#### WOPTS UNKNOWNS

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### **DISEASE CATEGORIES**

Cataract: 3, 5, 8,10, 15, 16, 22, 24, 58, 69, 78, 79, 80, 87, 92, 94

Congenital Abnormalities: 15, 16, 18, 76, 77

**Glaucoma:** 1, 9, 10, 17, 18, 19, 22, 29, 42, 44, 49, 51, 52, 53, 54, 57, 58, 59, 63,

69, 74, 75, 77, 87, 92, 95

**Inflammation:** 1, 2, 3, 4, 5, 6, 8, 11, 13, 14, 17, 22, 24, 25, 27, 28, 29, 34, 38,

39, 41, 42, 44, 46, 48, 53, 56, 57, 59, 61, 62, 63, 64, 65, 70, 71

**Metabolic:** 23, 41, 94

**Neoplasm:** 6, 7, 8, 9, 10, 11, 12, 19, 20, 21, 25, 26, 33, 34, 36, 37, 38, 43, 44, 45, 47,

49, 50, 54, 55, 56, 57, 60, 68, 70, 72, 78, 79, 81, 84, 90, 91, 95, 96

**Organisms:** 1, 2, 3, 4, 5, 24, 28, 34, 46, 48, 62, 64, 74, 93

**Post-operation:** 29, 42, 58, 59, 65

**Trauma:** 24, 25, 30, 31, 32, 35, 65, 67, 69, 73, 76, 82, 83, 85, 88, 89, 92

#### Slide 1, Inf 683, 95RD052

This slide is a vertical section is of an intact canine globe. On subgross examination, there is retinal detachment and protein rich exudative material in the collapsed vitreous. Histologically, there is an intact corneal epithelium. There is midstromal corneal vascularization. The endothelium is separated but appears within normal limits. There is a segment of the superior iris leaflet where the endothelium appears to be plastered against the iris. Despite the apparent anatomic relationship, I believe this phenomenon is an artifact. The anterior uvea is surprisingly clean of inflammation, however, the iris profile demonstrates a very shallow anterior chamber and an outward bowing of the posterior chamber and then at the pupillary margin, the iris tissue extends backwards, contacting the lens (some sections do not show the posterior synechia, however, there is a cellular membrane on the anterior surface of the lens). This iris profile is typical of **iris bombé.** There is a rich protein exudate in both the anterior and posterior chamber, which is relatively cell poor. There is hemorrhage and broad tissue edema of the ciliary processes extending to the lens equator. The lens capsule appears to be intact. There is a rich protein exudate in the collapsed central vitreous, and adjacent to the detached retina, there is a **pyogranulomatous vitreitis.** The neutrophilic inflammation is primarily seen immediately adjacent to the inner limiting membrane of the detached retina. In addition, intermittently there are also little clustered aggregates of foamy macrophage cells indicative of granulomatous **inflammation**. Often the little granulomas have adhering fibrils to the inner limiting membrane. The retina is wrinkled and distorted and there is a mild perivascular lymphocytic retinitis. There is complete **retinal detachment.** The subretinal space is largely empty, however, there are small amounts of both hemorrhage and fibrin exudation, and there is marked hypertrophy of retinal **pigment epithelium.** These features are morphologic indicators of pathologic (as opposed to artifactual) retinal detachment. Careful scrutiny of the exudative reaction immediately internal to the retinal internal limiting membrane will demonstrate the presence of fungal hyphae which are very difficult to discern with the H&E sections. A silver stain for fungus (GMS stain) is provided for this case.

#### **Diagnoses:**

- 1. Midstromal corneal vascular infiltrate (stromal keratitis)
- 2. Iris bombé
- 3. Thin preiridal fibrovascular membrane
- 4. Complete retinal detachment
- 5. Pyogranulomatous vitreitis

- 6. Mycotic vitreitis
- 7. Secondary glaucoma as per history
- 8. Retinal detachment
- 9. Hypertrophy of retinal pigment epithelium
- 10. Granulomatous inflammation

**Comment:** This animal is reported to have glaucoma. Evaluation of the retina shows the presence of a surprisingly large amount of ganglion cells. I have observed in several cases that when there is retinal detachment preceding the development of glaucoma, ganglion cells seem to be spared.

## Slide 2, Inf 712, 95RD145

This section is of an intact canine globe. Subgross evaluation shows that there is a rich protein exudate in the vitreous and subretinal space, and retinal detachment. Histologically, the corneal epithelium is intact. There is keratinization of segments of the central corneal epithelium. There is a mid-stromal vascular infiltrate in the corneal stroma. The anterior chamber is narrow. There is a rich protein infiltrate in the posterior chamber. There is a rich protein infiltrate in the vitreous. There is complete **retinal detachment** and there is an extensive inflammatory infiltrate in the retina and in the subretinal space as well as the choroid. Multifocally, the inflammatory infiltrate in the retina is a mixture of histiocytes and neutrophils (pyogranulomatous retinitis). Localized foci show **retinal necrosis**. There is a pyogranulomatous infiltrate in the subretinal space, most prominently seen immediately adjacent to the retina and also internal to the retinal pigment epithelium. Lymphocytic and histiocytic infiltrates extend into the choroid segmentally. The presence of pyogranulomatous exudate in the eye, especially in the subretinal space, should initiate a careful search for fungal organisms, and in this case we are rewarded by finding numerous circular yeast profiles. Typical organisms are distinctly circular with a refractile capsule approximately 12 µm in diameter. This profile is typical of *Blastomyces dermatitidis*. The other feature to look for is the presence of broad-based budding.

- 1. Corneal stromal vascularization
- 2. Pyogranulomatous retinitis
- 3. Pyogranulomatous choroiditis
- 4. Mycotic chorioretinitis (Blastomyces dermatitidis)
- 5. Retinal detachment
- 6. Retinal necrosis

### Slide 3, Inf 436, 92RD194

This slide is of a feline globe. On subgross evaluation there is **retinal detachment** with exudate in the vitreous and in the subretinal space. Histologically, there is artifactual wrinkling of the cornea. The central corneal epithelium is markedly attenuated and absent over much of the cornea. There is inflammatory cell infiltrate within and disrupting the corneal endothelium over much of the central cornea. The predominant endothelial inflammatory cells are neutrophils (suppurative endotheliitis). There are both clusters of neutrophils and foamy macrophage cells adherent to the anterior iris surface and filling the iridocorneal angle. Notice the difference in the cellular population of the superior and dependent iridocorneal angle. There is a moderate lymphoplasmacytic inflammatory infiltrate around blood vessels of the anterior uvea. There is a spindle cell membrane extending from the ciliary body to the lens equator and an early spindle cell membrane progressing posterior to the posterior capsule along the anterior vitreous face (developing cyclitic membrane). There are Morgagnian globules and cortical cataract changes at the equatorial cortex and there is posterior migration of lens epithelial cells (posterior subcapsular cataract). Filling the vitreous there is a complex of protein globules, hypereosinophilic cells, and poorly staining pleomorphic fungal yeast organisms without cellular reaction. The characteristic organisms are poorly staining pleomorphic to round bodies almost always with a clear zone around the central structure. Moving to the detached retina, retinal morphology is variably interrupted by solid aggregates and sheets of macrophage cells containing numerous fungal yeast forms. Broad sheets of the inner choroid are thickened and displaced by thick membranes of phagocytic cells containing yeast organisms in their cytoplasm. Smaller numbers of neutrophils and lymphoplasmacytic cells are seen. Lymphoplasmacytic cells tend to be within the substance of the choroid and the organisms tend to be in the subretinal space or inner choroid. The organisms are approximately 10-20 µm and have poorly staining central bodies and a thick, non-staining mucinous capsule typical of *Cryptococcus neoformans*. Budding forms are easily found. This organism can be highlighted with the Alcian blue PAS stain which stains the mucinous capsule Alcian blue positive and the organism PAS positive. The silver stain GMS also stains the organism black.

- 1. Suppurative inflammation in the corneal endothelium
- 2. Mild lymphoplasmacytic uveitis
- 3. Mild cortical cataract
- 4. Developing cyclitic membrane
- 5. Early posterior subcapsular cataract
- 6. Pyogranulomatous endophthalmitis, retinitis, and choroiditis with *Cryptococcus neoformans*
- 7. Retinal detachment

#### Slide 4, Inf 822, 96RD57

This slide is a section of an intact feline globe. On subgross evaluation, there is marked thickening and distortion of the anterior uvea and protein exudation in the chambers of the eye. Histologically, there is a broad segment of central cornea devoid of epithelium. Some fragments of epithelial lips are found in the section. Notice the tendency for epithelial cells to become keratinized on both surfaces and therefore, poorly attached or nonattached. In the central zone of the cornea devoid of epithelium, there is a thick corneal sequestrum. Within the sequestrum, the stroma is relatively cell poor. Neutrophils can be seen subtending the sequestered stroma and large colonies of bacteria can be found within the sequestrum tissue centrally. Deep in the stroma, there is a rich neutrophilic inflammatory cell infiltrate. In searching for features that distinguish this as a feline eye we are kind of stuck because both the iris and the tapetum are virtually destroyed by the inflammatory infiltrate. Some areas of retina are relatively preserved, and in these areas there are coarse Mueller cell fibers, which is a feline morphologic phenomenon. The iris tissue is almost completely lost in the solid sheet of inflammatory cells. The inflammation largely replaces the iris as well as the anterior portion of the ciliary body and extends full thickness through the sclera into the subconjunctival tissue. In almost all areas, the inflammation is largely a mixture of very large macrophage cells with smaller numbers of lymphocytes, plasma cells, and neutrophils. Macrophage cells are usually filled with numerous small dark staining red or blue dots. These dots are about 3 to 5 µ in diameter. Inner connecting areas of coagulation necrosis are seen within the **granulomatous uveitis**. The morphologic characteristics of the intracytoplasmic fungal organisms are typical of *Histoplasma capsulatum*. There are broad areas of similar granulomatous destruction of the choroid and chorioretinal junction with marked but intermittent retinal atrophy. Clusters and aggregates of macrophages and neutrophils with and without organisms are seen in the inner retina, usually around blood vessels. In most areas, the retina is markedly gliotic and the lamellar organization is lost. In some areas, with less inflammation, there is a spindle cell membrane subtending the retina, an indicator of retinal pigment epithelial disease, and spindle cell transformation.

- 1. Poor corneal epithelial attachment
- 2. Corneal sequestrum
- 3. Suppurative keratitis
- 4. Granulomatous anterior uveitis, scleritis, chorioretinitis
- 5. Histoplasma capsulatum
- 6. Outer retinal atrophy with gliosis

### Slide 5, Inf 763, 95B926, Inf 337, 91RD096

This slide is of an intact canine globe stained with Alcian blue PAS. On subgross examination, there is obviously a protein exudate in all ocular chambers, and the lens substance is largely absent. Histologically, there is severe corneal stromal disease in the central cornea just in the dependent side of the axial cornea. Although the epithelium is intact there is disruption of the stromal lamellae associated with a neutrophil-rich inflammatory reaction (suppurative stromal keratitis). Over much of the cornea the epithelium is intact, but the basement membrane is markedly thick and has a jagged sawtooth profile. The thickening of the basement membrane is an indication of a chronic process of recurring erosion and re-epithelialization. The PAS stain highlights the presence of fungal hyphae mostly in the superficial stroma but extending as far back as Descemet's membrane. Many sections do not have fungal hyphae within Descemet's membrane. Within the anterior chamber there is a cell-poor, granular protein exudate. Notice the difference in the cellular infiltrate in the dependent iridocorneal angle and trabecular meshwork compared to the superior angle. Inflammatory cells tend to gravitate, and the finding of multinucleate macrophage cells is common in suppurative endophthalmitis. There is a preiridal **fibrovascular membrane**, and the posterior chamber is markedly distorted because of the presence of a spindle cell membrane associated with a broad **posterior synechia**. Much of the iris pigmented epithelium is missing from the section. In addition, there are epithelial cysts in the superior iris segment. Much of the lens is empty, with a liquid cortex and solid nucleus (morgagnian cataract). There is a cell-poor collagen deposition on the inner aspect of the anterior lens capsule (anterior subcapsular cataract). Notice the presence of crisp PAS-positive membranes in the anterior subcapsular cataract. This is an indication that the cell-poor matrix was deposited by lens epithelial cells. Small numbers of elongate spindle cells remain. There is a mixed spindle cell and pigmented cell membrane on the anterior lens surface. This is a positive indicator for **posterior synechia**. There is a mild lymphoplasmacytic inflammatory infiltrate in the anterior uvea, mostly around blood vessels. There is granular protein exudate in the vitreous. There are small numbers of phagocytic inflammatory cells in the vitreous, some of which contain melanin. There are small numbers of lymphocytes and plasma cells around blood vessels in the retina. It is a good slide to look for the hallmarks associated with artifactual retinal detachment. Look carefully at the retinal pigment epithelial cells and notice the presence of the torn remnants of the photoreceptor outer segments. This finding is a clear indicator of artifactual retinal detachment. In addition, there is no evidence of degeneration of the outer retina and no hypertrophy of the retinal pigmented epithelial cells.

- 1. Suppurative stromal keratitis
- 2. Mycotic keratitis
- 3. Preiridal fibrovascular membrane
- 4. Posterior synechia
- 5. Artifactual retinal detachment

- **6. Iridociliary epithelial cysts** (not in all sections)
- **7. Anterior subcapsular cataract** (not in all sections)
- 8. Morgagnian cataract

### Slide 6, Neo 2423, 00RD753, Neo 548, 94RD042, Neo 530, 93RD242

This slide is an aggregate of the three most common nodular eyelid lesions. **Meibomian gland** adenoma is a well differentiated, circumscribed, nodular lesion made up of disorganized but fully differentiated meibomian glandular tissue and it is often surrounded by inflammatory infiltrate. In this case, there is a marked **lipogranuloma** or **chalazion** surrounding the meibomian gland adenoma. Lipogranuloma is characterized by the presence of irregular histiocytic cells containing granular to linear, hypereosinophilic, intracytoplasmic material sometimes with a sprinkling of pigmented granules. About half the time examination of the macrophages of lipogranuloma surrounding meibomian gland lesions will show the presence of birefringent particulate or linear material in the cytoplasm of the phagocytic cells. Ultrastructurally, this is made up of parallel arrays of membranous electron dense material, presumably tear film lipid. **Meibomian gland epithelioma** is a less well differentiated nodular lesion made up of mostly poorly differentiated basal cells. Sometimes it's easy to find the components of meibomian gland tissue (squamous differentiation and sebaceous differentiation), but in other cases it can be made up mostly of undifferentiated basal cells. A characteristic of this tumor is the presence of regularly dispersed pigmented cells and meibomian gland epithelioma can present as a black nodular mass. The sample in this slide also contains **chalazion** or lipogranuloma surrounding the meibomian gland epithelioma. Both meibomian gland adenoma and meibomian gland epithelioma are benign. They are the counterparts of these same tumors in the sebaceous gland of the haired skin. However, lipogranuloma surrounding sebaceous gland tumors never show birefringence. The third lesion is a reactive squamous papilloma. These lesions are characterized by an exophytic papillary mass covered by usually thickened stratified squamous epithelium. **Reactive squamous papillomas** can be secondary to tumors of meibomian gland origin, eyelid margin inflammation, or they can occur de novo without underlying disease. In the examples in this slide, the papilloma is associated with meibomian glandular tissue at the base. Some slides show the presence of a lymphoplasmacytic inflammatory infiltrate adjacent to the meibomian gland.

# Diagnoses (three separate tissues on the same slide):

- 1. Meibomian gland adenoma with surrounding lipogranuloma (chalazian)
- 2. Meibomian gland epithelioma with surrounding lipogranulomas (chalazian)
- 3. Reactive squamous papilloma associated with hyperplastic meibomian glandular tissue

### Slide 7, Neo 0572, 94RD106

The slide is a **near normal feline globe** cut vertically. Abnormalities are limited to the iris stroma. Histosections of iris stroma show redundant amounts of pigmented cells, both on the iris surface and extending into the iris stroma. On the inferior iris leaflet the redundant cells are mainly piled up on the iris surface, with small aggregates extending into the stroma. There is a very mild **ectropion uvei**. On the superior iris margin there is obvious and convincing extension of redundant pigmented cells into the substance of the iris. In all areas, the cells in question are round to polygonal pigmented cells with a round nucleus, often with a prominent nucleolus. The iridocorneal angles are within normal limits, and there are just a small number of similar pigmented cells attached to the trabecular meshwork in the dependent iridocorneal angle. The retina and optic nerve profile do not suggest glaucoma. This is an **early feline diffuse iris melanoma**. If the cells were only on the anterior surface of the iris I would call it **iris melanosis**.

- 1. Early feline diffuse iris melanoma
- 2. Near normal feline globe
- 3. Ectropion uvei
- 4. Melanosis

#### Slide 8, Neo 1156, 97RD086

This slide is of the globe of a cat. The anterior segment of the eye is markedly distorted due to a cellular infiltrate. In the plane of section there is no anterior chamber. There is corneal stromal vascularization throughout the entire cornea. Organized iris tissue is not apparent due to the infiltrative mass. Solid neoplastic tissue extends full-thickness through the sclera at the limbus, filling cavitated spaces in the sclera that presumably correspond to the scleral venous plexus. The mass extends deeply into the ciliary body, tapering into normal choroidal stroma in the peripheral choroid. Either only small segments or no retinal tissue remains. Neoplastic infiltrate consists of a solid sheet of pleomorphic neoplastic cells, many of which are heavily pigmented. Cells range from spindle cells to round cells and occasionally large cells with foamy cytoplasm (balloon cells) are seen as a component of the tumor. Localized foci of necrosis are occasionally seen. Occasional multinucleate cells or cells with giant nuclei (karyomegalic cells) are seen and occasionally nuclei have invagination of cytoplasm into the nucleus. This is a good example of an extensively infiltrative feline diffuse iris melanoma, and, in a case with this extensive infiltration, metastasis is a distinct possibility. There is a liquefied lens cortex with aggregates of spindle cells in collagen deposited in the inner aspect of the anterior capsule (anterior subcapsular cataract). There is a discontinuous posterior capsule with wrinkling and scrolling of the ruptured lens capsule (lens capsule rupture). There is a neoplastic cellular membrane extending over the posterior aspect of the lens capsule along the structure that also contains spindle cells. This may be a cyclitic membrane or it may be remnants of the detached retina. There is marked hypertrophy and hyperplasia of retinal pigment epithelial cells, indicative of pathologic retinal detachment.

- 1. Stromal keratitis
- 2. Extensive feline diffuse iris melanoma
- 3. Retinal detachment
- 4. Lens capsule rupture
- 5. Hypermature cataract
- 6. Anterior subcapsular cataract
- 7. Pathologic retinal detachment

## Slide 9, Neo 526, 93RD268

This slide is a vertical section of a canine globe. There is a pannus of fibrovascular tissue extending into the midcorneal stroma in the dependent periphery. The anterior uvea is markedly distorted by a nodular infiltrating mass. The mass involves the entire iris and most of the ciliary body and extends into the sclera in association with the scleral venous plexus. The neoplastic infiltrate is made up of sheets of pleomorphic neoplastic cells, often with a scant amount of cytoplasmic melanin. Neoplastic cells have a tendency to aggregate together in small easily disrupted clusters and intermittently throughout the mass there are multifocal areas of microscopic tumor necrosis. Neoplastic cells have pleomorphic nuclei, characterized by coarse peripheral chromatin and large, sometimes bizarre-appearing, nucleoli. Mitotic activity is common. The posterior iris epithelium and the ciliary body epithelium are relatively spared and the posterior segment of the eye returns to a surprisingly normal profile. Although profound retinal atrophy is not a feature, there is a proportionate decrease in ganglion cells, indicating glaucoma. Not all sections contain the optic nerve head. This is a malignant intraocular melanoma.

- 1. Canine malignant intraocular melanoma of the anterior uvea
- 2. Secondary glaucoma

# Slide 10, Neo 1111, 97RD007

This slide is a vertical section of an intact feline globe. The dependent anterior uvea is markedly distorted by a cavitated and lobulated solid mass bulging inward to make broad contact with the anterior and equatorial surface of the lens and stretching posteriorly across midline in the vitreous cavity. The tumor extends posteriorly almost to the posterior pole of the eye, pushing the retina out of place and abutting on the tapetum. At the margins of the neoplastic mass, remnants of wrinkled retina can be found. A few millimeters away, the retina is almost normal thickness, however, there are decreased ganglion cells and the retina has a gliotic appearance. At the lens equator where the lens is cradled in the tumor, there is wrinkling of the lens capsule and proliferation of lens epithelial cells showing spindle cell metaplasia (anterior subcapsular cataract). In addition, there is posterior migration of lens epithelial (posterior subcapsular cataract). The tumor is made up of solid sheets of small polygonal cells with a regular nuclear profile. Although cell margins are usually indistinct, there is a granular to vacuolated cytoplasm and a very regular cellular differentiation forming broad sheets positioned between regularly spaced blood vessels all throughout the mass. Multifocal segmental areas of tumor necrosis are seen throughout the tumor. There is little evidence of pigmentation of neoplastic cells and, although the tumor abuts on the sclera, there is little evidence of invasion into the sclera or scleral tissue or mitotic activity. The collection does not contain a PAS slide of this case, however, these tumors usually show thin delicate PAS-positive basement membranes, either around individual cells or small aggregates of cells. This is the typical appearance of **feline** iridociliary adenoma.

