EYE

Kenneth Alonso, MD, FACP

Embryologic development of ocular structures

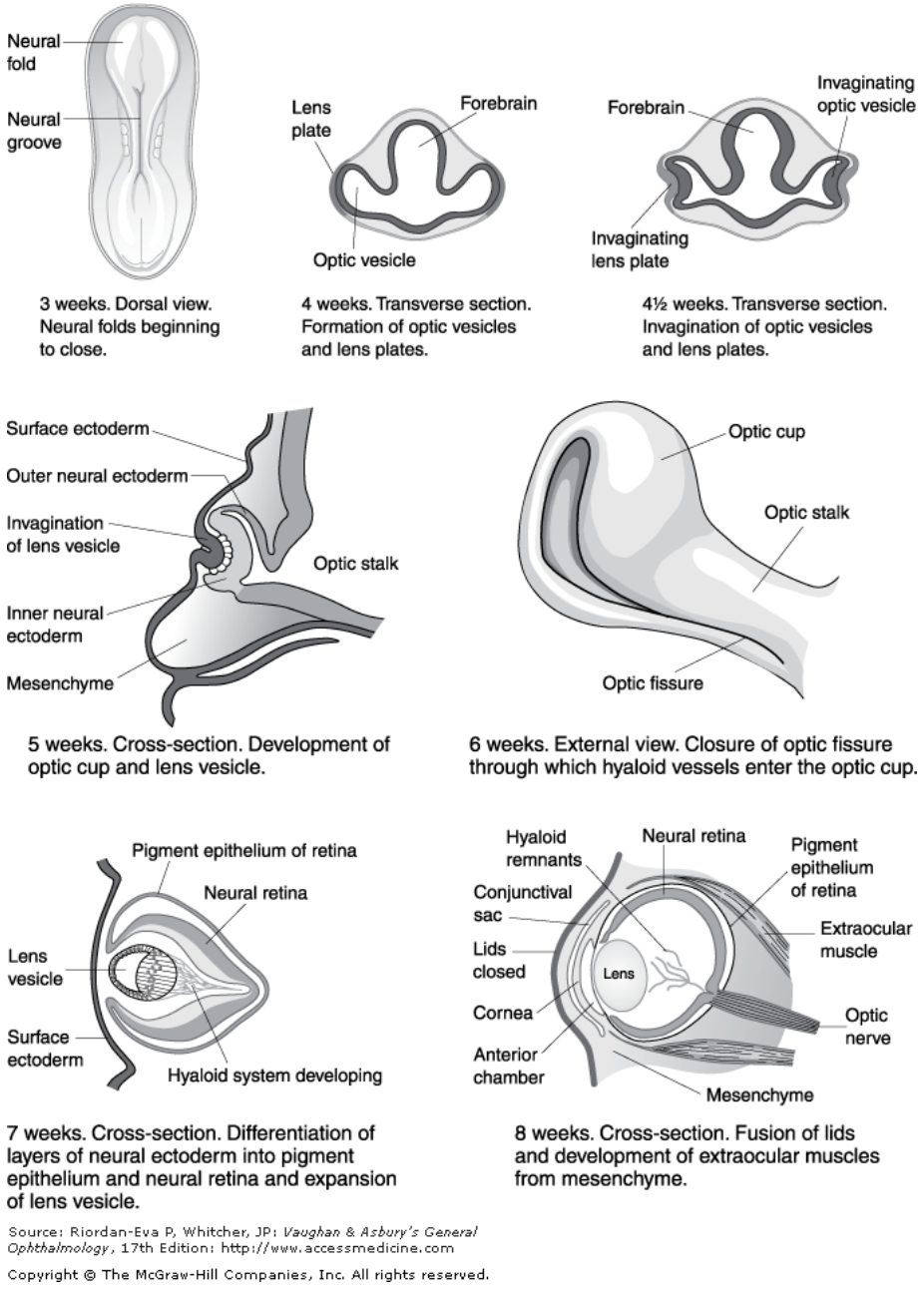


Fig. 1-28 Accessed 07/01/2010

Eye development

- Optic vesicles form as evagination of developing forebrain (day 22).
- Lens placodes induced when forebrain contacts surface ectoderm.
- Optic cup forms at week 5 from optic vesicle. (Intraretinal space noted.)
- Lens vesicle is induced from lens placode.
- Optic fissure (choroid) forms as outer layer of optic cup.
- Pigmented layer.

Eye development

- Hyaloid artery reaches the inner chamber of the developing eye.
- Becomes the central retinal artery.
- Developing lens induces overlying ectoderm to form corneal epithelium.
- The cornea is avascular.
- The remainder of cornea is mesodermal.
- The limbus cornea (between cornea and sclera) is vascularized.

Eye development

- At 7 weeks, cells of the posterior wall of the lens vesicle elongate and grow anteriorly.
- Axons leave neuroretina via the developing optic nerve.
- Hyaloid vessels supply the developing lens. Later will supply inner layers of retina.
- Loose mesenchyme around the the primordium forms inner choroid and outer scleral layers.

Anatomy of the eye

- The sclera consists of dense fibrous tissue. It forms the outer coat of the eye.
- Sclera is continuous with dura mater of optic nerve.
- The middle coat of the eye is the uvea.
- It is the vascular layer.
- It consists of the choroid, ciliary body, and iris.
- Served by choriocapillaris (outer layer) and central retinal artery (inner layer).
- Choroid continuous with pia-arachnoid

Anatomy of the eye

- The retina is the inner coat of the eye.
- The ora serrata is the area of transition from the 10-layered sensory retina to the 2-layered non-sensory retina.

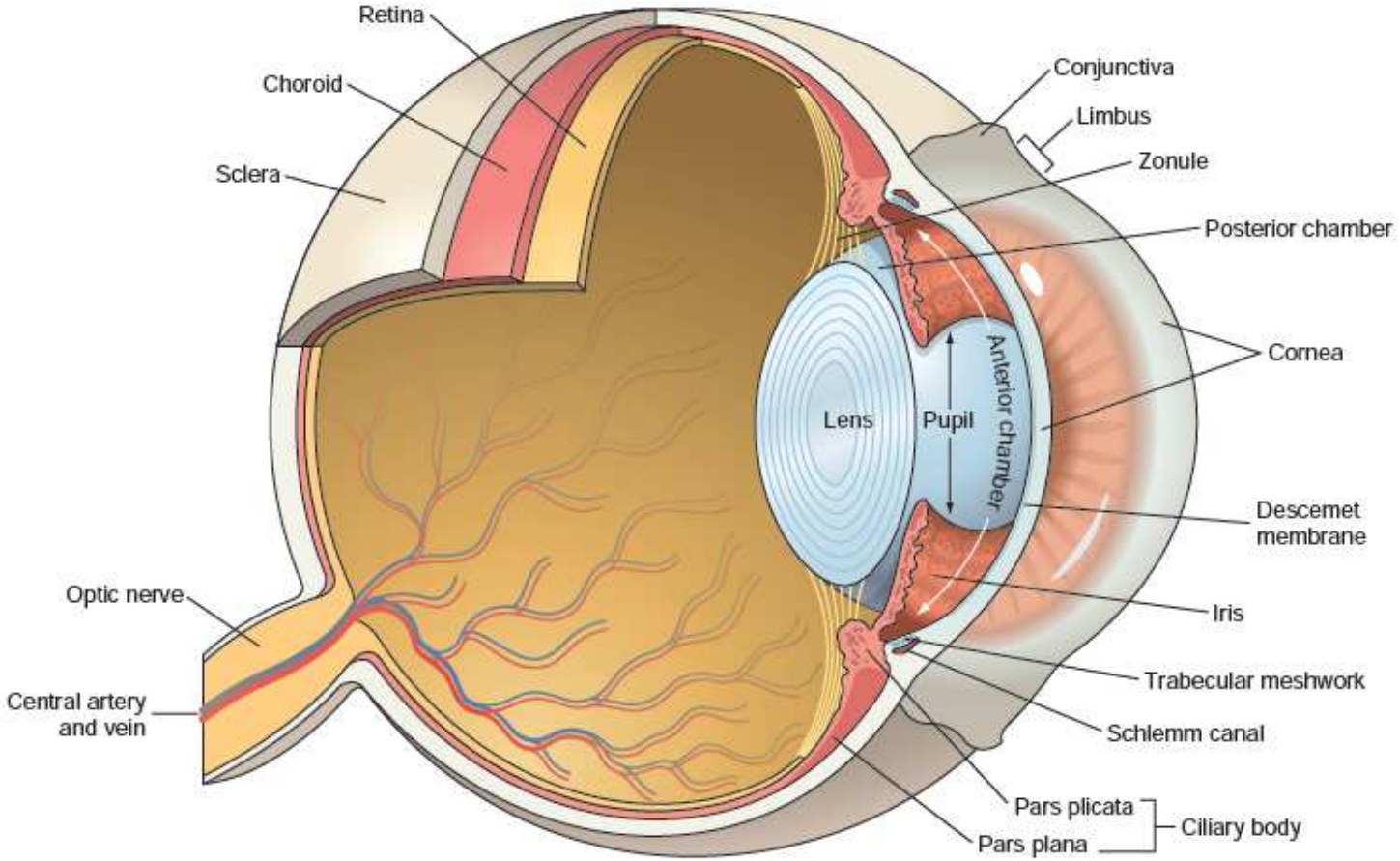


Figure 29-1 Anatomy of the eye.

