-specific DNA Binding Protein 2 (DDB2)*
- Strongly associated with cancer risk in Haflingers and Belgians

Breeds SCC & solar elastosis

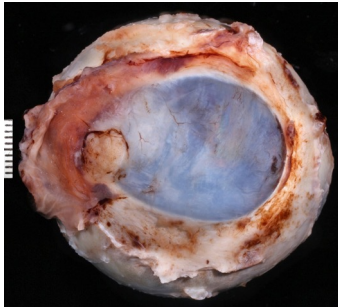
7.3%	4	0 breed not specified
3.6%	2	1 mixed breed
14.5%	8	American paint
1.8%	1	American quarter pony
9.1%	5	American quarterhorse
10.9%	6	Appaloosa
1.8%	1	Arabic
1.8%	1	Belgian
16.4%	9	Haflinger
1.8%	1	Knabstrupper
1.8%	1	Morgan
1.8%	1	Oldenburg
10.9%	6	paint
1.8%	1	palomino
1.8%	1	Pony of the Americas
7.3%	4	quarterhorse
1.8%	1	Rocky Mountain horse
1.8%	1	Tennessee walker
1.8%	1	thoroughbred

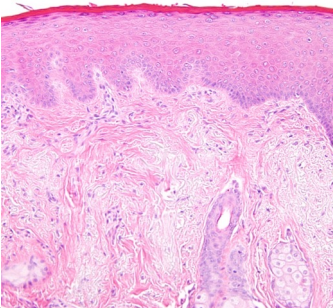
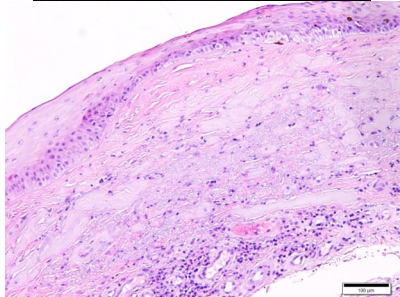
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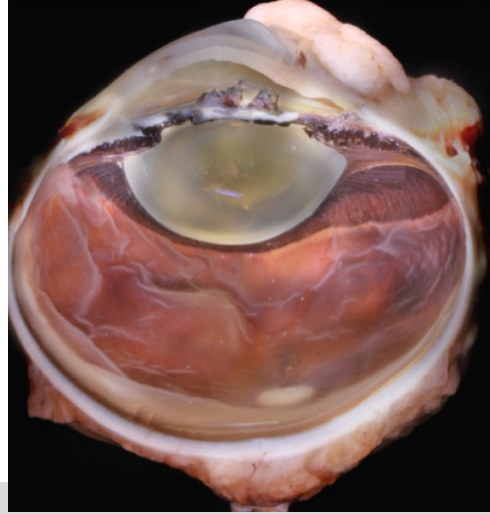
Solar elastosis

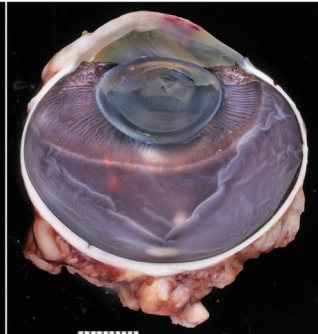
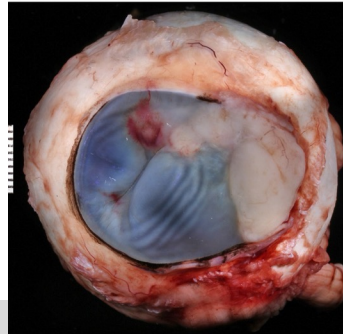
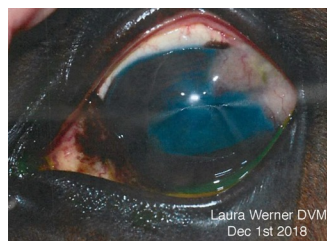
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Equine Ocular Surface SCC

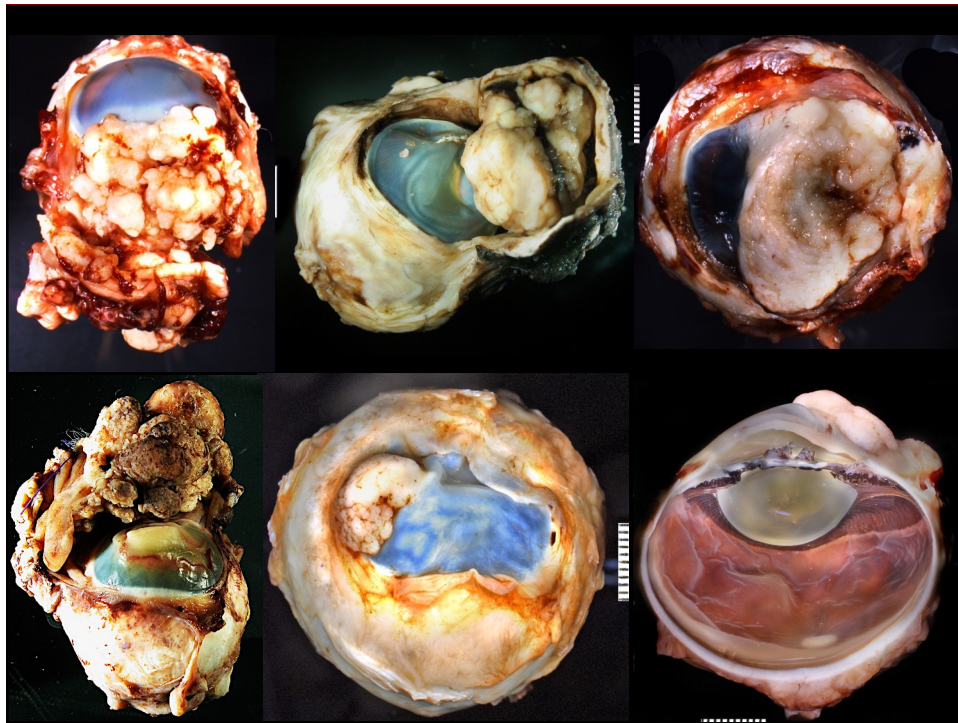


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Equine Ocular Surface SCC



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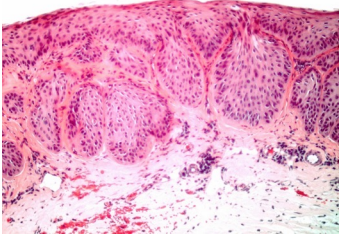
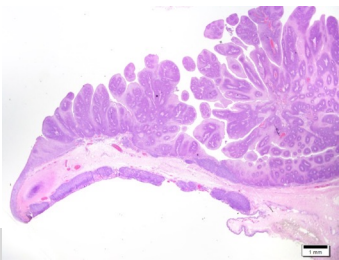
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Equine Ocular Surface SCC

Epithelial dysplasia – pre-neoplastic - 19 cases

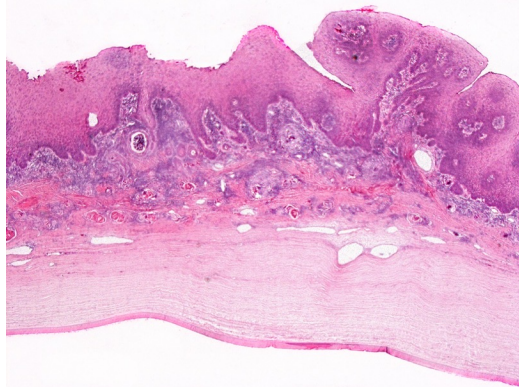
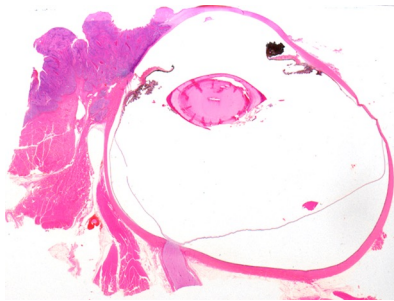


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Equine Ocular Surface SCC

- Keratectomy samples more common than enucleations
- Both SCC *in situ* and SCCs
 - Gradient of dysplastic to neoplastic lesions
- Associated chronic inflammation and solar elastosis

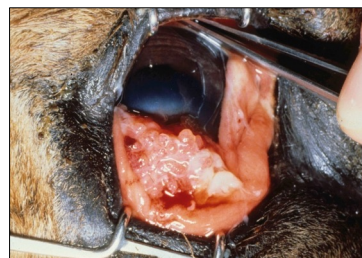


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Equine Ocular Surface SCC

Malignant potential

- Aggressive local invasion
 - orbit, maxilla, globe, intracranial
- Systemic metastasis
 - Late, only 5% of cases
 - 3rd eyelid lymphatics continuous with orbital lymphatics
 - Parotid Inn → regional Inn → thoracic duct → circulation → heart, lungs, pleura, liver, kidney



Slide courtesy of Dr. P. Miller

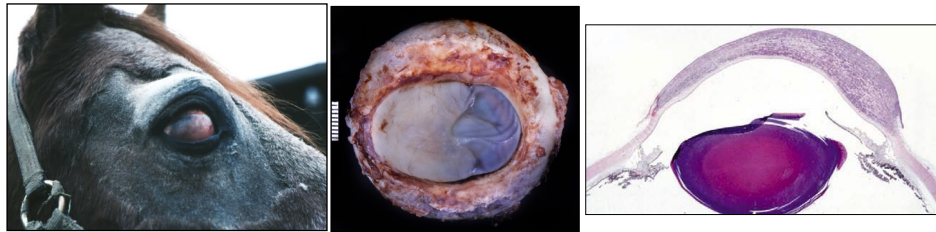


Slide courtesy of Dr. P. Miller

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Stromal invasive SCC in Horses

- 23 cases in the COPLOW collection
 - Variant of limbal conjunctival SCC which primarily infiltrates the corneal stroma
 - Masquerades as corneal stromal keratitis!!

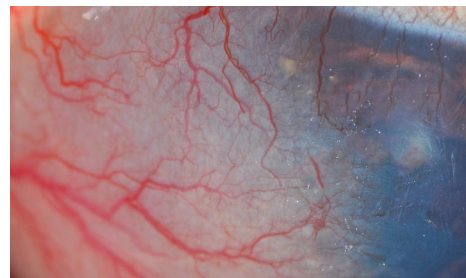


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Stromal invasive SCC



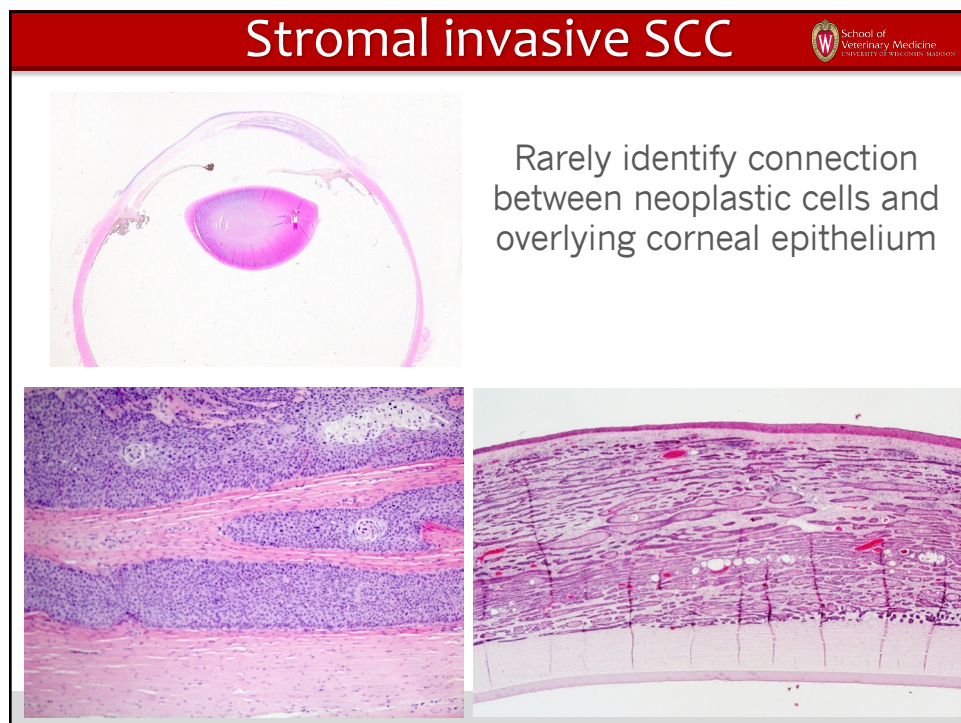
- Adult male Appaloosa: Uncooperative horse
- Original Dx: Stromal Keratitis
 - Failed to respond to treatment
- Diagnosed at the Vet School in Vienna
SISCC
- Treated with lamellar keratectomy, conj.
graft then mitomycin



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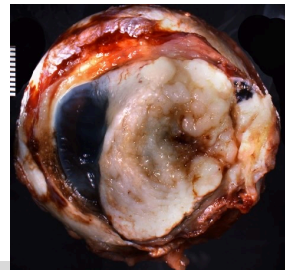
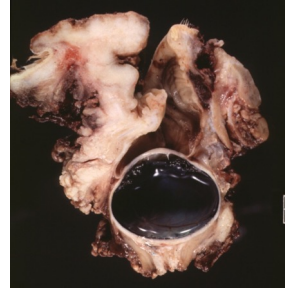
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OS-SCC Bovine

- Most common and economically important neoplasm of North American cattle;
- Major cause of carcass condemnation;
- *Bos taurus* cattle commonly affected
- 70% from bulbar conjunctiva at limbus, then, nictitating membrane, palpebra or cornea.