#### **Diagnoses:**

- 1. Feline solid, nonpigmented feline iridociliary adenoma
- 2. Secondary glaucoma
- 3. Anterior subcapsular cataract
- 4. Posterior subcapsular cataract

**Comment:** Iridociliary adenomas in cats are considerably different than those in dogs. The pattern you see in this tumor is quite typical. They usually are made up of nonpigmented epithelial cells forming solid sheets of polygonal cells formed into clusters and aggregates by thin lacy basement membranes visible with the PAS stain. The presence of cavitated spaces (Swiss cheese appearance) is a common, but not uniform, feature of feline iridociliary body tumors. Tumor cells stain positive for vimentin and are rarely positive for cytokeratin, which is an unusual staining pattern for an epithelial tumor.

## Slide 11, Neo 2091, 99RD937

The slide is of a canine third eyelid. Throughout the conjunctival surface there is a mild to moderate lymphoplasmacytic inflammatory infiltrate and intermittent areas of squamous metaplasia of the conjunctival epithelium. Toward the margin of the third eyelid there is a segment of non-neoplastic gland of the third eyelid, however, there are fairly abrupt margins with an infiltrating neoplastic gland of the third eyelid. Neoplastic glandular tissue is less organized, more basophilic, contains smaller cells with a larger nucleus to cytoplasm ratio, and mitotic figures are easily found. Neoplastic tissue forms small glandular aggregates that are distorted by solid sheets and clusters and elongate fingers or tubes of poorly differentiated epithelial cells. This tumor shows a fairly aggressive infiltrative pattern with nodules of neoplastic tissue extending into surrounding fibrovascular stroma and in some cases has the appearance of nodules of neoplastic tissue within lymphatic or vascular structures. At the surgical margin there is infiltration of neoplastic tissue within the loose connective tissue all the way to the margin causing this specimen to have a dirty surgical margin. Notice that even in the most poorly differentiated areas it is easy to find neoplastic cells that form rosette-like clusters with secretory protein material centered in the middle of the rosette, suggesting secretory activity. This case has little of a secondary inflammatory component, which is a common feature of this particular tumor. This is a typical adenocarcinoma of the gland of the third eyelid.

- 1. Lymphoplasmacytic conjunctivitis
- 2. Adenocarcinoma of the third eyelid gland with dirty surgical margins

## Slide 12, Neo 925, 96RD143

This slide is of fragments from an orbital tumor from an 11 year-old female Labrador Retriever dog. The tissue submitted is multiple lobules of friable translucent, slightly brown tissue. Histologically, the tissue sampled is a mixture of lobules of neoplastic epithelial glandular tissue and very small amounts of loose fibrovascular connective tissue including areas of adipose tissue. Neoplastic glandular tissue is made up of solid sheets and sometimes gland-like aggregates of large round to polygonal cells with an eccentric circular nucleus and foamy to eosinophilic granular cytoplasm. The solid sheets of secretory glandular epithelial cells are interspersed with fine capillary vascular structures and occasional fibrous trabeculae. Completely absent in any of the lobules are differentiated ductular structures which would be expected to be present in fully differentiated glandular tissues. In some foci, acini or tubular glandular structures can be discerned within the solid mass. The morphology of the glandular tissue is reminiscent of salivary or lacrimal gland tissue. I refer to this orbital neoplastic disease as **canine orbital adenomatosis**.

## **Diagnosis:**

#### 1. Canine orbital adenomatosis

**Comment:** This is an interesting disease. It usually presents as exophthalmus or bulging of the conjunctiva. The surgeon reports the presence of a lobulated friable tissue or in some cases more solid friable tissue. Usually, the report indicates that it is difficult to excise all the tissue and characteristic biologic behavior is to have one or several recurrences at approximately one-year intervals. I have a few cases of this disease that are bilateral. The unsuspecting pathologist might read this out as normal glandular tissue because of the high degree of differentiation of the secretory epithelial cells and the lobulated appearance of the tumor.

### Slide 13, Inf 525, 93RD203

This slide is a vertical section of the globe from a 12 year-old, spayed, female mixed breed dog. Subgrossly, it is obvious that there is thickening and a cellular infiltrate throughout the uvea, and retinal detachment. Histologically, the cornea is relatively intact. There is an intense, mixed, inflammatory infiltrate within the substance of the entire uveal tract. The posterior uvea is more affected than the anterior uvea. The infiltrate is characterized by a mixture of perivascular lymphoplasmacytic cells making up the minor portion of the infiltrate and sheets and sometimes aggregates of histiocytic cells, making up the major component. Histiocytic cells often show a scattering of melanin pigment in the cytoplasm, and in other areas they have vacuolated cytoplasm. Multinucleate giant cells are rare and difficult to find. The granulomatous or histiocytic infiltrate is more prominent in the choroid. In the choroid, there is granulomatous inflammation abutting on the choriocapillaris, most prominently seen in the tapetal retina. There is marked hyperplasia and hypertrophy of retinal pigment epithelial cells, typical of retinal detachment. There is complete retinal detachment. An interesting feature is the relative absence of inflammatory disease in the retina. The presence of aggregates of histiocytic inflammation distorting the profile of Bruch's membrane (**Dalen-Fuchs-like nodules**) is a feature to look for in making a diagnosis of canine uveodermatologic syndrome. This is a good example of canine uveodermatologic syndrome (also known as VKH-like syndrome). The morphologic and clinical features which I think are important in correctly diagnosing VKH-like syndrome are: 1) the presence of granulomatous uveitis widely dispersed over both the anterior and posterior uvea; 2) scattering of melanin pigment in the affected granulomatous uveitis; 3) the presence of **Dalen-Fuchs-like nodules**; 4) a relative absence of disease in the retina; 5) a tendency for remarkable bilateral symmetry. In cases where both eyes are available for evaluation, which is a common factor in this disease, the distribution of inflammation in the uveal tract will be similar or identical in both eyes. Depigmentation of the nose or lips is a clinical phenomenon in less than half the cases in my collection. The clinical aspect of this disease in the eye is usually associated with the development of glaucoma and retinal detachment.

#### **Diagnoses:**

- 1. Canine uveodermatologic syndrome
- 2. Retinal detachment
- 3. Dalen-Fuchs-like nodules
- 4. VKH-like syndrome

**Comment:** There are many features of this syndrome similar to human Vogt-Koyanagi-Harade syndrome (VKH). This syndrome has granulomatous uveitis with retinal detachment and glaucoma combined with cutaneous or hair depigmentation.

## Slide 14, Inf 324, 91RD76

This slide is of a vertical section through an intact feline globe. The lens is removed to facilitate sectioning. Approximately half of the cornea is fairly normal full thickness. The other half of the cornea shows marked distortion of the anterior stroma and epithelium and a return to near normal stroma in the deep stroma. The surface contour of the epithelium is markedly distorted with irregular wavy profile. The superficial stroma is no longer recognizable. There is a marked edema, irregular dilated vascular infiltrate, and a mixed inflammatory infiltrate. The inflammation is characterized by a mixture of lymphoplasmacytic inflammatory cells around blood vessels, histiocytic cells seen most commonly in the edematous area, and numerous eosinophils seen mostly in the deeper stroma. The surface epithelium is intermittently absent and in several areas, there is epithelial downgrowth into the superficial stroma. The rest of the globe is relatively intact and normal. The deep stroma, Descemet's membrane, and endothelium remain virtually normal even in the most effected segment of the cornea. This is a typical case of eosinophilic keratitis. Eosinophilic keratitis is not a disease that is very commonly seen by pathology. The features seen in this globe are typical. Typical features, in my experience, are: 1) regional involvement of extensive segments of the cornea, and sometimes conjunctiva; 2) marked irregular contour to the corneal surface; 3) extensive subepithelial stromal edema making it impossible to recognize corneal lamella superficially; 4) abrupt transition to virtually normal posterior lamellar stroma; 5) widely dilated blood vessels; 6) mixed inflammation. The presence of eosinophils is not an absolute determinant of the diagnosis of eosinophilic keratitis. Many cases are dominated by lymphoplasmacytic cells around blood vessels that include germinal follicle-like structures. Special stains usually show large numbers of mast cells in the edematous stroma.

#### **Diagnosis:**

1. Feline eosinophilic keratitis

#### Slide 15, Misc 288, 88R2820

The slide is an Alcian blue PAS-stained vertical section through the globe of an 8 week-old West Highland White Terrier thought to be congenitally blind. Histologically, many of the features of the anterior segment are those of a normal neonatal dog. Notice the thin Descemet's membrane, the lack of definitive formation of the corneal scleral trabecular meshwork, and the thin pars plicata of the ciliary body. Most sections show one or several strands of uveal tissue extending from the iris into the anterior chamber (**persistent pupillary membranes**). Although the equatorial cortex and the nuclear bow are well formed, there is posterior migration of lens epithelium (**posterior subcapsular cataract**) and **posterior cortical cataract** seen in the posterior pole and, to a lesser extent, in the anterior pole. The PAS stain shows multiple foci where the lens capsule is duplicated, both in the anterior capsule and in the posterior capsule. An additional feature is the presence of multiple **pathologic retinal folds (retinal dysplasia**).

### **Diagnoses:**

- 1. Persistent pupillary membrane
- 2. Anterior lens capsular fold wrinkling (not seen in all sections)
- 3. Posterior subcapsular cataract
- 4. Posterior cortical cataract
- 5. Duplication of lens capsule
- 6. Retinal folds
- 7. "Swedish puppy syndrome"

**Comment:** The combination of persistent pupillary membranes, congenital cataract focused on the posterior pole, sparing of the lens equator, duplication of lens basement membrane, focal wrinkling of the lens capsule (a feature not seen in all sections of this globe), and retinal folds characterize a syndrome which affects multiple puppies from litters of varying breeds of dogs always from Sweden and possibly always from the north of Sweden. Since these puppies are from many different breeds and since it is my impression that when it occurs, it affects all the dogs of a litter, this condition is thought to be a result of some teratogenic effect related to the husbandry of the pregnant bitch.

## Slide 16, Misc 202, 86R1867

This slide is a vertical section through the globe of a 7 week-old Doberman Pinscher dog. Grossly and histologically, there is **retinal detachment** with **hypertrophy of retinal pigment epithelial cells**. The margins of the detached retina, in some sections, are rounded, indicating a pathological **retinal tear**. In addition to these changes, there is a thin rim of extralenticular tissue plastered against the back of the lens capsule. The posterior capsule is thin and difficult to recognize. In most sections there are, in addition, lens epithelial cells migrated to the posterior pole (**posterior subcapsular cataract**). In most sections, some of the cells on the posterior pole of the lens are pigmented.

- 1. Retinal detachment
- 2. Retinal tear
- 3. Persistent hyperplastic primary vitreous
- 4. Posterior subcapsular cataract

### Slide 17, Misc 1572, 98RD636

This slide is a vertical section through the formalin-fixed right globe of a 10 year-old, neutered, male Golden Retriever dog. Histologically, on the posterior corneal surface there is a localized area with a **retrocorneal membrane**, which includes pigmented cells incorporated into the membrane. An attenuated endothelium extends over the retrocorneal membrane. There is **iris bombé** with posterior synechia at the pupillary margin of both iris flaps. In addition, there is a cell-poor protein membrane that extends across the pupil and is attached to the anterior lens capsule. Spindle cells and pigmented cells are incorporated in this membrane. The posterior chamber is distorted and filled by numerous, **thin-walled epithelial cysts** extending off the posterior iris and/or ciliary body. The cyst walls also line the anterior surface of the vitreous body on both sides and the pigmented epithelial membranes are adherent to the lens capsule. Inflammation is not a prominent feature of the uveal tissue. The ciliary cleft is closed. Free pigmented cells are seen in the vitreous, especially on the anterior margins of the vitreous. There is artifactual retinal detachment in the superior quadrant and throughout the retina there are decreased numbers of ganglion cells. Profound full-thickness retinal atrophy is not a feature in any segment. There is gliosis and cupping of the optic nerve head.

### **Diagnoses:**

- 1. Retrocorneal membrane
- 2. Iris bombé
- 3. Thin-walled iridociliary cysts
- 4. Chronic glaucoma
- 5. Pigmentary uveitis

**Comment:** This condition is often referred to clinically as **pigmentary uveits** in Golden Retrievers. The morphology in this section is typical. Thin-walled iridociliary cysts fill the posterior chamber, making contact with the lens capsule and, I believe, pulling the iris into the lens. In addition, the cysts probably push the iris forward, narrowing the iridocorneal angle. The role that inflammation plays in this disease is not clear on histopathology.

#### Slide 18, Misc 360, 89B829

This slide is a vertical section through the globe of a 9 year-old Cocker Spaniel dog with glaucoma. The eye was removed approximately three days after the initial presentation. Histologically, the iridocorneal angle is distorted due to the presence of a broad sheet of iris tissue extending from the iris base to the arborized terminus of Descemet's membrane (goniodysgenesis). The ciliary cleft is still visible in some sections. Some sections show the accumulation of neutrophils and pigmented debris in the dependent iridocorneal angle, and most sections show increased numbers of neutrophils in the limbus sclera, as well as plump nuclear profiles of spindle cells in the trabecular meshwork and scleral venous plexus. The corneoscleral trabecular meshwork is difficult to localize. In addition to pigmented debris in the anterior chamber, some sections show loss of pigment from the iris epithelium near the pupillary margin. The section illustrates the changes of the retina in acute glaucoma. Moving along the retina most sections show segmental areas of marked retinal edema and distortion. Full-thickness apoptosis is seen in areas destined to become full-thickness atrophy. Another lesion to look for is the presence of hypereosinophilic profiles of ganglion cells. These are necrotic ganglion cells and are usually seen only in the first few days following the initial onset of glaucoma. Only a few sections include the optic nerve, but those that do show vacuolar hypereosinophilia of the neuropil of the nerve head, indicating acute necrosis. Pyknotic debris can be seen scattered throughout the neuropil, with very little evidence of a cellular response at this early date. Within a short period of time macrophages will clear out the dead neuropil and leave a cupped optic disc. Progression of retinal atrophy also occurs rapidly and, within seven days after the onset of glaucoma, end stage retinal atrophy is expected.

#### **Diagnoses:**

- 1. Goniodysgenesis
- 2. Acute retinal necrosis, secondary to glaucoma
- 3. Acute optic nerve head necrosis, secondary to glaucoma
- **4. Pigment dispersion** (some sections)

**Comment:** In canine glaucoma, including glaucoma associated with goniodysgenesis, it is not unusual to find evidence of scraping away of pigmented epithelial cells from the posterior iris near the pupillary margin and migration of pigmented debris to the dependent iridocorneal angle within the anterior chamber.

# Slide 19, Neo 2456, 00RD858

This slide is a vertical section through an intact feline globe. The anterior uvea, and particularly the iris, is thickened and distorted due to the presence of a solid partially pigmented mass. The iris stroma is effaced by solid sheets of large polygonal to round cells characteristically with an eccentric round nucleus and a prominent nucleolus. Variable amounts of melanin pigment are seen in the cytoplasm and many cells have vacuolated or clear cytoplasm. In some solid aggregates the cellular boundaries are distinctly evident. In some areas, karyomegalic forms are easy to find, sometimes with eosinophilic intranuclear inclusions that are, in fact, cellular cytoplasm invaginated into the nucleus (**nuclear pseudoinclusion**). The tumor infiltrates into the ciliary body stroma, filling up most of the ciliary body. There is disruption of the iris epithelium and neoplastic cells spill over into the posterior chamber. The tumor infiltrates into the scleral venous plexus on both sides. The retinal profile shows a largely intact retina, but with dramatically decreased numbers of ganglion cells, indicative of glaucoma.

### **Diagnoses:**

- 1. Feline diffuse iris melanoma (extensive)
- 2. Secondary glaucoma

**Comment:** A tumor with this extensive distribution is likely to metastasize to the liver.

### Slide 20, Neo 2436, 00RD801

This slide is a section of a cat eye markedly distorted by disease. Histologically, there is fullthickness neovascular infiltrate in the corneal stroma. Descemet's membrane is segregated and separated by a more solid cellular infiltrate often on both sides of Descemet's membrane. Wrinkled remnants of empty lens capsule are seen in the expected place and the uveal tract, surrounding the lens capsule, is markedly distorted by a mixture of a lymphoplasmacytic inflammatory infiltrate and a marked mesenchymal neoplastic infiltrate. The neoplasm is characterized by the presence of highly pleomorphic and anaplastic, plump spindle cells. Neoplastic cells often have a very long profile and oval nuclei. It is easy to find mitotic figures, including abnormal mitotic figures, in the neoplastic cells. The tumor infiltrates throughout the anterior uvea, extending forward to the posterior corneal stroma and colonizing the posterior aspect of Descemet's membrane. Tumor extends deeply into the sclera, extending into the scleral venous plexus and peripheral nerves and, in some segments, there is diffuse invasion of the scleral tissue itself. Tumor extends posteriorly lining the inner aspect of the choroid and there is abundant infiltration of the tissue of the choroid, as well. Remnants of tapetal cells can sometimes be found heavily infiltrated by neoplastic cells. Some slides show a segment of metaplastic bone in the inner choroid adjacent to where the choriocapillaris would have been within the tapetal retina. The retina is confined to wrinkled remnants in the vitreous and is heavily infiltrated by neoplastic cells. In some segments of the tumor a periodic acid Schiff stain (PAS) shows the presence of thick PAS-positive membrane surrounding individual neoplastic cells, typical of cells showing lens epithelial differentiation and producing a thick basement membrane reminiscent of lens capsule around individual neoplastic cells.

#### **Diagnosis:**

1. Feline posttraumatic sarcoma showing lens epithelial differentiation

## Slide 21, Neo 1160, 97RD114

This slide is a vertical section through the globe of a 1 year-old female Alaskan Malamute dog. The dependent iridocorneal angle and ciliary body stroma subtending the pars plicata is infiltrated by a solid neoplastic mass. The neoplasm extends into the anterior chamber showing aggressive infiltration into the corneal stroma behind Descemet's membrane. Neoplastic tissue extends across the iris surface and on the opposite side of the globe there are neoplastic cells in the posterior chamber and subtending the ciliary body epithelium. Posteriorly, on the dependent side, cylindrical tubes of neoplastic tissue extend over the pars plana and peripheral retina within the vitreous. The neoplasm is made up of solid sheets of poorly differentiated small cells. There is a repeating pattern of survival of neoplastic cells around blood vessels and necrosis beyond that. Under high magnification, the individual neoplastic cells have the appearance of irregular round cells. An interesting and significant feature is the tendency for the nuclear profiles of individual neoplastic cells to push together, often molding the nuclear profile around one another. A second feature is the formation of variably distinct rosettes. Rosettes characterized by a circular rim of nuclei internal to which cytoplasm processes extend toward a pseudolumen center are seen occasionally in most sections. The retinal profile is within normal limits and there is no evidence of glaucoma.

## **Diagnosis:**

### 1. Medulloepithelioma (primitive neuroepithelial tumor)

**Comment:** The diagnosis of medulloepithelioma covers a fairly broad morphologic spectrum of tumors of primitive neural epithelial origin. In dogs, these are often tumors of young dogs and are found in the ciliary body, although they can occur in other places in the eye. This tumor has a very primitive neural appearance, but medulloepithelioma can also be a very epithelial tumor. If this tumor were in the retina, one would be hard pressed not to make a diagnosis of retinoblastoma.

