



Glaucoma

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Abbreviations Guide

- GD – Goniodysgenesis
- PIFM – Preiridal fibrovascular membrane
- PAS – Peripheral anterior synechia
- CC – ciliary cleft
- RD – Retinal detachment
- TM – Trabecular meshwork
- ICA – Iridocorneal angle
- AC – anterior chamber; PC – posterior chamber
- IOP – Intraocular pressure
- ON/ONH – Optic nerve/optic nerve head

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Glaucoma definition

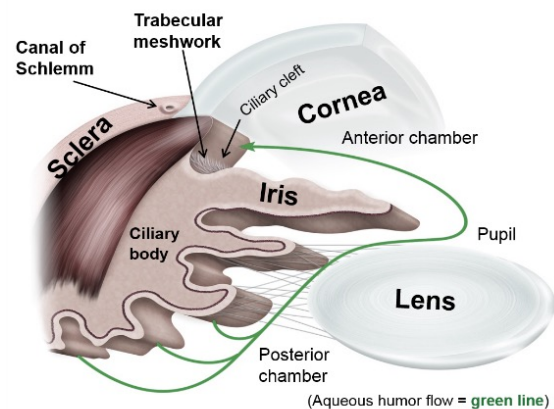
- A diverse group of ocular diseases which result in elevated intraocular pressure* which is incompatible with the maintenance of vision and health of the eye
 - In animals almost all glaucomas due to elevated IOP
 - Normal tension glaucoma common in humans
 - Elevated IOP $\neq$ Glaucoma
- Glaucoma is an optic neuropathy, with retinal ganglion cell death, optic nerve axonal loss, optic nerve cupping, and vision loss

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Morphologic Features of Glaucoma

Impairment of aqueous outflow

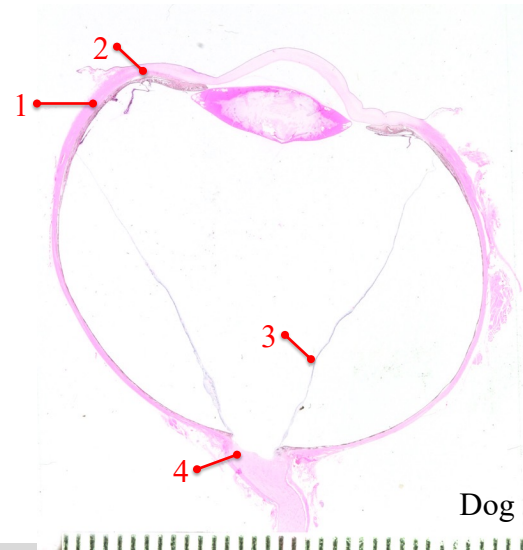
- Aqueous humor is produced at a constant rate by the ciliary body epithelium
- Drainage of aqueous humor occurs at the iridocorneal angle
- Increased Intraocular Pressure (IOP)



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Key Low Power Features

1. Buphthalmia, scleral thinning
Dogs/cats > horses > primates, others ?
2. Collapsed or inapparent ciliary cleft
3. Obvious retinal atrophy – ventral dog retina
4. Optic nerve head flattening/cupping

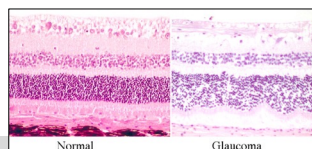
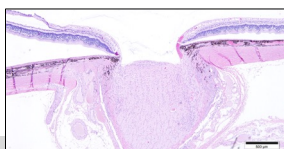


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Glaucoma Histology Tips

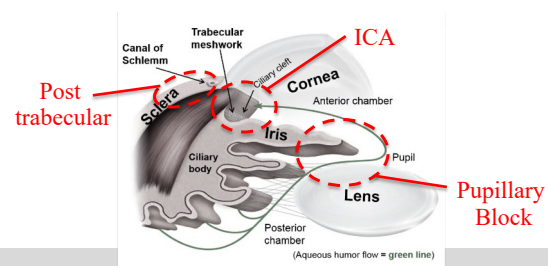
Posterior Segment

- Lesions are generally similar
- Not etiologically helpful in many cases, EXCEPT
 - K9 vs Most other species
 - Full thickness atrophy vs Inner retinal atrophy
 - K9 lens luxation glaucoma (more symmetrical)
 - Retinal detachment BEFORE (inner retinal sparing)



Anterior Segment

- Location of aqueous flow impairment
- Ciliary cleft almost always collapsed
- PATTERN of collapse is the difference
 - Goniodysgenesis vs GRU vs Neovascular vs Uveitis vs Melanosis, etc.

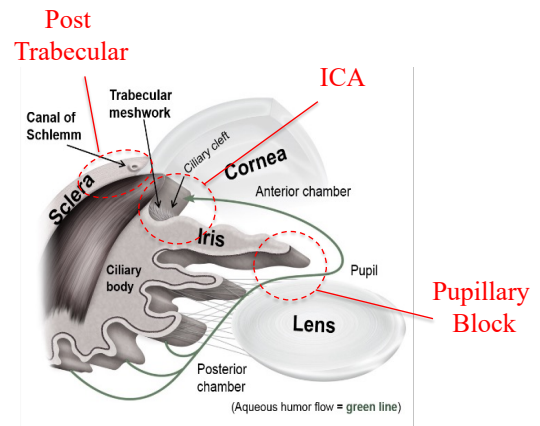


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Impairment of aqueous outflow

Causes

- Fibrovascular membranes and synechiae
- Pupillary block - Iris bombe
- Anterior lens luxation
- Angle recession
- Clogging of the trabecular meshwork
- Obliteration of iridocorneal angle by neoplasia
- Goniodysgenesis

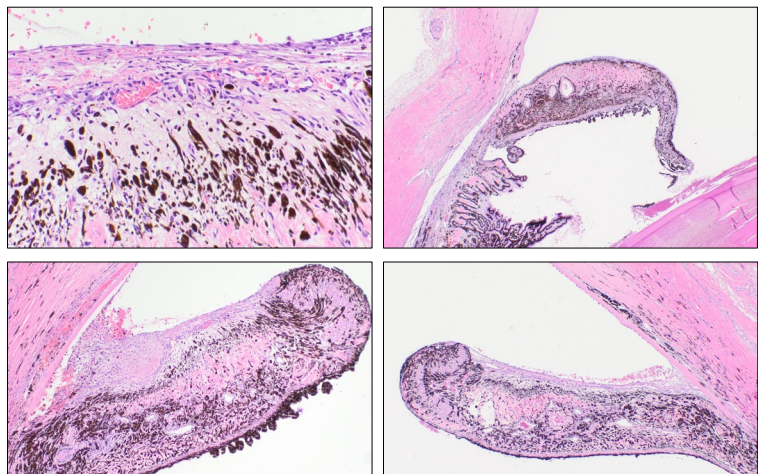


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Impairment of aqueous outflow

Causes

- **Fibrovascular membranes**
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 - Peripheral anterior synechia
 - Posterior synechia
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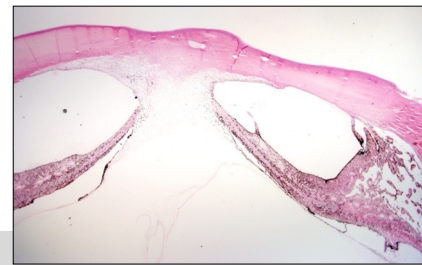
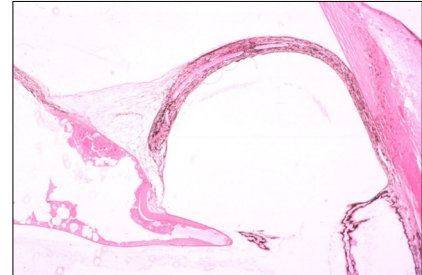
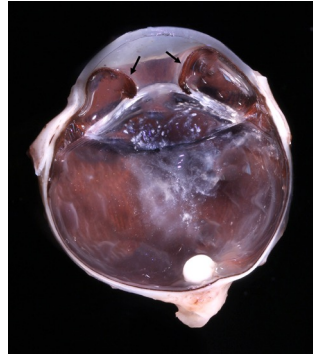


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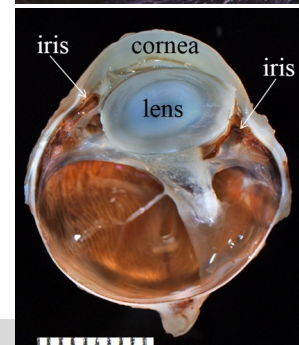
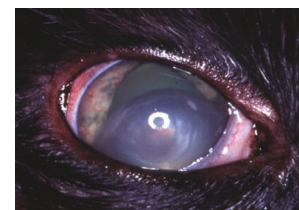
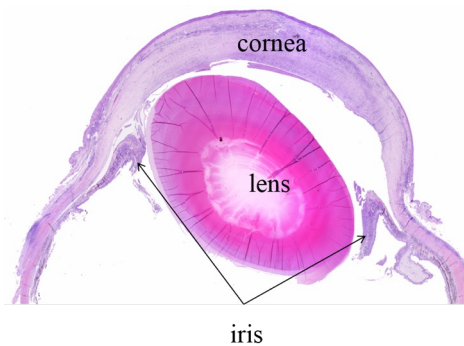


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Impairment of aqueous outflow

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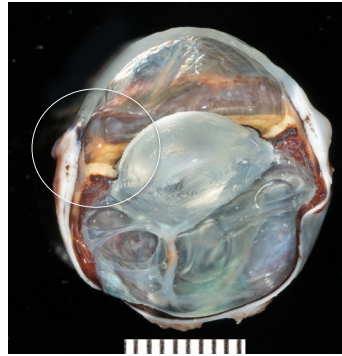