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Ocular Surface Vascular tumors

- Dogs > Horses > Cats > Others
- Strongly associated with excessive UV light exposure (actinic keratosis)
 - Non-pigmented eyelids and conjunctiva
 - Temporal bulbar conjunctiva and third eyelid margin
- More often benign (hemangioma) than malignant (hemangiosarcoma)

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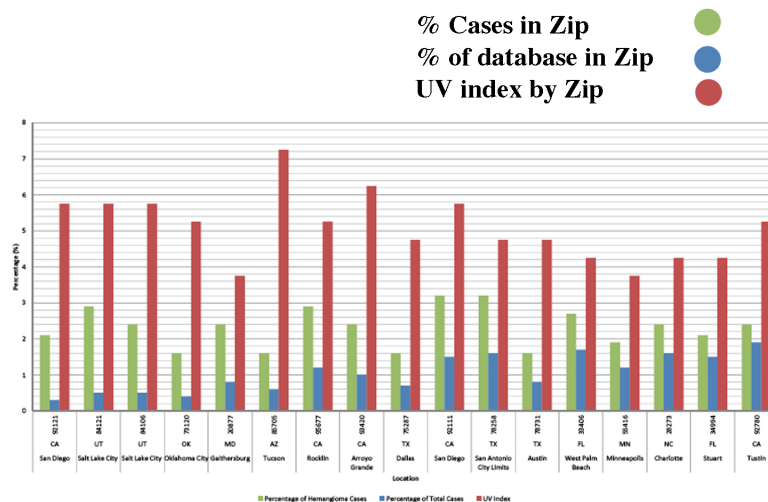
Canine Conjunctival Hemangioma/sarcoma

- 196 cases in the COPLOW database
 - 22 Boxer
 - 18 Australian Shepherd
 - 15 Basset Hound
 - 14 Border Collies
- Located either in the temporal bulbar
- or third eyelid margin
- Benign and malignant determined by histologic “standard criteria”
- Non-pigmented conjunctiva
- UV-light exposure is a risk factor

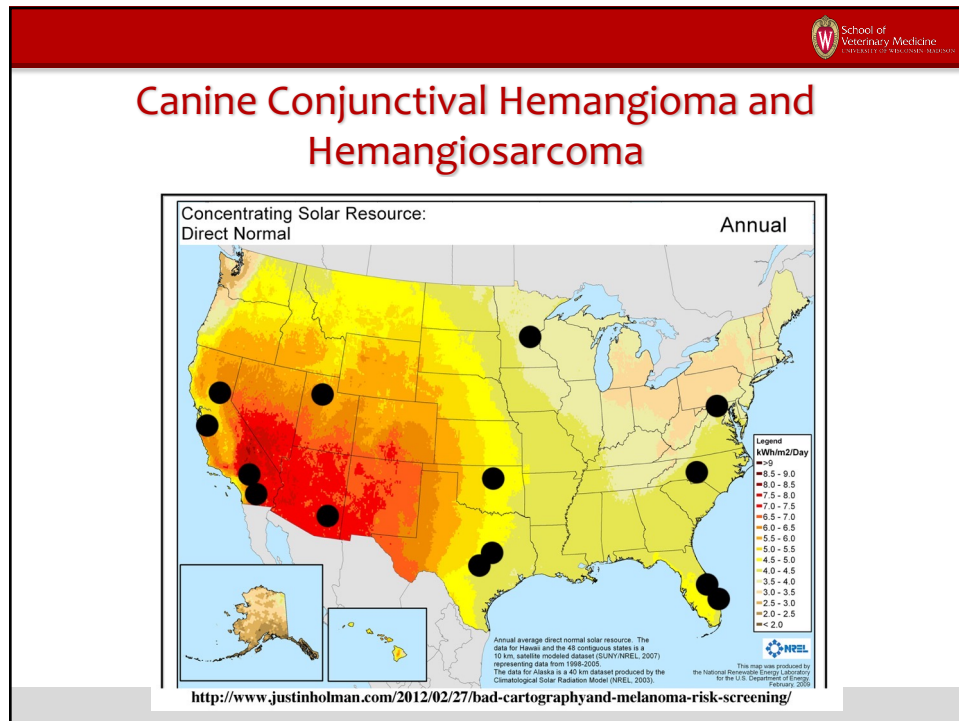


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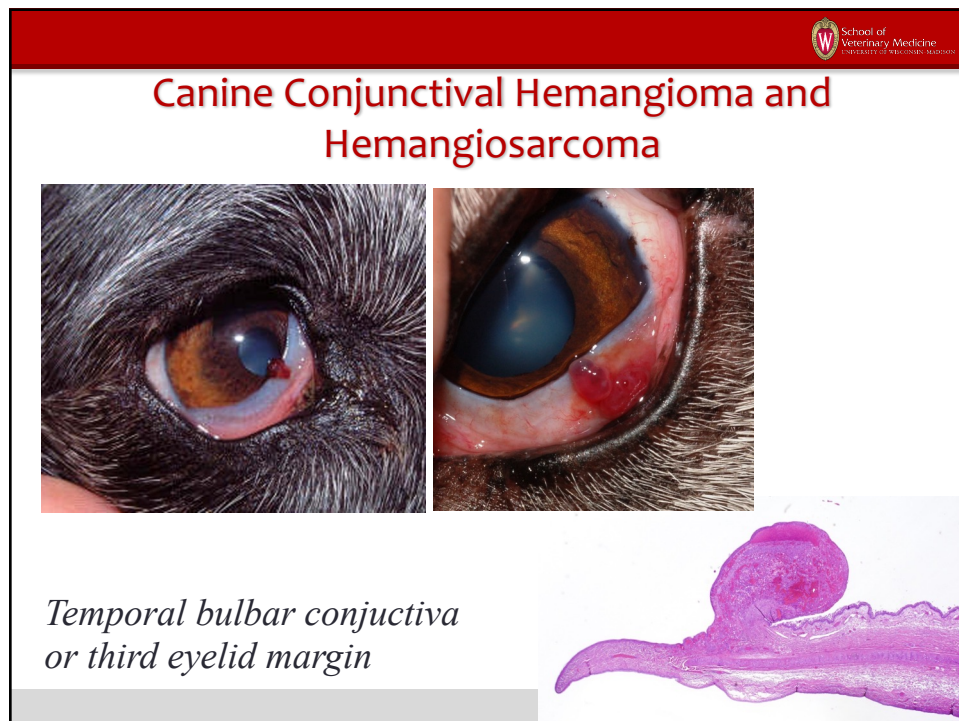
Canine Conjunctival Hemangioma and Hemangiosarcoma by Zipcode



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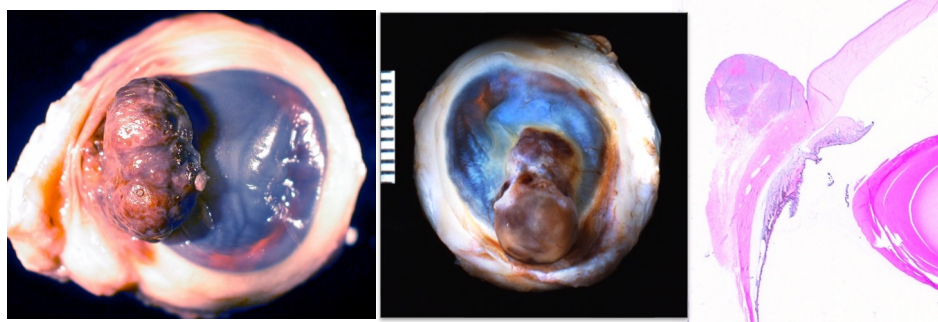


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Canine Conjunctival Hemangioma and Hemangiosarcoma

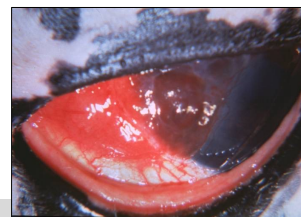


Temporal bulbar conjunctiva or third eyelid margin

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Equine conjunctival hemangiosarcoma

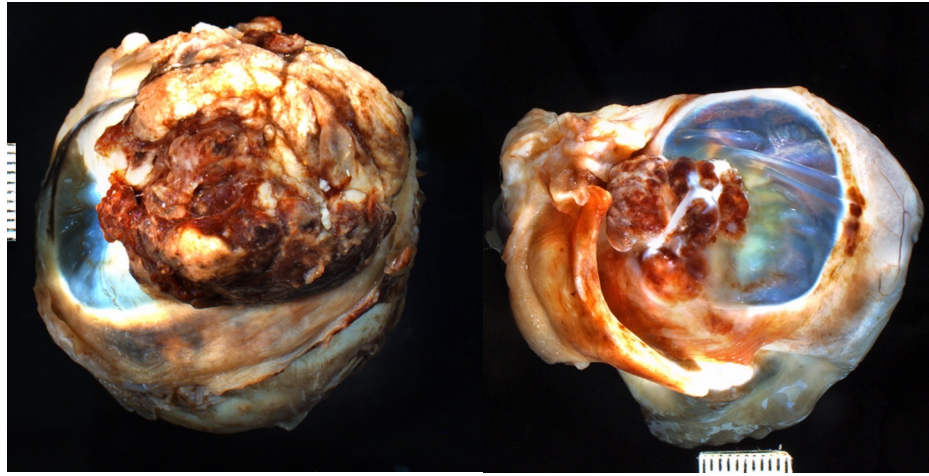
- Clinical appearance similar to other species
 - Most common locations:
 - Temporal conj. and third eyelid margin
 - More exposed to UV light
- Histologically variably
 - Solid, vascular, and HEAVILY inflamed areas
 - Can make misdiagnosis easy
 - May require IHC (Factor VIII > CD31)



