The Eye:
Anatomy, Histology & Histopathology

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Overview

- Macroscopic Anatomy
- Some clinical presentations of eye disease
- Microscopic Anatomy
  - Normal
  - Abnormal
- Methods of eye evaluation

- Abnormal
  - Inflammation
    - Terminology
    - Examples
  - Neoplasia
    - Examples
  - Degenerative conditions
    - Glaucoma
    - Macular Degeneration
    - Cataract
Anatomy

Uvea = pigmented parts of the eye = iris, ciliary body, choroid
Eye Embryology

- Surface Ectoderm: Corneal epithelium; Lens
- Neural Tube: Retina; Iris epithelium & muscles, Ciliary body epithelium
- Mesoderm: everything else
Ways to evaluate the eye structures

• External exam – orbit, eyelids, eyelashes, corneal surface
• Slit lamp exam – for examining the anterior part of the eye (cornea, sclera, iris, anterior aspect of lens)
• Fluorescein dye
  – Corneal surface – diagnoses corneal surface disease (ulcers)
• Ultrasound – interior structures (lens, vitreous cavity, fundus)
• Indirect ophthalmoscopy – interior structures including fundus (back of the eye, also includes macula and optic nerve head)
• Optical Coherence Tomography (OCT) – mostly used for examining retinal layers
Ways to evaluate eye function

• Schirmer tear test – measures tear production
• Fluorescein Dye
  • Intravascular – evaluates vascular integrity when fundus is examined concurrently
• Visual evoked potentials – evaluates retina and whether the signal gets to the brain
• Electroretinogram – evaluates the cells that make up the retina (retinal degeneration)
• Perimetry – visual field testing (glaucoma)
Clinical Eye Lesions

- Buphthalmos – enlarged globe
- Exophthalmos – protrusion of the globe
- Phthisis bulbi – shrinkage of the globe after injury or inflammation
- Anisocoria – having pupils of different size
- Hyphema – blood in anterior chamber
- Hypopyon – inflammatory cells in anterior chamber
- Synechiae
  - Anterior = iris adhered to cornea
  - Posterior = iris adhered to lens
Buphthalmos

Exophthalmos

Anisocoria

Synechia

Phthisis Bulbi

Hypopyon

Hyphema

http://www.answers.com/topic/synechia
http://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/asymmetrical-bilateral-exophthalmus.html
http://www.mooresvet.com/Feline/FeLV.html


Slit Lamp Examination
Indirect Ophthalmoscopy - requires dilated pupils

Normal human retina
retinitis pigmentosa

Foreign body
Ultrasound
Inflammation : Terminology

Select examples:

• Conjunctivitis – conjunctiva
• Keratitis – cornea
• Iritis – iris
• Cyclitis – ciliary body
• Iridocyclitis – iris & ciliary body
• Hyalitis/Vitritis – vitreous body
• Uveitis
  – Anterior – iris & ciliary body
  – Posterior – ciliary body and choroid
• Retinitis – retina
• Chorioretinitis – retina & choroid
• Endophthalmitis – uvea, retina and ocular cavities
• Panophthalmitis – all ocular structures including sclera
• Optic Neuritis – optic nerve
Conjunctivitis

In this case, accompanied by chemosis – edema of conjunctiva
The Source of (all) this info

- UC Davis’s Ophthalmic Pathology Primer
Histology

Normal Dog Eye

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epathOverview_index.html
Histology - Cornea

Normal Dog Eye

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epath_overview_index.html
Cornea

- Epithelium (Ep) – stratified squamous cells
- Stroma (S) – dense collagen
- Descemet’s membrane – basement layer of endothelium
- Endothelium – single layer of cuboidal cells
Corneal Edema

Occurs when the endothelium’s ability to keep the corneal stroma relatively dehydrated is overwhelmed (endothelial specific damage or epithelial damage). Edema appears histologically as white space between tissue components.
Keratitis

Corneal neovascularization

Ulcerative keratitis with accompanying corneal edema and neovascularization


Keratitis

Corneal ulcers stain with fluorescein dye, which fluoresces green in UV light. The dye adheres to the exposed negatively charged corneal stroma.

http://www.aafp.org/afp/2004/0701/p123.html

Keratitis

Normal cornea

Ulcerative keratitis with acute inflammation within the stroma

http://eulep.pdn.cam.ac.uk/images/3307.0_TMB.jpg
Histology – Anterior & Posterior Chambers