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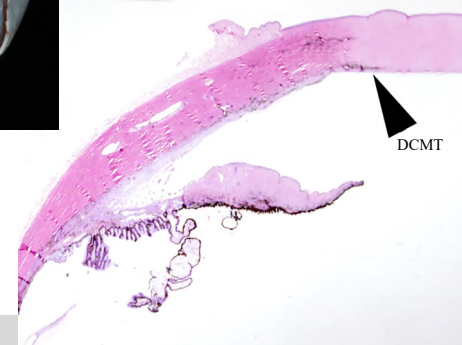
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- Clogging of the trabecular meshwork
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Cat, Blunt Trauma

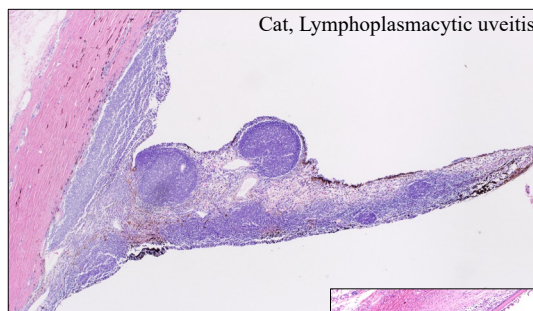


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Impairment of aqueous outflow

Causes

- Fibrovascular membranes
 - Anterior synechia
 - Peripheral anterior synechia
 - Posterior synechia
- Pupillary block - Iris bombe
- Anterior lens luxation
- Angle recession
- **Clogging of the trabecular meshwork**
 - **Cells**
 - **Inflammatory**
 - **RBCs**
 - **Neoplastic**
 - **Vitreous**
 - **Melanin (pigment dispersion)**
 - **ECM**
- Obliteration of iridocorneal angle by neoplasia
- Goniodysgenesis



Cat, Lymphoplasmacytic uveitis



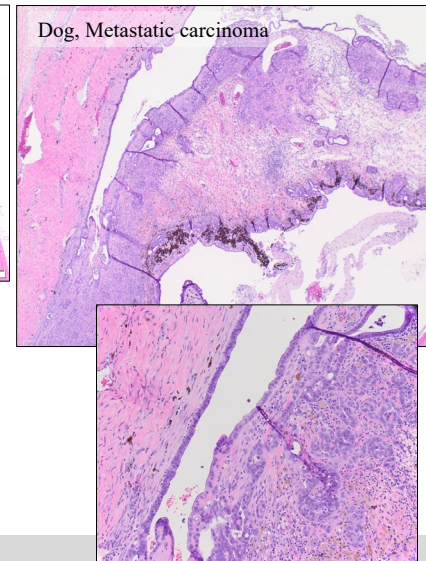
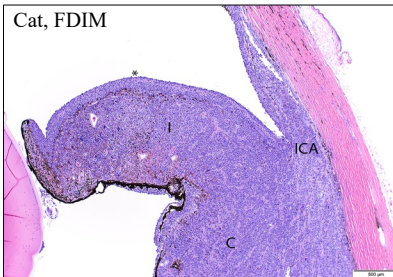
Dog, Asymmetric uveitis

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Impairment of aqueous outflow

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- Anterior lens luxation
- Angle recession
- Clogging of the trabecular meshwork with cells
- **Obliteration of iridocorneal angle by neoplasia**
- Goniodysgenesis



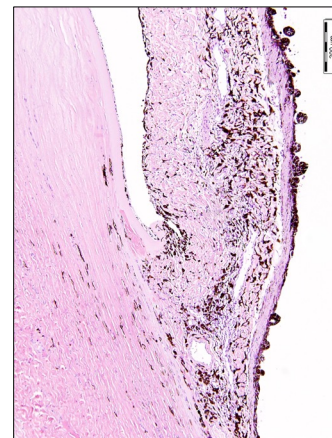
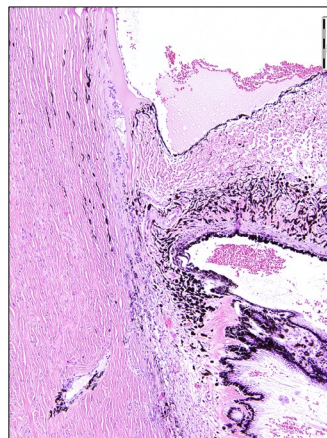
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- Clogging of the trabecular meshwork with cells
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- **Goniodysgenesis**

Dog, Goniodysgenesis



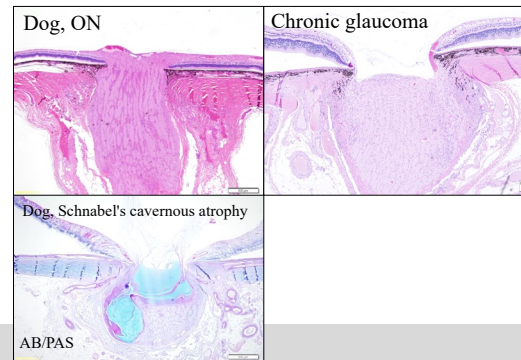
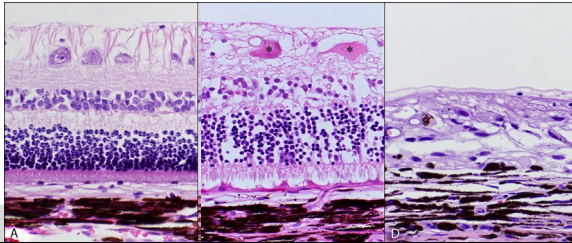
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Morphologic Features of Glaucoma

Posterior segment Changes

- Retinal atrophy
 - Decreased numbers of retinal ganglion cells
 - Atrophy of the nerve fiber layer
 - Tapetal sparing - less severe atrophy in retina overlying the tapetum (dorsal) - dogs
 - Full thickness retinal atrophy (in dogs only)
- Optic nerve atrophy
 - Atrophy and gliosis of the Optic nerve
 - Cupping of the optic nerve
 - Schnabel's cavernous atrophy

Dog, normal retina Acute glaucoma Chronic glaucoma



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Most common forms / Classification of Glaucoma Diseases

Dogs	Cats
• Congenital Glaucoma • Primary Glaucoma • Goniodysgenesis • Primary open angle glaucoma • Beagles ADAMTS10 gene mutation • Familial lens luxation and glaucoma • Multiple breeds ADAMTS17 gene mutation • Secondary Glaucoma	• Congenital glaucoma • Primary Glaucoma • Feline open angle glaucoma • Aqueous misdirection syndrome • Secondary Glaucoma

Note: These lists are not comprehensive!

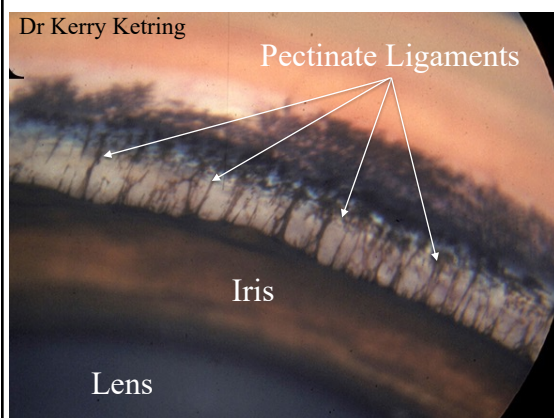
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Goniodysgenesis

- AKA:
 - Pectinate ligament dysplasia;
 - Mesodermal dysgenesis;
 - Goniodysgenesis associated-glaucoma
 - PCAG
 - Primary angle-closure glaucoma (Miller);
 - Open-angle, closed-cleft glaucoma (Peiffer)
- Malformation of the iridocorneal angle
- Congenital/developmental defect WITHOUT* congenital glaucoma
 - Mostly affects middle aged dogs
 - Severity of the malformation appears to be associated with early onset
- Breed predisposition

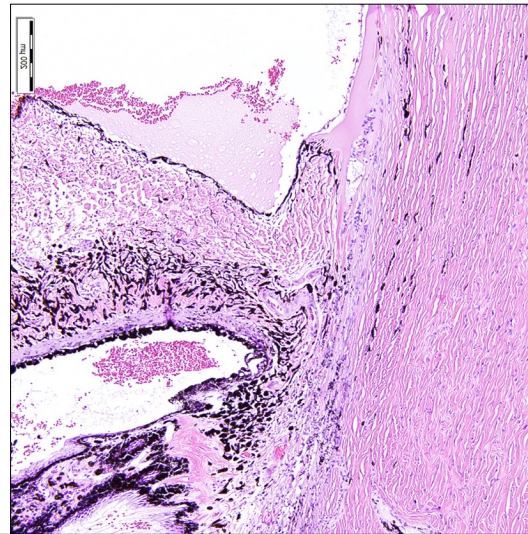
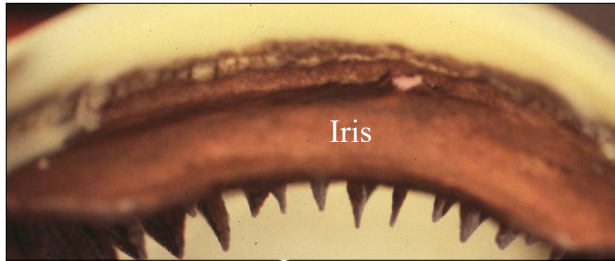
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The Normal Canine Angle