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Hemangiosarcomas

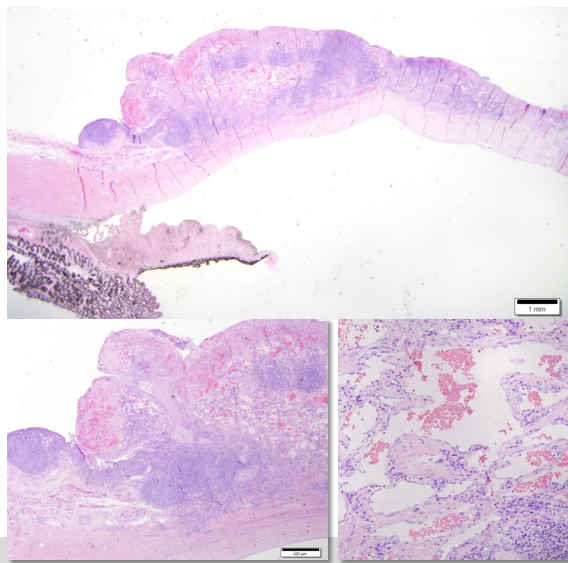
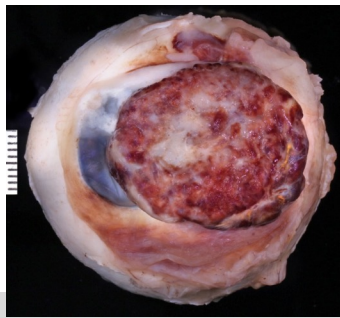
19 cases – 5 corneal



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Hemangiosarcoma -corneal

- Associated with chronic corneal disease
 - Requires pre-existing corneal neovascularization
- Ddx: Extension of conjunctival tumor



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Ocular/Periocular Melanocytic Tumors

Conjunctival
Palpebral, bulbar & 3rd eyelid

- Melanomas > melanocytoma
- Often recur, rarely met.
- Can be multifocal – pagetoid spread

Eyelid, Cutaneous

- Identical to cutaneous other sites
- Melanocytoma > Melanomas

Uveal

- Melanocytoma > Melanomas
- Iris/CB > Choroid
- Rarely met. or recur

Limbus

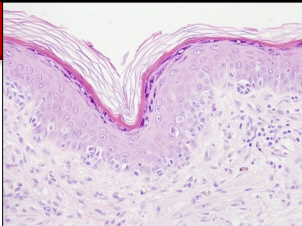
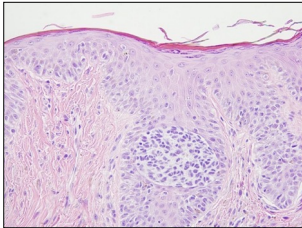
- Limbal melanocytoma
- Almost always benign

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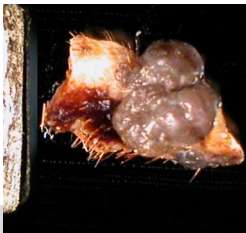
Eyelid Melanocytic Tumors *usually melanocytoma*

39 Cases in the COPLOW database

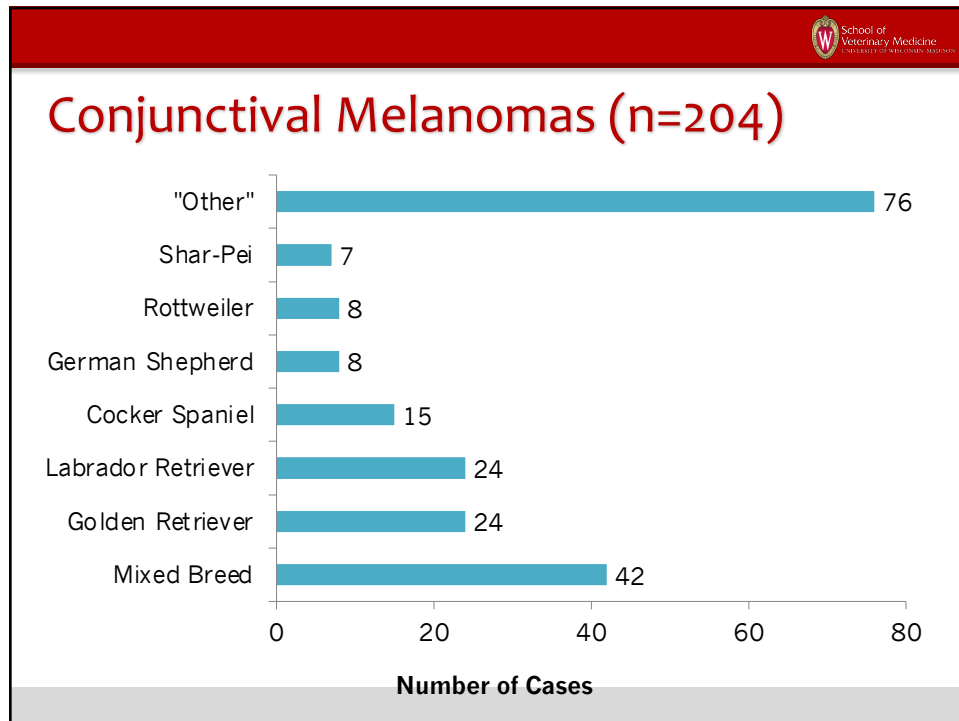
- 7 Mixed breed
- 6 Vizsla
- 4 Golden Retriever
- 3 Yorkshire Terrier
- 3 Doberman (White)





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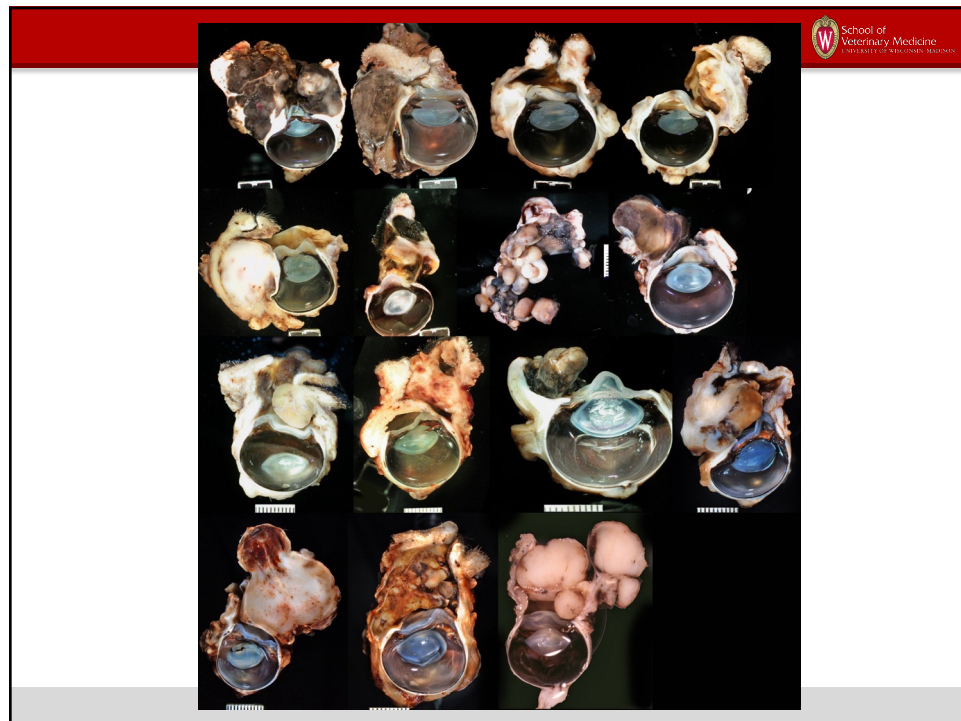
Conjunctival Melanomas

- Darkly pigmented conjunctiva are predisposed
- Malignant by morphologic criteria
- Most recur elsewhere in the conjunctiva
- Rarely metastasize

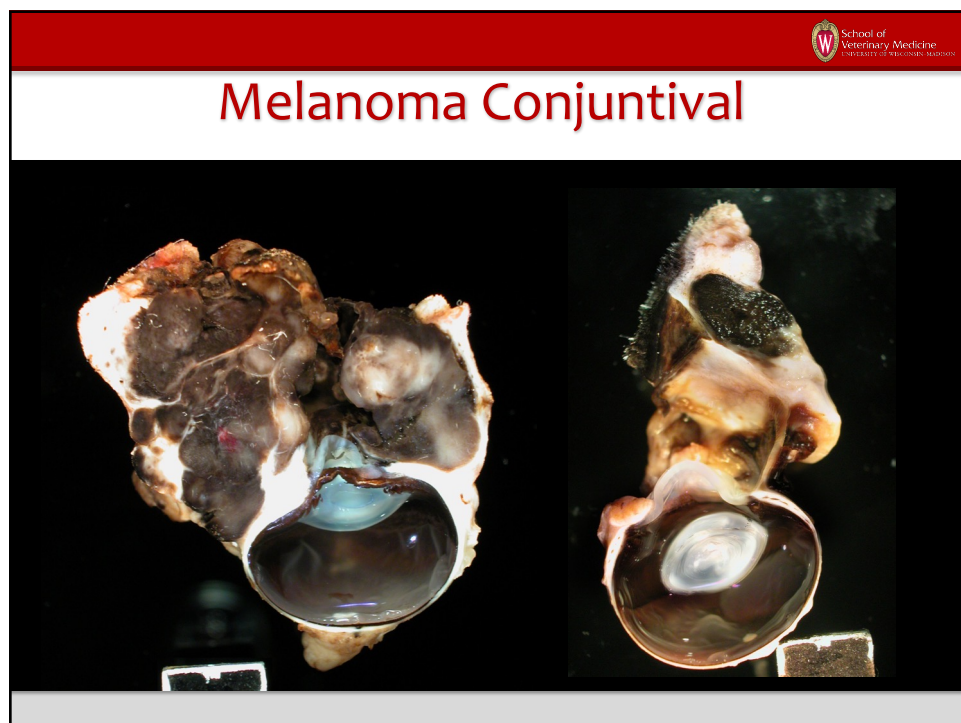


1. Reilly CR, Dubielzig RR, Newman SJ, Bergman PJ. (2005) Features of canine conjunctival Melanocytic Tumors. ACVO. Nashville.

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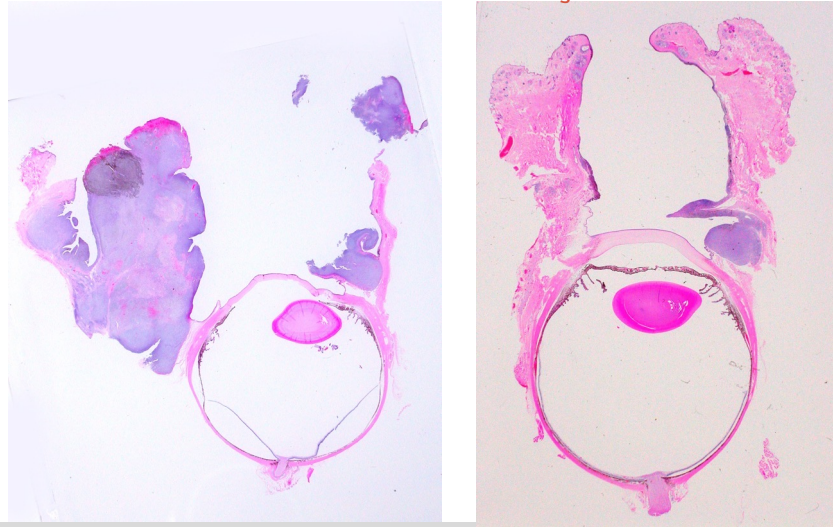
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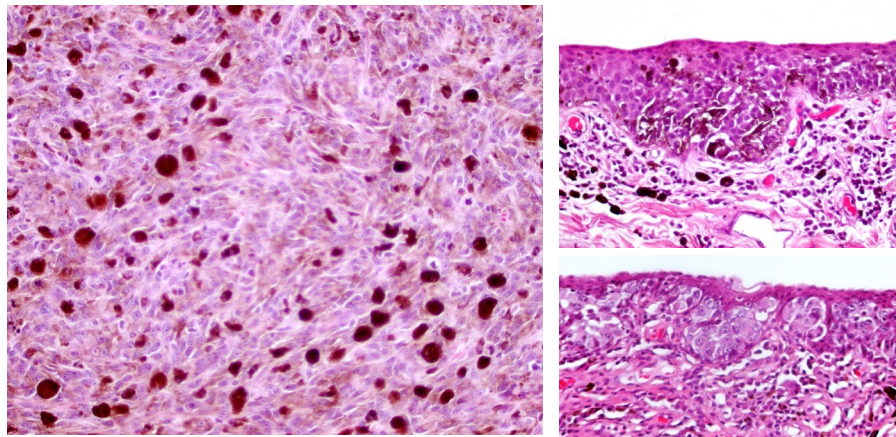
Melanoma Conjuntival