Orbit

- The orbit is a compartment that is closed medially, laterally, and posteriorly.
- Diseases that increase orbital contents therefore displace the eye forward (proptosis).
- Masses contained within the cone formed by the horizontal rectus muscles generate axial proptosis: the eye bulges straight forward.
- Optic glioma
- Menigioma
- Thyroid ophthalmopathy
- May result in chronic corneal exposure to air

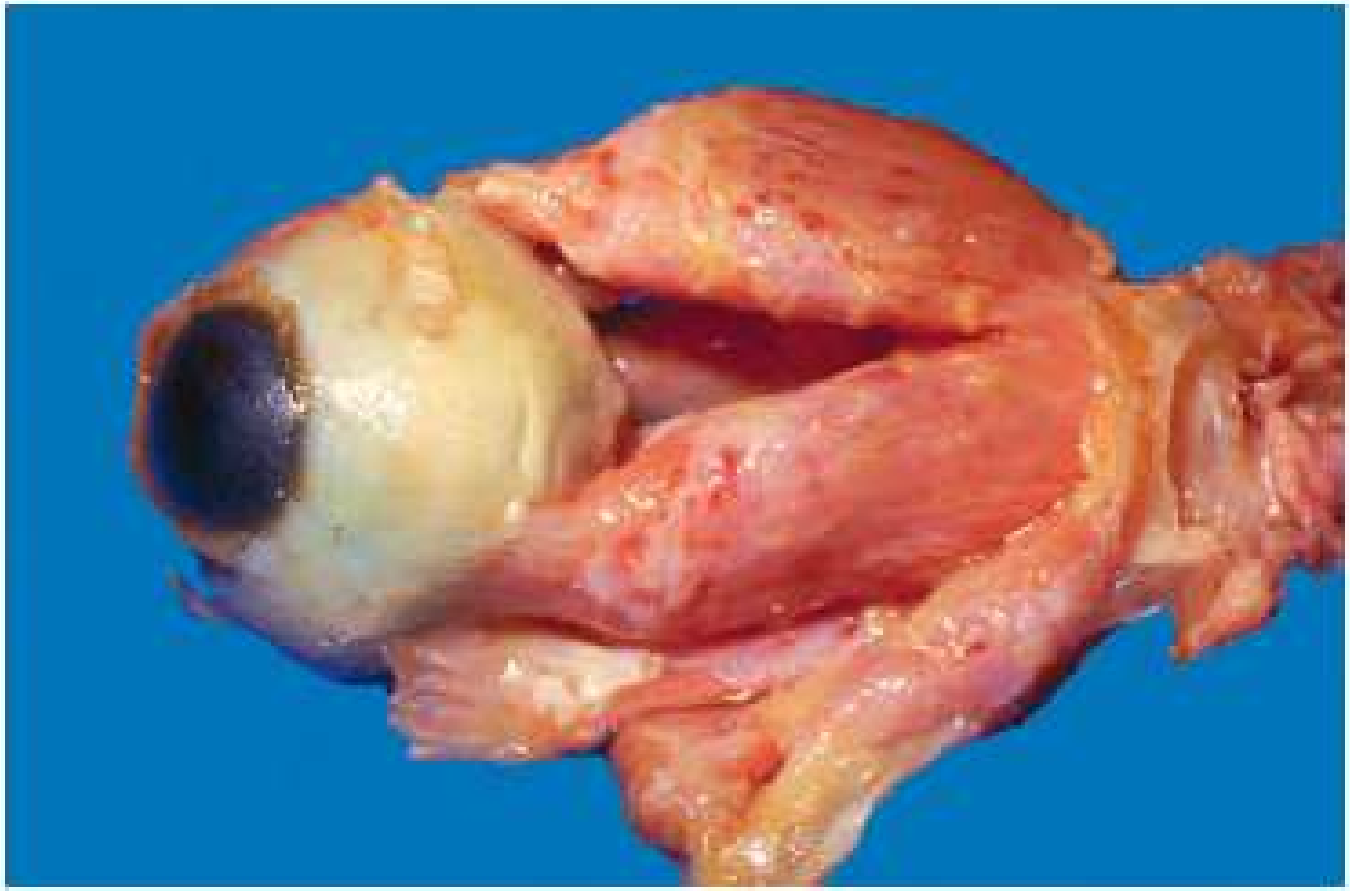


Figure 29-2 The extraocular muscles are greatly distended in this postmortem dissection of tissues from a patient with thyroid (Graves) ophthalmopathy. Note that the tendons of the muscles are spared. (Courtesy Dr. Ralph C. Eagle, Jr., Wills Eye Hospital, Philadelphia, Pa.)

Orbit

- Positional proptosis:
- Any enlargement of the lacrimal gland from inflammation or neoplasm produces a proptosis that displaces the eye inferiorly and medially as the gland is located superotemporally.
- The floor of the orbit is the roof of the maxillary sinus, and the medial wall of the orbit separates the orbit from the ethmoidal sinuses.
- Infectious agents may invade orbit directly
- Mucormycosis in diabetics

Orbit

- Idiopathic orbital inflammation (pseudotumor)
- Unilateral or bilateral
- May affect all orbital tissue elements
- May be confined to the lacrimal gland (sclerosing dacryoadenitis)
- May be confined to the extraocular muscles (orbital myositis),
- May be confined to Tenon's capsule, the fascial layer that wraps around the eye (posterior scleritis).

Orbit

- Histologically there is chronic inflammation and variable degrees of fibrosis.
- The inflammatory infiltrate typically includes lymphocytes and plasma cells and occasionally eosinophils.
- Germinal centers, when present, raise the suspicion of a reactive lymphoid hyperplasia.
- Vasculitis may be present, suggesting an underlying systemic condition.

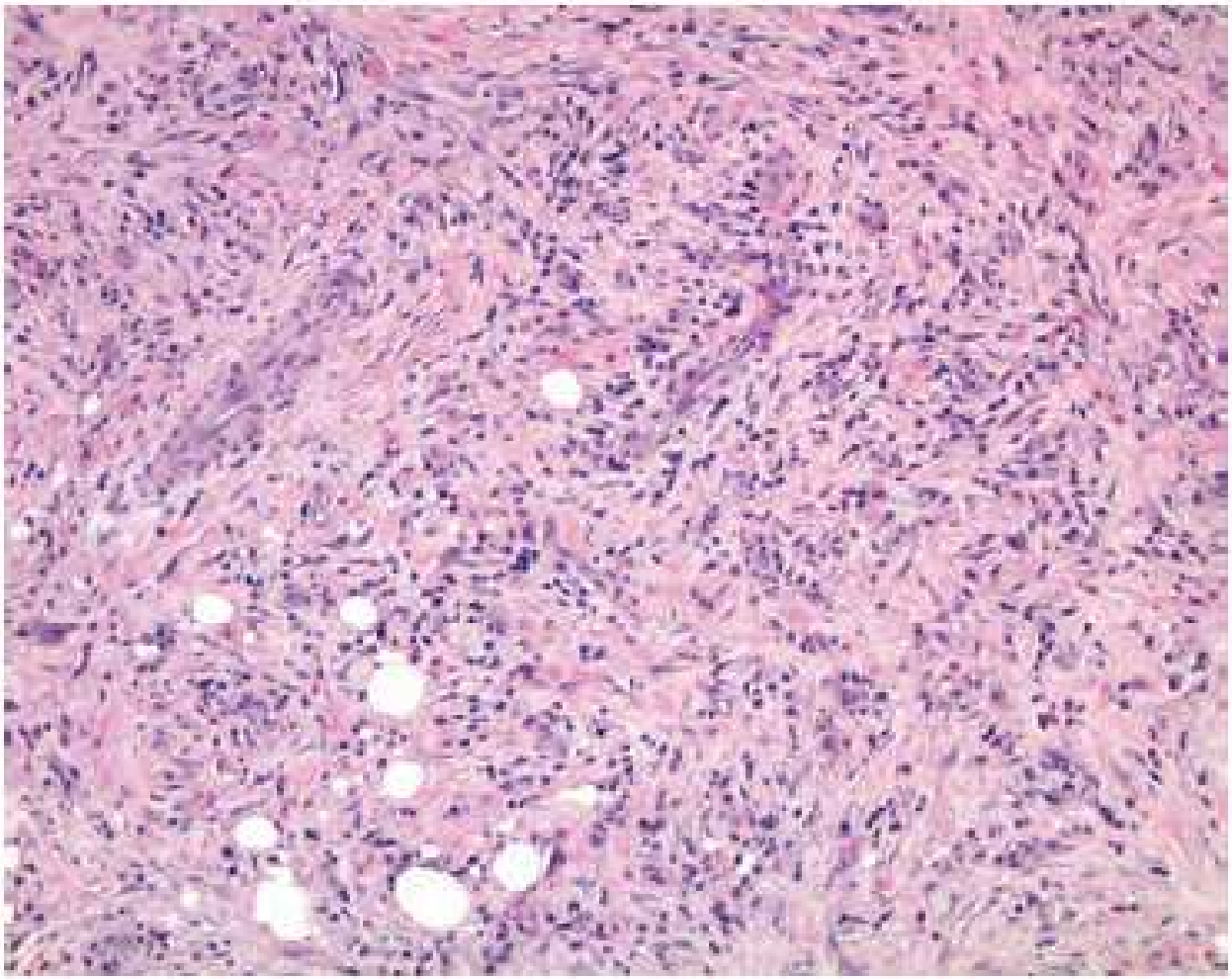


Figure 29-3 In idiopathic orbital inflammation (orbital inflammatory pseudotumor) the orbital fat is replaced by fibrosis. Note the chronic inflammation, accompanied in this case by eosinophils.

