

1

Pathology of the Eye and Periocular Tissues

Joseph S. Haynes

Department of Veterinary Pathology, Iowa State University, Ames, IA, USA

Introduction

Surgical pathology of the eye is unique in that the eye is a polarized organ with multiple segments, any of which may develop primary disease. A primary disease in one segment frequently will cause secondary disease in another segment. Microscopic examination of a diseased eye is somewhat analogous to performing a necropsy, in that each segment must be examined independently for lesions similar to the way each organ must be examined in an animal at necropsy, before a final diagnosis can be made.

Prefixation Preparation

In general, eyes removed at surgery and submitted for examination of ocular disease should have the periocular tissues, eyelids, and extraocular muscles removed prior to fixation. This should reveal the sclera and the long posterior ciliary arteries, which extend circumferentially around the globe from the optic nerve; these vessels denote the junction of the dorsal (tapetal) and ventral (nontapetal) portions of the fundus. This is important for the purpose of orienting the globe for sectioning, so that both tapetal and nontapetal fundus can be included in the microscopic slide. If the eye has been removed because of a lesion that involves the periocular or palpebral tissue and evaluation for surgical clearance is warranted, then the globe should not be stripped of periocular tissue, but the specimen should be left intact and the surgical margins should be marked with dye prior to fixation.

Fixation of Eyes for Histopathology

After eyes are removed and prepared, they should be immersed in 10–20× volumes of fixative as quickly as possible. Even a delay of few minutes will result in autolysis, especially of the retina. Several fixatives can be used with good results; however, all have some limitations. Traditionally, eyes were fixed in Bouin's fixative, which provided very good preservation of the globe and all internal segments, and it hardened the globe and thus retained the globe's prefixation turgor and shape. However, because of its environmental hazard, it is no longer routinely used. Davidson's fixative, which is composed of ethanol, formalin, and glacial acetic acid, has replaced Bouin's in our laboratory, and it provides the same level of fixation but much less hazardous than Bouin's. Ten percent neutral buffered formalin (10% NBF), which is the standard fixative for all biopsy and necropsy tissue specimens, can also be used. It is inexpensive; provides good fixation for the cornea, external ocular structures, and the anterior uvea and is not as hazardous as Bouin's fixative. However, it is slow to penetrate the globe, which results in a substantial amount of autolysis in the retina. In addition, it does not preserve the prefixation turgor of the globe; therefore, the globe will partially collapse and be more difficult to accurately section. This lack of rapid globe penetration and loss of turgor can be somewhat overcome by injecting 0.25–0.5 ml of formalin into the vitreous chamber with a 25-gauge needle.

Sectioning

Once the eye is fixed and rinsed, it needs to be sectioned. The globe is oriented so that the cornea is on the cutting board surface and the optic nerve is pointing to the ceiling. With a new razor blade (we use a new disposable microtome blade), the first cut is made lateral to the optic nerve, transecting the long posterior ciliary artery. The cut is continued all the way through the lens and cornea onto the cutting board; when the lens is encountered, the blade is pushed vertically through the lens to help avoid displacing it. Then a second cut is made parallel to the first cut on the medial side of the optic nerve, trying to avoid hitting the lens the second time. This produces a section out of the center of the globe that includes the optic nerve head, lens, tapetal, and nontapetal fundus. This section, along with the lateral and medial calottes (cup-shaped lateral and medial pieces of the globe), should be examined for lesions, such as hemorrhage, exudate, lens luxation, detached retina, and masses. An additional section is cut from the center of each calotte; these are perpendicular to the first section and allow evaluation of all four quadrants of the globe. These sections are placed in appropriately sized cassettes for processing and embedding in paraffin.

Processing and Staining

Once the tissues are processed and embedded, they are sectioned on the microtome to produce sections 3–5 μm thick. These are mounted on glass slides, deparafinized, and stained. **Hematoxylin and eosin (HE)** are the standard stains used for microscopic evaluation. Additional stains that may be helpful to identify certain structures or agents include **PAS stain** (basement membranes, fungi, yeasts, plant material); **GMS stain** (fungi, yeasts), and **Gram's stain** (bacteria). **Immunohistochemistry** is very useful for identifying certain molecules and the cells that contain them. Examples include IHC for coronavirus to confirm Feline infectious peritonitis, or glial fibrillary acidic protein (GFAP) to identify astrocytes in the retina and optic nerve.

Ocular Structure and Development

The eye is a complex structure in the shape of a globe that is designed to take in light from the outside and focus it, so it can be transmitted to the brain and form a visual picture of the world. The main components of the eye are **cornea, uvea (iris, ciliary body, and choroid), lens, retina, sclera, and optic nerve** (Figure 1.1). In addition, there are three chambers that are either filled with fluid, called **aqueous humor** (anterior and posterior chamber), or a gelatinous mass of **vitreous body** (vitreous chamber). In addition, the globe is surrounded by a set of periocular tissues that include the **conjunctiva** (bulbar and palpebral), **eyelids, third eyelid, lacrimal glands** and ducts, and **extraocular muscles**. Aqueous humor is produced by the nonpigmented epithelium on the ciliary processes and passes from the posterior chamber through the pupil into the anterior chamber, into the **ciliary cleft**, and ultimately is resorbed by the scleral veins. The **trabecular meshwork** is the complex of channels that forms the walls of the ciliary cleft. The angle formed by the junction of the cornea and iris is the **iridocorneal angle**. In most domestic mammals, the IC angle is spanned by a variably perforated structure, the **pectinate ligament** that originates at the termination of **Descemet's membrane** and inserts on the peripheral



Figure 1.1 Normal canine eye.

aspect of the **iris**. The **lens** is situated behind the iris and is held in place by **zonular fibers** from the **ciliary body**. The **vitreous body** sits behind the lens and fills the vitreous chamber, keeping the **retina** in place. In the vascular tunic of the globe, the **choroid** is the layer external to the retina, and the **sclera** is the densely fibrous external tunic of the globe.

Photons of light enter through the cornea, passing through the stratified squamous epithelium, corneal stroma, and corneal endothelium (inner lining of the cornea). Light continues through the aqueous humor in the anterior and posterior chambers and is then focused by the lens onto the retina. For light to get to the retina, it must pass through the vitreous body (humor). The fluid components of the eye (aqueous and vitreous humors) are important for nutrition and to help maintain the proper shape of the globe and organization of the internal segments; they must remain clear in order to transmit light. Light passes through the inner segment of the retina and is received by the photoreceptors in the outer segment. The photoreceptors (rods and cones) transduce photons of light energy into impulses of electrical energy that are transmitted to the neurons in the inner segment of the retina, especially the ganglion cells. These neurons, in turn, relay impulses through the optic tracts to the vision center in the cerebral cortex, where the visual image is formed.

The eye is formed in a series of steps initiated by an outgrowth of neural tissue from the primitive forebrain; this is the **optic vesicle**. As the optic vesicle grows toward the surface of the embryo, it stimulates the ectoderm to focally thicken into the **lens placode**. The lens placode then enlarges and grows to meet the optic vesicle; as it does this, it will form the **lens vesicle**. The lens vesicle will ultimately give rise to the lens. As the lens vesicle interacts with the optic vesicle, the optic vesicle caves in on itself to form the **optic cup**; this will give rise to the **retina** and **retinal pigment epithelium (RPE)**. This entire group of structures is surrounded by periocular mesenchyme, which will be induced to form the corneal stroma and endothelium, the stroma of the uvea, the sclera, and a transient set of blood vessels that will nourish the developing lens and retina. The development of the periocular mesenchyme into the aforementioned structures depends on appropriate RPE development; if this does not occur, then various ocular anomalies will occur. Such anomalies include **cystic eye**, in which the eye does not develop past the optic vesicle stage, and **microphthalmia**, in which abnormal development produces a small eye with discernible uvea and neuroepithelium that is dysplastic and disorganized (Figure 1.2a, b). There is a wide range in eye size and level of development with microphthalmia. In addition, an eye that is fairly normal in size may have a variety of incompletely developed or dysplastic interior segments, such as goniodysgenesis, choroid hypoplasia, retinal dysplasia, and/or nonattachment; these are frequently lumped together as **multiple ocular defects** (Figure 1.3).

Cornea

The cornea is the most rostral portion of the globe; the junction between the cornea and the sclera is the **limbus**. The cornea is derived from ectoderm and therefore is essentially a very specialized type of “skin” devoid of adnexae. It is composed of a superficial layer of **nonkeratinized stratified squamous epithelium**, that is five to eight cells thick, a superficial

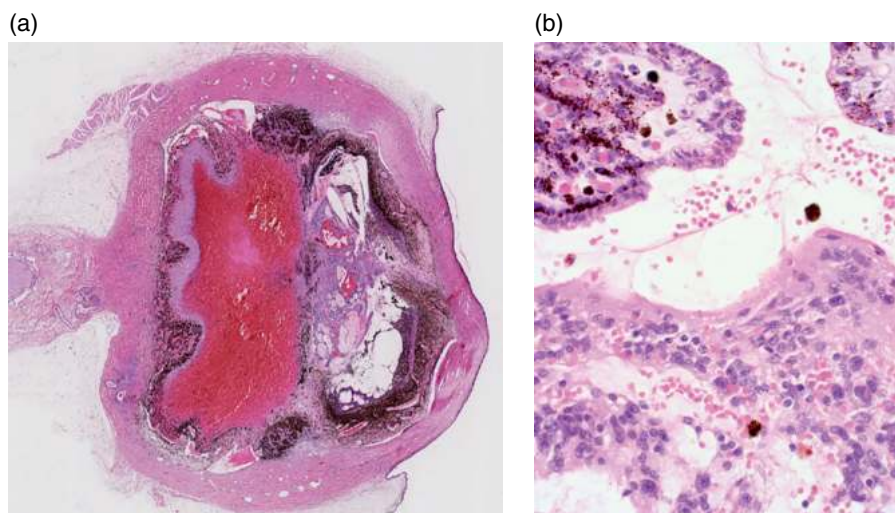


Figure 1.2 (a, b) Microphthalmia. Abnormal eye development that produces a small eye with discernible uvea and neuroepithelium that is dysplastic and disorganized.



Figure 1.3 Multiple ocular defects. Abnormal development has resulted in retinal dysplasia, goniodysgenesis, and congenital cataract.

basement membrane (**Bowman's membrane**), a stroma of avascular, highly structured fibrous connective tissue, and a layer of simple squamous epithelium, referred to as **corneal endothelium**. The stroma is maintained in a relatively dehydrated state by the epithelial layers on either side; this helps preserve its organization and clarity. Between the corneal stroma and the corneal endothelium is a thick basement membrane, known as **Descemet's membrane**, which terminates at the ciliary cleft. Since the cornea is avascular, it is nourished, hydrated, and lubricated by the tear film, which is composed of secretions from the lacrimal glands and cells lining the palpebrae and conjunctiva.

General Corneal Reactions to Injury

The cornea has a limited set of reactions to various injuries that occur. Acute reactions consist of **loss of epithelium** (erosion or ulcer), **edema**, serous, fibrinous, and/or purulent inflammation, or combinations of these (Figure 1.4). When the cornea develops edema or exudate in the stroma, the organization of the collagen fibers in the stroma is perturbed, which results in cloudiness of the cornea; this is common with ulcers. Chronic reactions consist of **epithelial hyperplasia** and **keratinization**, **fibrosis** of the stroma, and **neovascularization** (Figure 1.5). Epithelial hyperplasia can become severe enough to microscopically resemble epidermis, and coupled with superficial stromal fibrosis, resemble non-haired

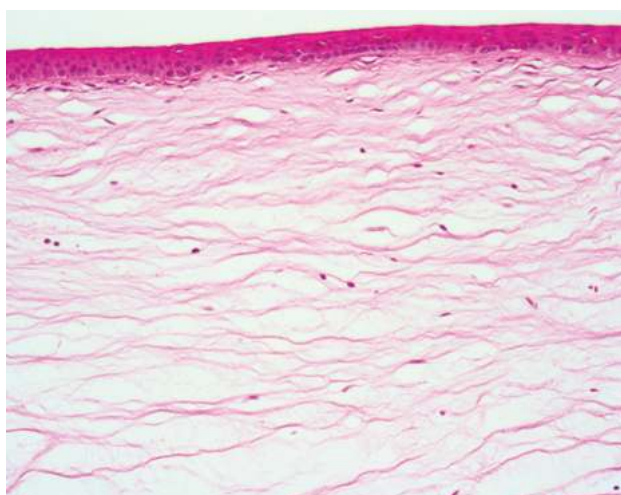


Figure 1.4 Corneal edema.

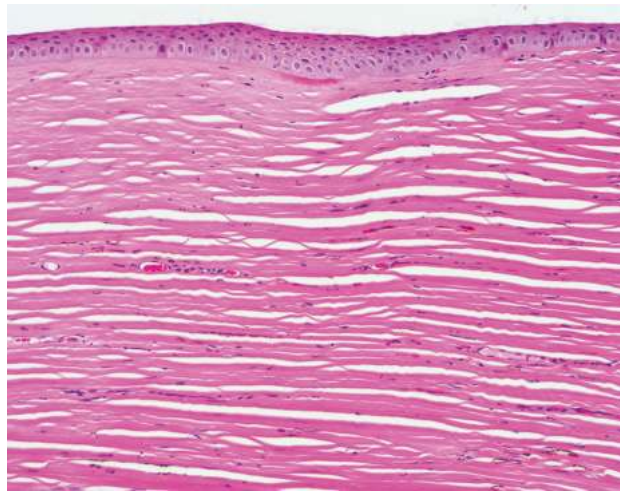


Figure 1.5 Moderate corneal stromal neovascularization.

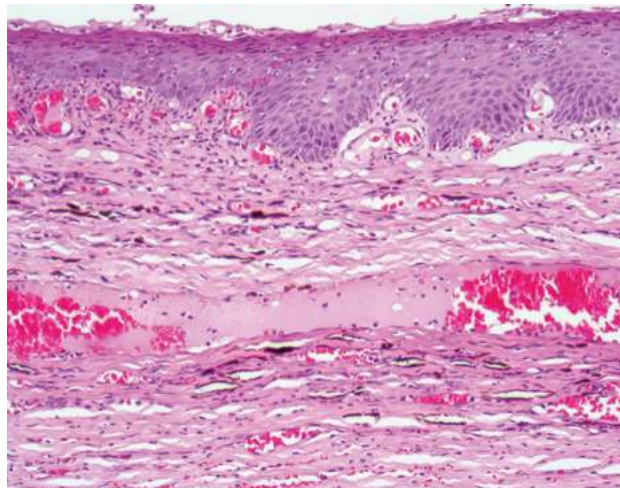


Figure 1.6 Corneal cutaneous metaplasia (epidermalization) due to chronic keratitis. There is hyperplasia with rete ridge formation of the surface epithelium. Also, there is marked fibrosis, hyperpigmentation, and neovascularization of the corneal stroma.

skin; therefore, this change is referred to as **cutaneous metaplasia** or “**epidermalization**” of the cornea (Figure 1.6). Fibrosis of the superficial stroma disrupts the normally precise organization of the stromal collagen fibers, causing corneal opacity (Figure 1.7). Neovascularization of the cornea commonly occurs secondary to ulceration, chronic keratitis, and uveitis; it will start from the limbus and progress toward the center of the cornea.

Developmental and Degenerative Corneal Disease

Corneal Dermoid

This is a developmental anomaly that consists of a patch of haired skin growing on the cornea.

Corneal Erosions and Ulcers

The loss of one or more layers of the superficial epithelium is **corneal erosion** (Figure 1.8). Loss of corneal epithelium through Bowman’s membrane with exposure of the corneal stroma is an **ulcer** (Figure 1.9). These are commonly due to trauma, injury from a foreign body, or drying. In addition, ulcers are commonly associated with keratitis (corneal inflammation). Occasionally, corneal ulcers are delayed in healing because the corneal epithelium does not establish appropriate

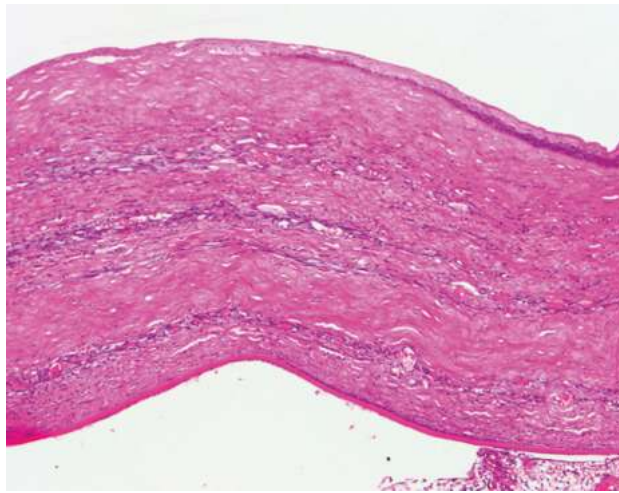


Figure 1.7 Corneal stromal fibrosis and neovascularization.

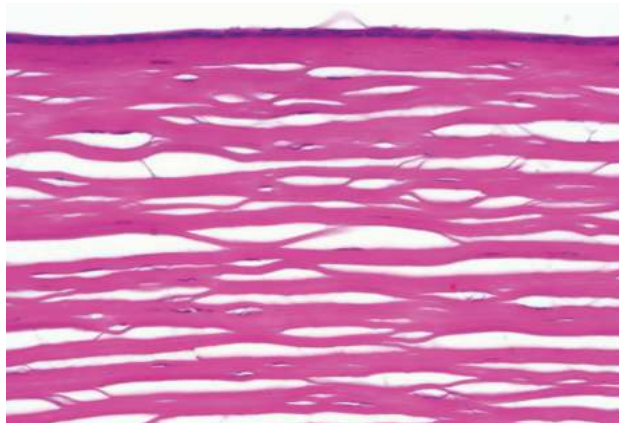


Figure 1.8 Feline corneal erosion. The surface epithelium is attenuated and only one to two layers thick.

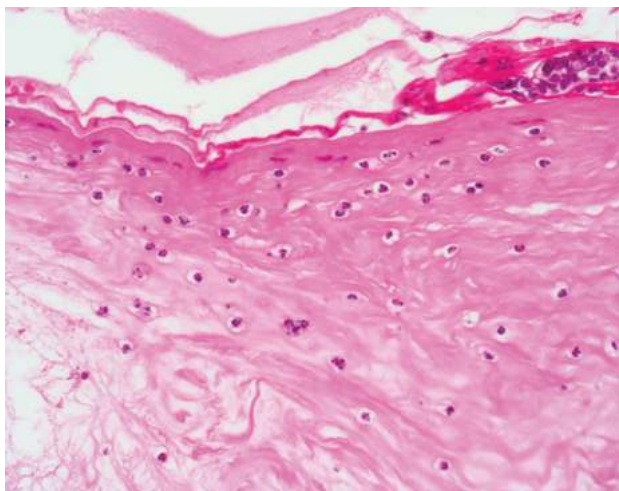


Figure 1.9 Corneal melting ulcer in a dog. The surface epithelium has been totally lost, the superficial stroma is necrotic and partially liquefied, and there are a few degenerate pmns evident.

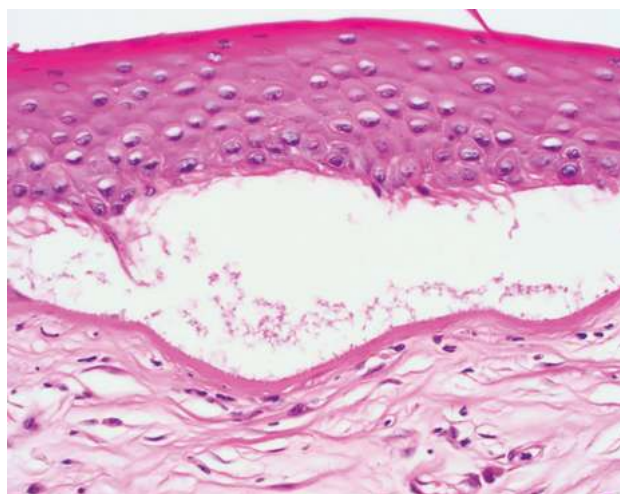


Figure 1.10 Persistent or recurring corneal ulcer. The surface epithelium regrows following ulceration but does not form hemidesmosomes for reattachment to the basement membrane, therefore ulceration recurs. Note the thickened, uneven basement membrane.

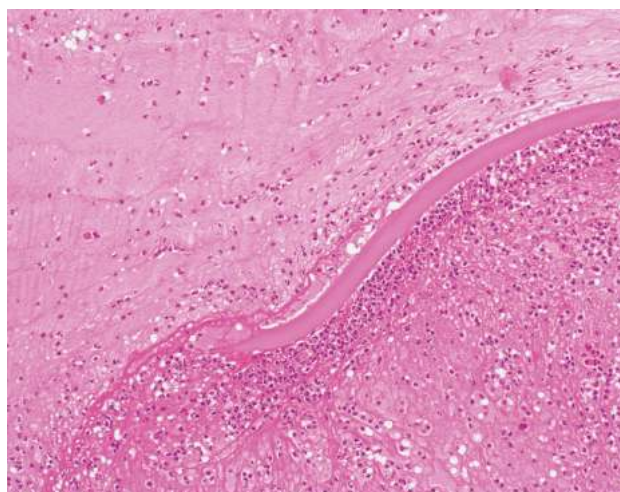


Figure 1.11 Rupture of Descemet's membrane associated with fibrinopurulent keratitis.

adhesion with the underlying basement membrane or stroma. These **persistent ulcers** occur primarily in dogs and are due to a failure of hemidesmosome production (Figure 1.10). There are several infectious agents that are noted for causing corneal ulcers in various species; **feline herpes virus** in cats is an example. A particularly deep ulcer that extends down to Descemet's membrane is very serious and will result in bulging of Descemet's membrane into the ulcer, which is called a **descemetocoele**. In this condition, the cornea is in jeopardy of perforation (Figure 1.11). If the cornea does perforate, then frequently the iris will prolapse into the perforation, acting like a plug; this is a **staphyloma** (Figure 1.12a, b). Healing of corneal ulcers (depending on the depth of the ulcer) is accomplished by a combination of stromal fibrosis, re-epithelialization, and possibly neovascularization.

Corneal Sequestration

This is death of a portion of the corneal stroma, which results in a characteristic brown focus, typically in the center of the cornea (Figure 1.13). The dead tissue apparently accumulates brownish pigment from the tear film, which results in this color change. This condition almost exclusively occurs in cats, especially Persian and Himalayan cats, and is frequently associated with chronic ulceration.

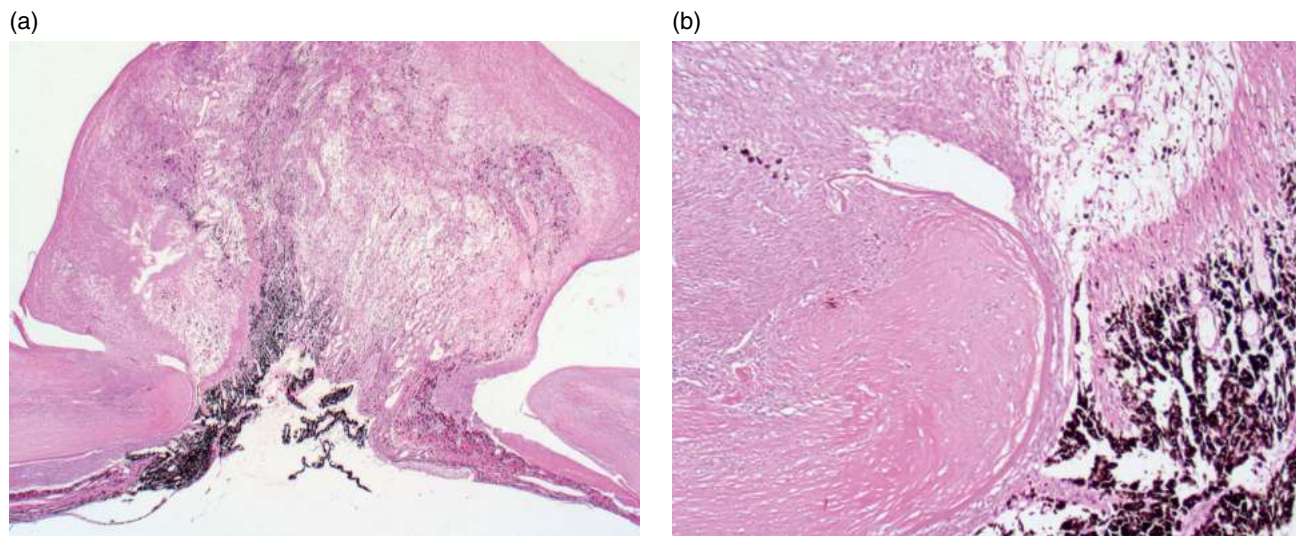


Figure 1.12 (a, b) Perforated corneal ulcer with prolapse of iris (staphyloma).



Figure 1.13 Keratectomy specimen from a cat with a corneal sequestrum. This is secondary to a chronic corneal ulcer with necrosis of the stroma. Note the characteristic brown discoloration.

Corneal Endothelial Dystrophy and Mineralization

Several breeds of dogs have a defect in corneal endothelial integrity due to degeneration, which results in seepage of aqueous humor into the corneal stroma. This results in corneal opacity due to edema (Figure 1.14a, b).

Corneal Stromal Dystrophy and Mineralization

Deposits of lipid, cholesterol, and/or mineral may occur in a variety of breeds of dogs and cats, which are recognized as specific corneal stromal dystrophies. In addition, these materials may also be deposited in the corneal stroma secondary to injury or metabolic abnormalities such as hypercholesterolemia or hypercalcemia.

Inflammatory Disease of the Cornea

Keratitis

Inflammation of the cornea is **keratitis**. As mentioned, keratitis commonly occurs with or leads to corneal ulceration (Figure 1.15). As with ulcers, keratitis also frequently is associated with abnormalities in the tear film. **Acute keratitis** is

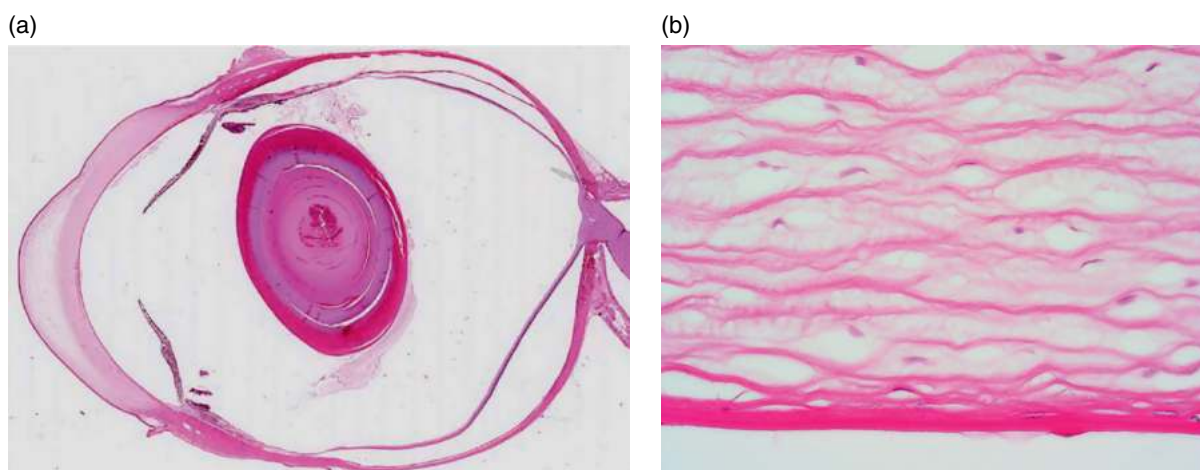


Figure 1.14 (a, b) Corneal endothelial dystrophy. There is degeneration and loss of corneal endothelium resulting in corneal edema.

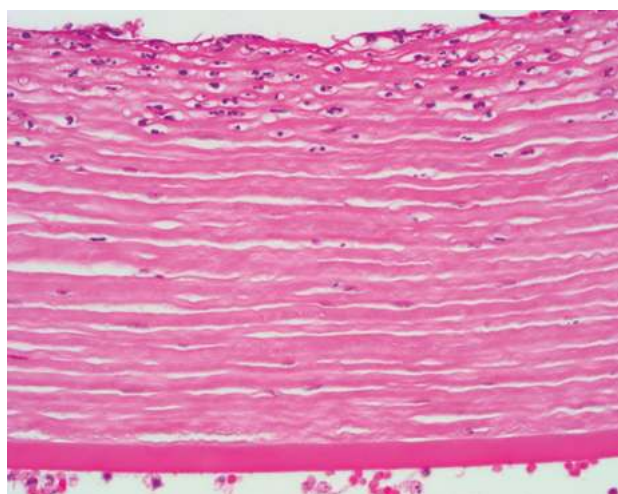


Figure 1.15 Acute ulcerative keratitis. The surface epithelium and basement membrane have been lost, and there is a moderate infiltrate of pmns within the superficial stroma.

frequently associated with conjunctivitis. Since the cornea is normally avascular, exudate that accumulates in acute keratitis must come from the tear film and adjacent vascular tissues, especially the bulbar and palpebral conjunctiva. Swelling of the cornea that occurs in acute keratitis is due to loss of epithelium and imbibition of fluid from the tear film and serous exudate from adjacent structures; this is usually referred to as “**corneal edema**” and causes the cornea to be cloudy. Neutrophils migrate into the cornea from the tear film and when numerous contribute to destruction of the corneal epithelium and stroma via the release of toxic oxidative molecules and enzymes. **Chronic keratitis** is typically characterized by neovascularization and fibrosis of the stroma with epithelial hyperplasia (Figure 1.16). Once corneal neovascularization is established, then inflammatory cells may enter the stroma through new vessels. Chronic keratitis is usually the result of a persistent injury, such as an eyelid abnormality.

Opportunistic bacteria, such as *Pseudomonas sp.* will occasionally colonize a small ulcer, and through production of potent enzymes that break down the stromal matrix (**matrix metalloproteinases**) and stimulate suppurative inflammation, make it much larger and progressive; this is **ulcerative and suppurative keratitis or keratomalacia** (also known as a “**melting ulcer**”) (Figure 1.17a, b).