### Slide 22, Inf 857, 96RD164

This slide is a vertical section through the globe of a 15 year-old Poodle dog. There is peripheral corneal stromal vascularization extending less than a millimeter into the peripheral cornea. The corneal epithelium is missing over most of the section and, in some areas, there is a very attenuated epithelium. There are no hallmarks to indicate that the epithelial loss is pathologic versus artifact. All of the chambers of the eye have a protein-rich and cellular infiltrate. There is retinal detachment and there are small numbers of cells in the subretinal space, as well as retinal pigment epithelial hypertrophy, especially in the nontapetal segment. The most striking change in this eye is an extensive mixed inflammatory infiltrate. Lymphocytes and plasmacytes tend to predominate in the substance of the uveal tract, however, histiocytes and neutrophils predominate in the anterior and posterior chamber, as well as in the vitreous. There is a repeating pattern of a solid line of histiocytes and neutrophils (pyogranulomatous inflammation) intermittently following a line surrounding the anterior uvea in both the anterior and posterior chamber, and then prominently following the ciliary body epithelium, filling the posterior chamber and the anterior vitreous space. A similar inflammatory infiltrate is seen intermittently on the anterior surface of the retina, extending into the vitreous. Causative agents are not seen. There is wrinkling of the lens capsule and **cortical cataractous** changes in the superior part of the section. Another prominent change is the pyogranulomatous inflammation seen in the limbus sclera. There is a tendency toward breakdown of limbal scleral collagen, although staphyloma is not yet a problem. Another prominent feature is a repeating tendency for the inflammation to involve blood vessels directly. There are several vascular profiles in the limbus sclera and also in the retina where the inflammatory infiltrate involves the blood vessels directly (vasculitis). Perhaps because of the vasculitis, sections of the peripheral retina show coagulation necrosis (**necrotizing retinitis**). Sections that include the optic disc show a rich lymphosuppurative and histiocytic **papillitis**. In the protein-rich vitreous behind the lens there are **asteroid hyalosis** bodies that are of no significance regarding the inflammatory disease. As is often the case with severe ocular inflammation, there is not an obvious cause of disease apparent in the eye. Broad sheets of pyogranulomatous inflammation lining the uvea are a flag to me suggesting that immunogenic processes are at work. I would worry about the possibility of inflammation in the second eye.

#### **Diagnoses:**

- 1. Lymphoplasmacytic suppurative and granulomatous panuveitis
- 2. Necrotizing retinitis
- 3. Multifocal vasculitis
- 4. Mature cortical cataract

- 5. Asteroid hyalosis
- 6. Papillitis
- 7. Pyogranulomatous inflammation
- 8. Asymmetric uveitis

**Comment:** The granulomatous change of the uveal surface along with retinal necrosis are features of what I call asymmetric uveitis because the second eye is at risk of similar disease and can be treated with anti-inflammatory drugs.

#### Slide 23, Misc 2155, 00RD701

This slide is a vertical section from the right eye of a 16 year-old Cockapoo. The corneal epithelium is intact and there is a moderate amount of mid-stromal corneal vascularization, with extensive hemorrhage in the posterior chamber. Broad sheets of iris pigmented epithelium are adherent to the anterior surface of the lens, suggesting **iris bombé**. Hemorrhage extends into the vitreous. There is complete retinal detachment, with multifocal areas of intraretinal hemorrhage and hemorrhage in the vitreous as well. There is extensive retinal atrophy, with anatomic disarray in the atrophic retina. There is asteroid hyalosis in the proteinaceous and hemorrhagic vitreous behind the lens. There is a **cortical cataract**, with posterior migration of lens epithelial cells forming a posterior subcapsular cataract, most prominent on the superior aspect of the globe. Although the retina is detached, there are several subretinal fibrous and neovascular membranes internal to the choriocapillaris. An Alcian blue PAS stain was also done on this eye and you should carefully examine both sections, looking at vascular profiles in both the retina and the choroid. Thick hypereosinophilic profiles or thick lamellar profiles are typical of vasculopathy associated with systemic hypertension (hypertensive vasculopathy). This lesion is most trustworthy when found in the choroid. Segmental areas of retinal necrosis, retinal fibrin deposition, or choroidal neovascular membranes are often associated with systemic hypertension and hypertensive vasculopathy should be checked for with an Alcian blue PAS stain whenever unexplained hemorrhage or fibrin exudates are seen in the retina or choroid.

### **Diagnoses:**

- 1. Corneal stromal neovascularization
- 2. Pre-iridal fibrovascular membrane
- 3. Peripheral anterior synechia
- 4. Iris bombé
- 5. Intraocular hemorrhage
- 6. Retinal detachment
- 7. Hypertensive vasculopathy
- 8. Asteroid hyalosis

**Comment:** It is important to stress the necessity to examine the eye with a PAS stain to look for hypertensive vasculopathy. The changes can be subtle and easily missed with only on H&E stain.

#### Slide 24, Inf 559, 94RD038

This slide is a vertical section through the globe of a 9 year-old, intact, female cat and there is a gram stain only. Histologically, there is protein and exudate in the anterior and posterior chamber, as well as the anterior vitreous. The iris is bowed forward and there is posterior synechia at the pupillary margin on both sides, suggesting **iris bombé**. There is a lymphoplasmacytic inflammatory infiltrate in the substance of the anterior uveal tract and a suppurative inflammation filling what remains of the posterior chamber. There is rupture of the anterior lens capsule with suppurative inflammatory infiltrate extending into the lens substance. If you look in the superficial cortex adjacent to the anterior capsule extending all the way to the nuclear bow on both sides within the lens under high magnification, you will see clusters of gram-positive cocci, gram-positive rods and, in some areas, gram-negative rods. You will find organisms in areas that do not have suppurative inflammation.

#### **Diagnoses:**

- 1. Endophthalmitis
- 2. Iris bombé
- 3. Suppurative inflammation associated with lens capsule rupture
- 4. Septic implantation syndrome

**Comment:** Suppurative inflammation associated with lens capsule rupture and broad posterior synechia should always cause a careful search for implanted bacteria in the lens. Even when bacteria cannot be found, it is my opinion that suppurative inflammation associated with lens capsule rupture is associated with traumatic implantation of bacterial organisms in the lens, usually associated with a cat scratch.

### Slide 25, Neo 1849, 99RD377

This slide is a vertical section through the eye of a 15 year-old domestic short hair cat. Much of the intraocular structure is missing. Only remnants of wrinkled lens capsule can be found in some sections. In other sections, no lens remnants are seen. The section is cut on the periphery of the cornea and the corneal stroma is heavily infiltrated with basophilic cellular infiltrate. Descemet's membrane is pathologically ruptured in several areas and some sections show scrolling of Descemet's membrane. Iris tissue and ciliary body tissue are not recognizable, except for a hint of pigmented cells. Choroidal tissue is more recognizable and the tapetum is easily discernible in the posterior quadrant. The uveal tract is circumferentially effaced by basophilic cellular infiltrate that extends into a zone of coagulation necrosis. Basophilic cells survive around blood vessels extending inward into the necrotic coagulated tissue. Careful examination of the sheets of basophilic cells shows a mixture of cells. In some areas there is clearly a lymphoplasmacytic inflammatory infiltrate. However, in other areas, there is a more monomorphic population of anaplastic round cells, typical of lymphosarcoma.

### **Diagnosis:**

## 1. Feline posttraumatic sarcoma (round cell variant)

**Comment:** This variant of the posttraumatic sarcoma fails to stain with PAS for basement membranes and fails to stain for other markers that might suggest a lens epithelial origin. In my opinion, this tumor is the equivalent of lymphosarcoma that occurs in the face of anterior uveal lymphoplasmacytic uveitis. The posttraumatic variant occurs circumferentially around the globe mimicking a more classical variety of posttraumatic sarcoma. The characteristic features are the presence of round cells in solid sheets, and the presence of coagulation necrosis centrally, and survival of tumor cells around blood vessels.

### Slide 26, Neo 949, 96RD189

The slide is a vertical section of a cat eye. The cornea is largely within normal limits, except that the endothelium is artifactually detached and disrupted because of a cellular infiltrate which consists of a mixture of neoplastic round cells, red blood cells, cellular fragments, and free melanin pigment. In addition, histiocytic cells, often containing melanin or hemosiderin pigment, are also disrupting the endothelium. In some areas, there is a **retrocorneal membrane**. The corneal epithelium is thin, but largely intact. The anterior uvea, including the ciliary body and iris stroma, is heavily infiltrated with a mixture of neoplastic round cells and smaller numbers of histiocytes, neutrophils, and tissue edema. Areas of neoplastic infiltrate consist of solid sheets of large lymphoblastic cells pushed between preexisting uveal stromal features. There is a tendency for the neoplastic cells to colonize the iris epithelium and, even more so, the ciliary body nonpigmented epithelium. Tumor cells extend in the ciliary body stroma to the pars plana. There is little evidence of a secondary inflammatory lymphoplasmacytic infiltrate and the neoplastic infiltrate is quite diffuse throughout the anterior uvea. Smaller numbers of neoplastic lymphocytes are seen intermittently in the choroid. The retinal profile returns to normal, with no evidence of glaucoma.

### **Diagnoses:**

- 1. Anterior uveal lymphosarcoma
- 2. Retrocorneal membrane

**Comment:** About half the cases of intraocular lymphosarcoma in cats occur in eyes that have a concurrent lymphoplasmacytic inflammatory infiltrate and neoplastic infiltrate and half the cases occur, as in this eye, as a purely neoplastic infiltrate. Those cases in which the neoplastic infiltrate occurs in the absence of lymphoplasmacytic inflammation, tend to have a more diffusely infiltrative neoplasm in the anterior uvea. In both cases, the tumor is primarily anterior uvea.

### Slide 27, 84R1410, New Zealand Dog Eyes

This slide is a vertical section through the eye of a blind adult sheep-herding dog from New Zealand. The lens has been removed. Disease is limited to the posterior segment. There is profound retinal atrophy ranging from areas where there is identifiable lamellar retina in the periphery, to other areas centrally where the retina consists of nothing more than glial cells, sometimes with perivascular fibrin deposition and occasional pigmented or nonpigmented phagocytes. The central nontapetal retina and choroid are usually the most severely affected. In addition to end-stage retinal atrophy, the most severely affected areas also have **choroidal fibrosis** with evidence of **vasculitis**. Careful examination in the area near the choriocapillaris shows the presence of mineralized lamellar deposits seen in small numbers subtending the markedly atrophied retina. Inflammation is minimal, but lymphoplasmacytic inflammatory infiltrates predominate, and occasional clusters and aggregates of macrophages are seen, both in the choroid and in the retinal remnants.

### **Diagnosis:**

# 1. Necrotizing, chronic chorioretinitis

**Comment:** This pattern of disease I have seen infrequently, but almost always in working dogs and in populations of dogs where one might expect a high exposure to *Toxocara canis*. Dogs affected with this type of disease usually go blind from bilateral chorioretinitis at about two years of age. The morphology is quite characteristic, but I have never been able to find parasites to document the cause and effect relationship. In the New Zealand dogs, younger dogs with less severe inflammation and still visual often have granulomatous disease with worm larvae present. Older dogs remain visual and have localized areas of retinal atrophy and pigment migration, and histologically these areas correspond to a mild lymphoplasmacytic inflammatory infiltrate. Again, no worms were recognized in the older population of dogs.

#### Slide 28, Inf 2048, 00RD1102

The slide is a vertical section through the globe of a 7 month-old domestic medium hair cat. Upon sectioning the globe, there was thick, fixed, semisolid protein material in all ocular compartments. Histologically, the cornea is relatively intact. There is a thick protein exudate in the anterior chamber. There is a mixed inflammatory infiltrate in the iris with a high lymphoplasmacytic component, but no germinal follicles. In addition, there are foamy macrophage cells free in the fluid in the anterior chamber. The posterior iris epithelium is infiltrated with a mixed inflammation, including neutrophils extending into the protein-rich exudate in the posterior chamber. In the dependent iridocorneal angle and in the dependent posterior chamber there are macrophage cells that appear to be phagocytosing neutrophils. There is a rich inflammatory infiltrate associated with the nonpigmented ciliary body epithelium, including lymphoplasmacytic cells, neutrophils, and macrophages. There is retinal detachment with a protein-rich fluid in the subretinal space, as well as a mixture of inflammatory cells. The retinal inflammation is quite striking. It is characterized by distortion of the retinal profile associated with edema and gliosis, and a marked vasocentric inflammatory infiltrate. Carefully examine the inflammation associated with retinal blood vessels, and you will find that in several instances the inflammation is not just around the blood vessels but incorporates the wall of the blood vessel as well. Again, the inflammation is mixed with a lymphoplasmacytic, histiocytic, and neutrophilic component, including retinal vasculitis. There is a lymphoplasmacytic and histiocytic inflammatory infiltrate in the meninges of the optic nerve, but the nerve itself is relatively spared. Within the vitreous there is a protein-rich fluid and a rich inflammatory infiltrate which is a mixture of large macrophage cells, lymphocytes, and neutrophils.

#### **Diagnoses:**

- 1. Lymphoplasmacytic and suppurative panuveitis
- 2. Lymphoplasmacytic retinitis with retinal vasculitis
- 3. Lymphoplasmacytic, histiocytic, and suppurative optic nerve meningitis
- 4. Consistent with a diagnosis of feline infectious peritonitis and ocular inflammation

Comment: The features of this inflammatory disease that are suggestive of FIP are: 1) the rich protein exudate in the chambers of the eye (on gross examination the protein-rich fluid appeared fixed as semisolid exudate); 2) mixed inflammation; 3) vasculitis. A fourth feature that I look for that is not particularly well illustrated here is the presence of solid granulomatous inflammation in some part of the inflammatory disease. This cat has a histiocytic component to the inflammation in most areas, but actual granuloma formation is not a prominent feature. In FIP, the granulomatous inflammation is often characterized by atypical features in the histiocytes.

#### Slide 29, Inf 1382, 98RD698

This slide is a vertically cut section of the left globe from a 12.3 year-old spayed female Bull Mastiff dog. The dog developed clinical disease after phacoemulsification. There is moderate peripheral vascularization of the corneal stroma. There are several ruptures of Descemet's membrane in the superior peripheral cornea. The more peripheral of these ruptures is presumed to be the surgical site (not in all sections). There are also several ruptures of Descemet's membrane in the dependent peripheral cornea (Haab's striae), and there is an anterior synechia in the dependent cornea. Notice that there is, intermittently, a doubling of Descemet's membrane (a tinctorial change creating the effect of two Descemet's membranes). This is probably due to damage to the endothelium or damage to Descemet's membrane at the time of surgery. Intermittently on the posterior cornea there is a **retrocorneal membrane** characterized by spindle cells and collagen rather than endothelial cells. The lens capsular bag is wrinkled and collapsed on itself. Within the capsule there is a cell-poor glassy collagen matrix. This collagen matrix was deposited by lens epithelial cells that have subsequently degenerated. There is a thick pre-iridal fibrovascular membrane with ectropion uvei on the superior iris leaflet. In addition, there is **peripheral anterior synechia**. The pre-iridal membrane extends through the pupillary margin and across the iris epithelium on the inner aspect lining the posterior chamber. There is an Alcian blue PAS stain of this eye also and that stain demonstrates basement membrane deposition around the spindle cells creating the pre-iridal and posterior iridal membranes, suggesting that they are of lens epithelial origin. A similar membrane can be seen streaming away from the wrinkled lens capsule posteriorly towards the pars plana. In the dependent aspect there is a glassy collagen membrane associated with wrinkling of the pars plana creating traction on the retina. Traction from this lens epithelial membrane may have been responsible for the retinal detachment. There is hemorrhage in the vitreous body. There is complete retinal **detachment** and there is retinal pigment epithelial cell hypertrophy. There is marked gliosis of the optic nerve head, typical of glaucoma. The detached retina is devoid of ganglion cells, also typical of glaucoma.

- 1. Status post-cataract surgery
- 2. Lens epithelial membrane on the iris and attached to the pars plana
- 3. Peripheral anterior synechia
- **4. Doubling of Descemet's membrane** (not in all slides)
- 5. Retrocorneal membrane
- 6. Ruptured Descemet's membrane
- 7. Complete retinal detachment
- 8. Secondary glaucoma

## Slide 30, Misc 590, 93B001

This slide is a vertical section through the globe of a 1 year-old female Weimaraner dog. The dog was kicked in the head by a horse 24 hours prior to enucleation. Lesions are limited to the retina. There is a segmental area of nontapetal retina with acute changes of tissue disruption and necrosis. Carefully follow the inner and outer segments of the photoreceptor layer starting within the tapetum and traveling ventrally and you can see the disruption of the retinal pigment epithelium. After noticing this change, then carefully go back and look at the nature of the outer segment nuclei using high magnification and you will see nuclear pyknosis in the affected retina. This is a good example of acute retinal contusion. Over about a three-day period of time this retina will implode and recruit macrophage cells and undergo a rapid degeneration.

# **Diagnosis:**

1. Acute (24 hours) retinal contusion with photoreceptor apoptosis

## Slide 31, Misc 1933, 99N723

This slide is a vertical section through a neutered male, 5 year-old, German Shepherd eye. Changes are primarily in the retina. Beginning in the nontapetal retina, there are segmental areas of retinal atrophy. The retinal atrophy involves only the outer segment in some areas, returning abruptly to a more normal configuration and then a more profound atrophy in the more peripheral retina. In some segments, there is a marked decrease in retinal integrity with apoptotic profiles of the photoreceptor nuclei and macrophage cells cleaning up necrotic debris. In at least two abrupt foci there is complete retinal atrophy, and in the most peripheral retina there is **retinal schisis**. Notice that the inner limiting membrane and the retinal blood vessels form a membrane covering the top of the gliotic posterior retina. This retinal schisis lesion extends to the far periphery, where it becomes incorporated in peripheral cystoid degeneration. Notice within the retinal schisis there are clusters and aggregates of macrophage cells hinting at the acute nature of the retinal degeneration.

## **Diagnoses:**

- **1. Retinal contusion** (3 to 5 days)
- 2. Retinal schisis

**Comment:** I would estimate that the retinal trauma in this case occurred 3-5 days prior to removal of the eye. This dog had neurologic disease (GME) and there was an incident of falling down the stairs several days before euthanasia. Abrupt retinal atrophy with gitter cells and involving any or all layers are the morphologic features that suggest trauma.

## Slide 32, Misc 2299, 00RD1081

This slide is a vertically sectioned globe from a 7 year-old, neutered male Golden Retriever dog. The most striking change is the presence of extensive subepithelial granulation tissue extending from about the axial cornea well into the conjunctival tissue on the superior aspect. Centrally in the cornea, the **granulation tissue** is recognizable as a pannus of blood vessels, with replacement of the lamellar stroma by granulation tissue. Within the cornea the blood vessels and fibroblasts are mainly oriented parallel to the anatomic corneal lamellae. In the conjunctiva the tendency is for blood vessels to run perpendicular to the surface and for collagen to be deposited parallel to the surface epithelium. The epithelium is intermittently lost with areas in which there is failure of attachment of the corneal epithelium. In the conjunctiva of the epithelium there is a thickened stratified squamous epithelium with intermittent areas of ulceration associated with exuberant granulation tissue bulging through the epithelium. The inflammatory component is minimal and, remarkably, the deep corneal stroma is almost normal, with the exception of artifactual folds, and the iridocorneal angle is open. The structures of the globe are largely within normal limits. There are incidental pigmented **iridociliary cysts** in the posterior chamber. This dog was exposed to muriatic acid (HCl) that caused an acid burn on the cornea and conjunctiva.

## **Diagnoses:**

- 1. Corneal and conjunctival ulceration and granulation tissue involving the superficial tissues secondary to acid burn
- 2. Incidental iridociliary epithelial cysts in the posterior chamber

**Comment:** Acid burns are notorious for the tissue damage that they cause, but acid does not tend to extend deeply into tissue, hence the sparing of the intraocular structures and the deep corneal and scleral structures.

# Slide 33, Neo 2555, 00RD1096, Neo 1083, 96RD530

The slide contains two fragments of conjunctival tissue from a 12 year-old Basset Hound and a 13 year old Labrador Retriever dog. Both fragments show an exophytic papillary growth covered in most areas by a thickened conjunctival epithelium with squamous metaplasia secondary to exposure. Subtending the epithelium in both pieces there is a cellular infiltrate made up of a mixture of lymphoplasmacytic inflammatory cells and a neoplastic infiltrate. In the larger tissue (Basset Hound) the neoplasm is a multilobulated mass made up of pleomorphic mesenchymal cells ranging from spindle cells to stellate cells. The neoplastic cells often line interconnecting small vascular channels filled with red blood cells. In other areas red blood cells percolate between solid sheets of neoplastic cells. The neoplastic cells have a relatively high nucleus to cytoplasm ratio and mitotic figures in neoplastic cells can be found fairly easily. Because of the lack of differentiation, cellular atypia, and mitotic activity this tumor would be characterized as a hemangiosarcoma. The smaller mass (Labrador Retriever) also shows an epithelial covered exophytic mass with squamous metaplasia secondary to exposure. Once again there is a prominent lymphoplasmacytic inflammatory response and, in the connective tissue, there are large well-differentiated interconnected vascular channels that interdigitate with the surface epithelium. Dilated vascular channels close to the surface, subtending the epithelium, often show thrombosis. Because of the high degree of differentiation and lack of cellular features of anaplasia this mass could be characterized as a conjunctival hemangioma. In both cases the tumors show an intimate interdigitating reaction with the surface epithelium. This intimate association is responsible for the exophytic papillary appearance frequently seen in conjunctival endothelial tumors.

