The Pathology and Pathogenesis of Acute Glaucoma in Dogs

Richard R Dubielzig

Overview of Glaucoma

Intraocular Pressure too High to Support a Healthy Optic Nerve

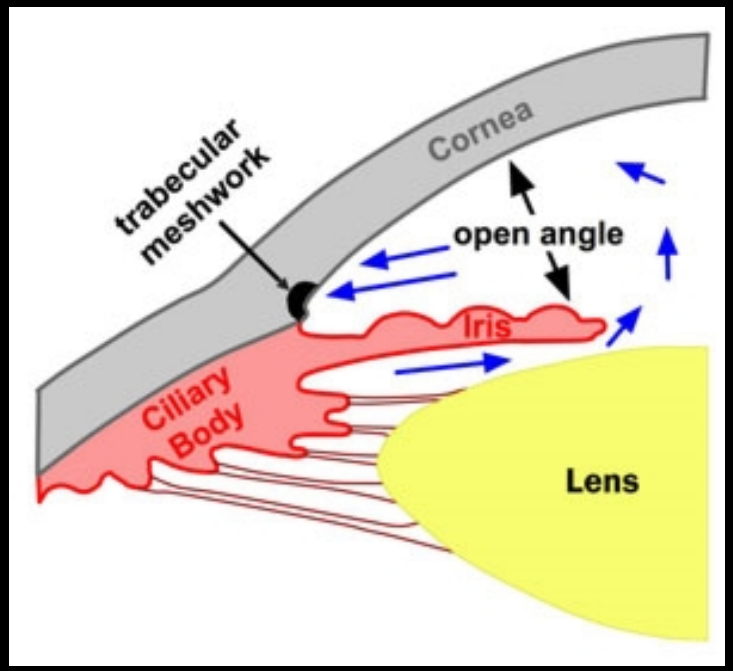
Terminology used in the classification of human glaucomas

I. Open-angle Glaucoma
   A. Primary (POAG)
   B. Secondary – selected varieties

II. Angle-closure Glaucoma
   A. Primary/acute
   B. Variants

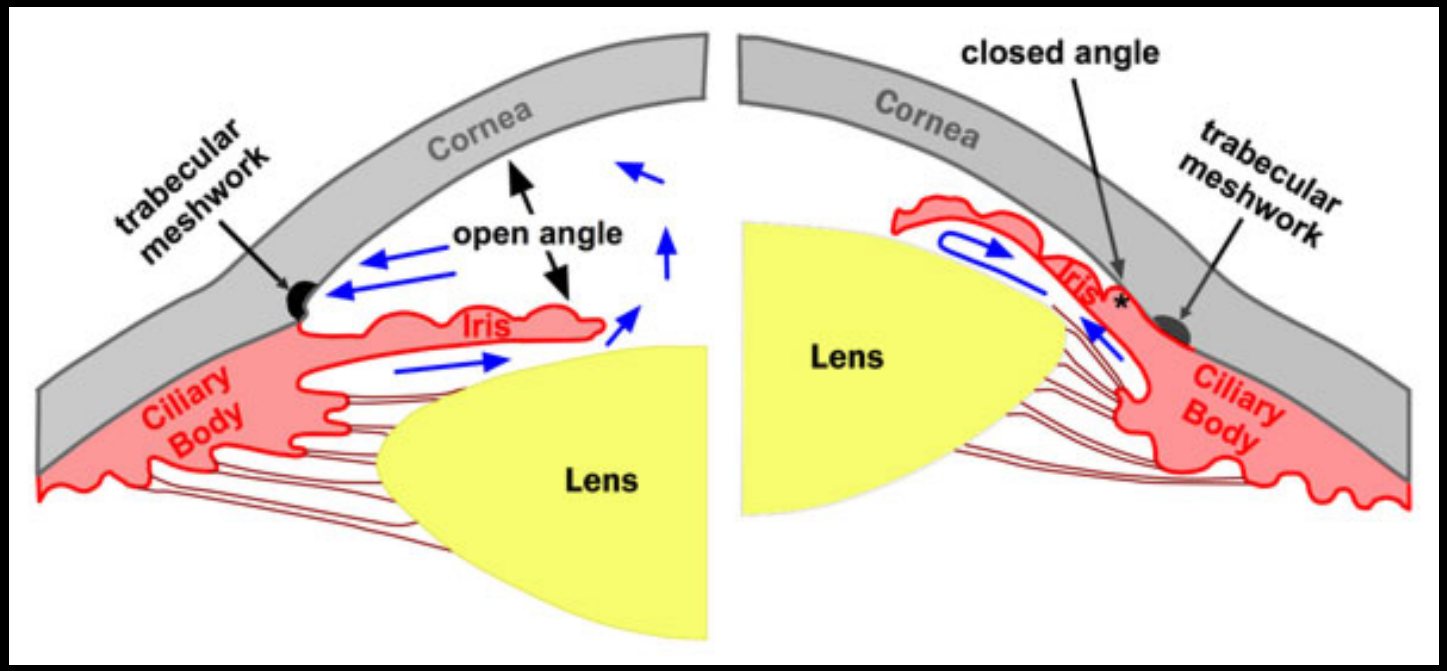
Aqueous Humor Dynamics

from human classification



- A Patient's Guide to Glaucoma www.medrounds.org

Aqueous Humor Dynamics
from human classification



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The Common Canine Glaucoma Diseases

- Primary glaucoma
- Primary open angle glaucoma , familial in the Beagle
- Familial lens luxation and glaucoma
- Pigmentary uveitis of Golden Retrievers
- Congenital glaucoma
- Glaucoma as a component of many disease processes
  - Neoplasia
  - Trauma
  - Uveitis

The Common Feline Glaucoma Diseases

- Aqueous mis-direct syndrome
- Feline open angle glaucoma
- Angel recession
- Congenital glaucoma
- Glaucoma as a component of many disease processes
  - Neoplasia…FDIM
  - Uveitis…Idiopathic L/P uveitis

The pathogenesis of glaucoma damage in the retina and optic nerve is controversial

Gradual ganglion cell loss from apoptosis and thinning of the nerve fiber layer of the retina is seen in animal models and also fits the pathology in most human glaucoma

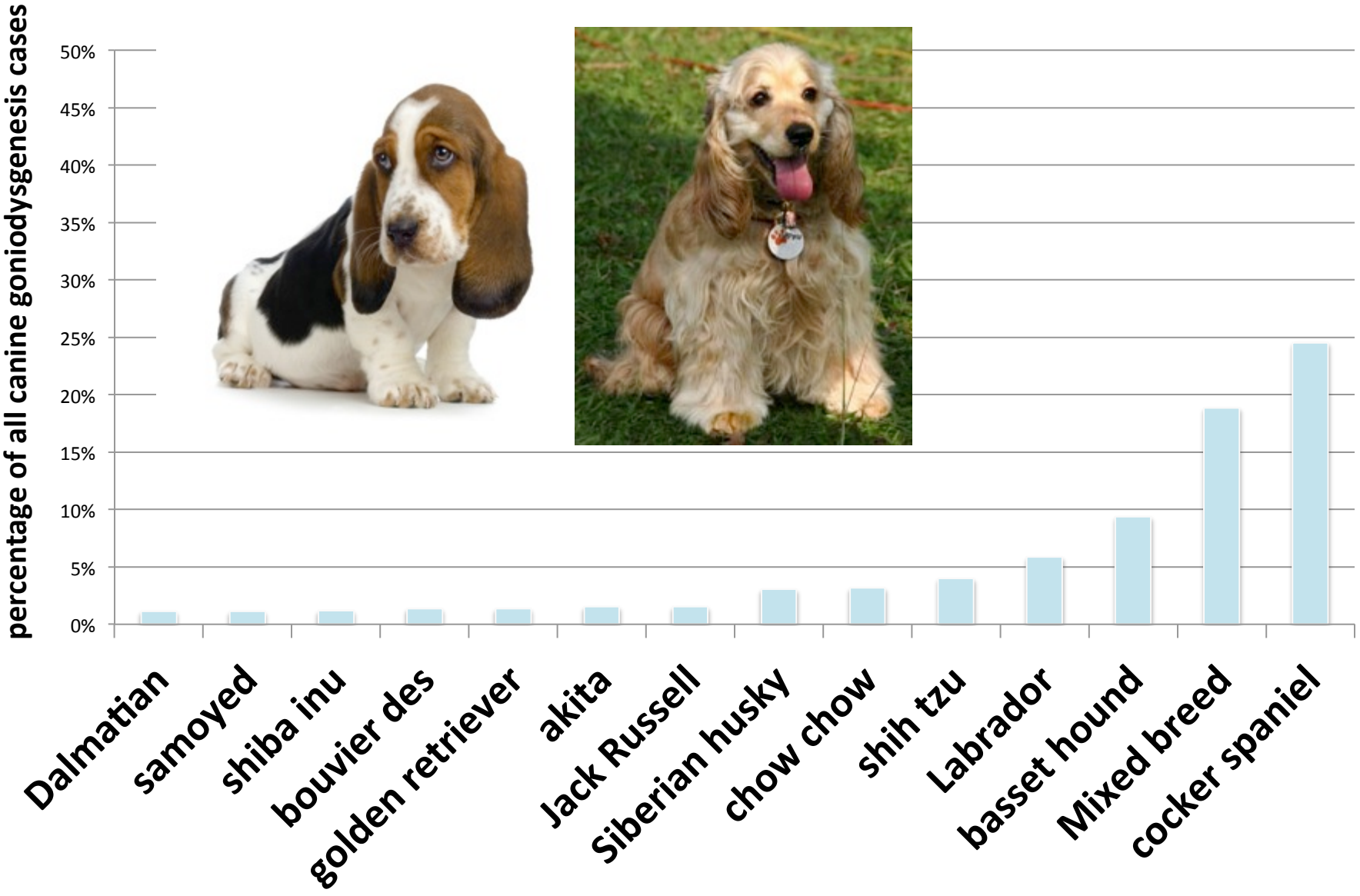
This change is thought to be the result of either axon or capillary obstruction in the scleral canal portion of the optic nerve (the level of the lamina cribrosa)

This scenario fits what we see in cats fairly well but it does not fit the pathology seen in most dog glaucoma. I will attempt to show why.

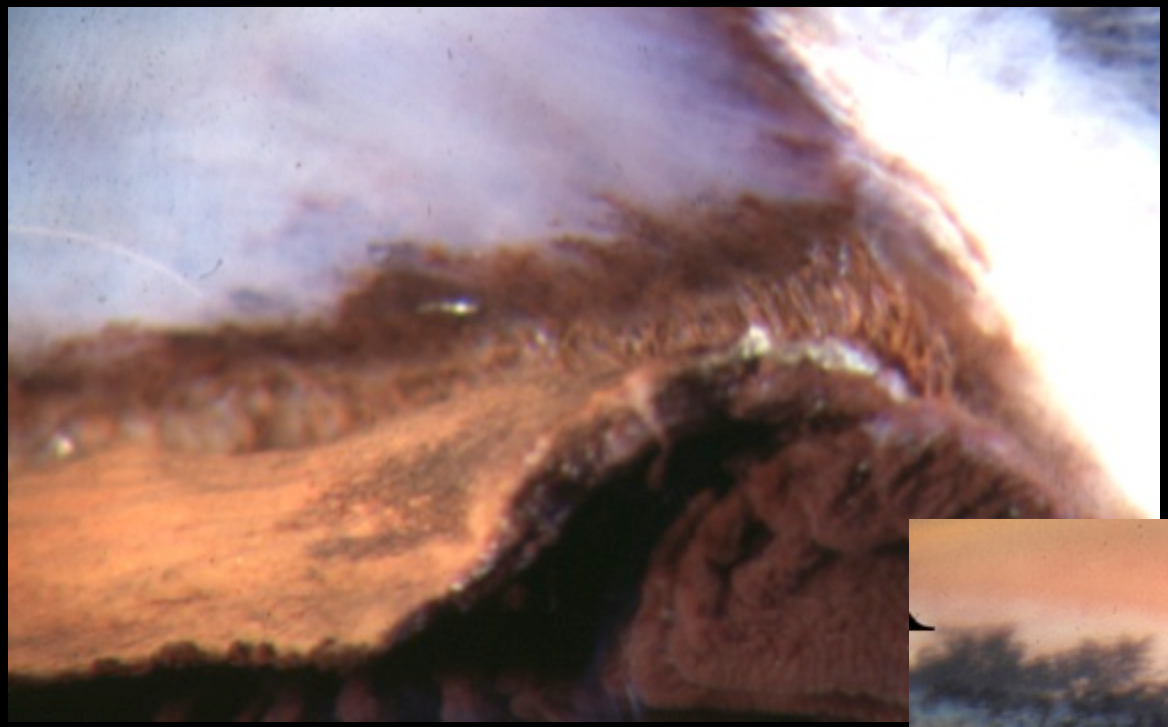
Canine Primary Glaucoma

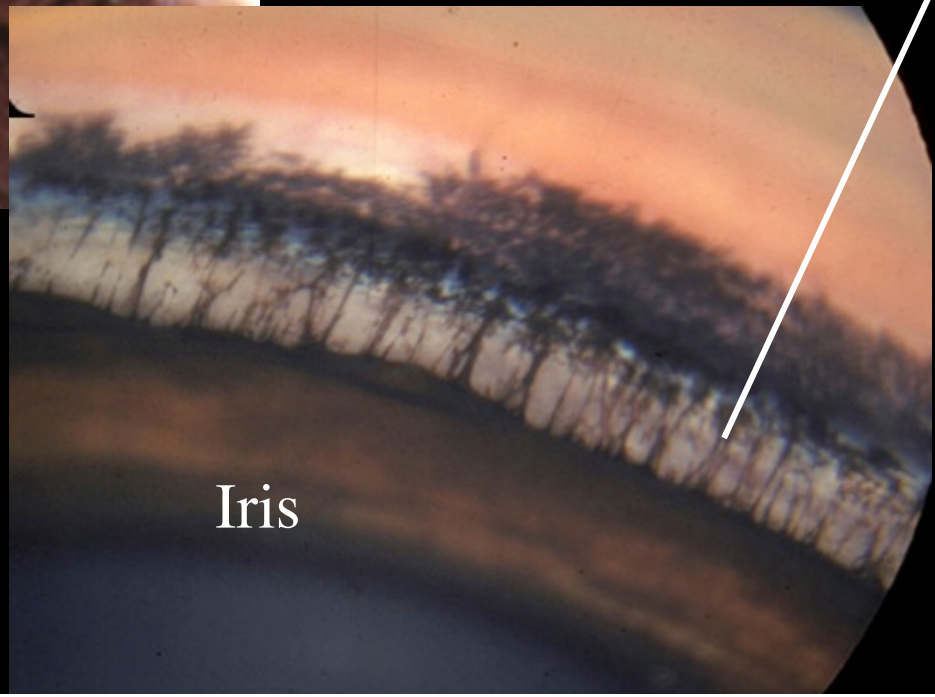
- Goniodysgenesis
- Pectinate ligament dysplasia
- Mesodermal dysgenesis
- Open-angle, closed-cleft glaucoma (Peiffer)
- Acute angle-closure glaucoma (Miller)
- Who knows what else