Normal Dog Eye

http://www.vetmed.ucdavis.edu/courses/vet_eye/eye_path/epath_overview_index.html
Drainage of Aqueous Humor

Ciliary body (blue & spongy in this figure) produces aqueous humor, which flows into posterior chamber, then thru the pupil into the anterior chamber and exits the eye via the drainage angle.
Anterior & Posterior Chambers

- Anterior chamber is between the cornea and the front surfaces of the iris and lens
  - Contains aqueous humor, which exits through the filtration angle (where the iris meets the cornea)

- Posterior chamber is between the posterior surface of the iris and the sides of the lens
  - Contains aqueous humor which is produced by the ciliary body
Histology – Iris

Normal Dog Eye

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epath_overview_index.html
Iris

- Anterior border layer
- Stroma – loose spongy connective tissue
- Dilator muscle layer – smooth muscle in mammals, striated muscle in birds
- Posterior epithelium
- Color determined by number of pigmented cells

Uvea

1- CORNEA

Trabecular meshwork
Schlemm’s canal

2 CONJUNCTIVA

2 collector vessels

3 SCLERA

3 ciliary process

4 POSTERIOR CHAMBER

ciliary muscle

5 ANTERIOR CHAMBER

6 IRIS

7 non-pigmented ciliary epithelium

8 VITREOUS

Beginning of choroid

9 LENS
Anterior & Posterior Uveitis

Inflammatory cells (purple/blue) expanding the choroid and iris. This case is due to a viral infection in a cat.

Histology – Filtration Angle

Normal Dog Eye

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epath_overview_index.html
Drainage/Filtration Angle

- Pectinate ligament (PL)
- Trabecular meshwork (TM)
- Collecting channel (CC) (canal of Schlemm)
- Problems with the filtration angle can lead to glaucoma
  - Congenital = goniodysgenesis

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epath_overview_index.html
Histology – Lens

Normal Dog Eye

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epath_overview_index.html
Lens

- Capsule (C)
  - Anterior is thicker than posterior
- Lens Fibers (LF) (cells)
- Lens bow is where the nuclei of elongating lens fiber cells line up towards the posterior part of lens
- Lens is prone to artifact in processing and sectioning
Cataract

• Any opacity in the lens
• Many different causes
  • Metabolic
  • Inflammatory
  • Degenerative
Cataracts

Bladder cells and epithelial proliferation

Fiber degeneration

Fibrous metaplasia of epithelium

Vacuolation
Histology – Retina

Normal Dog Eye

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epath_overview_index.html
Retina

- Retinal Pigmented Epithelium
- Photoreceptors (PRs) = rods and cones (contain photosensitive pigments), Outer Nuclear Layer
- Outer Plexiform Layer
  - Where PRs talk to Horizontal (HCs) and Bipolar cells (BCs)
- Inner Nuclear Layer & Plexiform Layer (HC and BC nuclei)
- Inner Plexiform Layer
  - Where HCs and BCs talk to Ganglion and Amacrine cells
- Ganglion Cell (GC) Layer
- Nerve Fiber Layer (axons of GCs – becomes optic nerve)

Fig. 2. Simple diagram of the organization of the retina.

http://webvision.med.utah.edu/imageswv/schem.jpeg
Retina

- Photoreceptors = rods and cones (contain photosensitive pigments), Outer Nuclear Layer
- Ganglion Cell Layer
- Nerve Fiber Layer (axons of GCs – becomes optic nerve)

Fig. 4. 3-D block of a portion of human retina.

http://webvision.med.utah.edu/imageswv/3dlabel.jpeg
Retina

• Photoreceptors = rods and cones (contain photosensitive pigments), Outer Nuclear Layer

• Ganglion Cell Layer

• Nerve Fiber Layer (axons of GCs – becomes optic nerve)

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epath_overview_index.html
Tapetum Lucidum

http://fr.academic.ru/dic.nsf/frwiki/1604972

http://www.4to40.com/qa/index.asp?id=3743
Macula

Macula – the area of the retina in primates (including humans) that is rich in cone photoreceptors and is responsible for fine, sharp, straight-ahead vision (entire retina in this photo is the macula)

Fovea – the area where there is a depression formed by thinning of the inner retinal layers to allow light to directly shine on the photoreceptor layer
Retinal Structure:
Optical Coherence Tomography (OCT)
Optical Coherence Tomography (OCT)

nerve fiber layer (NFL)
retinal pigment epithelium (RPE)
foveal depression
R-4300 for Greatest Depth, R-2200 for Greatest Resolution