Distribuição multifocal



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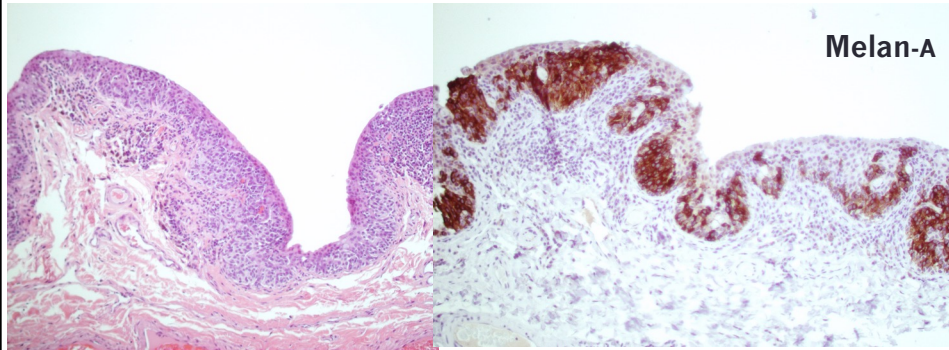
Melanoma Conjuntival



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Melanoma Conjuntival

“pagetoid” spread within the epithelium



Tumores tendem a reaparecer em outros locais da conjuntiva

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Feline conjunctival melanoma

- Variably pigmented
- Can be metastatic despite “bland nuclear features” and low mitotic rate
- Distinguish from “limbal melanocytoma”
 - Melanocytomas involve limbal stroma; heavily pigmented
 - Melanomas more substantia propria

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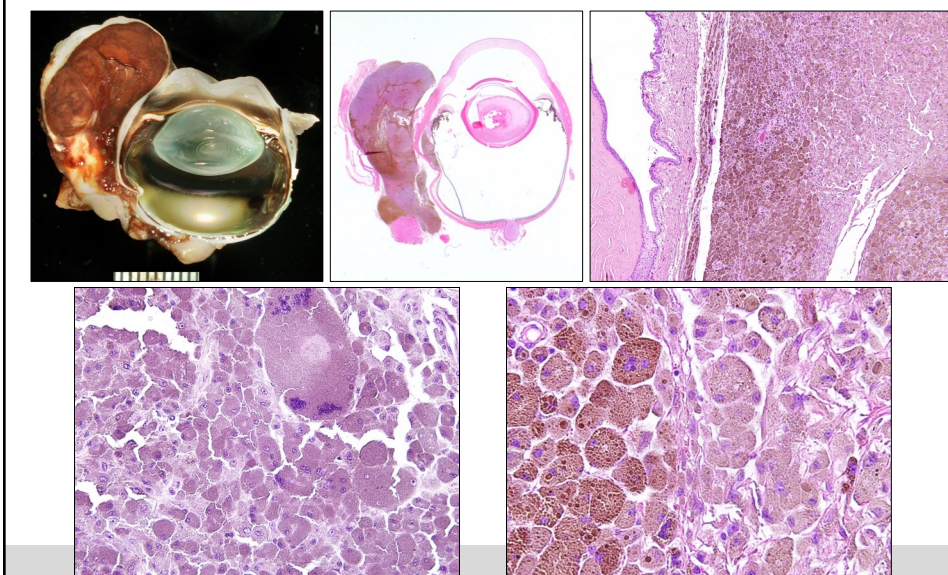
Feline Conjunctival Melanoma

50 cases in the COPLOW database



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Feline Conjunctival Melanoma



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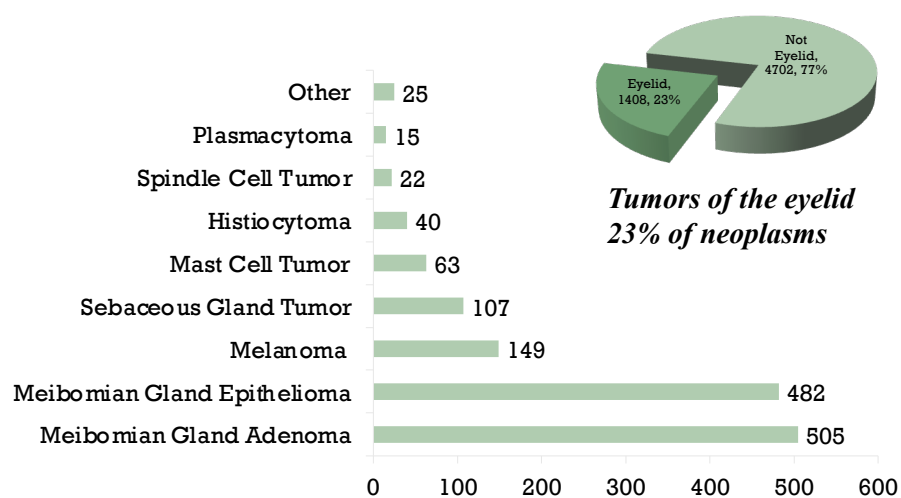
Eyelid margin and cutaneous palpebral neoplasm

General Considerations

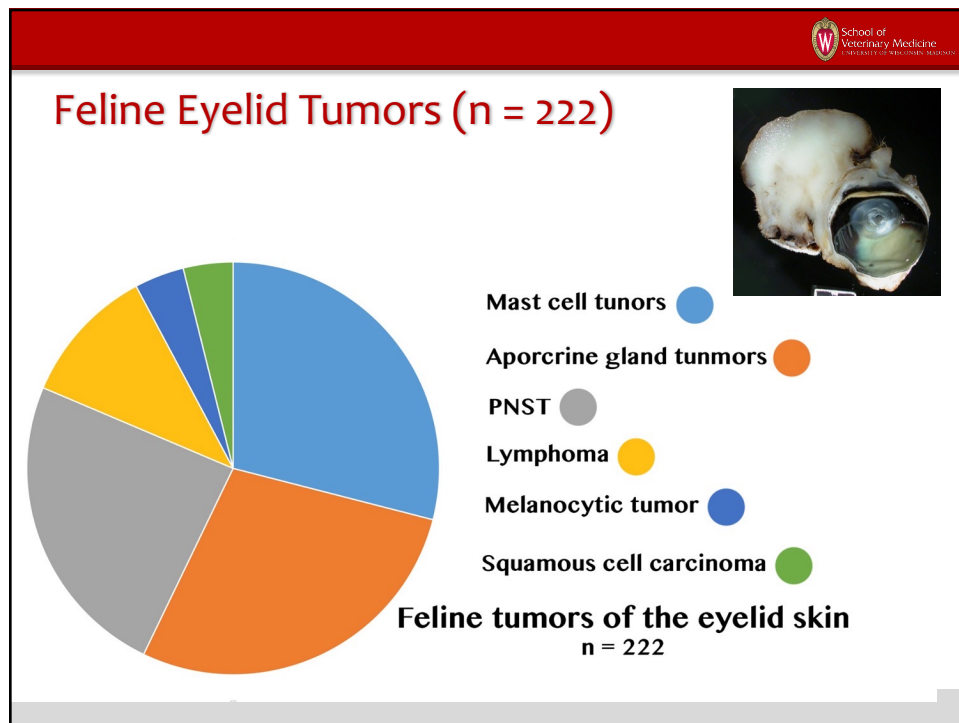
- Any cutaneous neoplasm can affect the eyelid skin
- Predisposition to the head/neck region
- Epithelial neoplasms
- Melanocytic neoplasia
- Round cell neoplasms
- Mesenchymal neoplasms
- Non-neoplastic masses

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Canine Primary Eyelid Tumors (n = 2705)



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Tumors of the Meibomian Gland

(Numbers from 2012)

1207 cases in the COPLOW database

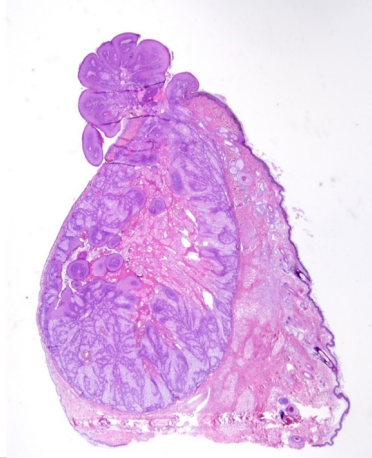
- 233 Mixed breed
- **222 Labrador Retriever**
- 91 Golden Retriever
- 66 Cocker Spaniel
- 47 Shih Tzu



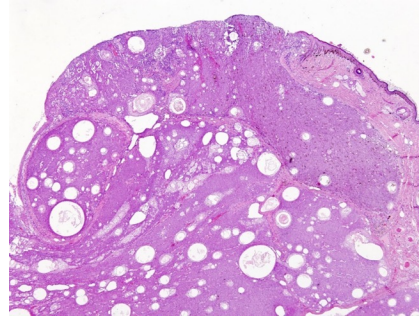
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Tumors of the Meibomian Gland

Adenoma: 648 cases



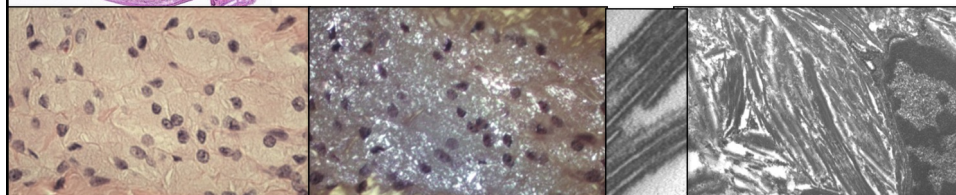
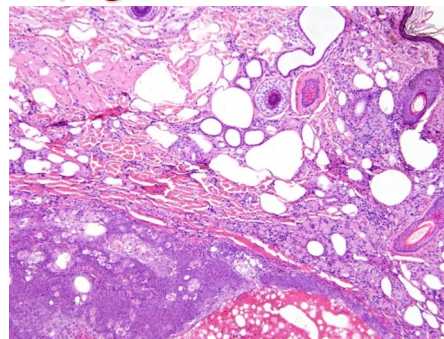
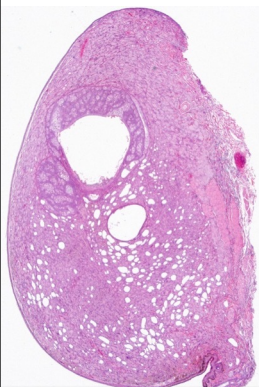
Epithelioma: 576 cases