Keratitis sicca

This is chronic keratitis that develops secondary to loss of adequate tear film production or maintenance.

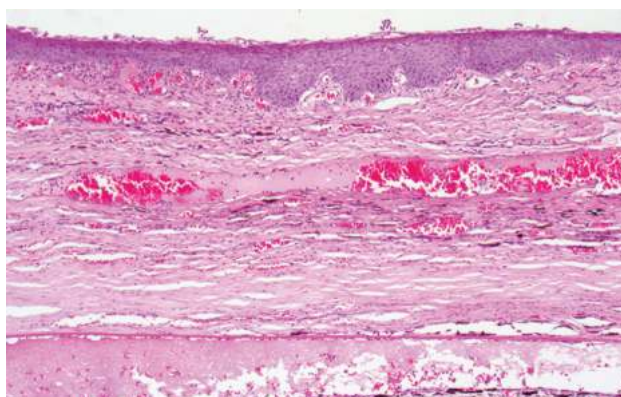


Figure 1.16 Chronic keratitis with cutaneous metaplasia. This is a common lesion that develops secondary to low-grade persistent injury associated with loss of tear film. In addition to cutaneous metaplasia, there is a moderate infiltrate of lymphocytes and plasma cells within the stroma.

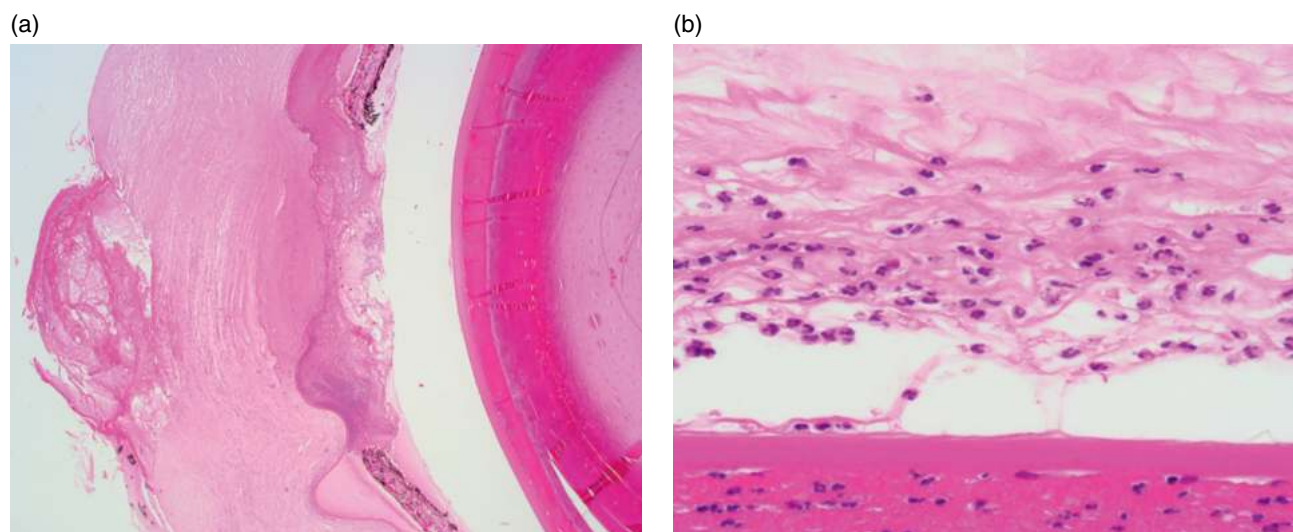


Figure 1.17 (a, b) Ulcerative and fibrinopurulent keratitis (melting ulcer). Note perforation of cornea.

Canine Pannus Keratitis (Chronic Superficial Keratitis)

This is a chronic progressive lesion that begins at the lateral limbus and spreads toward the center of the cornea. It occurs most commonly in German shepherd dogs but is not limited to this breed. Grossly, it is a red, fleshy plaque. Microscopically, it is characterized by an interface infiltrate of lymphocytes and plasma cells with vacuolar degeneration and scattered apoptosis of the basal epithelial cells, and occasionally, hyperpigmentation (Figure 1.18a, b). In addition, there is neovascularization of the superficial corneal stroma, and frequently, the superficial stroma contains scattered melanophages.

Feline Herpetic Keratitis

This disease is caused by **feline herpes virus 1 (FHV-1)**, which is characterized by corneal ulceration. There are two forms: **dendritic ulceration**, which typically involves the corneal epithelium only; and **stromal ulceration**, which is deeper, more chronic, and contains an infiltrate of lymphocytes and plasma cells.

Feline Eosinophilic Keratitis

This is a form of chronic stromal keratitis that is unique to cats. It is characterized by an inflammatory cell infiltrate of macrophages, lymphocytes, plasma cells, and few to many eosinophils (Figure 1.19). In addition, there is usually fibrosis and modest neovascularization with ulceration or hyperplasia of the overlying epithelium.

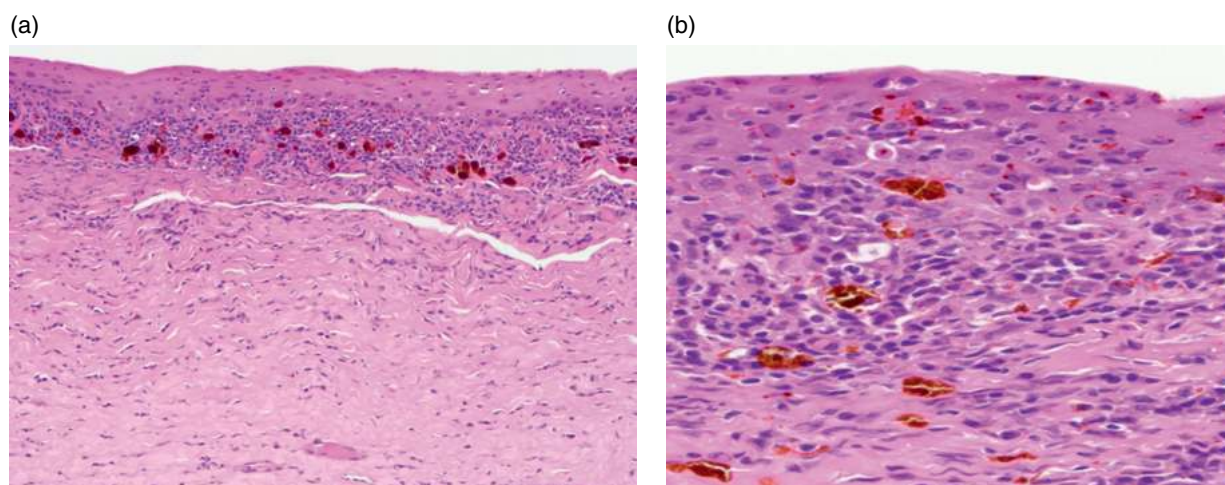


Figure 1.18 (a, b) Canine pannus keratitis (chronic superficial keratitis). There is a diffuse infiltrate of lymphocytes and plasma cells along with hyperpigmentation, pigmentary incontinence, and scattered apoptotic epithelial cells.

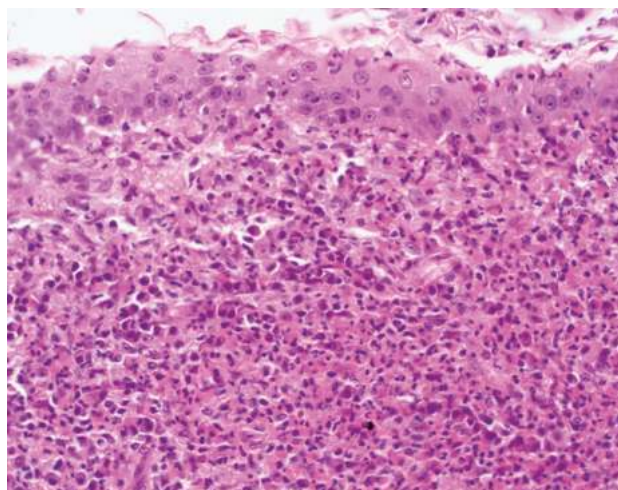


Figure 1.19 Feline eosinophilic keratitis. There is a marked diffuse infiltrate of eosinophils in the corneal stroma.

Mycotic Keratitis

Infection of the cornea with fungi is a fairly common, serious disease in horses and dogs. The agent involved is usually *Aspergillus sp.*, which typically enters through a corneal ulcer. *Aspergillus sp.* spreads through the corneal stroma and has a tropism for basement membrane; therefore, it typically invades the anterior basement membrane and Descemet's membrane. Fungal invasion incites a very necrotizing and fibrinopurulent reaction (Figure 1.20a–c). Occasionally, the cornea will perforate.

Equine Corneal Stromal Abscess

This is typically a collection of purulent exudate bordered by fibrovascular tissue deep in the corneal stroma (Figure 1.21a, b). Frequently, it is adjacent to Descemet's membrane. It is most likely the result of a small penetrating injury to the cornea with bacterial or fungal infection, although many times agents are not detected with histopathology.

Uvea

The uvea is composed of the **iris**, **ciliary body**, and **choroid**. It is pigmented with melanin and is very vascular. In fact, it is the main vascular supply to the outer half of the retina and provides nutrients to the lens and interior of the globe via the aqueous humor. **Aqueous humor** is an ultrafiltrate that is generated by the ciliary processes of the ciliary body and flows

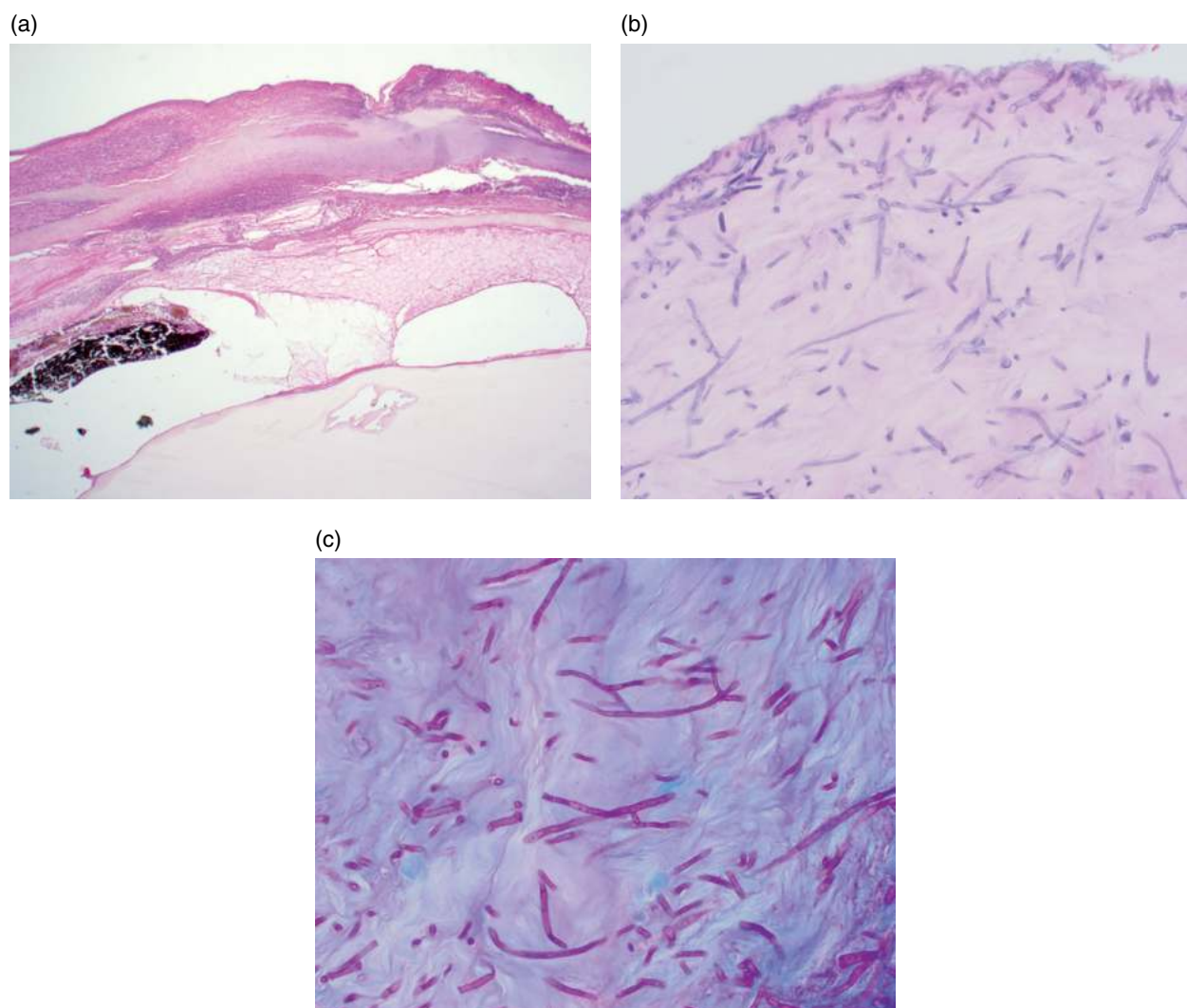


Figure 1.20 (a–c) Mycotic keratitis in a horse. There is marked ulcerative and fibrinopurulent inflammation of the cornea with fungal hyphae within the stroma.

anteriorly through the posterior chamber and pupil, into the anterior chamber, and then through the iridocorneal angle into the **ciliary cleft**. Here, aqueous humor flows into a series of interconnected vascular channels within the **trabecular meshwork** and exits the globe via scleral vessels. The iris helps regulate the amount of light passing to the lens and retina. The anterior surface of the iris is covered by a layer of melanocytes. The ciliary body is covered by epithelium, which is derived from neural tissue from the optic vesicle. The **zonular fibers** extend from the ciliary body and attach to the lens and thus hold it in place. The choroid is situated between the sclera (outside) and retina (inside). It is a fibrovascular layer, which also includes the **tapetum lucidum**. The tapetum is a reflective layer present in the dorsal portion of the globe in many mammals; it helps concentrate light for vision during relative darkness.

General Uveal Reactions to Injury

Since the uvea is a vascular structure, perhaps the most common reaction to injury is inflammation (**uveitis**). In fact, exudate that accumulates within the eye necessarily comes from the uvea and can take on various patterns that provide insight as to cause, as discussed later. **Intraocular hemorrhage** is a common lesion that can develop secondary to coagulopathy, trauma, uveitis, and intraocular neoplasms (Figure 1.22). It typically originates in the uvea, and depending on its location, may cause retinal detachment or hyphema. If severe, it will impair vision, and as it begins to organize, it will result in fibrosis that will distort intraocular structures.

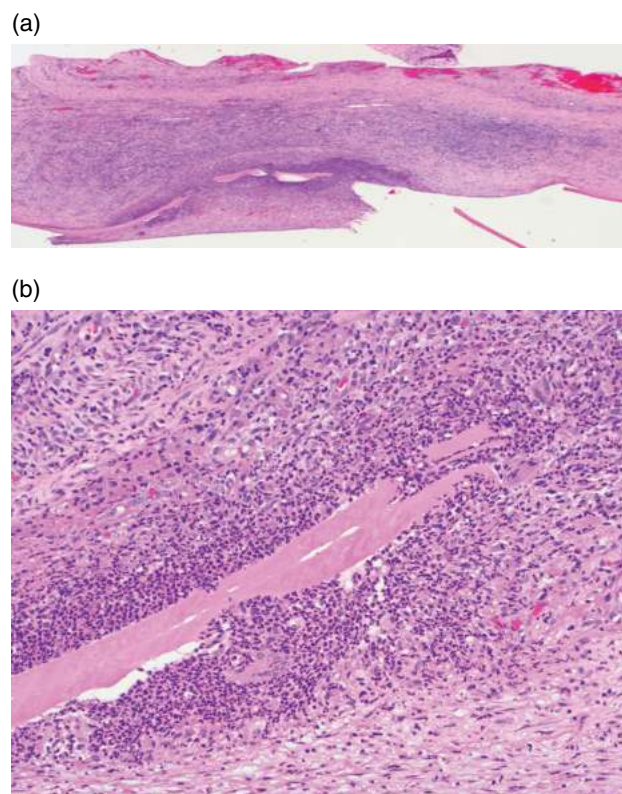


Figure 1.21 (a, b) Equine corneal abscess. En bloc removal of a deep corneal abscess in a horse.

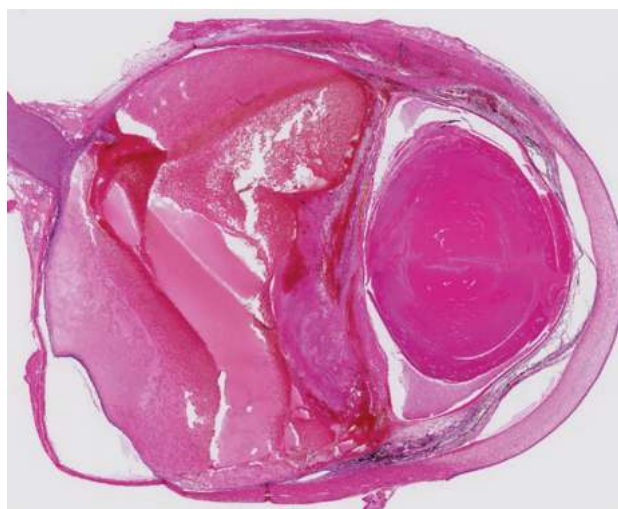


Figure 1.22 Intraocular hemorrhage filling the vitreous chamber.

Developmental and Degenerative Uveal Disease

Defective formation of the uvea during development is a common reaction to injury. Developmental defects of the uvea can vary widely in severity from mild goniodysgenesis that has little clinical significance to severe hypoplasia associated with multiple ocular defects.

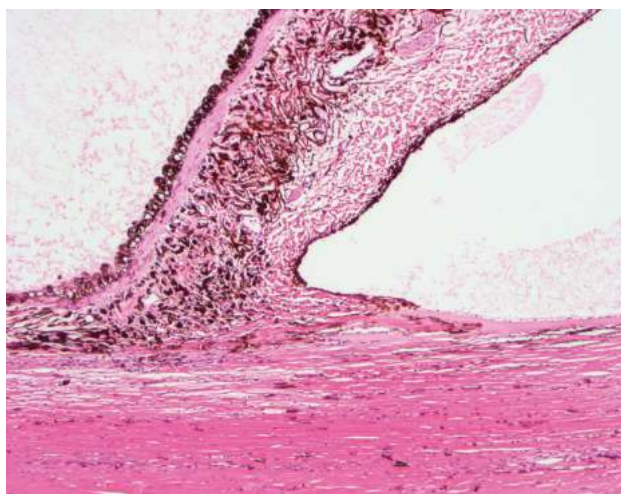


Figure 1.23 Goniodysgenesis. The termination of Descemet's membrane is split, and there is not a clearly distinct pectinate ligament or trabecular meshwork.

Goniodysgenesis and Pectinate Ligament Dysplasia

This is failure of the iridocorneal angle to develop normally. It may involve the entire circumference of the iridocorneal angle or only one or more segments (Figure 1.23). It is usually characterized by failure of the pectinate ligament to form correctly, a bulbous or abnormal termination of Descemet's membrane, failure of the ciliary cleft to open and a sheet of mesenchymal tissue in place of the trabecular meshwork. It is frequently a feature of eyes that have primary glaucoma.

Persistent Pupillary Membrane

Persistent pupillary membrane (PPM) is a developmental anomaly that is formed by the persistence of strands of the primary tunica vasculosa lentis. It is characterized by the attachment of strands of tissue (endothelial lined tubes) extending from the minor arterial circle of the iris to the cornea or anterior lens capsule. Fibrous metaplasia is usually present where these strands insert on the lens or cornea.

Choroidal Hypoplasia

This is an underdevelopment of the choroid characterized by thinning and hypopigmentation. It occurs in many species and is common in animals that have color-dilution of the hair coat. It may not be clinically significant in many instances, but it is a characteristic feature of the **Collie eye anomaly syndrome**, which is an inherited set of ocular lesions that occur in collies (Figure 1.24). The extent of the lesions may vary from case to case, but the characteristic components are choroidal hypoplasia and hypopigmentation, mild microphthalmia, scleral ectasia, and posterior coloboma adjacent to the optic nerve. The basic defect is an abnormality in RPE development, which results in failure of proper induction of the

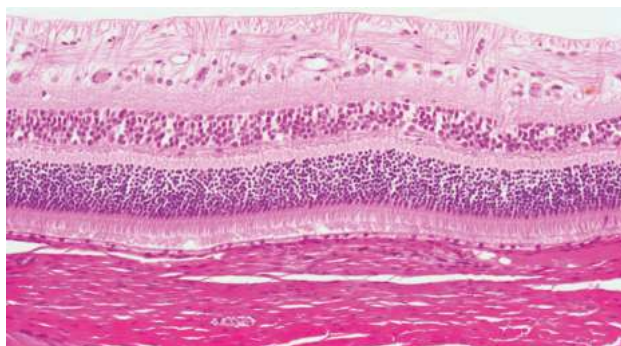


Figure 1.24 Choroidal hypoplasia in the Collie eye anomaly syndrome. The retina is fairly normal in this section, but the choroid is very thin and difficult to recognize.

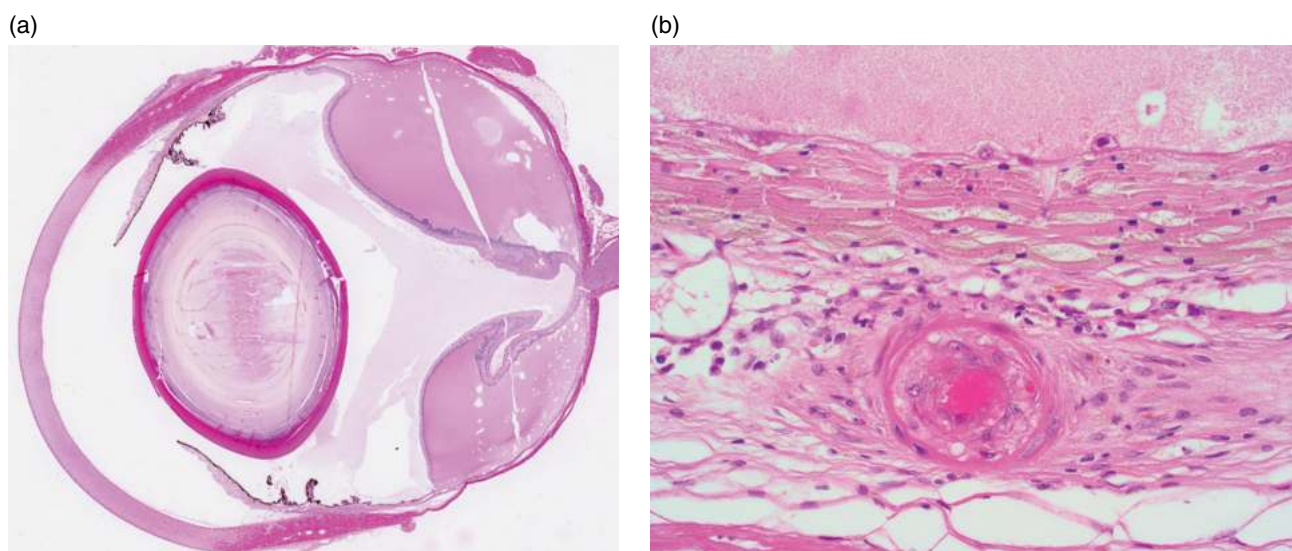


Figure 1.25 (a, b) Retinal detachment secondary to hypertensive vasculopathy in a cat with chronic renal failure.

periocular mesenchyme. This results in the failure of the choroid and sclera to develop properly and failure of the optic fissure to close properly. The retina bulges into the optic fissure, further impeding scleral development, resulting in scleral ectasia and posterior coloboma.

Hypertensive Vasculopathy

Hypertensive vasculopathy occurs in dogs and cats that have prolonged hypertension, which is frequently the result of chronic renal failure, especially in cats. The characteristic lesion is thickening and hyalinization of the walls in arterioles within the choroid and retina. This commonly leads to accumulation of transudate between the RPE and retina, resulting in retinal detachment (Figure 1.25a, b).

Inflammatory Disease of the Uvea and Ocular

Uveitis

Uveitis, inflammation of the uvea, is the most common reaction to uveal injury and is classified according to the portion of the uvea that is involved, the duration of the inflammation, and the type of exudate produced. The types of exudate that occur in uveitis vary and frequently give a clue as to the possible cause. Exudate not only is present within the uvea but may also accumulate in one or all of the ocular chambers. Most types of exudate are possible – serofibrinous, purulent, pyogranulomatous, and lymphoplasmacytic. Inflammation of the iris is **iritis**; inflammation of the ciliary body is **cyclitis**; and inflammation of the choroid is **choroiditis**. **Anterior uveitis** is inflammation of the iris and the ciliary body (also called iridocyclitis). **Panuveitis** is inflammation of all components of the uvea. **Acute uveitis** is characterized by hyperemia of the iris and the production of serous or serofibrinous exudate (and possibly pmns), which accumulates on the surface of the iris and within the anterior chamber. **Plasmoid aqueous** is a term used for the accumulation of protein from serous exudate in the aqueous humor (Figure 1.26). Accumulation of purulent exudate in the anterior chamber is **hypopyon** (Figure 1.27a, b). Occasionally exudate will adhere to the endothelial side of the cornea (the clinical term for this is **kera-titic precipitates**). Injury to the corneal endothelium can result in corneal edema. An inflamed iris is prone to adhere to the endothelial surface of the cornea (**anterior synechia**) or anterior surface of the lens capsule (**posterior synechia**). Acute uveitis may resolve or progress to chronic uveitis. **Chronic uveitis** is characterized by an infiltrate of lymphocytes, plasma cells, and/or macrophages. In addition, a layer of fibrovascular tissue will frequently develop over the anterior surface of the iris; this is a **pre-iridial fibrovascular membrane (PIFM)** (Figure 1.28). **Rubeosis iridis** is the clinical term for the gross appearance of a PIFM. PIFM is a serious complication of chronic uveitis because this tissue may grow into the ciliary cleft, resulting in occlusion and secondary glaucoma. Also, PIFM may distort the pupillary margins of the iris (causing **entropion uveae** or **ectropion uveae**), cause posterior synechia with pupillary block, or anterior synechia. When

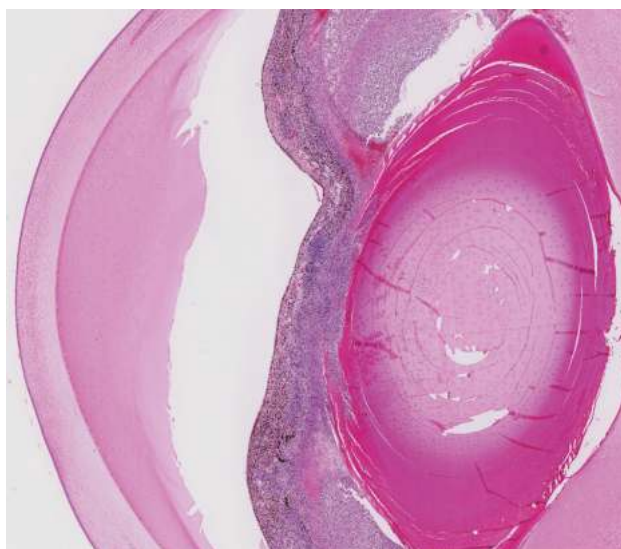


Figure 1.26 Plasmoid aqueous. This is a term used for the accumulation of protein from serous exudate in the aqueous humor. There is a marked infiltrate of lymphocytes and plasma cells in the iris.

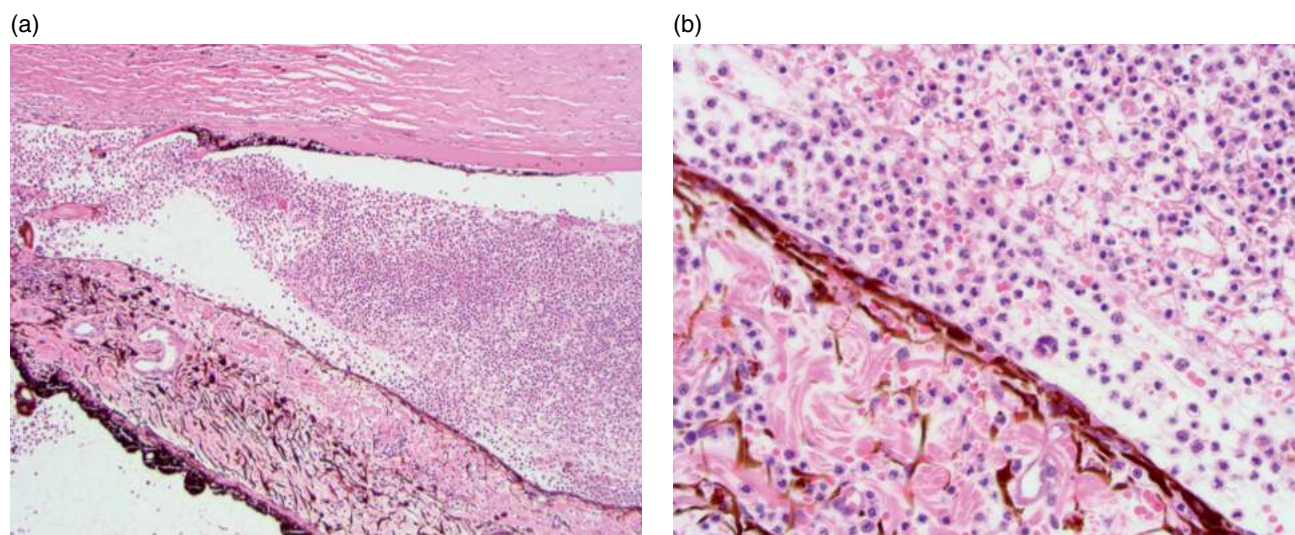


Figure 1.27 (a, b) Acute purulent anterior uveitis. The anterior chamber and ciliary cleft are filled with purulent exudate (hypopyon).

pupillary block occurs, i.e. a 360° posterior synechia, aqueous humor will accumulate in the posterior chamber, pushing against the iris; this will make the iris bulge anteriorly, a condition known as **iris bombe** (Figure 1.29). Fibrinous exudate or hemorrhage adjacent to the ciliary body will frequently be organized into a membrane that extends along the zonular fibers, covering the posterior surface of the lens; this is a **cyclitic membrane** (Figure 1.30). Another complication of chronic uveitis is the stimulation of corneal neovascularization. The end-stage inflammatory lesion of chronic uveitis or endophthalmitis is **phthisis bulbi**, which is characterized by a shrunken, fibrotic globe with partially destroyed remnants of the inner segments and lymphoplasmacytic to granulomatous exudate (Figure 1.31a, b).