Goniodysgenesis by breed, n=1710



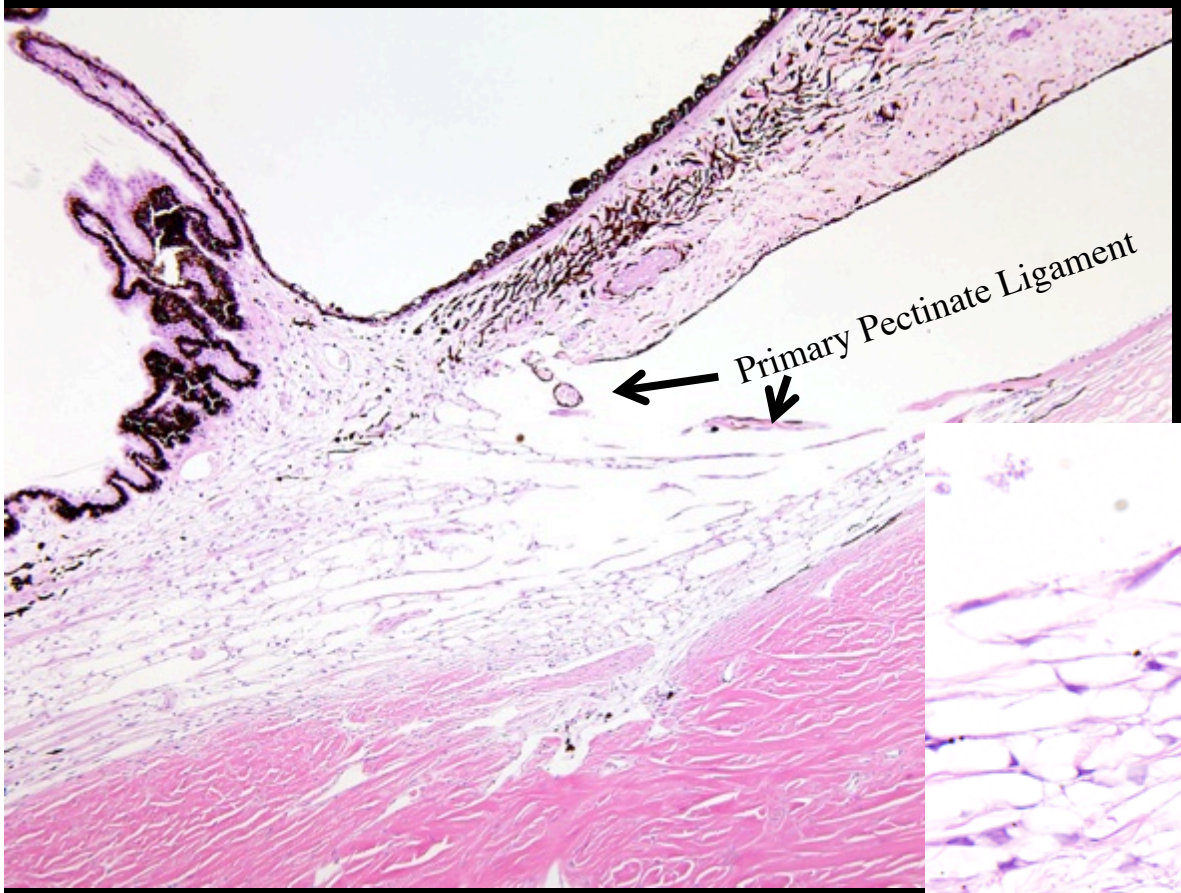
The Normal Canine Angle

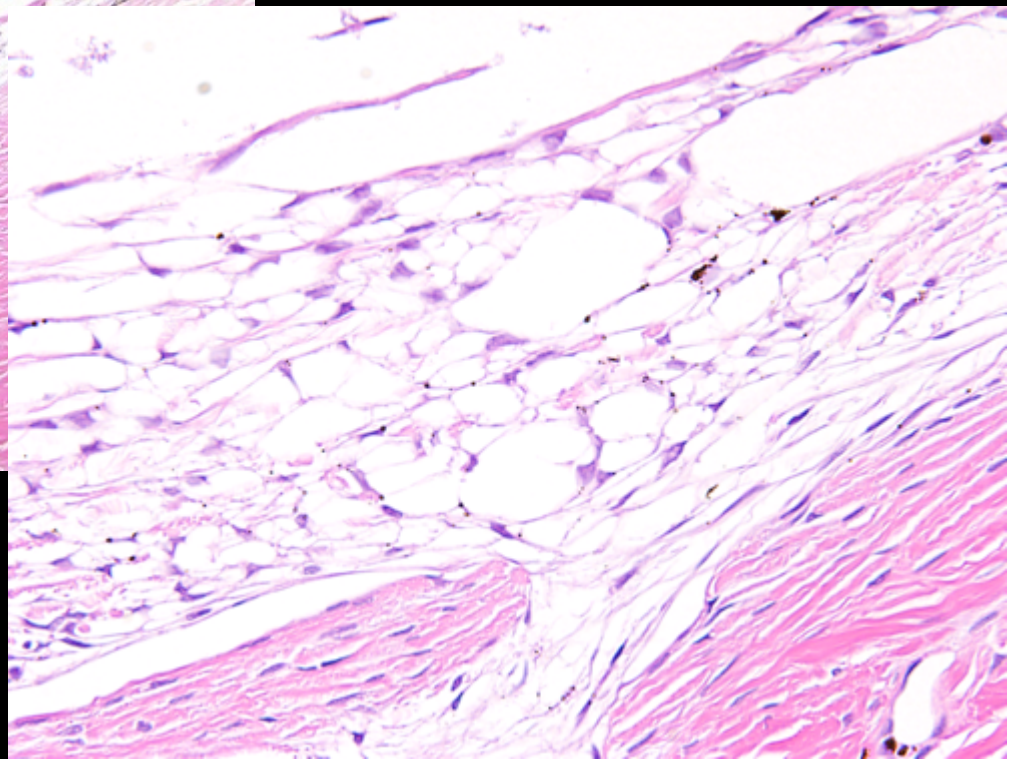




Dr Kerry Ketring

The Normal Canine Angle





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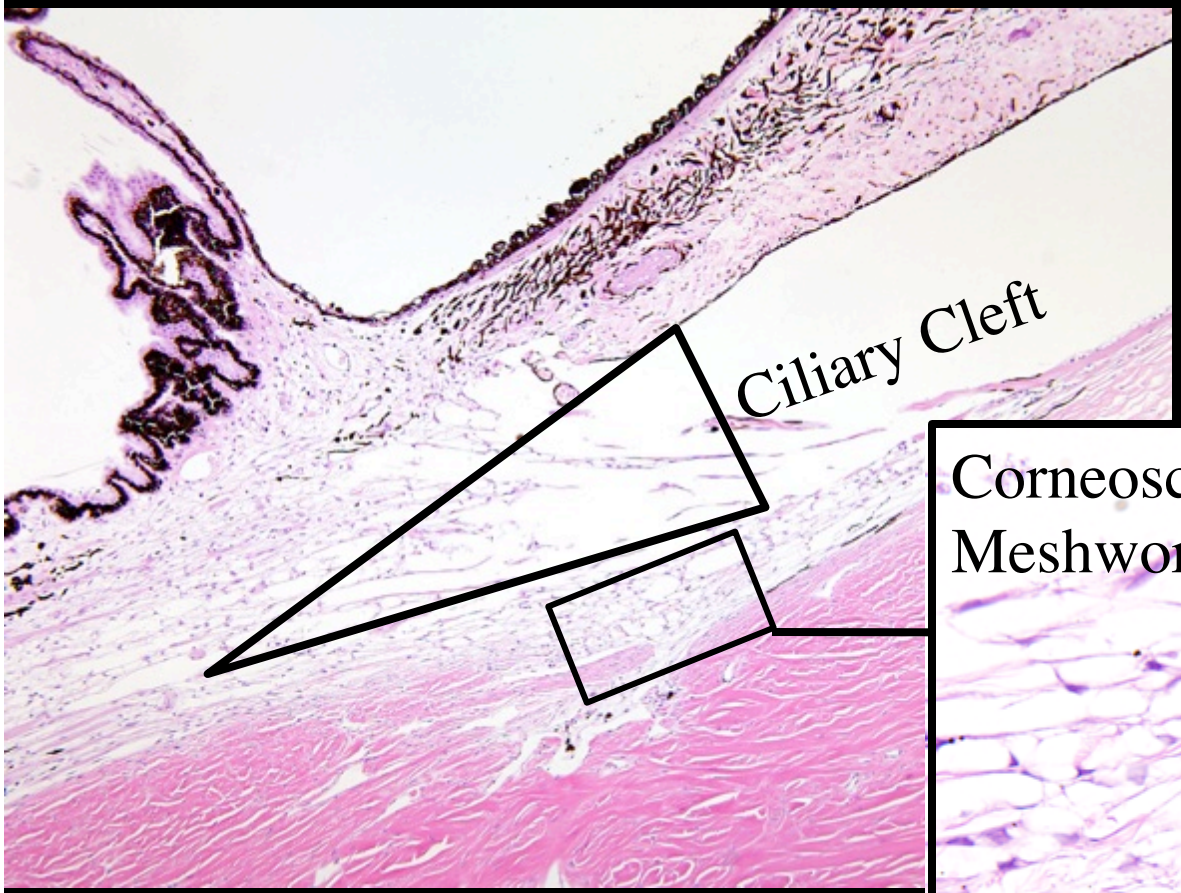
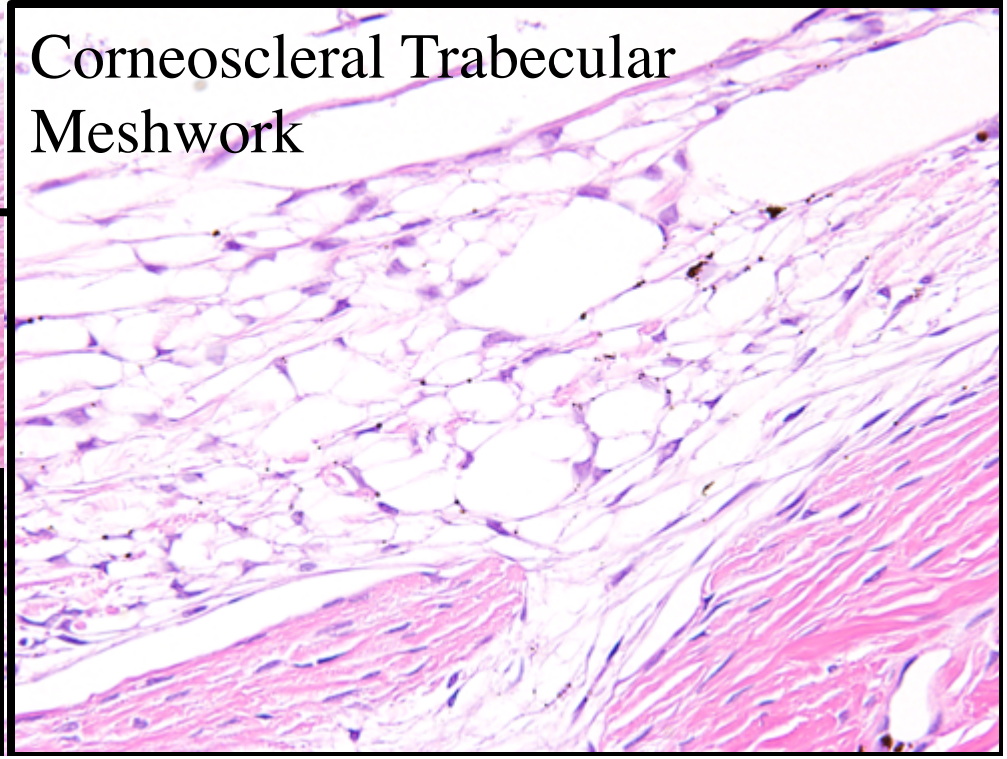
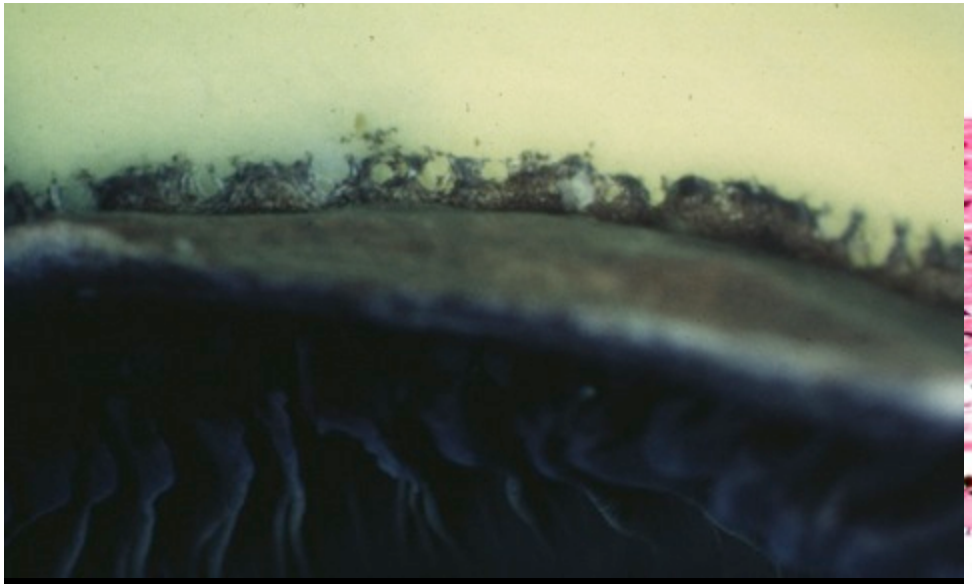
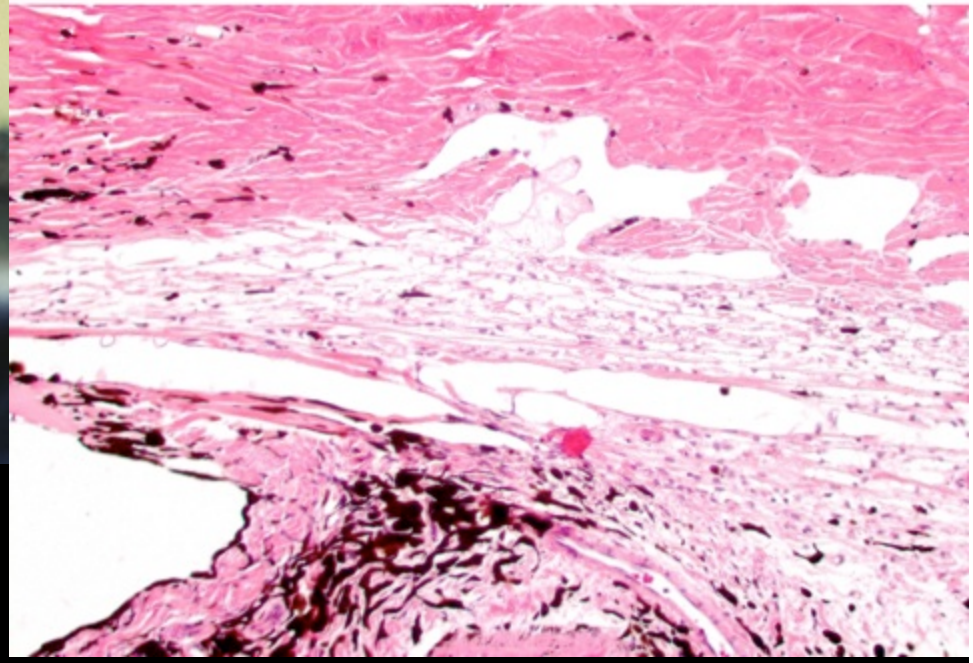


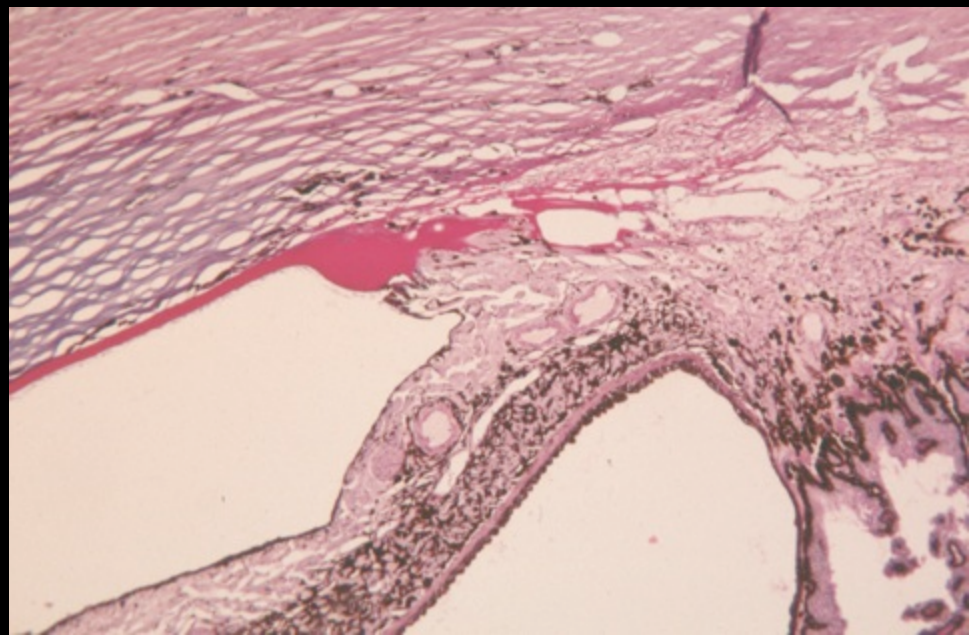




Goniodysgenesis
Normal
Pressure

Normotensive Basset Hound with Goniodysgenesis





Canine Primary Glaucoma the Clinical Disease Syndrome

- Sudden onset of painful, red, often blind eye with very high pressures
  - In this talk, the time of disease is measured from when the owner first notices a painful red eye (Hour 0)
- The response to treatment is variable, but severe cases are blind from the start
- Enucleation is a common outcome
  - When dealing with the second eye, enucleation is often chosen very early (24 hours from the first signs of disease)

Canine Primary Glaucoma the Histopathology

Anterior Segment

- Pigment dispersion
- Ciliary cleft collapse
- Neutrophilic infiltrate and stromal cell activation
- Thinning of the sclera at the limbus

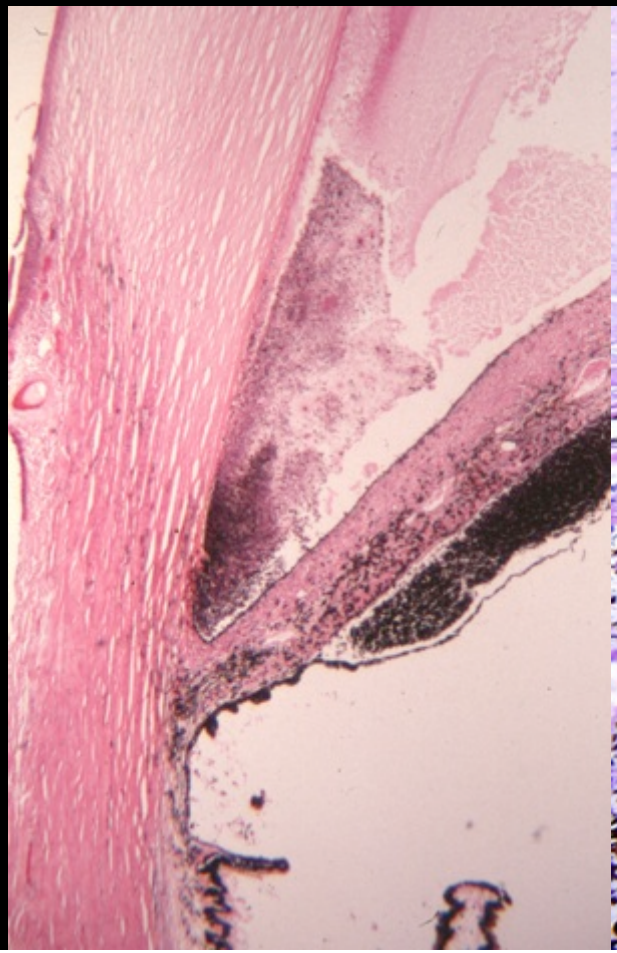
PosteriorSegment

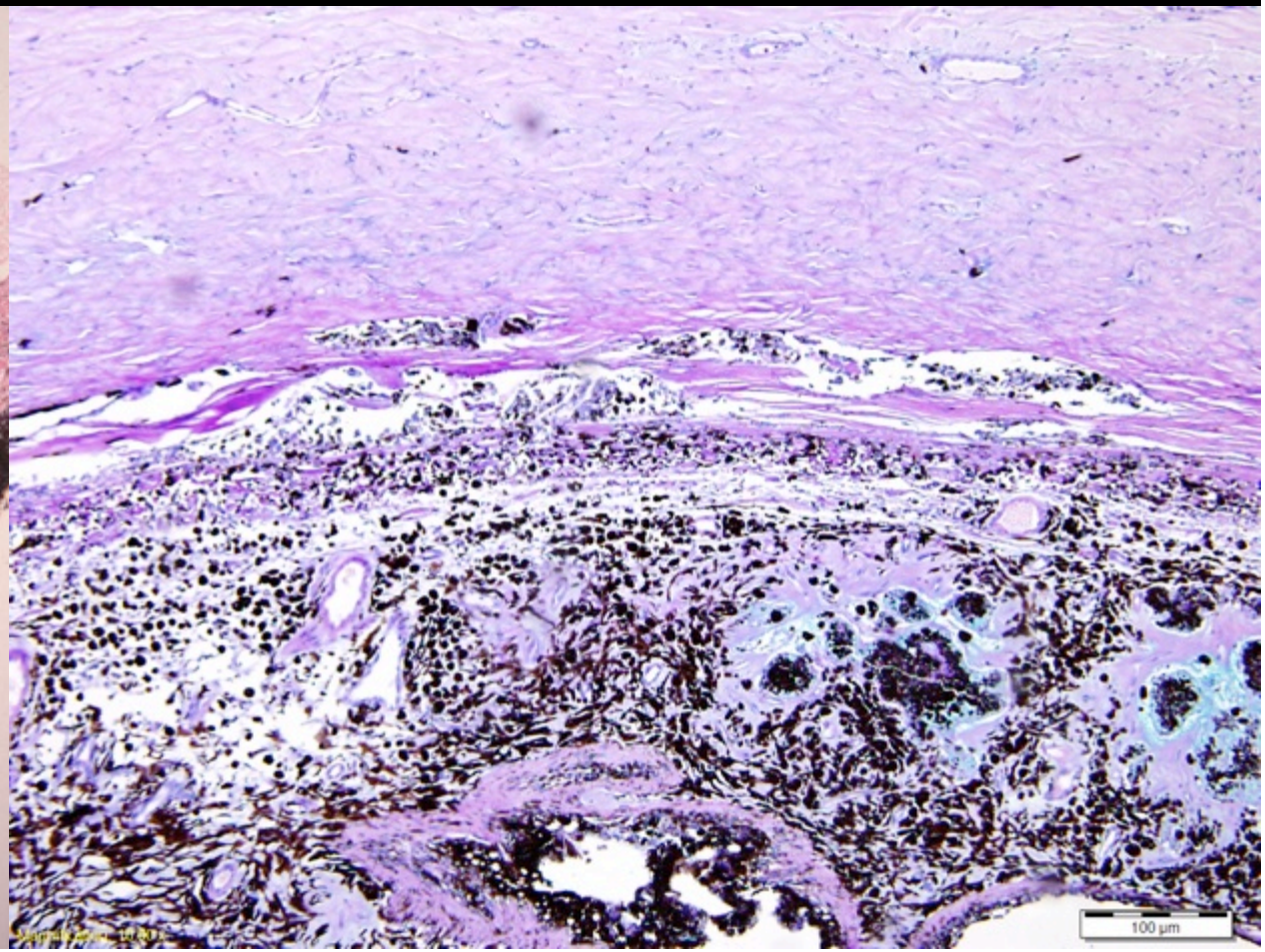
- Optic nerve head necrosis and malacia, infarction
- “Red dead” ganglion cells
- Apoptosis of all layers of the retina
- Formation of a deep optic cup (Schnabel’s cavernous atrophy)
- A progressive loss of axons

Pigment Dispersion

and

Neutrophilic Inflammation





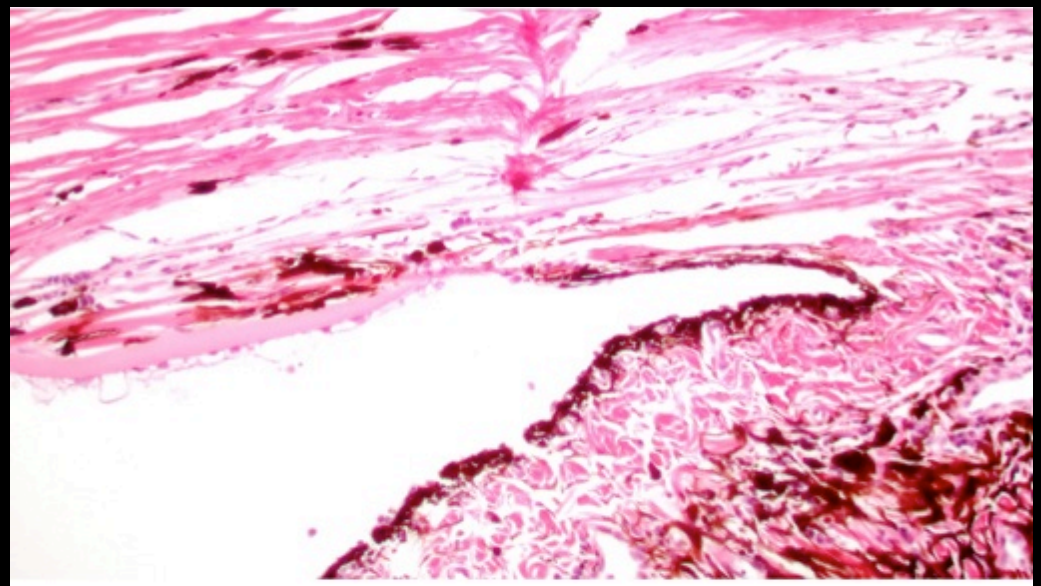
Pigment Dispersion in Primary Glaucoma

- Distinguish superior from inferior angle by pigment alone
  - 1 to 3 Days: 92%
  - 4 to 7 Days: 95%
  - Chronic: 79%
- Cells Stripped from Iris
  - 1 to 3 Days: 43%
  - 4 to 7 Days: 75%
  - Chronic: 55%
- Pigmented Cells in the Angle
  - 1 to 3 Days: 64%
  - 4 to 7 Days: 95%
  - Chronic: 50%

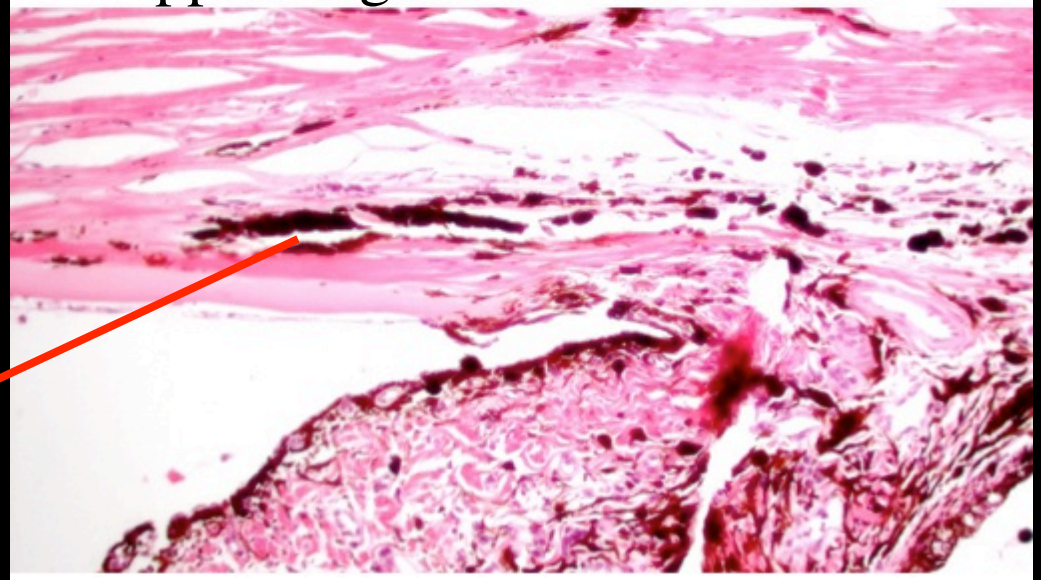
Reilly CM et al. (2005) Canine goniodysgenesis-related glaucoma: a morphologic review of 100 cases looking at inflammation and pigment dispersion. *Vet. Ophthal.*

