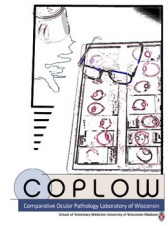
AAPSP
Australian Animal Pathology Standards Program

Davis-Thompson Foundation

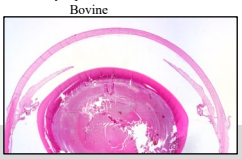
School of Veterinary Medicine
UNIVERSITY OF WISCONSIN-MADISON

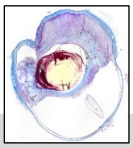
Veterinary Pathology Roadshow
2026

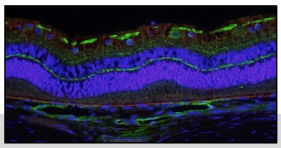


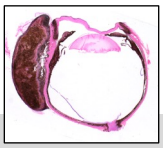
2. Congenital and Developmental Ocular Diseases

Arhinencephaly
Synophthalmos
Bovine









1

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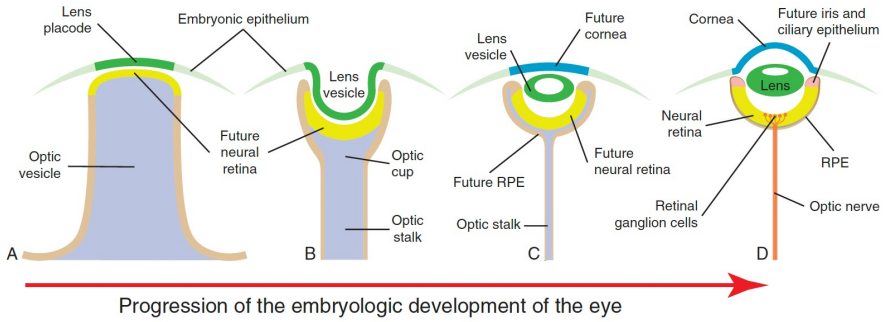
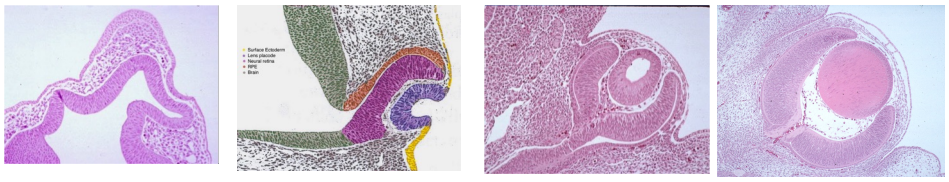
Congenital diseases are seldom submitted to a pathology service

- 2% of cases in the COPLOW collection
- Tends to be cases severe enough to warrant enucleation or euthanasia

2

Basics of Ocular Embryology





3

Congenital ocular malformations in dogs and cats: 123 cases

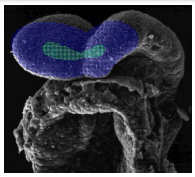
Veterinary Ophthalmology. 2020;23:964–978.

Inês Q. Saraiva | **Esmeralda Delgado**

- Incidence: 0.3% in dogs and 0.1% in cats
- Most common breed:
  - Mixed & French Bulldog for dogs & DSH for cats
  - Ocular dermoids & French Bulldog breed significantly associated (12/16)
- Median age of diagnosis:
  - 12 months for dogs and 6 months for cats
- Most frequently identified abnormalities:
  - Congenital cataract (dogs: 31.1%; cats: 30.0%)
  - Microphthalmia (dogs: 35.0%, cats: 25.0%)
  - Persistent pupillary membrane (dogs: 27.2%, cats: 40.0%)

4

Cyclopia & Synophthalmia



- Cyclopia
  - Formation of a single median globe
- Synophthalmia
  - Two incompletely separated or fused globes
- Concurrent severe craniofacial defects

Cyclopia

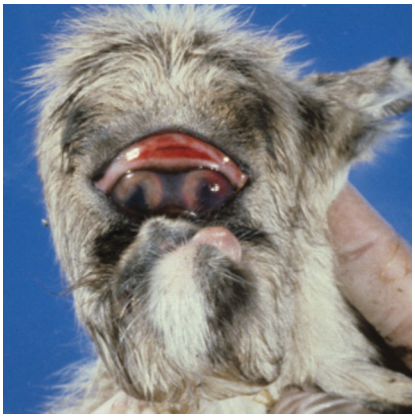
Synophthalmia

5

Cyclopia & Synophthalmia

Western False Hellebore or Corne Lily

- *Veratrum californicum*
  - Sheep:
    - Ingestion by pregnant ewe on **day 14** of gestation
- Steroidal alkaloids
  - Cyclopamine and jervine
  - Inhibit sonic hedgehog signal transduction during gastrulation
- Affects midline neural plate