Orbit

- The presence of necrosis and degenerating collagen along with vasculitis should raise the suspicion of granulomatosis with polyangiitis (Wegner's)
- Idiopathic orbital inflammation is typically confined to the orbit but may develop concomitantly with sclerosing inflammation in the retroperitoneum, the mediastinum, and the thyroid, especially as a manifestation of IgG4-related disease.

Orbit

- The most frequently encountered primary neoplasms of the orbit are vascular in origin:
- Capillary hemangioma of infancy and early childhood
- Lymphangioma
- Both of which are unencapsulated
- Cavernous hemangioma found typically in adults.
- Encapsulated
- Other encapsulated orbital masses are, pleomorphic adenoma of the lacrimal gland, dermoid cyst, and neurilemmoma

Orbit

- Non–Hodgkin lymphoma
- May affect the entire orbit or can be confined to compartments of the orbit such as the lacrimal gland.
- Primary orbital malignancies may arise from any of the orbital tissues.
- Metastases
- Metastatic prostatic carcinoma may present clinically like idiopathic orbital inflammation
- Metastatic neuroblastoma and Wilms may produce periocular ecchymoses.

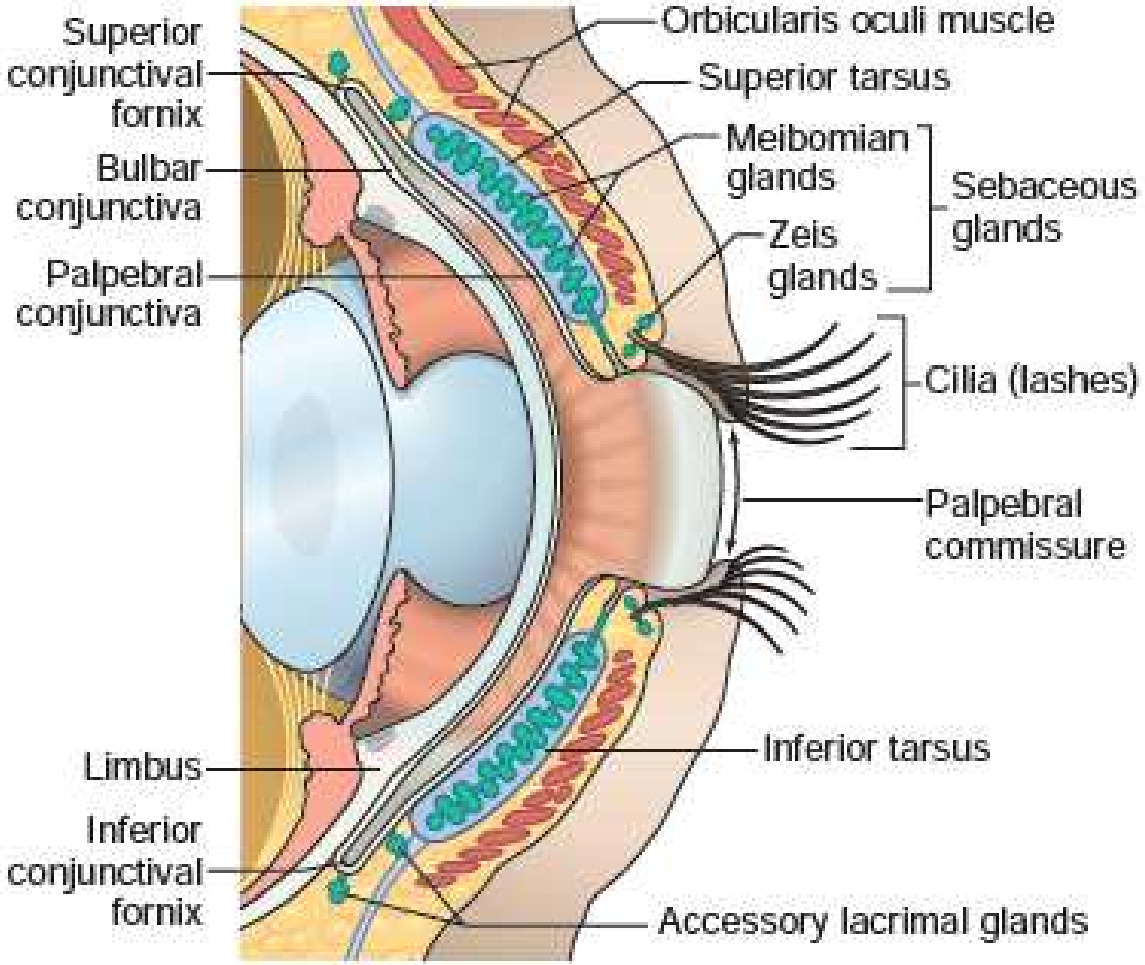


Figure 29-4 Anatomy of the conjunctiva and eyelids.

Eyelid

- The eyelid is composed of skin externally and mucosa (the conjunctiva) on the surface apposed to the eye.
- Covers the eye
- Accessory lacrimal glands within the eyelid generate the tear film.
- If the drainage system of the sebaceous glands is obstructed at the eyelid margin (blepharitis), then lipid may extravasate into surrounding tissue and provoke a granulomatous response producing a lipogranuloma (chalazion).

Eyelid

- The most common neoplasm of the eyelid is basal cell carcinoma.
- Melanoma is rare.
- Sebaceous carcinoma may form a local mass that mimics chalazion or may diffusely thicken the eyelid.
- May also resemble inflammatory processes such as blepharitis or ocular cicatricial pemphigoid
- Predilection for intraepithelial (Pagetoid) spread
- Spreads to parotid and submandibular nodes
- 22% mortality

Eyelid

- In moderately differentiated or well-differentiated sebaceous carcinoma, vacuolization of the cytoplasm is present
- May resemble a variety of other malignancies histologically, including basal cell carcinoma.
- Pagetoid spread may mimic Bowenoid actinic keratosis in the eyelid and carcinoma in situ in the conjunctiva.
- Sebaceous carcinoma may spread through the conjunctival epithelium and the epidermis to the lacrimal drainage system and the nasopharynx.
- It may also extend into the lacrimal gland ductules and thereby into the main lacrimal gland.