- 1. Conjunctival hemangiosarcoma (larger tissue)
- 2. Conjunctival hemangioma (smaller tissue)

# Slide 34, Neo 2598, 00RD1194, Neo 3050, 01RD1025, Neo 631, 94RD247, Neo 3101, 01RD1173

This slide contains two specimens from different dogs. Both specimens show verrucous, exophytic, wart like proliferations made up of keratinizing stratified squamous epithelium. The specimen with the looser papillary arrangement is a reactive squamous papilloma that can occur in dogs of any age on the eyelid margin, conjunctiva, third eyelid, or cornea. Often but not always there is a history of exposure, inflammation, irritation, or other underlying disease processes related to the development of reactive squamous papilloma. The tumor is papilliferous with arborizing branches of keratinizing stratified squamous epithelium. Each frond proliferative epithelium is associated with a mesenchyme containing blood vessels, fibroblasts, and usually inflammatory cells. There may or may not be a strata of granulosum and you will not find large dysplastic clear cells in the stratum granulosum. The other specimen is a canine viral papilloma. These tumors usually developed young dogs in the can occur at on the eyelid, conjunctiva, third eyelid, or cornea. The proliferating stratified squamous epithelium tends to be more tightly aggregated and interconnected. A prominent stratum granulosum is a hallmark feature of viral papilloma. Diffuse search in the stratum granulosum you will find localized areas where the epithelial cells become large round with clear cytoplasm and abnormal keratohyalin granules. These cells are referred to as koilocytes.

- 1. Reactive squamous papilloma
- 2. Canine viral papilloma

## Slide 35, Misc 2323, 00RD1204

The slide is a vertical section through a cat eye. Disease is limited to the posterior segment. There is profound **retinal atrophy** involving the whole tapetal retinal and the central nontapetal retina. Over most of the field there is end stage retinal atrophy with only a thin glial membrane remaining. Intermittently, short segments of intact retinal pigment epithelial cells can be found. Centrally, the atrophied retina shows more preservation of the inner retina and then intermittently becomes end stage atrophy until there is a point where, abruptly, the retina returns to a normal profile in the dependent retina and the normal retinal profile extends all the way to the far periphery. No other lesions are seen in the rest of the globe.

# **Diagnosis:**

## 1. End stage retinal atrophy, secondary to trauma

**Comment:** This cat was a student's surgery cat and was thought to have an eyelid mass, as well as the fundoscopic changes noted. The eyelid mass turned out to be a copper BB and the retinal lesions are consistent with traumatic retinal atrophy. The features that suggest trauma as a cause of disease in this cat are the abrupt margins of the retinal degeneration, the fact that any segment of retina can be involved, and in much of the retina the entire retina is atrophied. The date of the traumatic event was not known.

## Slide 36, Neo 2616, 00RD1247

The slide is a vertical section through the globe of an 8 year-old neutered male dog. There is mild mid-stromal vascularization in the dependent peripheral cornea. The obvious lesion is a destructive mass that effaces the stroma of the dependent iris and ciliary body. Clusters and aggregates of pigmented cells are all that remain of the iris and ciliary body stroma. About 80% of the mass tissue is made up of cell-poor, eosinophilic material that has ghost-like remains of neoplastic tissue (coagulation necrosis). At the margins of the necrotic areas there are surviving clusters and aggregates of neoplastic epithelium, often forming palisaded ribbons of poorly differentiated epithelial cells. There is aggressive infiltration of very poorly differentiated neoplastic cells extending into the inner aspect of the sclera and into the cornea behind Descemet's membrane. In addition, there are aggregates of neoplastic cells infiltrating into the peripheral retina tissue, and in the subretinal space in some sections. In the anterior vitreous there are asteroid hyalosis bodies, and in the iris on the opposite side of the eye from the mass there is a pre-iridal fibrovascular membrane, but it does not span the iridocorneal angle. There is retinal detachment with hypertrophy of retinal pigment epithelial cells. The detached retina has numerous ganglion cells, suggesting that glaucoma is not a problem in this eye.

## **Diagnoses:**

- 1. Iridociliary adenocarcinoma
- 2. Pre-iridal fibrovascular membrane
- 3. Asteroid hyalosis
- 4. Retinal detachment

**Comment:** Asteroid hyalosis and pre-iridal fibrovascular membrane are common findings concurrent to iridociliary epithelial tumors. I use a designation of adenocarcinoma when iridociliary epithelial tumors aggressively infiltrate into the sclera. Even with infiltration into the sclera, the tumor virtually never metastasizes.

## Slide 37, Neo 2634, 00RD1248

This is a section of the nictitans gland from a 9 year-old, neutered, male Cocker Spaniel dog. The section shows the leading edge of the nictitans with glandular tissue on both sides of the nictitans cartilage. There is squamous metaplasia intermittently on the conjunctival surface and, in addition, there is a moderate to intense lymphoplasmacytic inflammatory infiltrate subtending the epithelium. There is a nodular mass bulging on the bulbar surface of the nictitans conjunctiva. The nodular mass is within the gland of the nictitans. Also, in the gland of the nictitans, there is a periductular lymphoplasmacytic inflammatory infiltrate including lymphoid follicles. Away from the inflammation and away from the nodular mass, the gland of the nictitans returns to near normal configuration. The mass is sharply delineated and encapsulated. The mass is composed of a complex interplay of tubular and ductular epithelium, sometimes forming papillary structures. There is also a distinctive mesenchyme made up of stellate cells and abundant light bluish extracellular matrix and other areas where the extracellular matrix dominates. In the bluish areas the mesenchymal cells exist in lacunar-like spaces typical of cartilage tissue. This is an encapsulated complex adenoma of the gland of the third eyelid. This tumor is in every way analogous to a complex adenoma of the mammary gland and all of the glandular tissues of the body which contain a myoepithelium as a component of the secretory apparatus (mammary, sweat glands, salivary glands, and lacrimal glands) have the potential of forming complex tumors with a myxomatous, cartilaginous, or osseous component. In most instances, these tumors are benign and that is the case in this particular tumor.

#### **Diagnosis:**

1. Complex adenoma of the third eyelid

## Slide 38, Inf 1969, 00RD900, Inf 1858, 00RD473

The tissues on the slide are from two different dogs with nodular masses in the conjunctiva. Both masses are fairly sharply delineated, surrounded by normal subconjunctival connective tissue and made up of a solid mass that effaces the connective tissue. In one of the sections the epithelium is not apparent. In both sections there is a mixture of lymphoplasmacytic inflammatory cells with a more abundant population of larger pink cells. In the smaller mass, the larger pink cells form solid sheets, often sprinkled with lymphoplasmacytic inflammatory cells. The nuclear morphology is variable but lacks distinctly anaplastic features. Multinucleate cells can sometimes be found in this lesion, but are difficult to find in this particular example. The larger mass is similarly arranged, but many of the larger pink cells in much of the mass are made up of spindle cells, sometimes forming tight clusters and aggregates or whorls. Once again, the nuclear morphology is somewhat variable, but clearly anaplastic features are lacking. Both of these lesions are **nodular granulomatous episcleritis**. The larger mass with the prominent spindle cell component has a pattern that is often referred to as **nodular fasciitis**.

# **Diagnoses:**

- 1. Nodular granulomatous episcleritis (granulomatous type)
- 2. Nodular granulomatous episcleritis (nodular fasciitis type)

**Comment:** The diagnostic features of NGE are: 1) a distinct mass lesion; 2) mixture of histiocytic and lymphoplasmacytic inflammation; 3) a lack of clearly granulomatous nodules; 4) minimal neutrophils.

## Slide 39, Inf 1968, 00RD898

This slide is a vertical section of the globe from a 4 year-old, spayed, female Dachshund dog. Histologically, in the peripheral cornea, there is a moderate corneal stromal vascular infiltrate at all levels of the cornea. In the central cornea, there is a full-thickness defect characterized by interruption of all layers of the cornea and held together purely by fibrinous exudate and hemorrhage. At the margins of the full-thickness corneal defect are lesions classical for keratomalacia and characterized by lysis of the collagen of the lamellar stroma. The collagenolysis is associated with a suppurative inflammatory infiltrate. There is also a rupture of Descemet's membrane but no evidence of iris prolapse. Some sections show small microscopic foci of what appear to be epithelial cells hugging the anterior iris surface, which is perhaps the earliest evidence of epithelial downgrowth. In addition, there is a very thin, preiridal fibrovascular membrane. The iridocorneal angle is surprisingly open on both sides and there is a mild lymphoplasmacytic inflammatory infiltrate around blood vessels of the iris and ciliary body. The other obvious disease in this eye affects primarily the dependent sclera of the limbus and, to a lesser extent, the superior sclera extending all the way around to almost the optic nerve. Scleral lesions are characterized by lysis of scleral collagen and accumulation of inflammatory cells which, in some areas, are lymphoplasmacytic but, in many areas, also contain sheets of histiocytic cells and, in some cases, suppurative inflammation with necrosis in the center of the granulomatous inflammation (granulomatous scleritis). Degenerate or hyalinized collagen is often a feature and some people use the word collagen necrosis or collagenolysis to describe this tinctural collagen change. In addition to scleral disease, there is **retrobulbar fibrosis** with collagen-rich scar tissue accumulating on the orbital side of the sclera. The sclera of the superior limbus is thinned and probably at risk of **staphyloma** formation. There is artifactual retinal detachment and a moderate amount of lymphoplasmacytic choroiditis.

#### **Diagnoses:**

- 1. Central corneal keratomalacia
- 2. Central corneal rupture
- 3. Granulomatous scleritis
- 4. Thin preiridal fibrovascular membrane
- 5. Microscopic evidence of epithelial downgrowth

**Comment:** Granulomatous scleritis is a disease of unknown etiology in dogs. In my experience, there is a risk of similar disease occurring in the second eye.

## Slide 40, Neo 2988, 01RD907

The slide contains a vertically sectioned left globe from a 5 year-old neutered male German Shepherd dog. The iris on both sides and to a minimal extent the ciliary body on the dependent side are infiltrated by a neoplastic spindle cell mass. The iris pigmented epithelium is largely spared. Noticed that there is profound **choroidal hypoplasia** and an absence of pigment in the choroid and ciliary body. These changes are consistent with a **blue eyed dog**. The tumor is made up of pleomorphic spindle cells with a background of collagen. Spindle cells are arranged in fascicles showing a different spatial arrangement in different fascicles. Occasional cells with large nuclei are found. Multiple localized areas of perivascular lymphoplasmacytic inflammatory infiltrate are seen at all levels of the tumor. The tumor extends a short distance into the ciliary body stroma. The retina is devoid of ganglion cells suggesting glaucoma.

## **Diagnoses:**

- 1. Spindle cell tumor of the iris of a blue eyed dog
- 2. Secondary glaucoma

**Comment:** These spindle cell tumors occur almost exclusively in blue eyes. For that reason there is a breed predilection for breeds that commonly have blue eyes such as Siberian Husky. Glaucoma is a common secondary consequence. The cell of origin of these tumors is not completely understood, however at least some of these tumors appear to be derived from Schwann cells.

# Slide 41, Misc 2347, 01RD25

This slide is a keratectomy specimen from the superficial cornea of a 6 year-old, Cocker Spaniel dog. The epithelium is intact, however there is a cellular infiltrate subtending the epithelium and superficial stroma. The infiltrate has several components, including blood vessels, perivascular lymphoplasmacytic inflammation, and aggregates of histiocytic cells, often showing multinucleate giant cells. Histiocytic cells tend to surround elongate spindle-shaped, empty spaces that are classical cholesterol clefts.

# **Diagnosis:**

1. Superficial, granulomatous keratitis with intrastromal cholesterol granuloma

## Slide 42, Misc 2376, 01RD73

This slide is the vertically sectioned, formalin-fixed left globe from a 12 year-old, spayed, female Lhasa Apso dog. There is a history of lens removal two years prior to enucleation. The globe is a very large aphakic globe. Histologically, there is extensive, neovascular, and inflammatory infiltrate in the superficial cornea. The corneal epithelium is thickened and there is a prominently thickened corneal basement membrane intermittently. The thickened corneal basement membrane suggests repeated bouts of ulceration with healing. Descemet's membrane is only intermittently found on the back of the cornea. Lining the back of the cornea and extending over the anterior surface of the iris there is a layer of variably differentiated stratified squamous epithelium, sometimes with keratinization (epithelial downgrowth). In the superior limbus there is an island of stratified squamous epithelium in the midstroma, suggesting the presence of a deep scar at this point, probably the source of epithelial downgrowth. There is inner retinal atrophy with decrease in ganglion cells, and cupping and gliosis of the optic nerve head, typical of **chronic glaucoma**. There are cavitated clear lesions surrounded by glial cells in several levels of the optic disc filled with poorly-staining mucinous material, typical of Schnabel's cavernous atrophy. There is artifactual retinal detachment. The choroid is markedly thin but, nonetheless, pigmented and there is no evidence of lens tissue.

# **Diagnoses:**

- 1. Chronic superficial keratitis
- 2. Intrastromal corneal epithelial downgrowth in the superior peripheral cornea
- 3. Epithelial downgrowth into the anterior chamber
- 4. Multiple and broad ruptures in Descemet's membrane
- 5. Preiridal fibrovascular membrane
- 6. Aphakic globe (post-op lens removed)
- 7. Cupping and gliosis of the optic nerve head (Schnabel's cavernous atrophy)
- 8. Inner retinal atrophy
- 9. Chronic glaucoma

**Comment:** Segments of retinal tissue have large numbers of ganglion cells. There is not an obvious explanation for this. I have a theory that, when glaucoma occurs following retinal detachment, the ganglion cells are relatively spared. That does not appear to be the case in this animal, since the retinal detachment has morphologic features suggesting that it is an artifact, specifically, remnants of inner and outer segments are still adherent to the normal retinal pigment epithelium. Epithelial downgrowth probably occurred along the surgical incision site and, over the two years' time postoperatively, normal-appearing stratified squamous epithelium has colonized the anterior chamber.

# Slide 43, Neo 2702, 01RD2.5

This slide shows tissue sampled from the third eyelid conjunctiva and segments of haired skin from a 10 year-old spayed female Labrador Retriever dog. The pertinent abnormalities are in the conjunctival sections. Bulging outward from the palpebral surface of the third eyelid, there is a nodular mass lesion. In some areas, especially at the margin, there are prominent numbers of heavily pigmented round cells, however, most of the mass is nonpigmented. In the center of the mass, the normal connective tissue is effaced by solid sheets of highly pleomorphic polygonal cells with a large nucleus to cytoplasm ratio and abundant mitotic activity. The nuclei are irregular, with coarse chromatin clumping, and often contain very large single or multiple nucleoli. Only occasional clearly neoplastic cells can be found that have cytoplasmic melanin pigment. However, a careful search near the areas of pigmentation show clearly pigmented neoplastic cells. Closely examine the surface conjunctival epithelium adjacent to the mass. There is a mixture of lymphoplasmacytic inflammatory cells and a very complex interdigitation of the epithelium and the subepithelial tissue. In some areas where the mass is largest, the epithelium is lost and there is an ulcerative reaction. Notice the presence of small clusters of neoplastic cells, either abutting on the epithelium, or in many cases, directly within the epithelium. Move now to the conjunctival surface on the bulbar surface of the third eyelid. Again, you will notice a nonspecific lymphoplasmacytic inflammatory infiltrate and drop-off of melanin pigment. However, you will also see many small clusters of neoplastic cells either abutting on the epithelium or directly within the epithelium. This is a classical appearance of **conjunctival** malignant melanoma. The presence of aggregated dysplastic or neoplastic melanocytes, both immediately adjacent to the tumor and in the conjunctiva away from the tumor, are fairly typical of malignant melanoma of the conjunctiva. Solitary primary tumors which are removed will often recur as multifocal tumors of the conjunctiva because of these aggregated rests of neoplastic cells widely distributed in the conjunctival tissue. This tumor not only has a propensity to recur locally, but lymph node and hematogenous metastasis are reported.

## **Diagnosis:**

1. Conjunctival amelanotic malignant melanoma

## Slide 44, Neo 1133, 97RD051

This slide is a horizontally sectioned globe from an 11 year-old neutered male domestic shorthair cat. On subgross examination, there is an asymmetrical nodular distortion of the iris. Histologically, away from the mass lesion there is a prominent lymphoplasmacytic inflammatory infiltrate most prominently seen on the anterior surface of the iris and in the trabecular meshwork of the iridocorneal angle. A similar infiltrate can be seen on the iris leaflet that was distorted by the mass lesion. However, the mass itself is composed of solid sheets of large, irregular, round cells with coarse chromatin clumping, often with a prominent nucleolus and a fairly prominent mitotic index. Intermittent areas of coagulation necrosis are scattered across the mass lesion. The retina is largely depleted of ganglion cells and the optic nerve (in sections cut through the optic nerve) shows cupping and gliosis of the neuropil. Notice that the retina, although deficient in ganglion cells, is largely within normal limits in every other way. This is typical of glaucoma in cats. Whereas in dogs the entire retina is at risk of necrosis and atrophy, in cats, unless there is some other factor in place such as infarction or trauma, the only segment of the retina at risk of atrophy are ganglion cells. The diagnosis for this is lymphosarcoma with concurrent **lymphoplasmacytic uveitis**. About half the cases of lymphosarcoma in cat eyes occur in eyes in which there is a concurrent lymphoplasmacytic inflammatory infiltrate. The tumors in these eyes tend to be nodular, whereas eyes with a purely neoplastic infiltrate tend to have a more diffuse anterior uveal involvement. No difference could be found in survival between ocular lymphosarcoma concurrent with uveitis and independent of uveitis. There were some differences in the immunophenotype of the neoplastic cell.

- 1. Lymphosarcoma of the anterior uvea
- 2. Lymphoplasmacytic uveitis
- 3. Chronic glaucoma
- 4. Gliosis and cupping of the optic nerve
- 5. Loss of ganglion cells in the retina

## Slide 45, Neo 2664, 01RD113

This slide is a horizontally sectioned globe from a 7 year-old spayed female Boxer dog. On gross examination, there is a heavily pigmented mass bulging inward in the posterior segment. The mass effaces the normal tissue of the choroid. The mass is composed of a mixture of heavily pigmented round cells and heavily pigmented spindle cells. This mixture of cells is typical of melanocytoma. The mass effaces the choroidal tissue and shows a small amount of infiltration into the sclera, where the mass is largest. However, there is an abrupt switch to normal choroid and ciliary body stroma at the lateral margins of the neoplastic mass. Over most of the mass, the choriocapillaris is intact and there is hypertrophy of the retinal pigment epithelial cells. Pigmented drusen-like lesions are seen, as well as papillary projections of retinal pigment epithelial cells. Intermittently, the neoplastic mass breaks through the Bruch's membrane, and in these areas there is profound retinal atrophy and evidence of **retinal tearing**. Away from the mass, there is complete retinal detachment, however, the retinal profile returns to fairly normal. There is hypertrophy of retinal pigment epithelial cells indicative of pathologic retinal detachment. The structures of the iridocorneal angle are within normal limits and the detached retina has large numbers of ganglion cells. The submitting ophthalmologist reported that this dog did not have glaucoma, and the morphologic features back that up. Most sections do not pass through the optic nerve head.

- 1. Choroidal melanocytoma
- 2. Pathologic retinal detachment
- 3. Retinal tear

## Slide 46, Misc 2400, 01RD151

This slide is the vertically sectioned globe from a 3 year-old female Vizsla dog. On subgross evaluation, there is extensive protein and cellular exudate in the anterior and posterior chambers, as well as the vitreous. Histologically, there is corneal mid-stromal vascular ingrowth. There is a moderate lymphoplasmacytic inflammatory infiltrate in the iris stroma. The iris epithelium is largely absent, and there is posterior iridal spindle cell proliferation and fibrinous exudate. The lens is turned around backwards in the section, however, on the thick anterior lens capsule there is a mixture of adherent spindle cells, pigmented epithelial cells, and inflammatory infiltrate typical of posterior synechia. There are obvious breaks in the anterior lens capsule, with suppurative inflammatory infiltrate extending into the underlying lens substance. Numerous branching septate fungal hyphae can be found in the thick anterior lens capsule. There is retinal detachment with subretinal protein exudate and cellular infiltrate, indicating a pathologic retinal **detachment**. Notice that the retinal pigment epithelium is not hypertrophied in all areas. Retinal pigment epithelial cell hypertrophy is not a consistent finding with pathologic retinal detachment. There is a prominent suppurative and histiocytic inflammatory infiltrate in the vitreous. In many areas, the inflammation hugs and distorts the anterior retinal surface. Vitreous **inflammation**, with an inflammatory membrane that hugs the anterior surface, is a common finding in fungal infections. It is difficult to find fungi attached to the anterior retina, however, special stains showed the presence of septate fungal hyphae in this area also.