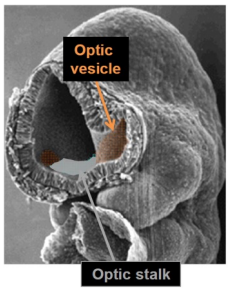


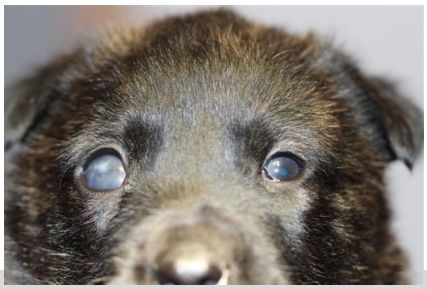
Arhinencephaly / Synophthalmos

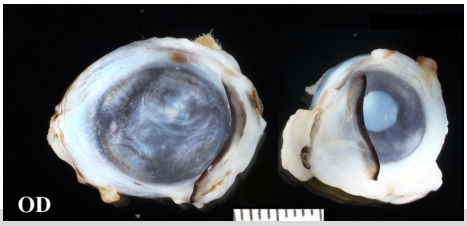
6

Microphthalmia

- Improper optic vesicle formation
  - Corresponding small palpebral fissure
- Failure of normal optic cup growth
  - Failure of fusion of the choroid fissure → colobomas
- Failure to establish normal IOP







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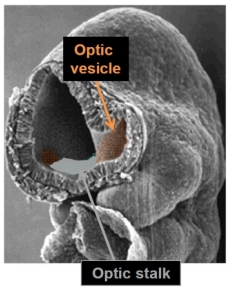
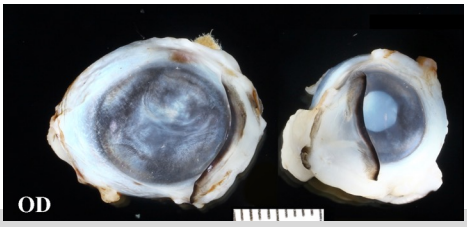
Microphthalmia

- Associated with many of ocular defects
  - ASD
  - PHPV
  - Cataract
  - Retinal dysplasia
  - Colobomas
    - Merle ocular dysgenesis





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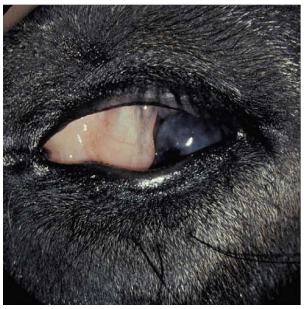
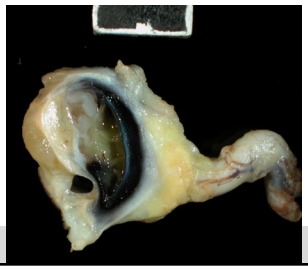
Microphthalmia in foals

- Sporadically seen,
- Foal otherwise normal
- Thoroughbred overrepresented
- Bilateral but not symmetrical involvement
- Not inherited
- Nonophthalmos – Microphthalmos
- Similar condition seen in deer fawns





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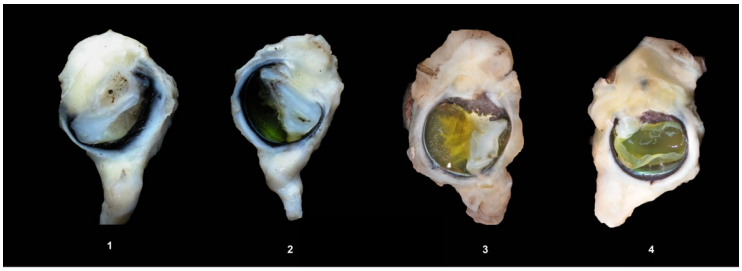
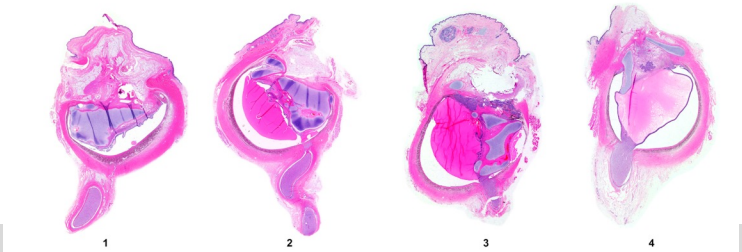
Equine Microphthalmia





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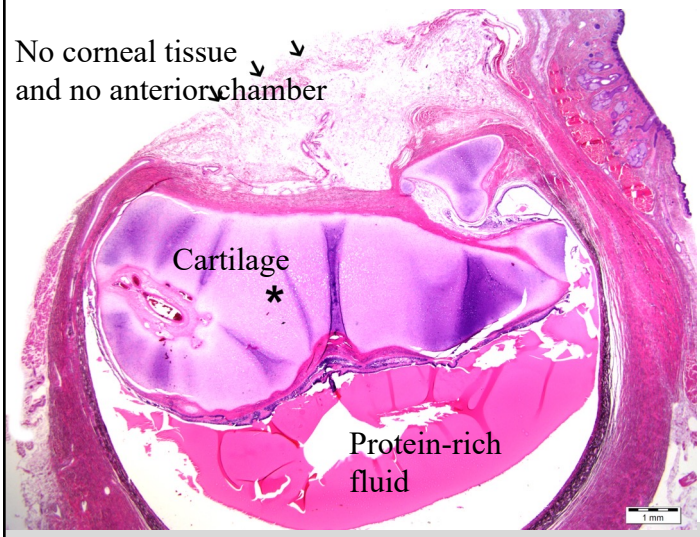
Equine Microphthalmia