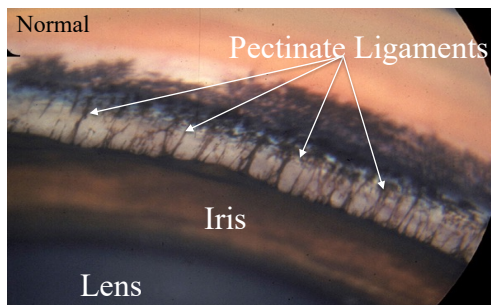


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Goniodysgenic Angle

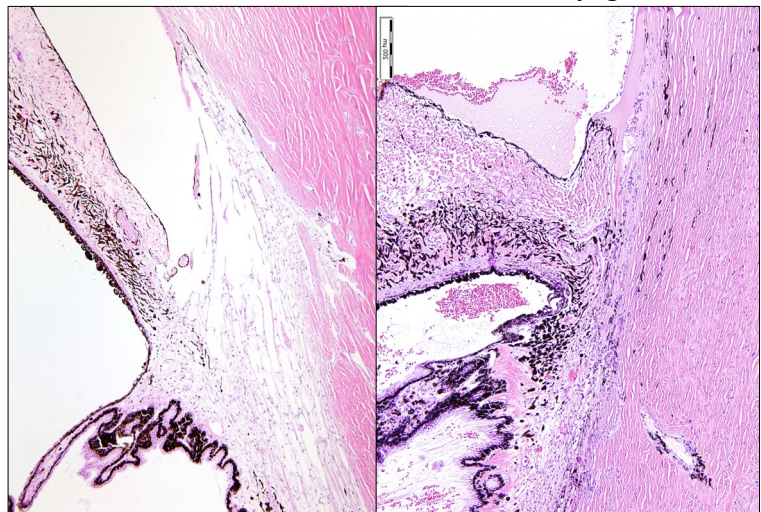


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Normal

Goniodysgenesis



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Controversy

- Recent article suggests histopathology inaccurate to diagnose goniodysgenesis

"The results indicate the histologic ICA changes proposed to be characteristic of PLD are also noted in canine globes affected with chronic secondary glaucoma. Therefore, using routine histologic evaluation, a histologic diagnosis of PLD is not possible in the face of chronic canine glaucoma."

- Reality is much more nuanced than that!**
 - There are cases you CAN'T and there are cases you DEFINITELY CAN diagnosed goniodysgenesis in histopathology
- Communication is key!
- i.e.: use a pathologist you trust
- Communicate suspicions and ancillary findings
 - Gonioscopy, prior trauma, etc
 - GD may lower threshold for glaucoma of other causes

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Can you diagnose goniodysgenesis with histopathology??

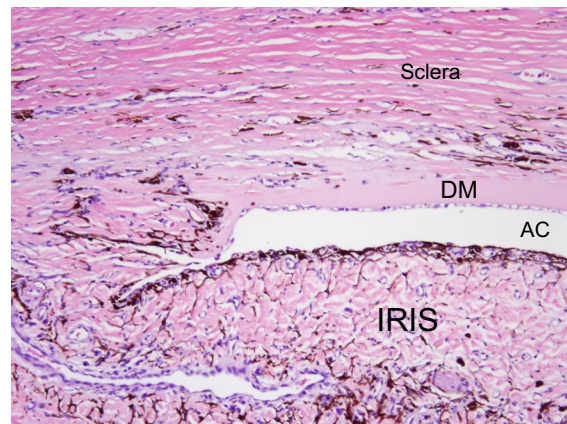
Look for:

Major Findings:

- Iris-like tissue crossing over the iridocorneal
 - Can connect to, overlie, undermine or abut end of DM
- Arborization end of DM
- Complete or partial lack of identifiable ICA structures
 - i.e. Pectinate ligament, Ciliary cleft, Trabecular meshwork, Aqueous venous plexus

Minor findings:

- Posterior extension of dilator muscle
 - Extension of the iris dilator muscle beyond iris base



Multiple sections of ICA helpful Let pathologist know if suspicious or unsure

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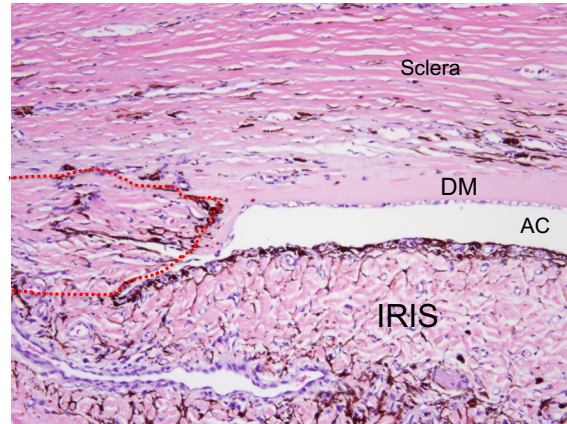
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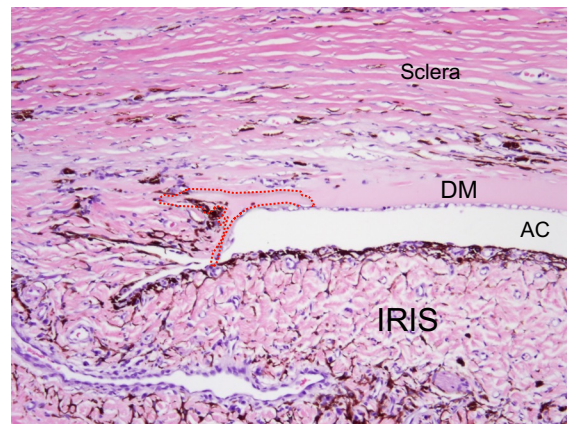
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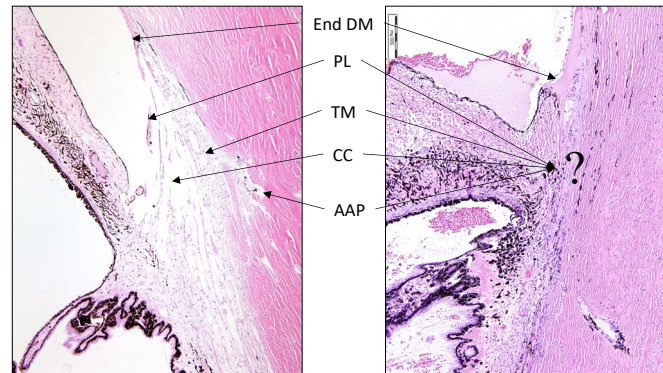
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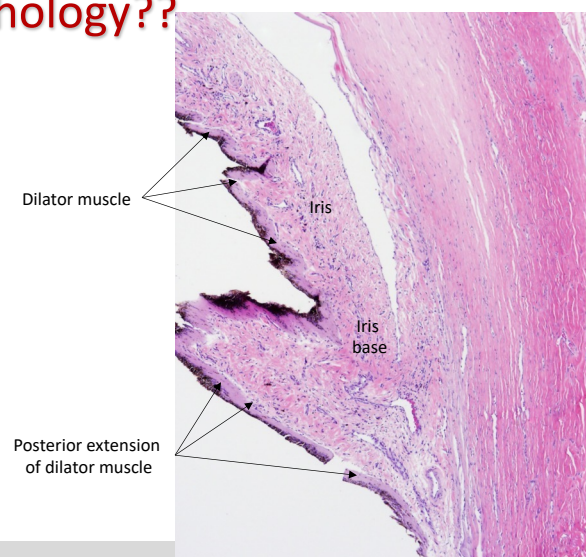
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 - i.e. Pectinate ligament (PL), Ciliary cleft (CC), Trabecular meshwork (TM), Angular aqueous plexus (AAP)

Minor findings:

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Glaucoma progression

- Studies in dogs have demonstrated fairly orderly sequence of events
- Progressive lesions in ICA/TM, retina, and optic nerve
- Rapid in dogs – end stage in as little as 7d
- Slower, more limited to inner retina in most other species, including humans

Let's see this progression in goniodysgenesis-related glaucoma

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Acute – Goniodysgenesis-related Glaucoma

Histopathologic lesions

Anterior Segment

- Ciliary cleft collapse
- ICA Pigment dispersion
- Neutrophilic infiltrate AC and limbal sclera
- Initial “degeneration” of scleral collagen at the limbus

Posterior Segment

- Optic nerve head and central retinal infarction (necrosis/malacia)
- “Red dead” ganglion cells
- Cell apoptosis in all layers of the retina