R4300 Whole Eye

R2200 Posterior

R2200 Anterior

R2200 Periphery

Mouse

Histology

SD-OCT

bioptigen

Envisu
Retinal Function: Electroretinogram (ERG)

- **b-wave**
  - Bipolar cells

- **a-wave**
  - Photoreceptors

- **3rd order neurons**

- **Rod**
- **Cone**

- Bipolar cells
Abnormal Electroretinogram

Visual function: Optokinetic Device

Eye – Species Differences

Normal mouse eye – rodents have shallow anterior chambers and relatively large lenses that take up a large portion of the vitreous cavity

http://www.aomf.ca/appl6.html
Eye – Species Differences

Normal rabbit retina. They have large retinal blood vessels on the surface of the retina, with capillary extensions down into retinal tissue. This would be considered a pathological lesion in other species.

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epath_overview_index.html
Murine Retinal Degeneration Models

Ocular Neoplasia

• Neoplasia can arise from any part of the eye
• Some common examples:
  – Melanoma (iris, choroid, conjunctiva)
  – Ciliary body adenoma / carcinoma
  – Glioma (optic nerve)
  – Squamous cell carcinoma (cornea)
Melanoma


http://www.merckvetmanual.com/mvm/htm/bc/eene909.htm
Melanoma

- Can arise from the iris, ciliary body epithelium or the choroid.
- Well differentiated tumors are composed of heavily pigmented cells that can be round to spindle shaped. Poorly differentiated tumors can be composed of poorly pigmented cells.

http://www.merckvetmanual.com/mvm/htm/bc/eene05.htm


Ciliary Body Adenoma / Carcinoma

http://www.merckvetmanual.com/mvm/htm/bc/eene910.htm

Ciliary Body Adenoma / Carcinoma

Cuboidal to polygonal shaped cells arranged in papillary to tubular patterns. One prominent characteristic is the thick basement membranes (stained with PAS stain in upper right photo).

Optic Nerve Glioma

Spindle shaped cells arranged in bundles and streams

Corneal Squamous Cell Carcinoma

http://www.vetmed.wisc.edu/pbs/dubielzig/pages/coplow/PowerPoints/Neoplasia08.pdf
Glaucoma

• Historically thought to be vision loss due solely to increased intraocular pressure
  – Can happen in some people despite normal intraocular pressure
  – Now considered to be an “optic neuropathy” leading to death of retinal ganglion cells and thus blindness

• Hallmarks:
  – Loss and/or death of retinal ganglion cells
  – Optic nerve degeneration (causes optic disk cupping)
  – Closure of filtration angle
  – Breaks in Descemet’s membrane (corneal endothelium basement membrane)
Glaucoma

Closed filtration angle

Retinal ganglion cells missing

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epath_overview_index.html
Glaucoma

Cupping of optic disc

Break in Descemet’s membrane

http://www.vetmed.ucdavis.edu/courses/vet_eyes/eye_path/epath_overview_index.html
Vascular eye disease models

• Age-related macular degeneration
  – Dry = drusen deposition between choroid & RPE
  – Wet = vascular problem caused by unhappy (hypoxic) cell signalling

• Diabetic retinopathy & Retinopathy of prematurity
  – Pathogenesis similar to wet AMD

http://jirehdesign.com/eye-illustrations/eye-conditions-illustrations/co0069.html
Fluorescein Angiography
Macular Degeneration

• Affects older adults
• The macula is affected primarily, so central vision is lost
• Two types:
  – Wet form – new blood vessels invade the subretinal space from the choroid and leak fluid thus separating the retina from the RPE, which leads to photoreceptor degeneration
  – Dry form – cellular debris (drusen) builds up between the RPE and the retina leading to photoreceptor degeneration
Macular Degeneration

http://www.ahaf.org/macular/about/understanding/normal-macula-compared.html
Macular Degeneration

- **Dry AMD** – drusen under RPE

- **Wet AMD** – retinal neovascularization
P7 mice are exposed to 75% oxygen, which induces loss of immature retinal vessels and slows development of the normal retinal vasculature, leading to a central zone of vaso-obliteration (VO). After returning mice to room air at P12, the central avascular retina becomes hypoxic, triggering both normal vessel regrowth and a pathologic formation of extraretinal neovascularization (NV).
Questions?