Dermoid

No lens

Detached and
dysplastic retina

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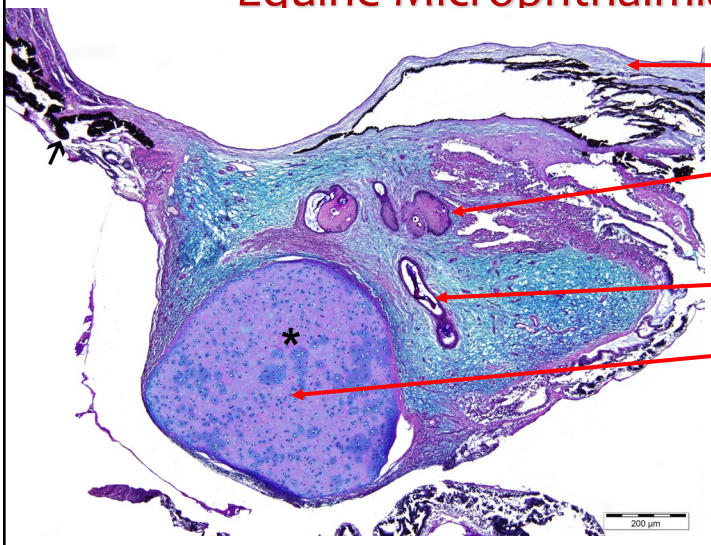
Equine Microphthalmia



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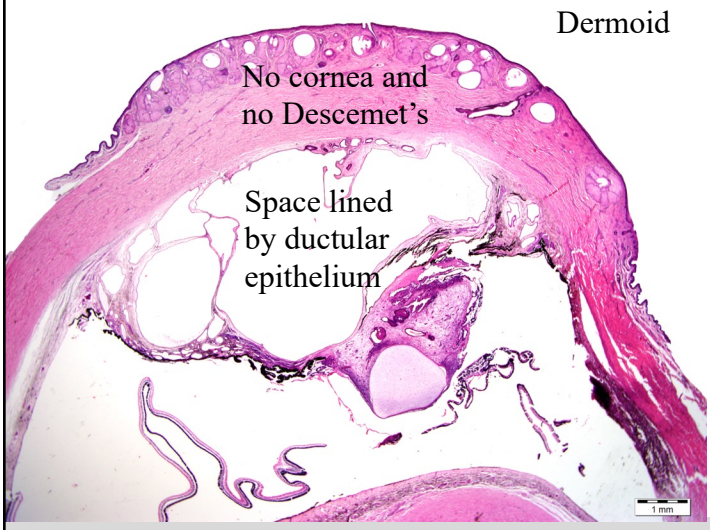
Equine Microphthalmia



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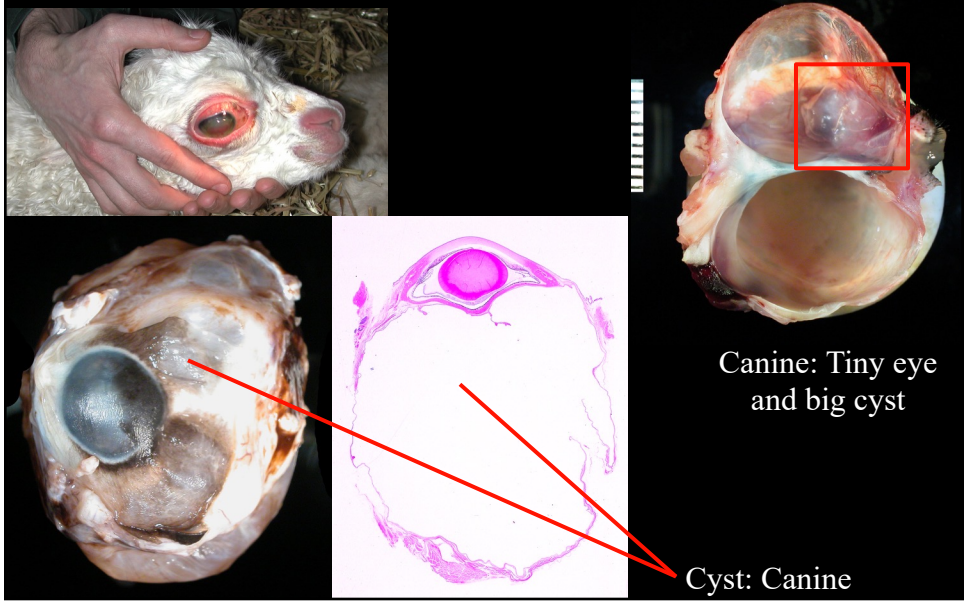
Microphthalmos with Cyst



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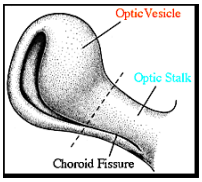
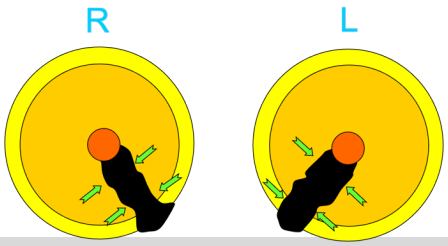
Coloboma



- "Defect"
- Failure of fusion of the choroid fissure
  - "Typical colobomas" at the 6 o'clock position
- Abnormal differentiation of the outer optic cup
  - "Atypical colobomas" at other location