Lymphoplasmacytic Anterior Uveitis

This is the most common form of uveitis in dogs, and it is usually an idiopathic condition. It is characterized by a perivascular to diffuse infiltrate of lymphocytes and plasma cells within the iris and ciliary body (Figure 1.32a, b).

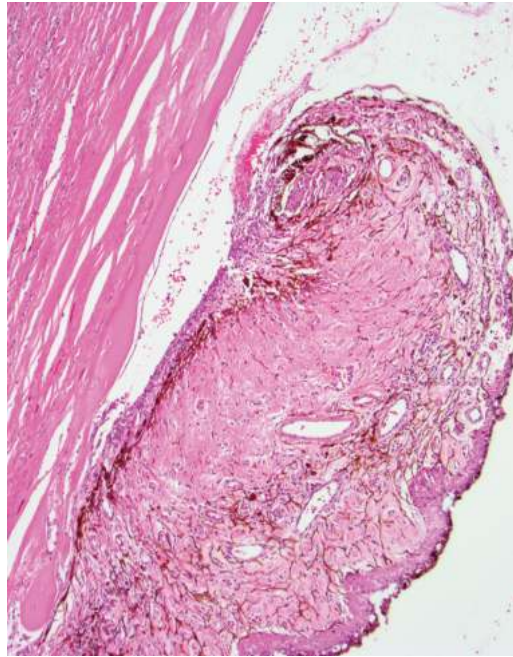


Figure 1.28 Chronic anterior uveitis with preiridial fibrovascular membrane that has distorted the iris pupillary margin (ectropion uveae) and collapsed the iridocorneal angle.



Figure 1.29 Iris bombe. Chronic anterior uveitis with a 360° posterior synechia, resulting in iris bombe. Also, the anterior chamber is filled with serofibrinous exudate and hemorrhage.

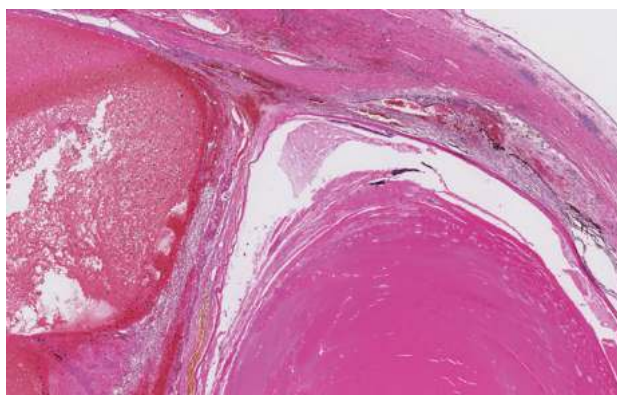


Figure 1.30 Cyclitic membrane of partially organized hemorrhage extends from the surface of the ciliary body along the posterior lens capsule.

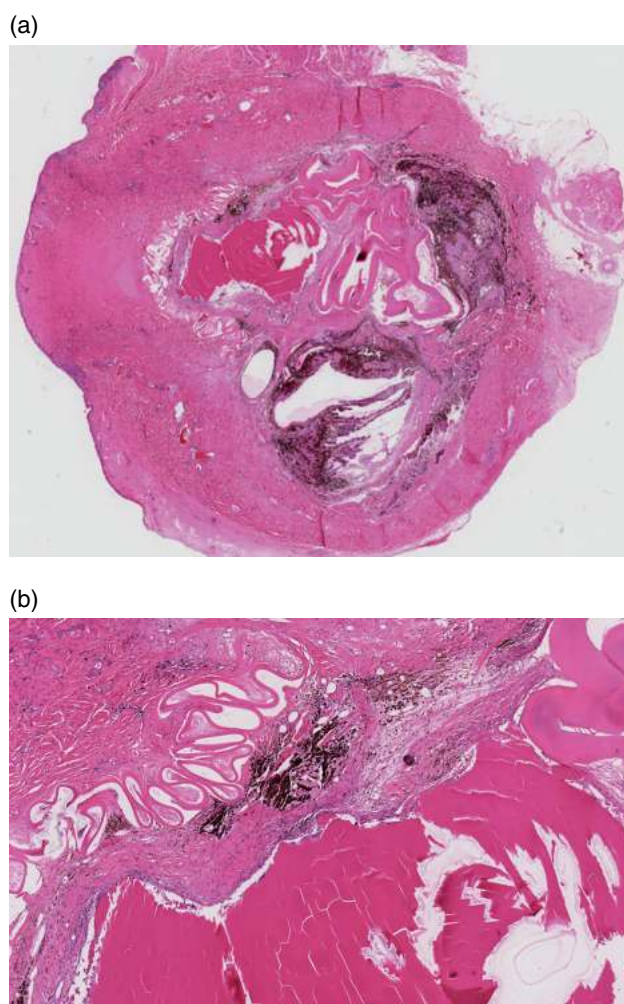


Figure 1.31 (a) Phthisis bulbi secondary to a penetrating wound through the cornea and chronic endophthalmitis. (b) Note the fibrotic cornea, convoluted Descemet's membrane, and remnants of the anterior uvea, lens capsule, and lens fibers.

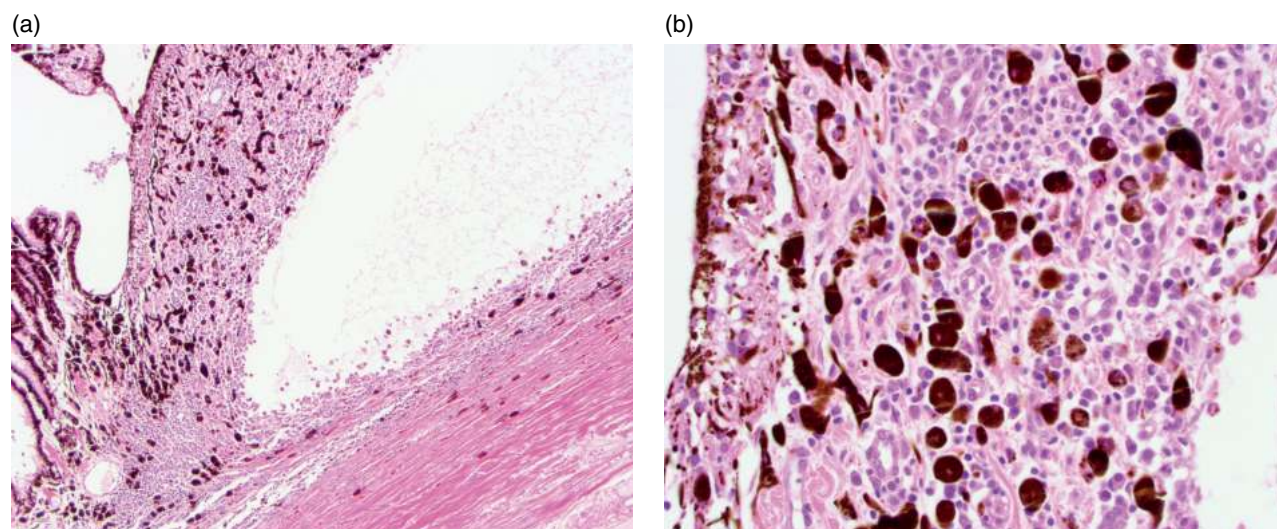


Figure 1.32 (a, b) Lymphoplasmacytic anterior uveitis. There is a diffuse infiltrate of lymphocytes and plasma cells within the iris and ciliary body that has resulted in closure of the ciliary cleft.

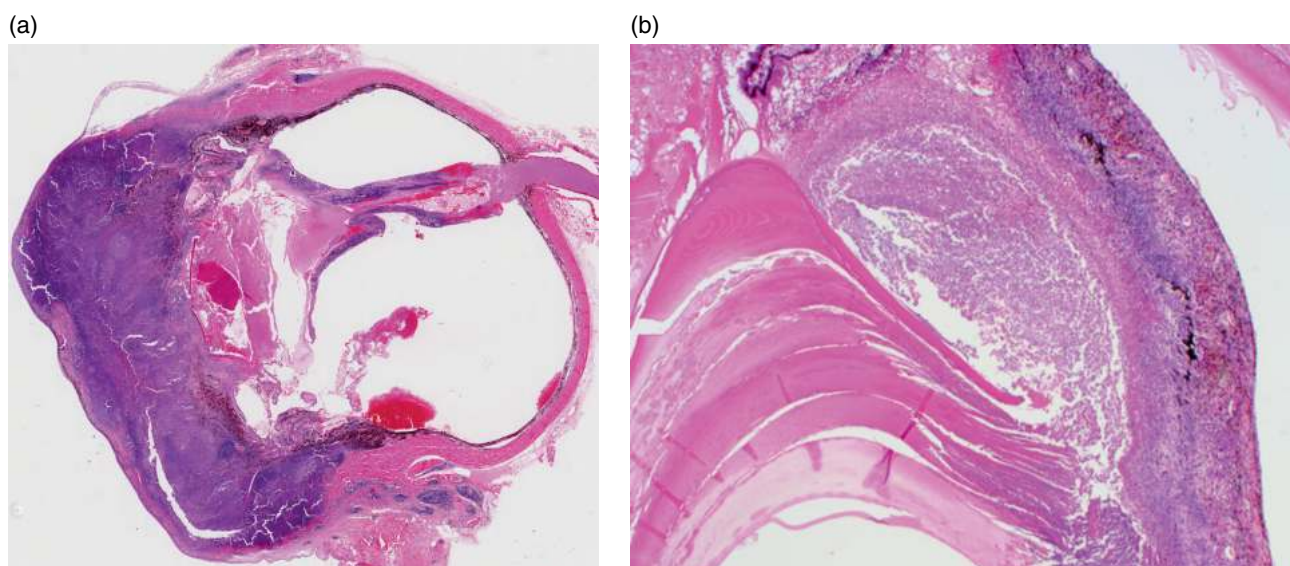


Figure 1.33 (a, b) Phacoclastic uveitis. The lens capsule has been ruptured, and the lens proteins have incited severe lymphoplasmacytic to pyogranulomatous inflammation of the uvea.

Phacoclastic Uveitis/Endophthalmitis

This is a severe form of uveitis that develops following traumatic rupture of the lens capsule. Rupture of the lens capsule allows abrupt leakage of lens proteins into the chambers of the eye, which stimulates severe inflammation within the lens (phacitis), adjacent uvea, and ocular chambers (Figure 1.33a, b). Accumulation of purulent to pyogranulomatous exudate between lens fibers, within the anterior uvea and ocular chambers, frequently with posterior synechia, is characteristic.

Phacolytic Uveitis

This is a milder form of uveitis that is caused by a less severe leakage of lens proteins, frequently secondary to maturing cataract. An infiltrate of lymphocytes and plasma cells within the anterior uvea is typical.

Equine Recurrent Uveitis

This is the most common form of uveitis in horses, and it is characterized by lymphoplasmacytic exudate with a thick layer of **amyloid-like material** covering the epithelium of the ciliary body (Figure 1.34a, b). Equine recurrent uveitis (ERU) is considered to be an autoimmune disease triggered by infection with *Leptospira* spp. The theory for the pathogenesis of ERU is that lesions occur in the uvea because it contains antigens that are similar to those on *Leptospira* sp., therefore, the immune response generated to the bacteria also targets the cross-reactive antigens in the uvea.

Uveitis Due to FIP Coronavirus

Vasculocentric pyogranulomatous and lymphoplasmacytic panuveitis are characteristic of the ocular lesions that occur in **feline infectious peritonitis** (Figure 1.35a–c). This is an important multisystem disease that is caused by infection with a feline coronavirus (FIP virus) and the profound, yet ineffective immune reaction to this virus. The disease develops in cats that are unable to clear the virus but continually mount an ineffective immune response to the virus. The eyes are a common location for lesions with FIP.

Canine Uveodermatologic Syndrome (VKH-like Syndrome)

This is an autoimmune disease that occurs in dogs, primarily in Akitas, Samoyeds, and Siberian Huskies, which targets the pigmented segments of the eye and skin. This results in **severe granulomatous panuveitis/endophthalmitis** and **interface dermatitis** (Figure 1.36a, b).

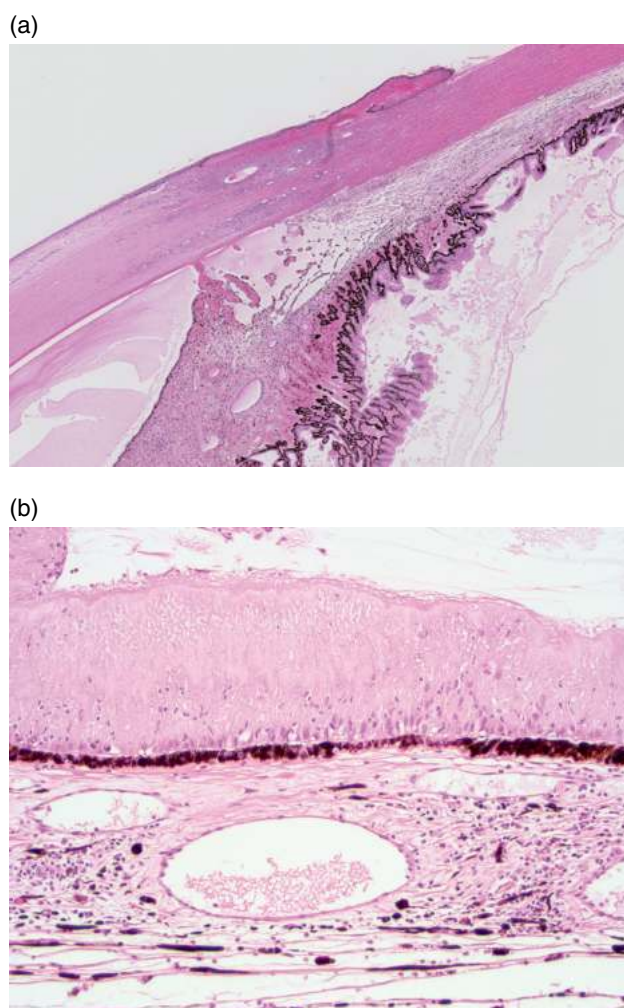


Figure 1.34 (a, b) Equine recurrent uveitis. There is serous exudate in the anterior chamber along with a perivascular to diffuse infiltrate of lymphocytes and plasma cells in the iris and ciliary body. Also there is amyloid-like material covering the neuroepithelium of the ciliary body.

Pigmentary Uveitis

This is a condition that occurs primarily in Golden Retrievers and is characterized by multiple thin-walled uveal cysts, usually on the ciliary body and posterior surface of the iris (Figure 1.37a, b). In addition, there is substantial melanin pigment throughout the anterior chamber, vitreous, ciliary cleft, trabecular meshwork, and adhered to the lens capsule. However, there is only a minimal inflammatory infiltrate in the uvea. This results in cataract and secondary glaucoma.

Endophthalmitis and Panophthalmitis

Endophthalmitis is not a specific disease but is an inflammatory condition of the eye characterized by **inflammation of all interior segments and chambers of the eye**. Typically exudate is present within the anterior, posterior, and vitreous chambers. **Panophthalmitis** is essentially endophthalmitis plus inflammation of the sclera and cornea. The character of the exudate can vary from serous to granulomatous, but usually it includes fibrin and pmns. When serofibrinous exudate is grossly evident in the aqueous and/or vitreous chambers, it is referred to as **plasmoid aqueous** or **plasmoid vitreous**, respectively. Endophthalmitis and/or panophthalmitis are characteristic of several diseases, including blastomycosis, cryptococcosis, feline infectious peritonitis, and intraocular bacterial infections, especially those from corneal perforation or penetrating foreign objects.

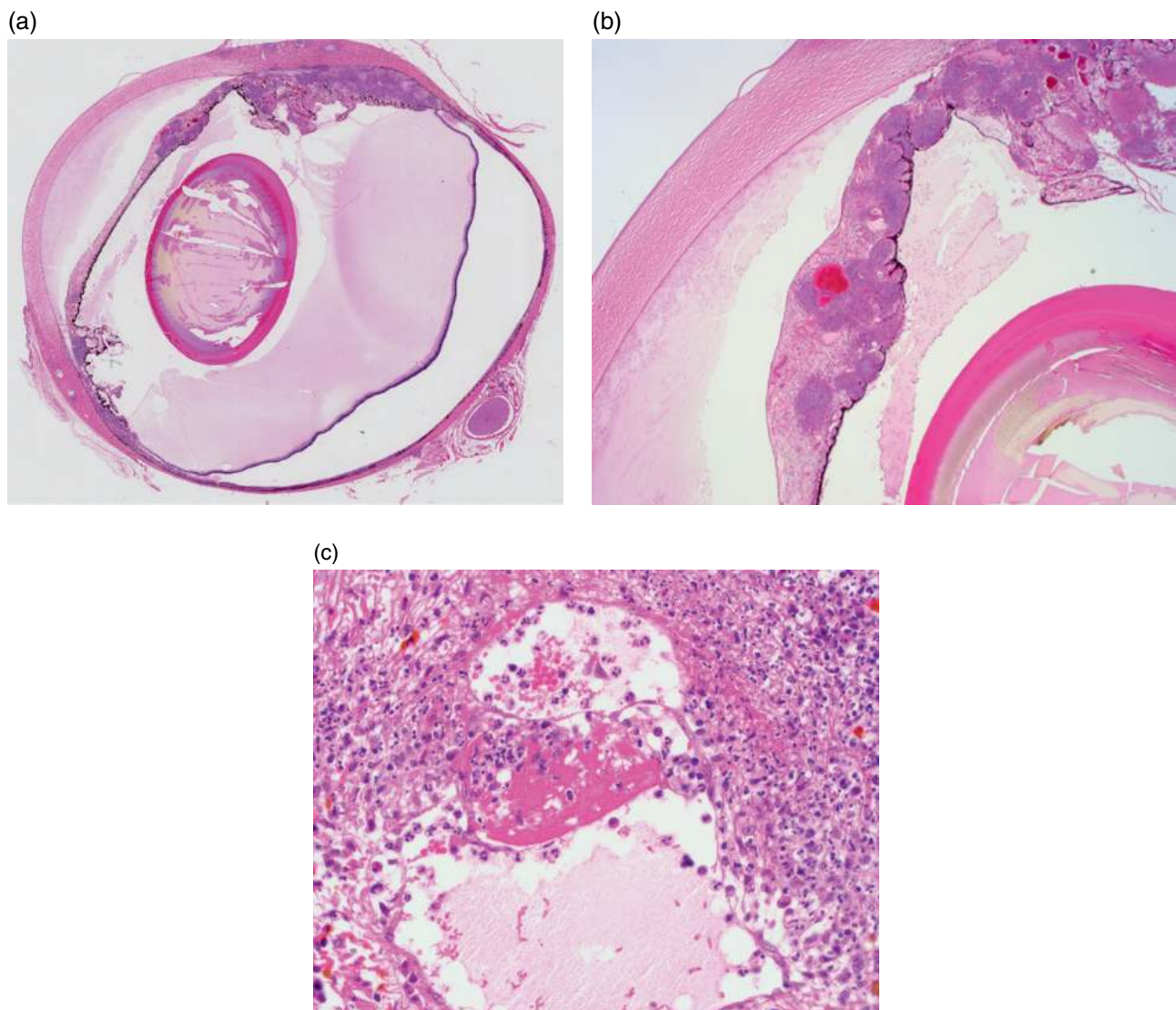


Figure 1.35 (a–c) Feline infectious peritonitis-associated panuveitis. The eye lesion with FIP is typically a lymphoplasmacytic to pyogranulomatous vasculocentric infiltrate in the iris, ciliary body, and choroid.

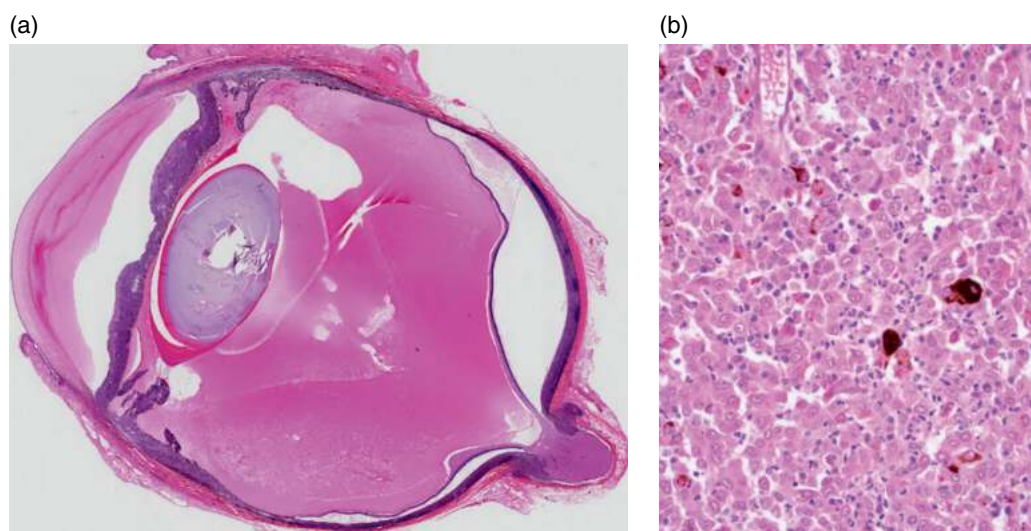


Figure 1.36 (a, b) Canine uveodermatologic syndrome (Vogt–Koyanagi–Harada-like syndrome). Granulomatous panuveitis/endophthalmitis focused on the melanocytes within the eye.

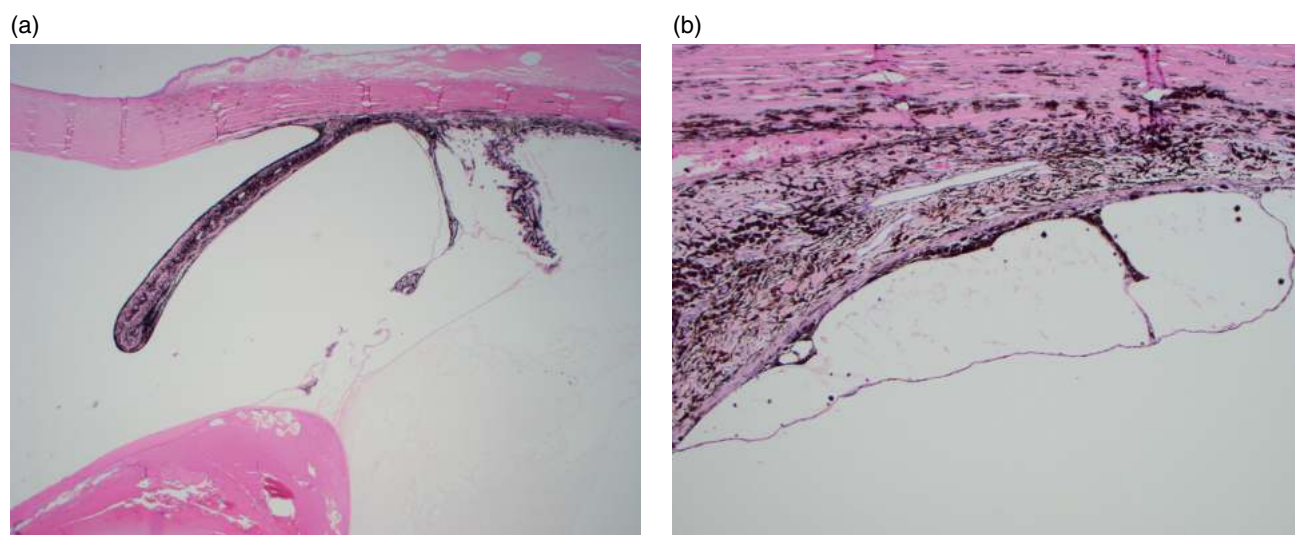


Figure 1.37 (a, b) Pigmentary uveitis is characterized by proliferation of melanin-containing cells throughout the uvea, along with multiple thin-walled uveal cysts.

Bacterial Endophthalmitis

Intraocular bacterial infections can occur from blood-borne pathogens or from a wound, especially those from a perforated corneal ulcer or a penetrating foreign object. Hematogenous intraocular infection most commonly occurs in neonatal animals, especially those with failure of passive transfer of maternal immunity. Intraocular bacterial infection from a penetrating wound is the more common route in enucleated eyes submitted for pathologic evaluation. In these eyes, there is commonly a mixed population of bacteria, both bacilli and cocci. The infection spreads throughout the eye, and all chambers are typically filled with purulent or fibrinopurulent exudate (Figure 1.38a–c).

Ocular Blastomycosis

Blastomycosis is a disease caused by the yeast form of the dimorphic fungus *Blastomyces dermatitidis*. It is typically a systemic disease in dogs that frequently involves the lungs, bones, lymph nodes, eyes, and a variety of other organs. The characteristic lesion, regardless of the organ involved, is pyogranulomatous inflammation centered on one or more organisms. In microscopic sections, the yeasts are round, have a thick refractile wall, are 15–30 μm in diameter, and replicate via broad-based budding (Figure 1.39a, b). Ocular involvement has a characteristic distribution in which organisms and associated pyogranulomatous exudate first accumulate in the choroid and subretinal space, and then spread into the retina and vitreous chamber; occasionally, inflammation may extend through the sclera. The anterior uvea is frequently inflamed; however, organisms rarely are found in the anterior chamber or iris. Since the interior segments of the eye (uvea, retina) and all chambers (vitreous, posterior, aqueous) are involved, this becomes endophthalmitis; if the cornea and sclera are also involved, then it becomes panophthalmitis.

Ocular Cryptococcosis

Cryptococcosis is another disease caused by yeast, similar to blastomycosis. *Cryptococcus neoformans* is the agent; it is an oval to spherical yeast that is 5–20 μm in diameter and surrounded by a thick mucinous capsule, which produces a clear zone around the yeast in microscopic sections. This may be a systemic disease, but also it is commonly limited to the nasal cavity, brain, and eyes in dogs and cats. The distribution within the eyes is similar to blastomycosis, although the reaction is more purely granulomatous with few pmns but numerous macrophages surrounding yeasts (Figure 1.40a, b).

Ocular Coccidioidomycosis

Coccidioidomycosis induces granulomatous to pyogranulomatous inflammation that primarily starts in the choroid. The yeast form of *Coccidioides immitis* replicates by endosporulation, forming spherules that are much larger than the other yeasts found within the eye. Organisms range up to 50 μm in diameter and have a double-refractile wall.

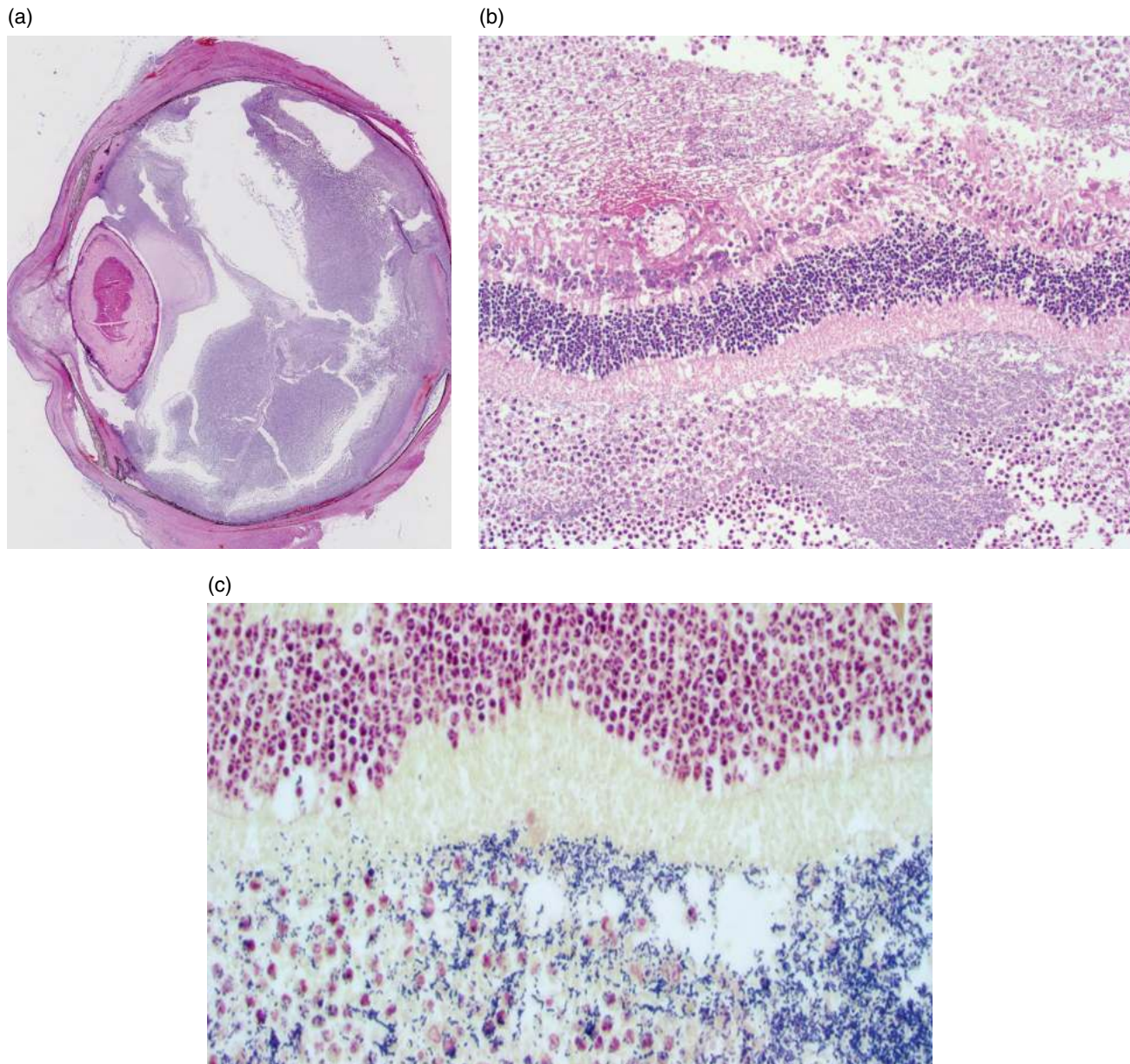


Figure 1.38 (a, b) Purulent endophthalmitis caused by an intraocular bacterial infection. There is inflammation of the interior segments of the eye with accumulation of exudate within all chambers. (c) Gram + coccoid bacteria.