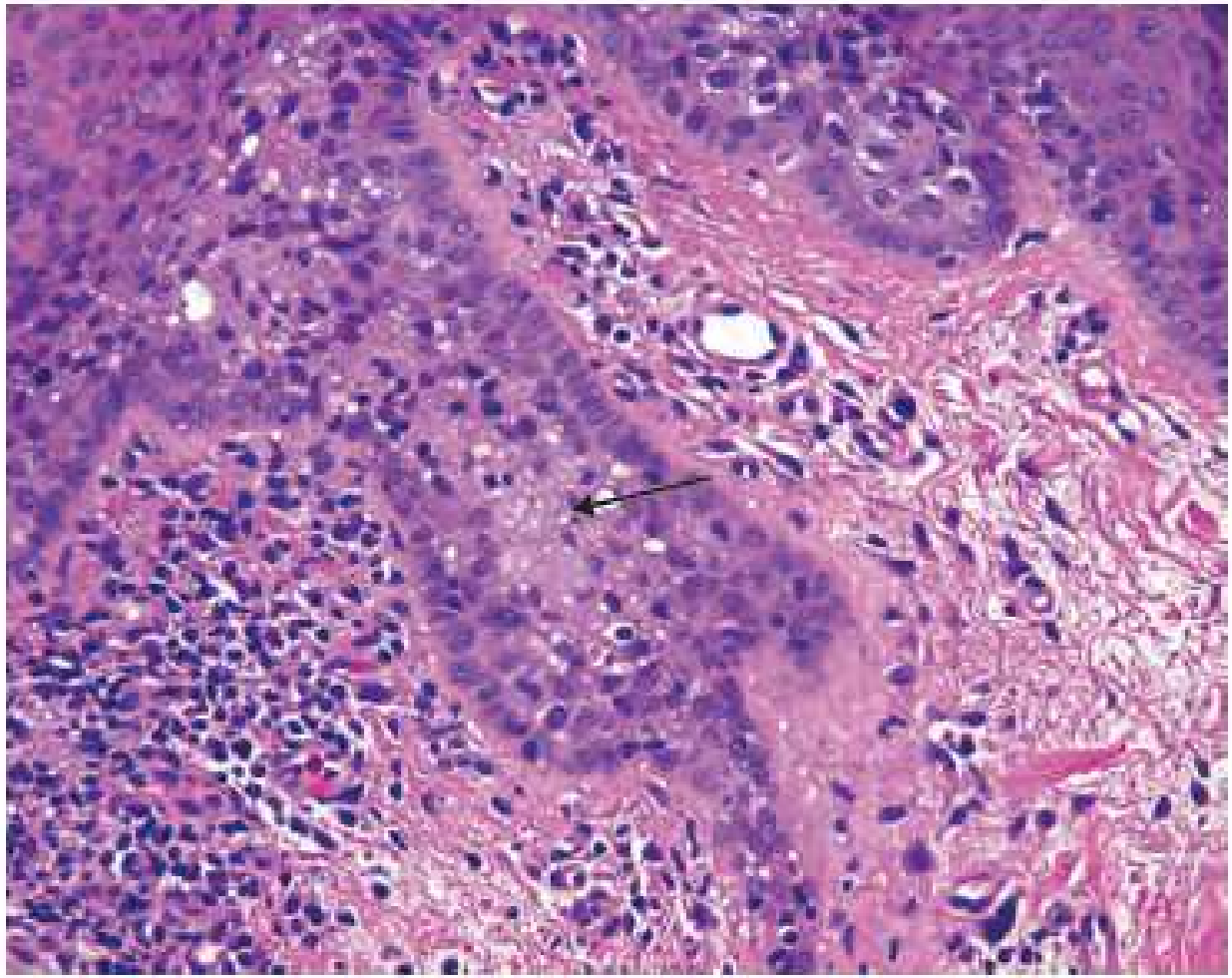
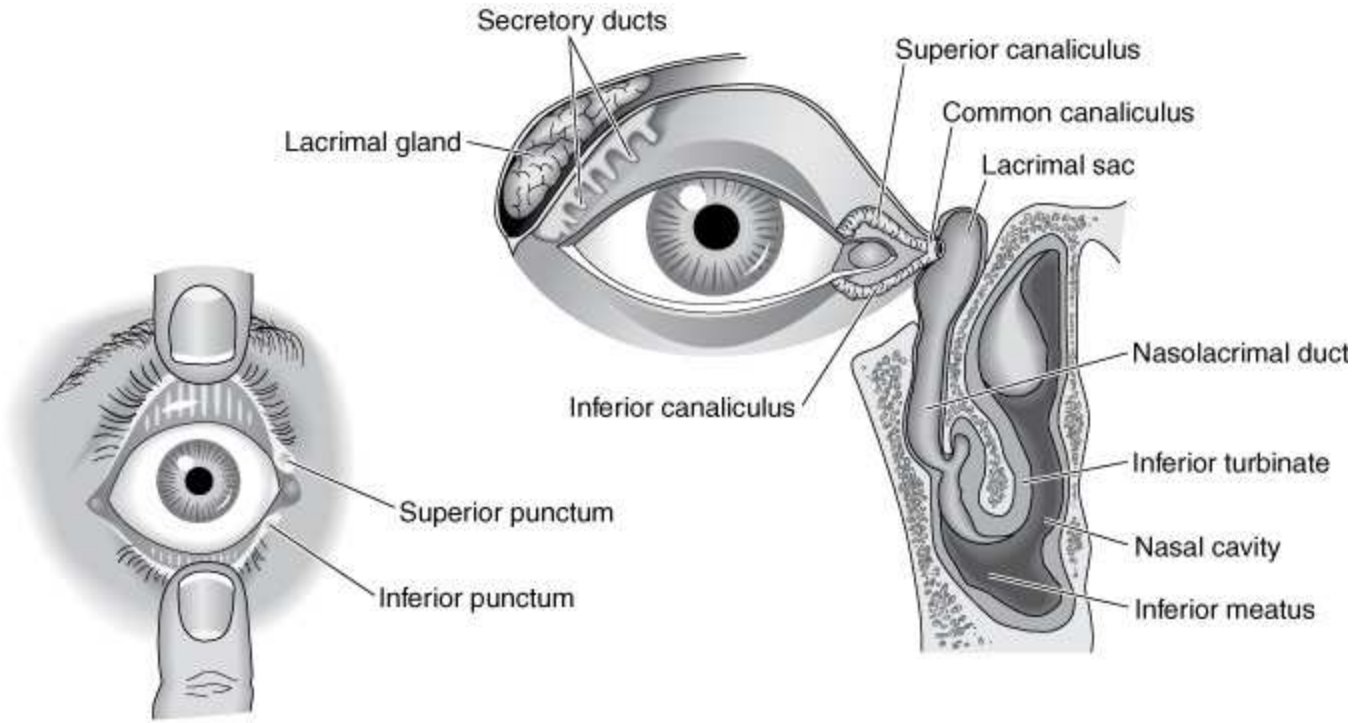


Figure 29-5 Pagetoid spread of sebaceous carcinoma. Neoplastic cells with foamy cytoplasm are present within the epidermis (arrow). Invasive sebaceous carcinoma was identified elsewhere in this biopsy sample.

Conjunctiva

- The conjunctiva that covers the surface of the eye, bulbar conjunctiva, is a nonkeratinizing stratified squamous epithelium.
- The limbus, the intersection between the sclera and cornea, also marks the transition between conjunctival and corneal epithelium
- The conjunctiva lining the interior of the eyelid, the palpebral conjunctiva, is tightly tethered to the tarsus and may respond to inflammation by being thrown into minute papillary folds.
- Conjunctivitis (allergic and bacterial)

Lacrimal drainage



Source: Riordan-Eva P, Whitcher, JP: *Vaughan & Asbury's General Ophthalmology*, 17th Edition: http://www.accessmedicine.com

Fig. 1-24 Accessed 07/01/2010

Conjunctiva

- The conjunctiva in the fornix is a pseudostratified columnar epithelium rich in goblet cells.
- The fornix also contains accessory lacrimal tissue, and the ductules of the main lacrimal gland pierce through the conjunctiva in the fornix superiorly and laterally.
- Lymphoid follicles may be prominent in the fornix.
- Conjunctivitis (viral)
- Sarcoid
- Lymphoma

Conjunctiva

- Bilateral conjunctivitis is usually a manifestation of an allergic or autoimmune disorder.
- Unilateral conjunctivitis is a result of:
- Rhinovirus
- Adenovirus
- Hemophilus influenzae
- Staphylococcus aureus
- Neisseria gonorrheae
- Chalmydia trachomatis.

Conjunctiva

- Many cases of bacterial or viral conjunctivitis cause redness and itching, but most heal without sequelae.
- However, infection with Chlamydia trachomatis (trachoma) may produce significant conjunctival scarring.
- Conjunctival scarring is also seen after exposure of the ocular surface to caustic alkalis or as a sequel to ocular cicatricial pemphigoid or following surgery.
- Decrease in tear production as well as surface mucin

Conjunctiva

- Both pinguecula and pterygium appear as submucosal elevations on the conjunctiva.
- They result from actinic damage
- Located in the sun-exposed regions of the conjunctiva (in the interpalpebral fissure).
- Pterygium typically originates in the conjunctiva astride the limbus.
- It is formed by a submucosal growth of fibrovascular connective tissue that migrates onto the cornea, dissecting into the plane occupied normally by the Bowman layer.
- Pterygium does not cross the pupillary axis

Conjunctiva

- Pinguecula is a small, yellowish submucosal elevation.
- Does not invade the cornea
- The presence of a focal conjunctival elevation near the limbus can result in an uneven distribution of the tear film over the adjacent cornea.
- As a consequence of focal dehydration, a saucer-like depression in the corneal tissue (delle) may develop

Conjunctiva

- Squamous papillomas and conjunctival intraepithelial neoplasia
- Presence of HPV 16 and 18.
- Mucoepidermoid carcinoma
- Conjunctival nevi are encountered commonly but seldom invade the cornea or appear in the fornix or over the palpebral conjunctiva.
- An inflamed juvenile nevus is benign.
- Melanoma and are usually unilateral and are found in the fornix or over the palpebral conjunctiva.