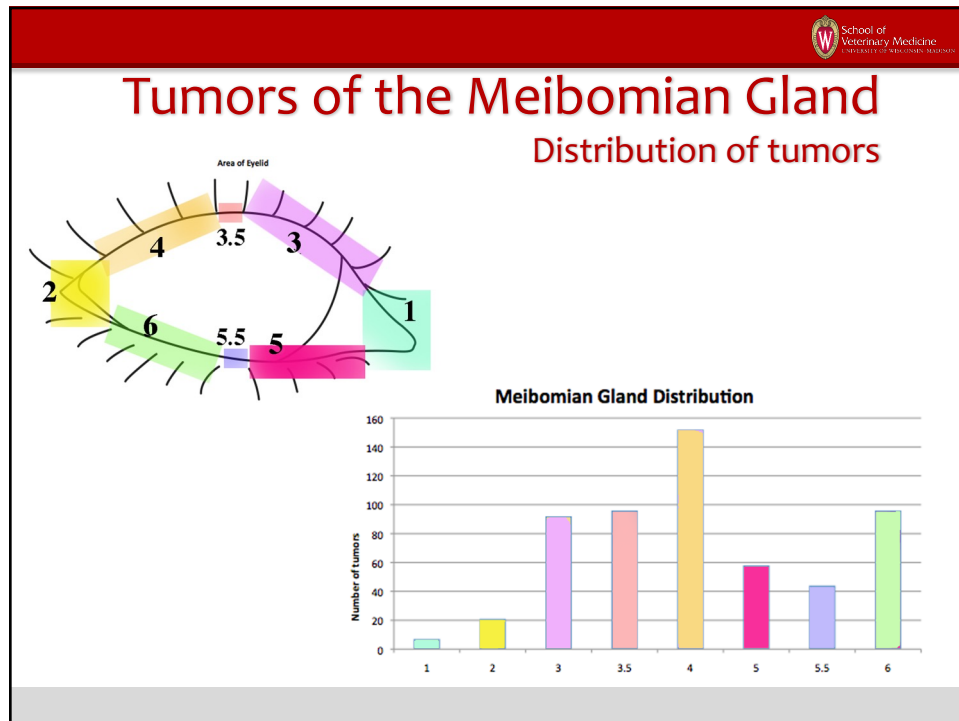
55

Tumors of the Meibomian Gland

Lipogranuloma



56



57

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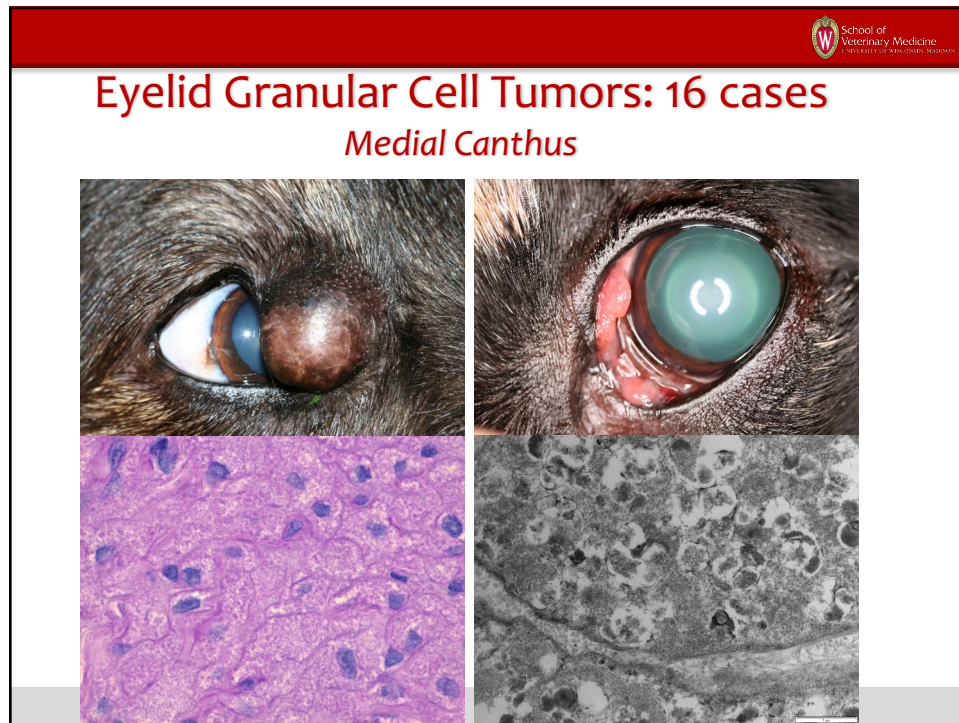
Eyelid Cutaneous Mast Cell Tumors

175 Mast Cell Tumors in the COPLOW database

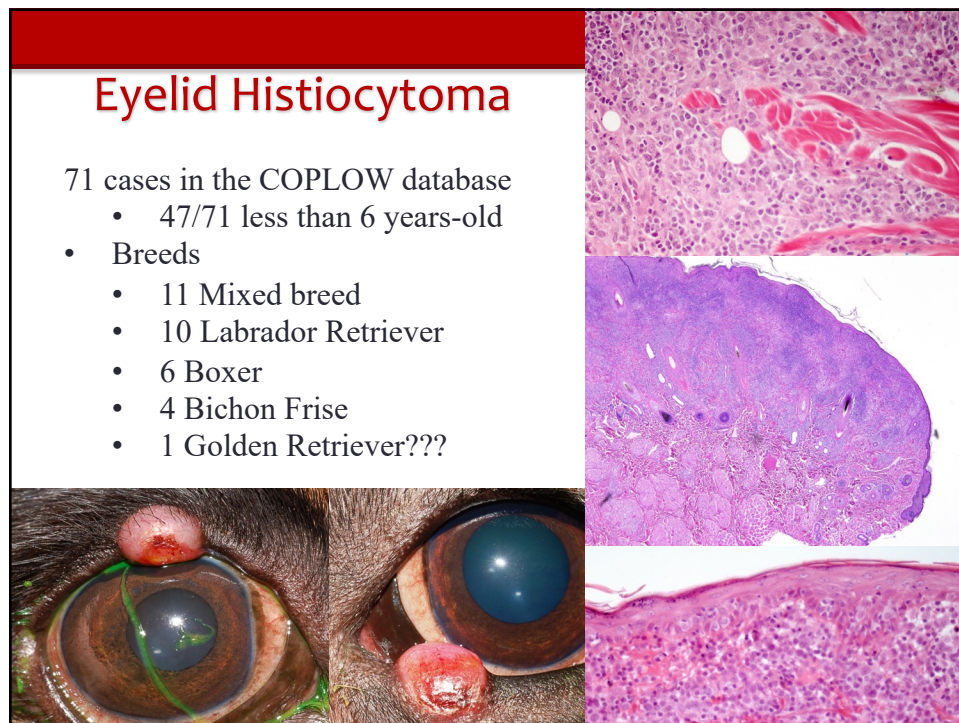
- 80 cases are conjunctival
 - 16 Mixed breed
 - 18 Labrador Retriever
 - 10 Golden Retriever
- Conjunctival tumors have a better prognosis than expected
- Grading systems are unproven in the conjunctiva

The three photographs show different presentations of conjunctival tumors: a large, fleshy, pinkish-red mass on the inner surface of the lower eyelid; a smaller, blue, nodular mass on the conjunctiva; and a large, fleshy, pinkish-red mass on the inner surface of the upper eyelid.

58



59

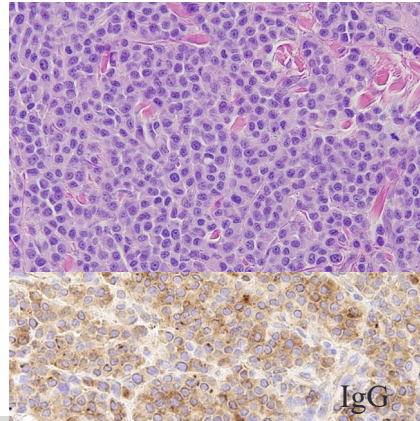
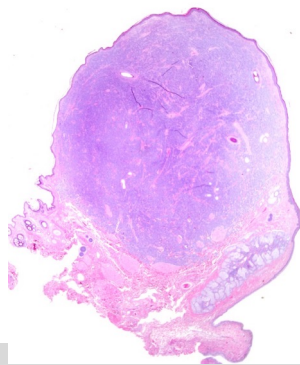


60

Eyelid/Conjunctival Plasmacytoma

- 39 cases of plasmacytoma in the COPLOW database
- 8 eyelid skin, 5 lid margin and 12 conjunctival

Lid Margin

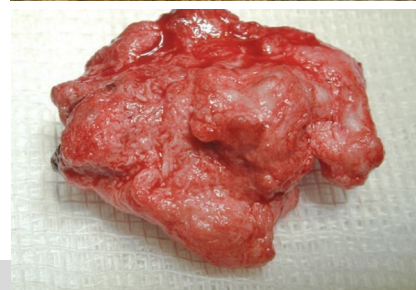
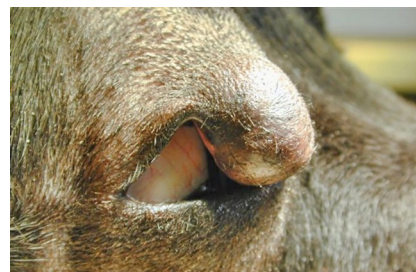


61

Canine Mesenchymal Hamartoma

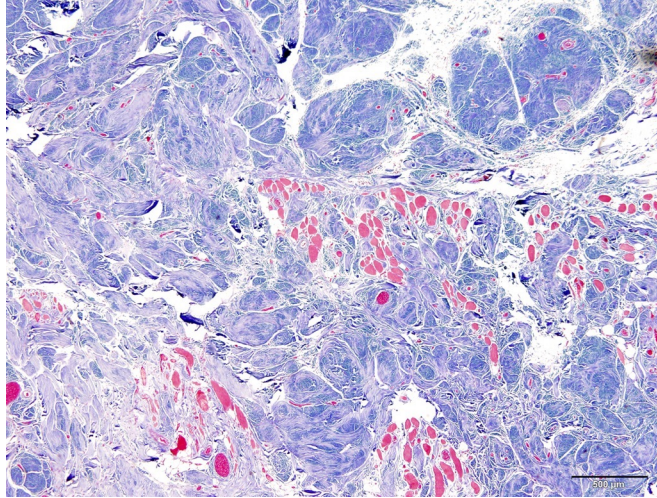
- 22 cases
- Almost all at lateral canthus
- Mostly large breed dogs
- 12 OD, 6 OS, 1 OU

1	1 mixed breed
1	Alaskan husky
2	basset hound
1	boxer
1	Doberman pinscher
1	English cocker spaniel
1	German shepherd
1	giant schnauzer
3	golden retriever
1	Jack Russell terrier
2	Labrador retriever
1	munsterlander
3	rottweiler
1	Staffordshire terrier
1	weimaraner
1	Wheaten terrier



62

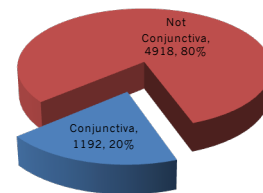
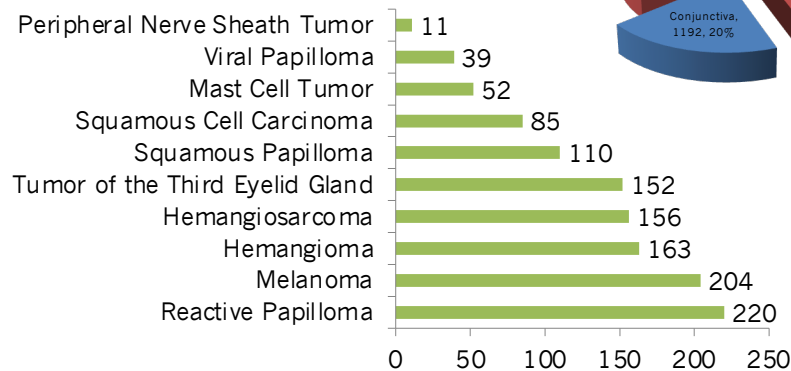
Canine Mesenchymal Hamartoma



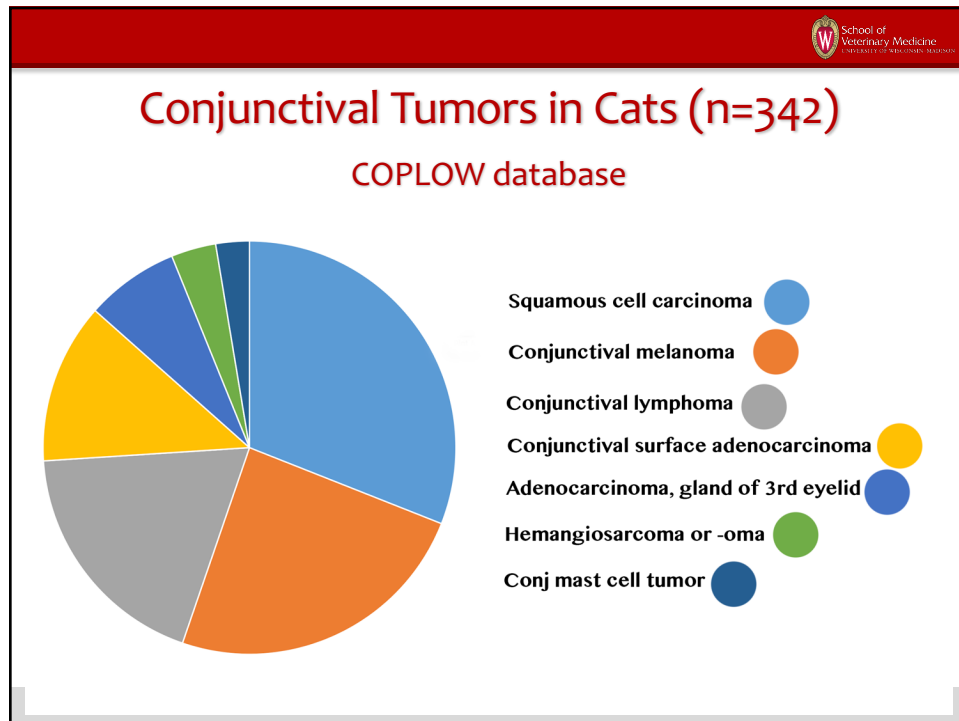
63

Conjunctival Tumors in Dogs

(n = 1280)