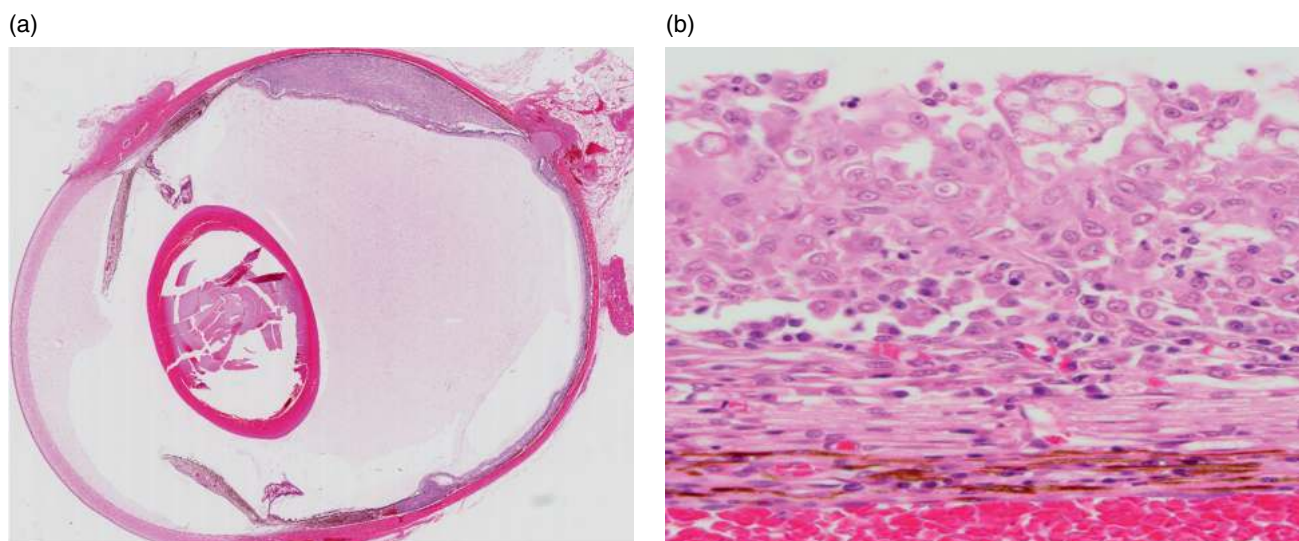


Figure 1.39 (a, b) Ocular blastomycosis. The characteristic lesion seen here is granulomatous exudate along with yeasts within the choroid and subretinal space. Also, there is serofibrinous exudate within the anterior, posterior and vitreous chambers.

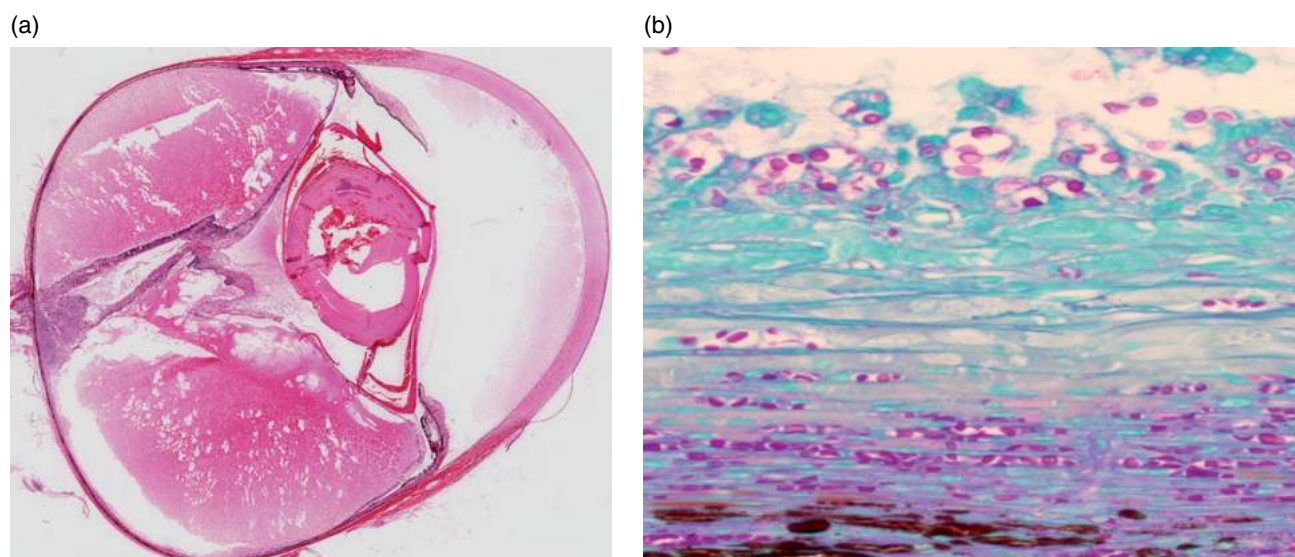


Figure 1.40 (a) Ocular cryptococcosis in a cat. The characteristic lesion is accumulation of exudate and yeasts within the choroid and subretinal space. There is marked retinal detachment as a result of exudate accumulation in the subretinal space. (b) PAS stain demonstrates yeasts.

Ocular Histoplasmosis

Histoplasmosis induces granulomatous inflammation that also starts in the choroid. Macrophages contain clusters of *Histoplasma capsulatum*, which are 2–4 μm diameter yeasts.

Ocular Protothecosis

Protothecosis is an uncommon disease that can involve the eyes in dogs. It is caused by one of two *Prototheca* sp., which are colorless alga. The organism is round to oval, 5–20 μm in diameter and replicates by endosporulation. The daughter cells number from 2 to 20, are wedge-shaped and remain within the cell wall of the parent cell. The cleavage lines between daughter cells form a variety of patterns, such as crosses, “Y”s and stars. The inflammatory reaction and distribution within the eye is similar to the intra-ocular dimorphic fungal infections: granulomatous exudate surrounding numerous organisms primarily in the choroid, subretinal space, and vitreous chamber (Figure 1.41a, b).

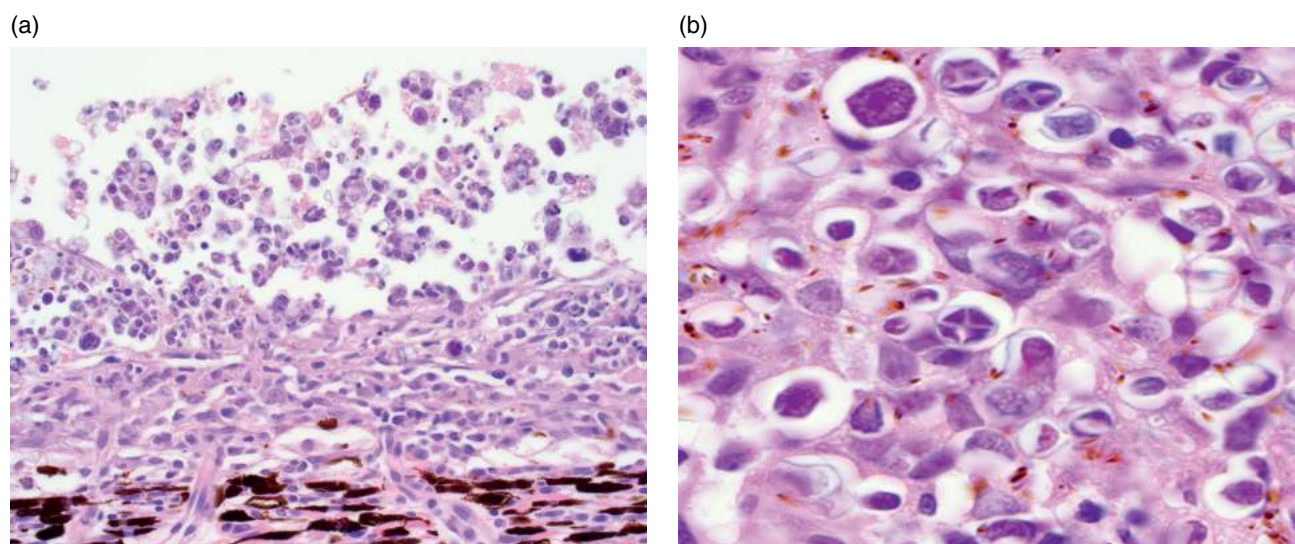


Figure 1.41 (a, b) Ocular protothecosis in a dog. The pattern of granulomatous inflammation is similar to intraocular dimorphic fungal infections, such as blastomycosis. The organism is round to oval, 5–20 μm in diameter and replicate by endosporulation. The daughter cells number from 2 to 20, are wedge-shaped and remain within the cell wall of the parent cell. The cleavage lines between daughter cells form a variety of patterns, such as crosses, “Y”s, and stars.

Lens

The lens is composed of epithelium surrounded by a basement membrane, the lens capsule. It is held in place between the iris (anterior) and the vitreous body (posterior) by zonular fibers from the ciliary body. The epithelium under the anterior surface of the lens capsule contains germinative cells that replicate throughout life. These epithelial cells migrate posteriorly and centrally, elongate, and become lens fibers. Also, over the years, lens fibers will compress centrally, forming the lens nucleus. In addition, as an animal ages, the anterior lens capsule will progressively thicken.

General Lens Reactions to Injury

The lens is a tough, durable structure, and it takes a significant injury to damage an otherwise healthy lens. There are a limited number of reactions to injury that occur, which include rupture of the capsule, epithelial fibrous metaplasia, mineralization, cataract, and inflammation. The subcapsular lens epithelium may proliferate and undergo **fibrous metaplasia** in response to injury to the capsule or posterior synechia (Figure 1.42). This change will interfere with the clarity of the lens. Injury to the lens epithelium from a variety of causes can result in cataract, which causes lens opacity and is discussed in more detail below. Ocular trauma or a penetrating foreign object may cause **rupture of the lens capsule**; this typically results in the inflammation of the lens (phacitis) and phacoclastic uveitis, as previously discussed (Figure 1.43).

Lens Luxation

Occasionally, the lens will break loose from its attachment sites and be displaced, usually anteriorly. This can result in pupillary block and acute glaucoma. Certain breeds of dogs, especially terriers, are prone to spontaneous lens luxation because they have somewhat weak zonules. Also, lens luxation can occur secondary to trauma or be a complication of buphthalmos. A luxated lens may occlude the pupil, causing pupillary block and secondary glaucoma.

Developmental and Degenerative Disease of the Lens

Microphakia and Aphakia

These are developmental defects that result in absence of a lens (aphakia) or a lens that is smaller than normal (microphakia) (Figure 1.44). Microphakia is the more common lesion, and it is usually associated with **multiple ocular anomalies**. It is common for microphakic lenses to also have congenital cataract.



Figure 1.42 Fibrous metaplasia of the subcapsular lens epithelium secondary to injury of the capsule.

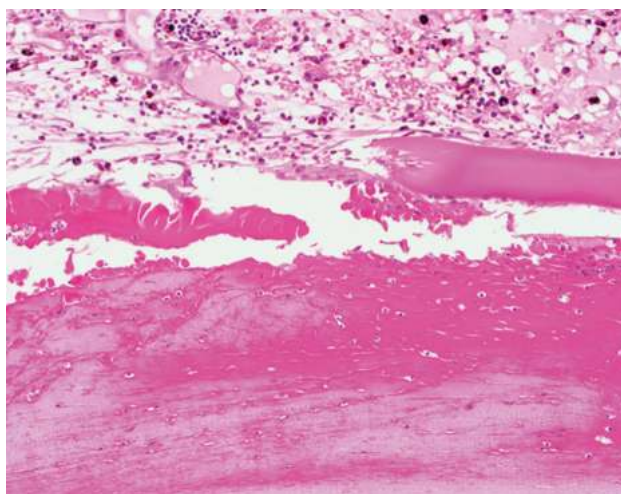


Figure 1.43 Rupture of the lens capsule with associated uveitis and phacitis.

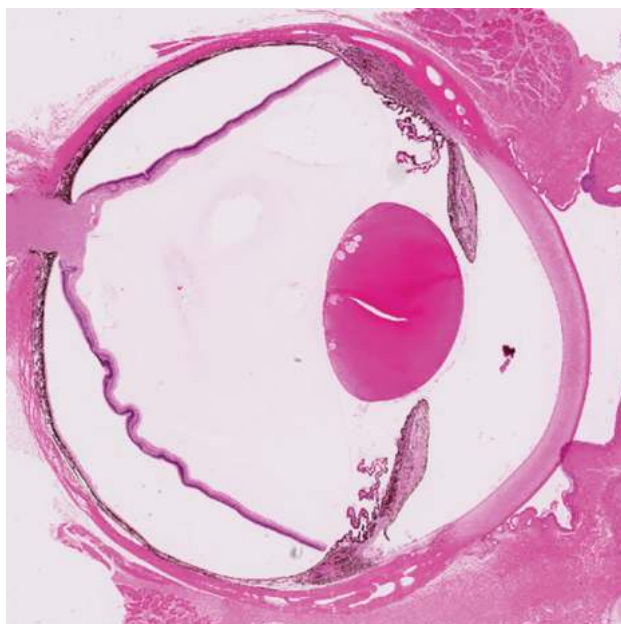


Figure 1.44 Microphthalmia with congenital cataract and retinal dysplasia.

Persistent Pupillary Membrane, Persistent Primary (Hyperplastic) Vitreous, Persistent Posterior Tunica Vasculosa Lentis, and Persistent Hyaloid Artery

These are developmental anomalies due to the persistence of remnants of the embryonal vascular and mesenchymal structure surrounding and supplying the lens, the **primary vitreous**. The vascular tunic around the lens, which is a subcomponent of the primary vitreous, is the **tunica vasculosa lentis**. Anomalies of these structures commonly occur with other developmental anomalies, such as microphthalmia, microphakia, and congenital cataract. **PPM** is characterized by the attachment of strands of tissue (endothelial lined tubes) extending from the minor arterial circle of the iris to the cornea or anterior lens capsule. Fibrous metaplasia is usually present where these strands insert on the lens or cornea. **PPV** or **PPHV** is characterized by a cord of vascular tissue and associated extracellular matrix extending from the optic disc to and covering the posterior lens capsule. **PPTVL** is characterized by a residual band of fibrovascular tissue along the posterior lens capsule (Figure 1.45a, b). In the developing eye, the **hyaloid artery** extends from the optic disk to the tunica vasculosa lentis on the posterior surface of the lens. Occasionally, remnants of this vessel will persist (Figure 1.46).

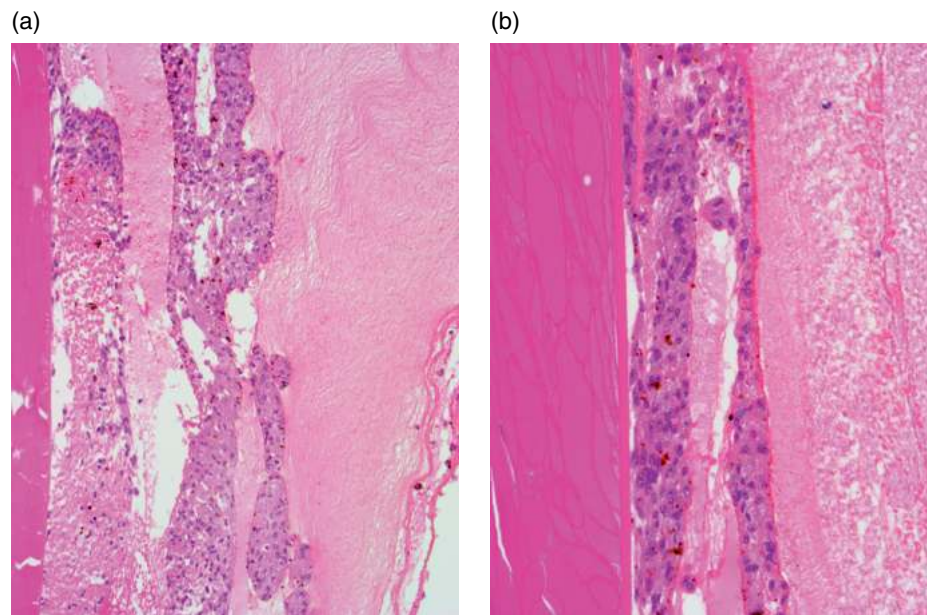


Figure 1.45 (a, b) Persistent primary tunica vasculosa lentis. This is a remnant of the embryonal vascular tunic that surrounds the lens. The PPTVL is adhered to the posterior lens capsule, which is on the left in this slide.

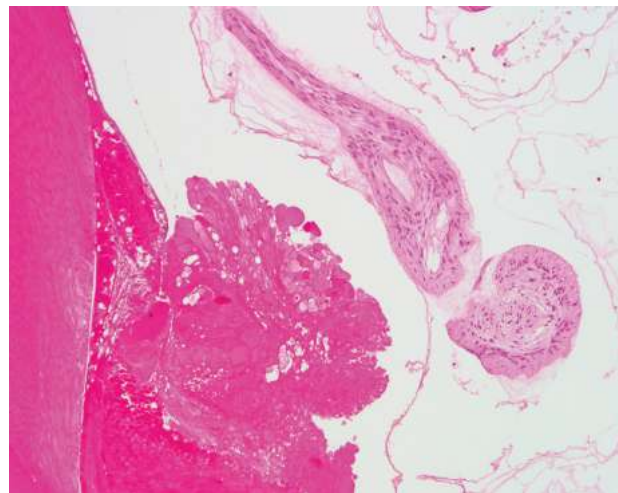


Figure 1.46 Persistent hyaloid artery and congenital cataract.

Cataract

Opacity of the lens is known as **cataract** (Figure 1.47). There are several different causes for cataracts, but the microscopic changes that occur are similar for all. Injury to the lens fibers results in the hydropic degeneration and swelling with the production of **bladder cells** (Figure 1.48). Denatured cytoplasm from the injured fibers is liberated and forms eosinophilic globules, known as **Morgagnian globules** (Figure 1.49). Also, degenerate lens fibers may fragment, liquefy, and/or mineralize. Certain types of cataracts have a genetic basis, others may be due to accumulated injury over many years, and still others are due to abnormality in lens metabolism. Cataracts that occur in **diabetes mellitus** are an example of the latter. When dogs are hyperglycemic due to DM, glucose accumulates within the lens fibers and is converted to sorbitol. Sorbitol will osmotically attract water, and therefore, the lens fibers swell (hydropic degeneration); this results in lens opacity.

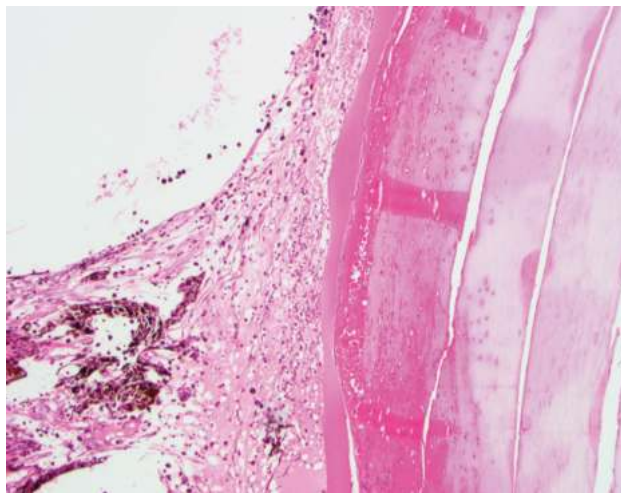


Figure 1.47 Posterior synechiae with cortical cataract.



Figure 1.48 Congenital cataract with swollen lens fiber.

Sometimes a cataract will totally liquefy and only the lens capsule and liquefied lens fibers remain; this is called a “**hypermature cataract**” (Figure 1.50).

Inflammatory Disease of the Lens

Phacitis

Inflammation of the lens is **phacitis** (Figure 1.51a, b). It usually occurs when there has been a penetrating injury through the lens capsule. Exudate, usually pmns, will accumulate under the perforated capsule and dissect between lens fibers. Abrupt leakage of lens proteins can result in a severe form of uveitis, **phacoclastic uveitis**, which was previously described. A less severe form of uveitis, **phacolytic uveitis**, may occur when lens proteins slowly leak from the lens.



Figure 1.49 Cortical cataract with fibrous metaplasia of lens epithelium along with fragmented lens fibers and liberated lens proteins forming Morgagnian globules.

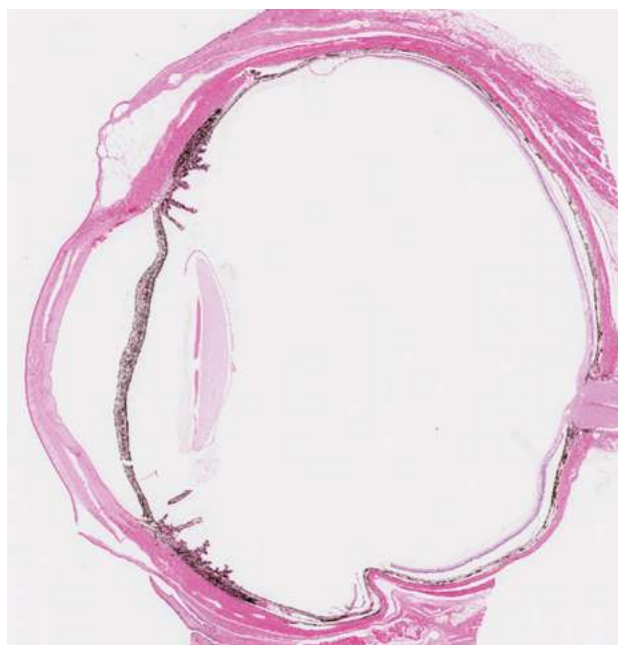


Figure 1.50 Hypermature cataract. The lens fibers are totally degenerate and liquefied. The lens shrinks, clears, and may leave only the capsule.

Retina

The retina is the neurosensory portion of the eye. It is derived from the optic vesicle, which is an extension from the brain. It is composed of eight distinct layers, from the innermost layer to the outermost layer: these are nerve fiber layer, ganglion cell layer, inner plexiform layer, inner nuclear layer, outer plexiform layer, outer nuclear layer, photoreceptor layer, and

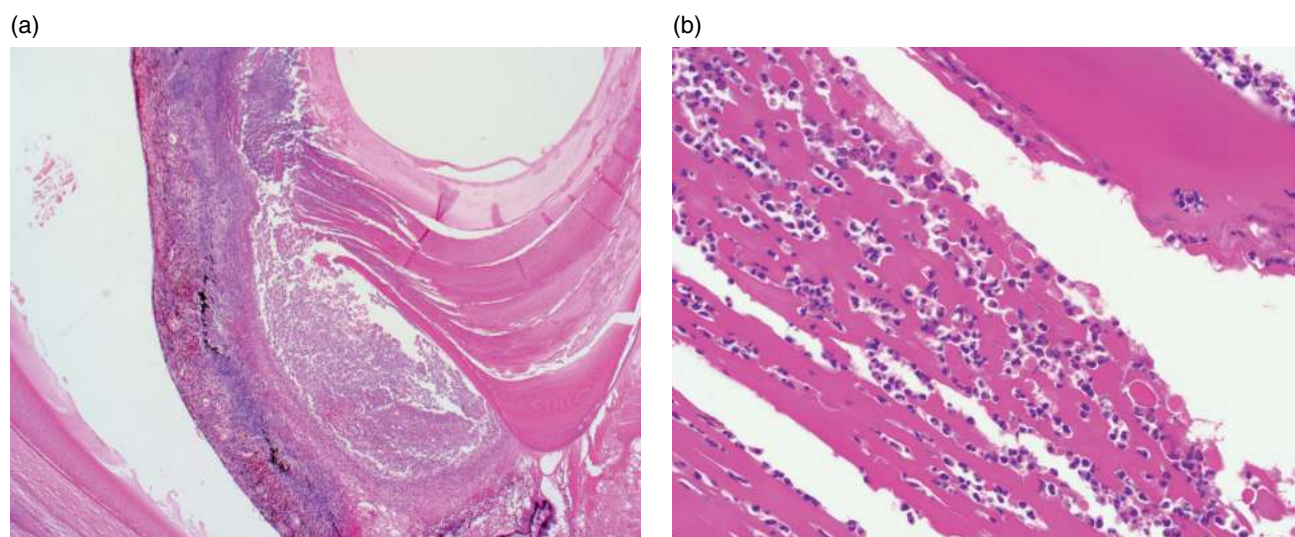


Figure 1.51 (a, b) Phacitis and phacoclastic uveitis secondary to rupture of the lens capsule. Note the pmns between the degenerate lens fibers.

RPE. The retina is only attached at its periphery (ora ciliaris retinae) and at the optic nerve head; it is held in place against the choroid by the vitreous body. The retina has its own blood supply, which enters through the optic nerve.

General Retinal Reactions to Injury

Degeneration, atrophy, inflammation, and glial scarring are the typical reactions to injury that occur in the retina. **Retinal degeneration (RD)** is best defined as loss of one or more retinal components, usually neural, as a result of injury. RD may occur as a primary disease, or it may develop secondary to other ocular diseases, such as glaucoma. RD can occur in several patterns and can be due to a variety of causes; the pattern of degeneration can indicate the cause. The patterns of RD are due to the segment(s) of the retina affected. The inner segments (ganglion cells and inner nuclear layer) can be preferentially affected compared to the outer segments (outer nuclear layer and photoreceptors); this is typical of **RD due to glaucoma**. Conversely, the outer segments may be preferentially affected, which is typical of **nutritionally-induced or inherited types of RD**. In certain diseases, such as glaucoma, the tapetal retina is preferentially spared (**tapetal-sparing effect**) from degeneration compared to the nontapetal retina. Specific cellular changes that occur in RD include acute neuronal swelling, acute neuronal necrosis resulting in loss of neurons, and loss of photoreceptors. There are a variety of causes for RD; these include too much light, inherited RD, specific nutritional deficiencies (vitamin A, taurine in cats), increased intraocular pressure, ischemia, and retinal detachment. **Retinal atrophy** is more or less the end stage of retinal degeneration or retinitis, when there has been such extensive loss of retinal components that the retina is thin, hypocellular, and gliotic. Primary **retinitis** is not a common lesion in surgical specimens, but may occur with certain neurotropic viral infections and along with uveitis and endophthalmitis.

Developmental and Degenerative Retinal Disease

Retinal Dysplasia

Dysplasia is a developmental abnormality that is characterized by folds, wrinkles, or rosettes in the retina. This is the result of injury to the developing retina. There are several recognized syndromes, such as the **skeletal-ocular dysplasia syndrome of Labrador retrievers**, in which retinal dysplasia is a component of an inherited disease with multiple ocular anomalies (Figure 1.52a, b).

Lysosomal Storage Diseases

These are a group of rare diseases in which a specific enzyme is deficient, resulting in failure of a metabolic pathway that allows intracellular accumulation of a substrate. In companion animals, these are inherited enzyme deficiencies. Affected

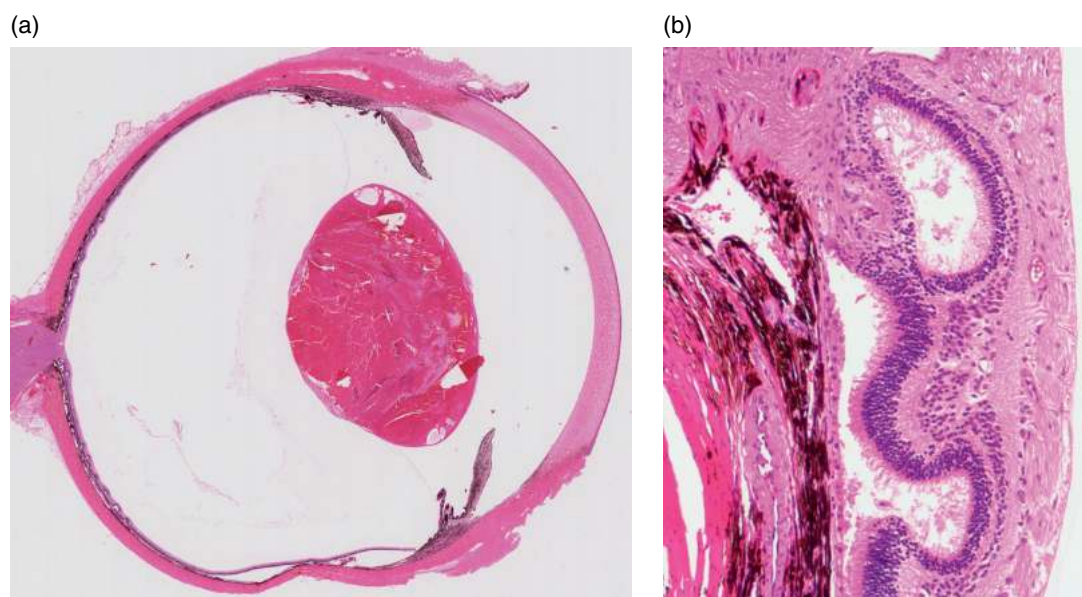


Figure 1.52 (a, b) Retinal dysplasia and congenital cataract. Retinal dysplasia is characterized by folds, wrinkles, and/or rosette-like structures.