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Typical Coloboma

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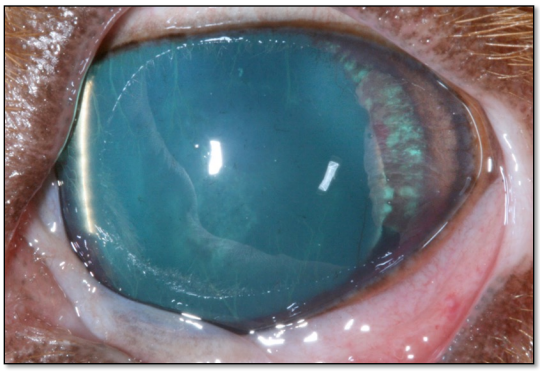
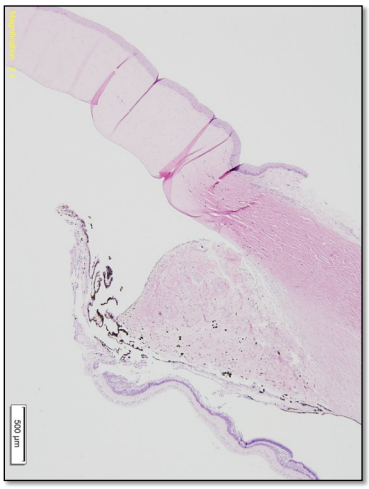
Aniridia

Alpaca





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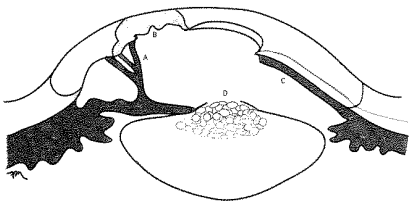
Anterior Segment Dysgenesis

- Persistent keratolenticular attachment
- Classic example: Peter's anomaly
- Corneal opacity with stromal & DM defects (B)
- Persistent pupillary membrane (A)
- Iris hypoplasia (C)
- Anterior polar cataract (D)



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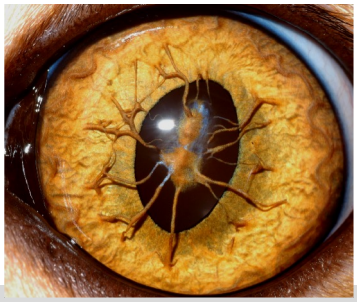
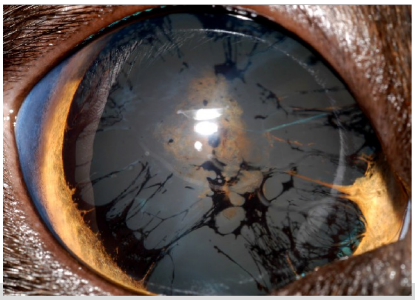
Anterior Segment Dysgenesis
Persistent Pupillary membrane

- Failure of the pupillary membrane to regress
- Strands arise from iris collarette
  - DDx: Synechiae arise from pupillary marginIris hypoplasia

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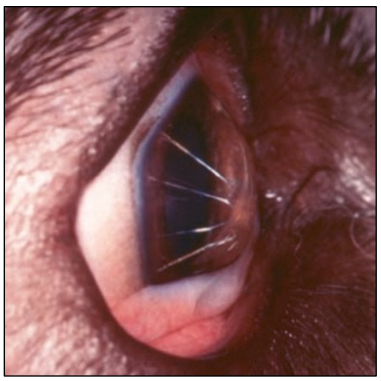
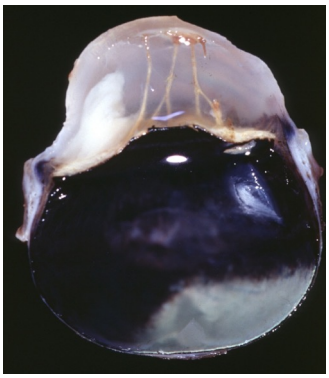
Anterior Segment Dysgenesis
Persistent Pupillary membrane

- Usually insignificant, may cause focal cataract or corneal opacity where PPM contacts the lens or cornea

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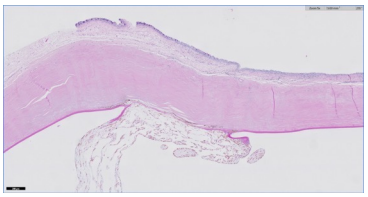
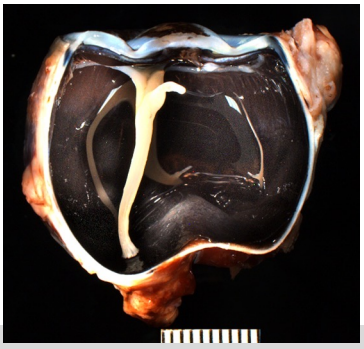
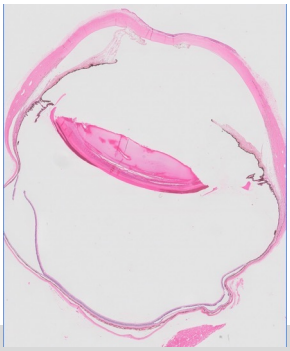
Anterior Segment Dysgenesis

Peter's anomaly

- Usually insignificant, may cause focal cataract or corneal opacity where PPM contacts the lens or cornea