64

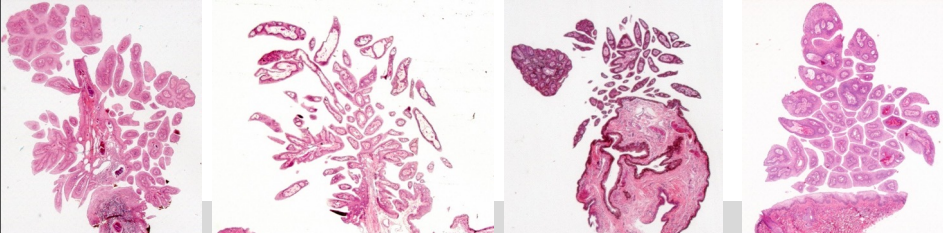


65

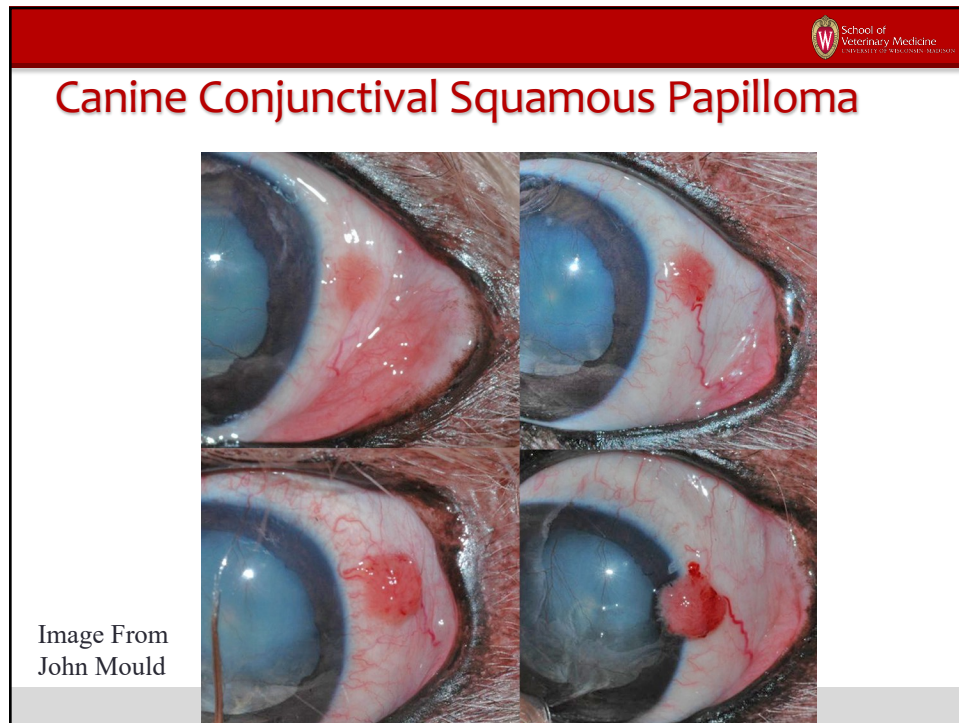
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Canine Conjunctival Squamous Papilloma

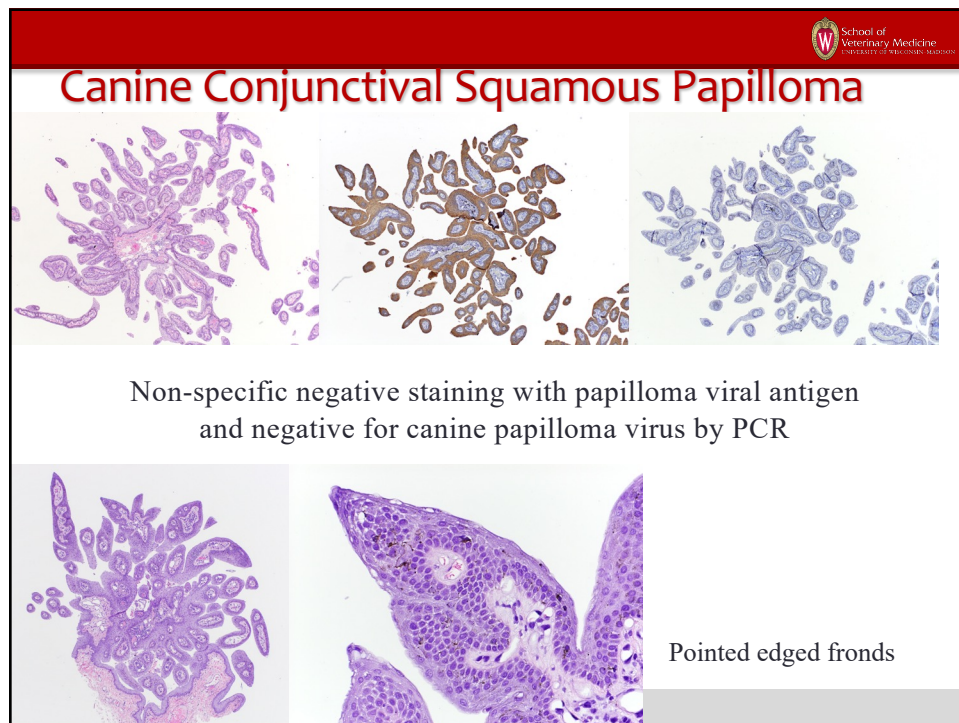
- 183 cases in the COPLOW database
 - 25 Golden Retriever
 - 24 Mixed breed
 - 12 Shih Tzu
 - 11 Labrador Retriever
- Characterized by pointed fronds of epithelium
- No underlying inflammation or neoplasia
- These are seldom correctly diagnosed clinically

66



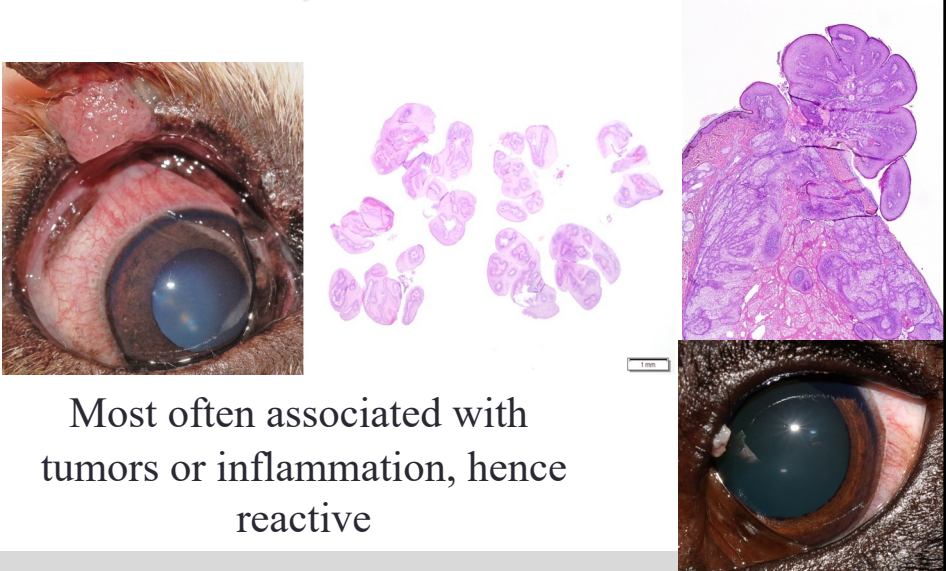
67



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Canine Conjunctival Reactive Papilloma



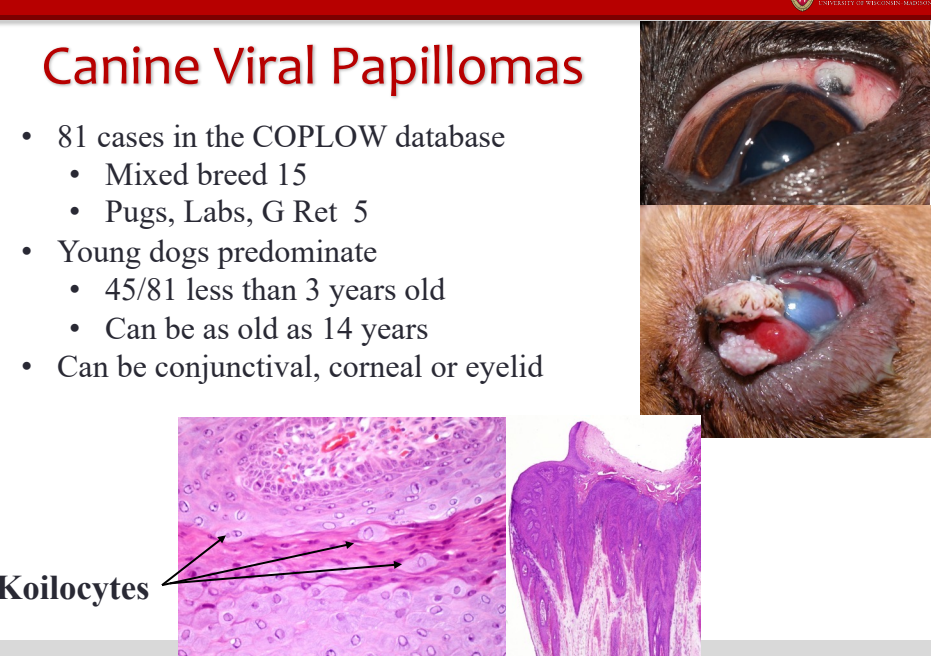
Most often associated with
tumors or inflammation, hence
reactive

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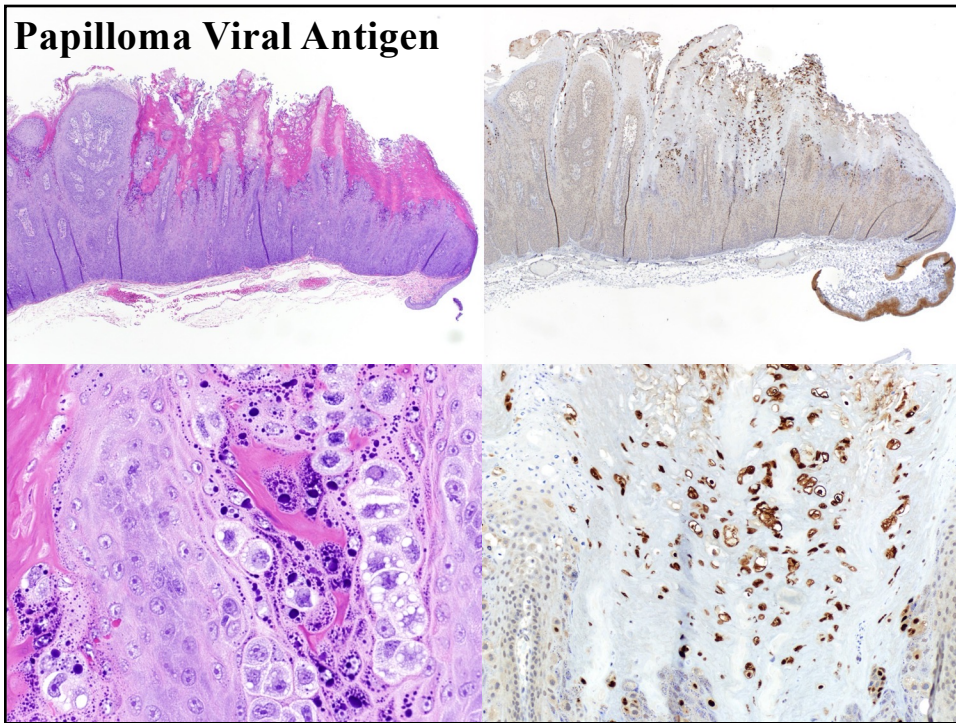
Canine Viral Papillomas