## **Diagnoses:**

- 1. Stromal keratitis
- 2. Posterior synechia
- 3. Lens capsule rupture
- 4. Suppurative inflammation in the lens
- 5. Fungal organisms in the lens capsule
- 6. Histiocytic and suppurative vitreitis and inner retinitis

**Comment:** This dog is most likely suffering from systemic aspergillosis. *Aspergillus* organisms tend to have parallel cell walls, septa, and dichotomous branching. Fungal organisms have an affinity for basement membranes, and in this case the lens capsule and interlimiting membrane of the retina are anchoring points for fungal hyphae.

# Slide 47, Neo 2706, 01RD207

This slide is a vertical section of the globe from a 10 year-old spayed female Yorkshire Terrier dog. There is an obvious nodular solid mass circumferentially surrounding the optic nerve and indenting the posterior sclera. Histologically, the anterior segment is relatively intact. Most sections pass through the optic nerve and there is an inward pouching of the optic nerve head with gliosis of both the nerve and the disc. There is a decrease in ganglion cells in the retina, although the retina is poorly sampled. There is a lymphoplasmacytic inflammatory infiltrate in the choroid, most prominently seen around the optic disc. There is a neoplastic infiltrate, both internal to the dura mater, and external to the dura mater. In both cases, the tumor is made up of aggregated clusters of large cells with a round nucleus and prominent nucleolus and abundant amounts of eosinophilic cytoplasm with indistinct cell boundaries. The cells have an epithelial appearance, both because of the large size and the extensive amount of eosinophilic cytoplasm, and also because they tend to form tight clusters and aggregates. Collagen secretion by the neoplastic cells is not seen, however, the tumor cells insinuate between orbital collagen bundles and orbital adipocytes. Widely disseminated throughout the tumor, there are localized aggregates of mesenchyme that have either a myxomatous appearance or evidence of cartilaginous differentiation or osseous differentiation. In this particular case the tumor does not infiltrate into the tissue of the optic nerve or the nerve head or the choroid, however, that is seen in some cases.

# **Diagnosis:**

# 1. Canine orbital meningioma

Comment: This case is typical of canine orbital meningioma. These tumors are different from meningiomas that occur within the calvarium. They are almost always made up of solid aggregates of plump cells, and the differential diagnosis of carcinoma needs to be considered. The presence of multifocal foci of bone cartilage or myxomatous nodules is also characteristic of this tumor and not seen in meningiomas developing in other locations. It is believed that this tumor arises from the arachnoid cap cells. These are clusters of arachnoid epithelial cells that extend through the dura mater into the perineural orbital tissue in a normal canine optic nerve. Canine orbital meningioma may exist entirely outside the dura, although, as in this case, tumor extension both within and outside the dura is also a common phenomenon. These tumors are slow growing and difficult to remove surgically. Tumor tissue remaining in the orbit will eventually cause local recurrence or blindness by extending through the optic chiasm. There are cases in the literature where metastasis has been recorded, but this is unusual.

# Slide 48, Inf 1499, 99RD174

This slide is a vertical section through the globe of a 5 year-old spayed female domestic shorthair cat. The ocular tissues show considerable distortion due to wrinkling and inflammatory infiltrate. There is a mid-stromal corneal vascular ingrowth. The anterior chamber is filled with a protein and red blood cell-rich exudate. The iris and ciliary body on the dependent side are largely effaced by an inflammatory infiltrate, and on the superior side there is evidence of **posterior** synechia and entropion uvei. The pupillary margin of the iris shows a backward bowing which suggests attachment to the lens capsule and there is a spindle cell membrane on the fragmented remnants of lens capsule. The lens itself is shattered, and fragments of retina with retinal inflammation are interdigitating with the exposed lens substance. In addition, there is a mixed neutrophilic and histiocytic inflammatory infiltrate interdigitating with the exposed lens substance, indicating a pathologic lens capsule rupture. In the superior choroid, there is a moderate to severe, lymphoplasmacytic, and histocytic inflammatory infiltrate most prominently seen in the choroid adjacent to the choriocapillaris. In the inferior choroid, the granulomatous infiltrate becomes markedly thickened, mostly positioned in the subretinal space interior to the choroid. There is a thick, solid cluster of a mixture of histiocytes and neutrophils with fragments of fibrin deposition and tissue necrosis. There is also marked proliferation of retinal pigment epithelium. Within the choroid, and within the sclera and extraorbital tissue, there is a perivascular, lymphoplasmacytic inflammatory infiltrate and tissue fibrosis indicating chronicity. The **pyogranulomatous inflammation** effaces the normal tissue through most of the dependent inner choroid, ciliary body, and iris. Throughout all of these areas, but most prominently seen in the inner choroidal inflammatory infiltrate, there are large numbers of spherical yeast organisms characterized by spherical organisms with a thick birefringent capsule and granular contents. These are spherules of *Coccidioides immitis* and the granular contents are referred to as endospores. The large size, birefractile capsule, and variable size are typical of this organism. The absence of budding and the presence of endospores are all typical of *Coccidioides immitis*. This animal lived in Arizona and the organism is indigenous to the desert southwest.

- 1. Pyogranulomatous panuveitis
- 2. Lens rupture
- 3. Retinal detachment with lymphoplasmacytic retinitis
- 4. Coccidioides immitis uveitis

## Slide 49, Neo 2375, 00RD664

This slide is a vertically cut section of the globe from a 12 year-old, spayed female Labrador Retriever dog. On gross examination, there is thickening of the iris and ciliary body and a relatively thickened hyperpigmented uveal tract. Histologically, the cornea is near normal. The iris tissue and anterior segment of the ciliary body is markedly distorted by a cellular infiltrate. In the dependent segment, there are clusters of pigmented and nonpigmented cells filling the iridocorneal angle, and there is **peripheral anterior synechia** where the thickened iris is adherent to the end of Descemet's membrane. In both sides of the globe, the iris epithelium and the dilator muscle are relatively intact. However, the iris stroma is distorted by a cellular infiltrate. The cellular infiltrate extends beyond the anterior limits of the iris, forming a cellular neoplastic pre-iridal membrane. Infiltrating cells in the iris tissue are quite variable. In some areas there are small stellate cells with a large nucleus to cytoplasm ratio and pigmented cytoplasm. In other areas, the cells become slightly plumper with large pleomorphic nuclear profiles, including dark staining, hypochromatic nuclei, and mitotic activity. Occasional binucleate or multinucleate cells are seen. Although most of the neoplastic cells are nonpigmented, it is easy to find neoplastic cells with melanin pigment in the cytoplasm. Extending posteriorly, the tumor gradually blends into thickened hyperpigmented posterior, ciliary body, uveal tissue, and hyperpigmented choroid. In sections of the optic nerve there is cupping and gliosis of the optic nerve head and hyperpigmentation of the uveal tissue and meningeal tissue, as well as the stromal tissue around the optic nerve head. The retina is artifactually detached (artifactual retinal detachment) and there are decreased numbers of ganglion cells in the retina, indicating secondary glaucoma. The lens is pushed out of position, but otherwise normal.

#### **Diagnoses:**

- 1. Ocular melanosis
- 2. Malignant anterior uveal melanoma arising from within ocular melanosis
- 3. Chronic secondary glaucoma
- 4. Artifactual retinal detachment

**Comment:** This tumor is designated as a malignant tumor because of the nuclear pleomorphism and the presence of mitotic figures. The fact that it is poorly pigmented is consistent with a malignant tumor, but is not by itself diagnostic. The tumor is not particularly invasive, with little evidence of scleral invasion or extension into the scleral venous plexus. It is not unusual for melanoma or melanocytoma to arise within melanosis.

## Slide 50, Misc 2872, 01RD546

The slide is a vertical section of the right globe from a 10 year-old neutered male Golden Retriever dog. The globe was removed because of intraocular hemorrhage and suspected uveitis. Grossly and histologically hemorrhage is detected in the anterior chamber and posterior chamber and to a lesser extent in the vitreous cavity. Look carefully at the pars plicatus on both sides of the globe. The morphology of the pars plicatus is distorted by multifocal areas of infiltrating plump basophilic cells that contain a hyperchromatic nucleus with one or more prominent nucleoli. If you look at all areas notice that these neoplastic cells have a tendency to have red blood cells contained in slit-like spaces or inner connected luminal spaces intimately associated with the neoplastic cells. This is a **metastatic hemangiosarcoma**. The pattern of tumor infiltration is typical of **metastatic cancer** of the canine eye. The typical pattern is to occur in the loose connective tissue of the ciliary body and breakthrough into the posterior chamber. Once the posterior chamber is colonized neoplastic cells often grow as if in thin tissue culture to surround the iris, ciliary body, and other structures. The retina has an adequate number of ganglion cells and the optic nerve and optic disc are within normal limits suggesting that glaucoma is not an issue.

# **Diagnosis:**

1. Metastatic hemangiosarcoma with intraocular hemorrhage

## Slide 51, Misc 1357, 98RD054

This slide is a vertical section through the globe of a 7 year-old spayed female Australian Blue Heeler dog. Histologically, there is mild peripheral corneal neovascular invasion of the midcorneal stroma. There is a segmental break in Descemet's membrane (Haab's striae) seen in the superior peripheral cornea. Segmentally, in the central inferior corneal stroma there is a collagenrich retrocorneal membrane on the posterior aspect of the cornea. Over most of the cornea the endothelium is artifactually nonattached. There is a thick, **pre-iridal fibrovascular membrane** with **peripheral anterior synechia** seen best in the superior iris leaflet. There is also mild ectropion uvei in the superior iris leaflet. Both superior and inferior leaflets have peripheral anterior synechia. When the globe was sectioned, the vitreous was liquid and the lens was out of position. Histosections of the ciliary body show a cell-poor glassy protein membrane adherent to the inner aspect of the nonpigmented ciliary body epithelium in both the pars plana and the pars plicata. A similar membrane is seen attached to the lens capsule irregularly. There is cortical cataract and evidence of posterior subcapsular cataract, although the lens is out of position. There is pathologic retinal detachment with hypertrophy of the retinal pigment epithelial cells. Sections across the optic disc show gliosis and cupping of the optic disc. Notice that the connective tissue in the caudal most aspect of the tissue sampled has a hypereosinophilic muddy staining quality. This is an artifact created by electrocautery.

- 1. Pre-iridal fibrovascular membrane
- 2. Peripheral anterior synechia
- 3. Haab's striae
- 4. Retrocorneal membrane
- 5. Lens luxation with abnormal zonular ligament protein seen in the ciliary body and on the lens capsule
- 6. Pathologic retinal detachment
- 7. Chronic glaucoma
- 8. Electrocautery artifact

# Slide 52, Misc 2466, 01N129

This slide is a vertically sectioned eye from a Basset Hound dog with no ocular symptomatology. This section is of a **near normal canine eye**. Sections across the iridocorneal angle show a thick uveal membrane stretching from the iris base and attached to the arborized end of Descemet's membrane. These changes are the hallmark of **goniodysgenesis**. Notice that the ciliary cleft is open and normal, and there is a clearly visible corneal scleral trabecular meshwork in this normotensive eye with goniodysgenesis.

- 1. Near normal canine eye
- 2. Normotensive goniodysgenesis in a Bassett Hound

## Slide 53, Inf 2187, 01RD302

This slide is a vertically cut section from a 13 year-old spayed female domestic shorthair cat. Grossly there is thickening, destruction, and hypercellularity to the central cornea, with exudation in the anterior uvea. Histologically, there is vascular and cellular infiltrate at all levels of the cornea stroma. Centrally, there is posterior stromal necrosis with mid-stromal **collagenolysis** associated with an extensive suppurative inflammatory infiltrate. Centrally, there is irregular corneal epithelial nonattachment with an unusual pattern of corneal epithelial duplication with basilar cells subtending a more tenuous epithelium, suggesting a scenario of **repeated epithelial erosion**. In several areas of the poorly attached corneal epithelium there is keratinization on both the inner and outer aspects. There is segmental rupture in Descemet's **membrane**, and there is a necrotizing suppurative inflammatory infiltrate adjacent to Descemet's membrane. The endothelium is intermittent and lost over much of the Descemet's membrane, and there is a fibrin-rich suppurative and necrotic exudate in the anterior chamber, most prominently seen in gravitating segment. Within the uveal tract there is a primarily lymphoplasmacytic inflammatory infiltrate which changes into suppurative inflammation in the posterior chamber. Also in the posterior chamber, there are large numbers of granular histiocytic cells often seen with phagocytosed neutrophils in the cytoplasm. The posterior segment is much less inflammatory. The retina shows a relative decrease in ganglion cells, and there is vacuolation of the optic nerve fiber layer, as well as vacuolation of the optic disc and optic nerve, and early evidence of gliosis, suggesting glaucoma. The lens is intact and the vitreous is normal except that there are increased amounts of granular protein.

#### **Diagnoses:**

- 1. Corneal epithelial erosion
- 2. Collagenolytic, necrotizing, suppurative keratitis
- 3. Suppurative endophthalmitis of the anterior segment
- 4. Lymphoplasmacytic uveitis
- 5. Secondary glaucoma

**Comment:** The cause of disease is not apparent. Special stains for bacteria are rarely helpful in locating organisms in the necrotic cornea.

## Slide 54, Neo 2757, 01RD270

This slide is a vertically sectioned globe from a 9 year-old spayed female Maltese dog. Corneal stroma shows a minimal anterior stromal neovascular infiltrate. The anterior chamber is largely distorted by a neoplastic mass that extends from the irides to the posterior cornea. On the less involved side, there is **broad anterior synechia**, and on the more involved side, there are columns and trabeculae of neoplastic tissue traversing the anterior chamber and broadly attached to the back of the cornea. On the less affected side, the iris profile is distorted by a neoplastic infiltrate made up primarily of fairly heavily pigmented polygonal cells, often with a round nucleus and a prominent nucleolus. Within this mass, there are intermittent localized foci where the cells become nonpigmented and have a larger nucleus to cytoplasm ratio and more prominent evidence of mitotic activity. On the side with the larger mass, most of the neoplastic tissue is made up of the more anaplastic cells, and the most malignant elements are seen in the almost completely nonpigmented focus within the ciliary body. In these areas, neoplastic cells have a large nucleus to cytoplasm ratio, pleomorphic nuclear profiles, and abundant evidence of mitotic activity. The tumor cells show a limited propensity to invade into the sclera. Interestingly, the iris epithelium remains identifiable over most of the back of the iris, although there is a thin spindle cell membrane distorting some of the posterior iris surface on both sides of the globe. The lens is pushed out of position but is otherwise unaffected. There is an absence of ganglion cells in the otherwise largely intact retina. Sections that pass through the optic nerve head show cavitation and gliosis of the optic nerve head.

## **Diagnoses:**

- 1. Malignant anterior uveal melanoma with broad anterior synechia
- 2. Secondary chronic glaucoma

**Comment:** The neoplastic tissue has elements of both melanocytoma and malignant melanoma, and it is possible that the malignant tumor is arising from within melanocytoma in this case.

## Slide 55, Misc 1454, 98RD311 and Misc 1671, 99RD112

This slide contains sections from two different dogs, one a 12 year-old spayed female Shih Tzu, and the other a 6 year-old female Cocker Spaniel, both with virtually identical disease profiles. Each slide set will have a section from one or the other, but not both of these globes. Histologically in both globes, there is a broad band of iris-like uveal tissue extending from the iris base and making contact with the thickened and arborized terminus of Descemet's membrane. The ciliary cleft is closed and it is impossible to find the corneal scleral trabecular meshwork. There is a varying degree of a neovascular infiltrate into the peripheral cornea. The lens is either normal or poorly sectioned. There should be at least some optic nerve tissue in all sections, and the optic nerve head is pushed back to form a cup, and there is permanent gliosis of the optic nerve head, the nerve tissue within the lamina cribrosa, and the nerve tissue behind the lamina cribrosa. The quality of the retinal sections is variable, however, in all sections it is clear that there is a loss of ganglion cells and a relative, more advanced, retinal atrophy in the nontapetal retina compared to the tapetal retina (tapetal sparing).

- 1. Goniodysgenesis
- 2. Chronic glaucoma

# Slide 56, Inf 2200, 01RD401

This slide is the obliquely sectioned globe from a 17 year-old neutered male Shih Tzu dog, sectioned so as to include the papillary mass extending outward from the limbal conjunctival surface. Grossly, the anterior cornea was opaque and darkly pigmented. Histologically, there is a thickening of the cornea epithelium, with irregular epithelial downgrowth and a thin keratinizing surface. There are numerous pigmented cells within the epithelium and pigmented phagocytes subtending the epithelium, and there is a vascular network immediately subtending the epithelium. Very few inflammatory cells are seen, and the mid and deeper stroma returns to a normal corneal profile with an intact Descemet's membrane and intact endothelium. On both sides of the cornea, there is **squamous metaplasia** of the conjunctival epithelium. On the side with the exophytic papillary mass, the epithelium is distorted in an outwardly proliferating papillary mass attached by a stalk to the conjunctival connective tissue of the limbus. There is a rich vascular bed with a primarily lymphoplasmacytic inflammatory infiltrate subtending the exposed epithelial surface. The epithelium is thickened and heavily keratinized, typical of **reactive papilloma**. In all other ways, the globe is within normal limits.

- 1. Chronic pigmentary superficial keratitis
- 2. Conjunctival squamous metaplasia
- 3. Acquired limbal conjunctival squamous papilloma secondary to chronic inflammation

## Slide 57, Neo 2800, 01RD447

This slide is a vertically cut section of the globe from an 11 year-old spayed female domestic shorthair cat. Some of the sections have a lens and some of the sections do not. As many sections as possible were cut through the optic nerve. Although wrinkled, the superficial corneal stroma is near normal. In the dependent cornea there is a retrocorneal membrane with lymphoplasmacytic inflammatory cells. There is extensive lymphoplasmacytic inflammation in the anterior uvea forming follicle-like structures in the iris and filling the trabecular meshwork of the iridociliary angle. Careful examination of the round cells in the trabecular meshwork complex on the superior portion of the section shows areas where a monomorphic population of large irregular cells replace the highly variable cell populations in the rest of the uvea. This feature is not obvious in all sections because the affected area was fairly small. In this area, the cells begin to look like neoplastic round cells and I would consider this an early variant of the feline ocular lymphoma occurring within uveitis. In all other areas, there are follicle-like clusters of lymphocytes and large numbers of plasma cells, including numerous **Mott cells** or Russell body cells. Look carefully at the nonpigmented ciliary body epithelium and you will see that lymphoplasmacytic inflammatory cells tend to aggregate directly within the nonpigmented ciliary body epithelium. Examine the anterior vitreous. The anterior vitreous can be seen in both sections that contain the lens and sections that don't contain the lens. You will find hypereosinophilic granular protein deposits, either behind the lens or on the margin of the anterior vitreous space. The formation of this granular protein aggregate is seen in about 20% of lymphocytic uveitis cases in cats, and the significance is unknown. The lens has fallen aside so that it is cut perpendicular. Poor lens attachment is a common phenomenon in lymphoplasmacytic uveitis in cats, and a fracture of the anterior vitreous space with vitreous prolapse into the posterior chamber or pupil is another common phenomenon. In sections that have an optic nerve head, you will find a mild lymphoplasmacytic papillitis and gliosis of the optic nerve head, and you will find a depletion of ganglion cells in the otherwise wellpreserved retina. In cats with glaucoma, the retina tends to remain largely intact, with a loss of ganglion cells, whereas in dogs, chronic glaucoma leads to a highly variable degree of retinal atrophy, including end-stage retinal atrophy.

- 1. Retrocorneal membrane
- 2. Lymphoplasmacytic uveitis with lymphoid follicles
- 3. Early development of lymphoma within uveitis (some slides)
- 4. Lens subluxation
- 5. Anterior vitreous rupture
- 6. Granular protein deposition in the anterior vitreous
- 7. Papillitis
- 8. Secondary glaucoma

# Slide 58, Misc 1059, 96B946

This slide is a vertical section of the globe of a 3 year-old neutered male Bichon Frise dog that had had **cataract surgery** 2 years prior to enucleation. The corneal stroma is largely free of neovascular infiltrate except minimal peripheral disease. Look at the epithelium, especially a superior portion of the section. Notice the **intra-epithelial vacuolation**. This change, I think, is the most reliable change to identify corneal edema. Look at the far periphery of the superior cornea and find the **surgical scar**. The surgical scar should extend to a **break in Descemet's membrane**. The iris profile on both sides shows **peripheral anterior synechia** and a forward bowing of the mid-iris, which extend posteriorly to touch on the capsular bag, creating a classical **iris bombé**. There is, in addition, a spindle cell membrane on the anterior iris surface and spanning the pupil, entrapping a segment of the capsular bag. Notice the reformation of lens fiber material and the formation of a **secondary cataract** within the capsular bag. The capsular bag is not entirely sectioned in all slides. Sections do not pass through the optic nerve, however, the histopathology of the retina and segments of the optic nerve away from the eye fail to show evidence of glaucoma. The history, and also the pathology of the anterior segment, both suggest that glaucoma would be a problem in this case, so reconciliation of that fact remains unresolved.