Neutrophilic Inflammation

- 1 to 3 Days: 86%
- 4 to 7 Days: 50%
- Chronic: 15%

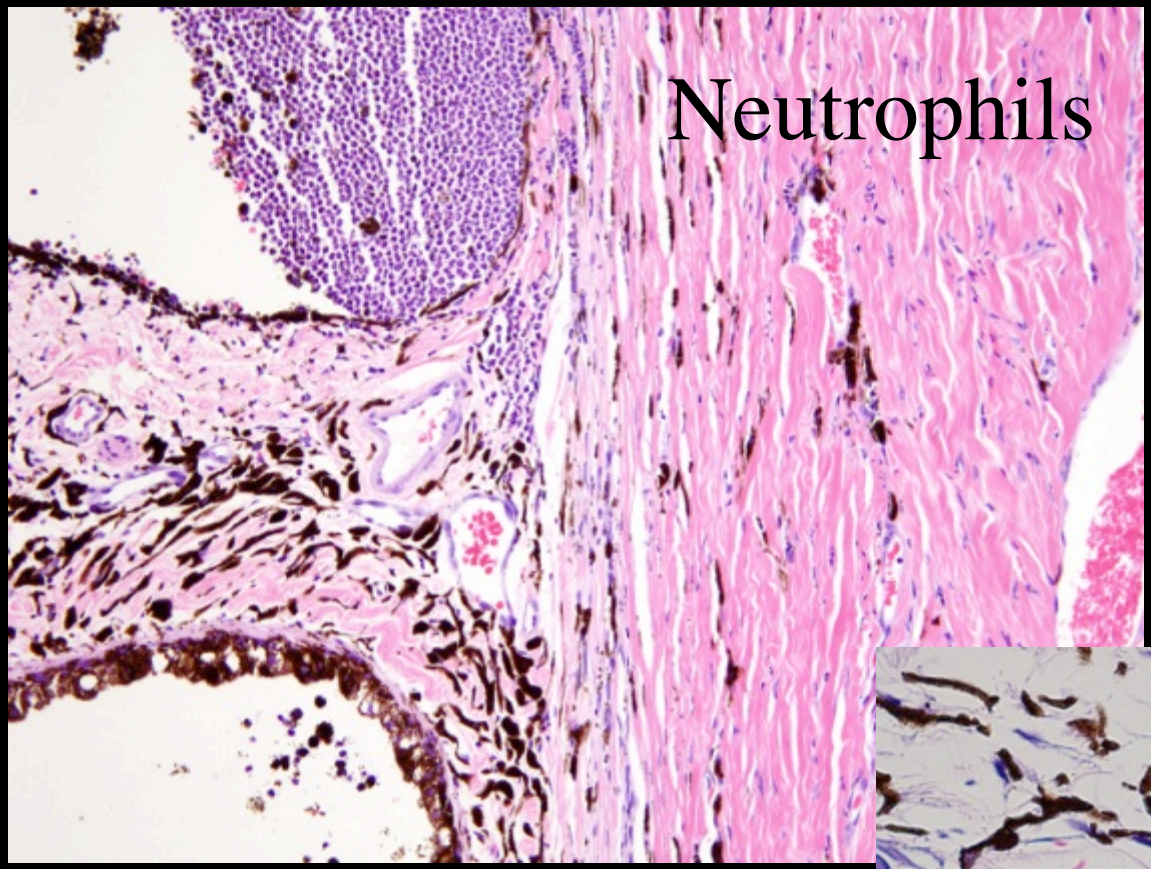


Upper Angle



Lower Angle

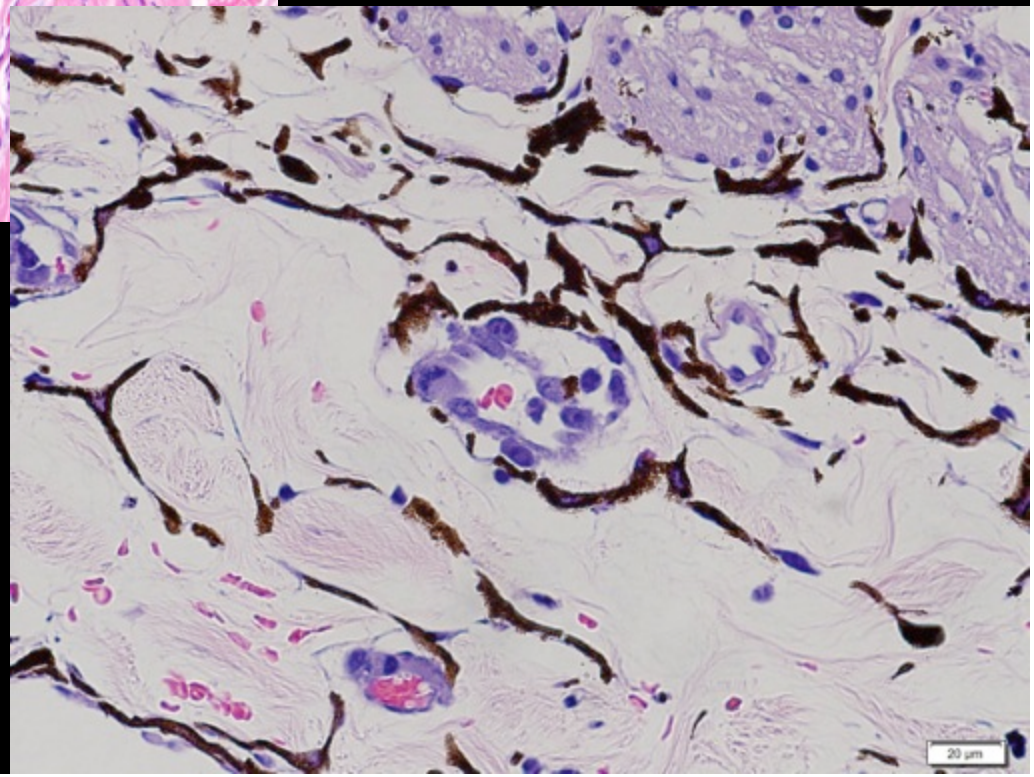
Pigment Dispersion



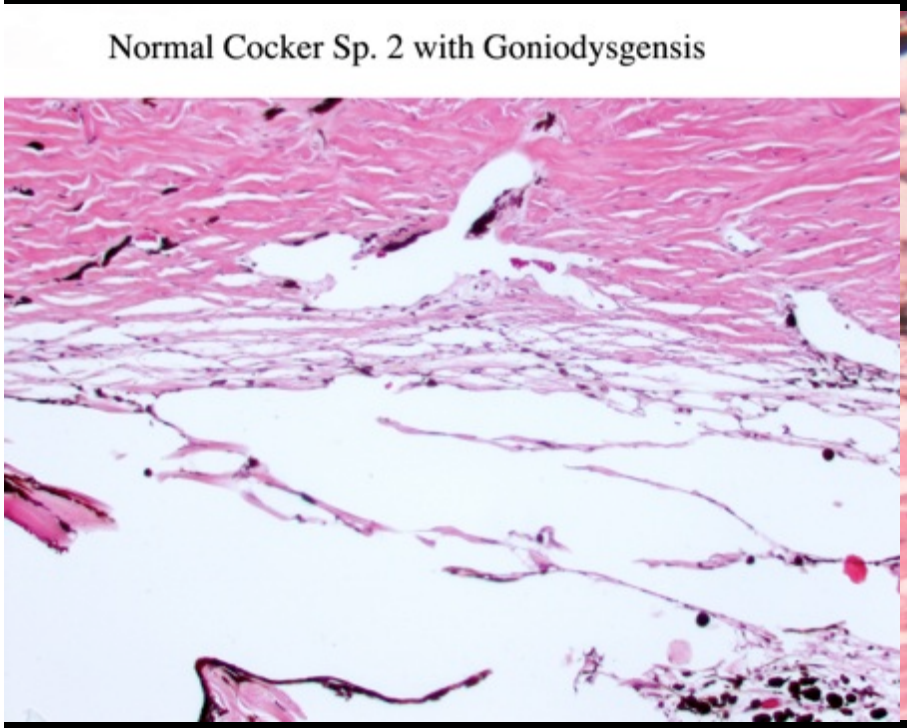
Early Changes in the Iridocorneal Angle

30 hour Glaucoma

Neutrophils and stromal and endothelial cell Proliferation



Evidence of Gradual Atrophy of the Corneoscleral Trabecular Meshwork

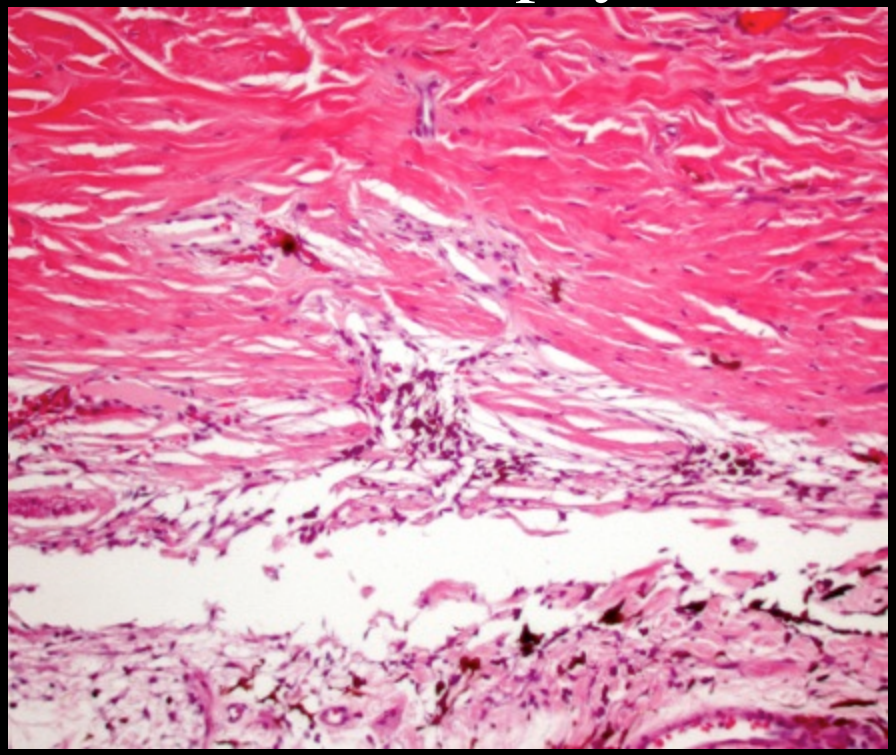


Normal

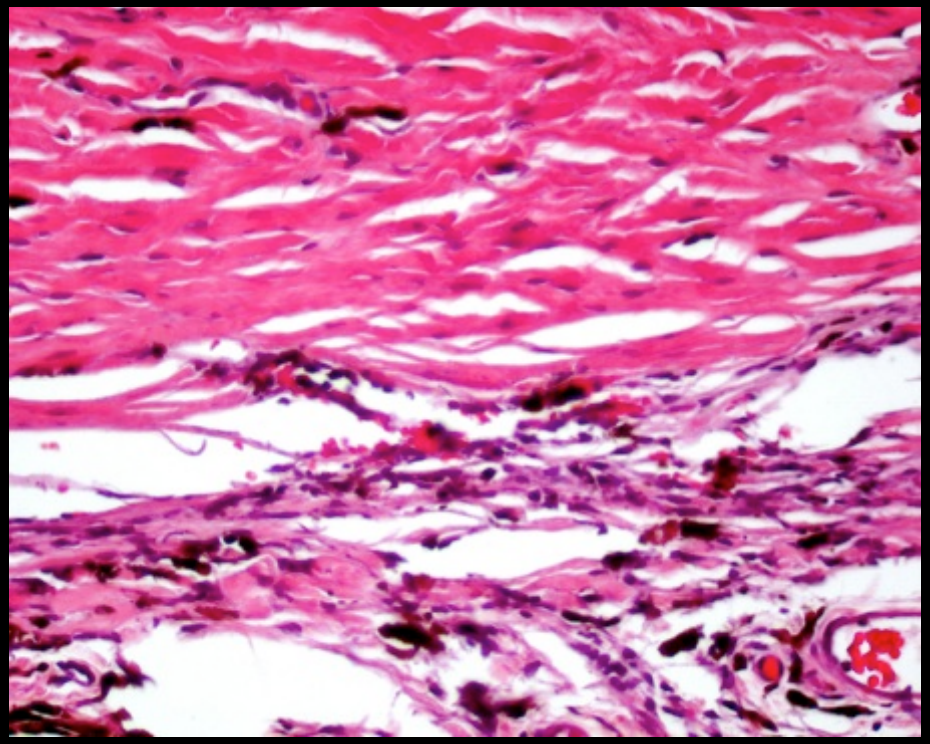
Atrophic

The Second Eye

Atrophy of the trabecular meshwork



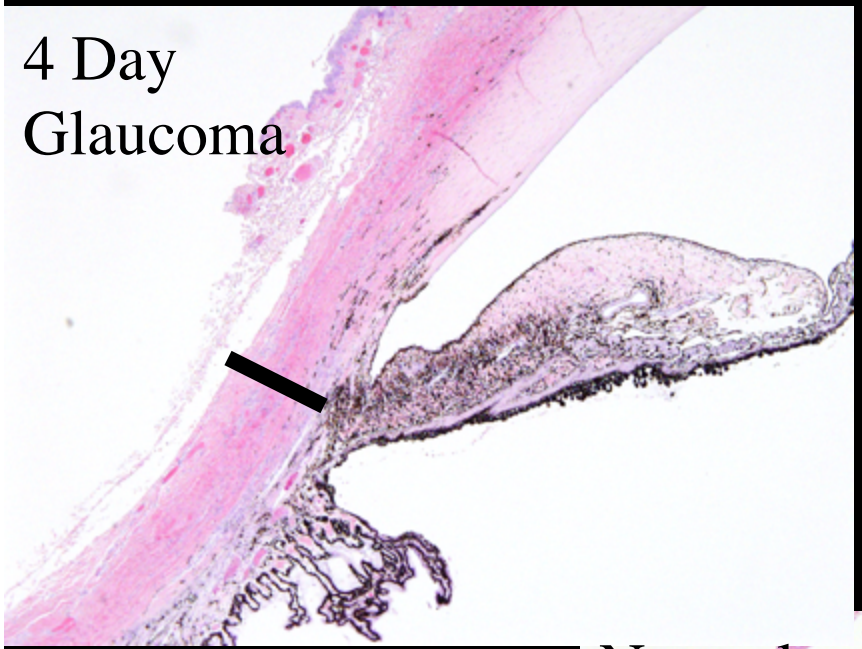
Up



Down

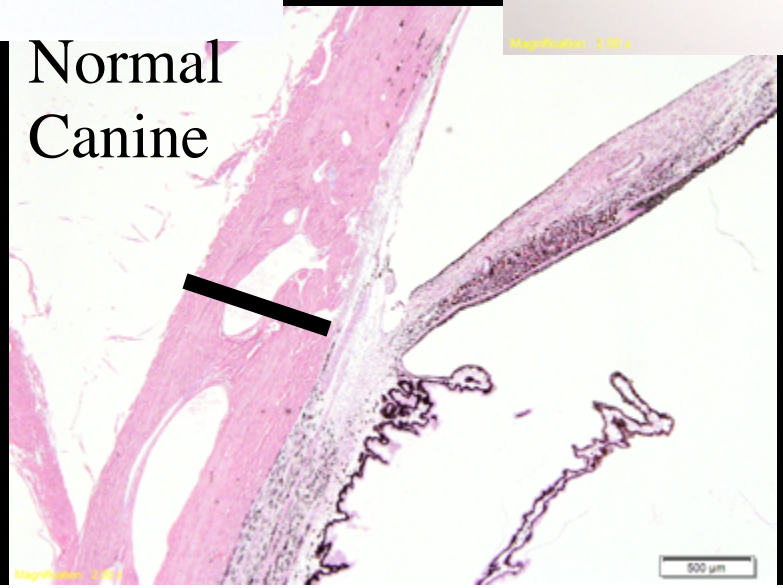
Buphthalmos
Scleral Thickness

4 Day
Glaucoma

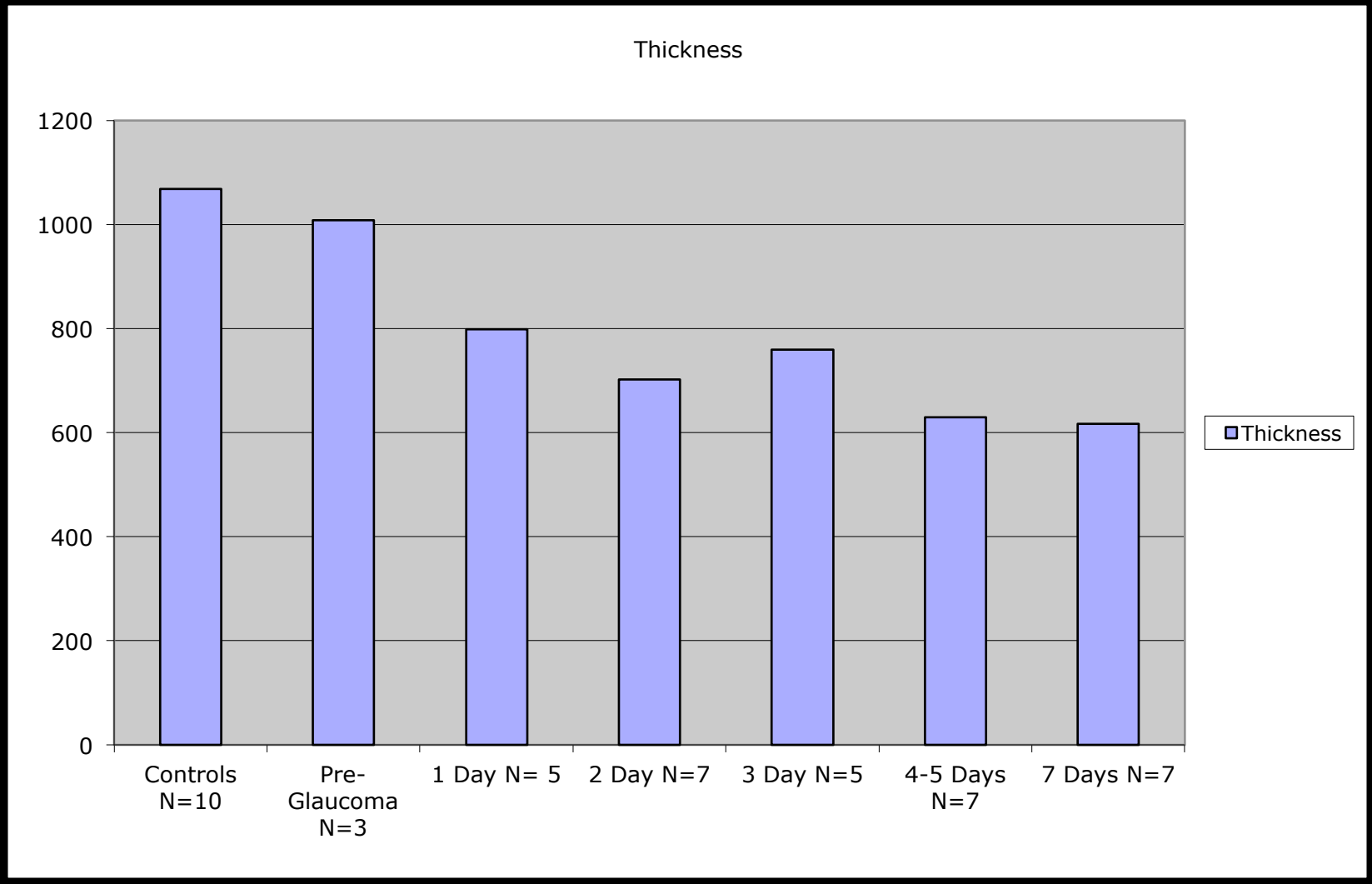


7 Day
Glaucoma

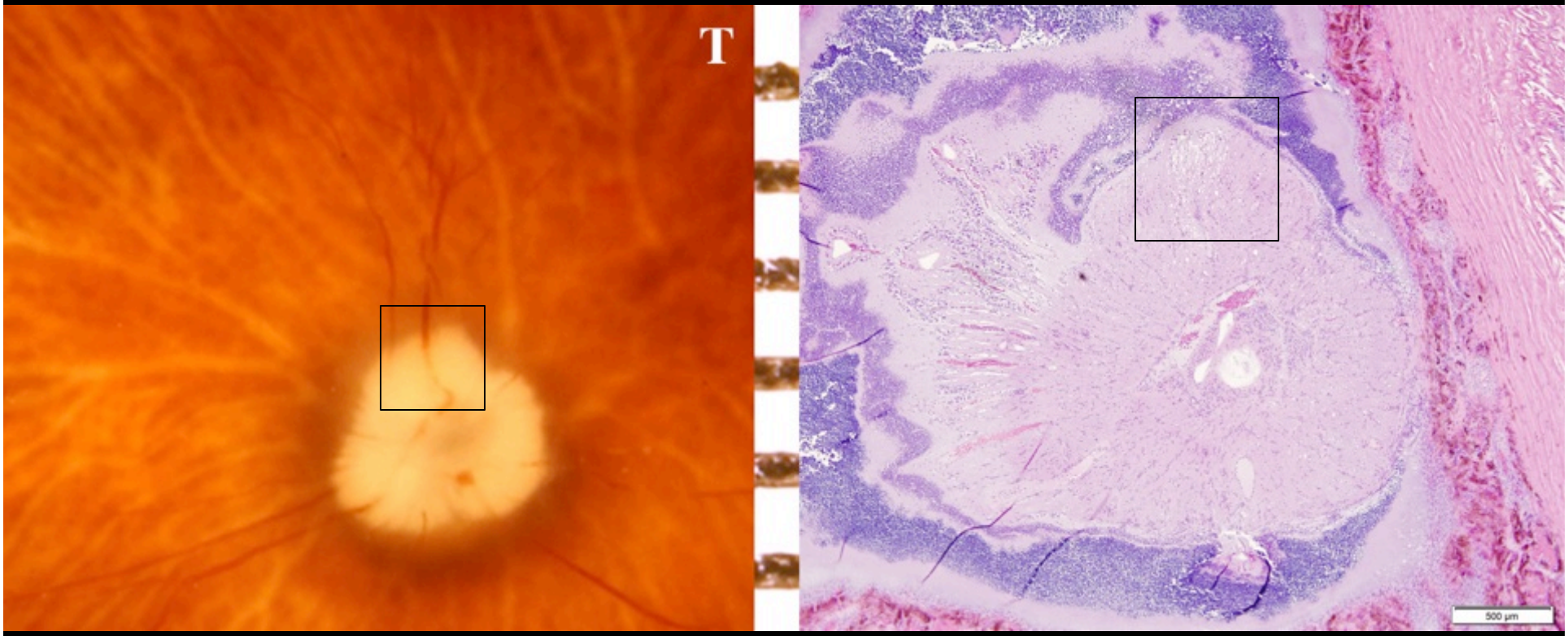
Normal
Canine



Average Scleral Thickness, μ



Effects of Primary Glaucoma on the Optic Nerve and the Retina



1-day Glaucoma

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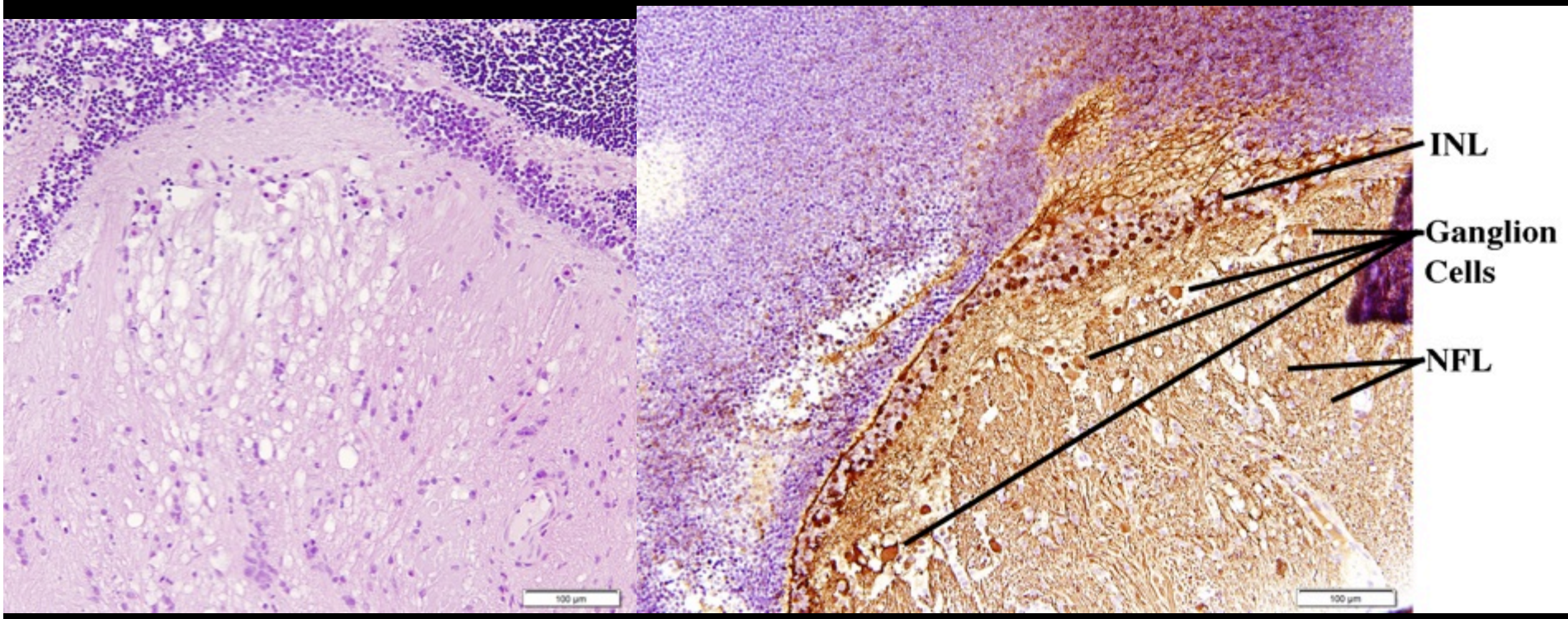