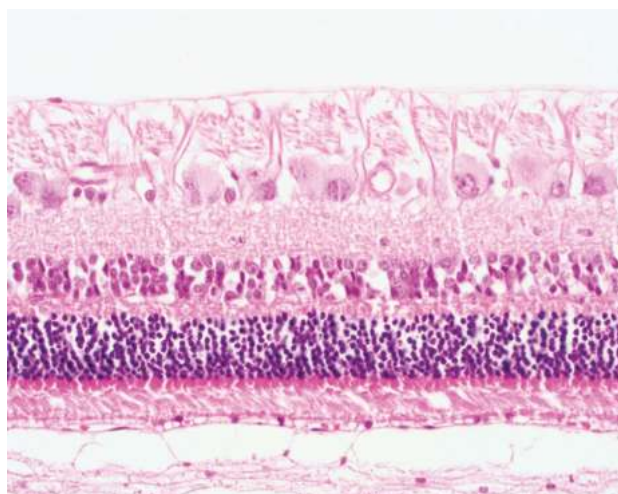


Figure 1.53 GM1 gangliosidosis. This is an example of a lysosomal storage disease in which incompletely metabolized substrate accumulates within ganglion neurons of the retina.

cells will become engorged with the substrate resulting in enlargement, vacuolization, and dysfunction. Since neurons are long-lived cells and frequently contain the dysfunctional pathway, they commonly have lesions. Neurons in the retina, especially ganglion cells, are frequently affected (Figure 1.53).

Cystic Retinal Degeneration

This occurs at the ora ciliaris retinae and is a common incidental lesion in older dogs (Figure 1.54).

Inherited Retinal Dysplasia and/or Degeneration (Progressive Retinal Atrophy)

This is a group of inherited retinal diseases that result in loss of rods, cones, or both and ultimately, neurons from the outer nuclear layer. One disease in this group is rod and cone dysplasia of Irish setter dogs. In this condition, the rods and cones do not develop normally due to a defect in the enzyme that breaks down cGMP (a phosphodiesterase). There are conditions in

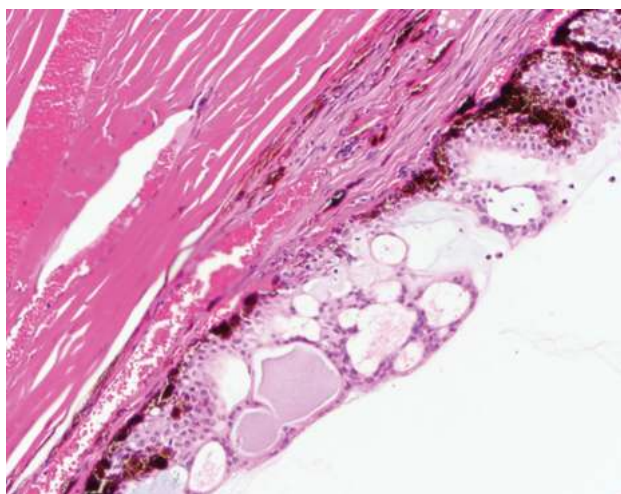


Figure 1.54 Cystic retinal degeneration. This is a common incidental aging lesion that occurs at the ora ciliaris retinae in dogs.

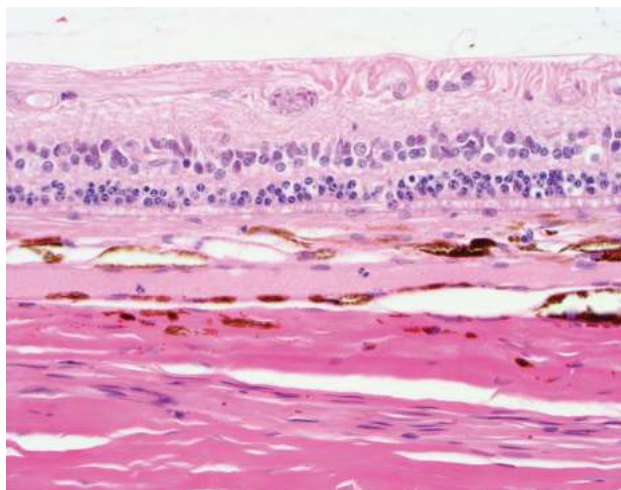


Figure 1.55 Progressive retinal atrophy (inherited retinal dysplasia/degeneration) in a Pug. The retina is thin due to hypocellularity of the outer nuclear layer and loss of the photoreceptor layer.

other breeds, in which the rods and cones develop normally, but begin to degenerate within a few years. The net result is atrophy of the retina, especially the central retina, due to loss of photoreceptors and neurons from the outer nuclear layer (Figure 1.55).

Nutritionally Induced Retinopathy

Several dietary deficiencies will cause retinal degeneration, including deficiencies of vitamin A and E. In companion animals, deficiency of the amino acid taurine is a notable cause of retinal degeneration in cats. The retinal lesion from **taurine deficiency** is degeneration of the outer nuclear and photoreceptor layers in the central area of the retina (Figure 1.56).

Toxic Retinopathy

This is not particularly common in companion animals. However, **enrofloxacin**, a widely used fluoroquinolone antibiotic, will cause retinal degeneration in cats, especially those receiving prolonged treatment. The resulting retinal lesion is thinning of the retina due to loss of the outer nuclear and photoreceptor layers, similar to taurine deficiency.

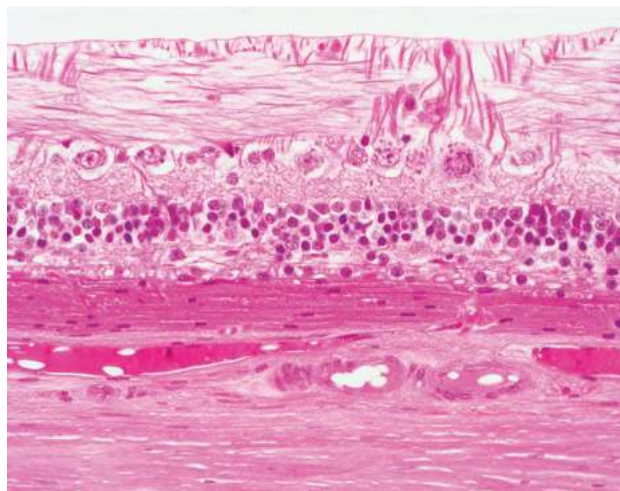


Figure 1.56 Retinopathy in a cat due to dietary taurine deficiency. There is diffuse loss of the photoreceptor layer and outer nuclear layer.

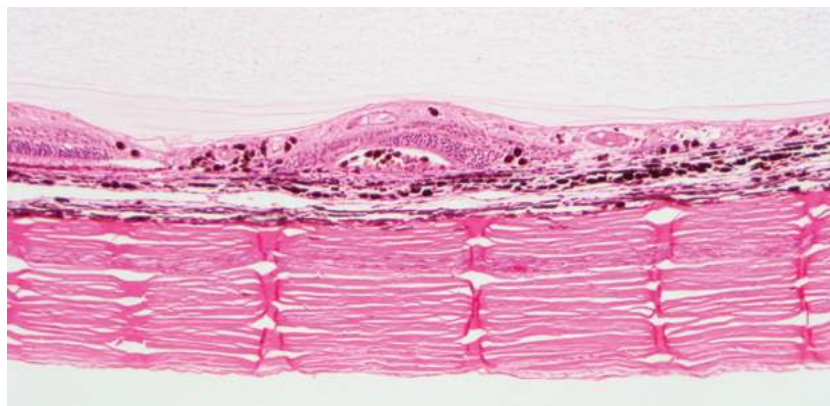


Figure 1.57 Multifocal retinal scars due to retinal ischemia and infarction. In the scarred areas of the retina, there is loss of all layers with replacement by glia and melanophages.

Ischemic and Infarctive Retinopathy

Retinal ischemia resulting in infarction can have a variety of causes including systemic thrombotic disease (DIC), vasculitis, hypertension, retinal detachment, and intra-ocular neoplasms. The acute retinal lesion that results is coagulative necrosis proceeds to liquefaction, much like necrosis in the brain. If the animal survives long enough for these lesions to heal, then one or more retinal scars will form, which are characterized by a thin, collapsed gliotic focus that lacks identifiable retinal layers and contains an accumulation of melanophages derived from injury to the RPE (Figure 1.57).

Glaucoma

Glaucoma is a disease characterized by increased intraocular pressure. It can be classified in several different ways, but the two main classifications are primary glaucoma and secondary glaucoma. Glaucoma can also be classified as open or closed-angle glaucoma, depending upon whether or not the iridocorneal angle is open (and looks normal) or closed. Primary glaucoma, as the name indicates, is glaucoma that occurs without any antecedent disease. Secondary glaucoma is an increase in intraocular pressure secondary to some other intraocular disease, such as uveitis. Primary glaucoma occurs preferentially in certain breeds of dogs, such as Basset hounds and cocker spaniels. Frequently, primary glaucoma is associated with abnormal development of the pectinate ligament, ciliary cleft, and trabecular meshwork; this is called goniodysgenesis. With goniodysgenesis, the flow of aqueous humor through the ciliary cleft is somewhat impeded, which leads to elevated IO pressure. Secondary glaucoma is usually caused by some process that closes or collapses the ciliary cleft. In primary or secondary, open or closed-angle glaucoma, the net result is the same. Increased IO pressure results in degeneration and atrophy of the

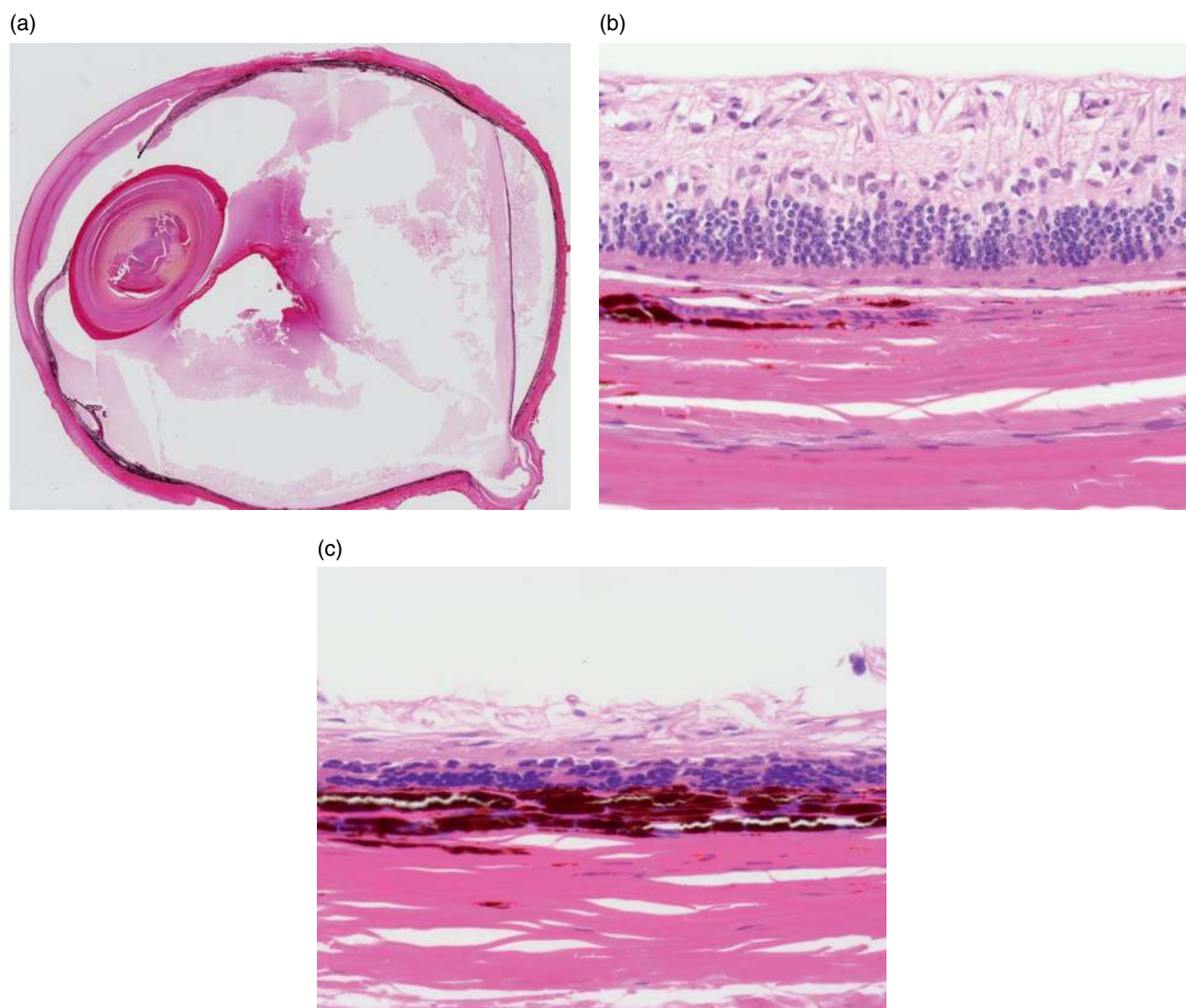


Figure 1.58 (a) Glaucoma secondary to uveitis. The iridocorneal angle is closed, and there is posterior synechia. Characteristic lesions of chronic glaucoma include buphthalmos, retinal degeneration, and cupping of the optic disk. (b, c) Characteristic retinal lesions are loss of the nerve fiber layer, ganglion neurons, inner nuclear layer neurons, and plexiform layers (left photo). The outer nuclear layer and photoreceptor layers are relatively spared until late in the disease. Retinal atrophy is the last stage of glaucoma.

inner layers (especially the ganglion and inner nuclear layers) of the retina, and eventually cupping of the optic nerve head. In addition, the increased in IO pressure is painful and frequently causes enlargement of the globe (buphthalmos) (Figure 1.58a–c). This can result in failure of the eyelids to cover the cornea and maintain an adequate tear film, thus leading to drying and chronic keratitis.

Sudden Acquired Retinal Degeneration Syndrome

This is an idiopathic disease that can affect any dog, young or old, which is characterized by a very rapid onset of blindness due to acute bilateral diffuse degeneration of the rods and cones, progressing to apoptosis of photoreceptor cells of the outer nuclear layer, and eventually loss of neurons in the inner retinal segments (Figure 1.59). Another similar syndrome, cancer-associated retinopathy, occasionally occurs in dogs with cancer; the microscopic lesions of which are similar to those in sudden acquired retinal degeneration syndrome (SARDS).

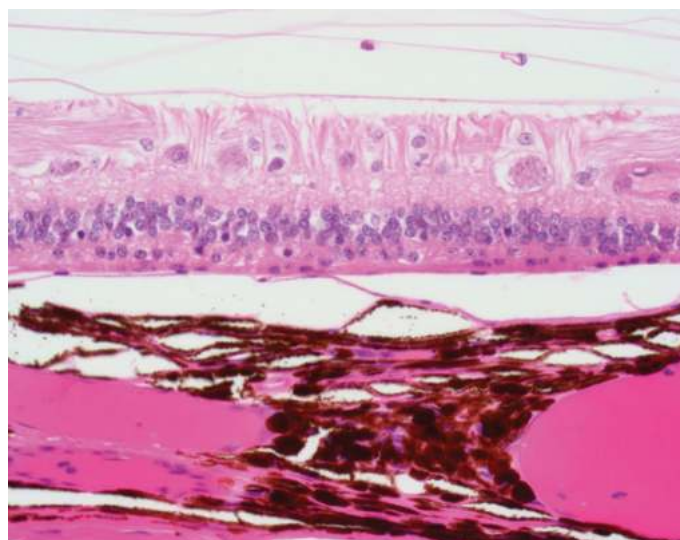


Figure 1.59 Sudden acquired retinal degeneration syndrome. This syndrome is characterized by loss of the outer nuclear layer and photoreceptor layer.

Retinal Detachment

Since the retina is only attached at the optic nerve head and the ora ciliaris retinae, sometimes it becomes pathologically separated from the adjacent tissue in the globe, and this is known as **retinal detachment**. The separation actually occurs within the retina – between the photoreceptor layer and the RPE. This is usually the result of one of the following: loss of the vitreous body, anterior traction on the retina due to intraocular hemorrhage, or accumulation of edema fluid, exudate, or hemorrhage in the subretinal space (Figure 1.60). Once the retina is detached, the outer segments of the retina, especially the photoreceptors, will begin to degenerate. Foci of retinal necrosis may develop. Also, the RPE will hypertrophy and resemble a row of little tombstones (Figure 1.61a, b).

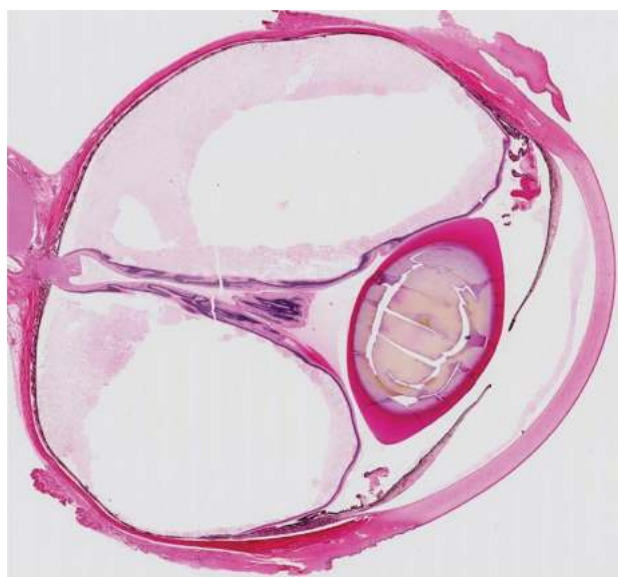


Figure 1.60 Retinal detachment in a dog with hypertension due to chronic renal failure. Serous fluid accumulates in the subretinal space secondary to hypertensive vasculopathy in the choroid.

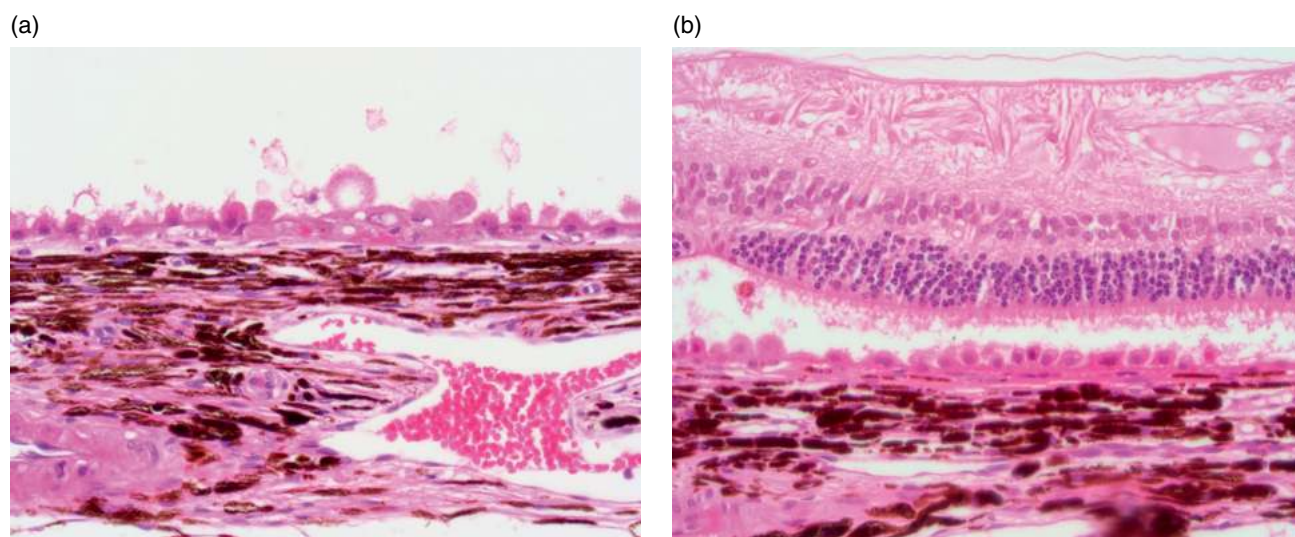


Figure 1.61 (a, b) Retinal pigment epithelium hypertrophy. There may be multiple causes for retinal detachment, but hypertrophy of the retinal pigment epithelium along with degeneration and loss of photoreceptors are characteristic changes of detachment due to any cause.

Inflammatory Disease of the Retina

Retinitis

Retinitis is inflammation of the retina. Although any type of exudate is possible, retinitis is usually characterized by a perivascular infiltrate of lymphocytes and/or plasma cells. Retinitis alone is fairly uncommon; it usually accompanies inflammation in the uvea, especially the choroid; however, some neurotropic viral infections, such as canine distemper, may localize in the retina and cause lymphocytic retinitis.

Optic Nerve

The optic nerve, cranial nerve II, is the mature structure derived from the stalk portion of the optic vesicle. Histologically, it is essentially an extension of the white matter from the brain and does not resemble peripheral or other cranial nerves. It is composed of myelinated axons that come from the ganglion neurons and nerve fiber layer of the retina. Within the globe, it begins as the optic disk, then exits the globe through the sclera at the lamina cribosa and is surrounded by the meninges. The right and left optic nerves meet at the optic chiasm before entering the brain.

Developmental and Degenerative Disease of the Optic Nerve

Hypoplasia of the Optic Nerve and/or Optic Chiasm

This may be the result of prenatal injury to the developing globe and/or skull, as caused by vitamin A deficiency or a variety of teratogens. Hypoplasia of the optic nerve may be associated with microphthalmia but is otherwise rarely seen in surgical pathology specimens.

Axonal Degeneration and Atrophy of the Optic Nerve

This is more common than hypoplasia and is typically caused by chronic injury from an adjacent expanding mass (such as a retrobulbar meningioma), ischemia, or long-standing glaucoma. Microscopic features include swelling of degenerate axons (spheroids), dilated axon sheaths containing axonal and myelin debris, gutter cells, and an increased number of activated astrocytes (Figure 1.62).

Cavitation of Optic Disk

Cavitation or cupping of the optic disk is a lesion that develops secondary to prolonged intraocular pressure and is indicative of long-standing glaucoma. In addition, microscopic changes usually associated with cavitation are axonal degeneration, myelin loss, and astrogliosis (Figure 1.63).

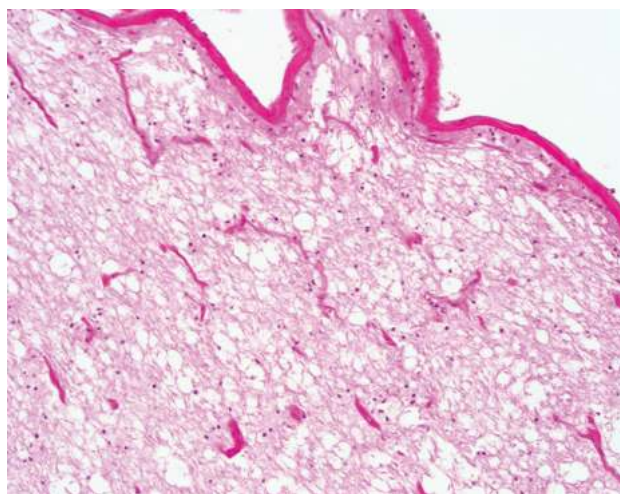


Figure 1.62 Axonal degeneration of the optic nerve characterized by numerous dilated axon sheaths.

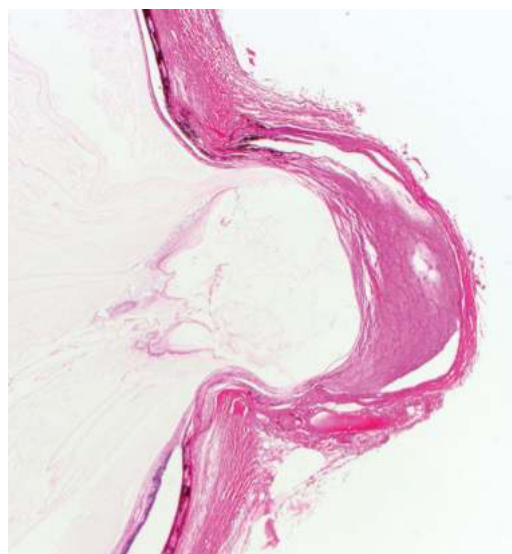


Figure 1.63 Cavitation of the optic disk due to glaucoma.

Canine Ocular Gliovascular Syndrome

This is a somewhat unusual set of lesions that primarily affects the optic disk. The optic disk is gliotic and covered with a layer of fibrovascular tissue and glial cells that protrudes into the vitreous chamber. In addition, there are usually several secondary lesions, including PIFM formation with the closure of the iridocorneal angle and secondary glaucoma. Canine ocular gliovascular syndrome (COGS) may occur more commonly in Labrador Retrievers (Figure 1.64a, b).

Inflammatory Disease of the Optic Nerve

Optic Neuritis

Inflammation of the optic nerve is not a particularly common lesion but will occasionally occur secondary to infection with agents that commonly infect the CNS. Examples would include canine distemper virus, arboviruses (EEE, WEE, West Nile), and aberrantly migrating ascarids (*Baylisascaris* sp., *Toxocara* sp.). With canine distemper, demyelination of the optic nerves is a classic lesion. Occasionally, inflammation can extend into the optic nerve from panophthalmitis or from retrobulbar cellulitis (Figure 1.65).

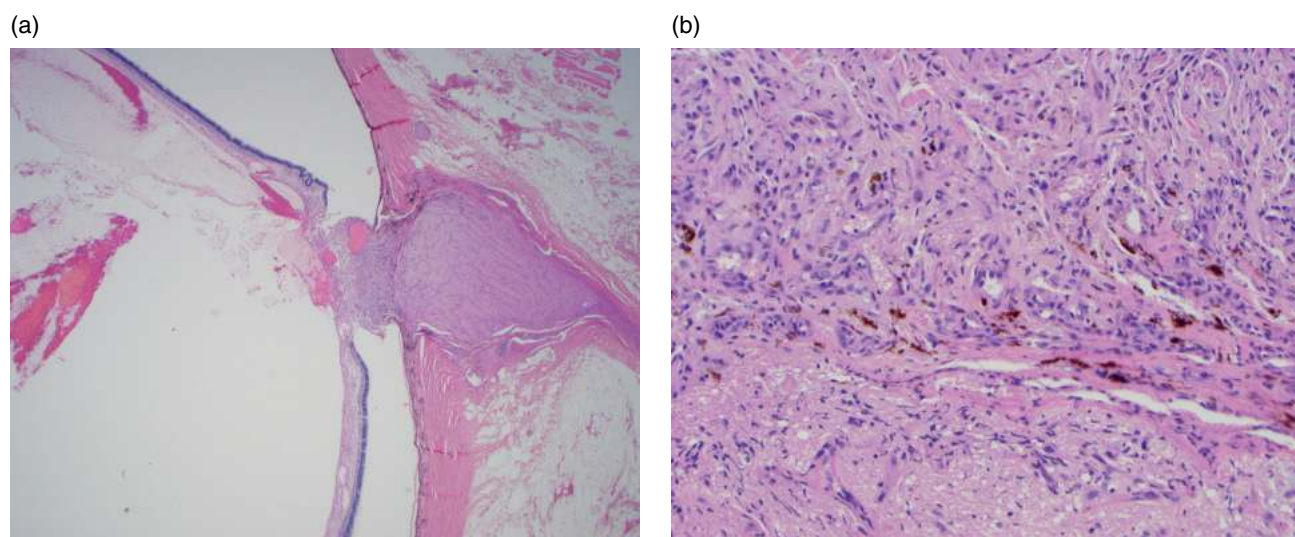


Figure 1.64 (a, b) Canine ocular gliovascular syndrome. The optic disk is gliotic and covered with a layer of fibrovascular tissue and glial cells that protrudes into the vitreous chamber.

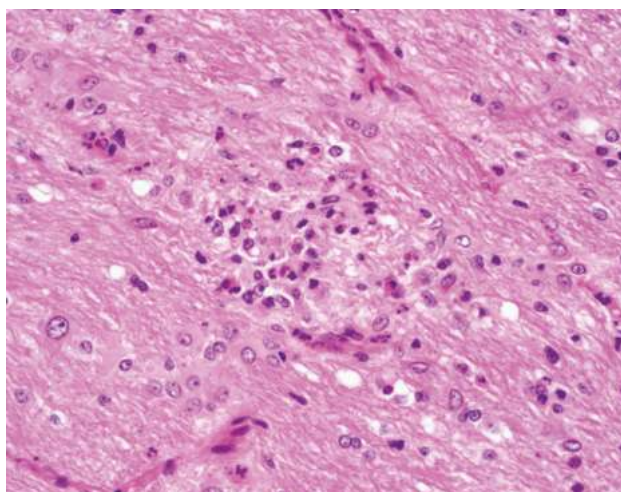


Figure 1.65 Optic neuritis due to aberrant migration of ascarid larvae. There is an infiltrate of eosinophils, macrophages and a few lymphocytes.

Granulomatous Meningoencephalitis

The idiopathic condition of canine granulomatous meningoencephalitis (GME) will occasionally extend into the optic nerves and meninges. This is characterized by an infiltrate of lymphocytes, macrophages, plasma cells, and occasionally a few pmns (Figure 1.66). The main differential diagnosis for optic nerve involvement would be lymphosarcoma.

Sclera

The sclera is the outer fibrous tunic of the eye, which is formed from periocular mesenchyme. It blends into the cornea at the limbus. The anterior portion of the sclera is covered by bulbar conjunctiva. The optic nerve exits the posterior of the globe through the lamina cribrosa.

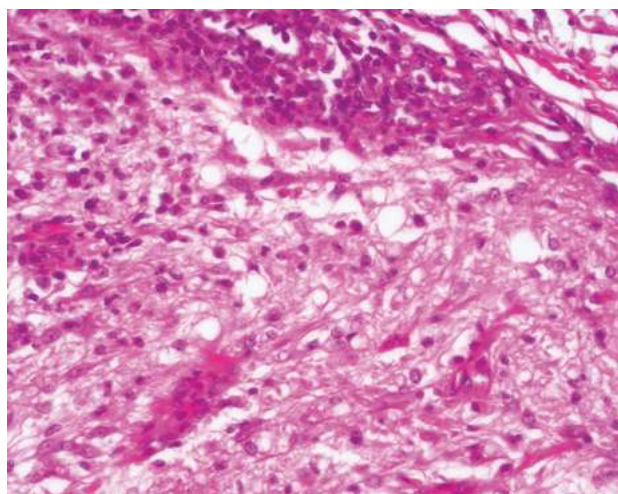


Figure 1.66 Optic neuritis due to granulomatous meningoencephalitis in a dog. There is an infiltrate of lymphocytes, plasma cells, and macrophages in the meninges and parenchyma of the nerve.