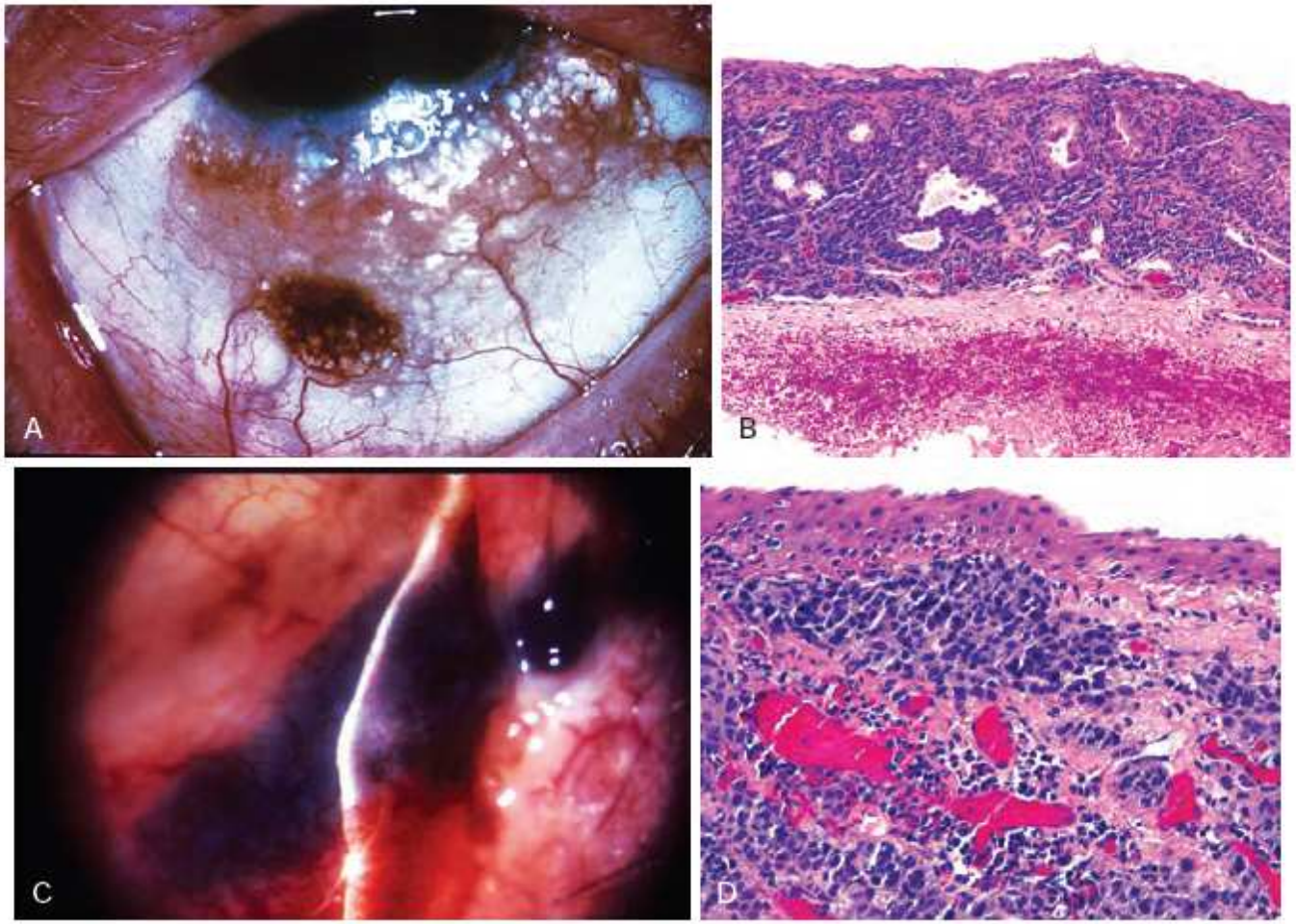


Figure 29-6 **A, B,** Cystic compound nevus of the conjunctiva. **C, D,** Conjunctival malignant melanoma. In **C**, note the deflection of the beam of the slit lamp over the surface of the lesion, indicative of invasion. (**A, B,** From Folberg R, et al: Benign conjunctival melanocytic lesions: clinicopathologic features. Ophthalmology 96:436, 1989.)

Sclera

- The sclera is continuous with the dura mater of the optic nerve.
- The sclera consist mainly of collagen and contain few blood vessels and fibroblasts.
- Immune complex deposits within the sclera, such as in rheumatoid arthritis, may produce a necrotizing scleritis.

Sclera

- Blue sclera are seen:
- Thinning following scleritis (optical Tyndall effect)
- Ectasia resulting from elevated intraocular pressure (staphyloma)
- Osteogenesis imperfecta
- Congenital melanosis oculi (nevus of uvea)
- Nevus of Ota also has periocular cutaneous pigmentation

Cornea

- The cornea and its overlying tear film make up the major refractive surface of the eye.
- Myopia typically develops because the eye is too long for its refractive power
- Hyperopia results from an eye that is too short.

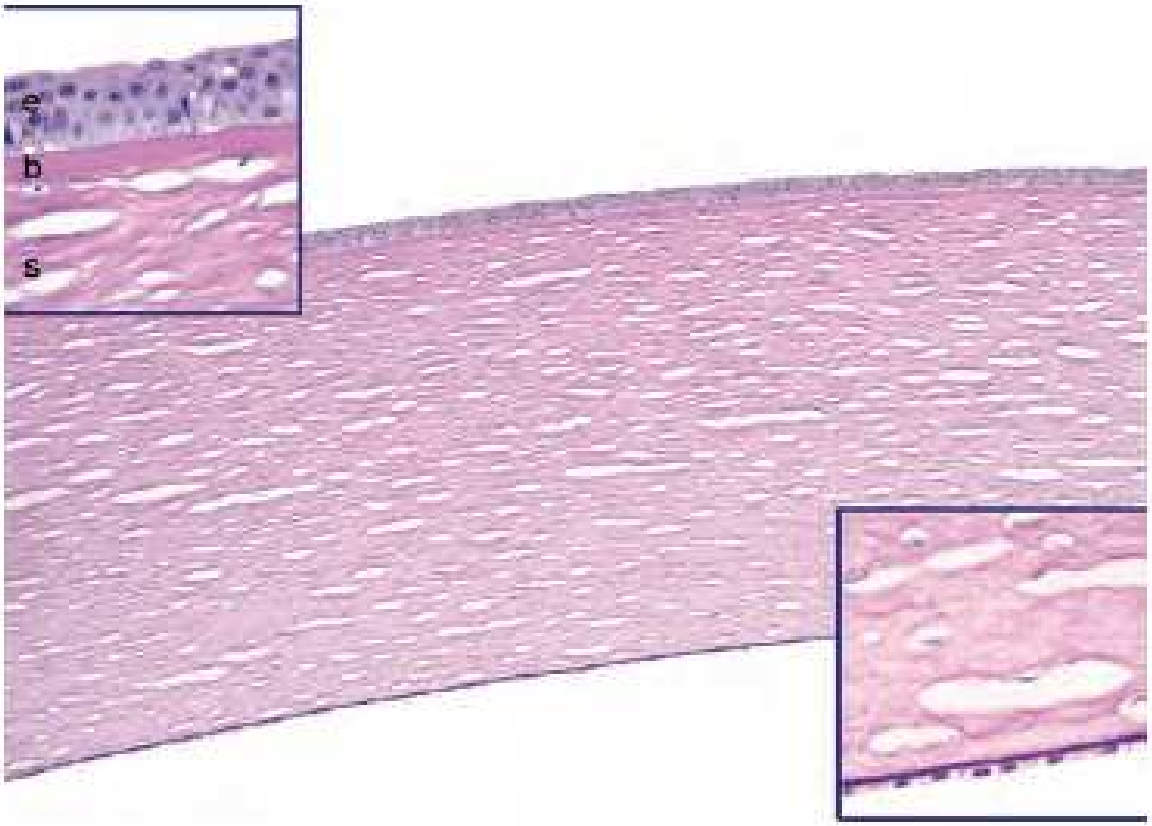


Figure 29-7 Normal corneal microarchitecture. The corneal tissue is stained by periodic acid–Schiff (PAS) to highlight basement membranes. The inset at the upper left is a high magnification of the anterior layers of the cornea: the epithelium *(e)*, Bowman layer *(b)*, and the stroma *(s)*. A very thin PAS-positive basement membrane separates the epithelium from the Bowman layer. Note that the Bowman layer is acellular. The *inset* at the *lower right* is a high magnification of the PAS-positive Descemet membrane and the corneal endothelium. The "holes" in the stroma are artifactitious spaces between parallel collagenous stromal lamellae.

Cornea

- In all forms of keratitis, dissolution of the corneal stroma may be accelerated by activation of collagenases within corneal epithelium and stromal fibroblasts (also known as keratocytes).
- Exudate and cells leaking from iris and ciliary body vessels into the anterior chamber may be visible by slit lamp examination and may accumulate in sufficient quantity to become visible even by a penlight examination (hypopyon).