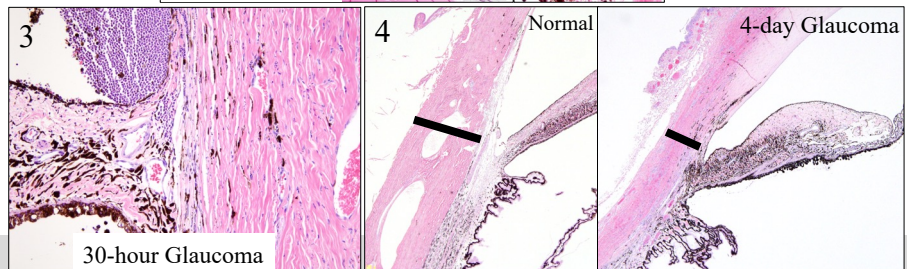
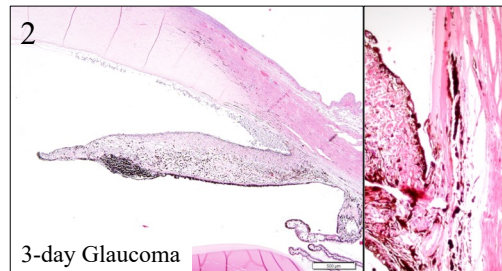
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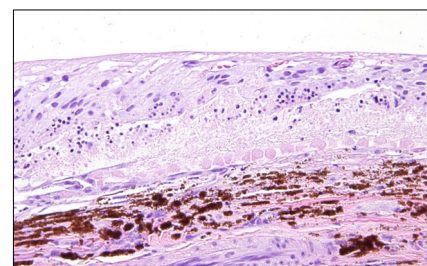
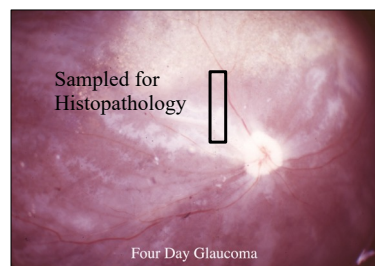
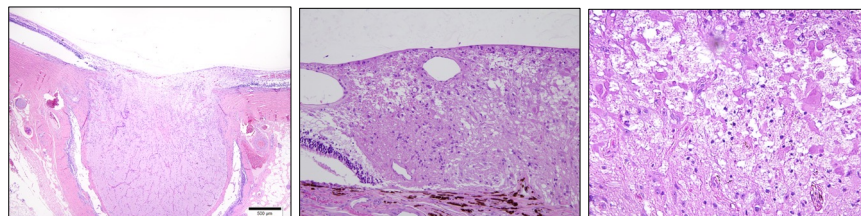
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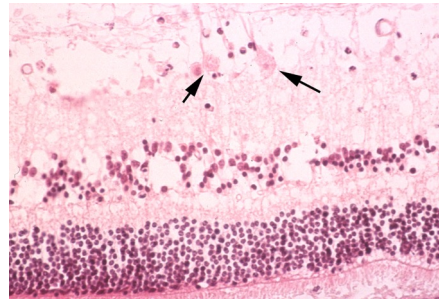
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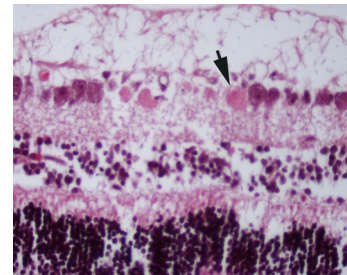
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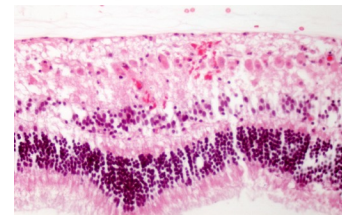
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1-Day Glaucoma



Glaucoma 2 Days after Laser Ablation of Melanocytoma

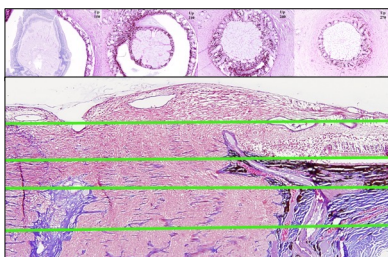
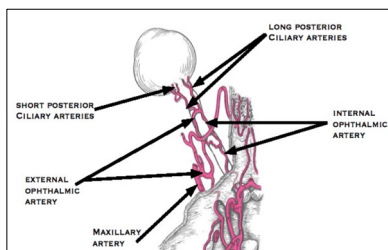


Proptosis, 3 days

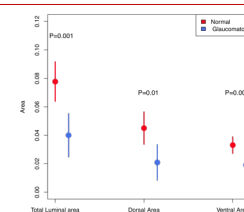
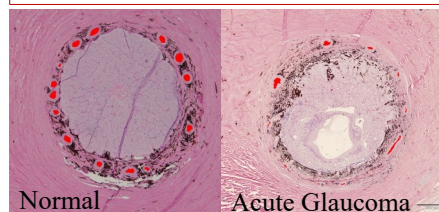
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Why is Acute Canine Glaucoma an Ischemic Disease?