- 1. Status post-cataract surgery
- 2. Corneal surgical scar
- 3. Microvesicular edema of the corneal epithelium
- 4. Iris bombé
- 5. Secondary cataract (lens fiber regrowth)
- 6. Absence of morphologic glaucoma

## Slide 59, Misc 1328, 97RD662

This slide is a vertical section through the globe of a 15 year-old spayed female Shih Tzu dog that had a history of cataract surgery two months prior to enucleation. Histologically, there is a moderate corneal stromal neovascular membrane on both sides. Most sections show a segmental area of **poor epithelial attachment**, characterized by a subepithelial cleft. In this area, the epithelium is disorganized, showing a loss of the basilar-oriented cells and a hint of keratinization on both sides of the epithelium, suggesting features of **indolent ulcer**. At the superior margin, there is a full-thickness surgical scar easily recognized because of a break in **Descemet's membrane** and a cleft in the scar tissue. Extending into the scar, there are several deeply seated tongues of stratified squamous epithelium, and in most areas there are clusters or circular aggregates of stratified squamous epithelium at the level of the penetrated Descemet's membrane (epithelial downgrowth). In addition, several sections show entrapped asteroid hyalosis bodies surrounded by macrophages within the connective tissue at the margins of the surgical scar. There is broad anterior adhesion of the iris to the area of the surgical scar, and there is distortion of the iris profile and a thick **pre-iridal fibrovascular membrane** on the iris away from the scar. Several sections show segments of disorganized neural retinal tissue entrapped in the pupillary aperture. No remnants of lens capsule are found in the sections. Posteriorly, there is pathologic retinal detachment of the superior retina, which is otherwise largely intact. Ganglion cells are reasonable in number, however, there is a moderate to mild, perivascular, lymphoplasmacytic inflammatory infiltrate. Macrophages with phagocytosed red blood cells are seen in the subretinal space, and there is atrophy of the photoreceptor outer processes. At the terminus of the detached retina the retinal profile has a smooth border, suggesting a retinal hole. The optic nerve head shows gliosis, but little evidence of cupping. There is retinal detachment of the nontapetal retina as well, and rather than a single hole, the nontapetal retina is pulled apart into multiple fragments and segments of gliotic retinal tissue, some of which are migrating into the anterior chamber. Going back to the anterior chamber and examining the dependent iridocorneal angle, a suppurative inflammatory infiltrate can be seen, sometimes adherent to the pre-iridal fibrovascular membrane. Within this suppurative inflammation, there are individual squamous cells, and entrapped in the iridocorneal angle, there are rafts of pigmented and nonpigmented iris epithelial cells or ciliary body epithelial cells.

- 1. Status post-cataract surgery
- 2. Indolent ulcer
- 3. Surgical scar
- 4. Epithelial downgrowth
- 5. Pre-iridal fibrovascular membrane
- 6. Anterior synechia

- 7. Squamous epithelial cells in the anterior chamber
- 8. Retinal detachment with retinal tear
- 9. Secondary glaucoma
- 10. Asteroid hyalosis

# Slide 60, Neo 2781, 01RD364

The section is of the third eyelid mass from a 13 year-old neutered male Samoyed dog. Histologically, the leading margin of the third eyelid is identifiable on the section. There is a sharply delineated mass effacing normal tissues occupying most of the slide. At the margin, adjacent to the leading edge of the third eyelid, there is a small amount of unaffected atrophied gland of the third eyelid adjacent to the mass. Both around the margins of the mass and within the mass there is an extensive lymphoplasmacytic inflammatory infiltrate. The mass is composed of solid sheets of tightly packed cells. Anaplastic epithelial cells, lymphoplasmacytic inflammatory cells, and fibrovascular stroma are mixed together with small localized areas of necrosis. Neoplastic cells most commonly form tight aggregates of highly pleomorphic and anaplastic epithelial cells. They have a large open nucleus with coarse chromatin clumping and one or several unusual-appearing nucleoli. Mitotic activity is easily found. These are pushed apart by a cell-rich stroma in which there are large numbers of lymphoplasmacytic, in some areas histiocytic, inflammatory cells. Occasional multinucleate inflammatory cells are found. In all areas, the tumor is sharply delineated, however, on the proximal edge there is no surrounding stroma, indicating a dirty surgical margin.

# **Diagnosis:**

1. Adenocarcinoma of the gland of the third eyelid with malignant features and dirty margins

## Slide 61, Inf 2239, 01RD472

The slide is vertical section through the globe of a 12 year-old spayed female mixed breed dog. Subgross evaluation shows that the limbus on both sides of the globe is distorted by cellular masses bulging outward into the subconjunctival connective tissue. Histologically, the masses on both sides of the cornea are similar. There are poorly delineated margins. There is a neovascular infiltrate extending into the peripheral cornea. The bulk of the mass is made up of a mixture of cell types commingling with subconjunctival and scleral collagen. The cellular infiltrate extends full thickness into the sclera at the limbus, including peripheral cornea in some areas. Histologically, the mass is primarily made up of elongate cells with oval or irregular nuclei and fairly abundant amounts of eosinophilic granular to vacuolated cytoplasm. There is a secondary population of lymphoplasmacytic inflammatory cells. Posteriorly, the mass bulges up into the subconjunctival connective tissue and begins to extend posteriorly into the orbital muscle tissue. The iris and ciliary body are almost not affected at all, and the internal structures of the globe are within normal limits. This mass is made up of a mixture of elongated phagocytic cells and lymphoplasmacytic cells. The mixture of cells is exactly identical to what would be expected in **nodular granulomatous episcleritis**. However, in this case the inflammatory disease extends full thickness into the sclera. It is cases like this that blur the margin between nodular granulomatous episcleritis and granulomatous or necrotizing scleritis.

# **Diagnosis:**

## 1. Granulomatous scleritis with extension to the conjunctiva

Comment: I don't have a firm opinion whether granulomatous scleritis is in fact related to nodular granulomatous episcleritis. Granulomatous scleritis usually has a much more aggressive behavior, and in most cases there is more inflammatory disease within the eye. The disease blends with granulomatous uveitis on the other side of the spectrum. This particular case has all the features of nodular granulomatous episcleritis in terms of the blandness of the inflammatory disease and the sharp delineation. However, clearly there is extensive involvement full thickness through the limbus sclera. Granulomatous scleritis often occurs in the second eye.

# Slide 62, Inf 591, 94RD136

This slide is a vertically sectioned globe from a 4 year-old Terrier mix dog. On subgross examination, there is obvious protein exudate in the anterior chamber, iris bombé, and retinal **detachment** with extensive protein exudate in the vitreous. Histologically, there is a neovascular infiltrate in the corneal stroma. In the superior aspect, there is **rupture of Descemet's membrane** and a spindle cell proliferation in the posterior corneal stroma. This lesion would suggest possible proximity to a full-thickness scar, but no full-thickness lesion is seen in the sampled tissues. There are broad adhesions of both iris tissue and fibrovascular connective tissue to the shattered anterior lens capsule and anterior lens. Although the iris profile is bulged outward suggesting **iris bombé**, there is also extensive complex proliferation of iris epithelium and neovascular tissue obliterating the posterior chamber. There is a suppurative inflammatory infiltrate in the tissue adjacent to the **ruptured lens capsule** and extending into the lens tissue. At the equator on one end of the lens there is a cluster of inflammatory cells separating lens fibers, and in this area there are several bacterial colonies. Small bacterial colonies are seen in other areas of the lens, sometimes in the area of inflammatory cell infiltration, but often away from inflammatory cells. There is a suppurative and histiocytic membrane on the anterior surface of the iris, and there are several areas of suppurative inflammation adherent to Descemet's membrane. Within the uveal tissue of the iris and ciliary body the inflammation is primarily lymphoplasmacytic. However, there is a histiocytic and suppurative inflammatory infiltrate internal to the ciliary body epithelium, posterior to the lens capsule, and in smaller numbers throughout the vitreous. The retina is detached, however, there is nothing in the subretinal space, and there is no evidence of cellular change in retinal pigment epithelium, so this detachment is an artifact. There is very little inflammation in the choroid, and inflammation in the retina is limited to the vitreous face and around blood vessels.

#### **Diagnoses:**

- 1. Stromal keratitis
- 2. Lymphoplasmacytic uveitis
- 3. Suppurative endophthalmitis limited to the anterior segment
- 4. Posterior chamber fibrosis
- 5. Lens capsule rupture with suppurative inflammation in the lens
- 6. Septic implantation into the lens
- 7. Rupture of Descemet's membrane, probably adjacent to a corneal scleral rupture

**Comment:** I call this syndrome "septic implantation to the lens" or, alternatively, "feline anterior capsulotomy". If you get a history, or if you dig into the history in these cases, it is remarkable how often a cat scratch is implicated as a causative process. The fact that there is collagen-rich fibrosis adherent to the anterior lens capsule suggests that this disease has been festering for a long period of time. It is not unusual to find that the cat scratch occurred months, or even years, before enucleation. It is common to attribute the suppurative inflammation to the presence of exposed lens fiber material and sequestered antigens from lens protein. In my

experience with this particular syndrome, in more than half the cases you can demonstrate the presence of bacteria in lens tissue. The bacteria are often away from the inflammatory infiltrates, suggesting they have been sequestered in pockets. In dogs, the bacteria are usually gram-positive cocci, however, this is the form of organism that is most easily found with a tissue gram stain. Tissue gram stain is not a very effective tool for finding bacteria in suppurative inflammatory lesions, so in my opinion this disease is a bacterial infection until proven otherwise, and for that reason I question the importance of exposure to sequestered lens protein antigens.

# Slide 63, Misc 2513, 01RD508

This slide is a vertically cut section from the globe of a 10 year-old female spayed Golden Retriever dog. On low magnification histopathology, the most obvious change is an **entropion uvei**. Careful examination of the iris shows the presence of a fairly thin, **preiridal**, fibrovascular membrane that expands over the iridocorneal angle, causing peripheral anterior synechia. Carefully look along Descemet's membrane and you will find localized areas where Descemet's is doubled and shows an unusual granular staining pattern. On low magnification examination, the posterior chamber appears normal, but on examination with high magnification shows the presence of multiple interconnected, thin-walled, epithelial-lined cystic structures. These cystic structures emanate from the iris epithelium and the ciliary body processes and they touch on the lens surface. If you go to high magnification and examine the surface of the lens, you will see that there is a cellular or cell-free collagen membrane stretching all the way across the surface of the lens. In some areas it becomes extremely thin. In sections that contain the optic nerve you will notice that there is marked gliosis, but little or no cupping. High magnification examination of the optic nerve head shows the presence of necrotic nerve tissue with neutrophils and dark shrunken nuclei, suggesting pyknosis or apoptosis. There is a **decrease in** ganglion cells over the entire retina, most prominently in the nontapetal retina, typical of chronic glaucoma. Looking at the connective tissue adjacent to and surrounding the segment of optic nerve sampled, you will see a dark purple muddy quality of the tissue. This is an artifact caused by electrocautery.

- 1. Preiridal fibrovascular membrane
- 2. Peripheral anterior synechia
- 3. Duplication of Descemet's membrane multifocally
- 4. Thin-walled iridociliary cysts stretching across the posterior chamber
- 5. Glaucoma with acute and chronic elements
- 6. Electrocautery artifact

## Slide 64, Inf 2260, 01RD556

This slide is a vertical section through the globe of a 7 year-old neutered male domestic shorthair cat. On gross examination, there is **retinal detachment** and there is a suppurative inflammatory infiltrate filling much of the posterior segment. Histologically, most of the cornea is devoid of epithelium. If you look at the margins, there are jagged-edged margins and fragments of epithelium covering the denuded stroma. There is no evidence of a cellular response or cellular remodeling that suggests that this change is an artifact. There is a protein-rich and suppurative inflammatory infiltrate in the anterior chamber that tends to gravitate to the dependent segment of the eye. There is complete retinal detachment with an extensive pyogranulomatous inflammatory infiltrate in the subretinal space, most obvious immediately adjacent to the retinal pigment epithelium and also hugging the posterior retina and, in many areas, extending into the retina. Careful examination in the areas of **pyogranulomatous inflammation**, especially where macrophages tend to cluster, will reveal the presence of yeast-like organisms. Organisms tend to be exquisitely round with a thin refractile capsule, and often contain a basophilic-staining central nucleus-like structure. Occasional budding forms are seen, and the morphology is typical of **blastomycosis**.

## **Diagnosis:**

## 1. Pyogranulomatous chorioretinitis associated with blastomycosis

**Comment:** *Blastomyces dermatitidis* is most common in dogs. It is said that dogs are ten times more likely to have blasto than humans, and humans, are ten times more likely to have blasto than cats. However, this case in a cat is a good example where organisms are easily found and has the classical features of ocular blastomycosis.

## Slide 65, Inf 2261, 01RD572

This slide is a vertically sectioned globe from a 2 year-old neutered male Persian cat. Histologically, most of the disease is in the anterior segment. There is a large full-thickness central corneal defect with iris tissue prolapsing (**iris prolapse**) through the defect. Descemet's membrane is disrupted and wrinkled. The deep corneal stroma contains a mixed inflammatory cell infiltrate at the defect margins. There are also blood vessels that seem to originate from the iris tissue extending into the corneal stroma at the defect. In the superficial stroma, on both superior peripheral cornea and the central portion of the inferior peripheral cornea, the stroma resembles subepithelial conjunctival stroma. This is because a **conjunctival flap** had been previously performed. Careful examination of the epithelium covering these areas, as well as the epithelium covering the prolapsed iris, will demonstrate the presence of goblet cells, suggesting that this is a conjunctival epithelium. There is a moderate lymphoplasmacytic inflammatory infiltrate in the anterior uvea. The posterior segment returns to a near-normal profile. Some sections may have embedded suture material left over from the conjunctival flap, with epithelium around the suture material.

- 1. Central corneal perforation with epithelial healing
- 2. Iris prolapse
- 3. Status post-conjunctival graft surgery

#### **WOPT**

## Slide 66, Neo. 2871, 01RD575

This slide is a vertical section from the globe of a 13 year-old spayed female Cocker Spaniel dog. The eye was removed following a previous evisceration and prosthetic implant surgery in a globe that had an iridociliary epithelial tumor. The section is of the scleral shell, with recurrent neoplasm extending through the sclera and into the orbital tissue. The cornea can be identified by the epithelium, as well as remnant corneal stroma and Descemet's membrane. There is superficial stromal vascularization throughout the whole section, and in addition there is a lymphosuppurative inflammatory infiltrate over much of the superficial stroma. In some areas, there is pigmentation of the cornea epithelium, indicating a **chronic superficial keratitis**. There is squamous metaplasia of the conjunctival epithelium. Although Descemet's membrane is intermittently intact, there is a thick retrocorneal membrane made up of a collagen-rich lamellar stroma subtending Descemet's, with no evidence of endothelium. Over broad areas, Descemet's membrane is absent. Continuing around the globe, there is a qualitative difference in the collagen stroma from the pre-existing sclera to the cell-free, collagen-rich, lamellar connective tissue that lines the cavity in which the silicon ball is inserted. Within this inner fibrous proliferation, there are remnant clusters and aggregates of uveal tissue. It is of interest to me that the remnant clusters of uveal tissue (choroid) show no evidence of fibrosis within the tissue. This is a general feature of ocular pathology that the uveal tract itself resists fibrosis. The tumor is seen as invasive, multilobulated, pleomorphic tumor extending full thickness through the sclera and into the surrounding loose connective tissue with aggregates extending into skeletal muscle, adipose tissue, and abutting on lacrimal glands. The tumor is made up of palisading epithelial components, and a PAS stain shows thick PAS-positive basement membranes typical of iridociliary adenoma. Centralized areas of necrosis are seen in interconnecting foci in the middle of the thickest part of the tumor.

### **Diagnoses:**

- 1. Status post-evisceration and prosthesis placement
- 2. Recurrence of iridociliary adenoma/adenocarcinoma following evisceration

**Comment:** I do not know the eventual outcome of this case. Metastasis of iridociliary tumors in dogs is almost unheard of. However, this dog's tumor does have invasive characteristics, and the tumor cells have features of anaplasia that would be worrisome. The original tumor did not appear invasive, but it was evaluated as an evisceration specimen.

## Slide 67, Misc 2524, 01B613, Misc 1833, 99RD616

This case is from globes from either of two 7 year-old Shih Tzu dogs. In both sections, there is a central corneal full-thickness **corneal perforation**. In both cases there is prolapse of iris tissue into the defect with varying degrees of epithelial proliferation to cover the defect. In one of the sections, the epithelialization is complete and lies on a granulation tissue bed that is derived from iris tissue, and in the other the epithelialization only occurs at the margins and occurs on fibrin and granulation tissue from the iris prolapse. In both sections, there is rupture of Descemet's membrane and varying degrees of protein exudation in the anterior chamber. The posterior segment returns to fairly normal in both globes, with no evidence of glaucoma.

- 1. Central corneal perforation with iris prolapse
- 2. Corneal epithelial regrowth
- 3. Corneal stromal neovascular proliferation extending from the prolapsed iris

## Slide 68, Neo 351, 92RD001

This slide is a vertically sectioned globe from a 13 year-old female Cocker Spaniel dog. To varying degrees, there is effacement of the iris and ciliary body by a solid neoplastic mass. The neoplastic mass is made up of solid sheets of large polygonal cells with abundant amounts of foamy to granular cytoplasm. Most of the sections show the mass primarily in the anterior chamber and iridocorneal angle, with some sections showing scleral invasion and posterior chamber involvement. In some areas where the tumor is compacted, the cells take on a smaller more spindle profile, but the characteristic cell is a large foamy cell forming solid sheets.

# **Diagnosis:**

## 1. Foam cell variant of iridociliary adenoma

**Comment:** This is a rare and unusual variant of the iridociliary adenoma. On electron microscopy, these cells are clearly epithelial with secretory cytoplasmic organelles and epithelial cell junctions. In addition, it is not too unusual to find small foci within iridociliary adenomas where there is foam cell differentiation. The significance is unknown. These seem to be tumors with no risk of metastasis, the same as more standard iridociliary adenomas.

## Slide 69, Misc 2551, 01RD635

This slide is a vertical section through the globe of an 11 year-old Cocker Spaniel dog. In the peripheral corneal stroma on both sides, there is a mixture of blood vessels, inflammatory cells, and abundant pigmented cells extending into the iris stroma. The inflammatory cells are primarily lymphocytes (**peripheral keratitis**). At the iris base there is a broad band of iris tissue extending from the iris to the arborized end of Descemet's membrane, a configuration typical of goniodysgenesis. Centrally, there is a broad posterior synechia. All that remains of the lens is the lens capsule, which is wrinkled. Attached to the anterior surface of the lens there is a spindle cell and pigmented cell membrane. The membrane reflected over the back of the iris contains a thin layer of epithelial cells and cell-poor collagen subtending it, suggesting that this membrane is derived from released lens epithelial cells. The profile of the ciliary body on the dependent segment is largely within normal limits. The profile of the ciliary body on the superior segment shows dense collagen deposition within the substance of the ciliary body and distorting the profile of the ciliary body. This is a typical reaction with a **laser photoablation** surgery. The retinal atrophy is extremely profound and, in addition, the retina is lost over segments of the choroid. Most sections do not pass through the optic nerve, however, those that do show gliosis and deep optic nerve cupping, typical of chronic glaucoma.

- 1. Peripheral keratitis
- 2. Goniodysgenesis
- 3. Hypermature cataract with evidence of lens capsule rupture
- 4. Broad posterior synechia
- 5. Proliferation of released lens epithelial cells
- 6. Photoablation-induced ciliary body atrophy

## Slide 70, Neo 1185, 97RD174

This slide is a vertically sectioned feline globe with a large central corneal full-thickness defect. There is complete **retinal detachment** and no lens is seen in the distorted globe. In the peripheral cornea there is anterior stromal neovascular proliferation, granulation tissue, and a lymphosuppurative inflammation. On the dependent segment the peripheral corneal surface epithelium is thickened, distorted, and disorganized. The disorganized and anaplastic epithelial fronds, characteristic of **squamous cell carcinoma**, extend deeply into the peripheral corneal stroma and subconjunctival stroma. In most areas there is a coexisting lymphoplasmacytic inflammatory infiltrate and a desmoplastic spindle cell proliferation. The neoplastic infiltrate extends into the globe lining the anterior iris and it is seen on both sides of the distorted Descemet's membrane. In the superior segment the neoplastic cells also line the anterior iris and extend deeply into the ciliary body stroma. Cords of neoplastic cells also dissect between corneal lamellae in the superior segment. The retina is detached however there are adequate numbers of ganglion cells. There are free red blood cells in the vitreous and there are inflammatory cells in the subretinal space. There is intermittent and mild retinal pigment epithelial cell hypertrophy indicative of retinal detachment.