Cornea

- Chronic herpes simplex keratitis may be associated with a granulomatous reaction involving the Descemet membrane.
- Varicella-zoster virus as well as the free-living amoeba, Acanthamoeba, may also cause keratitis.

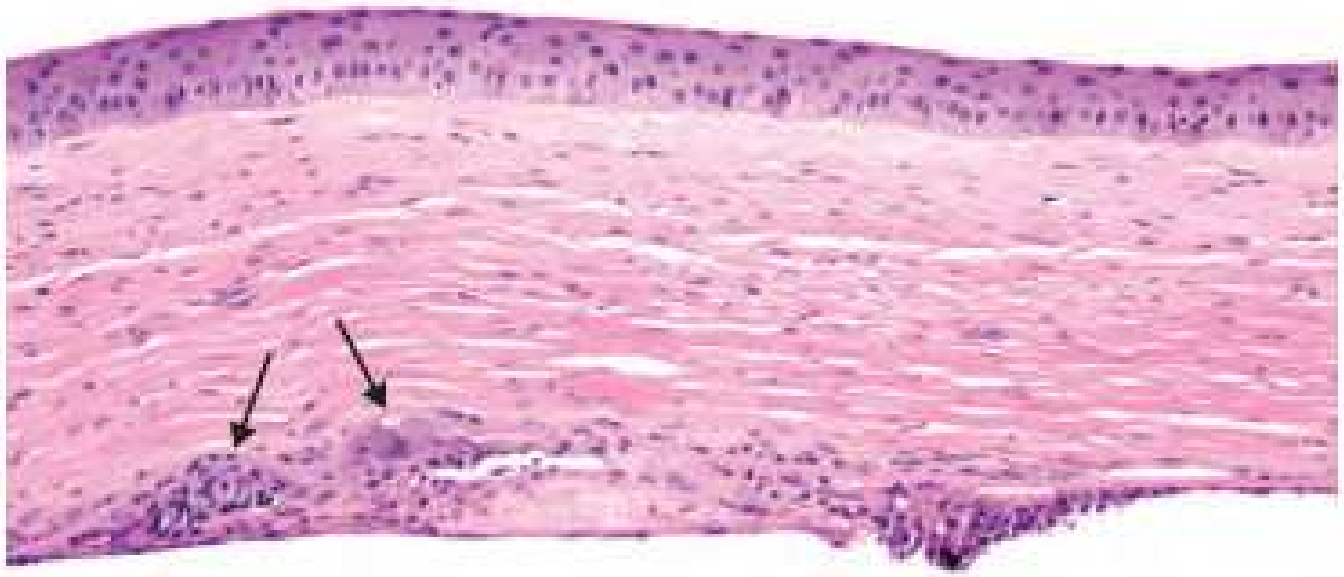


Figure 29-8 Chronic herpes simplex keratitis. The cornea is thin and scarred (note the increased number of fibroblast nuclei). Granulomatous reaction in the Descemet membrane, illustrated in this photomicrograph *(arrows)*, is a histologic hallmark of chronic herpes simplex keratitis.

Cornea

- Corneal dystrophies are typically bilateral and are hereditary.
- May affect selective corneal layers:
- Reis-Bückler dystrophy affects Bowman layer
- Posterior polymorphous dystrophy affects the endothelium
- The changes may be distributed throughout multiple layers.

Cornea

- Corneal degenerations are typically bilateral and are not hereditary.
- Calcific band keratopathy is characterized by deposition of calcium in the Bowman layer.
- May complicate chronic uveitis, especially in individuals with chronic juvenile rheumatoid arthritis

Cornea

- Actinic band keratopathy ("oil-droplet")
- Develops in individuals who are exposed chronically to high levels of ultraviolet light.
- Extensive solar elastosis develops in the superficial layers of corneal collagen in the sun-exposed interpalpebral fissure
- Horizontally distributed band of pathology
- Yellow

Cornea

- Keratoconus presents as irregular astigmatism and is difficult to correct.
- Microscopically there is corneal thinning with breaks in the Bowman layer.
- The Descemet membrane may rupture, permitting aqueous humor from the anterior chamber to reach the stroma (corneal hydrops).
- Rupture secondary to increased intraocular pressure in infantile glaucoma (Haab striae).
- May be associated with Marfan's and Down's syndromes

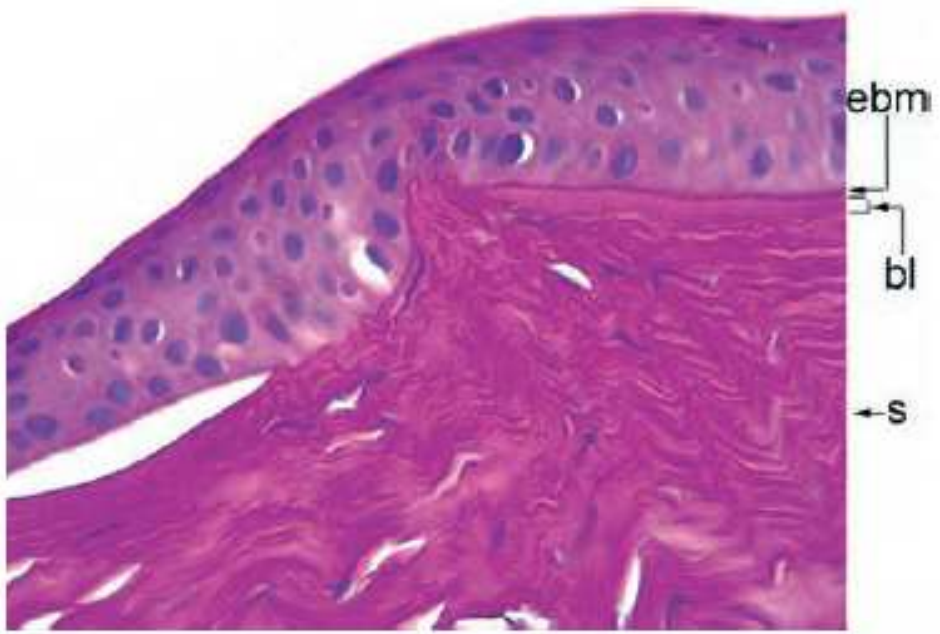


Figure 29-9 Keratoconus. The tissue section is stained by periodic acid–Schiff to highlight the epithelial basement membrane (ebm), which is intact, the Bowman layer (bl), situated between the epithelial basement membrane, and the stroma (s). Following the Bowman layer from the *right side* of the photomicrograph toward the *center*, there is a discontinuity, diagnostic of keratoconus. The epithelial separation just to the *left* of the Bowman layer discontinuity resulted from an episode of corneal hydrops, caused by a break in the Descemet membrane (not shown).

Cornea

- Fuch's endothelial dystrophy
- Stromal edema and bullous keratopathy characteristic.
- Initially, endothelial cells produce abnormal basement membrane material
- Drop-like deposits (guttata)
- With loss of endothelial cells, the stroma cannot be maintained fluid free
- Becomes edematous and thickens
- Ground glass appearance
- Vascularization may follow

Cornea

- Pseudophakic bullous keratopathy follows loss of endothelial cells following cataract surgery.
- Stromal dystrophies
- Deposits in the vicinity of the epithelium, its basement membrane, and Bowman layer may result in painful epithelial erosions and scarring.
- One such dystrophy, inherited as an autosomal dominant, is caused by mutations in the *TGFB1* gene which encodes an extracellular matrix protein (keratoepithelin).
- Some mutations cause improper folding of this protein which in turn causes depositions in the cornea.