Developmental and Degenerative Scleral Disease

Scleral Ectasia

Occasionally, the sclera will be focally thinner than normal; this is **scleral ectasia**. It is typically associated with a defect in the closure of the optic fissure and coloboma of the choroid. Scleral ectasia and/or coloboma are commonly associated with choroidal hypoplasia and the **Collie eye anomaly** (Figure 1.67).

Inflammatory Disease of the Sclera

Lymphoplasmacytic Scleritis

Inflammation of the sclera, **scleritis**, does not usually occur alone; it most frequently accompanies uveitis or occasionally is a component of generalized eye inflammation (panophthalmitis) (Figure 1.68). Accumulation of lymphocytes and plasma cells around scleral vessels at the limbus or adjacent to the ciliary body is a common lesion that accompanies

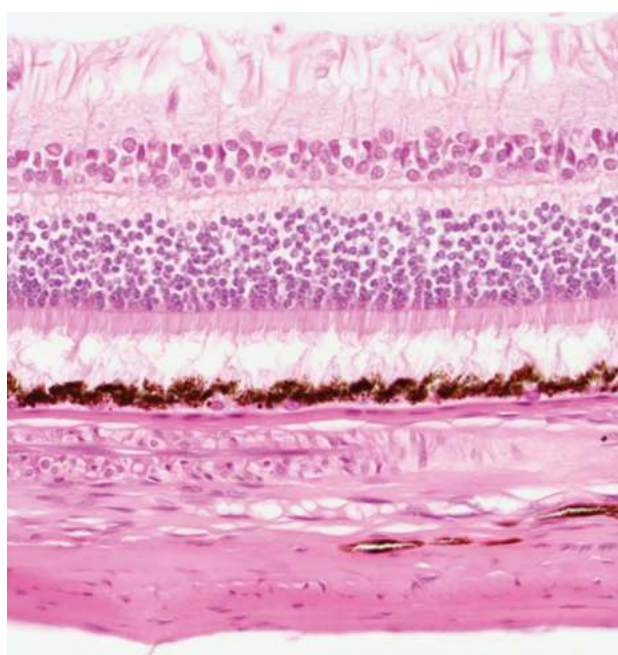


Figure 1.67 Scleral ectasia as a component of the Collie eye anomaly. The sclera is only about half of its normal thickness.

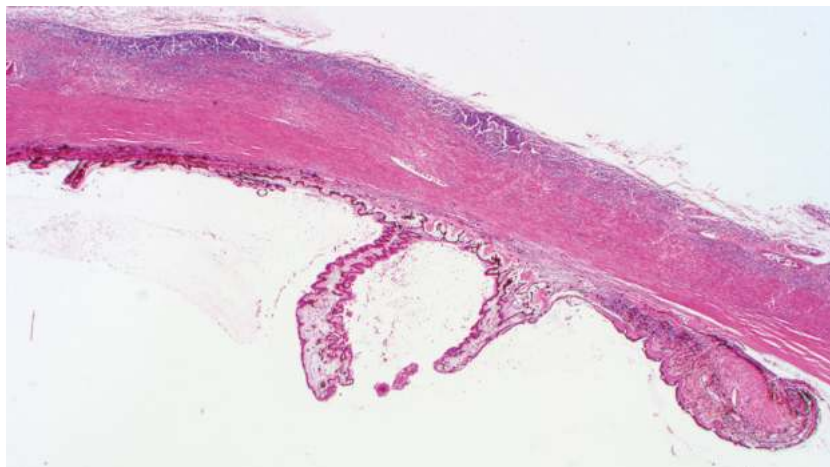


Figure 1.68 Lymphoplasmacytic scleritis. There is a perivascular to diffuse infiltrate of lymphocytes and plasma cells in the external surface of the sclera associated with chronic uveitis.

anterior uveitis. Occasionally, intraocular fungal diseases, such as blastomycosis, will extend through the wall of the eyeball and involve the sclera. Likewise, penetrating wounds into the eye that result in intraocular bacterial infection may also extend to involve the sclera.

Nodular Granulomatous Episcleritis and Necrotizing Scleritis

These are two apparently different syndromes that behave different clinically and have distinctive features and locations. Nodular granulomatous episcleritis (NGE) is more common and is composed of a mixture of macrophages, lymphocytes, plasma cells, and fibroblasts aligned in bundles and occurs in the bulbar conjunctiva at the limbus and may extend into the cornea; it also may occur on the membrana nictitans (Figure 1.69a). Necrotizing scleritis (NS) is a rare condition that contains foci of collagenolysis within the sclera along with a similar mix of inflammatory cells that may include granulomas. It is a more destructive lesion and may spread to involve the entire sclera and is frequently accompanied by lymphoplasmacytic uveitis (Figure 1.69b, c).

Eyelids, Conjunctiva and Retrobulbar Tissues

Developmental Disease of the Eyelids

The eyelids (palpebrae) are flaps of haired skin with a serous surface on the underside that is lined by palpebral conjunctiva. The edge of the eyelid contains a row of eyelashes (cilia) and associated sebaceous glands (Meibomian glands). The eyelids must meet properly to maintain an adequate tear film; eyelids that roll out (**ectropion**) or roll in (**entropion**) are unable to do this and result in eye irritation, especially the cornea. **Distichiasis** is the abnormal location of hairs along the eyelid margin; many times these will emerge from Meibomian gland openings. **Ectopic cilia** are frequently located on the conjunctival surface of the eyelid and cause irritation to the cornea.

Inflammatory Disease of the Eyelids

Granulomatous Blepharitis/Meibomian Adenitis

Blepharitis is inflammation of the eyelid. Inflammation of the Meibomian glands is Meibomian gland adenitis. Inflammation of these glands usually extends into the adjacent propria/submucosa causing blepharitis. **Granulomatous blepharitis** is the most common form of eyelid inflammation in the dog, and it is usually associated with leakage of secretion from the Meibomian glands. Granulomatous blepharitis typically forms a nodule along the lid margin, which is called a **chalazion** (Figure 1.70).

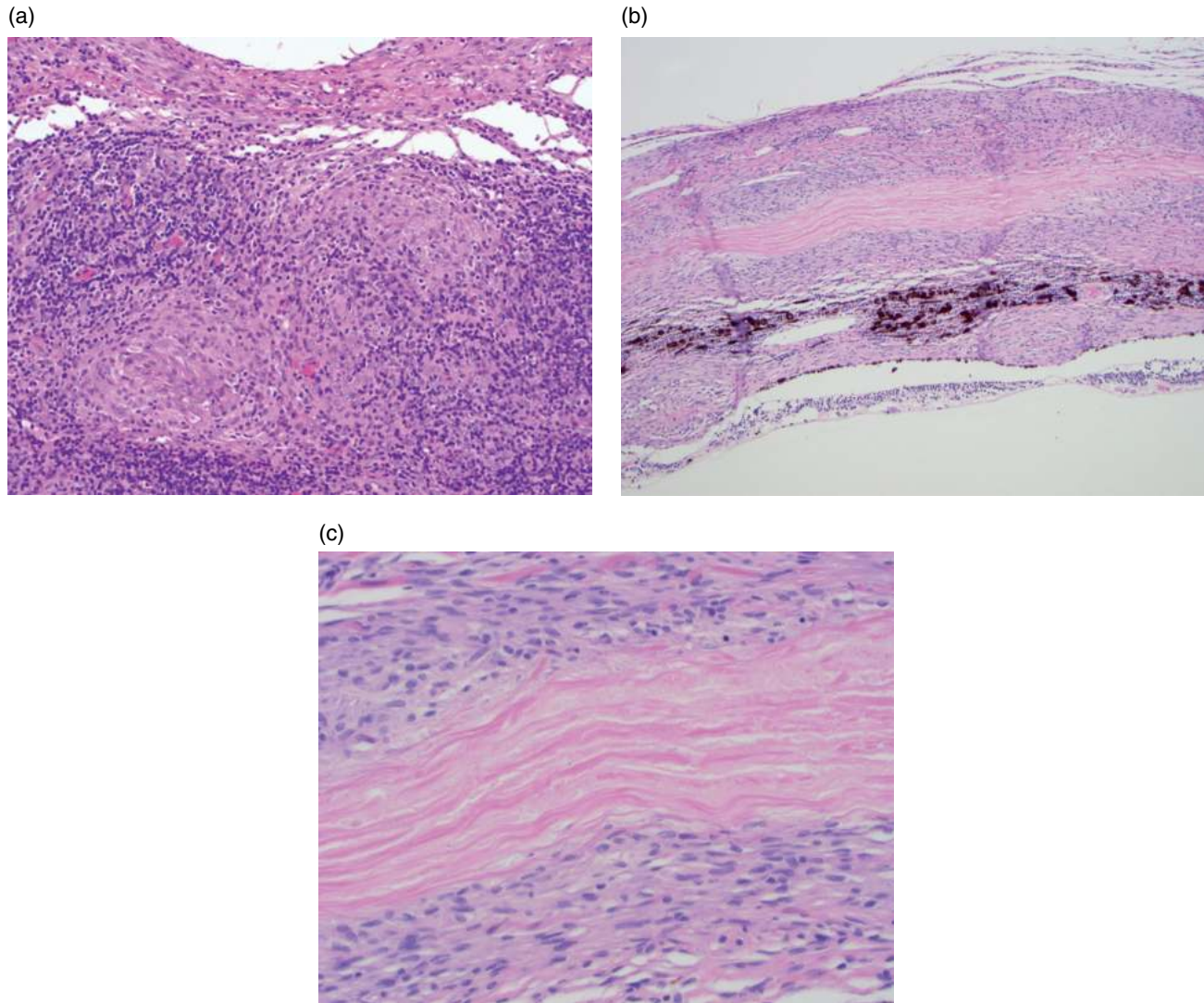


Figure 1.69 (a) Nodular granulomatous episcleritis in a dog. There is a multinodular infiltrate of lymphocytes and plasma cells associated with aggregates of macrophages in the external sclera. (b, c) Necrotizing scleritis in a dog. Also, there is lymphoplasmacytic uveitis and retinal atrophy.

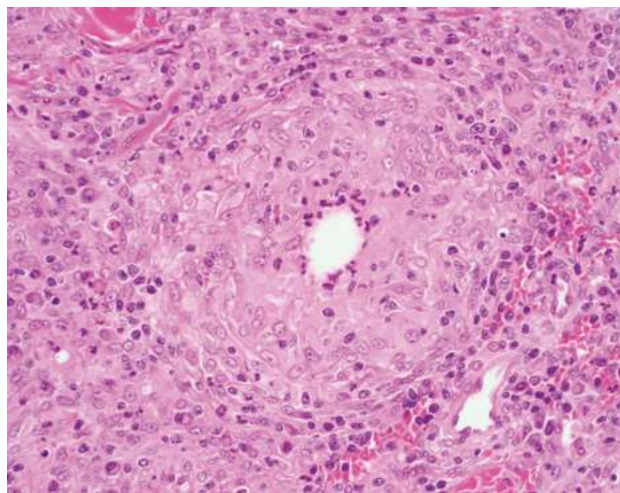


Figure 1.70 Granulomatous Meibomian blepharitis/adenitis (chalazion). This is a nodular sheet of epithelioid macrophages with a scattered infiltrate of lymphocytes, plasma cells and pmns centered on lipid material from a ruptured Meibomian gland.

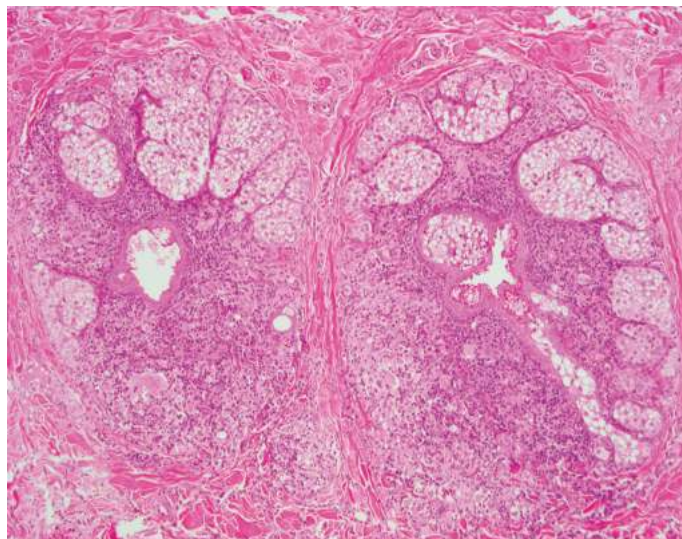


Figure 1.71 Marginal nodular Meibomian adenitis and blepharitis. This is granulomatous inflammation in multiple Meibomian glands along the eyelid margin.

Marginal Nodular Blepharitis/Meibomian Adenitis

This is an idiopathic disease recognized in dogs. It is characterized by multiple nodular foci of granulomatous inflammation involving multiple adjacent Meibomian glands along the eyelid margin (Figure 1.71).

Inflammatory Disease of the Conjunctiva, Membrana Nictitans, and Retrobulbar Tissues

The conjunctiva is located on the inner surface of the eyelid (palpebral conjunctiva) and the outer surface of the anterior portion of the sclera (bulbar conjunctiva). It is a thin layer of fibrovascular tissue that is covered with nonkeratinized stratified epithelium that varies from squamous to columnar. The membrana nictitans (third eyelid) is a specialized component of the conjunctiva, which is present at the medial canthus. In addition, to its serous mucosal surface, it contains a plate of cartilage, a lacrimal gland, and lymphoid tissue. In addition to the optic nerve and vessels that supply the eye, the retrobulbar tissue contains adipose tissue, extraocular muscles of the eye, and lacrimal gland.

Conjunctivitis

Conjunctivitis is inflammation of the conjunctiva. This is usually non-specific and due to irritation from foreign objects, dust, or chemicals. However, there are a few specific infectious agents that will produce conjunctivitis, such as *Chlamydomydia felis* in cats. Inflammation of the membrana nictitans is a form of conjunctivitis.

Nodular Granulomatous Episcleritis/Conjunctivitis

This is inflammation of the bulbar conjunctiva and superficial sclera, which may extend into the cornea. The most common syndrome in dogs is **nodular granulomatous episcleritis** (Figure 1.72a, b). This is an idiopathic disease, which tends to begin at the lateral limbus and form indistinct nodular lesions. Occasionally NGE extends into the cornea and may occur on the membrana nictitans.

Periocular/Retrobulbar Cellulitis/Abscess

Inflammation may develop in the tissues (including salivary and lacrimal glands) behind or adjacent to the eye. This can be caused by a penetrating or migrating foreign object, but most of the time, the cause is not clear. Typically purulent exudate will accumulate in the retrobulbar tissue, sometimes forming an abscess. This will result in **exophthalmos** and occasionally, secondary ulcerative keratitis.

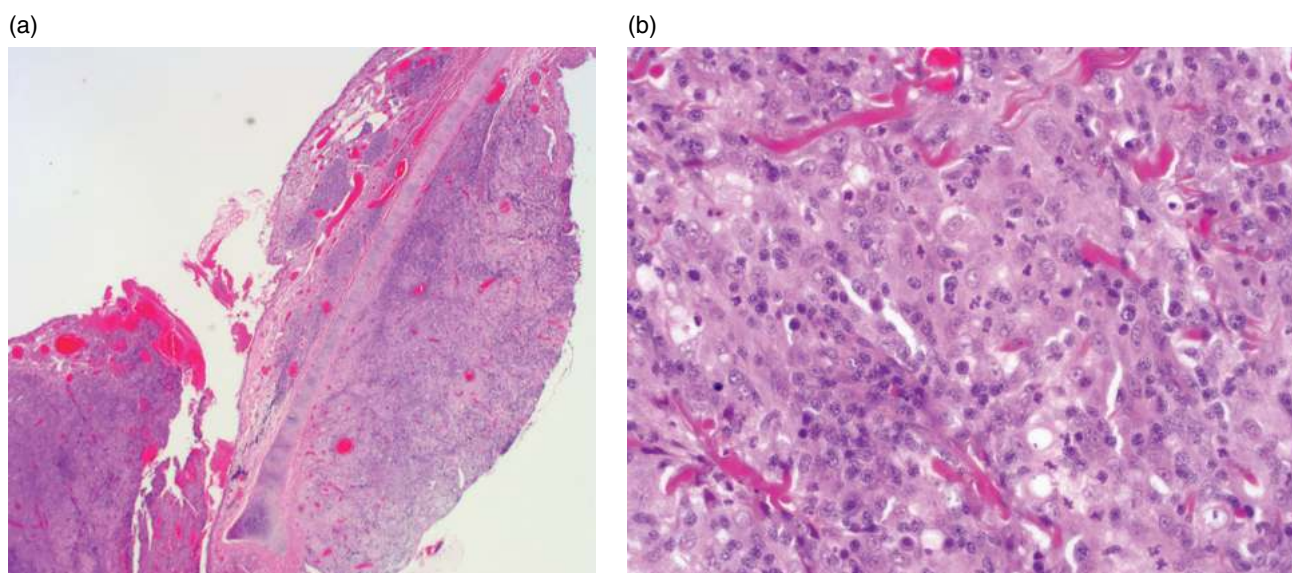


Figure 1.72 (a, b) Nodular granulomatous episcleritis/conjunctivitis on the membrana nictitans in a dog. There is a multinodular infiltrate of lymphocytes and plasma cells associated with aggregates of macrophages in the mucosa, extending down to the tarsal plate.

Neoplasia of the Eye and Periocular Tissues

Neoplasia of the Cornea

Primary neoplasia of the cornea is rare. Neoplasia within the cornea typically has invaded from a neoplasm that originates in the conjunctiva or anterior uvea. The most common primary neoplasm of the cornea is **squamous cell carcinoma** (Figure 1.73a, b). Although SCC can arise within the corneal epithelium, more commonly it originates in the adjacent conjunctiva and invades the cornea. **Squamous papilloma** also may occur (Figure 1.74a, b). **Uveal melanoma** may invade the cornea, tracking along Descemet's membrane, and **epibulbar melanoma** may invade into the cornea (Figure 1.75). There has been one case of a primary corneal melanoma with junctional activity reported in a horse. Also, there has been one case of a **primary corneal fibrosarcoma** in a cat, which was associated with a corneal ulcer and sequestrum (Figure 1.76a, b). **Hemangiosarcoma** has been reported to occur (Figure 1.77a, b).

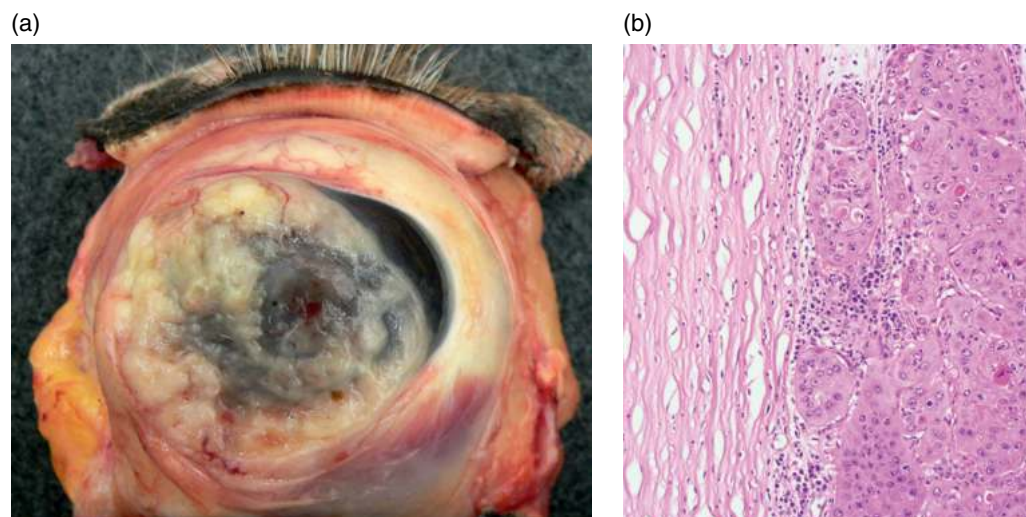


Figure 1.73 (a, b) Squamous cell carcinoma in the cornea of a horse.

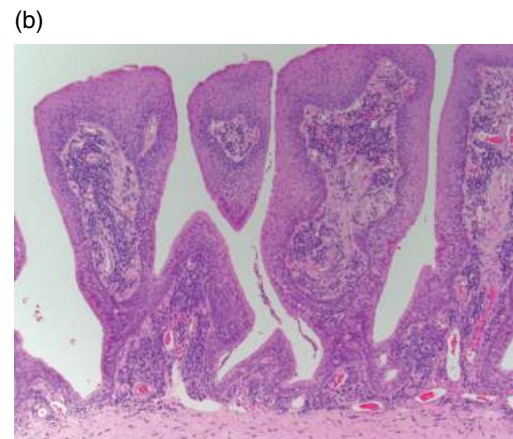


Figure 1.74 (a, b) Squamous papilloma on the corneal surface adjacent to the limbus.



Figure 1.75 Canine epibulbar melanoma extending into the cornea.

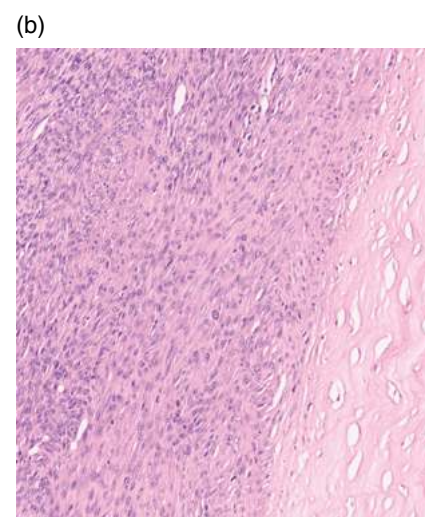
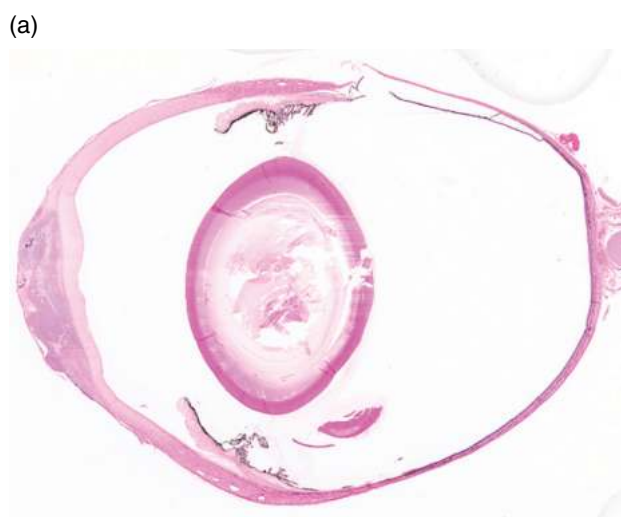


Figure 1.76 (a, b) Primary feline corneal fibrosarcoma.

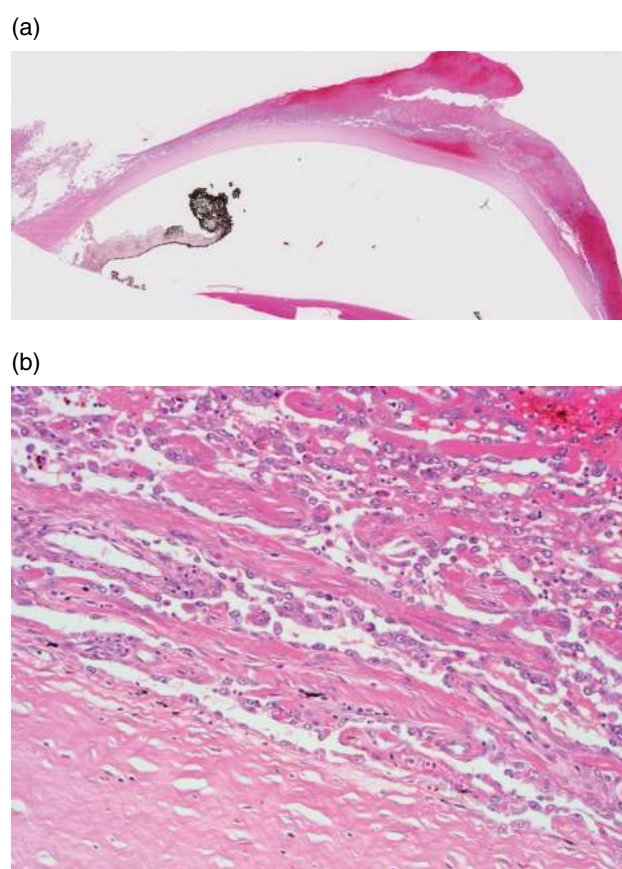


Figure 1.77 (a, b) Corneal hemangiosarcoma in a dog. Neoplastic endothelium forming vascular spaces, some of which contain blood.

Neoplasia of the Uvea

Intraocular Melanoma and Uveal Melanocytosis

Most intraocular melanomas originate in the anterior uvea. Uveal melanomas are very common in dogs, cats, and occasionally horses. **Canine uveal melanoma** is typically benign and originates in the iris or ciliary body; these typically are composed of heavily pigmented, round to spindle cells with a low mitotic index (Figure 1.78a, b). They may extend into the choroid and occasionally sclera; they can become fairly large and cause intraocular hemorrhage or secondary glaucoma. Intraocular melanoma in horses typically involves the anterior uvea and are benign. In cats, the typical melanocytic tumor is **diffuse iris melanoma**; these are considered to be malignant, and therefore may metastasize to other organs, although this is not very common. However, diffuse iris melanoma in cats will typically spread throughout the uvea and may obliterate much of the inner segments of the eye. Microscopically, the neoplastic cells can be quite pleomorphic and vary from well-differentiated round cells with a moderate amount of finely granular light brown pigment to very large round cells with one to several large nuclei with prominent nucleoli and minimal pigment (Figure 1.79a, b). Another condition that occurs primarily in Cairn Terriers is **uveal melanosis** (Figure 1.80). This condition is usually bilateral and characterized by progressive proliferation of heavily pigmented melanocytes in the anterior uvea that can extend along the scleral veins and exfoliate into the ciliary cleft and vitreous chamber. Uveal melanosis results in thickening of the affected iris and ciliary body and may be difficult to distinguish from a typical uveal melanoma. Also, it can cause secondary glaucoma.

Iridociliary Tumors

Ciliary body adenoma and adenocarcinoma are neoplasms derived from the neuroepithelium covering the ciliary body and/or the posterior surface of the iris. These are most common in the dog and are usually benign; even tumors that have cytological changes indicative of malignancy do not invade through the globe or metastasize. These are composed of cuboidal cells aligned in cords, tubules, or pseudotubules around vessels (Figure 1.81a–c). Iridociliary tumors frequently contain

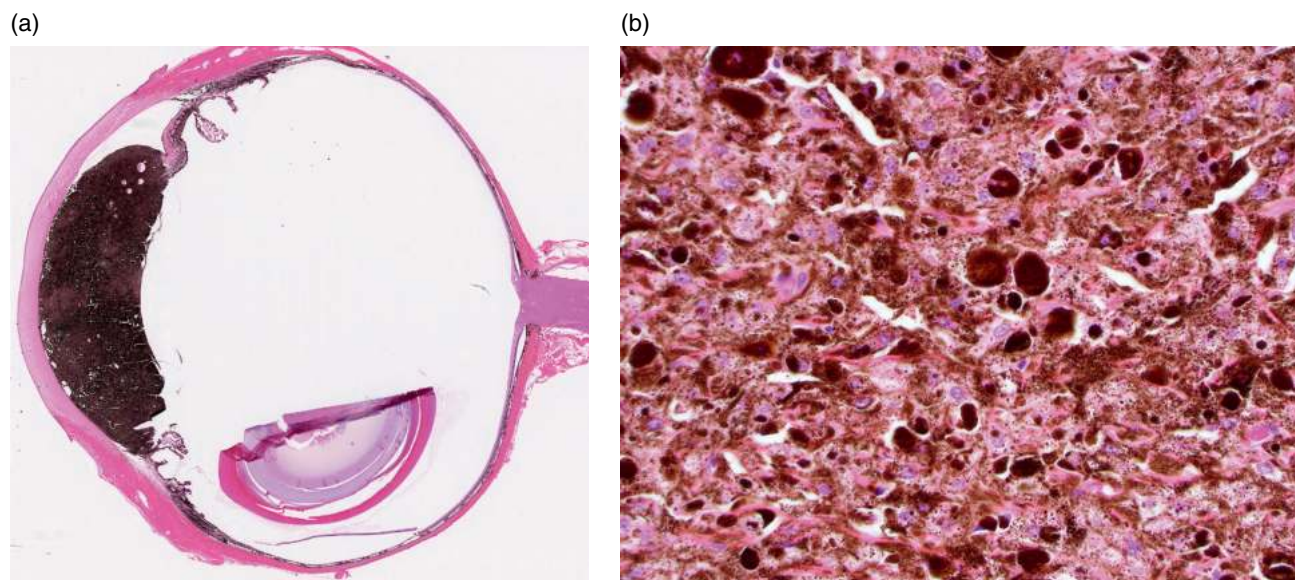


Figure 1.78 (a, b) Canine uveal melanoma. This uveal melanoma has developed within the iris and has formed anterior synechiae and partially closed the iridocorneal angle. The neoplastic melanocytes are large, round, heavily-pigmented cells. Also, the lens is luxated.

