Clinical and Pathology Correlation

- Ophthalmic lesions have excellent pathologic correlates. Many lesions, e.g. in cornea and lens, are seen with a resolution that is equal or higher than a histology section. Layers and focal disease can be readily identified.
- Provide either photographic documentation or a drawing for pathologist to cut the eye in the appropriate plane.
- Fixatives: Bouin (dog), Davidson (rodent, monkey, dog) are excellent for general pathology of eye. "Render fix" method is excellent. FORMALIN IS NOT GOOD!!!!!!!
Examples:
granular Groenouw Type 1 = CDGG1; Lattice type 1 = CDL1; Avellino = CDA; Reis-Buckler (Thiel-Benhke) = CDRB; lattice type IIIA = CDL1/IIIA

Siberian Husky: Crystalline Corneal Dystrophy

Cholesterolosis (lipid dystrophy)

Usually subepithelial, although pre-Descemet deposits are recognized. Rare in laboratory beagles. Generally found in older animals (>~2 yr)

These opacities in SD rats (Rx/control) were on the epithelial surface, and persisted

Sperificial (Punctate) Keratopathy: SK, SPK

These opacities in SD rats were on the epithelial surface, and persisted
Crl:CD®(SD)IGS BR rats: Eye Findings (1)

- Number examined: 335M/333F from different sources, ~5 wks of age
- Methods: 1% tropicamide, I.O.-40D lens, SL-14B (.1-.2 width, 16X)

**Cornea**
- crystalline opacity uni or bilateral, subepithelial (11-46%), M=F
- sporadic post-inflam: focal/diffuse stria or opacities (infrequent)

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**Compound XYZ-apnbt**

Abnormalities were limited to the eyelids (abnormal blink reflex) and cornea. By 1 hour, both upper and lower eyelids were retracted and a blink reflex could not be elicited. In the interpalpebral space, the cornea developed a focal, oval area of drying. In this area the epithelial and superficial stromal layers became indented and compressed. The epithelial surface was dry, irregular and corrugated, and a distinct precorneal tear film (PTF) layer was absent from the area of corneal drying.

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**Disorders of the Iris and Perilenticular Vascular Mesoderm**

- corectopia
- coloboma
**Anterior uvea** (my summary from 335M/333F rats examined from different colonies)
- anterior or posterior synechia, PPM, and anterior uveitis (sporadic)
- iris colobomas (6% in one colony)

Aguirre-Univ. of Penna.

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**Lens Structure**
- surrounded by a basement membrane (lens capsule)
- lens epithelial cells only present anteriorly after development
- cell division and fiber elongation only at equator (lens bow region)

The lens consists of an enveloping basement membrane (the lens capsule), an anterior epithelium and a cellular stroma made up of lens fibers. The shape of the lens is determined by the elastic lens capsule, and the tension on the lens by the ciliary body (i.e. ciliary muscle) acting through the zonular ligaments. The red boxes in the image identify the area of the peripheral anterior cortex of the lens near the lens bow region.

In postnatal life, the lens epithelium is present only on the anterior surface of the lens. The posterior lens epithelium, present in the embryo/fetus, was converted to lens fibers (primary lens fibers) during early prenatal lens development. The primary lens fibers are surrounded by the secondary lens fibers, and form the “nucleus” of the lens. The secondary lens fibers are the cortex of the lens.
Fine Cortical Lens Opacities are Common—record all changes.

Spontaneous Polar Anterior Subcapsular Opacity: Sprague-Dawley rats

- slight to no difference in incidence rates depending on country (US/Japan/France): from 0–8.5% (~2%). M>F
- does not increase with age.

- Lens (my summary from 335M/333F rats examined from different colonies)
  - normal/sporadic: sutural line prominence, nuclear haze, perinuclear opacities and posterior subcapsular opacities, uni or bilateral.
  - severe but focal anterior suture line, focal anterior nuclear-cortical interface, cortical cataracts, perinuclear cataracts, focal anterior or posterior subcapsular cataracts in the central axis.

Aguirre-Univ. of Penna.

Durand et al., 2001

Inherited Cataracts in Dogs

Drug Induced Cataracts in Dogs
(these are indistinguishable from inherited defect)

Drug Induced Cataracts in Dogs

Slides provided to Dr. Aguirre
Drug Induced (immunosupression) Cataract in Cynomolgus Monkeys

Lamellar zonular cataract

The sequence of changes in inherited and drug-induced retinal degeneration are the same. Drugs target pathways essential for photoreceptor function and viability, and these are the same as are involved in inherited degenerations in all species.

Diseases of the Retina/Retinal Pigment Epithelium

Note progressive changes in the retina in photographs of the SAME dog with PRA taken over a span of 4 years.


- Other diagnoses (my summary from 335M/333F rats examined from different colonies)
  - vitreal hemorrhage, persistent hyaloid artery, hyaloid artery remnant, retinal hemorrhage
  - retinal folds, disc colobomas and linear retinopathy
  - sporadic; low incidence and unilateral or bilateral

Linear Retinal Atrophy

- Hubert et al., 1994

Linear Retinal Atrophy (aka FCRA)

disc coloboma
peripapillary coloboma

Linear Retinal Atrophy-rat

a, b
Change in Fundus Coloration (yellow) in Rats

Examples of Drug-associated Findings in Dogs

papilledema
retinal degeneration
multifocal retinal edema/focal RPE damage
RPE: Autofluorescent Epitheliopathy

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Tapetal Degeneration in Dogs

Normal Tapetum Lucidum

control

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Drug-Induced Tapetal Degeneration

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Idiopathic Optic Atrophy (temporal) in Rhesus Macaque (Fortune et al., IOVS, 2005)

needs direct ophthalmoscopy to image the optic disc/vessels

Cynomolgus: Focal Macular Drusen/Window Defects

(Fortune et al., IOVS, 2005)
Drusen and RPE Window Defects

Lipoidal Epitheliopathy
Lipoidal accumulation (RPE "window defects")

Rhesus macaque: radial-like drusen

Autosomal dominant radial drusen (Malattia leventinese)

Is this a model for Mal. lev.??

Macular and Peripheral Degeneration with RPE Proliferation/Migration in Squirrel Monkeys
### Instruments/Methods Used for Routine Clinical Assessment

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
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<tbody>
<tr>
<td>Indirect scope</td>
<td>40D aspheric-rat</td>
</tr>
<tr>
<td>Indirect scope</td>
<td>60D aspheric-mouse</td>
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<tr>
<td>Slit lamp (table or hand held)</td>
<td></td>
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<tr>
<td>Indirect scope</td>
<td>2.2 Volk Pan Retinal</td>
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<tr>
<td>Direct scope</td>
<td>(Fundus camera: F-M)</td>
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<tr>
<td>Slit lamp (hand held)</td>
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