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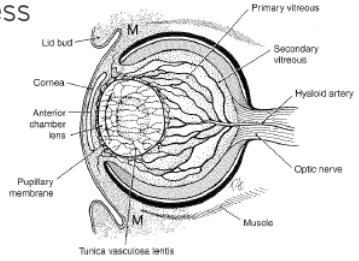
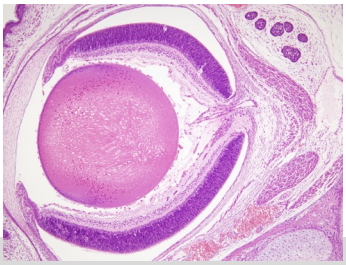
Persistent Fetal vasculature

- Failure of the fetal vasculature to regress
- Persistent Hyaloid Artery
- PHPV/PTVL
- Potential concurrent anomalies
  - Microphthalmia
  - Microphakia
  - Cataract
  - Retinal dysplasia
- Inherited trait
  - Doberman
  - Staffordshire Bull Terrier





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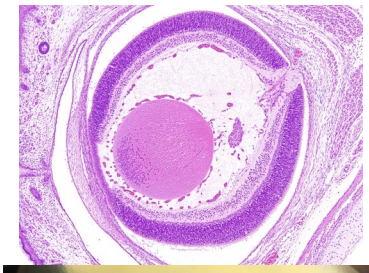
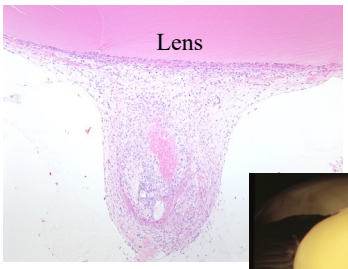
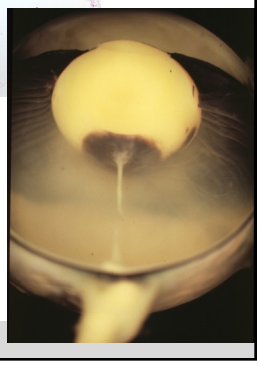
Persistent Fetal vasculature

Persistent Hyperplastic Primary Vitreous - PHPV







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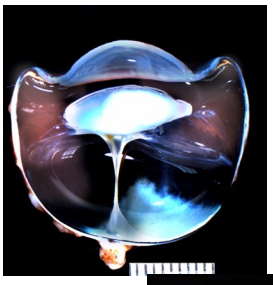
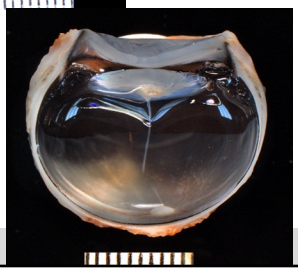
Persistent Fetal vasculature

Persistent Hyperplastic Primary Vitreous - PHPV





- First abnormalities gestation (30–33 days)
- Abnormalities centered on the vitreous +/- retro-lental vascular system, and anterior tunica vasculosa lentis
- Moderate to severe cases:
  - Cartilage
  - Pigmented tissue
  - Nests of glial tissue

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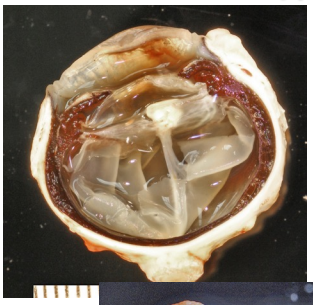
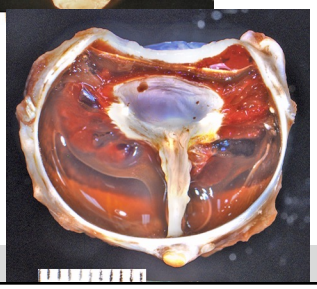
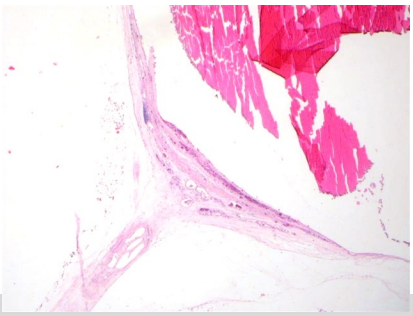
Persistent Fetal vasculature

Persistent Hyperplastic Primary Vitreous - PHPV





- Posterior lenticonus,
- Cataract
- Posterior lens capsule defect
- Intralenticular hemorrhage



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Others

- Dermoid
- Eyelid Agenesis
- Lens
  - Congenital cataract
  - Microphakia
- Retinal Dysplasia
- Optic nerve hypoplasia/ aplasia

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Defined "Syndromes"

- Collie Eye Anomaly (CEA)
- Merle Ocular Dysgenesis (MOD)
- Oculoskeletal dysplasia
- Microphthalmia in Portuguese Water Dogs
- Equine multiple congenital ocular anomalies (MCOA)
- Multiple ocular defects in Japanese Black Cattle

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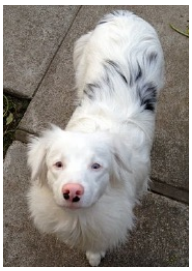
Merle Ocular Dysgenesis (MOD)

- Merle gene
  - Mottled color patches within a solid coat
  - SINE insertion into SILV (formerly PMEL17)
  - Genetic test (IDEXX)
  - Double merles (mm)
    - Predominantly white coat
    - Eye defects
    - Deafness
- Multiple breeds
  - Australian Shepherd
  - Great Dane
  - Dachshund
  - Shetland Sheepdog