- 81 cases in the COPLOW database
 - Mixed breed 15
 - Pugs, Labs, G Ret 5
- Young dogs predominate
 - 45/81 less than 3 years old
 - Can be as old as 14 years
- Can be conjunctival, corneal or eyelid



Koilocytes

70



71



72

Third Eyelid Gland Neoplasms

- Most are adenocarcinomas (80-85%)
- Adenomas
- May be complex/mixed (myoepithelial or metaplastic components)
- Rare: squamous cell carcinoma, leiomyoma

Dees DD et al. VO 2016; Mathes RL et al. VO 2016; McKeever JM Clin Case Rep 2022

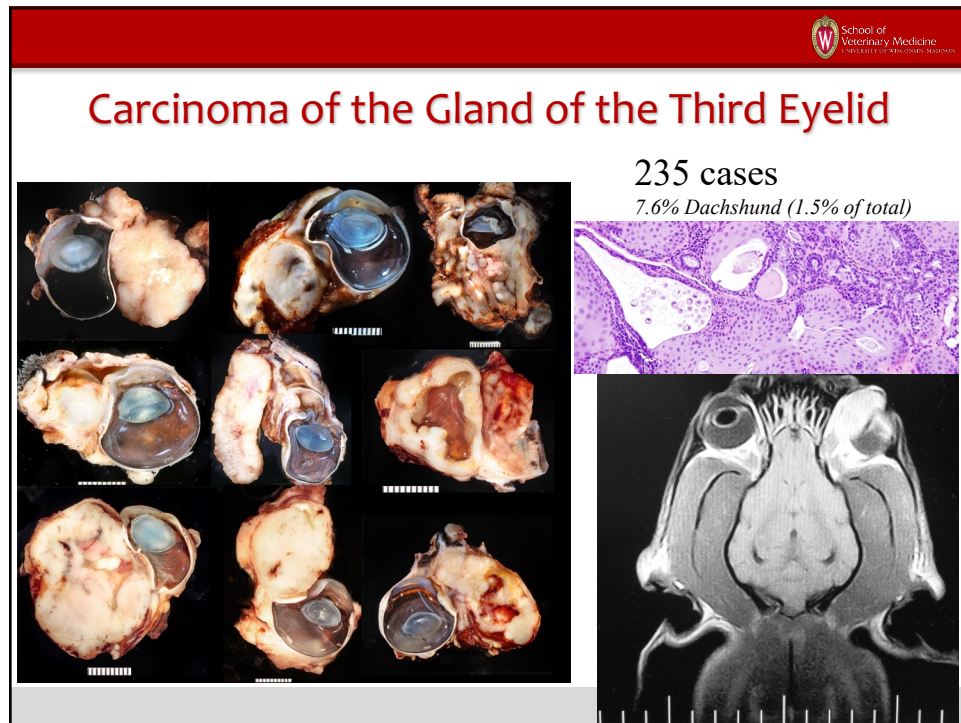
73

Third Eyelid Gland Adenocarcinoma

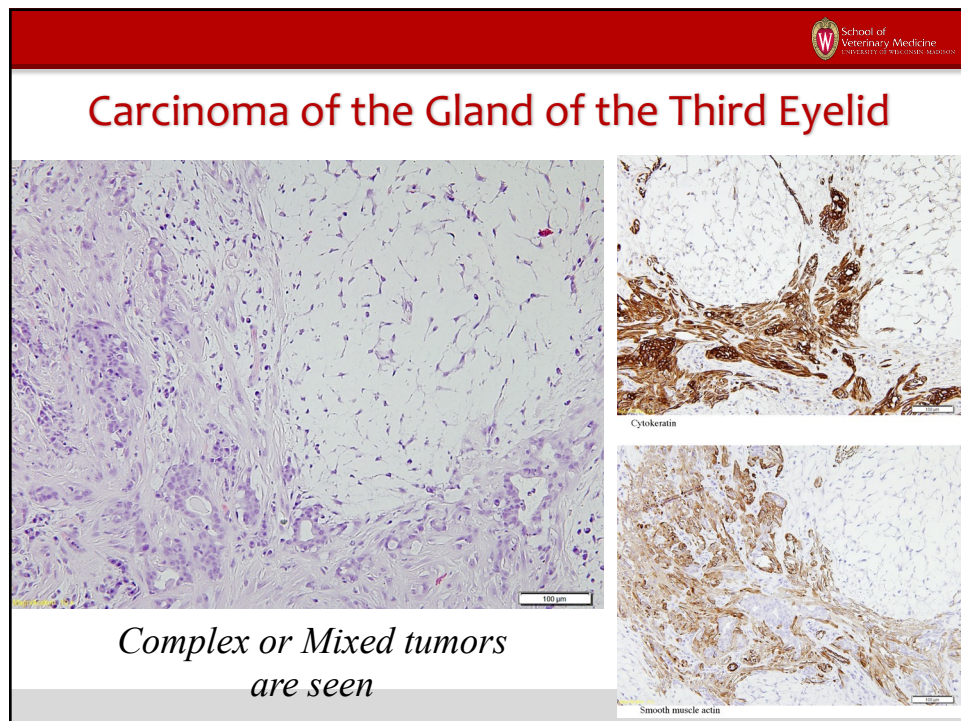
- Pink, firm
- Infiltrative
- Nests and tubules, or solid
- Squamous metaplasia
- Mitotic count highly variable (not predictive)
- More aggressive and more mets in cats than dogs

Wilcock B et al. JAVMA 1988; Dees DD et al. VO 2016; Komaromy AM et al. JAAHA 1997; Giudice C et al. Vet Pathol. 2021

74



75



76

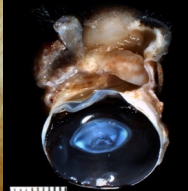
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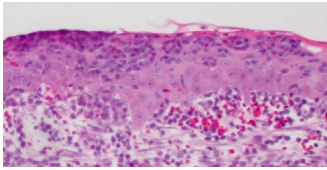
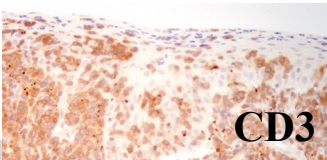
Conjunctival Lymphoma

(Numbers from 2012)

- 30 cases in the COPLOW database
 - 5 Mixed breed
 - 6 Golden Retriever
 - 5 Labrador Retriever
 - 3 Boxer
- 9 cases of epitheliotrophic T-cell lymphoma
- 18 left eye and 7 right eye





CD3

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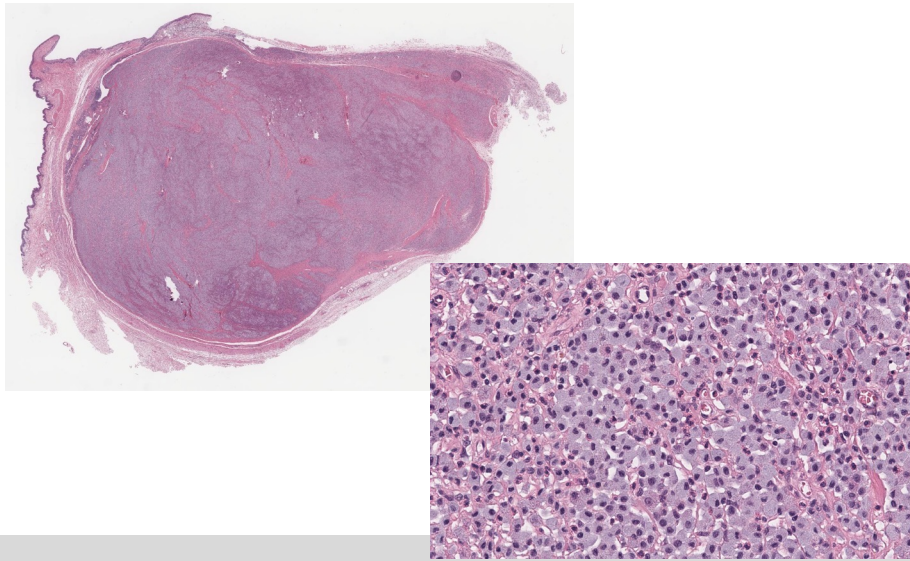
Conjunctival Mast Cell Tumor in dogs

- Smooth, firm, subconjunctival
- Well-circumscribed
- Sheets of mast cells
- Admixed with eosinophils
- Edema
- Grading only prognostic for skin
 - 2-tier system can be applied to conjunctiva
- Most respond to excision and cryotherapy

Fife M et al. VO 2011; Fischer BM et al VO 2023

78

Conjunctival Mast Cell Tumor in dogs



79

Feline Eyelid or Conjunctival Mast Cell Tumors

83 Cases in the COPLOW Database

- 2nd Most common cutaneous tumor in cats overall
- COPLOW
 - All but 3 are cutaneous
 - Most common at medial canthus
- Smooth, pink, alopecic
- Sheets of round cells with cytoplasmic granules

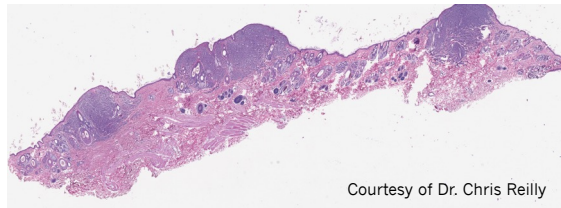


80

Feline Mast Cell Tumor

Prognosis

- The majority of feline MCTs are clinically benign
 - But up to 22% of cases may show an aggressive behavior
 - Lymph node metastases, visceral organ involvement, and/or cutaneous dissemination
- Grading system for cutaneous MCTs¹
 - No grading system for Conjunctival MCTs

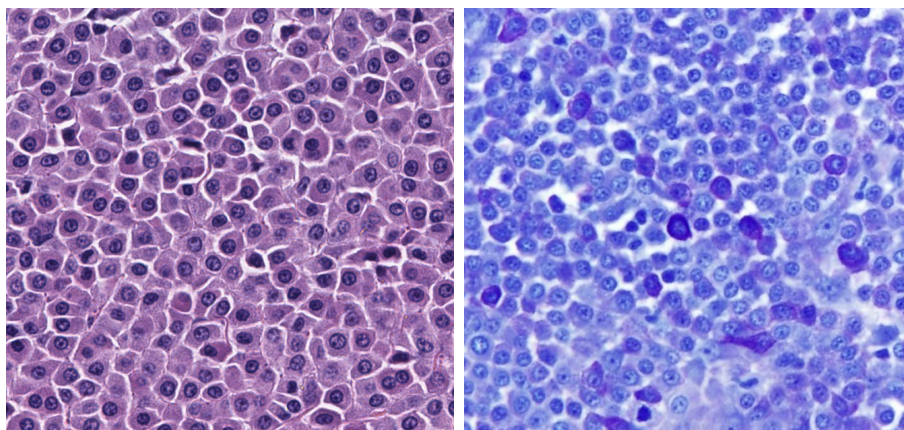


Courtesy of Dr. Chris Reilly

1. Sabattini; Bettini. Grading Cutaneous Mast Cell Tumors in Cats Vet Path. 2019, Vol. 56(1) 43-49

81

Feline Mast Cell Tumor



Courtesy of Dr. Chris Reilly

Giemsa Stain

82

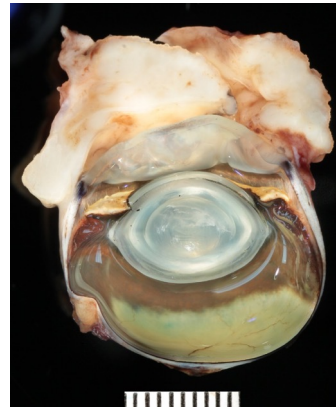
Feline Conjunctival Surface Adenocarcinoma Formerly Mucoepidermoid Carcinoma

Definition

Malignant epithelial tumor that originates from the conjunctival epithelium and/or possibly the third eyelid gland ducts.