### **Diagnoses:**

- 1. Broad central corneal perforation
- 2. Conjunctival or corneal squamous cell carcinoma invading the globe
- 3. Retinal detachment

**Comment:** This case was mistakenly treated for inflammatory disease for a long period time while the tumor developed. Squamous cell carcinoma often develops in a background of intense inflammation. In both cats and dogs aggressive infiltration into the globe is not uncommon. Neoplastic elements dissecting between corneal lamellae are also a common feature. When a tumor of conjunctival or corneal epithelial origin invades deeply into the globe one must carefully distinguish between infiltrative tumor, metastatic disease, and inflammation.

### Slide 71, Misc 2086, 00RD454

This slide is a vertically section globe from an 11 year-old spayed female Afghan dog. The abnormalities are limited to the cornea. There is a broad superficial corneal neovascular infiltrate and spindle cell proliferation. Throughout the section there is intermittent corneal epithelial disorganization or thinning. There is a segment of corneal epithelium that is not attached. This flap of epithelial tissue shows disorganized differentiation with keratinization in both the inner and outer margins of the flap. The disorganization begins abruptly in the area of nonattachment. Looking carefully at the superficial stroma subtending the non-attached epithelium you find a very thin layer of stromal matrix that is acellular. Over most of the surface there is a basophilic discoloration suggesting mineral deposition. Peripherally in the thickened cornea there are localized areas of epithelial disorganization in areas where the epithelium is still attached. Careful examination will show a very narrow space sometimes occupied by red blood cells between the epithelium and the underlying stroma in these foci. This area is at risk of **indolent ulcer**.

## **Diagnoses:**

- 1. Chronic superficial keratitis
- 2. Indolent ulcer

**Comment:** The features of corneal ulceration seen in this case are typical of indolent ulcer. The characteristic features are disorganized differentiation with keratin formation on both sides of the unattached lip and a thin layer of acellular stroma subtending the ulcer. The changes characteristic of indolent ulcer are often found on enucleated globes as an incidental finding presumably unrecognized or unimportant in the clinical syndrome.

### Slide 72, Neo 370, 92N69

This slide is a vertically sectioned globe from a 4 year-old male Bernese Mountain dog. The tissues of the globe are distorted due to a cellular infiltrate. The infiltrate affects the superior sclera, ciliary body stroma, and choroid with lesser involvement of the inferior sclera. In all areas the infiltrate is a nearly pure population of histiocytic cells. The infiltrating cells tend to push apart the tissues of the eye but there is little evidence of destruction of ocular structures. Careful examination of the dependent sclera shows that the infiltrating histiocytic cells have a tendency to invade within or adjacent to blood vessels. Although there are some areas in the choroid where the infiltrating histocytes contain melanin pigment in most areas melanin containing cells of the eye are not disrupted and the histiocytes are not pigmented. Specifically the retinal pigment epithelium, the pigmented epithelium of the iris and ciliary body, and the uveal melanocytes do not tend to be destroyed by the infiltrating cells. Careful examination of the histocytes shows occasional mitotic figures however, for the most part, the cells do not appear to be neoplastic. The pure population of histocytes, the vasocentric tendency, and the lack of destruction of pigmented ocular tissues are features that suggest malignant histiocytosis as opposed to VKH or other granulomatous inflammatory processes. Notice that the retinal tissue is completely within normal limits with no inflammation and no evidence of degeneration or glaucoma.

## **Diagnosis:**

## 1. Malignant histiocytosis of the globe affecting the uvea and sclera

**Comment:** Differential diagnoses that should be considered in granulomatous disease of this sort would be VKH, asymmetric uveitis, and fungal disease. In VKH and asymmetric uveitis one would expect destruction of ocular pigmented cells, both within the uvea and in epithelial tissue such as retinal pigment epithelium and ciliary body and iris pigmented epithelium. In VKH the retina tends to be considerably less affected than the rest of the eye however in asymmetric uveitis there is usually segmental retinal necrosis. Fungal disease has a tendency to occur in the subretinal space and inner choroid, however, the distribution is variable in the deep mycosis.

## Slide 73, Misc 2672, 01B1068

The slide is an oblique section of the globe of a 14 year-old spayed female Chow Chow dog. There is a neovascular infiltrate in the superficial half of the corneal stroma extending approximately 3 mm from the limbus on both sides of the cornea. Centrally there is a large full-thickness corneal defect with an almost intact Descemet's membrane bulging forward (descemetocele). The iris is prolapsed into the corneal defect and one can recognize an early neovascular proliferation extending from the iris tissue toward the corneal stroma. Vascularization of the corneal stroma from the iris is impeded by the intact Descemet's membrane. This barrier is broken segmentally in some of the sections and in the area of the broken Descemet's membrane uveal neovascularization of the margins of the corneal defect can be appreciated. Notice that the corneal epithelium has proliferated over much of the descemetocele surface. There is hemorrhage, fibrin deposition, and neovascular proliferation but the extent of inflammation is minimal. Only a moderate suppurative infiltrate is seen on the surface and in the subtending edematous tissue adjacent to the descemetocele. This animal was treated aggressively and the treatment allowed the eye to stay quiet enough for healing to occur, but the defect was too large.

- 1. Central corneal perforation
- 2. Descemetocele
- 3. Corneal stromal neovascularization
- 4. Epithelialization of the descemetocele
- 5. Iris prolapse

## Slide 74, Inf 588, 94RD096

The slide is a vertical section through the globe of a 6 year-old neutered male German Shepherd dog. The globe is distorted by a mass extending from the limbus deep into the orbital tissue. There is a superficial vascularization affecting most of the corneal stroma. There is a thick **preiridal fibrovascular membrane** and **peripheral anterior synechia** with hemorrhage in the dependent iridocorneal angle. There is a lymphoplasmacytic inflammatory infiltrate in the uvea. The vitreous face is hypercellular with lymphoplasmacytic inflammatory cells and spindle cells. There is a **deep optic nerve head cup with gliosis**. There is **inner retinal atrophy** suggesting chronic glaucoma. The mass lesion extends from the subconjunctival connective tissue deep into the orbit. The exposed conjunctival epithelium shows **squamous metaplasia**. The mass itself is made up of granulation tissue with a lymphogranulomatous inflammatory infiltrate. In the deepest segments of the mass there are several **nematode parasite** profiles. The nematodes have an outer cuticle and a body cavity. In some sections a uterus structure with microfilaria can be seen. The nematode morphology is typical of **Dirofilaria**.

### Diagnoses:

- 1. Preiridal fibrovascular membrane
- 2. Peripheral anterior synechia
- 3. Chronic superficial keratitis
- 4. Retrobulbar lymphogranulomatous inflammation
- 5. Retrobulbar aberrant Dirofilaria

**Comment:** Aberrant heartworm can be seen in virtually any part of the body. Nematode parasites are recognized by their outer cuticle, body cavity and internal organs.

## Slide 75, Misc 819, 94RD374

This slide is a vertical section of the globe of a 3 year-old spayed female Chow Chow dog. Histologically there is a vascular ingrowth in the midstroma of the peripheral cornea. The iridocorneal angle is distorted by a band of uveal tissue that stretches from the iris base to the arborized end of Descemet's membrane in a profile typical of **goniodysgenesis**. In the dependent segment there is a combination of fibrin and pigment-laden macrophage cells aggregated at the iridocorneal angle (**pigment dispersion syndrome**). If you look at the iris pigmented epithelium near the pupillary margin you see that the pigmented epithelial cells have been stripped away probably from touching and rubbing on the lens. There is a mild lymphocytic inflammatory infiltrate around blood vessels in the anterior uvea. Small numbers of pigmented cells are seen in the vitreous adjacent to the ciliary body and retina. There is profound **retinal atrophy** with relative sparing of the retina on the tapetal side of the optic nerve (**tapetal sparing**). At the optic nerve head there is tissue malacia with gitter cells as well as gliosis and cupping.

## **Diagnoses:**

- 1. Goniodysgenesis
- 2. Pigment dispersion syndrome
- 3. Chronic glaucoma
- 4. Optic nerve malacia

**Comment:** Disruption of the iris pigmented epithelium and the accumulation of pigmented debris in the dependent iridocorneal angle is a feature occasionally seen in glaucoma especially in association with goniodysgenesis. In people the entrapment of pigment in the trabecular meshwork is thought to play a role in the pathogenesis of glaucoma with pigment dispersion syndrome. The role of pigment dispersion in glaucoma associated with goniodysgenesis is not at all clear.

### Slide 76, Misc 2928, 02RD112

This slide is a vertically sectioned 6 month-old spayed female domestic shorthair cat globe. The animal had neonatal inflammatory disease diagnosed as herpes virus prior to opening of the eyes. Histologically there is virtually no corneal stroma. In the periphery on one side there is approximately 1 mm of stromal tissue in the vascular infiltrate. In this area there is an intact thin Descemet's membrane with coiling of Descemet's at the point of perforation. Over most of the globe the ocular surface is formed by an epithelium and subepithelial scar tissue forming on top of a prolapsed iris. In one segment there are numerous mineralized fragments of epithelial basement membrane (**band keratopathy**) surrounded by multinucleate giant cells and lymphoplasmacytic inflammation in the superficial granulation tissue. Subtending much, but not all, of the surface epithelium there is a lymphoplasmacytic inflammation, however, there is almost no inflammation in the deeper iris tissue or in the remainder of the ocular structures. Only some sections have fragments of retinal tissue however the retinal tissue when sampled is within normal limits.

## **Diagnoses:**

- 1. Extensive corneal perforation
- 2. Extensive iris prolapse with epithelialization
- 3. Band keratopathy and granulomatous inflammation

**Comment:** I believe that this pathology is the result of severe inflammatory keratitis in the neonatal animal prior to opening of the eyelids. The absence of intraocular inflammation and the formation of a largely intact epithelium over the prolapsed iris are remarkable. A similar healing can occur in adults intensively treated for sepsis and inflammation.

### Slide 77, Misc 2008, 00RD205

The slide is a vertical section through the globe of a 12 year-old neutered male Cocker Spaniel dog. There is an extensive superficial corneal vascular ingrowth from the superior limbus. Over the vascular ingrowth there is a lip of unattached corneal epithelium. Notice that the unattached epithelium is disorganized with keratinization occurring on both the inner and outer surface. Also notice that there is a variably thick eosinophilic cell free zone in the immediate superficial stroma underneath the ulcerative lesion. In some areas there is dark basophilia of the basement membrane suggesting mineralization. These changes are typical of recurrent erosion or **indolent ulcer**. At the iridocorneal angle there is a solid band of uveal tissue stretching from the iris base to the arborized terminus of Descemet's membrane in a pattern typical of goniodysgenesis. There is deep cupping of the optic nerve head and profound retinal atrophy with relative tapetal sparing. Pay attention to the cupped optic nerve head. Deep within the nerve tissue there are cavitated lesions filled with smudgy eosinophilic material that would stain brightly positive with alcian-blue (Schnabel's cavernous atrophy). Adjacent to the optic nerve head on the tapetal side just posterior to the sclera, there is a triangular cellular lesion where nerve tissue has an organization more suggestive of peripheral nerve then optic nerve. This type of lesion is seen fairly often in chronic glaucoma and I refer to it as **optic nerve neuroma**, although I do not know for sure there if it is derived from peripheral nerve tissue.

## **Diagnoses:**

- 1. Peripheral stromal keratitis
- 2. Indolent ulcer or recurrent erosion syndrome
- 3. Goniodysgenesis
- 4. Chronic glaucoma
- 5. Schnabel's cavernous atrophy
- 6. Optic nerve neuroma

**Comment:** Indolent ulcer or recurrent erosion is seen surprisingly frequently in enucleated globes. Seldom is the presence of indolent ulcer mentioned in the clinical workup either due to oversight or failure to diagnose. Schnabel's cavernous atrophy has been interpreted as the pushing of hyaluronic acid from the vitreous into the necrotic optic nerve. This pathogenesis is supported by the fact that this process is frequently seen in association with severe and acute disease.

## Slide 78, Neo 2929, 01RD740

The slide is a vertical section through the left globe of an 11 year-old male Labrador Retriever dog. Upon gross sectioning there was a 1 cm pigmented mass filling the superior iridocorneal angle and cradling the lens. Histologically the mass effaces the iris base, ciliary body, and extends a short distance into the inner sclera at the limbus. The mass is made up of solid tissue intermittently organized in long ribbons and cords of variably pigmented epithelium. The AlcBPas stain shows the presence of thick smooth PAS positive basement membrane structures typical of **iridociliary epithelial tumors**. Sections of the distorted lens show the presence of **morgagnian globules** at the lens equator at the point of contact with the posterior chamber mass.

### **Diagnoses:**

- 1. Pigmented iridociliary adenocarcinoma
- 2. Minimal cortical cataract

Comment: It is not unusual for iridociliary epithelial tumors to have a heavily pigmented profile. Grossly these tumors are hard to differentiate from melanoma or melanocytoma. I categorize iridociliary epithelial tumors in dogs in 3 groups depending on the degree of infiltration. The least infiltrative tumors are confined to the posterior chamber or the anterior chamber but show no uveal invasion, the intermediate tumors show invasion of the iris and ciliary body stroma but do not extend into the sclera, and the most invasive tumors show invasion of the sclera as does this tumor. By my own convention I designate tumors that invade the sclera as adenocarcinoma. There is no known risk of metastatic disease. Tumors that show scleral invasion also usually show advanced changes of anaplasia supporting the designation of adenocarcinoma.

# Slide 79, Neo 1117, 97RD15

The slide is a vertically sectioned right globe from a 10 year-old neutered male Cocker Spaniel dog. On gross sectioning the globe was small and filled with solid hard translucent material. There is intermittent corneal stromal vascularization. Remnants of lens with liquified lens contents are seen pushed against the Descemet's membrane in the anterior chamber. The empty lens capsule has **hypermature cataract**. There is a thin **retrocorneal membrane** replacing corneal endothelium. The remainder of the uveal tract is intact but distorted due to the presence of a solid mass of well-differentiated **hyalin cartilage** tissue filling the vitreous chamber of the globe and pushing the lens forward. At the margins of the cartilage there is a glassy collagen membrane with varying numbers of mesenchymal spindle cells forming an interface between the abnormal cartilage and the uvea. No retinal tissue is observed. Very little inflammation is seen. In the superior ciliary body there is stromal hemorrhage.

### **Diagnoses:**

- 1. Stromal keratitis
- 2. Hypermature cataract in anteriorly displaced lens
- 3. Intraocular chondroma (Alternative diagnosis: Intraocular chondromatous metaplasia)

**Comment:** I have only seen a few globes with lesions like this. Osseous metaplasia can be seen in chronically damaged globes, usually occurring near the lens capsule or near Bruch's membrane. No evidence of osseous changes is found in this globe. There is well-differentiated cartilage tissue filling the vitreous cavity and distorting the position of the lens. Because this is a mass lesion filling the vitreous cavity I prefer the designation ocular chondroma, however, because this is a well-differentiated, cartilaginous tissue metaplasia cannot be ruled out.

## Slide 80, Inf 2287, 01RD739

This slide is a section of a vertically cut globe from a 7 year-old neutered male Chow cross dog. Histologically there is irregular thickening of the corneal epithelium with corneal epithelial pigmentation (pigmentary keratitis). Most of the cornea has the corneal endothelium replaced by a spindle cell membrane that includes lymphoplasmacytic and suppurative inflammation (retrocorneal membrane). The sclera at the limbus on both sides of the section is thickened in association with an inflammatory infiltrate that extends from the sclera into the anterior uvea. There is a **preiridal fibrovascular membrane**, which blends with the retrocorneal membrane. There is a spindle cell pupillary membrane spanning the space of the pupil and cradling the anterior lens capsule although the lens itself is artifactually pulled away. There is profound entropion uvei and a spindle cell membrane on the posterior iris. There is artifactual retinal **detachment** and **fibrosis** and mixed inflammation involving the inner sclera and outer choroid almost circumferentially around the globe. In the limbus there is a mixed inflammatory infiltrate, which is full-thickness in the sclera and extends into the ciliary body stroma and iris base. Localized foci of collagen necrosis around granulomatous inflammation are seen in the sclera and granulomatous inflammation extends into the ciliary body. (granulomatous scleritis) Bladder cells and morgagnian globules are seen in the lens cortex (cortical cataract).

- 1. Granulomatous and necrotizing scleritis
- 2. Chronic superficial keratitis
- 3. Retrocorneal membrane
- 4. Broad posterior synechia
- 5. Acquired pupillary membrane
- 6. Granulomatous and lymphoplasmacytic uveitis
- 7. Cortical cataract

# Slide 81, Neo 2932, 01RD748

The slide is a vertically sectioned globe from a 15 year-old male Beagle dog. There is a large pigmented mass bulging inward in the globe extending from the ciliary body to the peripheral choroid. The mass is fairly sharply delineated and is composed of a mixture of heavily pigmented spindle cells with scant numbers of heavily pigmented round cells. Features of nuclear anaplasia or mitotic activity are not seen. The lens is not in the plane of section. The tumor pushes the iris anteriorly such that both the tumor and the iris are plastered against the peripheral cornea and there is a neovascular membrane in the superficial corneal stroma. The cellular features of the mass are typical of **melanocytoma**.

## **Diagnosis:**

## 1. Anterior uveal spindle cell melanocytoma (benign)

**Comment:** The morphologic features that distinguish benign melanocytic tumors (melanocytomas) from malignant ocular melanoma are the features of anaplasia, nuclear atypia, and mitotic activity seen in the neoplastic cells. In my opinion, the size of the original mass, the predominance of spindle cells, and even the invasiveness of the original mass will not help in distinguishing benign from malignant.

### Slide 82, Misc 2591, 01RD790

The slide is the vertically sectioned globe from a 5 year-old male Chow Chow Schnauzer cross dog. At gross sectioning the globe was filled with solid tissue and blood. Histologically there is corneal stromal vascularization with perivascular mixed inflammation. There is a thick retrocorneal membrane that blends to a preiridal fibrovascular membrane obliterating the anterior chamber. There is a moderate lymphoplasmacytic inflammatory infiltrate in the anterior uvea. The posterior chamber is collapsed in association with a collagen rich spindle cell membrane adherent to the wrinkled equator of the lens. Although the lens capsule is empty there are phagocytic cells on the inside of the lens capsule and in addition there is a collagen rich, cell poor membrane in the posterior capsule with duplication of the capsule. All of which suggest **lens capsule rupture** although the rupture is not apparent in all sections. In some areas there is hemorrhage within the lens capsule with hemosiderin laden macrophage cells and the formation of cholesterol clefts within macrophage cells seen in some sections. The collagen rich membrane in the anterior chamber is contiguous with a cyclitic membrane with adhesion of the detached retina to the cyclitic membrane. There is a vitreous and subretinal hemorrhage with hemosiderophage cells in both areas. There is a morning glory retinal detachment. Noticed that the hypertrophy of the retinal pigment epithelial cells is not very impressive. The presence of hemorrhage and hemosiderophages in the subretinal space as well as the configuration of the detached retina leave no doubt that the retina is pathologically detached. There is a rich lymphoplasmacytic inflammatory infiltrate subtending the conjunctiva at the limbus.

# **Diagnoses:**

- 1. Stromal keratitis
- 2. Retrocorneal membrane blending with preiridal fibrovascular membrane
- 3. Lens capsule rupture with hypermature cataract
- 4. Posterior and anterior subcapsular cataract
- 5. Fibrovascular membrane in the posterior chamber
- 6. Cyclitic membrane
- 7. Complete retinal detachment with lymphoplasmacytic retinitis

**Comment:** Hypertrophy of the retinal pigment epithelial cells is not always seen after retinal detachment. In this case there is clearly pathological retinal detachment and the RPE hypertrophy is not impressive. At least some of the collagen rich membrane surrounding the lens capsule is probably associated with released lens epithelial cells. Changes in this globe are most likely associated with some blunt traumatic event.