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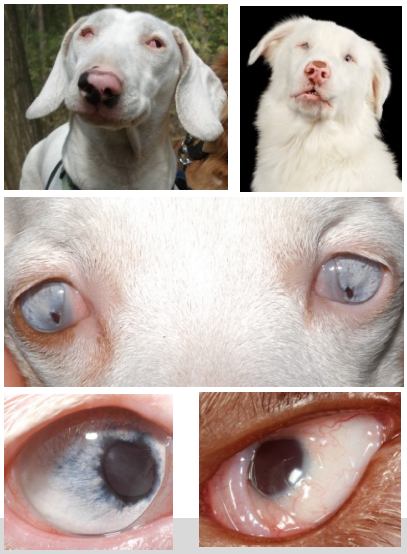
Merle Ocular Dysgenesis (MOD)

- Decreased pigment within outer cup
  - Failure to induce overlying neural crest
- Merle gene → Color dilution.
- Many breeds or mixed breed dogs have merle coat color variants
- Homozygous merle and abundant white spots are at risk of congenital abnormalities in ocular development



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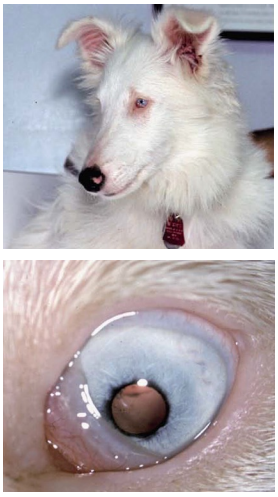
Merle Ocular Dysgenesis (MOD)

- **Lesions:**
  - Microphthalmia
  - Iris hypoplasia
    - Corectopia
    - Congenital miosis
    - Dyscoria
  - Iris coloboma
  - Cataract
  - Choroidal hypoplasia
  - Staphyloma
  - **<u>Affected dogs frequently also deaf</u>**



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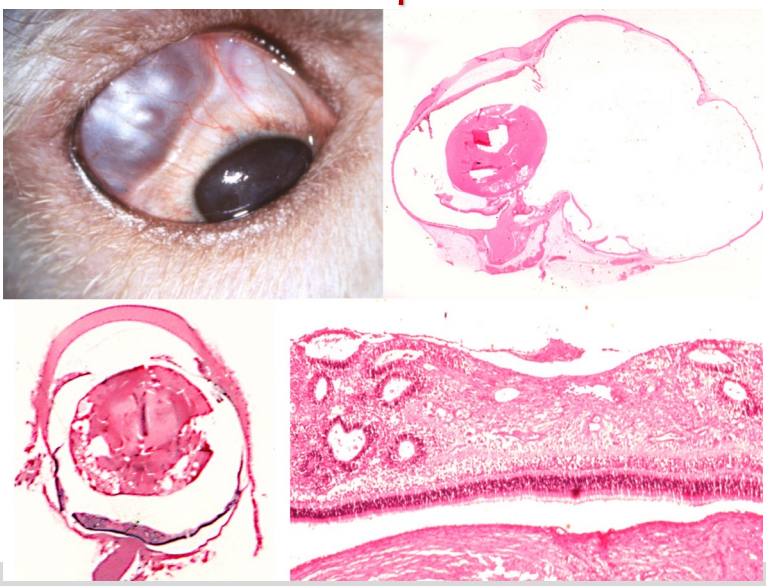
Merle and white spot coat color



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Collie Eye Anomaly (CEA)

- Failure of RPE to induce choroid &/or sclera
- Large deletion *NHEJ1* gene
  - Autosomal recessive
  - Genetic test (Optigen)
- Primary lesions:
  - Choroidal hypoplasia
  - Posterior polar colobomas
  - Retinal detachment
  - Hyphema
- Can be bilateral

- Multiple breeds (Incidence in USA)
  - Rough & Smooth Collie (67%)
  - Border Collie (2.2%)
  - Shetland Sheepdog (0.39%)
  - Australian Shepherd (0.22%)
- No association with coat color

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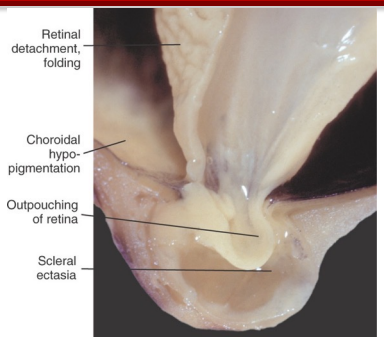
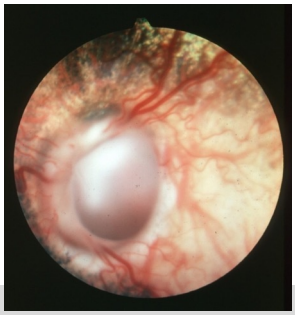
Collie Eye Anomaly (CEA)

- Choroidal hypoplasia is the hallmark*
- Severe cases may have focal defect in sclera and optic nerve adjacent to the optic disc
- 5-10% develop retinal detachment and/or hyphema





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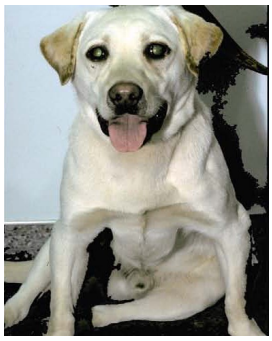
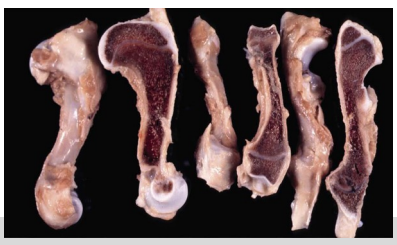
Oculoskeletal dysplasia

- 7 cases in the COPLOW collection.
- Labrador and Samoyeds
- Autosomal dominant with incomplete penetrance
  - Heterozygous animals → mild retinal dysplasia
  - Homozygous animals → skeletal changes and mild to severe retinal dysplasia
- Decreased amounts of type II collagen in the vitreous of affected Labrador retrievers.