Vascular Anatomy of the Posterior Segment

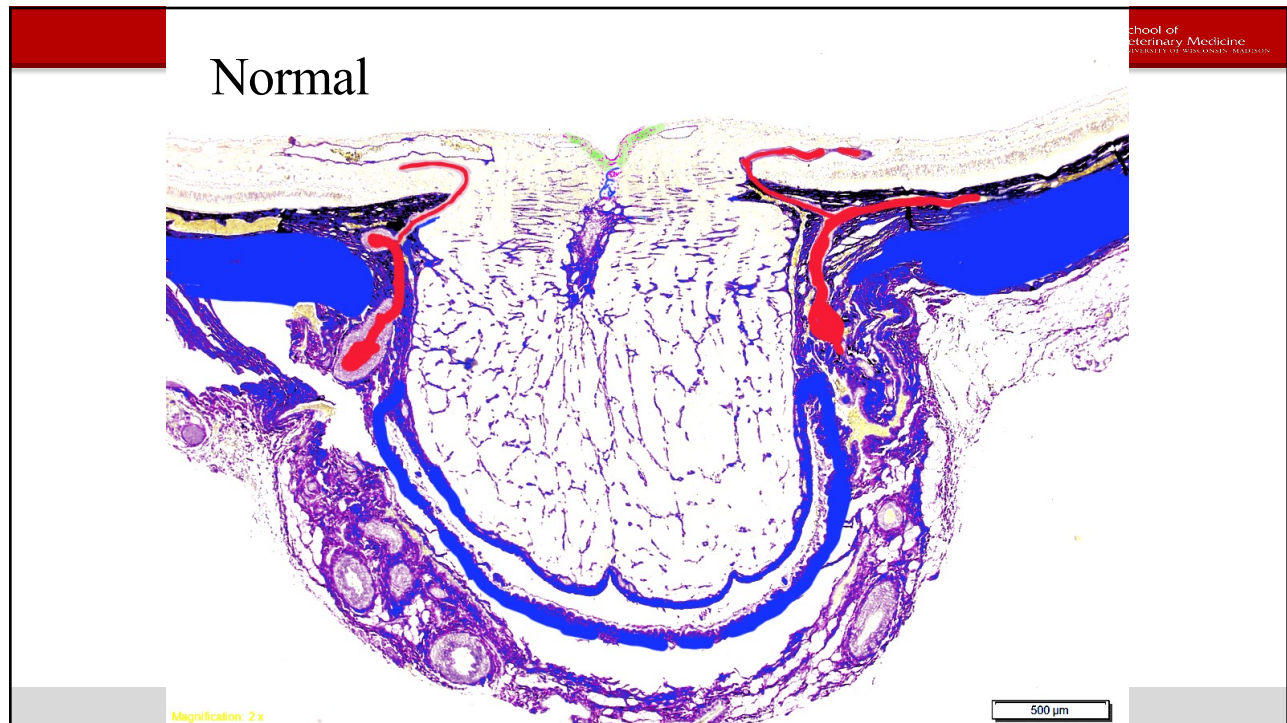


Blood Vessel Area Measurements

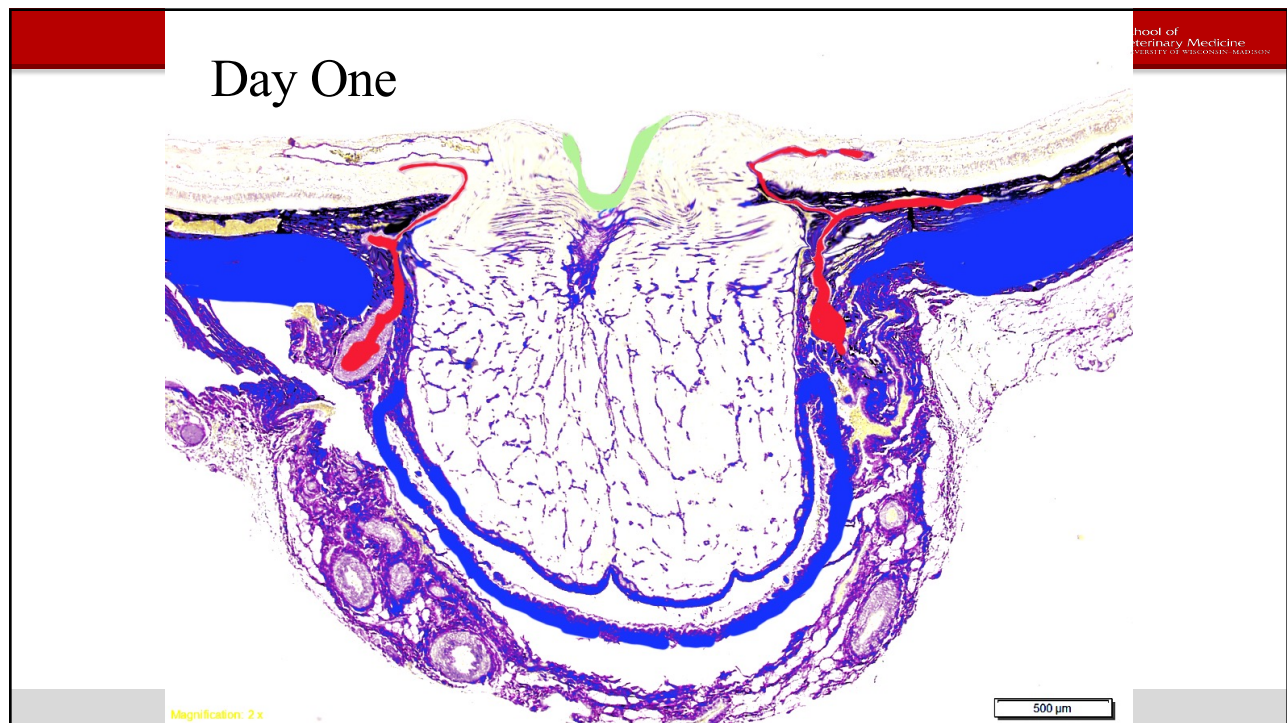


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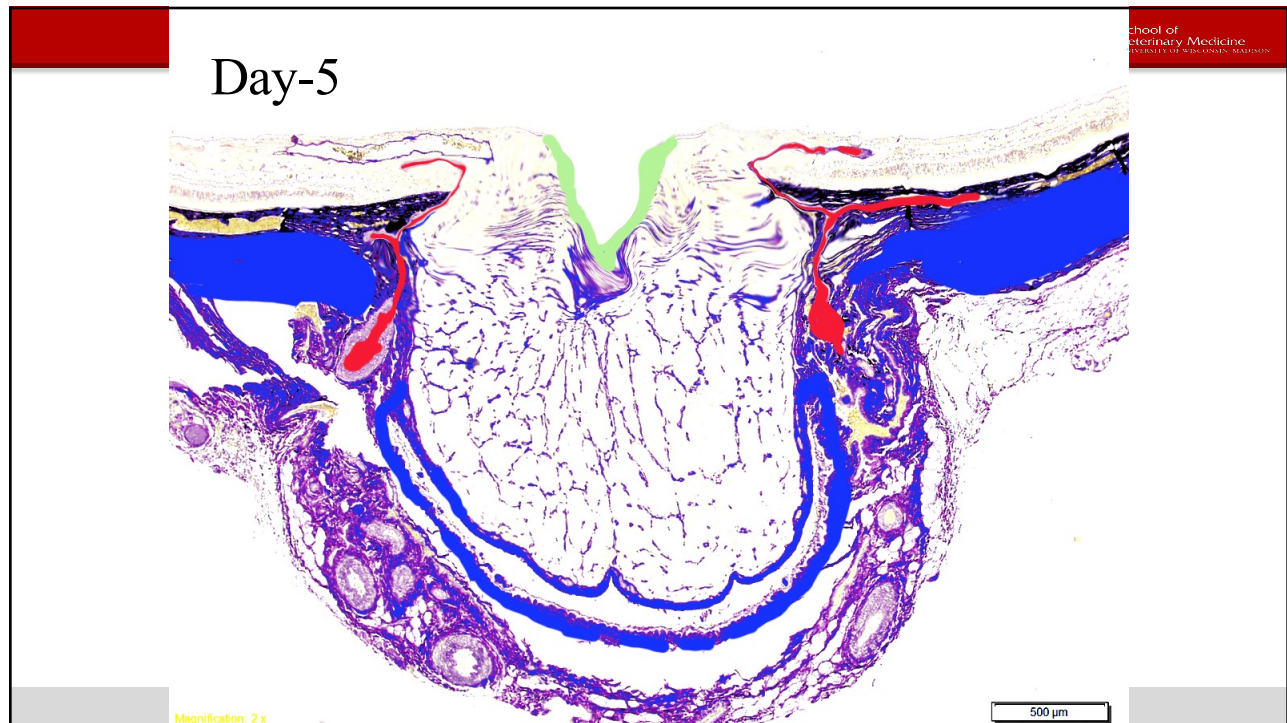
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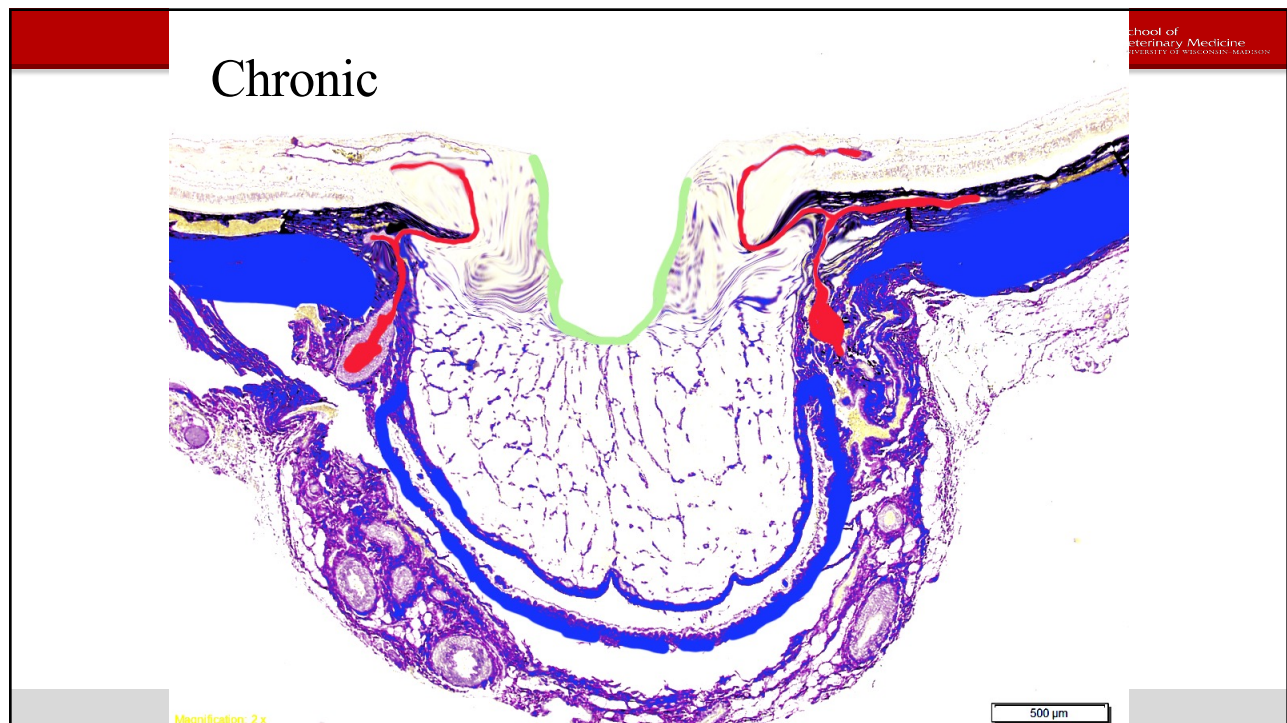
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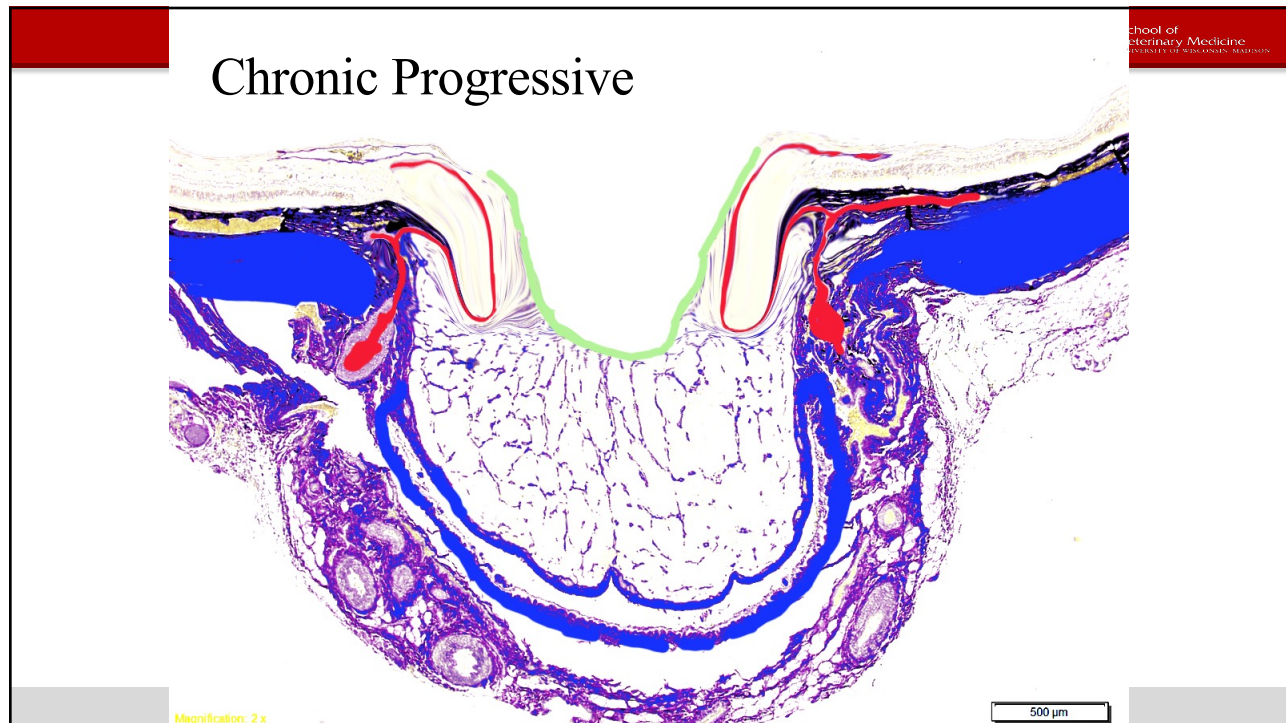
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Glaucoma in cats

- Relatively common indication for enucleation.
 - 29% of submissions to COPLOW
- Generally an insidious, gradually progressive disease.
 - 73% of glaucomatous cats blind at presentation (Blocker, 2001).
- Diagnosis:
 - IOP $\geq$ 25 or IOP asymmetry > 12 .
- Clinical signs
 - Buphthalmos, ON cupping*, retinal atrophy, mydriasis, vision loss etc.