### Slide 83, Misc 2577, 01RD665

The slide is of the wrinkled globe from a 2 1/2 year-old spayed female Siamese cat. In some of the sections there is a cavitated lesion in the subconjunctival adipose tissue characterized by an empty space surrounded by a thin fibrous capsule in which there is extensive hyperbasophilic staining of the collagen capsule with a moderate number of lymphoplasmacytic and neutrophilic inflammatory cells. Look at the capsule under high magnification to see refractile pigmented bodies and the hyperbasophilic appearance of collagen that suggests absorption of metallic material into the connective tissue. A metallic fragment, presumed to be a BB, was removed from this site at the time of tissue trimming. Sections of the globe itself showed a wrinkled but fairly acellular cornea. Look carefully at both iridocorneal angles and you will see that there is a mixture of inflammatory cells anterior of the trabecular meshwork and on one side there are fragmented remnants of the terminus of Descemet's membrane. There is a mixed inflammatory infiltrate in the tissue of the iridocorneal angle as well as in the remainder of the anterior uvea. There is marked attenuation of the remainder of the corneal endothelium and adjacent to the fragmented Descemet's membrane there is a doubling of Descemet's membrane suggesting deposition of new Descemet's material by damage endothelium. The lens is out of place and there is liquefaction of cortical lens substance and there is formation of a thick subcapsular cataract associate with transformation of lens epithelial cells. Most sections show a zone of dense collagen rich granulation tissue replacing the pars plana and peripheral choroid at the equator of the globe. None of the sections pass through a convincing scleral rupture, however granulation tissue and disruption of uveal tissue as seen in this eye is strong evidence of scleral rupture. Only remnants of retinal tissue are seen, however, the retinal tissue sampled is markedly atrophied and gliotic. The tapetum is clearly sampled in the posterior segment, however sections show fibrosis internal to the tapetum. RPE cells are either not visible or atrophied.

### **Diagnoses:**

- 1. Posttraumatic degeneration of ocular tissues
- 2. Embedded metallic fragment (not seen in all slides)
- 3. Iridodialysis
- 4. Scleral rupture (predicted from uveal fibrosis)
- 5. Hypermature cataract with subcapsular cataract (lens epithelial cell metaplasia)
- 6. Profound retinal atrophy secondary to trauma

**Comment:** This globe has a number of morphologic features that suggest severe ocular blunt trauma that occurred several weeks prior to enucleation. Of particular interest to me is the uveal fibrosis. Fibrovascular tissue proliferation in the globe usually occurs in the chambers of the eye (anterior chamber, posterior chamber, or vitreous body). When granulation tissue replaces uveal tissue itself there is reason to believe that there is scleral rupture even if the rupture is not seen in the plane of section. Only fragments of retinal tissue are seen in this section and those show end-stage atrophy and gliosis. Profound retinal atrophy of this sort in cats is highly suggestive of contusion.

## Slide 84, Neo 2952, 01RD840

The slide is a vertical section through the globe of an 11 year-old spayed female Himalayan cat. Many of the sections are off-center and do not include the optic nerve. The iris tissue is distorted and thickened due to the presence of a neoplastic infiltrate. Neoplastic cells are solid sheets of highly pleomorphic cells commonly with expanded vaculated cytoplasm. The nuclear profiles range from small round quiescent appearing nuclei, sometimes containing a prominent nucleolus, to karyomegalic nuclei with hyperchromatic chromatin and giant nucleoli. Cytoplasmic melanin pigment is not a prominent feature in this tumor. In some areas the prominent cell is a smaller cell with a larger nucleus to cytoplasm ratio and vacuolated clear cytoplasm. Notice that the iris pigmented epithelium is relatively intact although neoplastic cells can be seen in the posterior chamber and also entangled with the zonular ligaments. This is not a central cut and the retinal morphology is distorted by artifact however there is no evidence of glaucoma.

### **Diagnosis:**

## 1. Feline diffuse iris melanoma, balloon cell variant

**Comment:** Cellular variants of feline diffuse iris melanoma include round cell, spindle cell, balloon cell, and any combination of the above. Giant cellular forms with karyomegalic nuclear profiles are a common feature in all of the forms of feline diffuse iris melanoma. It is rare to see tumors with this high proportion of balloon cells. The balloon cell variant is usually seen as a component in tumors expressing other morphologic variants.

## Slide 85, Misc 2416, 01RD187 and Inf 2213, 01RD437

The globes sectioned for this case are from two different animals with similar abnormalities. In both cases the globes were small and wrinkled and after sectioning both halves were embedded in the same cassette. For this reason some of the sections have a corneal defect with full-thickness epithelial downgrowth and prolapse of uveal tissue through the defect. The other section has a segmental scleral defect. Both cases have prominent **chronic superficial keratitis**. There is extensive wrinkling of the globe with either no evidence of lens capsule or wrinkling of the empty lens capsule. Both cases have extensive fibrovascular tissue filling the anterior vitreous space and distorting the globe in association with **phthisis bulbi**. A phenomenon that I always find interesting is the absence of fibrovascular connective tissue proliferation within uveal tract. Notice that the iris, ciliary body, and choroid may be distorted or entrapped in an unusual configuration but scar tissue is usually not deposited directly within the uvea unless there is disruption of the sclera. In a phthisical globe the retinal tissue is usually absent or markedly atrophic. One of the sections has marked retinal atrophy and large numbers of hemosiderin-laden macrophages secondary to long-standing hemorrhage.

- 1. Phthisis bulbi
- 2. Intraocular fibrovascular membrane formation
- **3. Lens capsule rupture** (only seen in one of the cases used)
- **4. Corneal rupture with uveal prolapse and epithelial downgrowth** (only seen in one of the cases used)
- **5. Ocular hemosiderosis** (only seen in one of the cases used)

## Slide 86, Misc 588, 92RD218 and Misc 690, 93RD218

Globes from two cases are used to illustrate this disease. In both globes concentrate on the cornea. You find a segment of brown-discolored acellular stromal material surrounded by vascularized and inflamed corneal stroma. In some of the sections from one of the cases the necrotic stroma has separated from the highly cornea in the transection. In this case there is discolored acellular stroma full-thickness to Descemet's membrane and a separate segment. Noticed that the **corneal sequestrum** remains a cellular while the corneal tissue around it becomes highly vascularized and inflamed. Suppurative inflammation, granulation tissue, macrophages, and epithelium proliferate and migrate around the margins of the sequestrum and in many cases there will isolate the sequestrum that then has the potential of sloughing off. In one of the globes are samples there are opportunistic bacterial organisms growing in the necrotic sequestrum material. There is also a foreign body macrophage reaction at the margins of the necrotic and pigmented corneal stromal tissue. You conceive that the corneal epithelium has turned inward and is attempting to surround the sequestrum. Once that happens the sequestrum will slough.

## **Diagnosis:**

1. Feline corneal sequestrum syndrome

### Slide 87, Misc 2678, 01RD938

The slide is a vertically sectioned globe from an 11 year-old neutered male Maltese dog. Grossly and histologically the lens is entrapped in the anterior chamber (anterior lens luxation) and there is moderate midstromal corneal neovascular infiltrate. The iris is displaced backward on both sides adjacent to and adherent to the lens equator. Supporting the notion that the anterior iris is adherent to the lens equator notice that there are spindle cells and some pigmented cells adherent to the anterior capsular. There are morgagnian globules and bladder cells in the equatorial cortex and lens epithelial cells extend posteriorly to the posterior pole (cortical cataract and posterior subcapsular cataract). The corneal endothelium is either absent or markedly attenuated probably secondary to contact with the luxated lens. There is a spindle cell membrane extending along the anterior vitreous face (cyclitic membrane). The retina shows an absence of ganglion cells, more prominently seen in the nontapetal retina than in the tapetal retina (tapetal sparing). In addition there is a perivascular lymphoplasmacytic retinitis. Not all sections pass through the optic nerve however there is cupping and gliosis of the optic nerve head indicative of **chronic glaucoma**. In the anterior chamber adjacent to the lens there are increased numbers of macrophage inflammatory cells and smaller numbers of neutrophils and lymphoplasmacytic inflammatory cells. There is **peripheral anterior synechia** and closure of the ciliary cleft on both sides. Inflammatory cellular infiltrate is probably secondary to cataract formation (lens induced uveitis).

- 1. Anterior lens luxation (chronic)
- 2. Secondary glaucoma
- 3. Corneal endothelial attenuation
- 4. Posterior synechia
- 5. Peripheral anterior synechia
- 6. Cyclitic membrane
- 7. Equatorial cortical cataract
- 8. Posterior subcapsular cataract
- 9. Lens induced uveitis

### Slide 88, Inf 2361, 01RD985

The slide is a vertical section from the eye of a 2 year-old female domestic shorthair cat. There is a broad **corneal rupture** with **iris prolapse**. The peripheral cornea is markedly distorted with a vascular ingrowth and an intense suppurative inflammatory infiltrate. The epithelium is intermittent even on the intact stroma. At the perforated margin there is evidence of **collagenolytic inflammation**. At the margins of the prolapsed iris there is a vascular and fibroblast cellular proliferation, an attempt by the cells to colonize the necrotic corneal stroma. What remains of the anterior chamber is filled with fibrin and suppurative inflammation. No lens is present in the sections. There is complete **retinal detachment** and evidence of **retinal necrosis**. Following the sclera around the eye you find that segmental areas of sclera are lost in both the superior and inferior posterior segments. **Orbital fibrosis** and **choroidal fibrosis** are confluent over most of the back of the eye. In the superior segment there is a cavitated lesion filled with serum protein and fibrin as well as macrophage cells and neutrophils which is confluent with the attenuated sclera on one side and the fibrotic choroid on the other. This lesion is, in essence, a choroidal seroma.

### **Diagnoses:**

- 1. Broad corneal rupture
- 2. Iris prolapse
- 3. Collagenolytic lysis of the margins of the corneal defect
- 4. Aphakic globe
- 5. Complete retinal detachment with retinal necrosis
- 6. Multifocal and broad scleral rupture
- 7. Confluent orbital and choroidal fibrosis
- 8. Cavitating choroidal seroma
- 9. Severe ocular consequences of blunt trauma

**Comment:** Normally the uveal tract is resistant to fibrosis. An exception to this rule is in the face of scleral rupture as this case has illustrated nicely.

### Slide 89, Inf 2368, 01RD989

The slide is a vertically cut section through the globe from a 4 month-old female domestic shorthair cat. The internal contents of the eye contained large amounts of exudate. In the anterior chamber the exudate has gravitated to the dependent segment and consists of suppurative inflammatory infiltrate and fibrin. Co-mingled with neutrophils are large macrophage cells often containing numerous engulfed neutrophils. A similar cell population is seen in the posterior chamber and extensively in the subretinal space (endophthalmitis). There is complete retinal detachment with neutrophil and macrophage driven retinal necrosis and retinal lysis. Notice the cavitated and vacuolated appearance of the substance of the retina. The subretinal space is filled with suppurative and fibrinous exudate. Notice the exaggerated proliferation of blood vessels extending from the choroid and subretinal space. With suppurative endophthalmitis in both dogs and cats there is an activation and proliferation of blood vessels from the choroid extending into the subretinal space. In cats these lesions also stimulate RPE cell proliferation as in this case. There is episcleral edema and early fibrosis around the optic nerve. The sclera is intact and the lens capsule appears to be intact. In the superior segment the iridocorneal angle is pulled away from the end of Descemet's membrane suggesting cyclodialysis and resulting in an angle **recession**. In a globe like this it may be helpful to search for the presence of a penetrating foreign body such as a plant fragment. Evaluation for localize scleral rupture or lens capsule rupture as well as special stains for bacteria may also be helpful.

- 1. Suppurative endophthalmitis
- 2. Retinal detachment and neutrophil driven retinal necrosis
- 3. Inflammation driven choroidal neovascularization and RPE proliferation
- 4. Cyclodialysis with angle recession
- 5. Presumed penetrating foreign body

### Slide 90, Misc 2686, 01RD994

The slide is a vertical section of the globe of a 3 year-old spayed female mixed breed dog. The most obvious lesion is a dramatic hyperpigmentation of uveal tissues. The iris, iridocorneal angle, and limbus tissues are distorted in association with the increased numbers of pigmented cells. There is an **acquired staphyloma** involving the limbus sclera and dependent iridocorneal angle. There is extensive pigmentation full-thickness through the limbus and pigmented nodules in the orbital tissue. The choroid is markedly thickened and hyperpigmented and there are pigmented cells around the optic nerve head and extending into the orbital tissue. In all areas redundant pigmented tissue is made up of heavily pigmented round cells and small numbers of heavily pigmented spindle cells. There is artifactual retinal detachment. The retinal morphology and optic nerve head morphology remain normal and the animal did not have glaucoma. (Not all sections pass through the optic nerve head.) The diffuse nature of the hyperpigmentation in this case is typical of **ocular melanosis**.

## **Diagnoses:**

- 1. Diffuse ocular melanosis (unilateral)
- 2. Acquired limbal staphyloma

**Comment:** Many pathologists would interpret this as a diffuse form of a melanocytoma. The same populations of heavily pigmented round cells and heavily pigmented spindle cells are typical of melanocytoma. I diagnose melanosis when there is redundant pigmented tissue in the iris, ciliary body, choroid, around the optic nerve and within the limbal sclera, with or without distortion of the iris and filtration angle. Pigment invasion of the limbal sclera from melanosis, melanocytoma, or inflammation often leads to scleral weakening and acquired staphyloma.

## Slide 91, Misc 2685, 01RD995

The slide is a vertically sectioned globe from a 10 year-old neutered male domestic medium hair cat with coalescent pigmented foci on the iris surface. Histologically over much of the iris surface there is a variably thick layer of pigmented cells. The anterior layer of pigmented cells is made up of heavily pigmented polygonal cells with small dark nuclei. Although there are rounded iris melanocytes in the stroma behind the abnormal pigmented cells, there is no evidence of invasion of the iris stroma by abnormal pigmented cells. Rafts of similar pigmented cells can be seen on the trabecular meshwork especially in the dependent segment. A thin membrane of angular heavily pigmented cells with small round nuclei and no evidence of invasion of the iris stroma is characteristic of what I call **feline iridal melanosis**. When the cells begin to invade the iris stroma usually there is a morphologic change with a larger nucleus and rounded configuration. By my criteria, stromal invasion is the hallmark of early feline diffuse iris melanoma.

# **Diagnosis:**

1. Feline iridal melanosis with no evidence of melanoma

## Slide 92, Misc 2684, 01RD980

The slide is a vertically sectioned globe from a 10 year-old male Shih Tzu dog. There is an extensive anterior stromal neovascular infiltrate in the cornea. In addition to blood vessels there is fibrosis and a mixed lymphoplasmacytic and suppurative inflammatory infiltrate. Axially there is a superficial ulcer and the margins of the ulcer have detached epithelial flaps that show a loss of polarity typical of **indolent ulcer** or **recurrent erosion syndrome**. There is **luxation of the lens into the anterior chamber** that is characterized by a backward bending of the iris. There is a thick **preiridal fibrovascular membrane** with prominent and broad **peripheral anterior synechia**. There is a mature **cortical cataract** with **posterior migration of lens epithelial cells** and **proliferation of lens epithelial cells**. There is rupture of the lens capsule characterized by migration of lens epithelial cells across the ruptured margin in several areas. In addition, there is a macrophage driven inflammatory infiltrate seen on the exposed margins of the lens fibers in the area of capsular rupture. The retina is **artifactually detached** with a relative loss of ganglion cells. In this specimen there is mainly ganglion cell loss with little other retinal atrophy. There is **cupping and gliosis of the optic nerve head** typical of chronic glaucoma.

- 1. Stromal keratitis
- 2. Indolent ulcer or recurrent erosion syndrome
- 3. Mature cortical cataract
- 4. Posterior migration and proliferation of lens epithelial cells
- 5. Preiridal fibrovascular membrane with peripheral anterior synechia
- 6. Anterior lens luxation
- 7. Lens capsule rupture with a histiocytic response
- 8. Chronic glaucoma

## Slide 93, Misc 2796, 01RD1267

The slide is a vertical section through the globe of a 5 year-old spayed female German Short Hair Pointer dog. There is a pathologic **morning glory retinal detachment** with a cellular infiltrate hugging the outer retina and inner choroid. There is little inflammation away from these two areas. Focusing on the cellular infiltrate at the level of the inner choroid, subretinal space, and within the retina, there is a mixture of macrophage cells and small numbers of lymphoplasmacytic cells. Large numbers of poorly stained organisms are seen. The organisms are characterized by a poorly stained refractile capsule that contains one to several poorly stained irregular organisms. These organisms stain intensely with the PAS stain and have the typical morphology of **Prototheca**. Morning glory retinal detachment with a bland granulomatous inflammation and large numbers of poorly stained organisms is characteristic of ocular protothecosis.

- 1. Granulomatous chorioretinitis
- 2. Morning glory retinal detachment
- 3. Ocular protothecosis

## Slide 94, Inf 2499, 02RD172

The slide is a vertical section through the globe of a 12 year-old neutered male Yorkshire Terrier dog with a history of **diabetes mellitus**. Histologically there is a peripheral midstromal neovascular infiltrate in the cornea. There is an intense protein rich exudate in the anterior chamber, posterior chamber, and vitreous space. The iris is entrapped in an inflammatory membrane made up of lymphoplasmacytic cells in the stroma and histiocytic cells in the anterior chamber and facing the lens. There is a **mature cortical cataract**. Globular hypereosinophilic protein deposits are seen around the outside of the lens capsule suggesting released lens proteins. There is an intense, mainly histiocytic, inflammatory infiltrate on the inner aspect of the pars plana and inner retina with distortion and destruction of the inner retina. There is a perivascular lymphoplasmacytic inflammatory infiltrate deeper in the retinal tissue. The retina is artifactually detached.

## **Diagnoses:**

- 1. Mature cortical cataract (diabetic cataract)
- 2. Histiocytic driven endophthalmitis (phacolytic endophthalmitis)
- 3. Lymphoplasmacytic uveitis

**Comment:** Rapidly progressing diabetic cataract often incites a histiocytic driven endophthalmitis as seen in this case.

## Slide 95, Neo 2534, 00RD1064

The slide is a vertical section of the right eye of a 5 year-old Golden Retriever spayed female dog. There is extensive protein and cellular infiltrate in the anterior chamber. There is a corneal neovascular infiltrate in the superficial stroma throughout the section. There is a neovascular infiltrate in the deep stroma anterior to Descemet's membrane. There is a thick **preiridal fibrovascular membrane** with **peripheral anterior synechia**. There are multifocal hemorrhages in the distorted iris tissue, posterior chamber, ciliary body stroma, and retina. Look carefully at the iris and ciliary body stroma and notice that there are multiple dilated blood vessels that are occluded by **thrombosis**. The retina is detached with atrophy and absence of ganglion cells as well as multifocal **retinal coagulation necrosis**. Look carefully at the stroma of the ciliary body and iris and you will find clusters and aggregates of anaplastic cells that have a large nucleus to cytoplasm ratio. The cells are clustered together to form solid sheets, sometimes within blood vessels and sometimes extending through blood vessels into the posterior chamber. Neoplastic cells colonize the lens capsule, iris base, and posterior aspect of the Descemet's membrane. The pattern of infiltration in this globe is typical of **metastatic carcinoma** in the dog.

- 1. Metastatic carcinoma
- 2. Preiridal fibrovascular membrane with peripheral anterior synechia
- 3. Multifocal vascular thrombosis
- 4. Retinal detachment with retinal necrosis
- 5. Secondary glaucoma

# Slide 96, Neo 2105, 99RD950

The slide is a vertically sectioned globe from a 13 year-old neutered male domestic shorthair tabby cat. The cornea and anterior uvea are largely within normal limits. There are **epithelial cysts in the pars plana** in the superior segment. The tissue around the optic nerve is distorted due to the presence of numerous infiltrating aggregates of anaplastic epithelium sometimes coalescing to form solid sheets. Typically there is a basilar layer with smaller cells and large nucleus to cytoplasm ratio. In most areas there is differentiation of keratinizing squamous cells. Individual foci extend out into the extraocular muscles and are seen within the lumen of blood vessels throughout the tissue of the orbit adjacent to the optic nerve. In addition there is extensive involvement of the meninges. Neoplastic keratinizing cells are seen within blood vessels in both the choroid and retina and there is extensive evidence of retinal edema and folding seen most prominently in the central retinal tissue. This pattern of orbital, choroidal, and retinal vascular involvement is typical of **metastatic squamous cell carcinoma in cats**.

## **Diagnoses:**

- 1. Metastatic squamous cell carcinoma in the orbit, choroid, and retina
- 2. Retinal edema

**Comment:** Metastatic tumors in cats tend to occur in the choroid and orbit. Squamous cell carcinoma is secondary to lung cancer, however nasal cancer, middle ear cancer, oral cancer, or skin cancer is most common.