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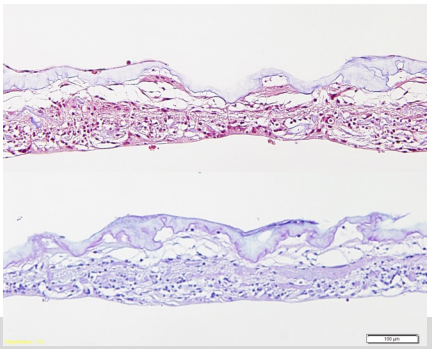
Oculoskeletal dysplasia

- Severely affected eyes → pronounced chondrodysplastic dwarfism
- Ocular changes:
  - Focal/multifocal retinal dysplasia and prominent vitreous strands
  - Focal retinal detachment, liquefied vitreous and thick vitreous strands attached to the inner retina
  - Severely affected: Complete retinal detachment, with disinsertion and wrinkling of the peripheral retina inward towards the optic disc



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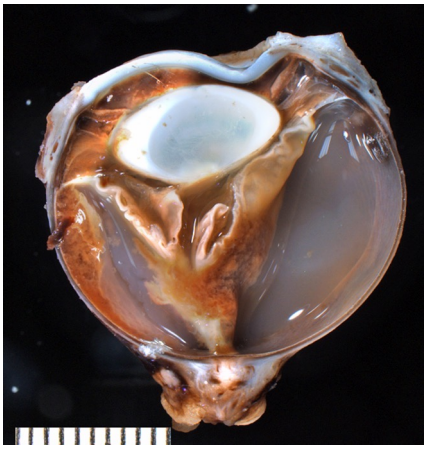
Oculoskeletal Dysplasia



- The end-stage ocular disease:
  - Retinal detachment
  - Neovascular glaucoma
  - Hemorrhage

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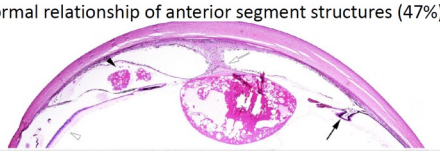
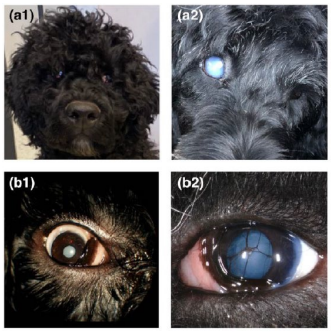
Microphthalmia in Portuguese Water Dogs

Microphthalmia With Multiple Anterior Segment Defects in Portuguese Water Dogs
Gillian C. Shaw[1], May P. Y. Tse[2], and Andrew D. Miller[2]

Veterinary Pathology
2019, Vol. 56(2) 269-273

- Microphthalmia (97%)
- Lens abnormality (congenital cataract or aphakia; 100%)
- Lack of a ciliary cleft & trabecular meshwork (47%)
- Abnormal relationship of anterior segment structures (47%)





- Additionally
  - Tooth enamel malformations
  - Stunted growth
  - Hematopoietic defects
    - Anemia & thrombocytopenia

OXFORD G3 Genes | Genomes | Genetics

A naturally occurring canine model of syndromic congenital microphthalmia

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Equine MCOA

Equine Multiple Congenital Ocular Anomalies and Silver Coat Colour Result from the Pleiotropic Effects of Mutant *PMEL*
PLOS ONE September 2013 | Volume 8 | Issue 9 | e75639

Lisa S. Andersson[1], Maria Wilbe[1], Agnese Viluma[1], Gus Cothran[2], Björn Ekesten[3], Susan Ewart[4], Gabriella Lindgren[1]*

- Silver dapple gene (*PMEL17*) on ECA6q
- Chocolate coat + flaxen mane & tail
- Missense mutation in exon 11 of *premelanosome protein*
- Genetic test (UC Davis VGL)
- MCOA – Incomplete dominant
  - Heterozygote – less severe phenotype
  - Homozygote – wide range of anomalies
- Rocky Mountain Horse, Kentucky Mountain Saddle Horse, Icelandic Horse, Morgan Horse and Silver Ponies

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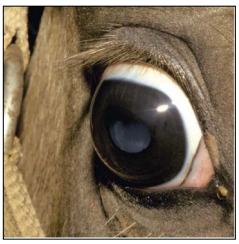
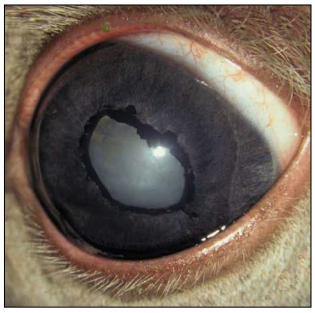
Equine MCOA