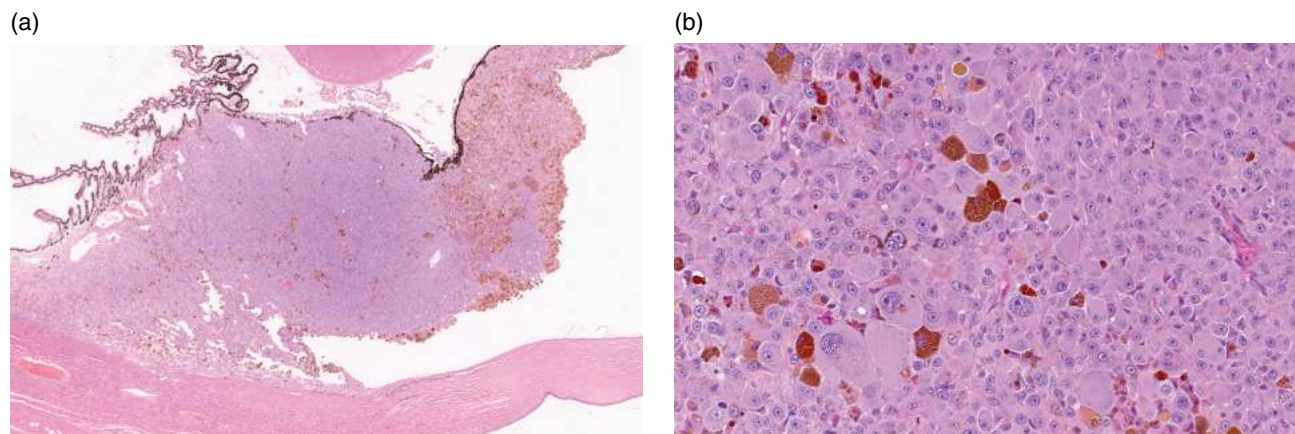


Figure 1.79 (a) Feline diffuse iris melanoma. This uveal melanoma has developed within the iris and has expanded into the ciliary body and closed the iridocorneal angle. (b) Marked anisocytosis and anisokaryosis with variable amounts of cytoplasmic pigmentation are common features.

basement membrane material surrounding lobules, foci of necrosis, are prone to hemorrhage and may stimulate the production of a PIFM.

Anterior Uveal Sarcoma of Blue-Eyed Dogs

This is an aggressive sarcoma that develops in the anterior uvea of dog breeds that typically have blue eyes, especially Siberian huskies (Figure 1.82a, b).

Intraocular Osteosarcoma

These are uncommon but occur, especially in the dog. These are aggressive neoplasms that obliterate all structures within the globe, so it is difficult to determine the specific intraocular site of origin. Their microscopic appearance is similar to osteosarcomas that occur in the appendicular skeleton (Figure 1.83a, b).

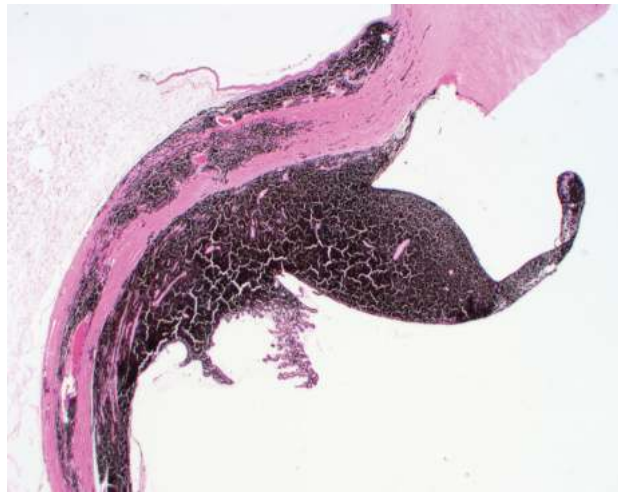


Figure 1.80 Uveal melanosis of Cairn Terriers. There is a diffuse infiltrate of large, heavily pigmented melanocytes and melanophages expanding the uvea and extending along scleral vessels.

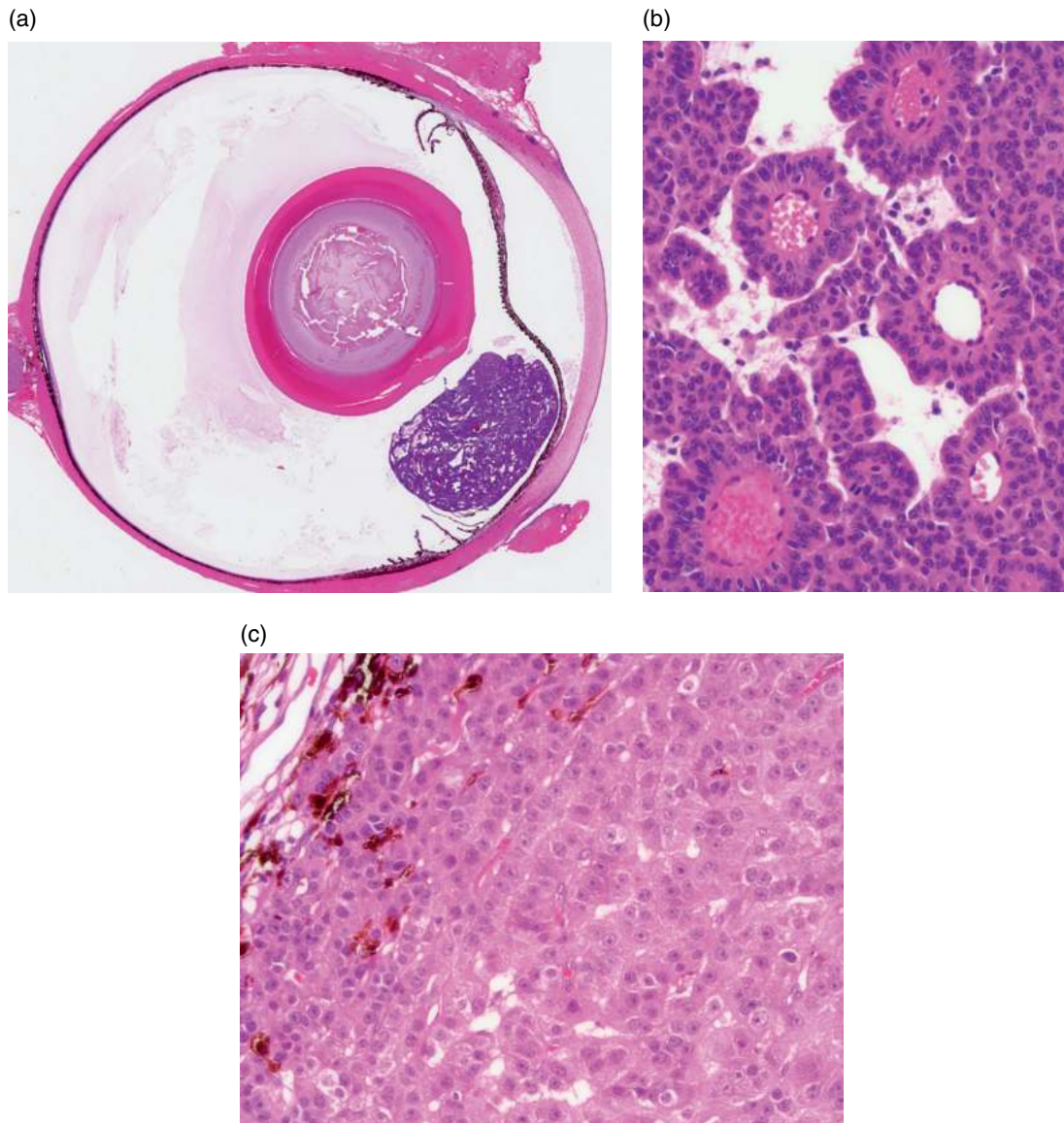


Figure 1.81 (a) Iridociliary tumor. These arise from the neuroepithelium covering the ciliary body and are typically a benign circumscribed mass. (b, c) These arise from the neuroepithelium covering the ciliary body and are composed of cells aligned in cords, tubules, or pseudotubules around vessels.

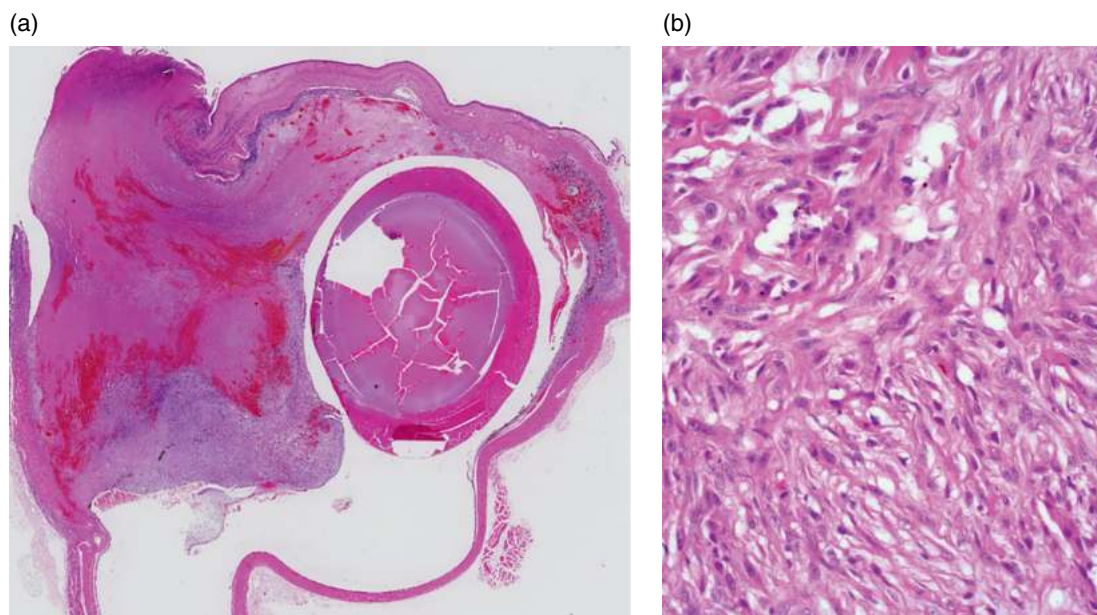


Figure 1.82 (a, b) Uveal sarcoma of blue-eyed dogs. This is an invasive poorly-differentiated sarcoma originating in the uvea.

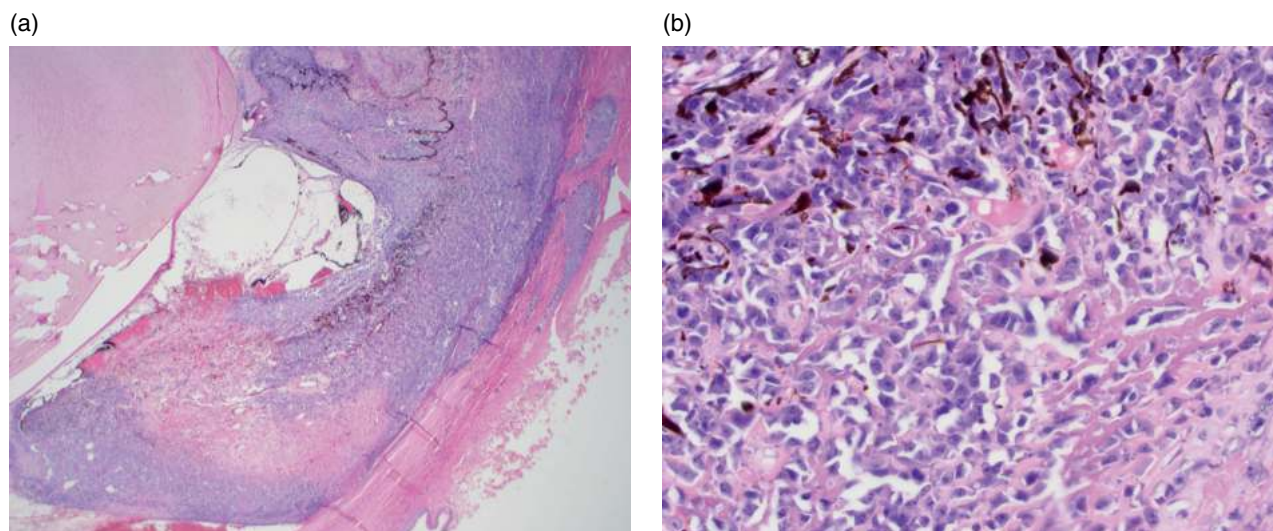


Figure 1.83 (a, b) Intraocular osteosarcoma. This is an invasive sarcoma that appears to originate in the uvea. It is composed of pyriform to polyhedral cells, some of which are surrounded by wisps of osteoid.

Intraocular Adenocarcinosarcoma (Malignant Mixed Tumor)

This is an uncommon malignant neoplasm that contains both neoplastic epithelial glandular tissue and mesenchymal tissue, which may include bone and/or cartilage (Figure 1.84).

Lymphoma

Ocular involvement is fairly common in lymphoma in most species. Usually, the uvea, including the choroid, is primarily infiltrated with neoplastic lymphocytes, which may efface the normal architecture, as in other tissues (Figure 1.85a–d). Ocular lymphoma may be a component of multicentric lymphoma, or it may apparently be limited to the eye. A form of lymphoma known as **presumed solitary ocular lymphoma (PSOL)** has been recognized in dogs and cats and may have a better prognosis than intraocular lymphoma that is a component of multicentric lymphoma. The immunophenotype of intraocular lymphoma can be B-cell, T-cell, or non-B/non-T cell.

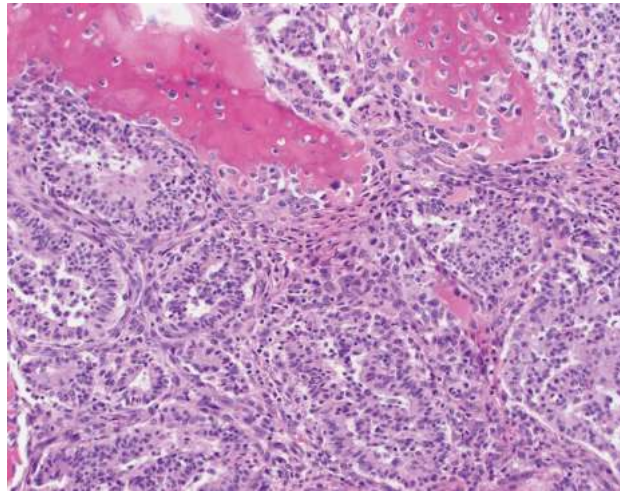


Figure 1.84 Intraocular adenocarcinoma (malignant mixed tumor). This is an invasive neoplasm that appears to originate in the uvea. It is composed of cuboidal to columnar cells aligned in tubuloacinar structures along with polyhedral to spindle cells, some of which are surrounded by wisps of osteoid or bone.

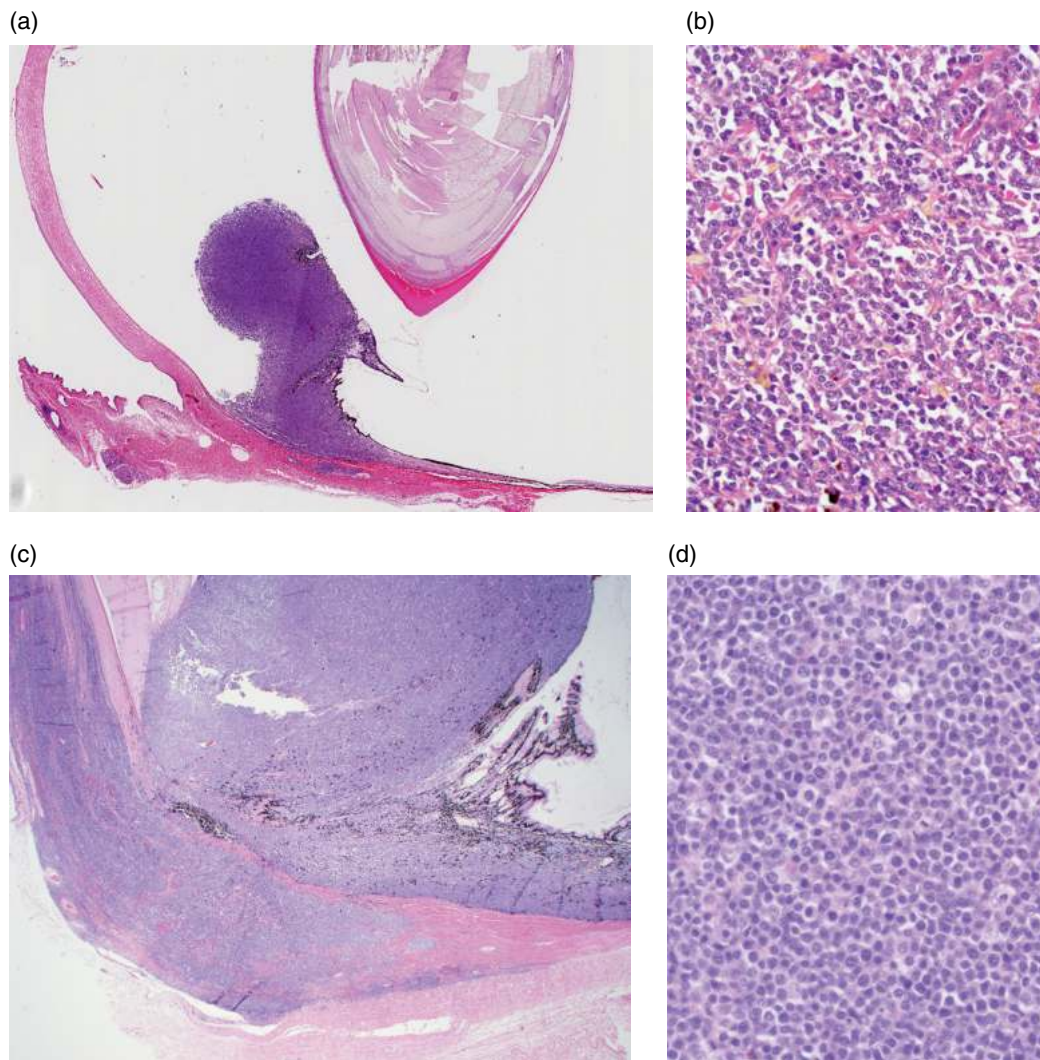


Figure 1.85 (a, b) Ocular lymphoma in a cat. Ocular lymphoma may involve any or all segments of the uvea. In this slide, an infiltrate of neoplastic lymphocytes has expanded and distorted the iris and ciliary body and has extended into the cornea and sclera. (c, d) Ocular lymphoma in a dog. Ocular lymphoma may be limited to the eye (presumed solitary ocular lymphoma), involving any or all segments of the uvea, or it may be a component of systemic lymphoma. In this slide, an infiltrate of neoplastic lymphocytes has expanded and distorted the iris and ciliary body and has extended into the cornea and sclera.

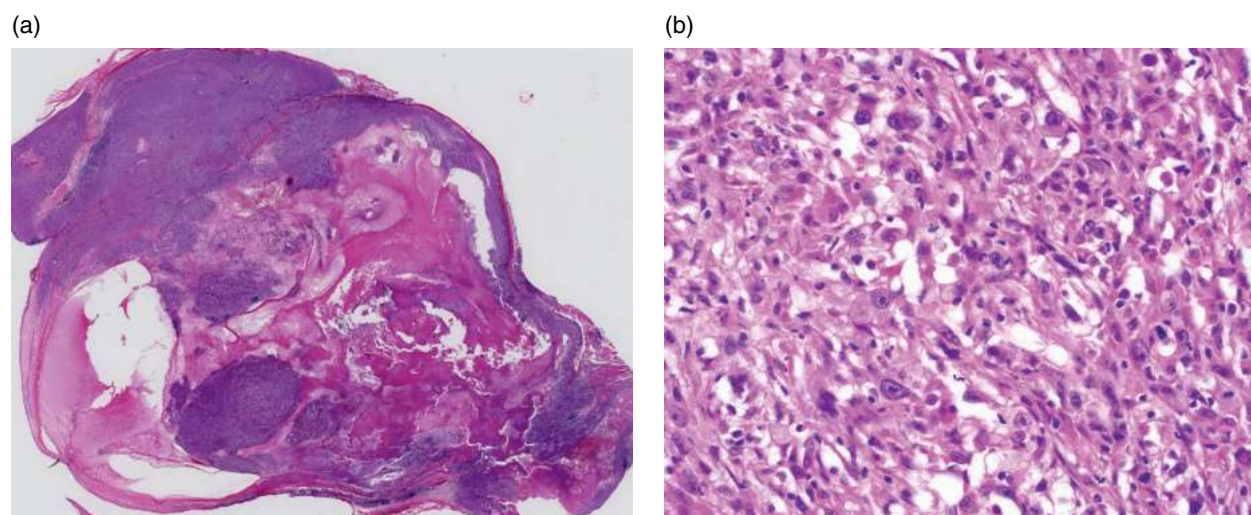


Figure 1.86 (a, b) Feline trauma-induced intraocular sarcoma. This is an invasive poorly-differentiated sarcoma that is presumed to originate from lens fiber epithelium following traumatic injury of the lens.

Neoplasia of the Lens

Trauma-Induced Intraocular Sarcoma of Cats

Trauma-induced intraocular sarcoma (TIIS) is a malignant neoplasm that is unique to cats. It occurs in an eye that has been severely traumatized, usually with a penetrating injury that has ruptured the lens capsule. It takes months to years to develop. It is thought to be due to neoplastic transformation of the lens epithelium, a step beyond fibrous metaplasia. Morphologically, TIIS can vary from a fibrosarcoma to osteosarcoma, and they frequently contain an infiltrate of lymphocytes and foci of necrosis. These typically invade circumferentially within the globe, obliterating all internal ocular components and can extend through the sclera into the periocular tissue (Figure 1.86a, b).

Neoplasia of the Retina

Primary neoplasia of the retina is extremely rare. Retinoblastoma and astrocytoma have been reported (Figure 1.87a–d).

Neoplasia of the Eyelids

Palpebral Melanocytoma and Malignant Melanoma

Melanomas and melanocytomas frequently occur on the eyelids as pedunculated or sessile masses, similar to other locations on the skin. These are typically benign, but many will have junctional activity. Neoplastic cells may vary from round with abundant pigment to spindle-shaped with little or no pigment (Figure 1.88a, b). Malignant melanoma of the eyelid in dogs is not common but microscopically resembles those of the oral cavity. These are invasive, rapidly growing neoplasms that frequently have satellite foci within the adjacent substantia propria and junctional activity (Figure 1.89a–c).

Squamous Cell Carcinoma

This is one of the most common neoplasms of the eyelids, third eyelid, and conjunctiva in dogs, cats, and horses. In draft horses, SCC is frequently multifocal and bilateral. Animals with little pigment in the eyelids are at increased risk due to the effect of ultraviolet radiation.

Squamous Papilloma

This is a common benign neoplasm that occurs on the eyelids of dogs. They may be caused by canine papillomavirus and are identical to those that occur in the skin and oral cavity.

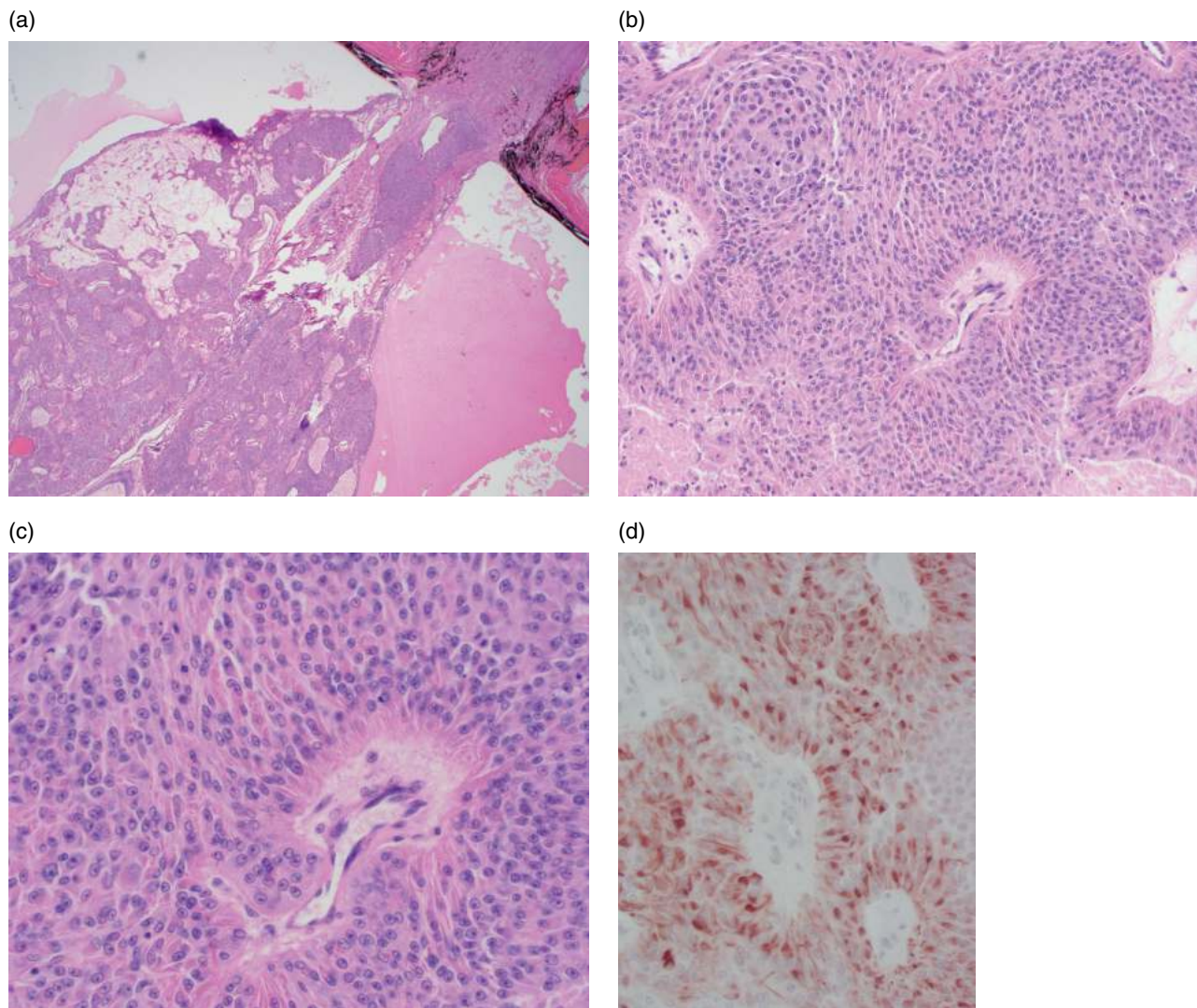


Figure 1.87 (a, b) Retinal astrocytoma. This is composed of polyhedral to spindle cells, some of which are aligned perpendicularly to the vessels. (c, d) These cells are immunoreactive for glial fibrillary acidic protein.

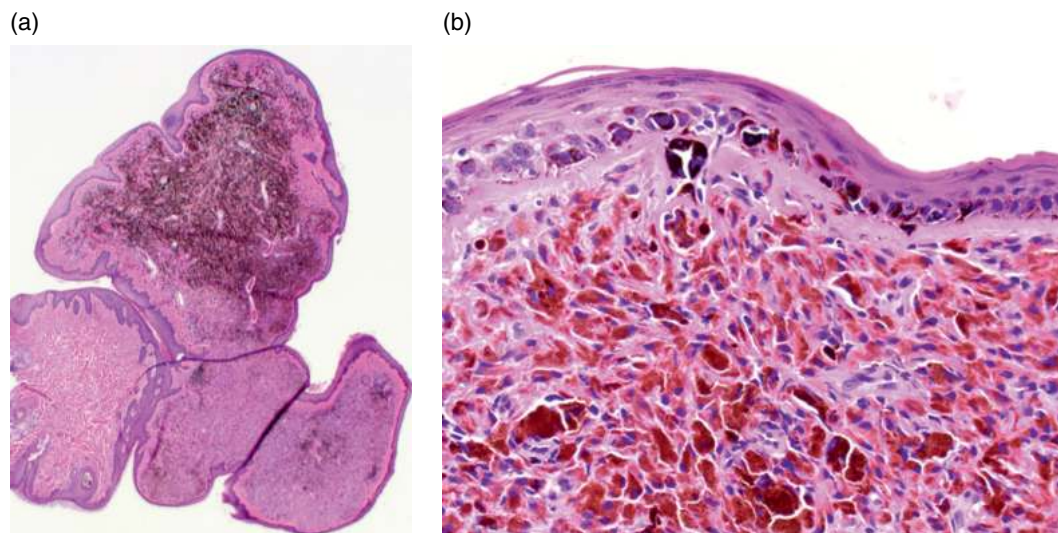


Figure 1.88 (a, b) Melanoma on the eyelid. Heavily pigmented cells are typical of melanoma in this location. Note the pigmented neoplastic cells within the epidermis; this is junctional activity.