1-day Glaucoma

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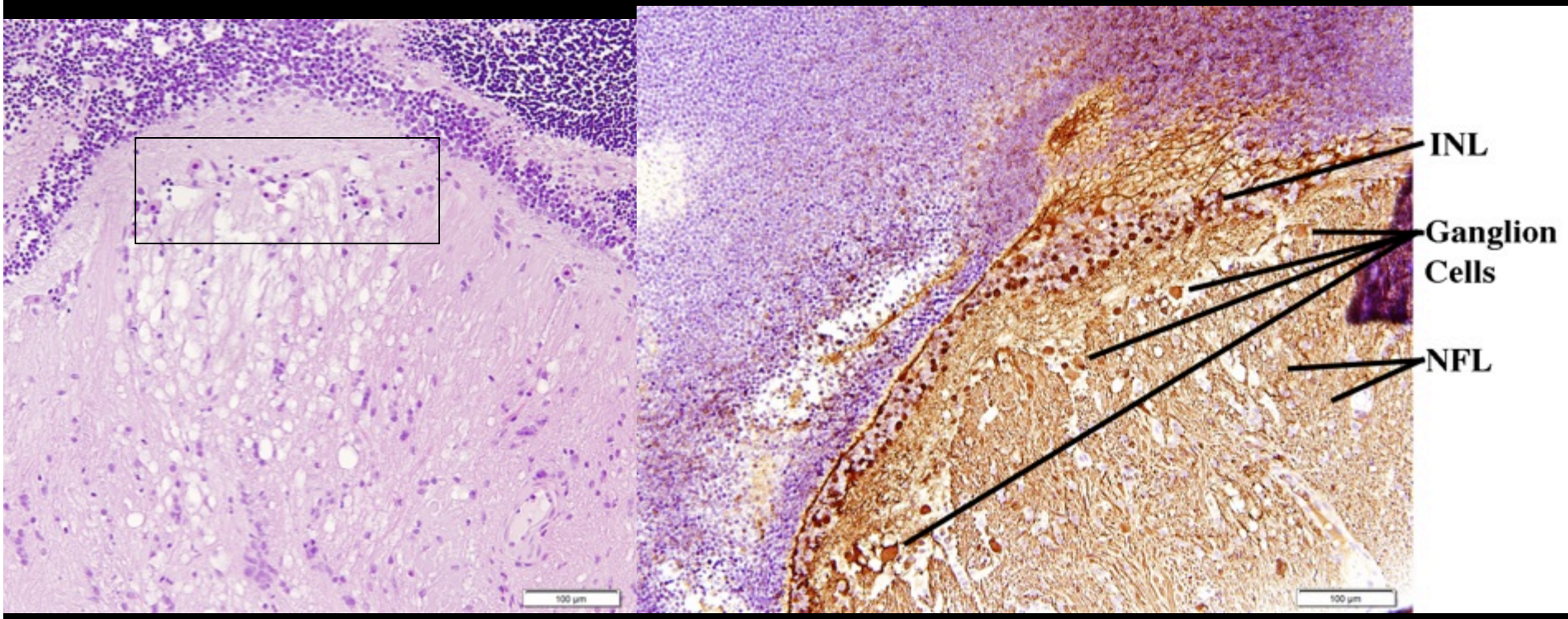

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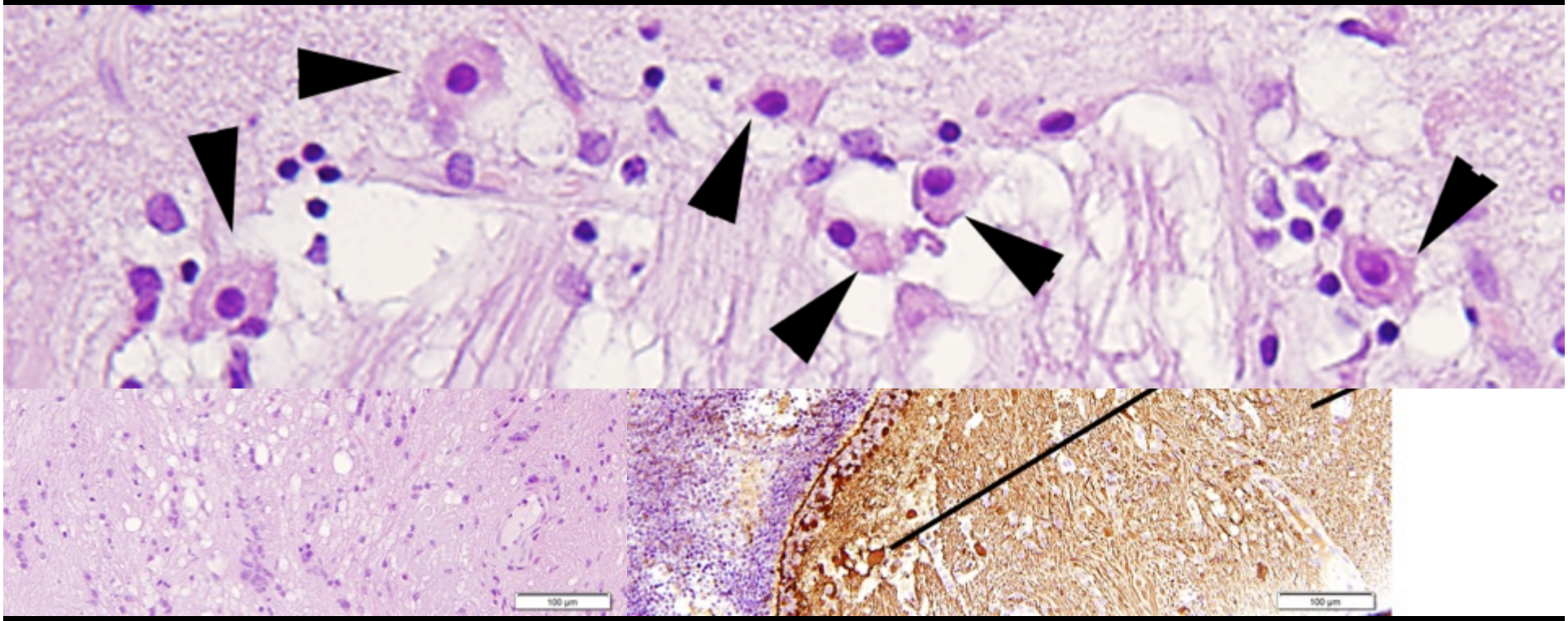
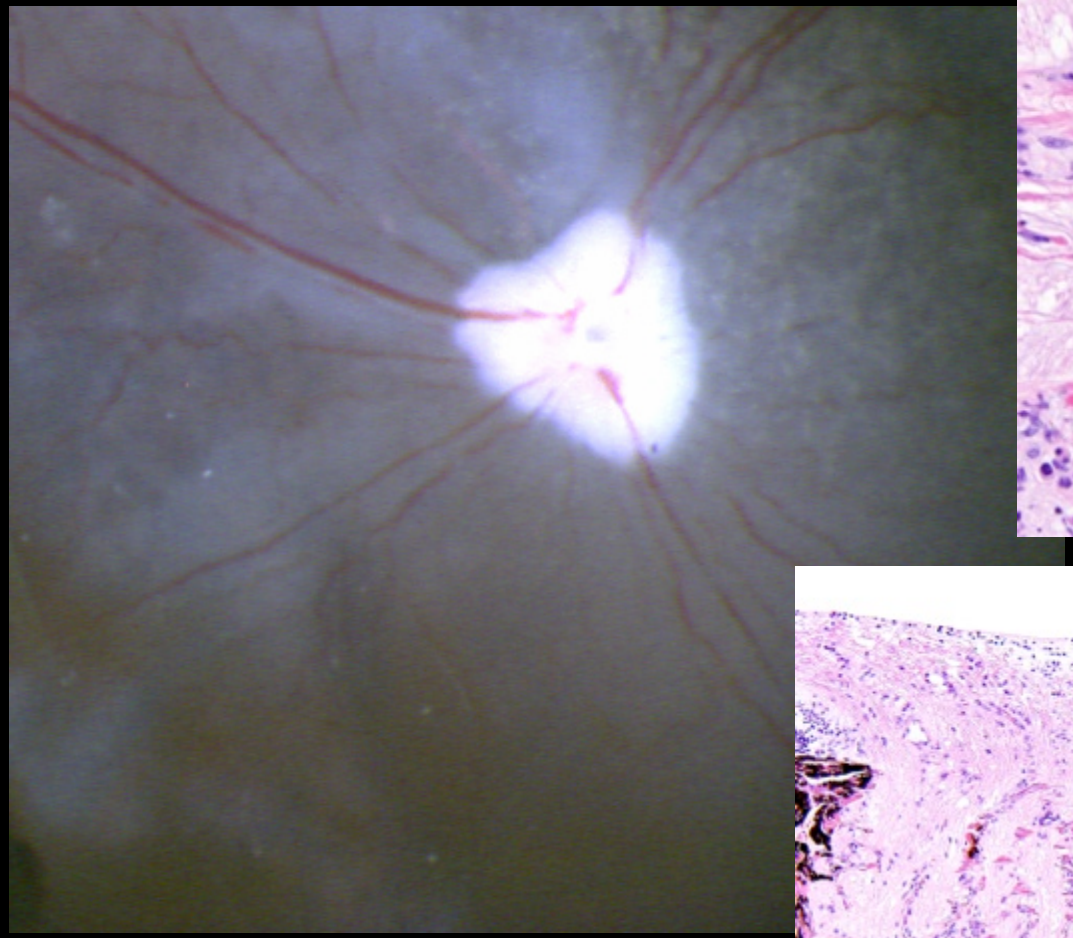
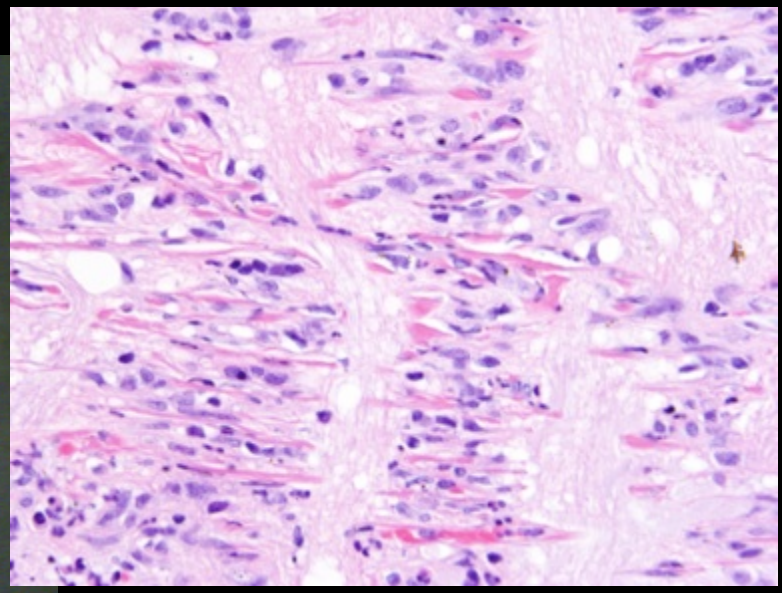
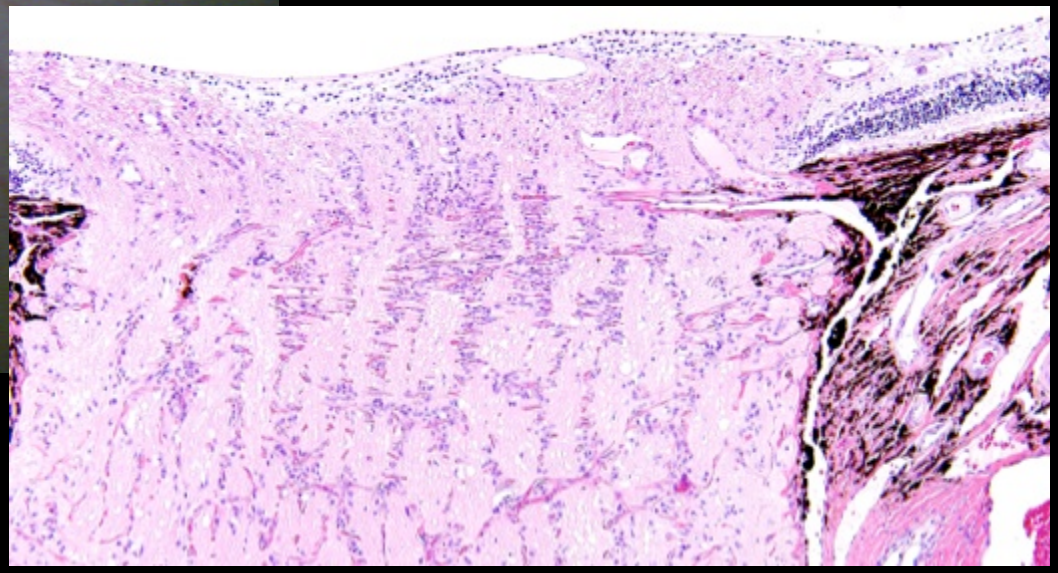