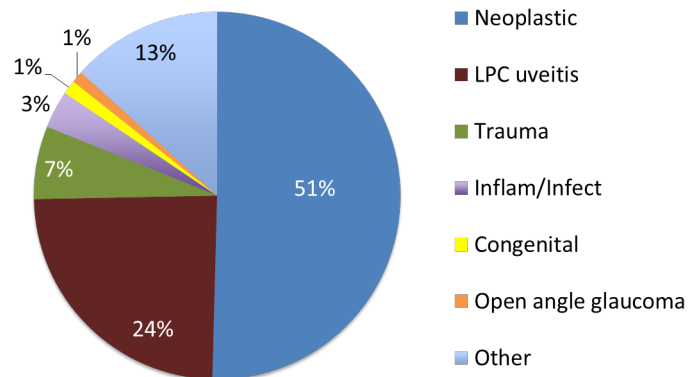
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UNIVERSITY OF WISCONSIN, MADISON

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Glaucoma classification in cats

- **Congenital Glaucoma**
- **Primary Glaucoma**
 - Open Angle Glaucoma
 - Narrow/Close angle Glaucoma (Burmese)
 - Goniodysgenesis (Siamese)
- **Secondary Glaucoma**
 - Anterior uveitis
 - Lens luxation (trauma/primary/cataract)
 - Hyphema
 - Intraocular tumors
 - Aqueous misdirection syndrome

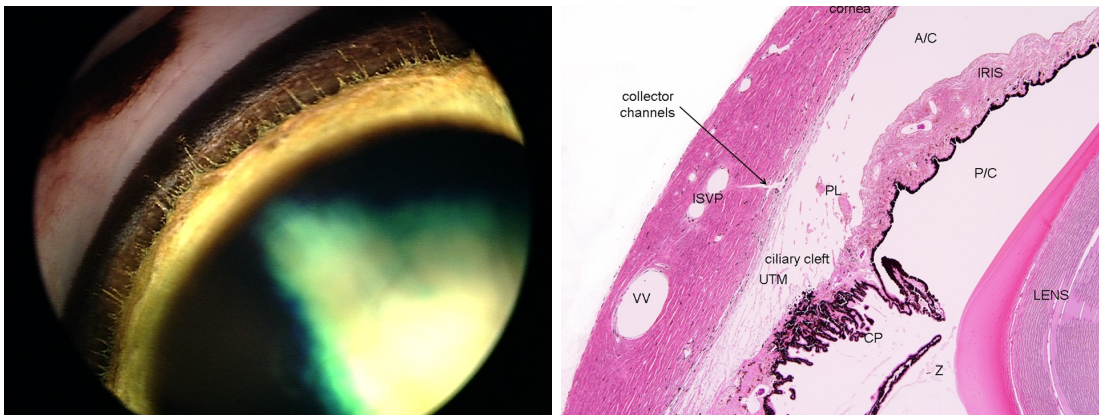
Causes of glaucoma in cats - COPLOW database



n3812

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Normal feline angle



Courtesy Dr. Gill McLellan

McLellan GJ, Teixeira LBC. Feline Glaucoma. *Veterinary Clinics of North America: Small Animal Practice*. June 2015.

Advancing animal and human health with science and compassion

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Glaucoma classification in cats

Congenital Glaucoma

Primary Glaucoma

- Open Angle Glaucoma
- Narrow/Close angle Glaucoma (Burmese)
- Goniodysgenesis (Siamese)

Secondary Glaucoma

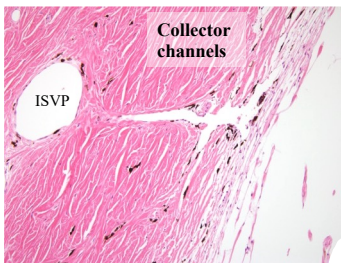
- Anterior uveitis
- Lens luxation (trauma/primary/cataract)
- Hyphema
- Intraocular tumors
- Aqueous misdirection syndrome

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Feline Open Angle Glaucoma

ICA and aqueous outflow anatomy in cats

Angular Aqueous Plexus(AAP)



Cat Aqueous outflow

Conventional Pathway 97%

Uveal scleral pathway 3%



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Feline Open Angle Glaucoma

Veterinary Ophthalmology (2008) 11, 3, 162-165

Feline primary open angle glaucoma

Susan Jacobi* and Richard R. Dubielzig†

- Increase in IOP with absence of significant ocular abnormalities.
 - “Open angle, open cleft”.
- 8 cats.
- Older cats (mean age 9.1years).
- Unilateral presentation.
- Burmese, DSH and DLH cats.

New COPLOW Data 2019

33 total cases

68% Female

Mean age 10.1 (5-18 y/o)

Breeds:

- DSH (n16)
- DHL (n8)
- DMH (n4)
- Burmese (n3)
- Persian (n2)

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Feline Open Angle Glaucoma

Mean IOP at time of enucleation- 47.7±18.5 mmHg

57% Bilaterally affected (11/19)

- 26% OD only (5/19)
- 15% OS only (3/19)

Glaucoma in the contralateral eye:

- **27.3%** (3/11) glaucoma OU at first presentation.
- **54.5%** (6/11) developed glaucoma other eye < 1 year.
- **18.2%** (2/11) developed glaucoma other eye > 1 year.

Average time to glaucoma in the 2nd eye after diagnosis:

≈9 months (299.5 days; range 0 - 1795d).

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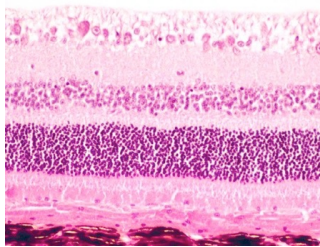
Feline Open Angle Glaucoma

Histopathology

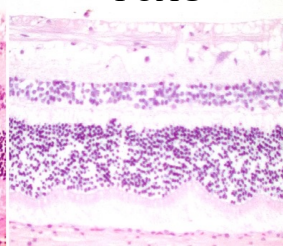
Retina

- Typical lesions of feline glaucoma:
 - Loss of RGCs with relative sparing of the remaining retina

Normal cat

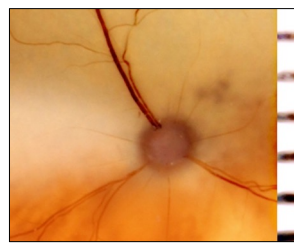


FOAG



Optic nerve:

- Deep cupping, atrophy and gliosis.
- Cupping FOAG cases more severe than other forms of glaucoma in cats



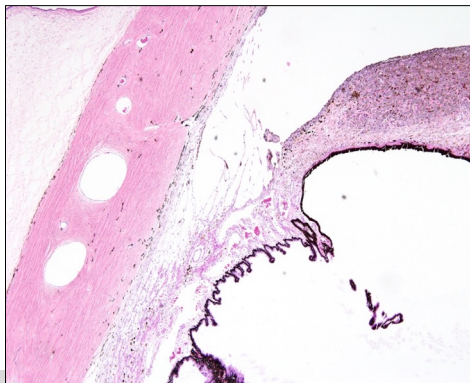
45

Feline Open Angle Glaucoma

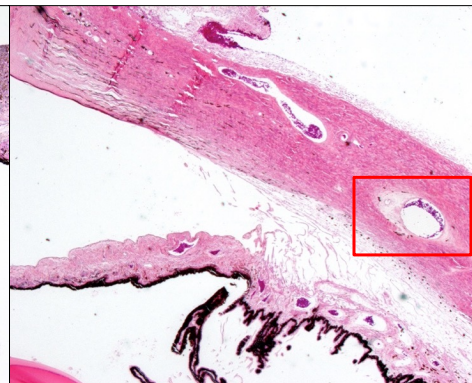
Histopathology

“Open Angle” = Open ciliary cleft and normal PLs and TM morphology

Normal Feline Angle



FOAG



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Feline Open Angle Glaucoma

Histopathology

Myxomatous matrix deposition(*) around vessels of the
intrasccleral venous plexus (ISVP)