- Cornea globosa
- Abnormal pectinate ligaments
- Iris & corpora nigra hypoplasia
- Congenital miosis
- Temporal iris & ciliary body cysts
- Retinal cysts
- "High-water marks" – focal detach/reattach
- Retinal dysplasia or detachment
- Cataract
- Lens luxation





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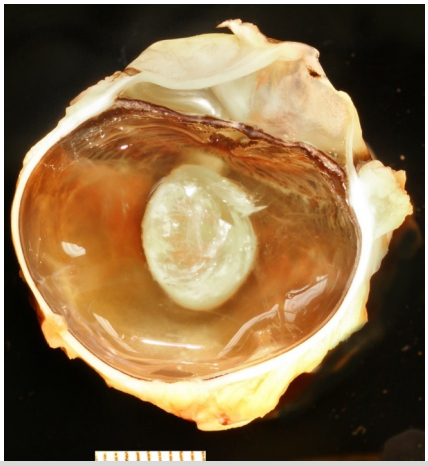
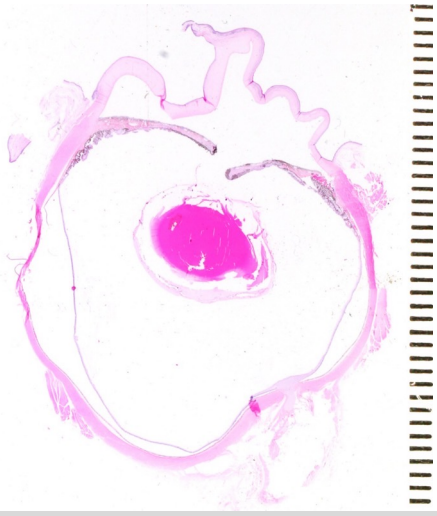
Ocular anomalies in Rocky Mountain Horses

Cornea globosa

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Ocular anomalies in Rocky Mountain Horses

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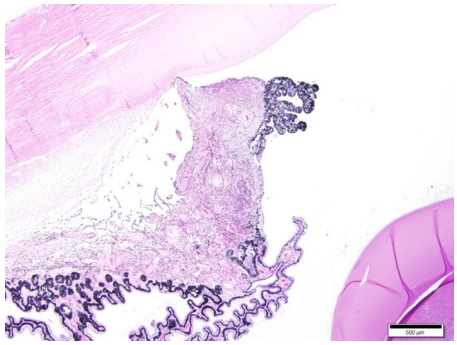
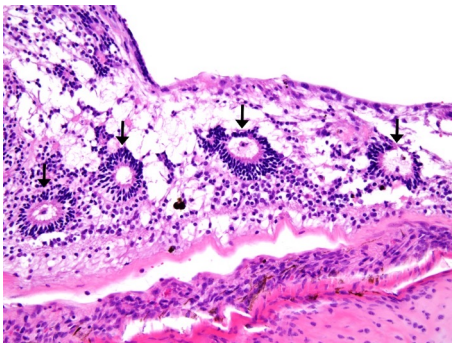
Ocular anomalies in Rocky Mountain Horses

Iris aplasia



Retinal dysplasia



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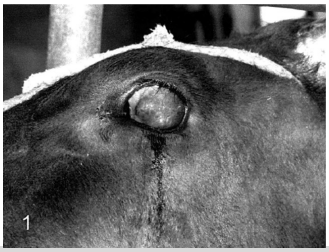
MCOA in Japanese Black Cattle


Genomics

A mutation of the *WFDC1* gene is responsible for multiple ocular defects in cattle

Abdol Rahim Abbasi [a,1], Maryam Khalaj [a], Takehito Tsuji [a], Muki Tanahara [b], Kazuyuki Uchida [c], Yoshikazu Sugimoto [d], Tetsuo Kunieda [a,*]

- Autosomal recessive
- WFDC1 mutation
  - 1 nucleotide insertion → frameshift mutation → stop codon
  - Small secretory protein
- Multiple ocular defects
  - Microphthalmia
  - Retinal detachment
  - Persistent hyaloid artery
  - Lens abnormalities



K. Uchida et al. Vet Pathol 2006;43:1017-1021

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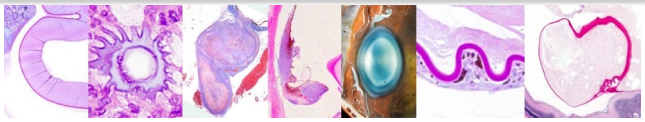
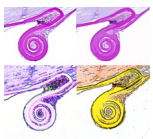
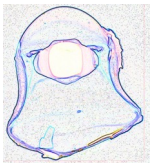
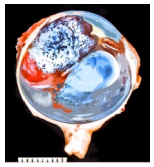
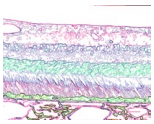


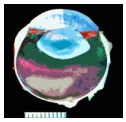


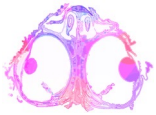
Questions?

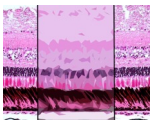


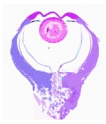


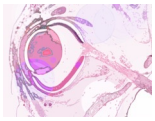












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