1-day Glaucoma

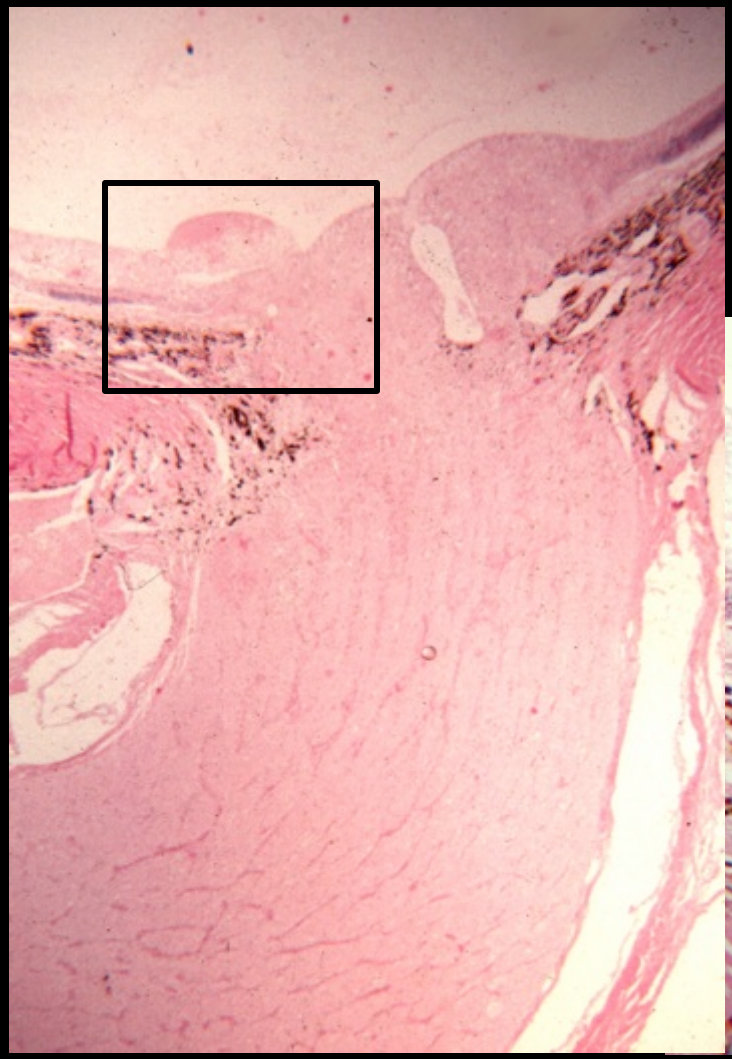
30 hour Glaucoma



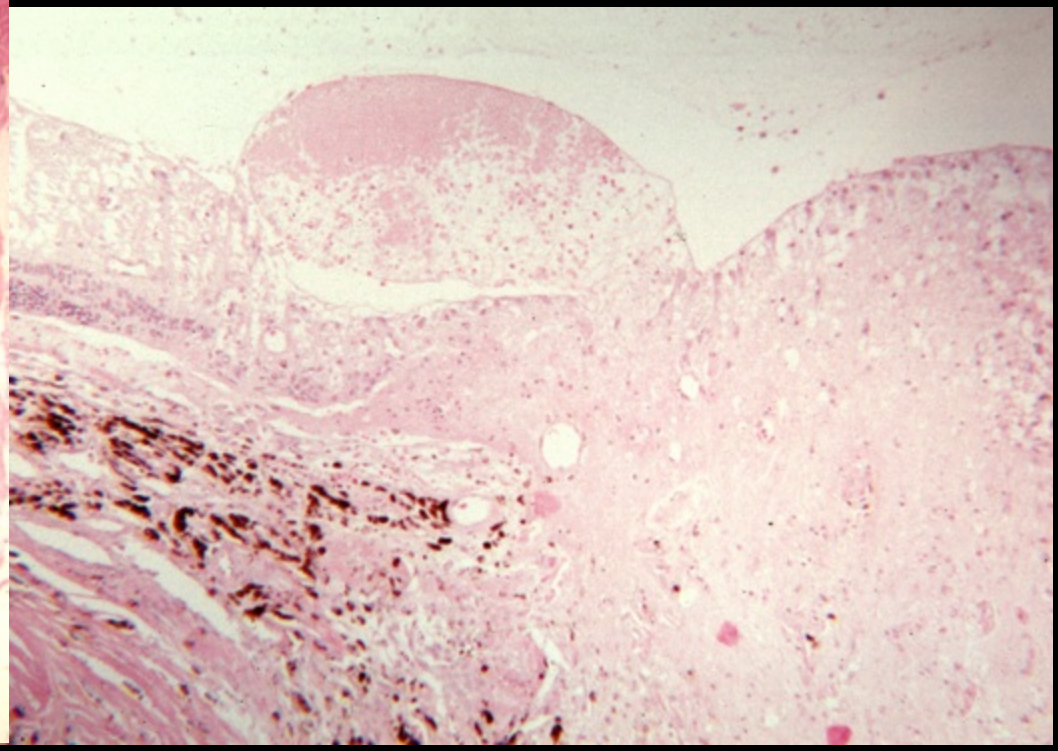


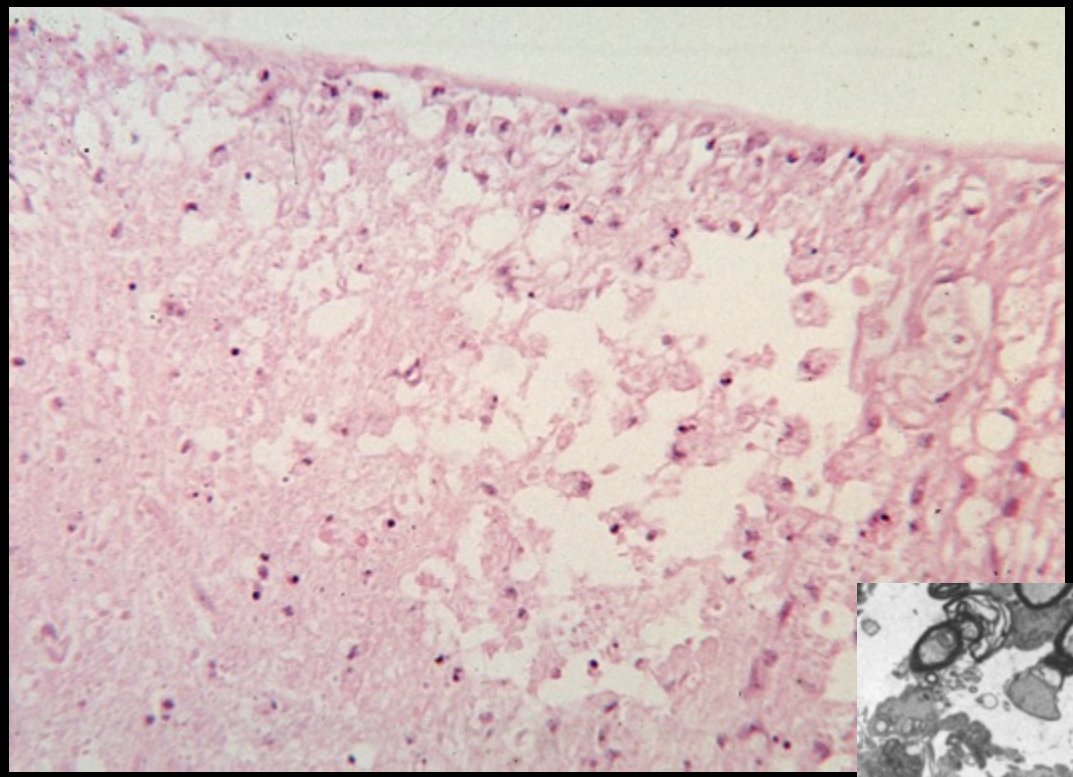


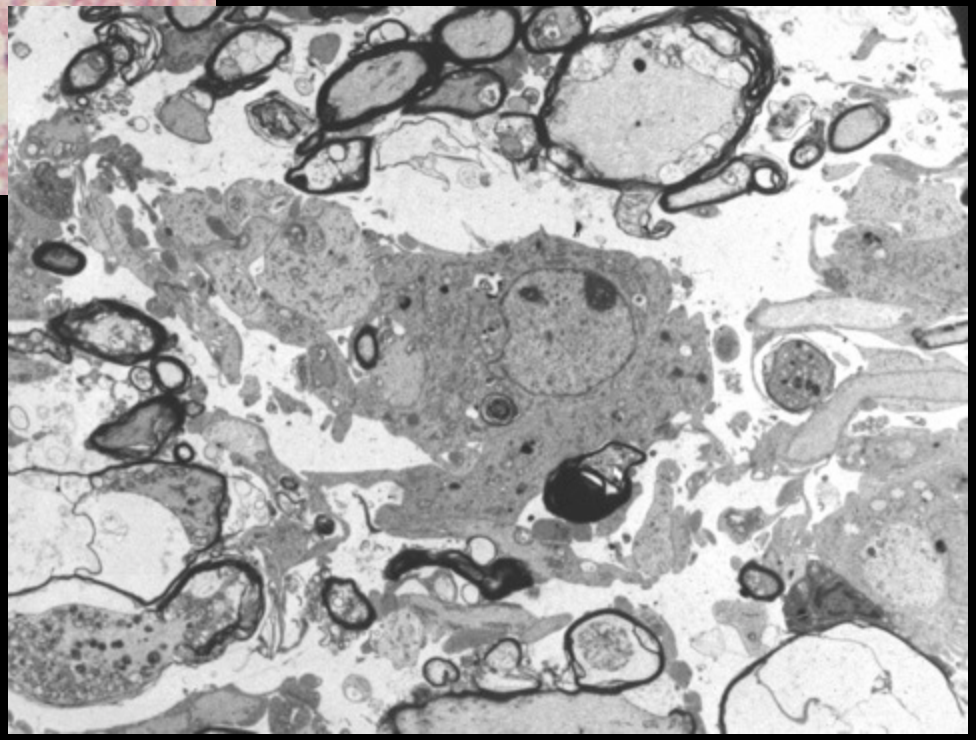
Optic Nerve 2 to 4 Days



Necrosis of the neuropil

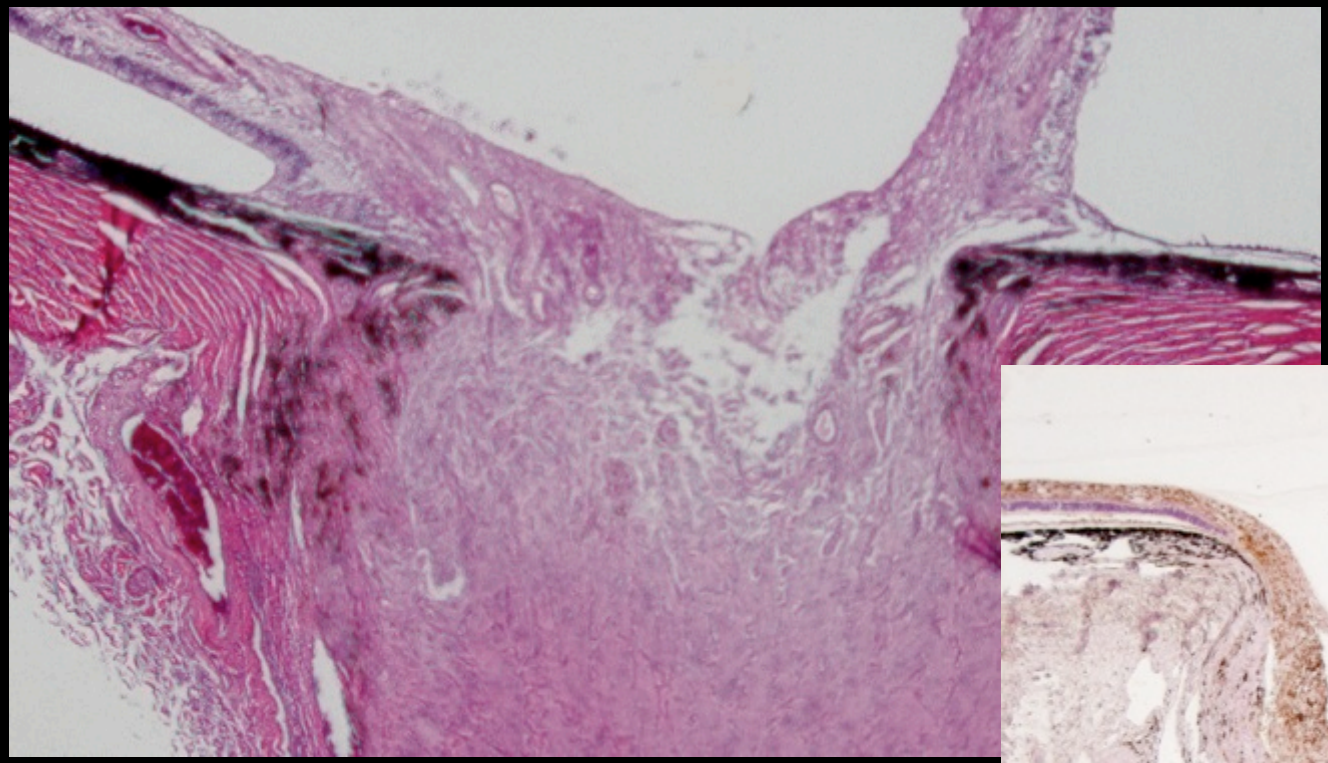


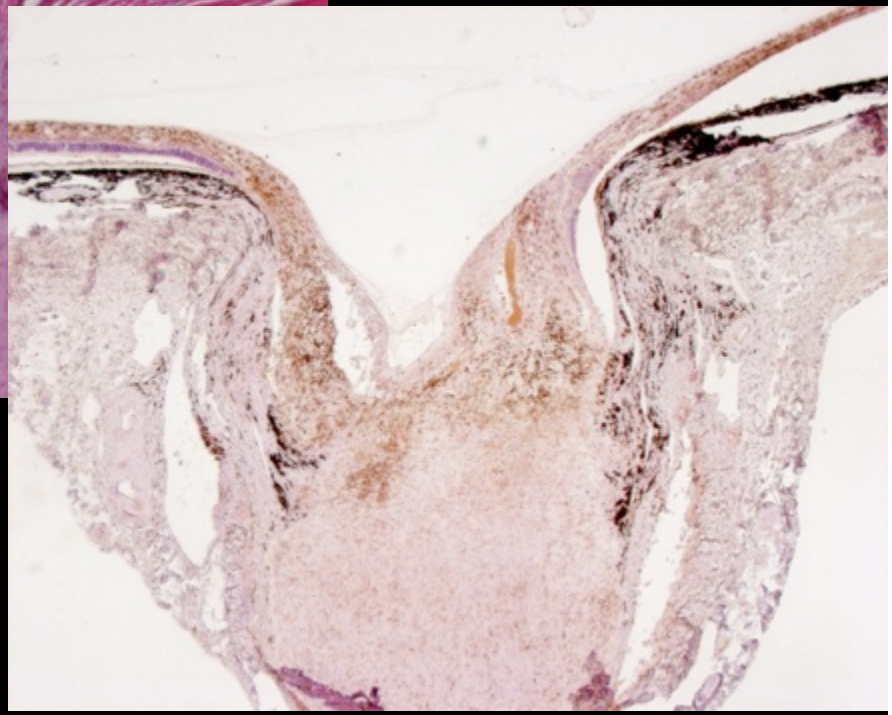




4 Day Optic Nerve Head
Phagocytosis/Malacia

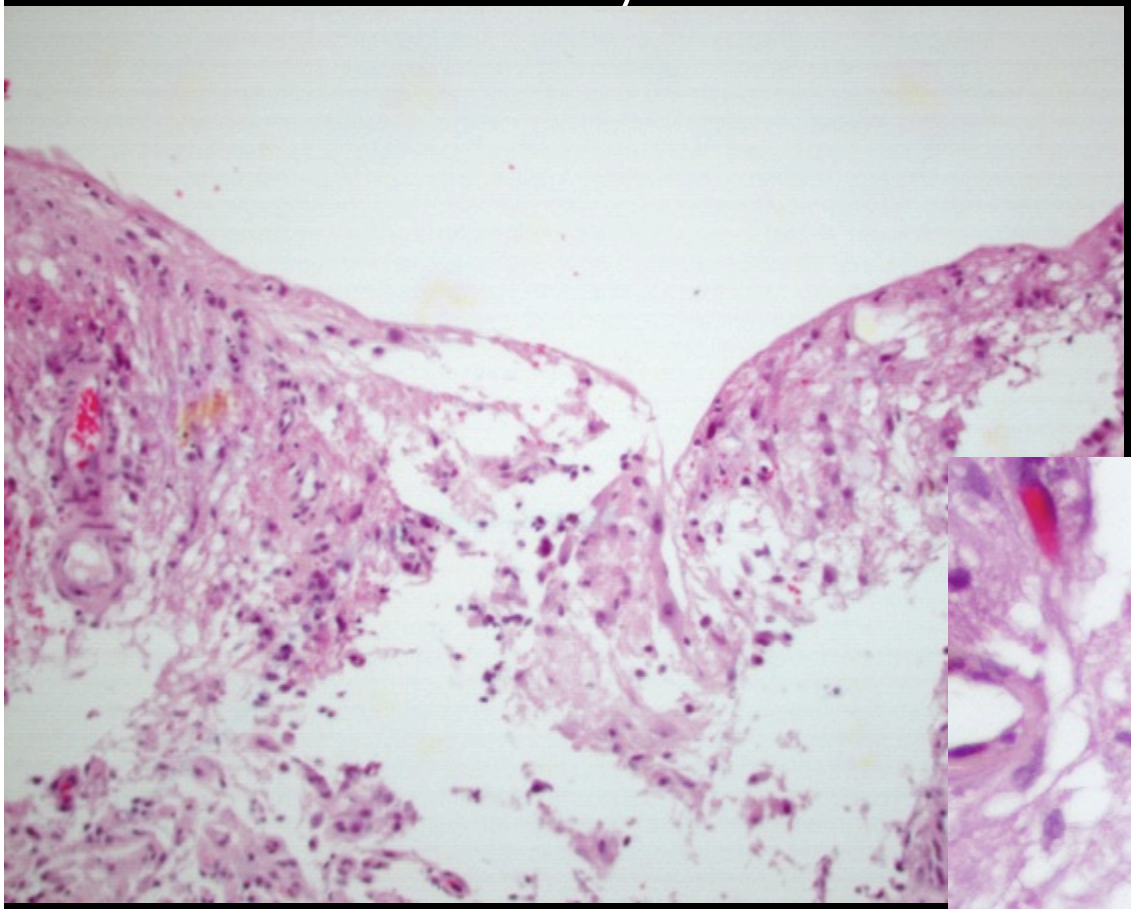
Five day Canine Glaucoma

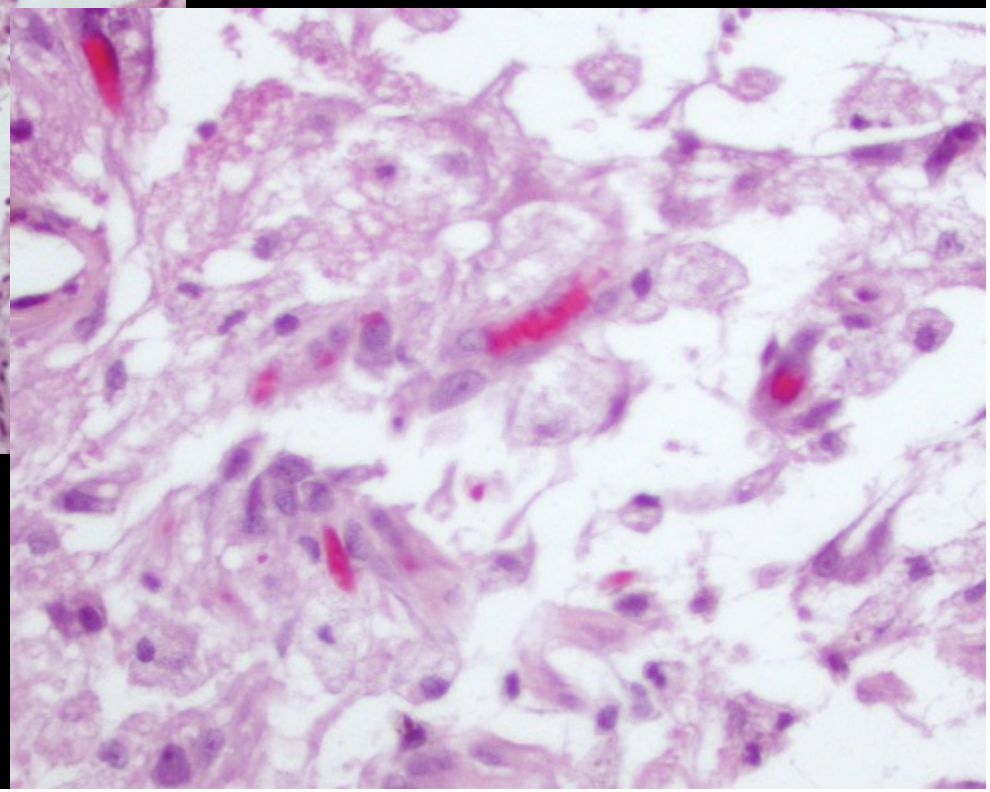




Stained for phagocytes

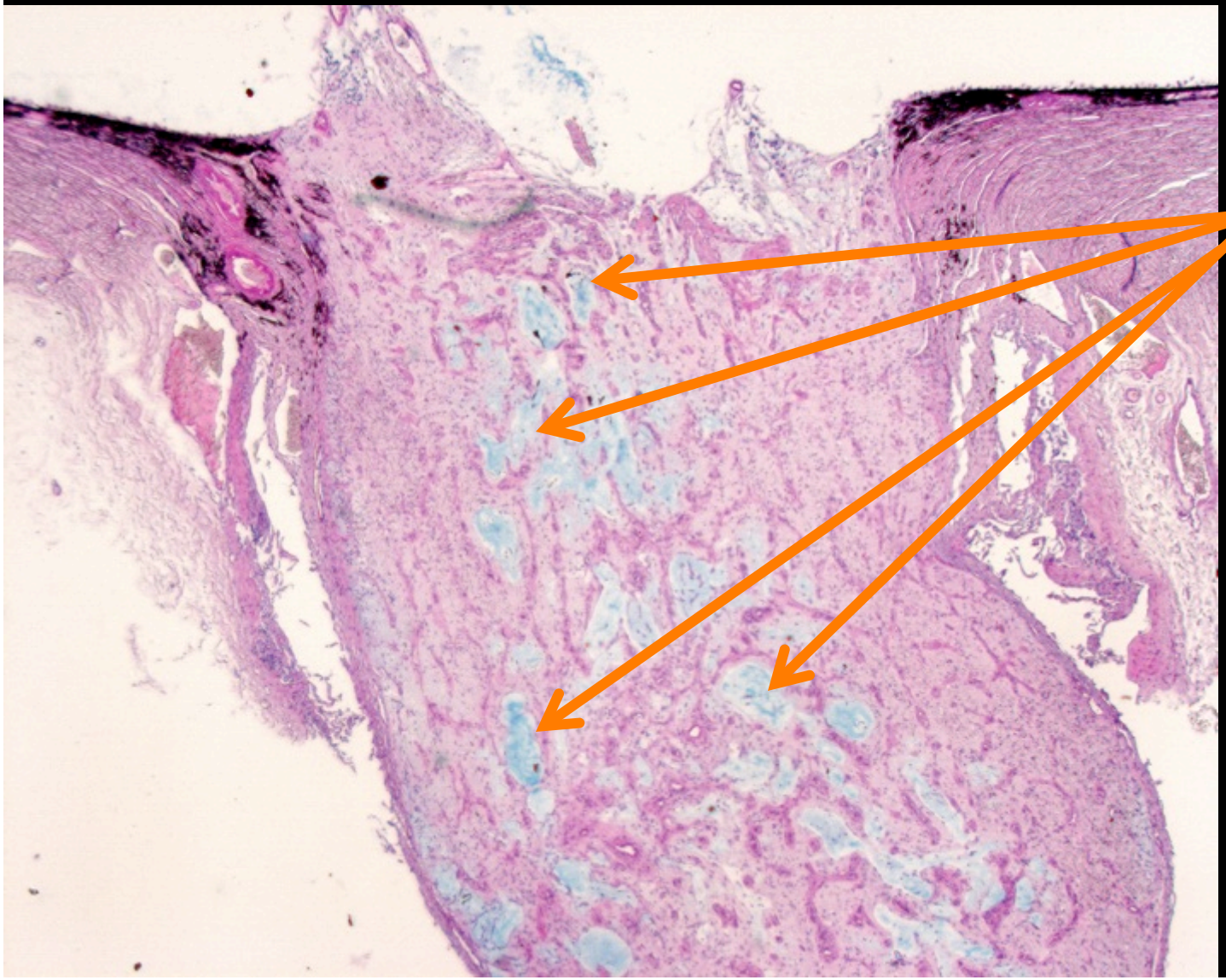
5 day Canine Glaucoma