COPLOW numbers

- 49 cases in the COPLOW collection.
- No breed or sex predisposition.
- Median age of affected animals is 12 years old (range 3-19).
- Both eyes are affected equally
- One cases presented bilateral disease.

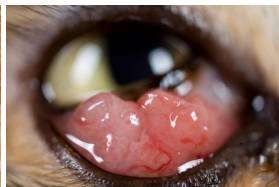
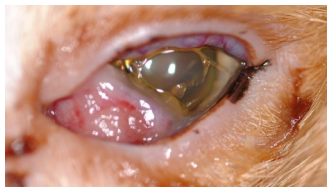


83

Feline Conjunctival Surface Adenocarcinoma

Clinical presentation

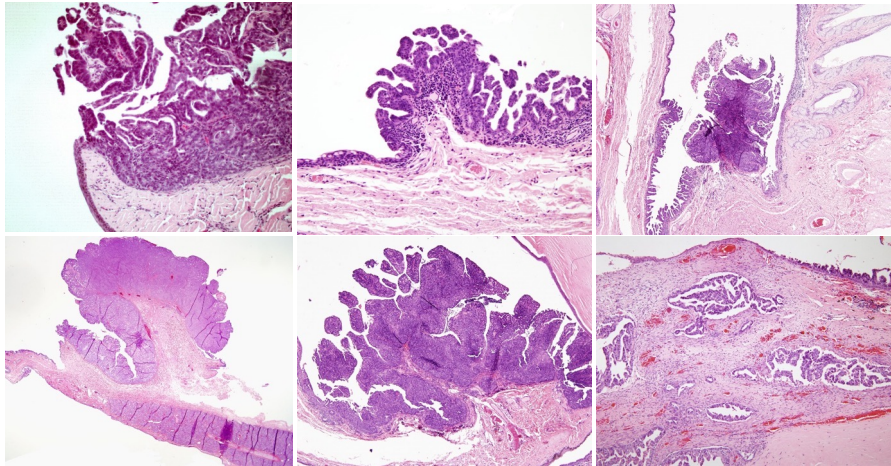
- Third eyelid +/- bulbar and palpebral conjunctiva
- Focal mass or diffuse thickening of the conjunctiva
- Hyperemic, friable mass, often papillary with frond-like projections.



84

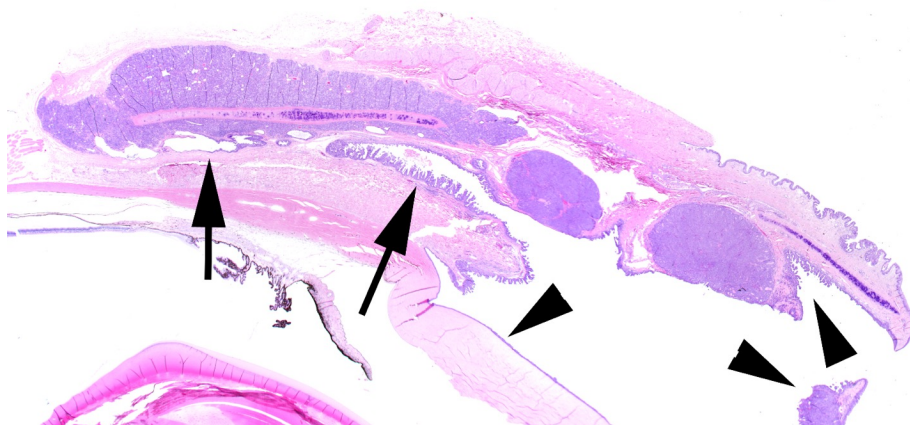
Feline Conjunctival Surface Adenocarcinoma

Diagnosis



85

Feline Conjunctival Surface Adenocarcinoma



Tumor appears to arise in the ducts of the TEL gland and spread across the conj. surface

86

Feline Conjunctival Surface Adenocarcinoma

Prognosis

- Infiltrative tumor
 - Surgical margins often dirty → Recurrence common
- Potential for regional and distant metastasis,
 - Regional lymph nodes
 - (parotid and submandibular)
 - Lungs
 - Skin



Parotid LN



Skin

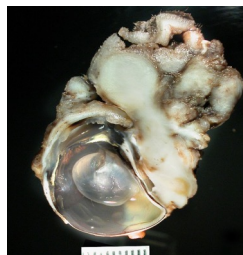
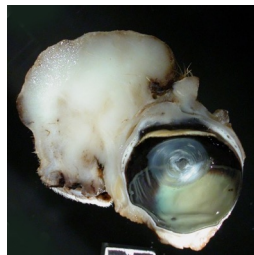


Lungs

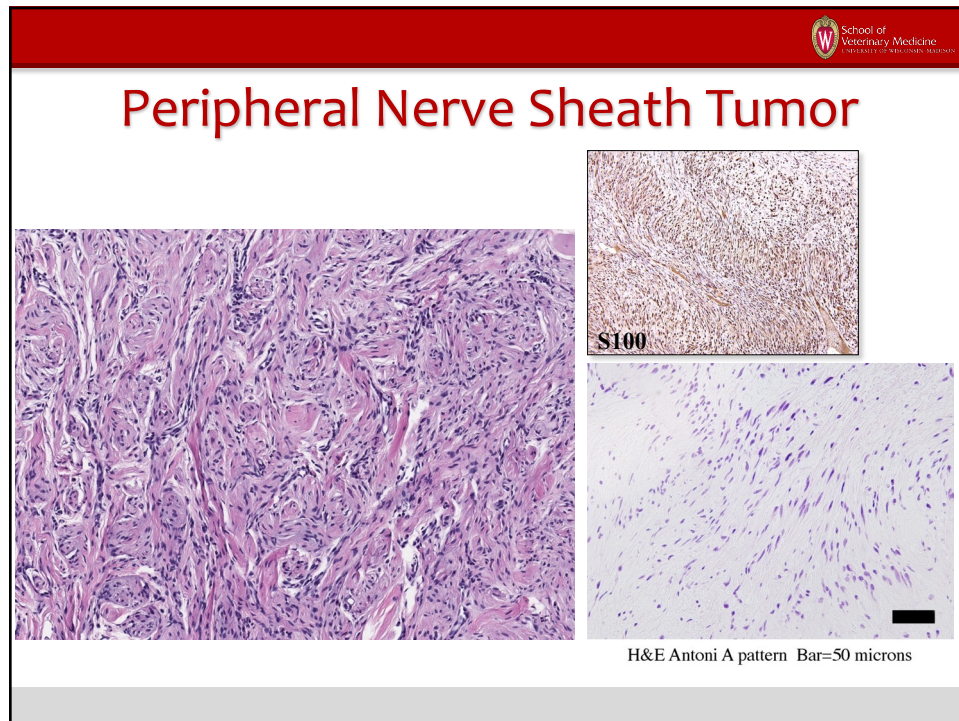
87

Peripheral Nerve Sheath Tumor

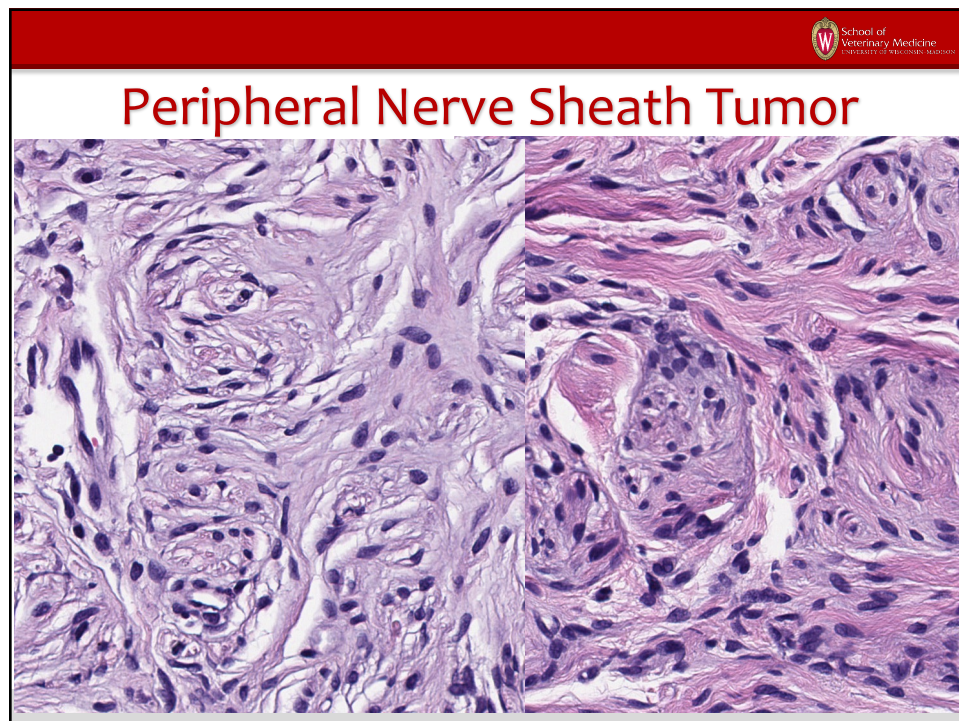
- 70 cases in the COPLOW Database
- Solitary, pink, firm
- Bundles, streams, whorls
- Antoni A/B
- IHC: laminin; +/- GFAP; S100



88



89



90

Peripheral Nerve Sheath Tumor

Prognosis

- Locally infiltrative tumors
- Dirty surgical margins are common
- Often necessitate enucleation /exenteration
- Unlikely to metastasize

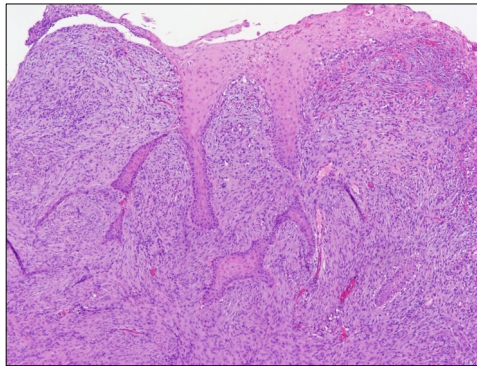
91

Equine Sarcoid

- Most commonly diagnosed tumor of equids
 - 20% of all equine neoplasms
 - 36% of all skin tumors in horses
- Benign, mesenchymal neoplasm
 - Bovine papillomavirus types 1 and 2
- Mass effect (with variable clinical appearance)

92

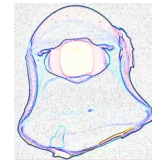
Equine Sarcoid



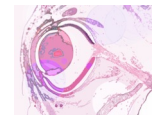
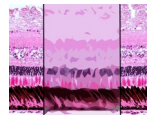
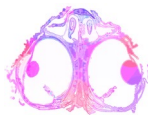
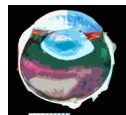
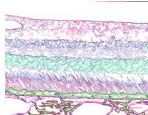
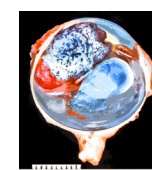
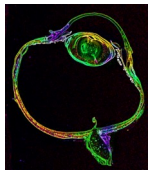
- Spindle cell proliferation
- Bundles
- No significant pleomorphism, low mitotic index
- Thin rete pegs extend in the mass

Dr. Chris Reilly

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Questions?



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