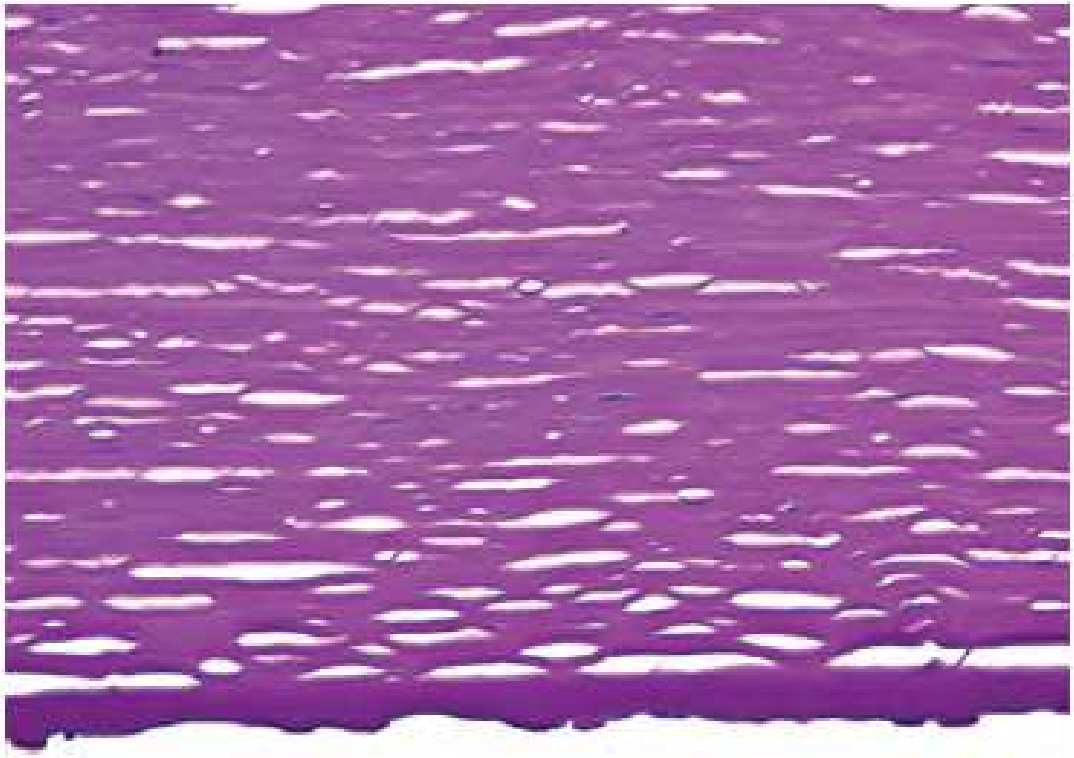
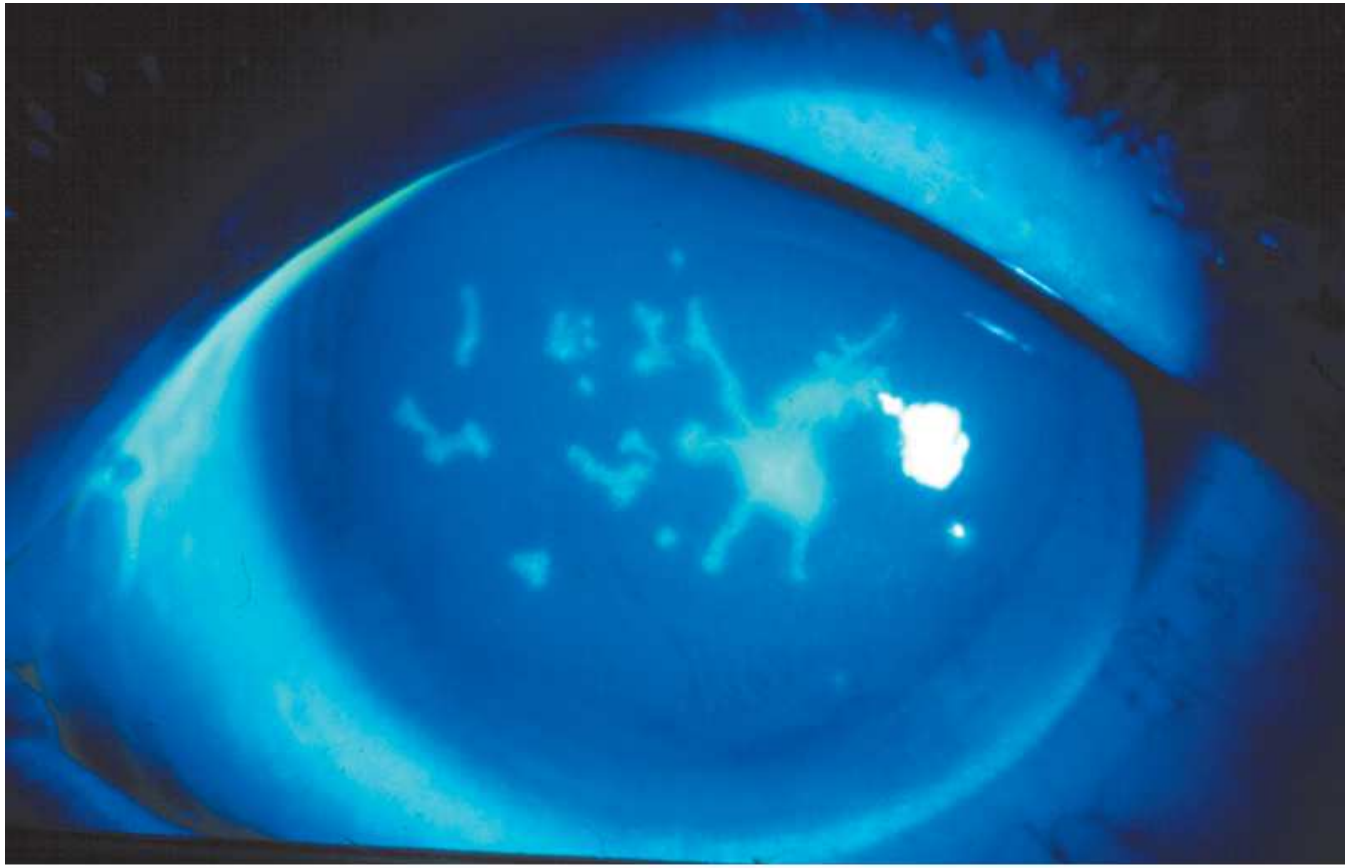
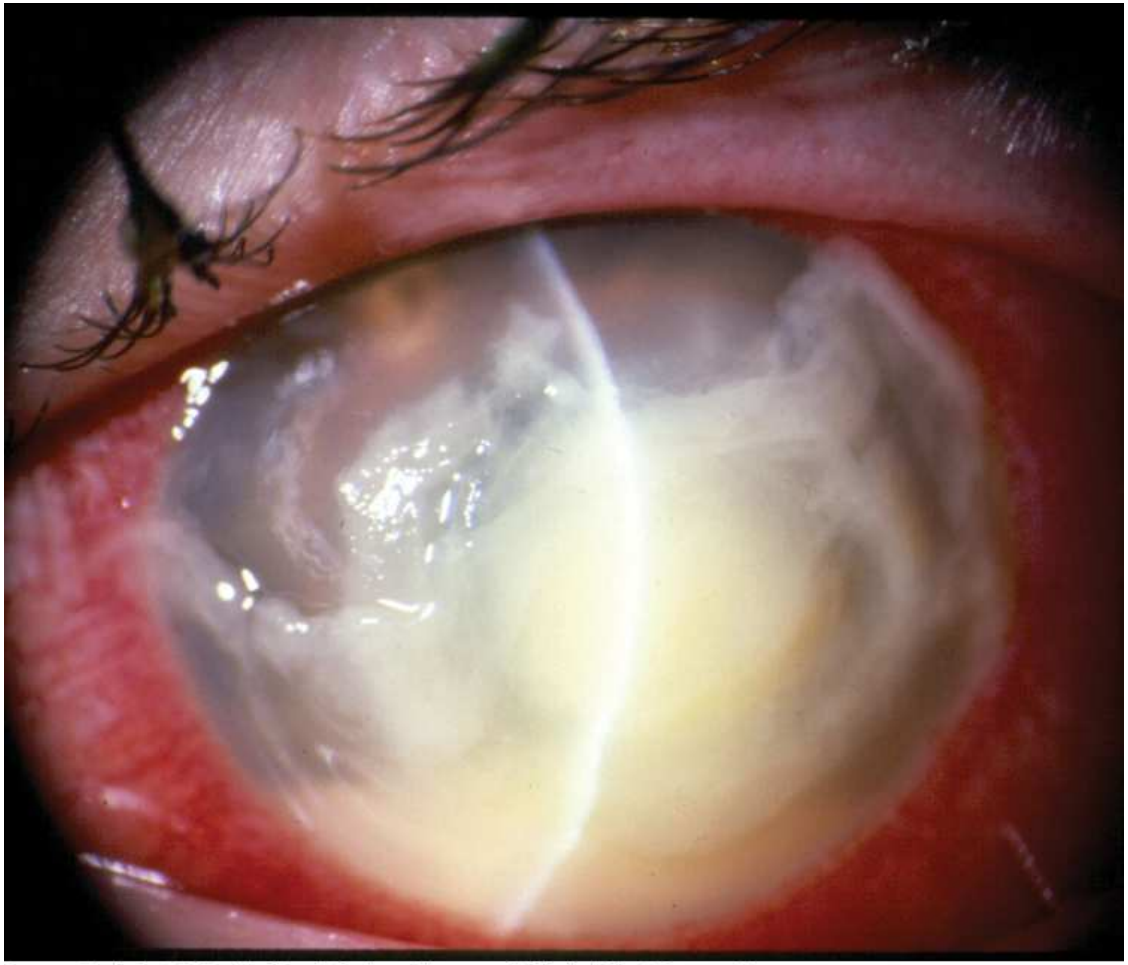


Figure 29-10 Fuchs dystrophy. This tissue section is stained by periodic acid–Schiff to highlight the Descemet membrane, which is thick. Numerous droplike excrescences—guttata—protrude downward from the Descemet membrane. Endothelial cell nuclei are not seen. Epithelial bullae, not shown in this micrograph, were present, reflecting corneal edema.