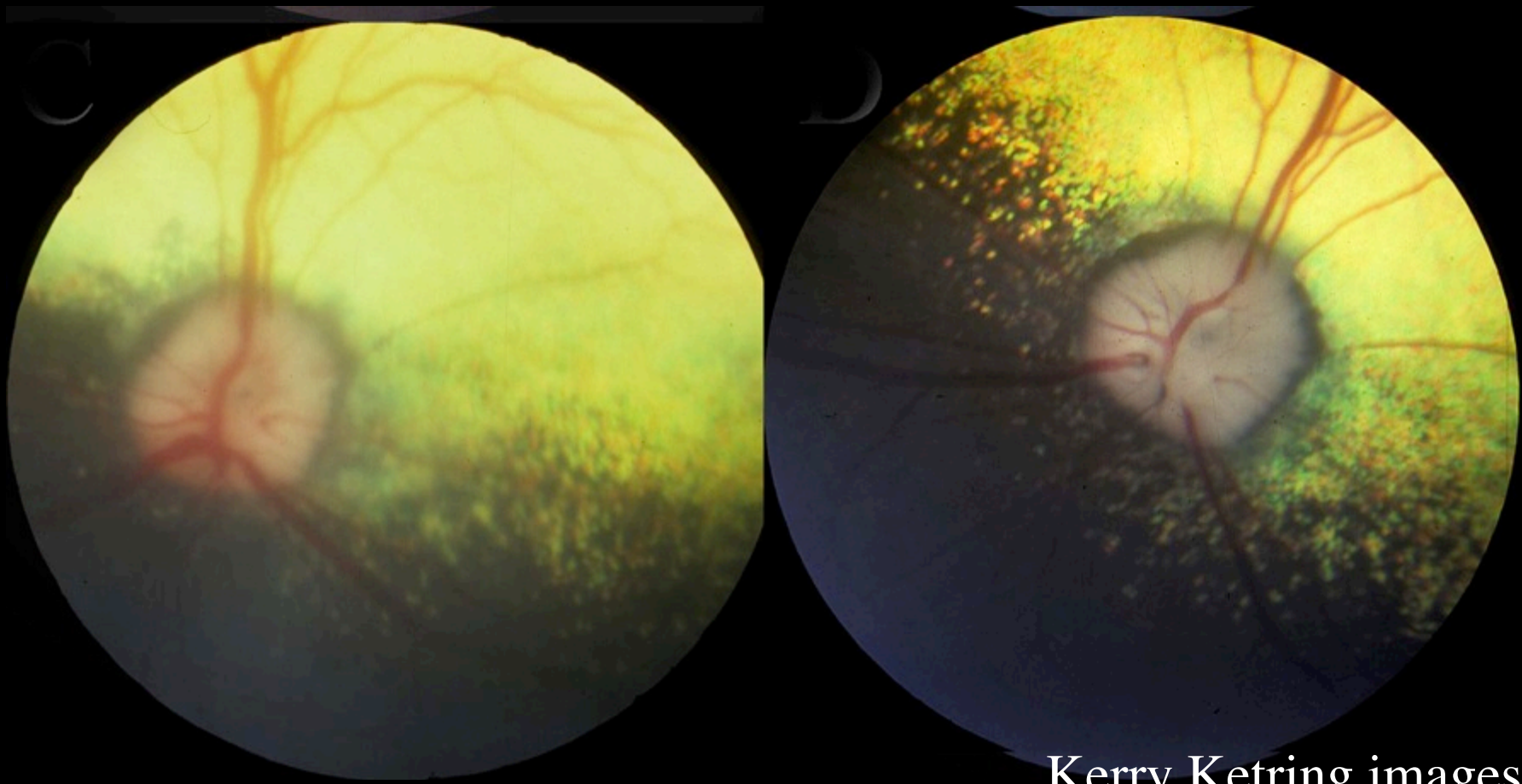
Gitter cell macrophages

Schnabel's cavernous optic atrophy



Entrapped vitreous

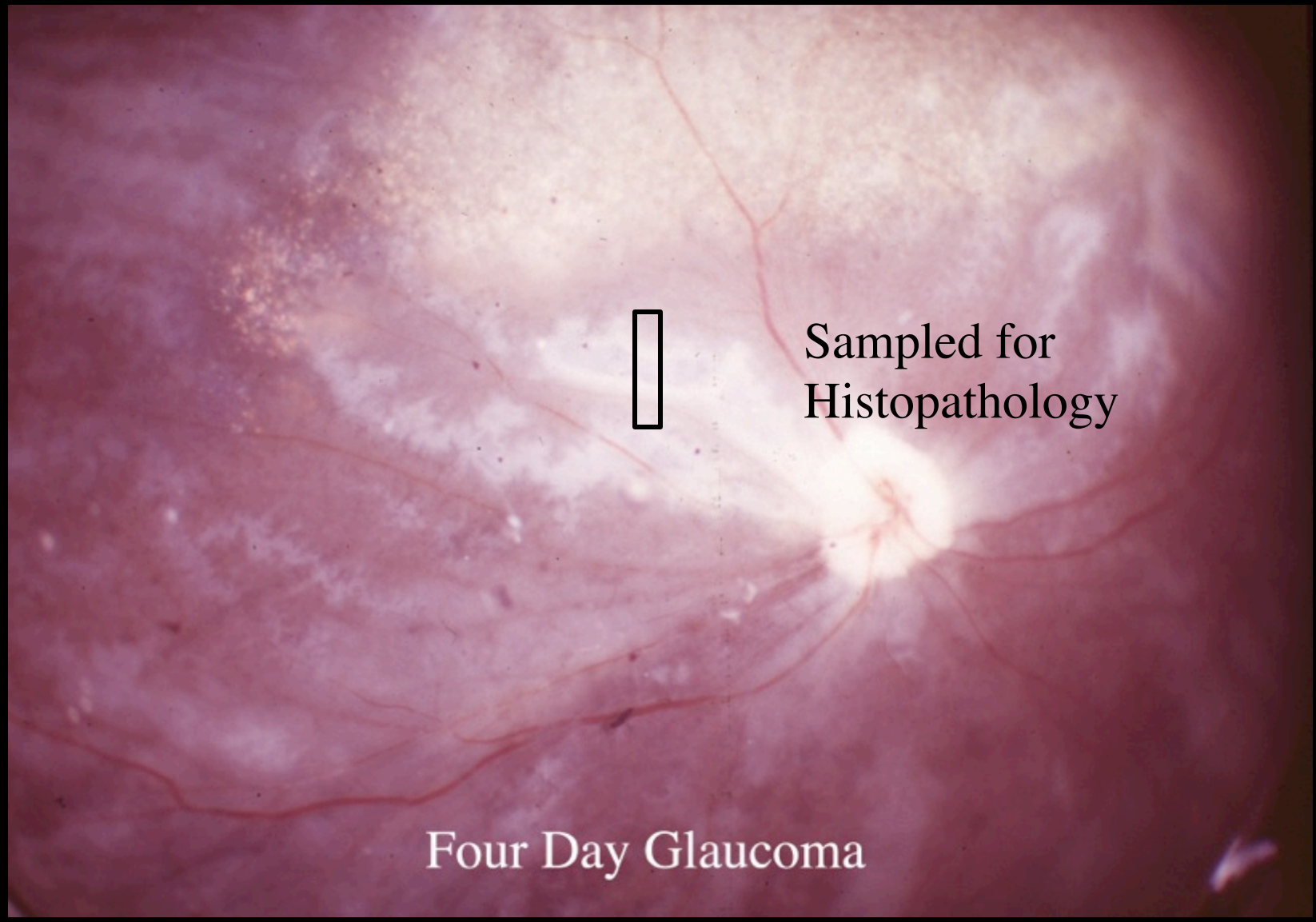
Early Progression of Retinal Disease

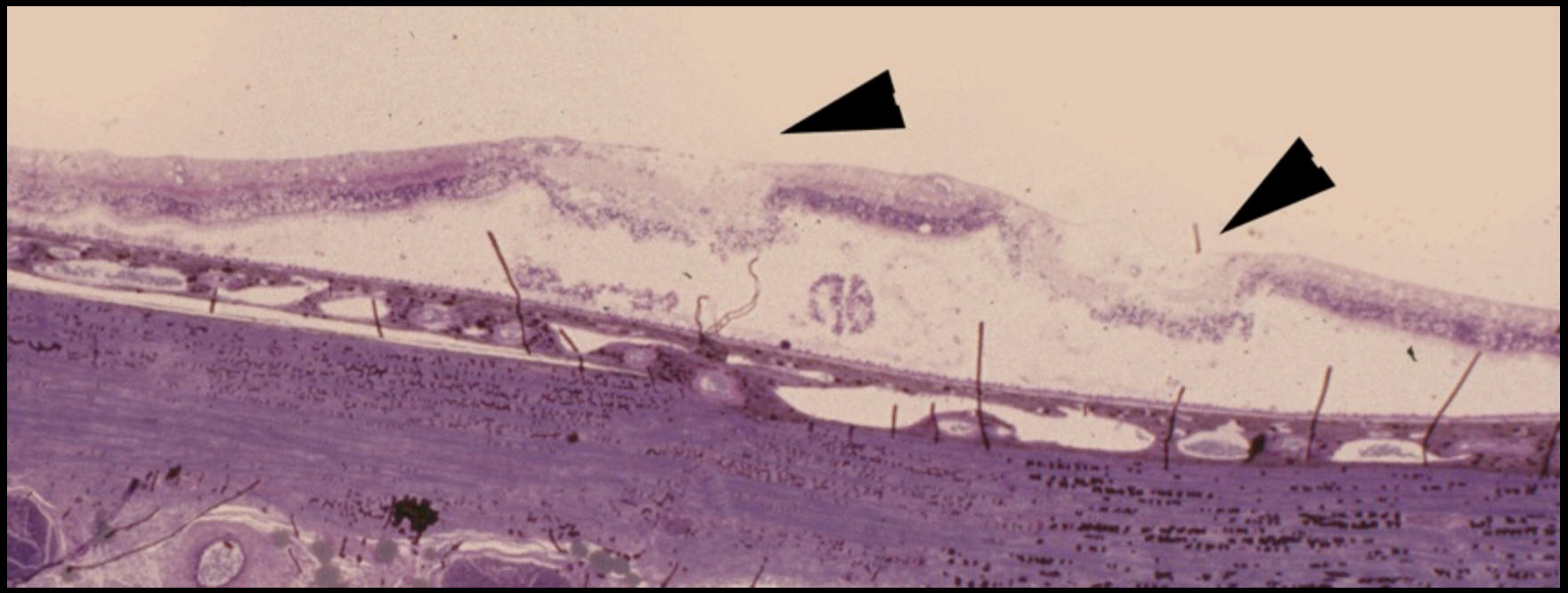


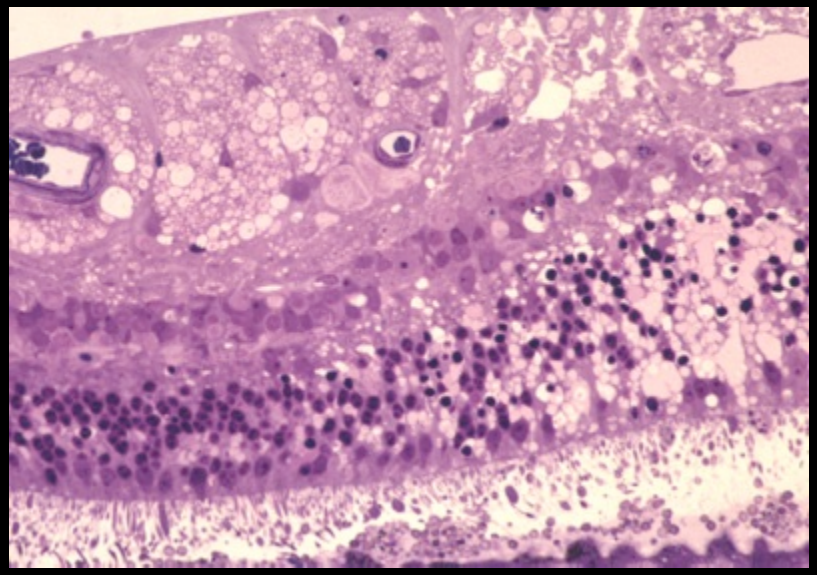
Kerry Ketring images

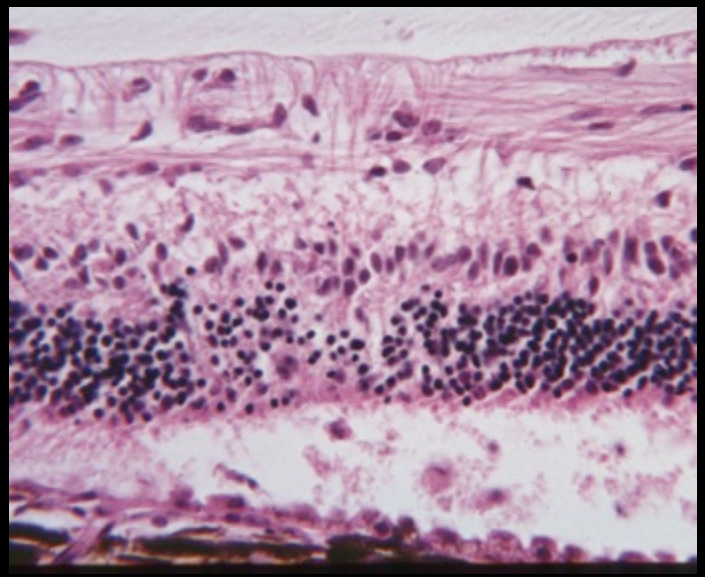
2 to 4 Day Glaucoma (Canine)

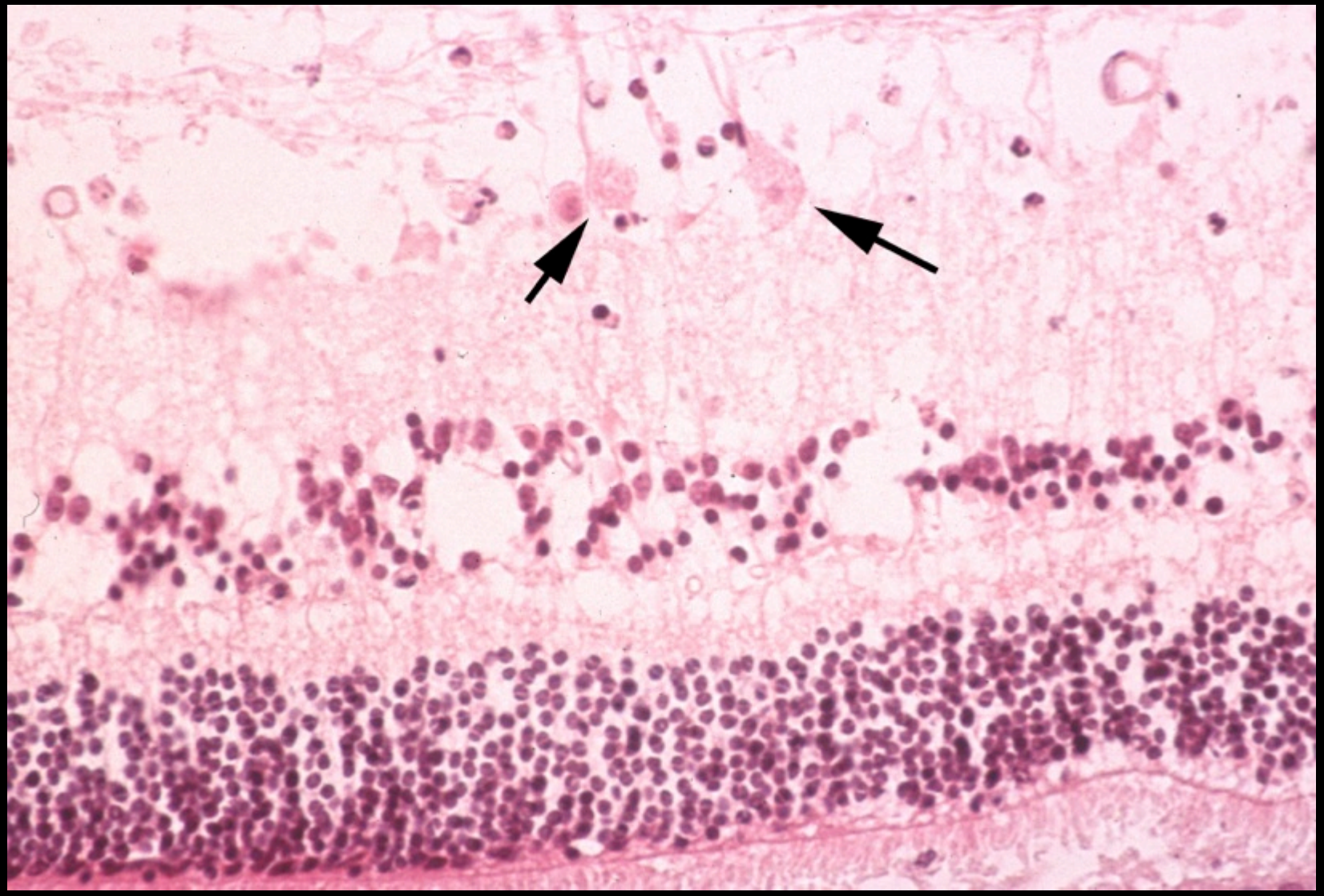
2 to 4 Day Glaucoma (Canine)



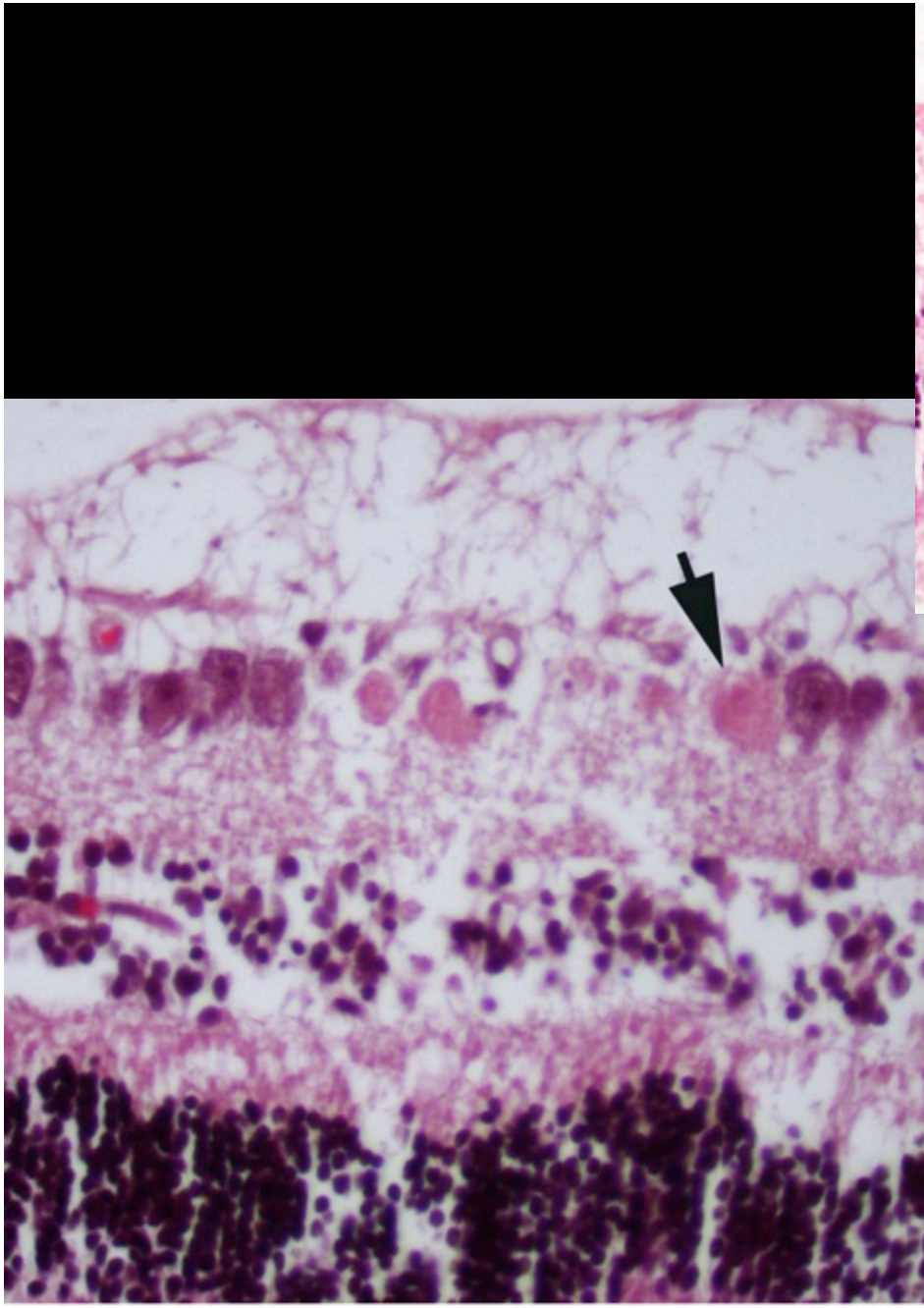




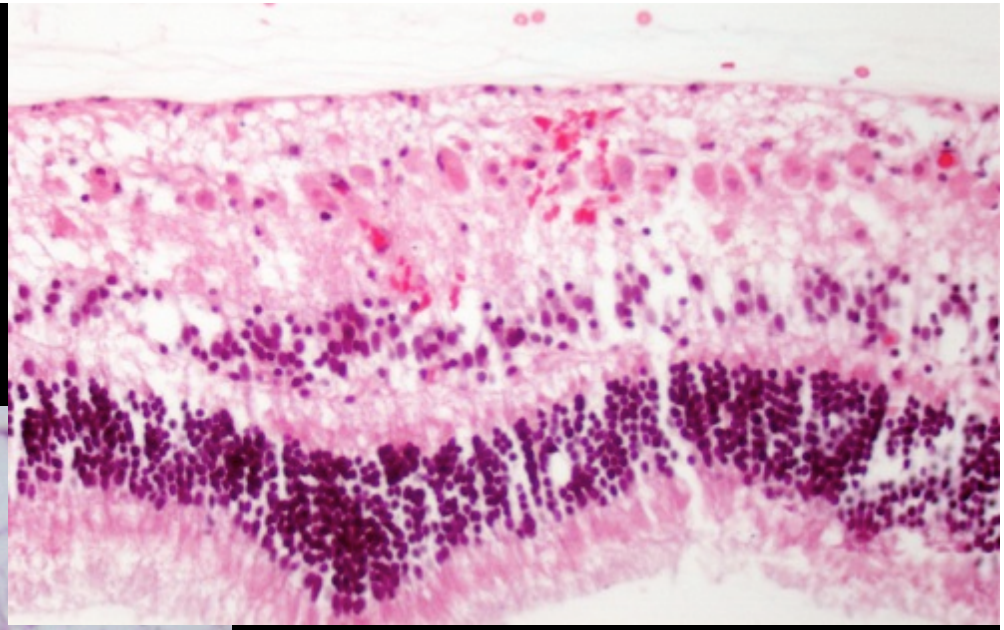




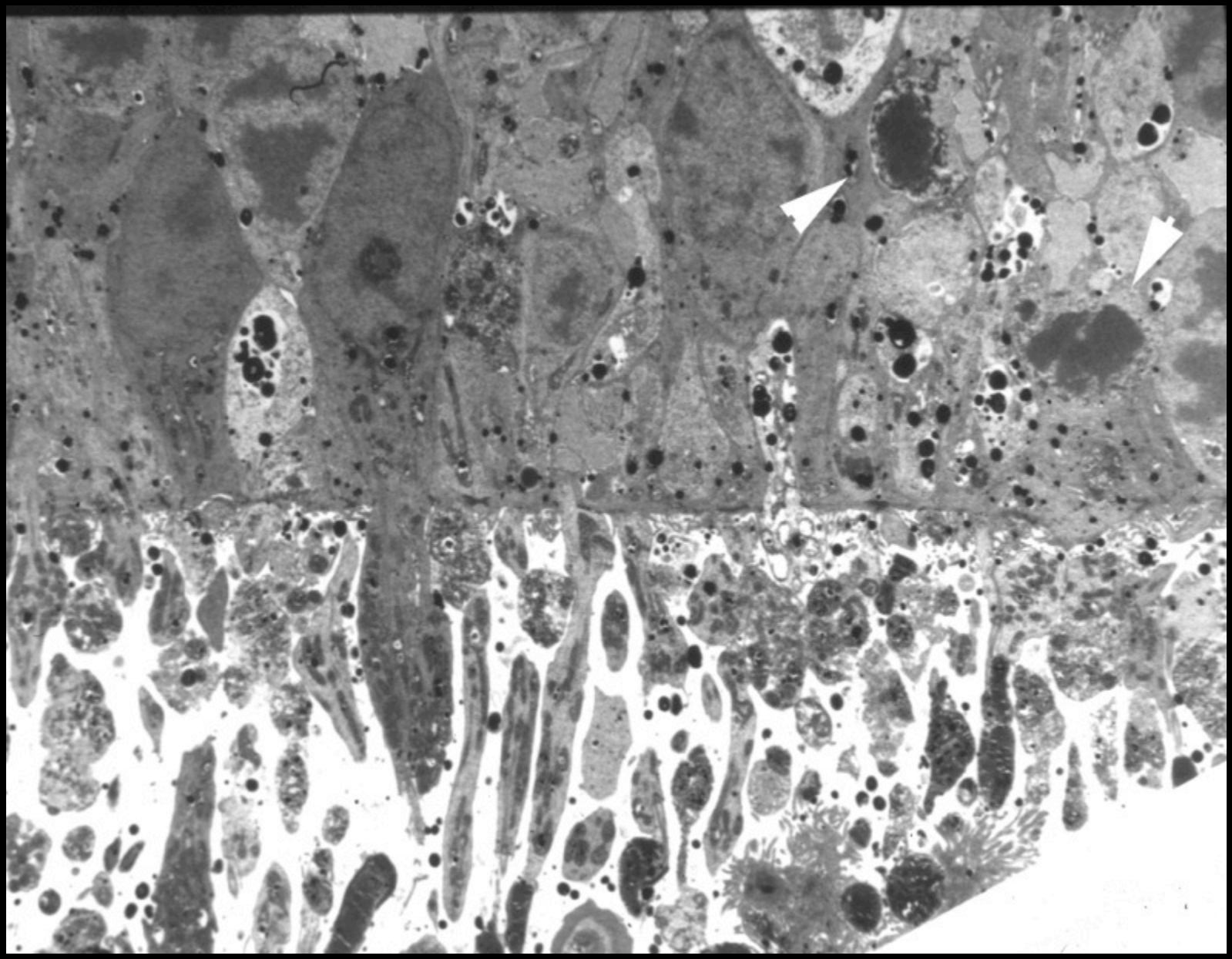
One Day Glaucoma
Red-Dead Ganglion Cells