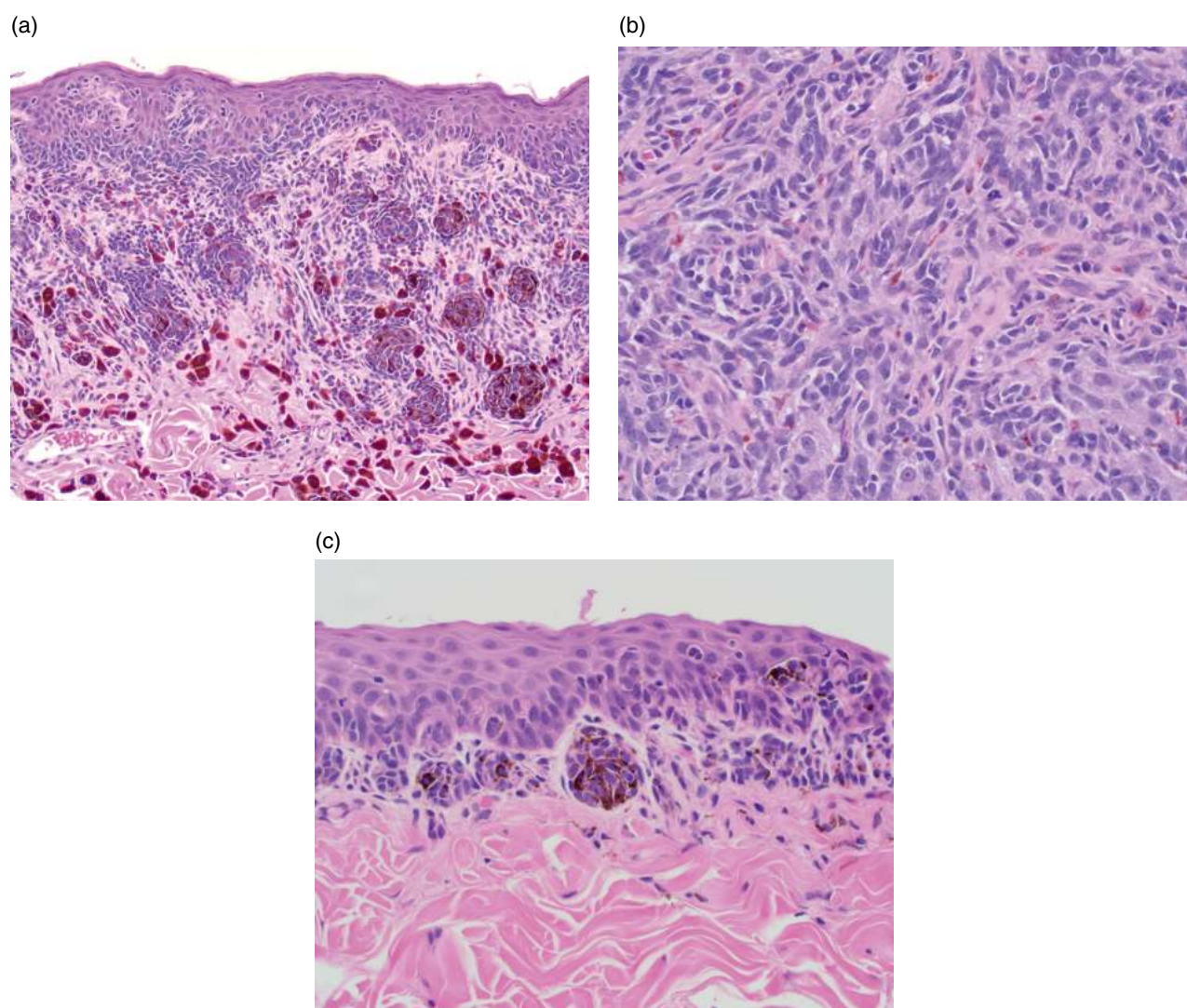


Figure 1.89 (a) Malignant melanoma on the eyelid. Heavily pigmented round cells along with poorly-pigmented spindle cells. Note the pigmented neoplastic cells within the epidermis (junctional activity). (b) Poorly-pigmented spindle cells with high mitotic index. (c) Aggregates of pigmented neoplastic cells within the epidermis (junctional activity).

Meibomian Gland Tumors

Meibomian gland tumors are extremely common in old dogs and less so in cats; they resemble sebaceous tumors that commonly occur in the skin. **Focal Meibomian hyperplasia** is typically a small mass that still retains some degree of gland architecture (Figure 1.90). **Meibomian adenoma** is typically a pedunculated mass on the eyelid margin composed of multiple lobules of well-differentiated sebaceous glands surrounding a duct lined by stratified squamous epithelium (Figure 1.91a, b). **Meibomian epithelioma** is less differentiated and is predominantly composed of proliferative basal reserve cells with scattered sebocytes; these are considered to be a premalignant lesion (Figure 1.92). Occasionally, **Meibomian adenocarcinoma** occurs. It is common for any of these Meibomian tumors to be ulcerated and partially surrounded by pyogranulomatous to pyogranulomatous exudate (chalazion) secondary to trauma.

Neoplasia of the Conjunctiva and Membrana Nictitans

Squamous Cell Carcinoma

Squamous cell carcinoma is a serious disease of the conjunctiva and typically occurs on the third eyelid and bulbar conjunctiva in white-face horses, dogs, and cats (Figure 1.93a, b).

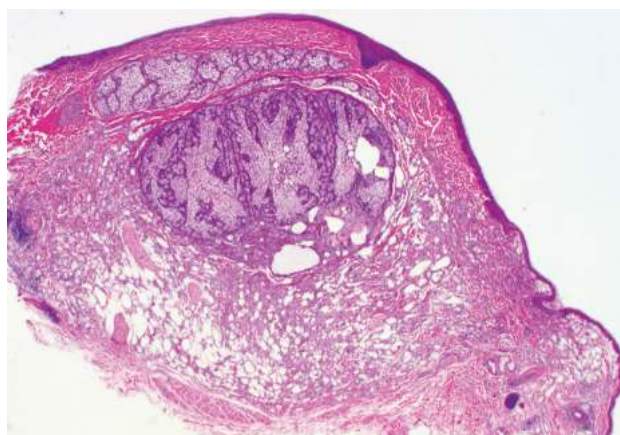


Figure 1.90 Meibomian gland hyperplasia surrounded by granulomatous inflammation.

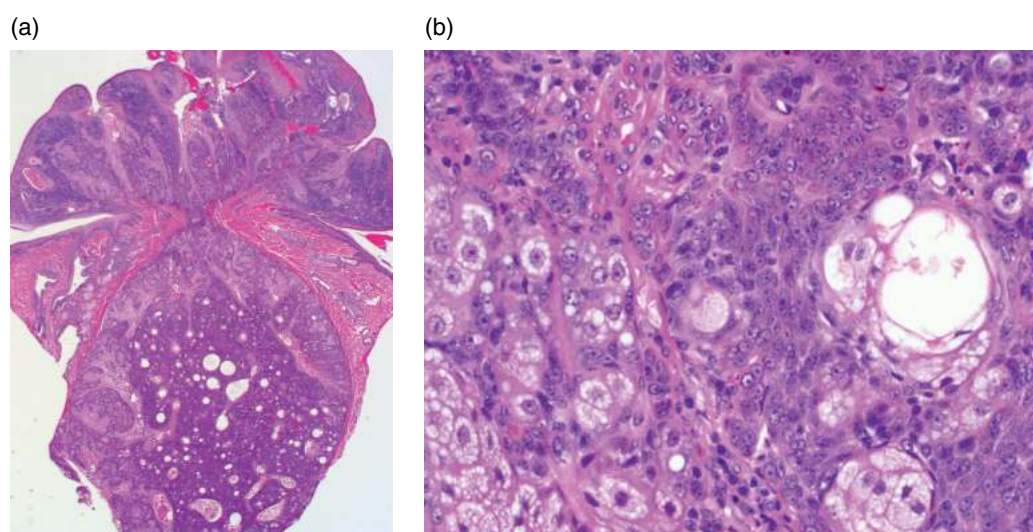


Figure 1.91 (a, b) Meibomian gland adenoma. These are nodular or papillomatous masses composed of lobules of well-differentiated sebocytes and a moderate number of spindle-shaped basal cells along with small ductular structures.

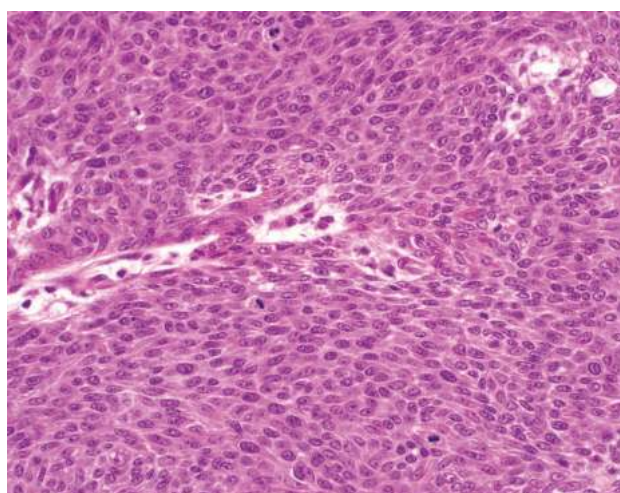


Figure 1.92 Meibomian gland epithelioma. These are composed primarily of spindle-shaped basal cells and a few scattered sebocytes. The mitotic index is typically high.

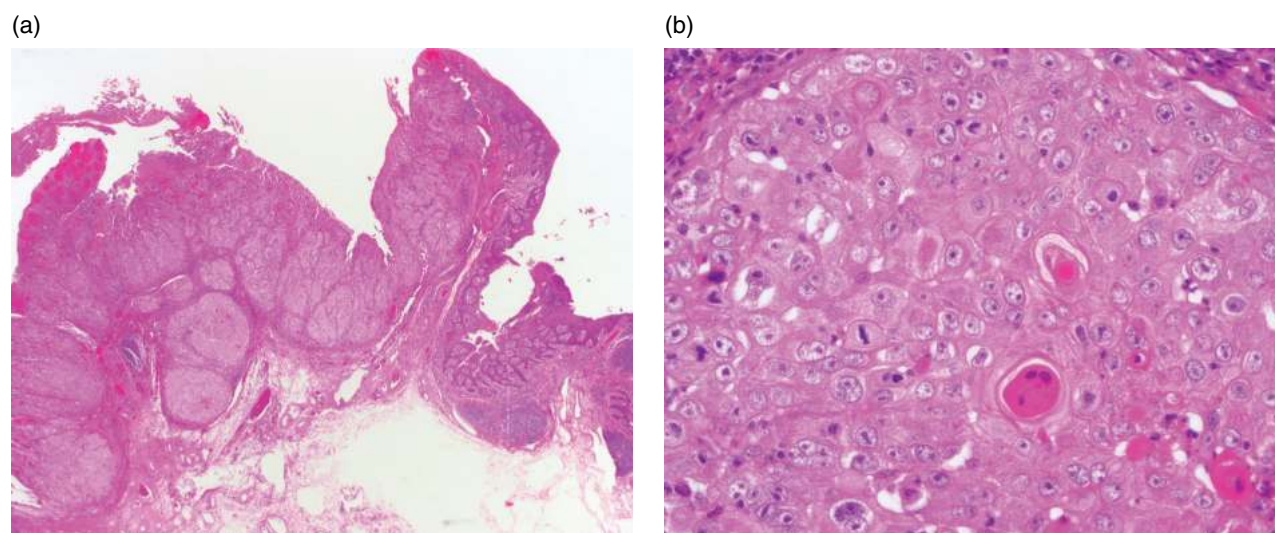


Figure 1.93 (a) Squamous cell carcinoma on the third eyelid. (b) Neoplastic cells are round to polygonal, have a large round to oval nucleus, one to two prominent nucleoli, abundant eosinophilic cytoplasm, and prominent desmosomes. Occasional cells are keratinized.

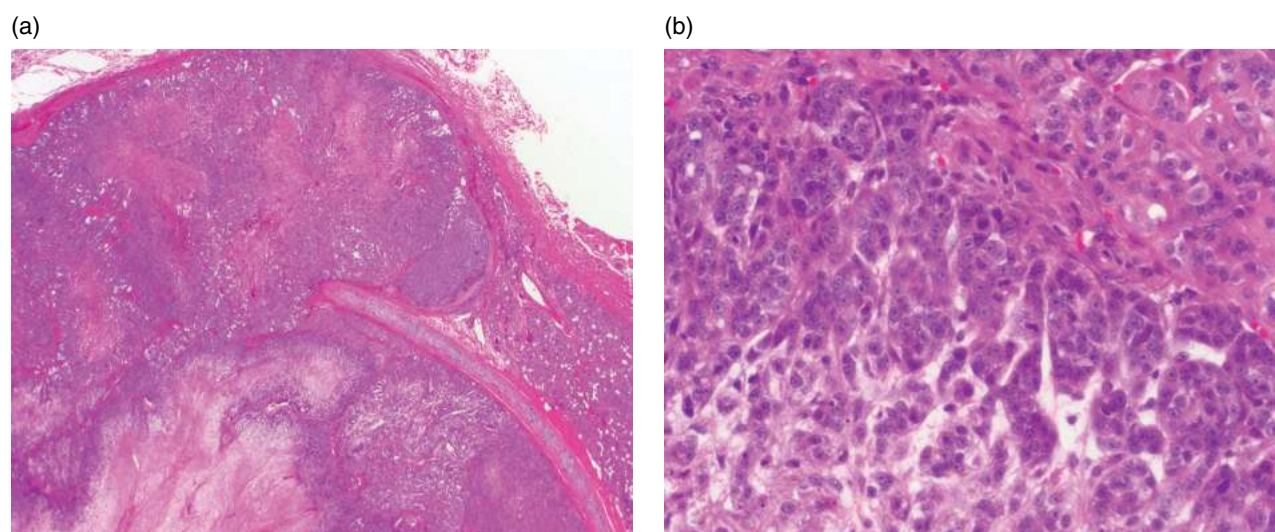


Figure 1.94 (a, b) Adenocarcinoma of the gland of the third eyelid. Neoplastic cells are cuboidal and are aligned in clusters or crude tubuloacinar structures.

Adenocarcinoma of Gland of Third Eyelid (Membrana Nictitans)

These are rare neoplasms in all species but are most common in old dogs. Microscopically, they are locally invasive and are composed of cells that are cuboidal and aligned in clusters or crude tubuloacinar structures (Figure 1.94a, b).

Epibulbar Melanoma

Melanomas also occur on the surface of the globe at the limbus in dogs. These are called limbal or **epibulbar melanomas**; they are considered to be benign.

Neoplasia of Retrobulbar Tissues

Retrobulbar Meningioma

Occasionally, a meningioma will develop in the meninges surrounding the optic nerve in dogs. These have a similar microscopic appearance to meningiomas in the CNS that are composed of spindle to polyhedral cells aligned in small sheets or clusters that frequently have a swirled pattern (Figure 1.95a–c). However, a distinctive feature that is common in

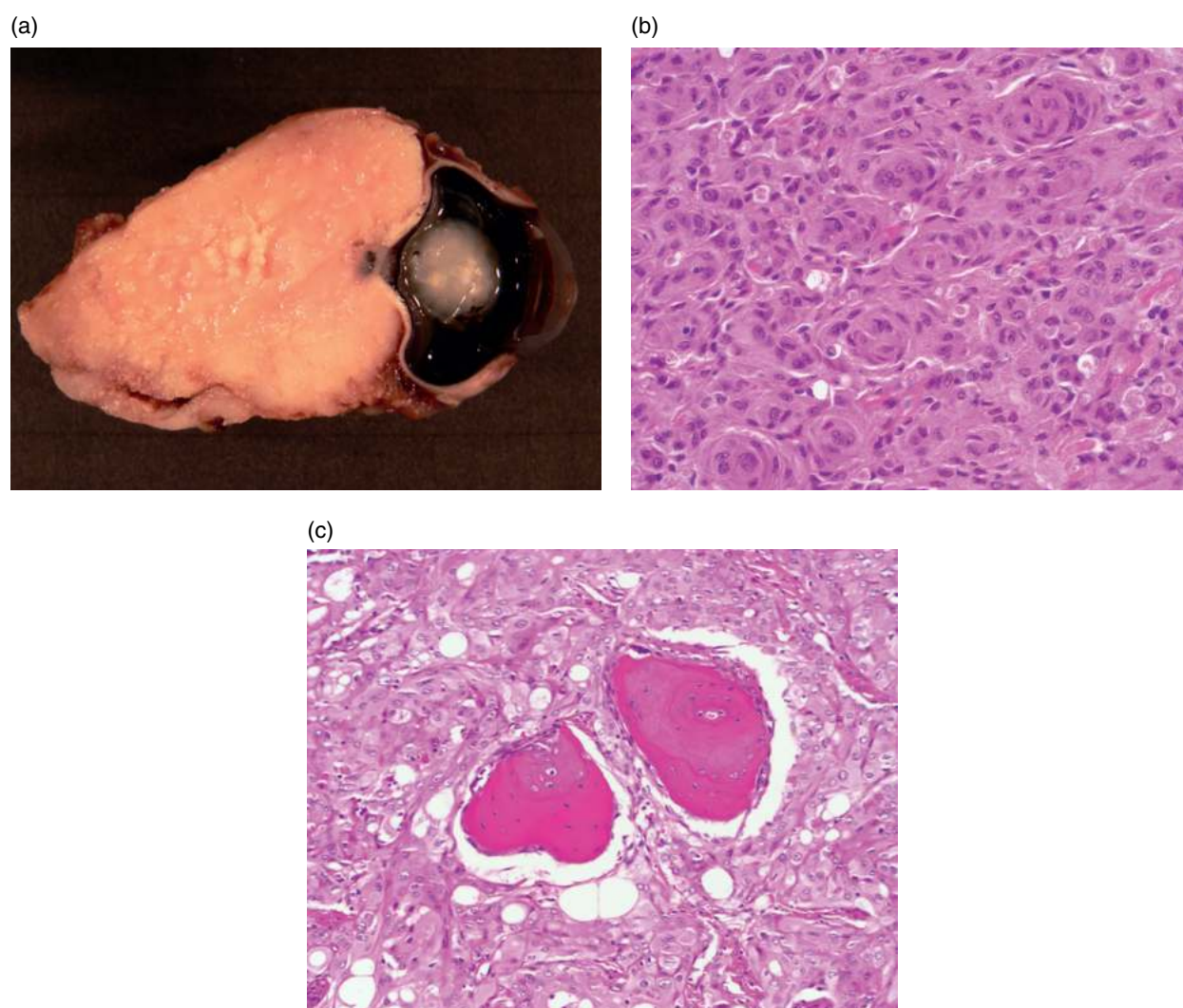


Figure 1.95 (a, b) Canine retrobulbar meningioma. (c) In addition to clusters or swirls of neoplastic spindle to polyhedral cells, these neoplasms commonly contain foci of metaplastic bone and cartilage.

retrobulbar meningiomas is foci of metaplastic bone and cartilage. Biologically, these neoplasms are generally benign, but they will surround the optic nerve and compress the globe frequently producing exophthalmos and atrophy of the optic nerve.

Retrobulbar Peripheral Nerve Sheath Tumor

Occasionally these arise from nerves within the orbit, branches of cranial nerves III, IV, and VI. They resemble peripheral nerve sheath tumors of the limbs and are characterized by interlacing, palisading, and swirling bundles of spindle cells (Figure 1.96).

Lymphoma

Multicentric lymphoma may develop in the retrobulbar tissues and surround and invade into the optic nerve.

Adenoma/Adenocarcinoma of Lacrimal Gland or Zygomatic Salivary Gland

There are several possible glandular neoplasms that occur in the retrobulbar/periocular tissues, but these are difficult to distinguish from each other. Adenomas of the lacrimal gland and zygomatic salivary gland have a very similar microscopic appearance and are mainly distinguished based on their location. These are circumscribed neoplasms composed of cuboidal to columnar epithelium aligned in multiple acinar structures (Figure 1.97). Adenocarcinoma of the lacrimal or zygomatic gland is composed of invasive cuboidal to columnar epithelium aligned in multiple crude acinar structures separated by immature fibrous tissue (desmoplastic response) (Figure 1.98).

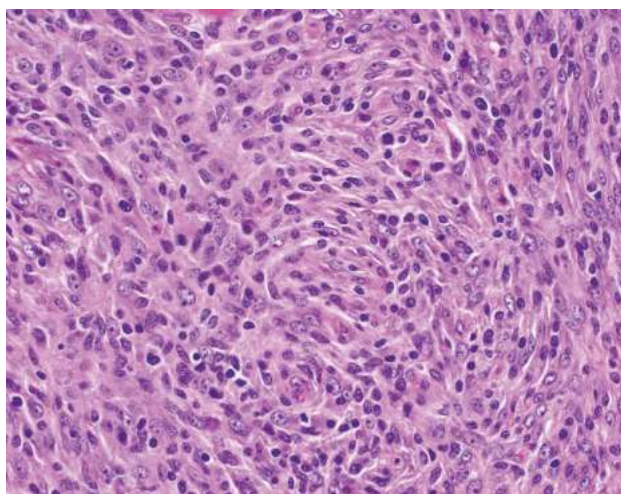


Figure 1.96 Retrobulbar nerve sheath tumor. Interlacing, palisading, and swirling bundles of spindle cells are characteristic. These may also contain an infiltrate of lymphocytes.

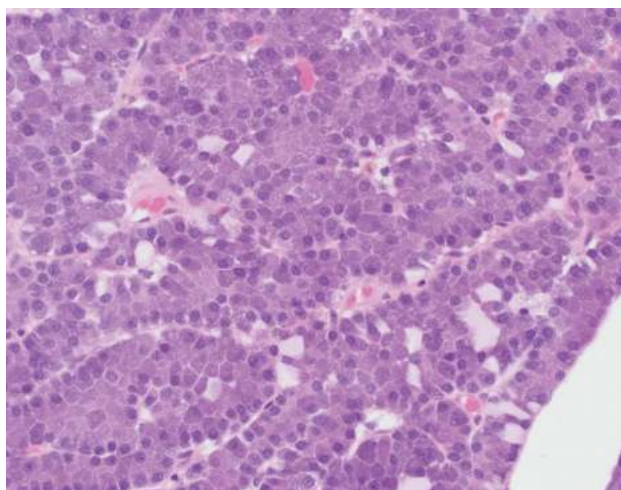


Figure 1.97 Lacrimal gland adenoma. This is composed of cuboidal to columnar epithelium aligned in multiple acinar structures.

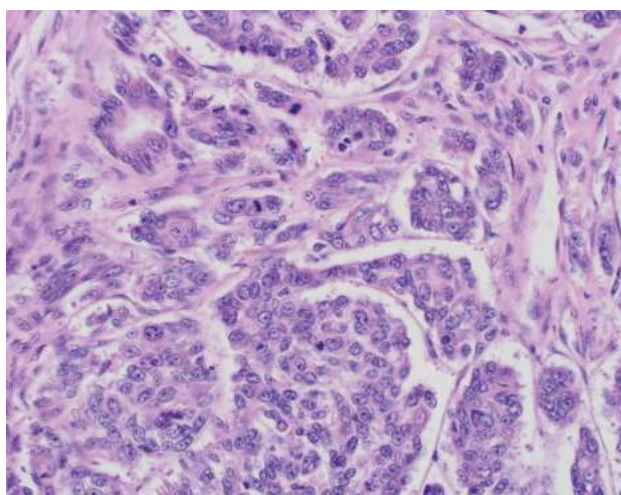


Figure 1.98 Lacrimal gland adenocarcinoma. This is composed of invasive cuboidal to columnar epithelium aligned in multiple crude acinar structures separated by immature fibrous tissue.

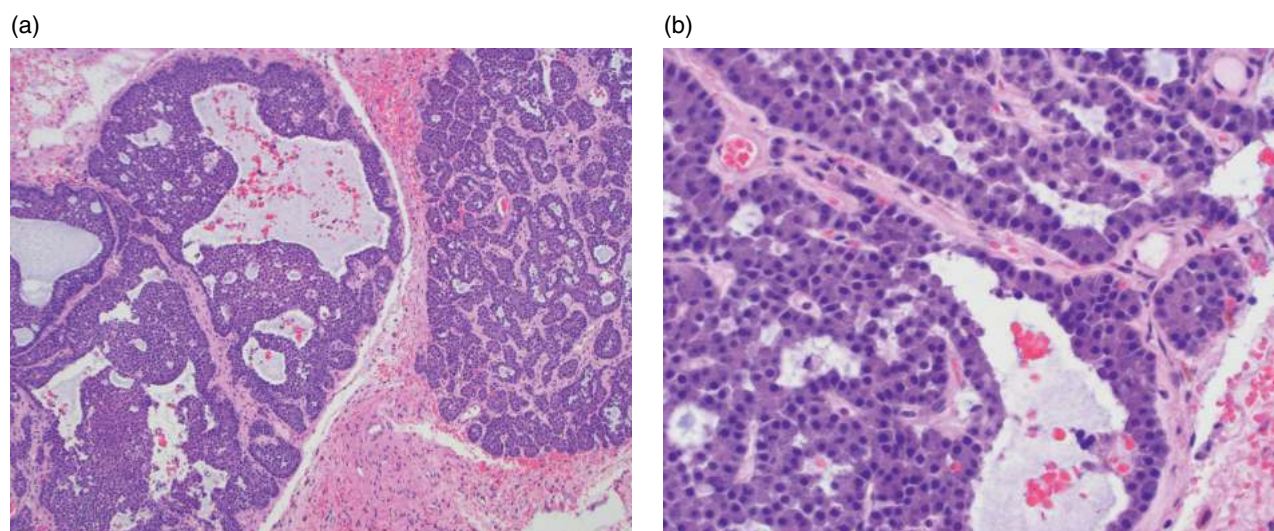


Figure 1.99 (a, b) Canine orbital lobular adenoma. This is composed of multiple lobules of well-differentiated cuboidal to columnar epithelium aligned in acini. The lobules are separated by loose fibrovascular tissue that makes the mass very friable and poorly demarcated.

Canine Orbital Lobular Adenoma

This is also a benign neoplasm that occurs in the retrobulbar tissues. It is composed of multiple lobules of well-differentiated cuboidal to columnar epithelium aligned in acini. The lobules are separated by loose fibrovascular tissue that makes the mass very friable and poorly demarcated; this is the main distinguishing feature of this neoplasm (Figure 1.99a, b).

References and Additional Readings

- Komaromy, A.M., Abrams, K.L., Heckenlively, J.R. et al. (2016). Sudden acquired retinal degeneration syndrome (SARDS) – a review and proposed strategies toward a better understanding of pathogenesis, early diagnosis, and therapy. *Vet. Ophthalmol.* 19 (4): 319–331.
- Beamer, G., Reilly, C.M., and Pizzirani, S. (2015). Microscopic lesions in canine eyes with primary glaucoma. *Vet. Clin. North Am. Small Anim. Pract.* 45 (6): 1213–1233. <https://doi.org/10.1016/j.cvs.2015.07.001>.
- Cooper, A.E., Ahonen, S., Rowland, J.S. et al. (2014). A novel form of progressive retinal atrophy in Swedish vallhund dogs. *PLoS One* 9 (9): e106610. <https://doi.org/10.1371/journal.pone.0106610>. Erratum in: *PLoS One* 2015; 10(2): e0118128. PMID: 25198798; PMCID: PMC4157785.
- Dean, E. and Meunier, V. (2013). Feline eosinophilic keratoconjunctivitis: a retrospective study of 45 cases (56 eyes). *J. Feline Med. Surg.* 15 (8): 661–666. <https://doi.org/10.1177/1098612X12472181>.
- Deehr, A.J. and Dubielzig, R.R. (1998). A histopathological study of iridociliary cysts and glaucoma in Golden Retrievers. *Vet. Ophthalmol.* 1 (2–3): 153–158. <https://doi.org/10.1046/j.1463-5224.1998.00018.x>.
- Denk, N., Sandmeyer, L.S., Lim, C.C. et al. (2012). A retrospective study of the clinical, histological, and immunohistochemical manifestations of 5 dogs originally diagnosed histologically as necrotizing scleritis. *Vet. Ophthalmol.* 15 (2): 102–109. <https://doi.org/10.1111/j.1463-5224.2011.00948.x>.
- Gelatt, K.N., van der Woerd, A., Ketrings, K.L. et al. (2001). Enrofloxacin associated retinal degeneration in cats. *Vet. Ophthalmol.* 4 (2): 99–106.
- Headrick, J.F., Bentley, E., and Dubielzig, R.R. (2004). Canine lobular orbital adenoma: a report of 15 cases with distinctive features. *Vet. Ophthalmol.* 7 (1): 47–51. <https://doi.org/10.1111/j.1463-5224.2004.00323.x>.
- Grahn, B., Peiffer, R., and Wilcock, B. (2019). *Histologic Basis of Ocular Disease in Animals*. Wiley Blackwell.
- Jost, H.E., Townsend, W.M., Moore, G.E., and Liang, S. (2020). Golden retriever pigmentary uveitis: vision loss, risk factors for glaucoma, and effect of treatment on disease progression. *Vet. Ophthalmol.* 23 (6): 1001–1008. <https://doi.org/10.1111/vop.12841>.

- Maxie, M.G. (ed.) (2016). Chapter 5 – special senses. In: *Jubb, Kennedy and Palmer's Pathology of Domestic Animals*, 6e, vol. 1, 407–488. Brian Wilcock.
- Lanza, M.R., Musciano, A.R., Dubielzig, R.D., and Durham, A.C. (2018). Clinical and pathological classification of canine intraocular lymphoma. *Vet. Ophthalmol.* 21 (2): 167–173.
- Petersen-Jones, S.M., Mentzer, A.L., Dubielzig, R.R. et al. (2008). Ocular melanosis in the Cairn Terrier: histopathological description of the condition, and immunohistological and ultrastructural characterization of the characteristic pigment-laden cells. *Vet. Ophthalmol.* 11 (4): 260–268. <https://doi.org/10.1111/j.1463-5224.2008.00640.x>.
- Sebbag, L., Riggs, A., and Carnevale, J. (2020). Oculo-skeletal dysplasia in five Labrador Retrievers. *Vet. Ophthalmol.* 23 (2): 386–393. <https://doi.org/10.1111/vop.12715>.
- Treadwell, A., Naranjo, C., Blocker, T. et al. (2015). Clinical and histological characteristics of canine ocular gliovascular syndrome. *Vet. Ophthalmol.* 18 (5): 371–380. <https://doi.org/10.1111/vop.12209>.
- Meuten, D. (ed.) Chapter 20 – tumors of the eye. In: *Tumors in Domestic Animals*, 5e, 892–922. Richard Dubielzig.
- Gelatt, K. (ed.) (2007). *Veterinary Ophthalmology*, 4e. Blackwell Publishing.
- Zarfoss, M.K., Tusler, C.A., Kass, P.H. et al. (2018). Clinical findings and outcomes for dogs with uveodermatologic syndrome. *J. Am. Vet. Med. Assoc.* 252 (10): 1263–1271. <https://doi.org/10.2460/javma.252.10.1263>.
- Zeiss, C.J., Johnson, E.M., and Dubielzig, R.R. (2003). Feline intraocular tumors may arise from transformation of lens epithelium. *Vet. Pathol.* 40 (4): 355–362. <https://doi.org/10.1354/vp.40-4-355>.