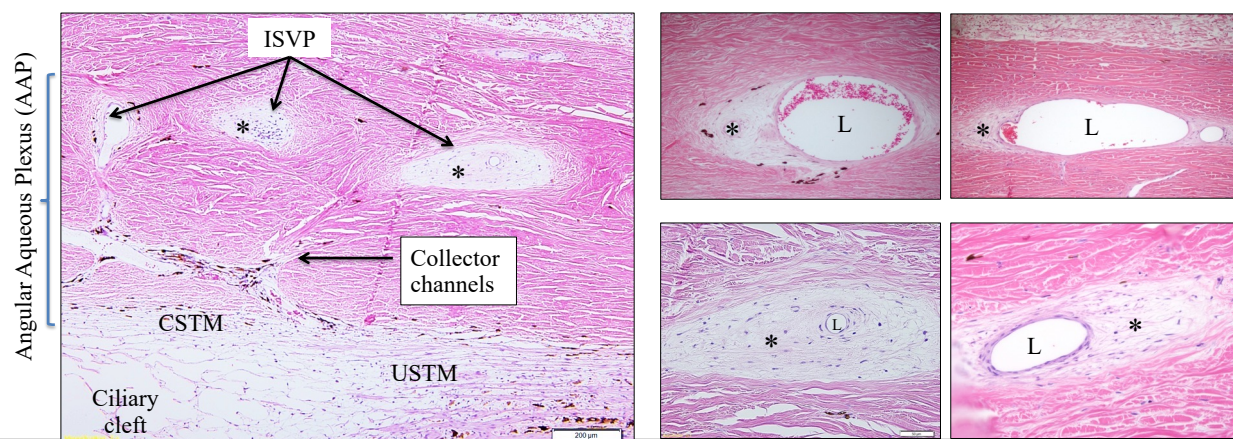
47

Feline Open Angle Glaucoma

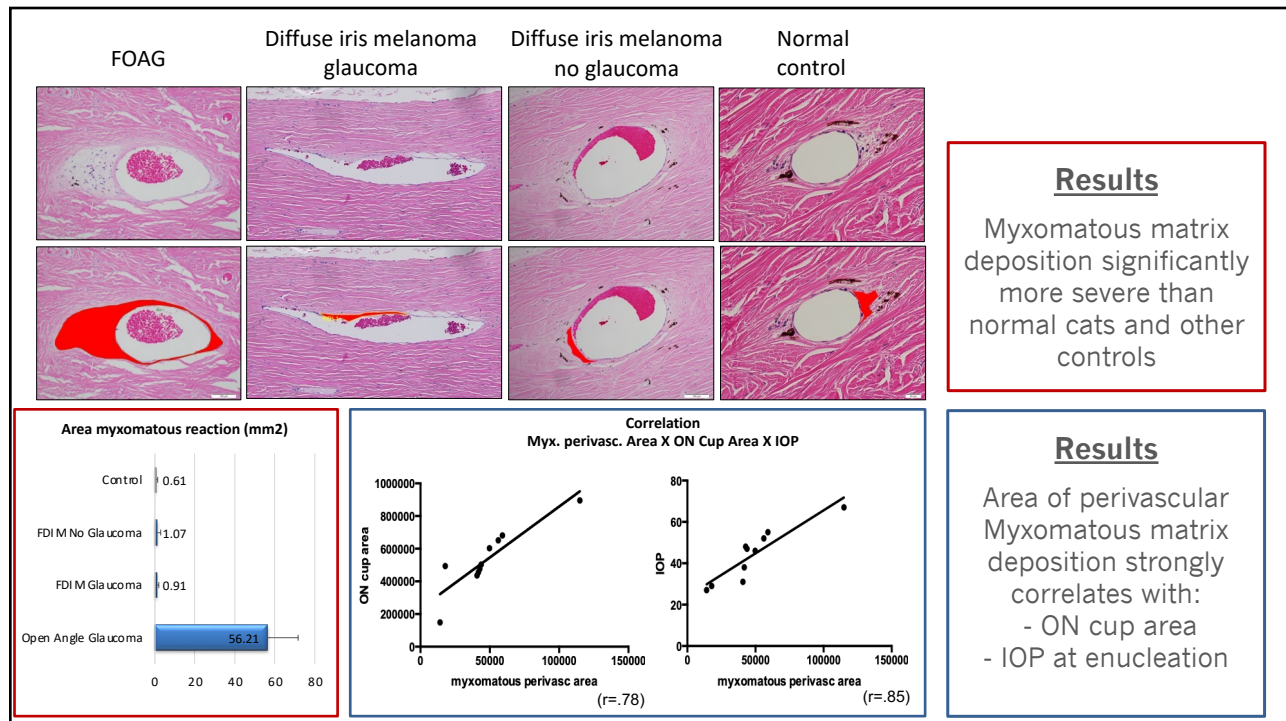
Histopathology

ISVP veins

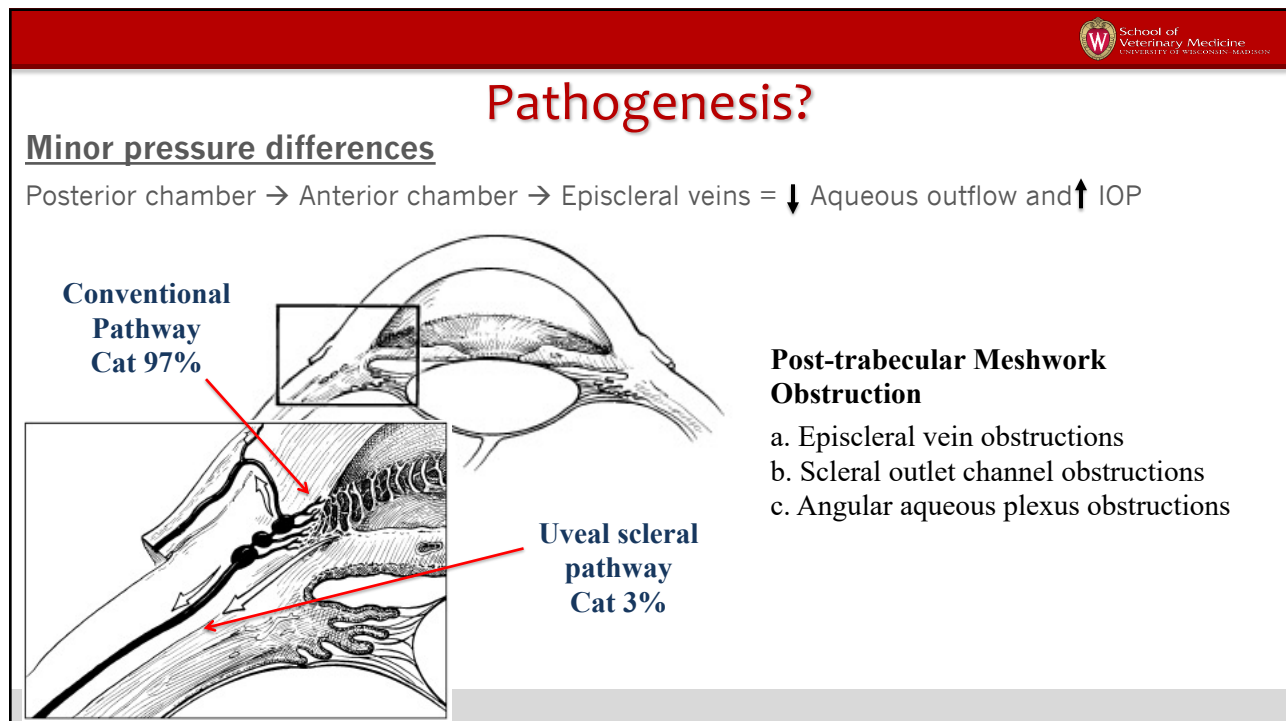
(L= lumen; *= Myxomatous matrix)



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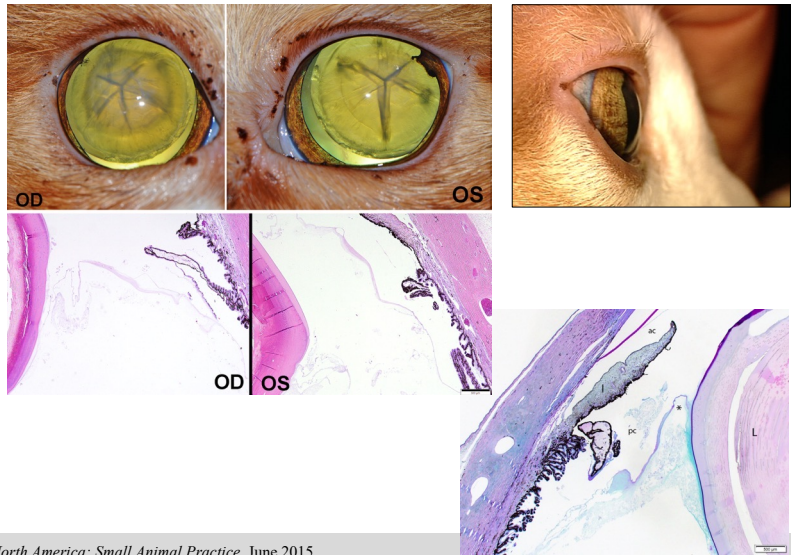


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Aqueous misdirect syndrome

Challenging diagnosis

- Shallow anterior chamber
- Forward shifting of the Iris, CB and lens
- Anterior vitreal face bowing forward
- Pools of aqueous in vitreous (hard to see histologically)



McLellan GJ, Teixeira LBC. Feline Glaucoma. *Veterinary Clinics of North America: Small Animal Practice*. June 2015.

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Glaucoma in Horses

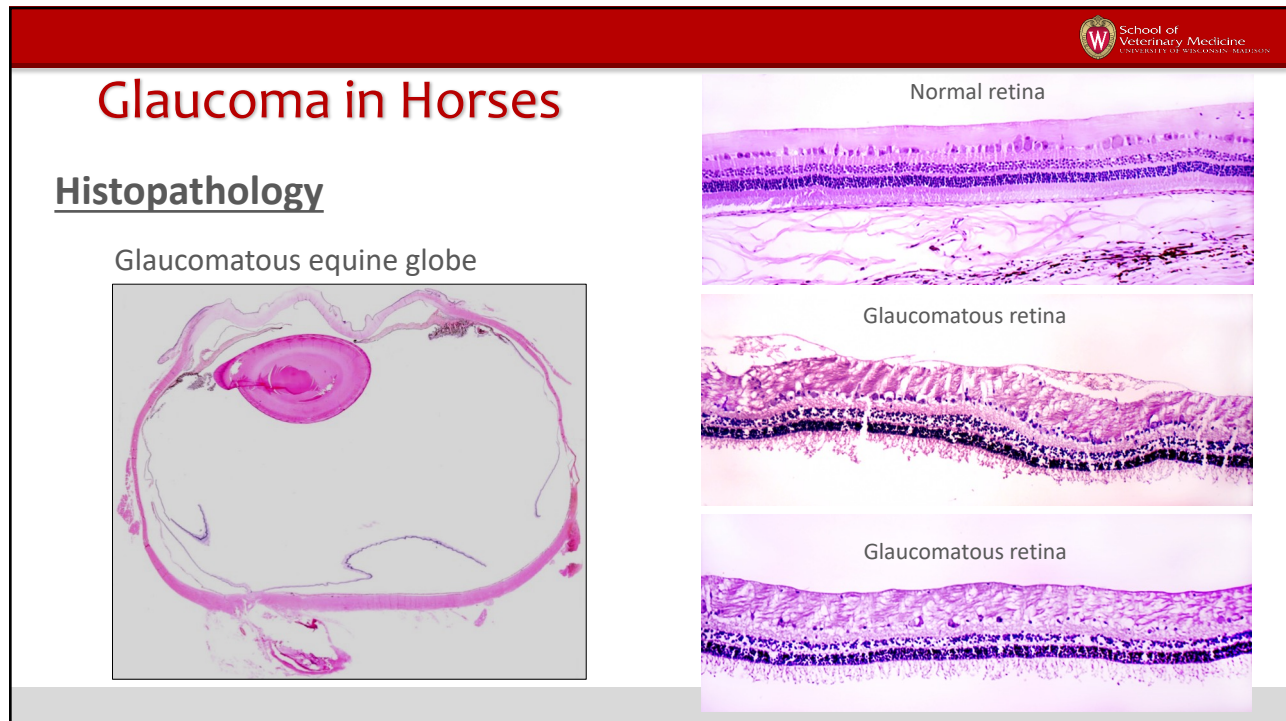
Glaucoma “classification” in horses

- **Congenital Glaucoma**
- **Primary Glaucoma**
 - Open Angle Glaucoma
- **Secondary Glaucoma**
 - ERU, Neoplasia, Trauma, etc.