Glaucoma 2 Days after Laser Ablasion of Melanocytoma



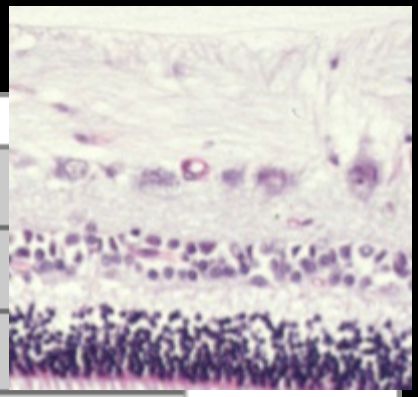
Proptosis, 3 days

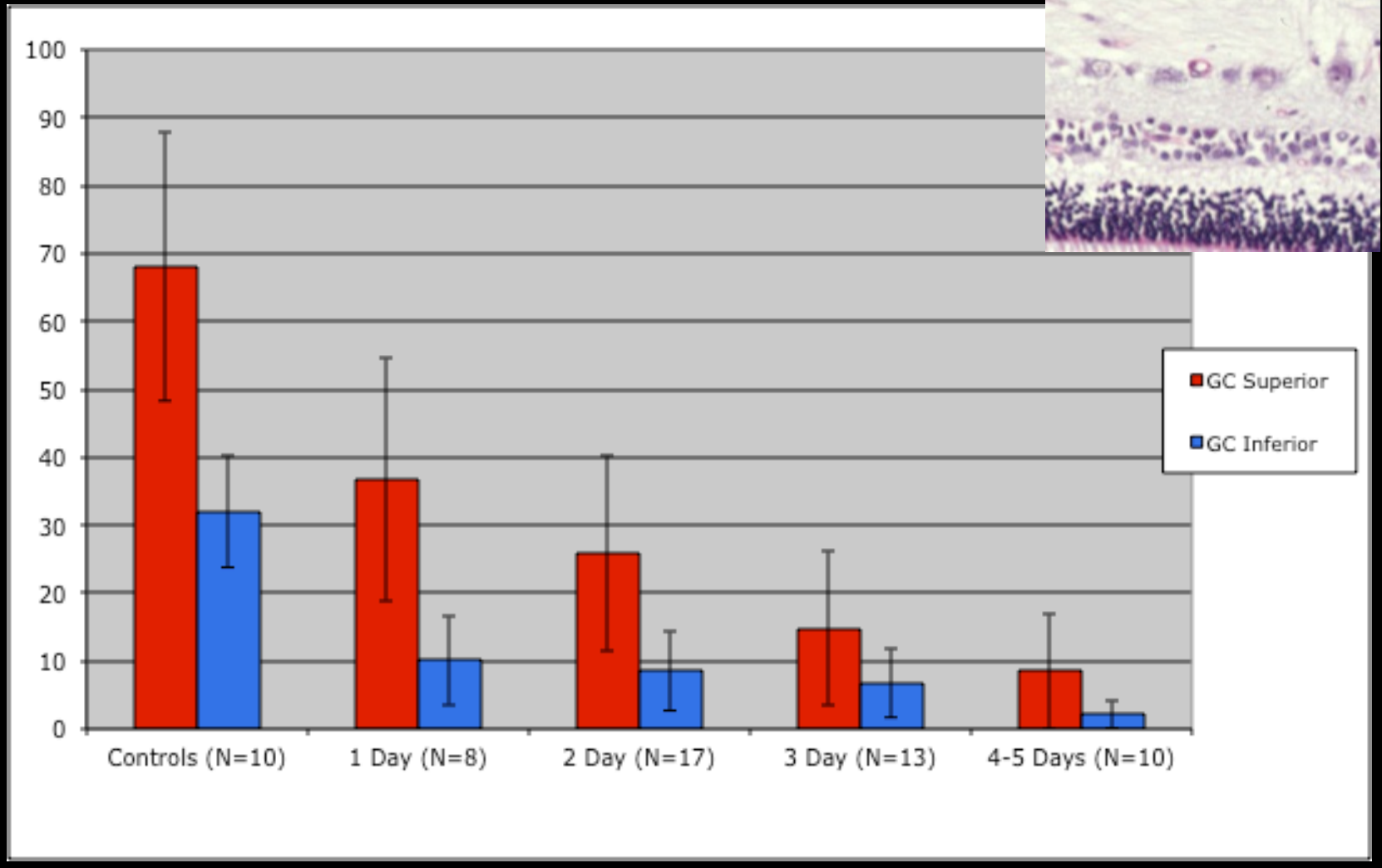


Electronmicrograph of 4-Day Glaucoma
Apoptosis

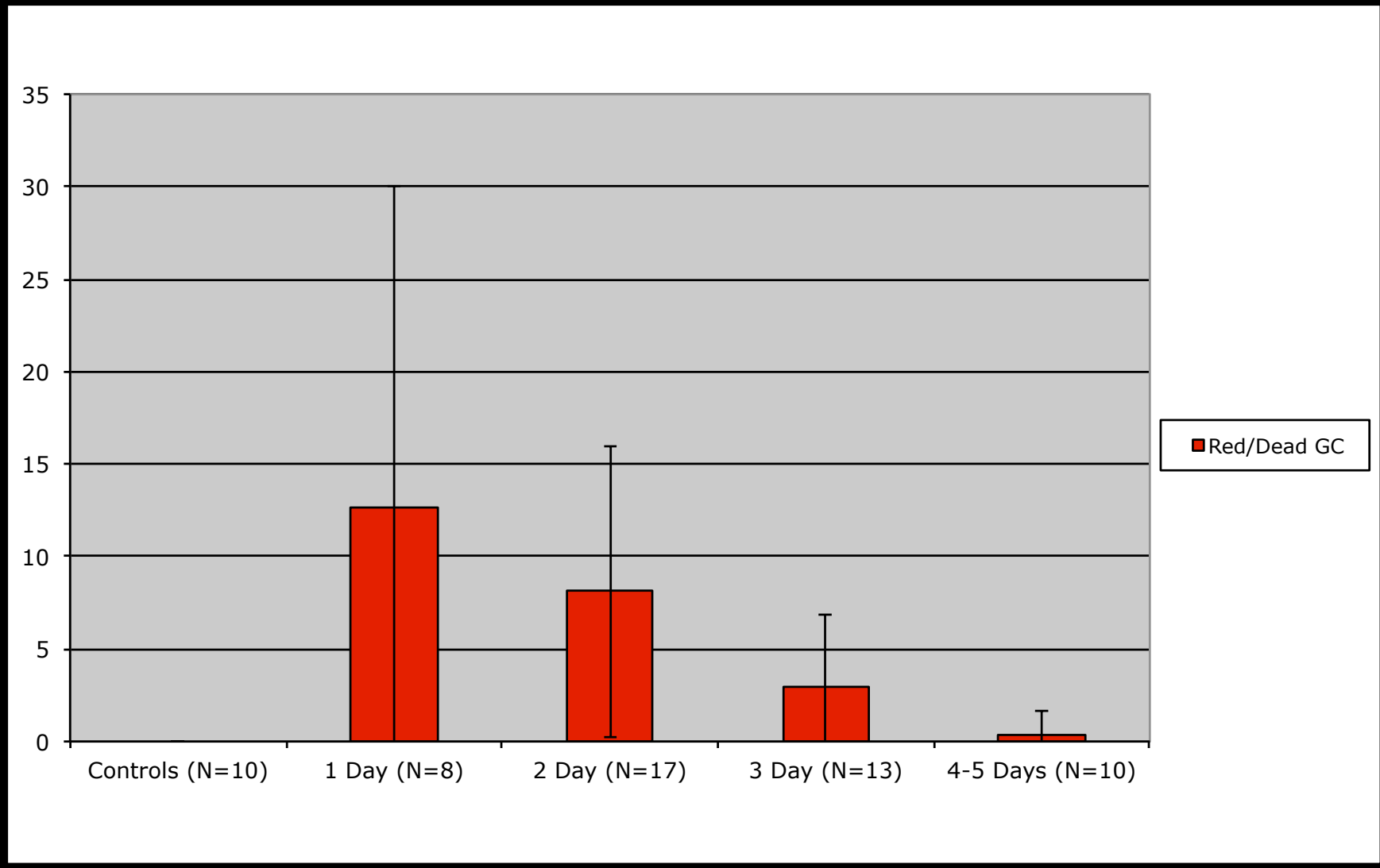
Average Ganglion Cell Counts

This count includes "Red Dead" cells

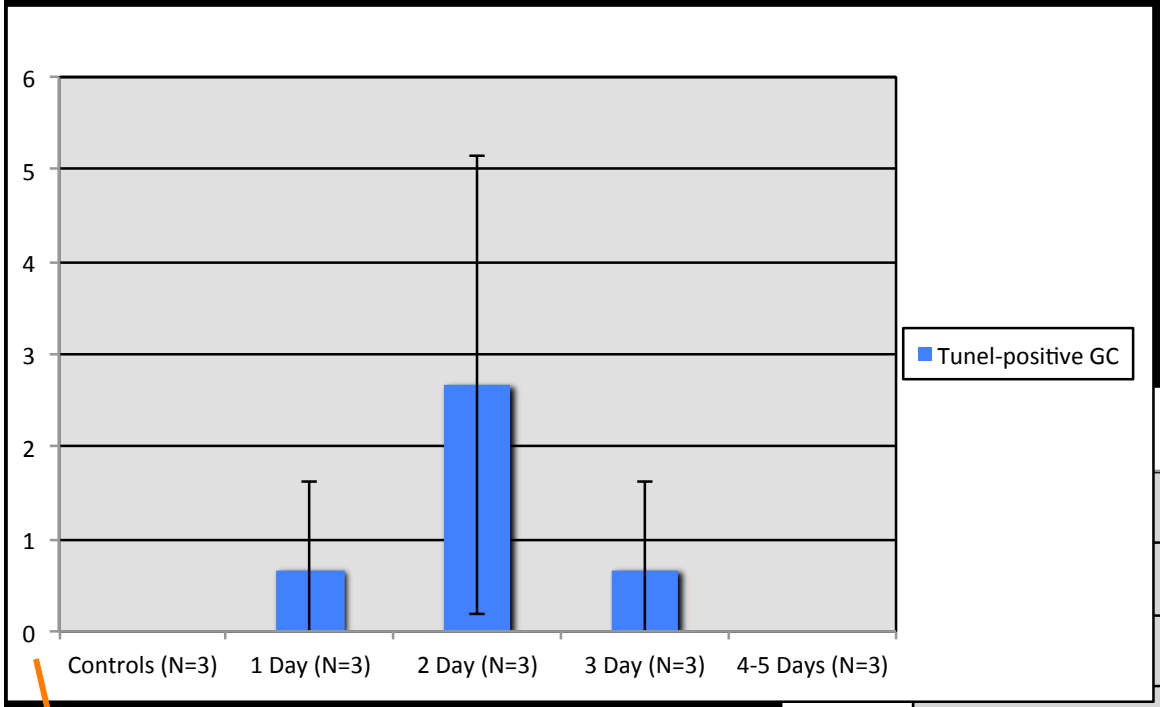




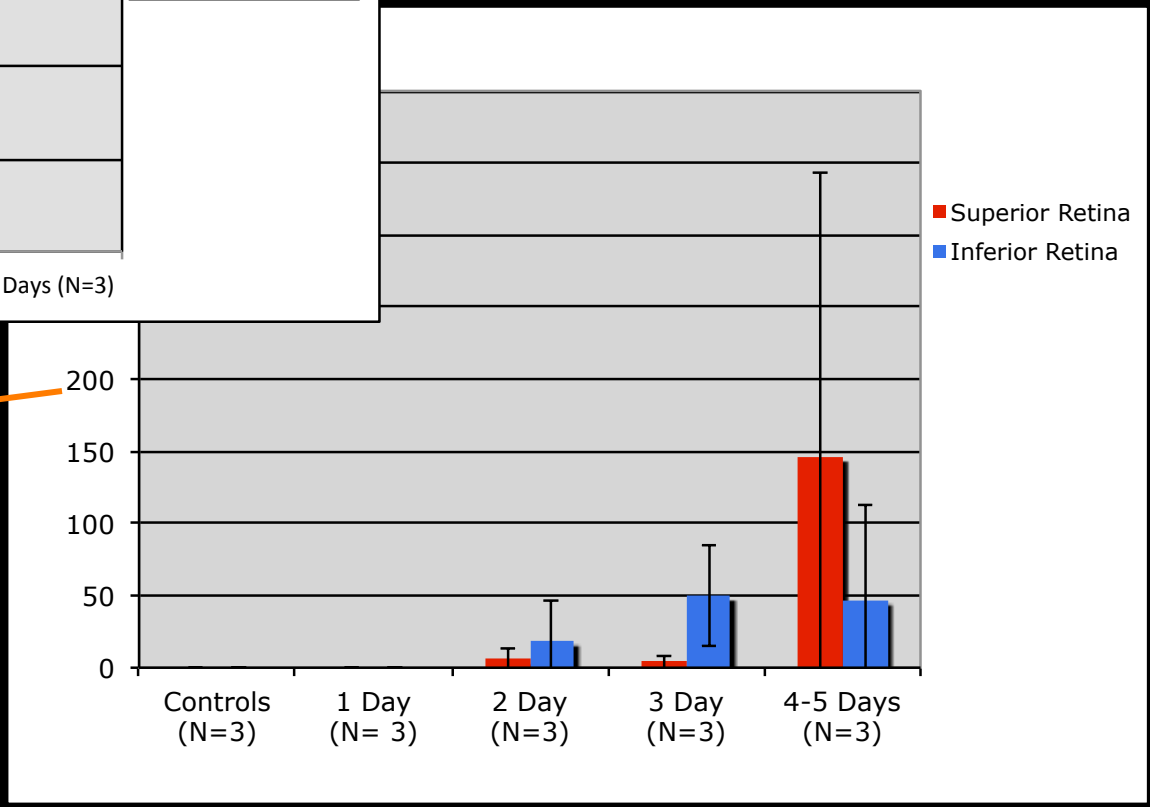
“Red Dead” Ganglion Cells



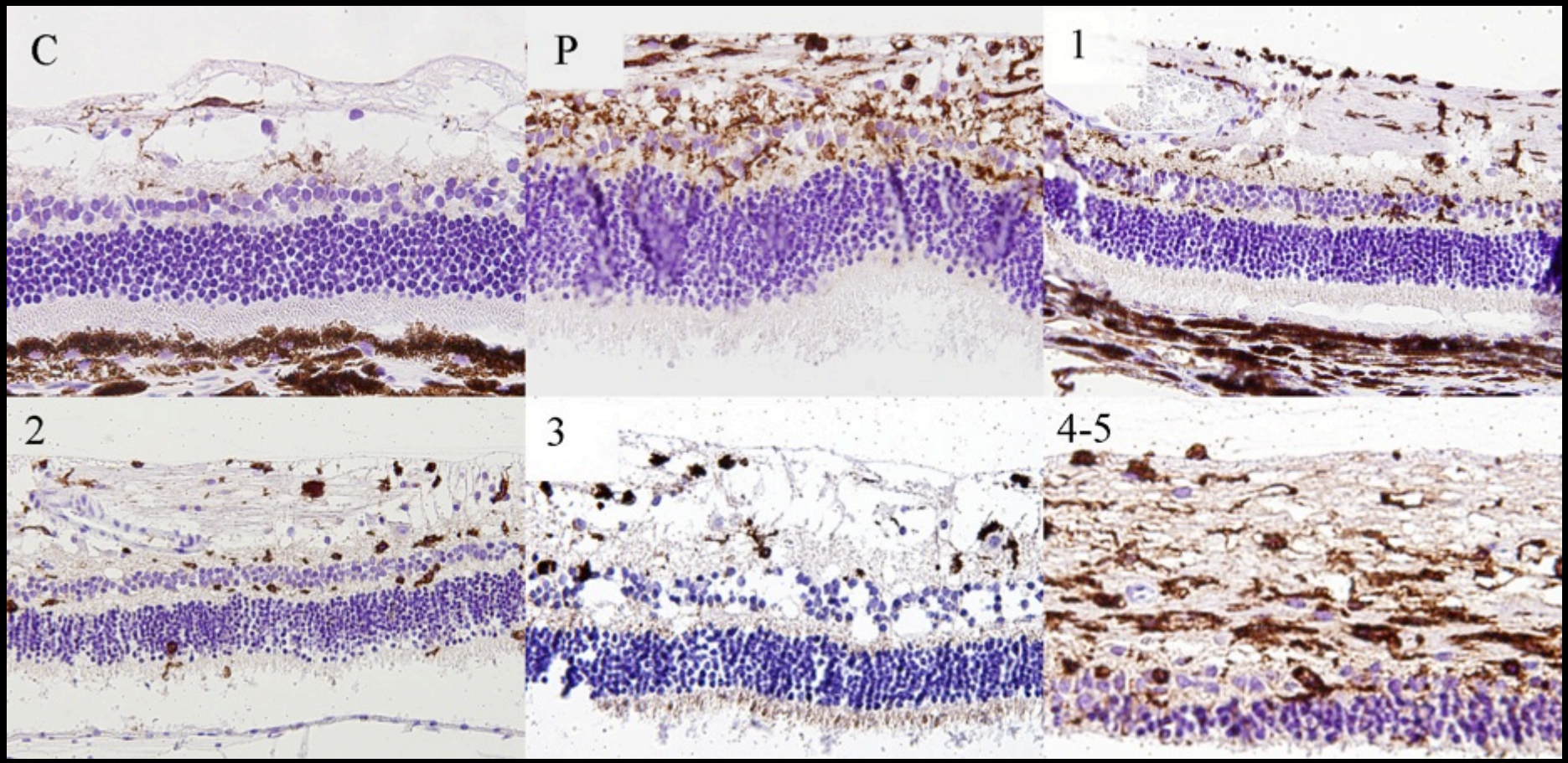
TUNEL + cells by day



Notice the scale change

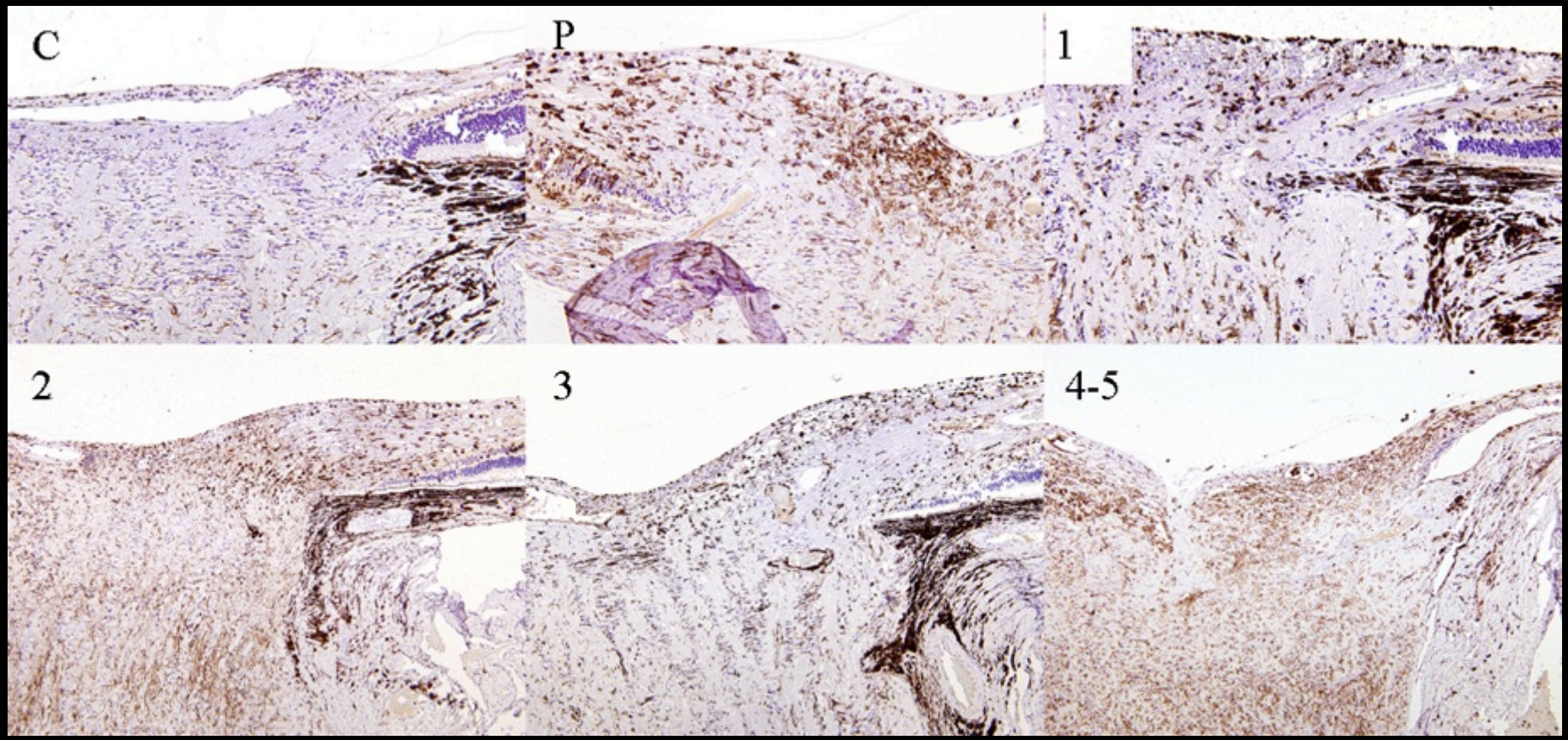


Retinal MHC-2 Phagocytes Retina

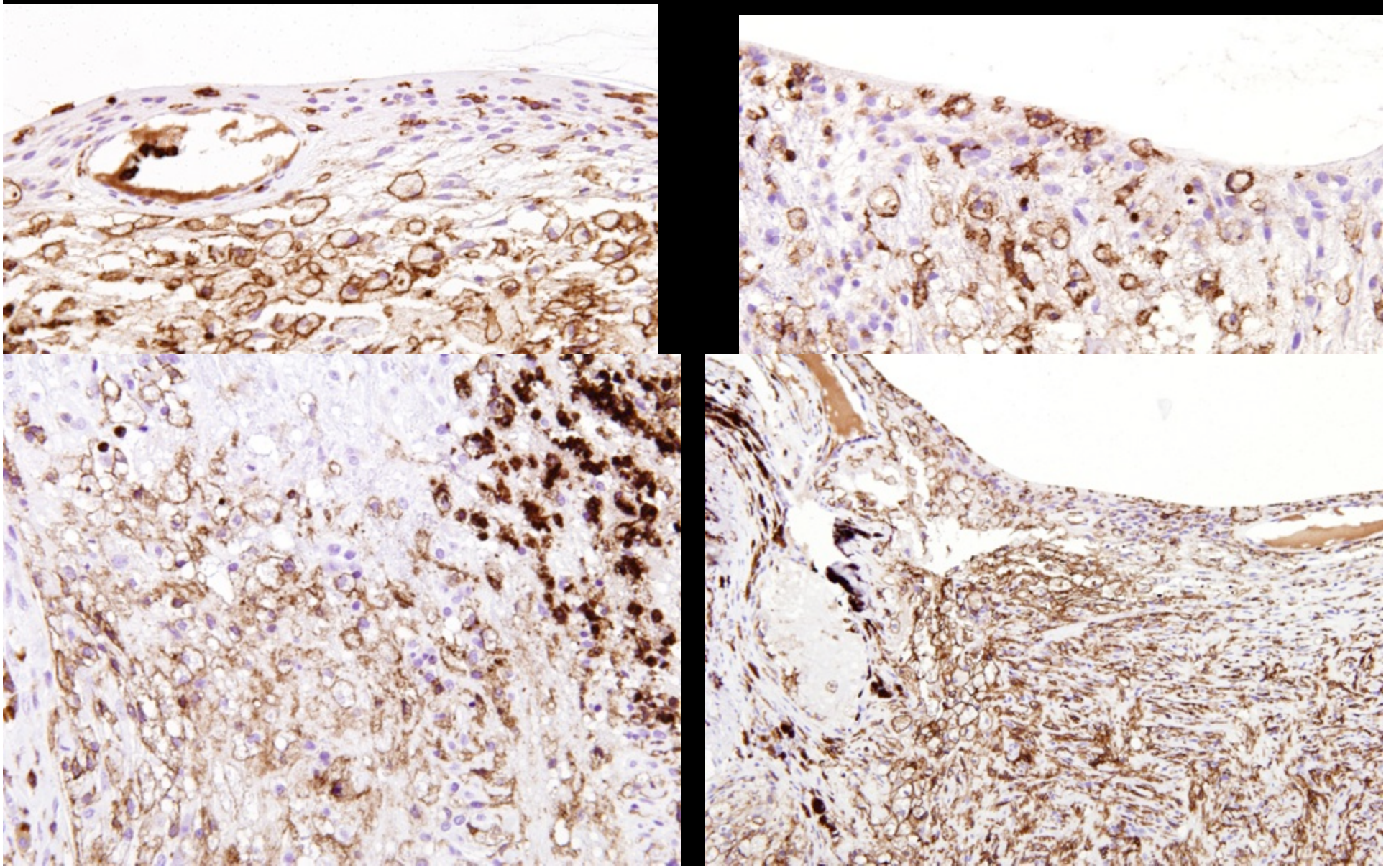


Phagocytic cells are the same at all time points

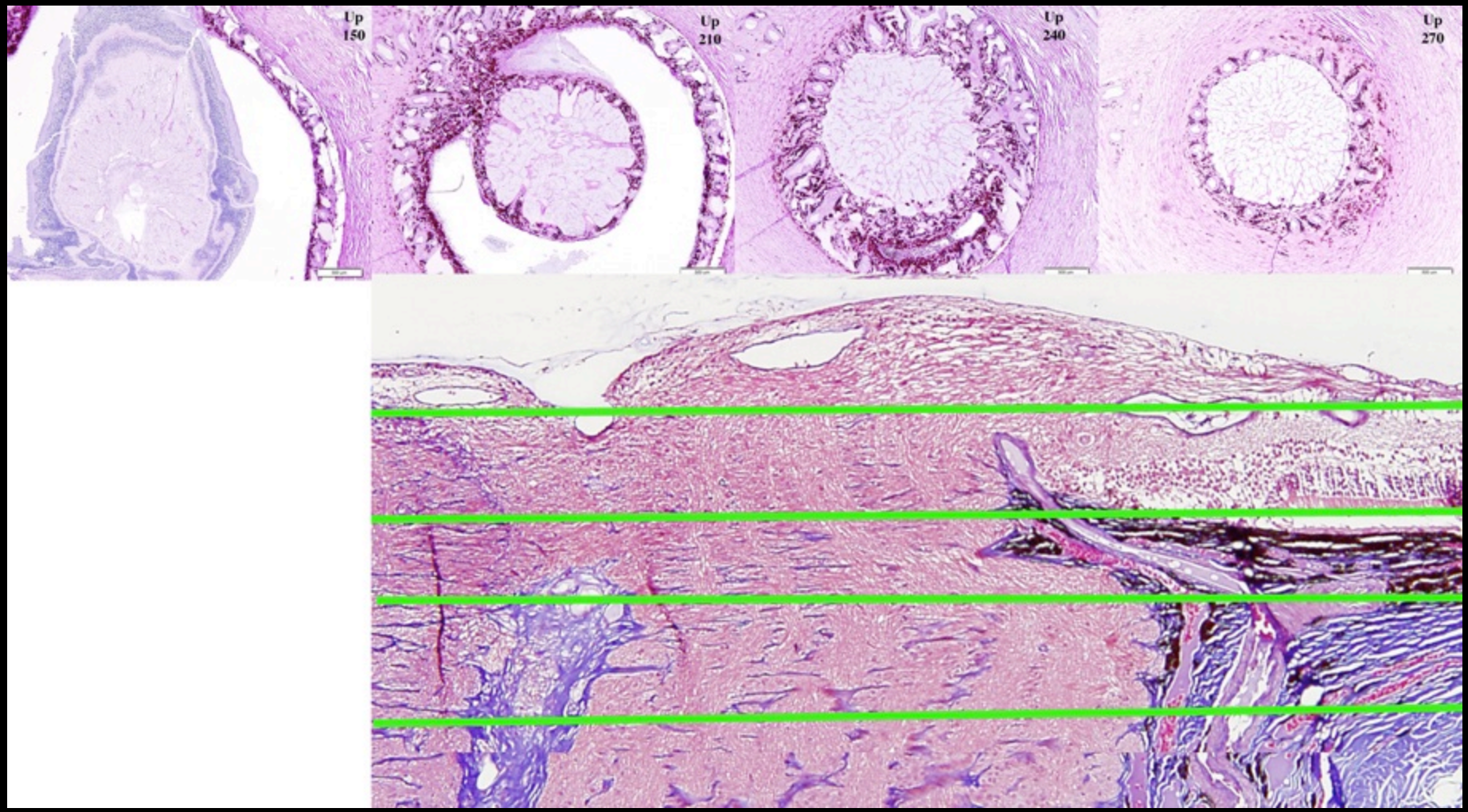
Optic Nerve MHC-2 Phagocytes Optic Disk



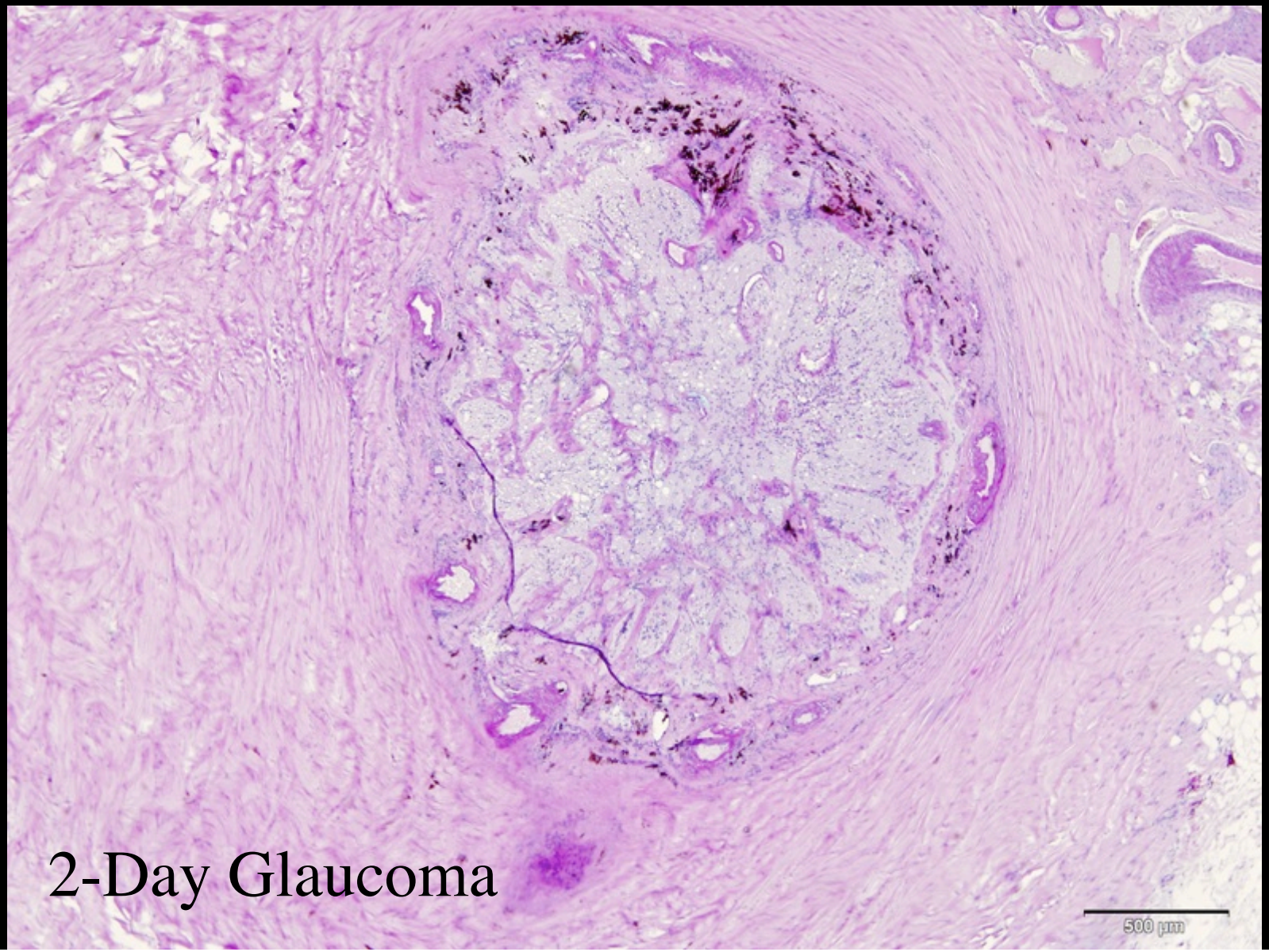
MHC-2 on 4-5 Day Glaucoma Optic Nerve



Why is Acute Canine Glaucoma an Ischemic?

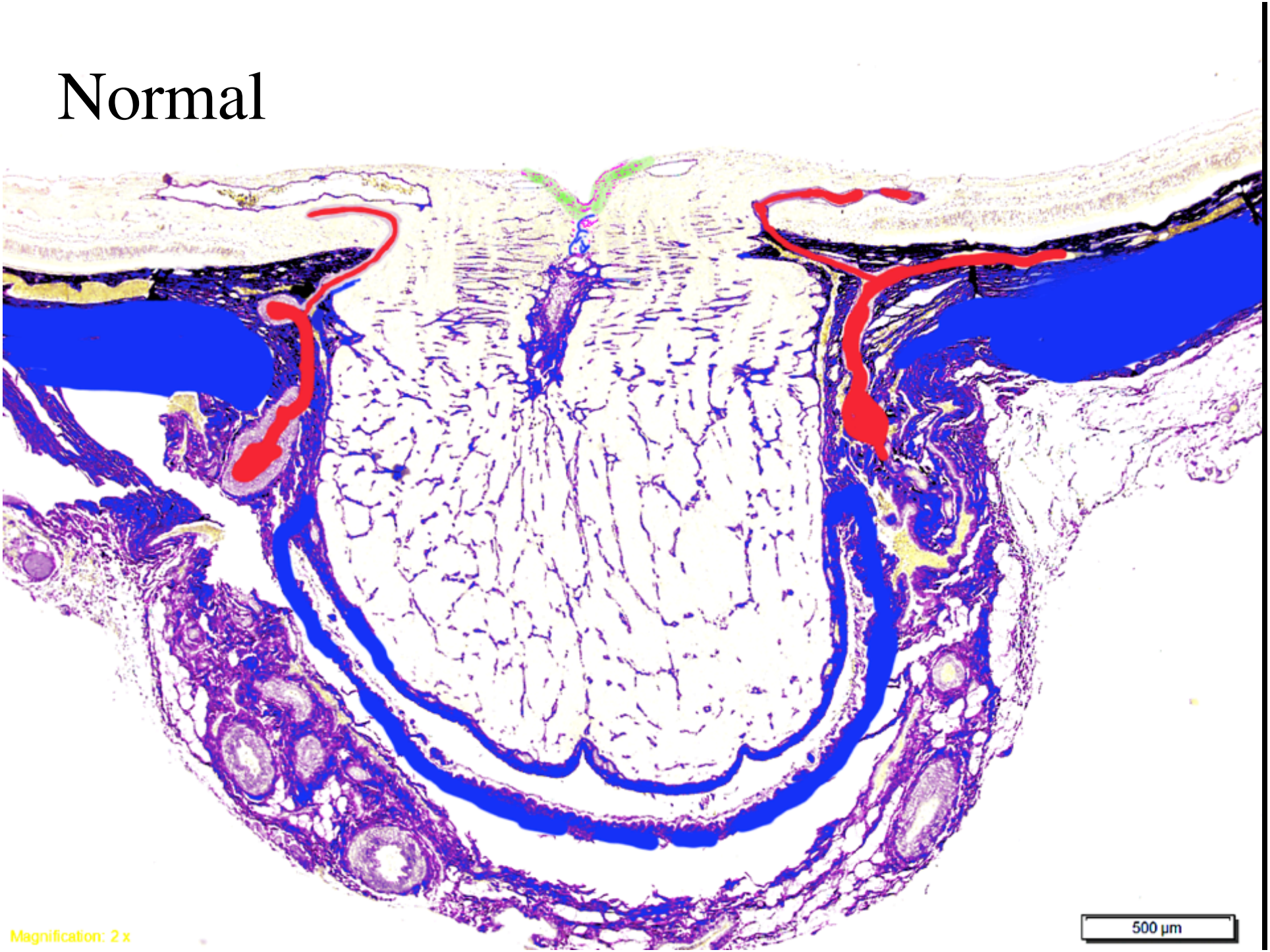