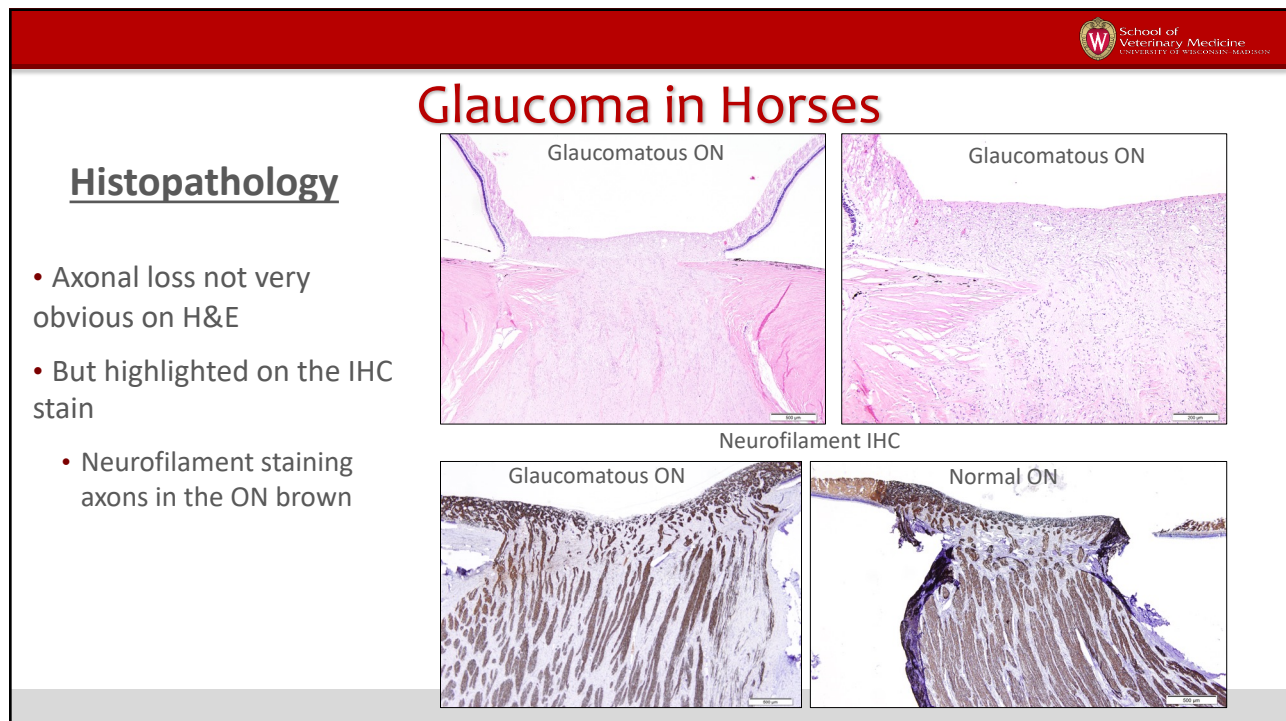
General Points

- Histologic diagnosis of glaucoma in horses is challenging
 - Not many RGC in a given sections
 - ON lesions might not be obvious

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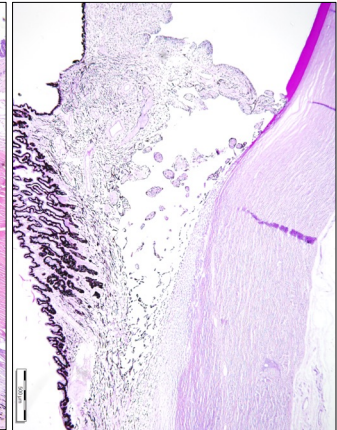
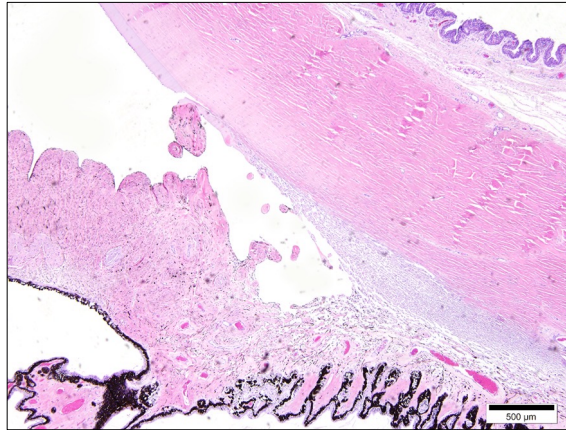
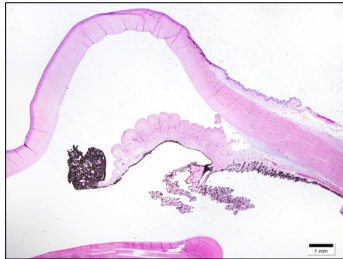


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Glaucoma in Horses

Histopathology

- Normal horse ICA

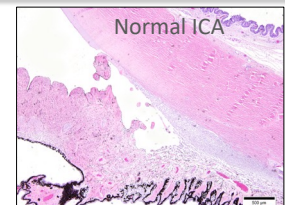
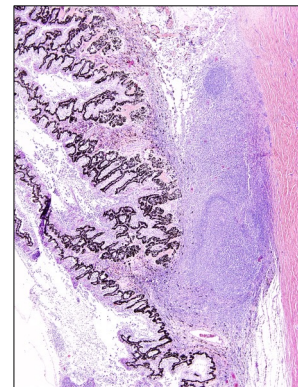
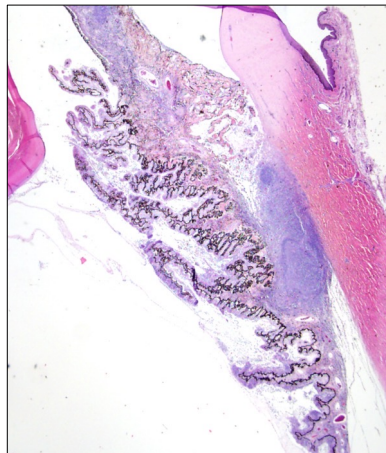
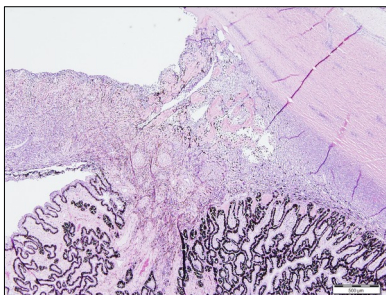


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Glaucoma in Horses

Histopathology

- ERU, Secondary Glaucoma
 - Lymphoplasmacytic inflammation in the ICA tissue



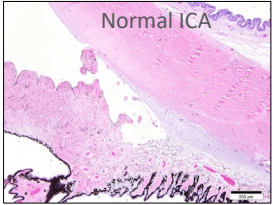
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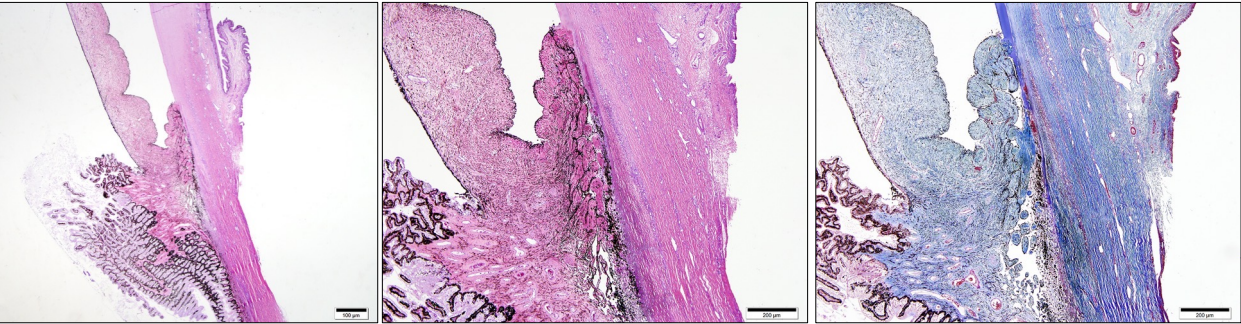
Glaucoma in Horses

Histopathology

- Horse diagnosed clinically with primary Glaucoma
 - Collapsed ICA



Normal ICA



Fibrosis TM – Masson's trichrome stain

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Questions?



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