Why is Acute Canine Glaucoma an Ischemic?

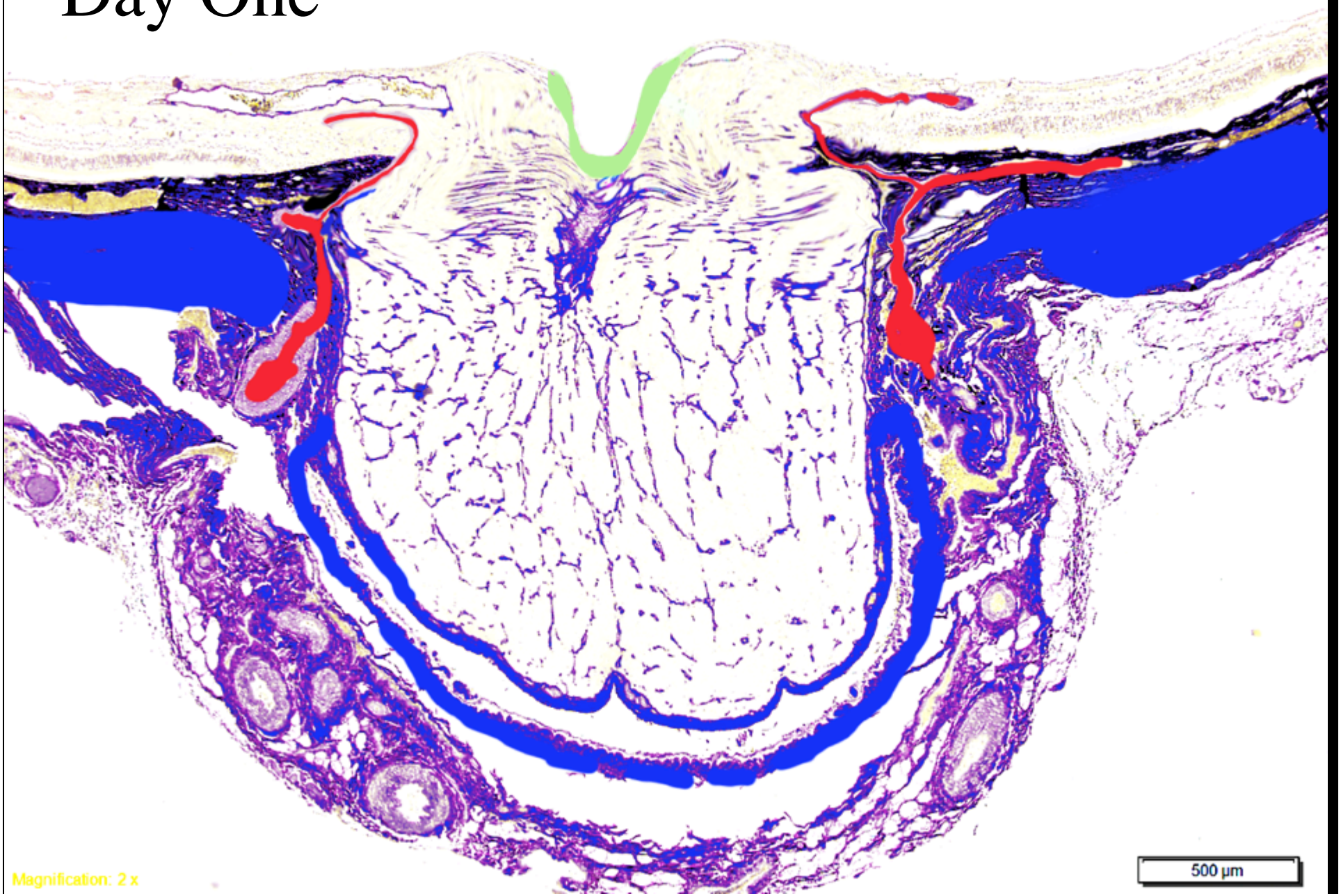


2-Day Glaucoma

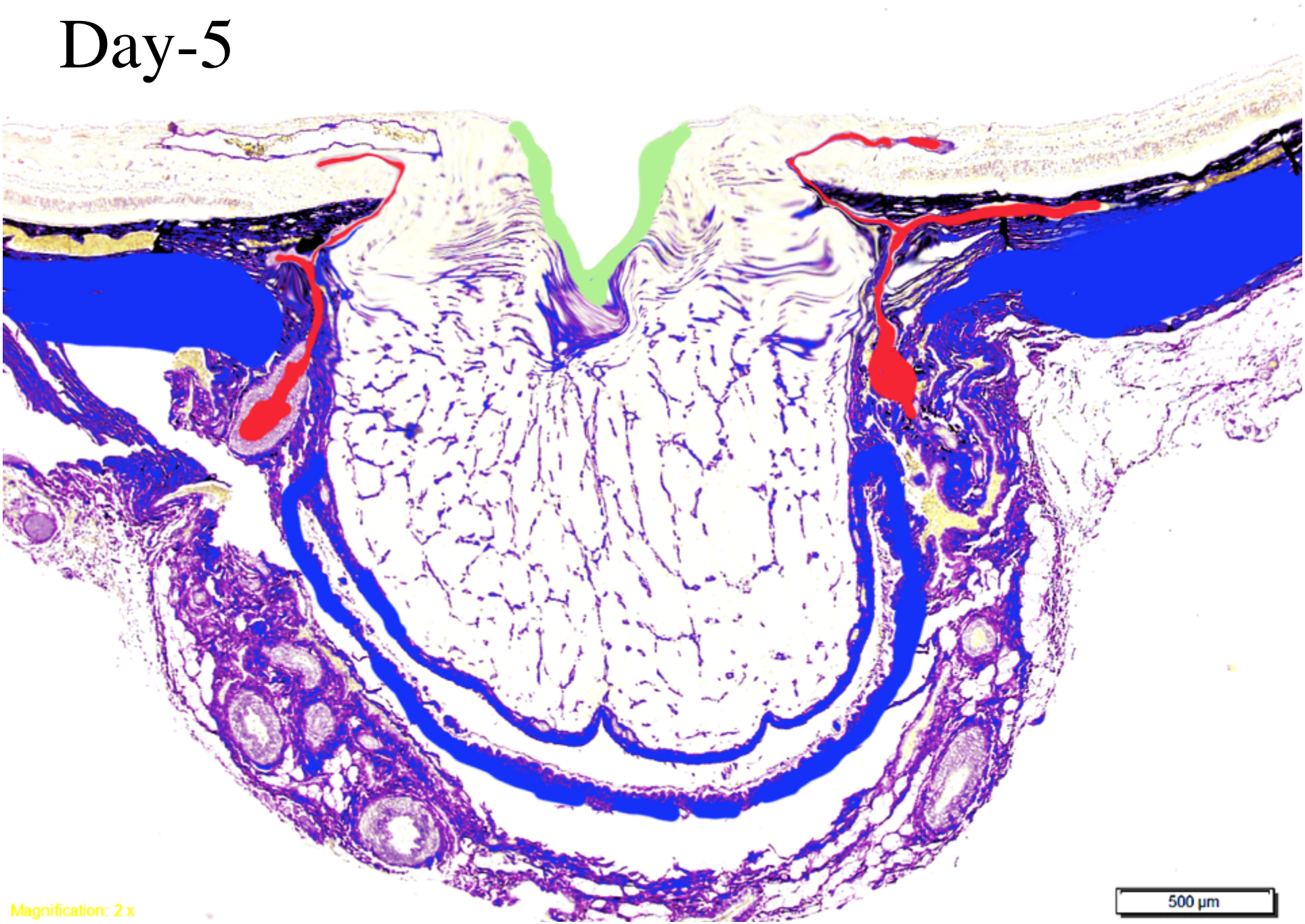
Normal



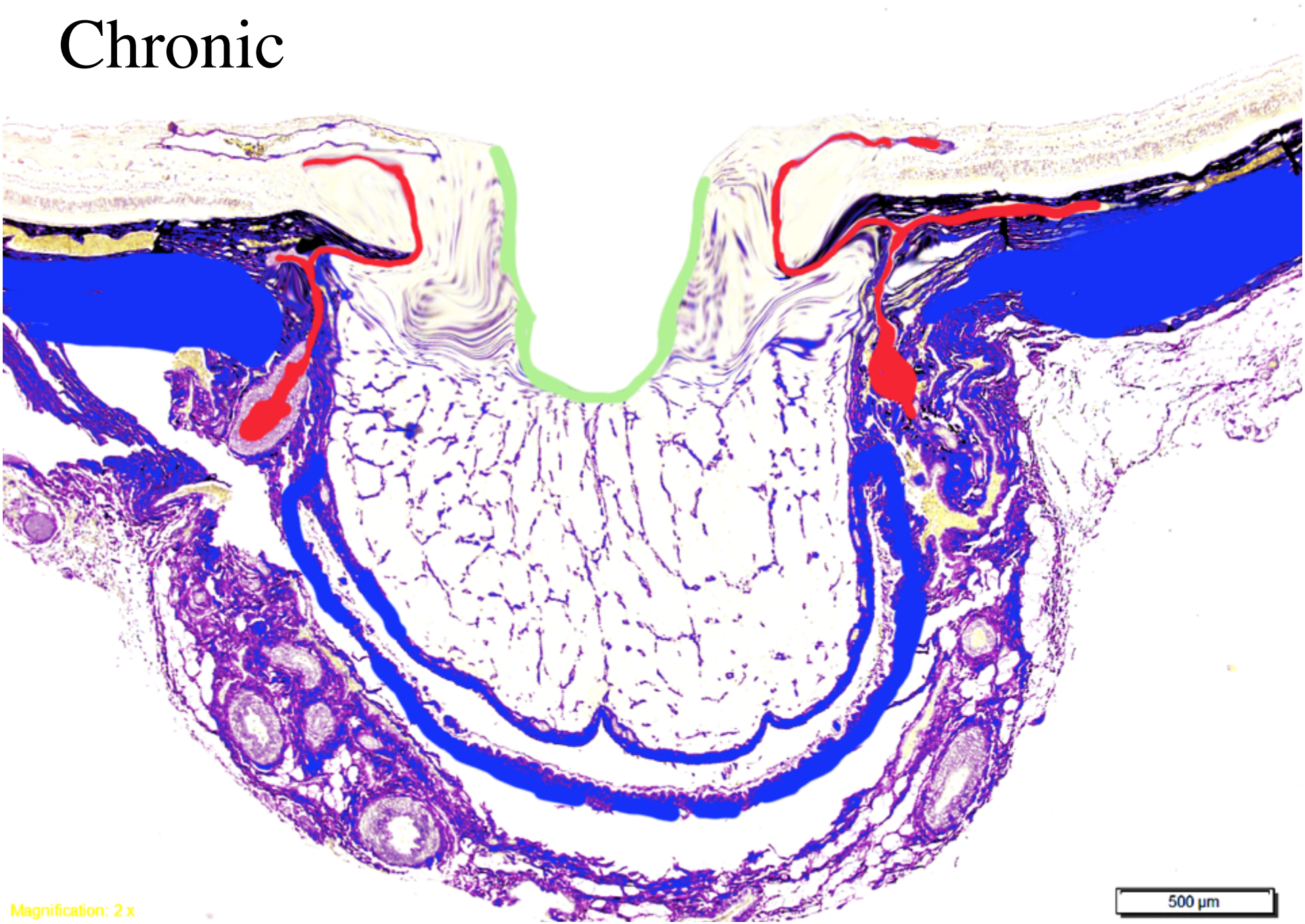
Day One



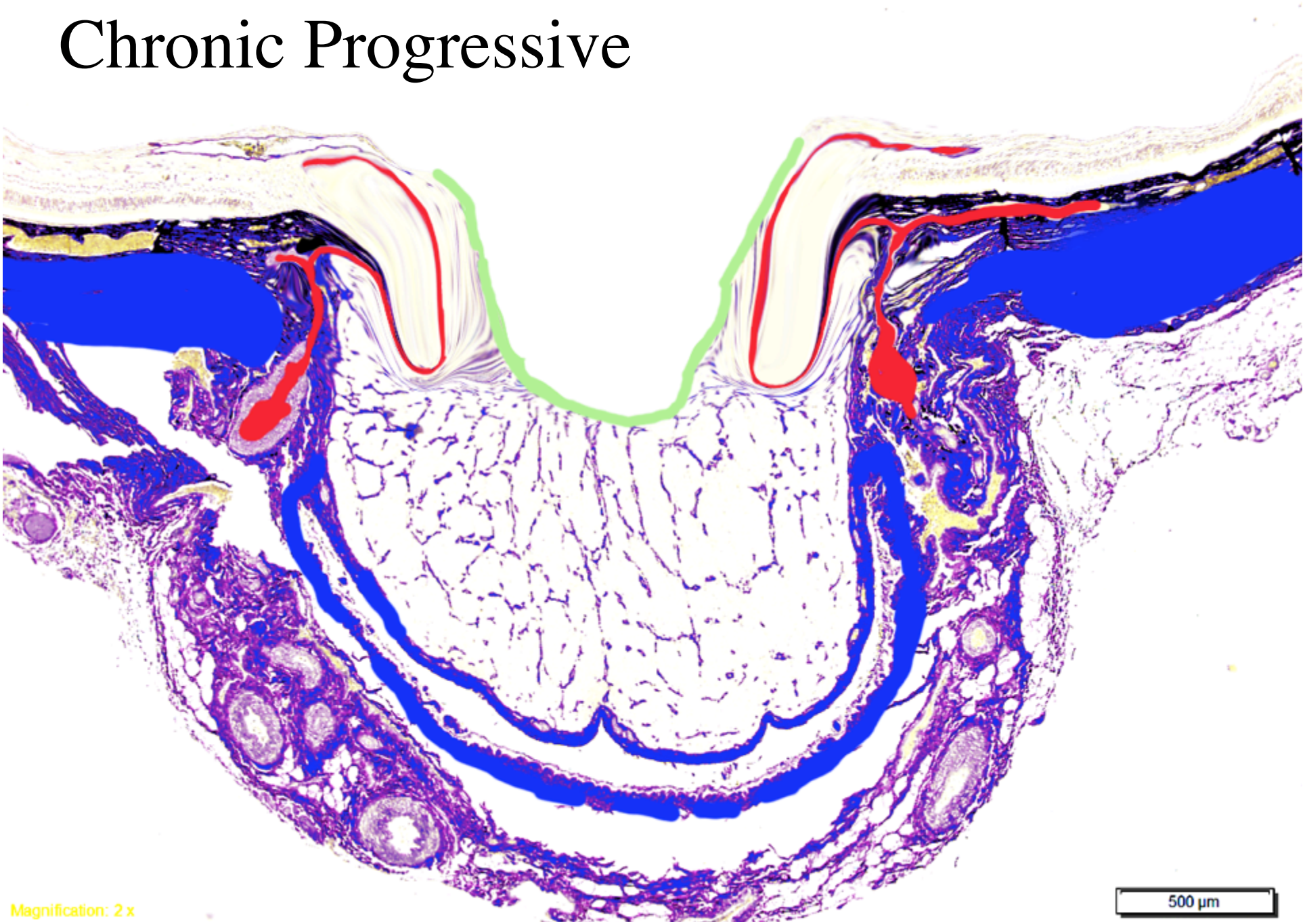
Day-5



Chronic



Chronic Progressive



Suggested Timeline

Before the Owner Detects Pain

1. Young normotensive dog with goniodysgenesis
    a) Ciliary cleft open at first
2. Gradual loss of ganglion cells
    a) Likely bouts of pressure spikes
    b) Pigment dispersion?
3. Gradual atrophy of the corneoscleral trabecular meshwork
4. Collapse of the ciliary cleft
    a) Detected with ultrasound biomicroscopy

Suggested Timeline

After the Owner Detects Pain

1. Sudden painful crisis
   a) Pathology suggests an event 2-3 days before owner detects
2. Stepwise rapid necrosis of the optic nerve and retina
   a) Neutrophils, dead ganglion cells, apoptosis, and finally phagocytosis
3. The second eye progresses through the same cycle