Herpes keratitis. Fluorescein stain shows the typical dendritic corneal lesions of herpes simplex. (Picture courtesy of Dr. William Driebe, University of Florida College of Medicine.)



Pseudomonas aeruginosa keratitis. Note the large hypopyon that accompanies the severe corneal opacification in this patient who used tap water to wash hard contact lenses. (Picture courtesy of Dr. William Driebe, University of Florida College of Medicine.)

Anterior chamber

- The anterior chamber is bounded anteriorly by the cornea, laterally by the trabecular meshwork, and posteriorly by the iris.
- Aqueous humor, formed by the pars plicata of the ciliary body, enters the posterior chamber, bathes the lens, and circulates through the pupil to gain access to the anterior chamber.
- The posterior chamber lies behind the iris and in front of the lens.

Lens

- The lens is a closed epithelial system
- Totally avascular
- Nourished by aqueous and vitreous humors
- The basement membrane of the lens epithelium (the lens capsule) totally envelops the lens.
- The lens epithelium does not exfoliate but accumulates with its derivative fibers within the confines of the lens capsule, thus “infoliating.”
- With aging, therefore, the size of the lens increases.

Lens

- Lens is transparent.
- Plasma membranes impermeable even to small ions (necessary to maintain transparency).
- Normal state is thickened (for near vision).
- Suspensory (or zonule) fibers hold the lens in a falttened state.
- Contraction of pupillary muscle reduces tension on the zonule fibers.
- The lens thickens; the pupil constricts. (Accommodation).

Lens

- Cataract describes lenticular opacities that may be congenital or acquired.
- Age-related cataract typically results from opacification of the lens nucleus (nuclear sclerosis) and the accumulation of urochrome pigment.
- Pigment distorts perception of blue colors
- Migration of the lens epithelium posterior to the lens equator may result in posterior subcapsular cataract secondary to enlargement of abnormally positioned lens epithelium.

Lens

- The lens cortex may liquefy (hypermature or Morgagnian cataract).
- Phacolytic protein may clog trabecular meshwork and lead to secondary open angle glaucoma.

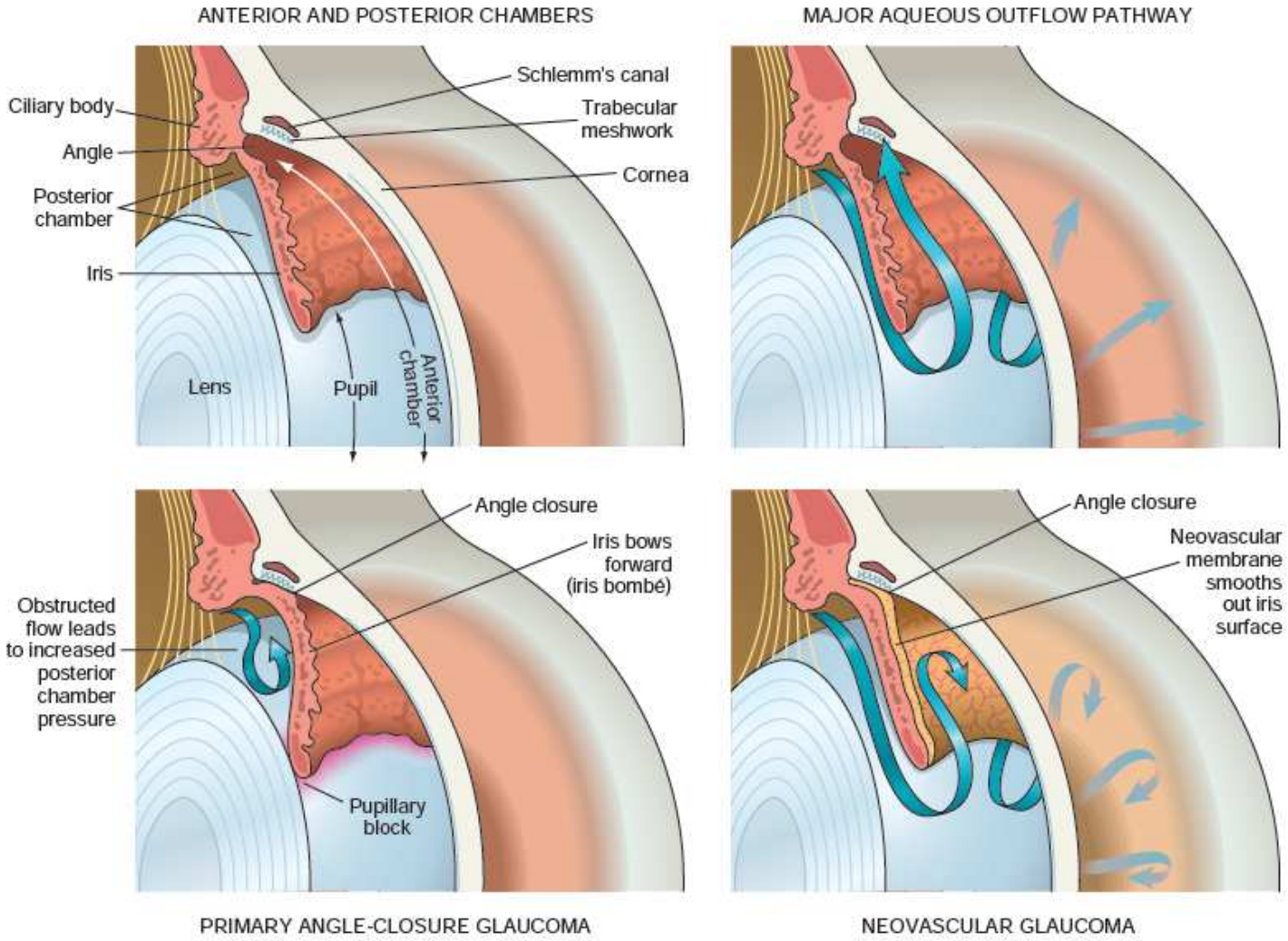


Figure 29-11 *Upper left*, The normal eye. Note that the surface of the iris is highly textured with crypts and folds. *Upper right*, The normal flow of aqueous humor. Aqueous humor, produced in the posterior chamber, flows through the pupil into the anterior chamber. The major pathway for the egress of aqueous humor is through the trabecular meshwork, into the Schlemm canal. Minor outflow pathways (uveoscleral and iris, not depicted) contribute to a limited extent to aqueous outflow. *Lower left*, Primary angle-closure glaucoma. In anatomically predisposed eyes, transient apposition of the iris at the pupillary margin to the lens blocks the passage of aqueous humor from the posterior chamber to the anterior chamber. Pressure builds in the posterior chamber, bowing the iris forward (iris bombé) and occluding the trabecular meshwork. *Lower right*, A neovascular membrane has grown over the surface of the iris, smoothing the iris folds and crypts. Myofibroblasts within the neovascular membrane cause the membrane to contract and to become apposed to the trabecular meshwork (peripheral anterior synechiae). Outflow of aqueous humor is blocked, and the intraocular pressure becomes elevated.

Glaucoma

- Aqueous humor is produced by the ciliary processes of the eye.
- Drains through the trabecular meshwork.
- Aqueous humor flows from the ciliary processes into the posterior chamber.
- The posterior chamber is bounded posteriorly by the lens and the zonules of Zinn, and anteriorly by the iris.
- From the posterior chamber it flows through the pupil of the iris into the anterior chamber.
- (The anterior chamber is bounded posteriorly by the iris and anteriorly by the cornea.)

Glaucoma

- Refers to a collection of diseases characterized by distinctive changes in the visual field and in the cup of the optic nerve secondary to increased intraocular pressure.
- Some individuals with normal intraocular pressure may develop characteristic optic nerve and visual field changes (normal or low-tension glaucoma).
- In open-angle glaucoma the aqueous humor has complete physical access to the trabecular meshwork, and the elevation in intraocular pressure results from an increased resistance to aqueous outflow in the open angle.

Glaucoma

- Primary open-angle glaucoma.
- Mutations in the myocilin (MYOC) gene
- Juvenile and adult
- Mutations in optineurin (OPTN)
- Adult

Glaucoma

- Secondary open-angle glaucoma
- Pseudoexfoliation glaucoma
- LOX1 gene mutation (lysyl oxidase)
- Phacolysis
- Senescent red cells after trauma (ghost cell glaucoma)
- Iris epithelial pigment granules (pigmentary glaucoma)
- Necrotic tumors (melanomalytic glaucoma)
- Sturge-Weber
- Increased episcleral venous pressure

Glaucoma

- In angle-closure glaucoma the peripheral zone of the iris adheres to the trabecular meshwork and physically impedes the egress of aqueous humor from the eye.
- Primary angle-closure glaucoma typically develops in eyes with shallow anterior chambers, often found in individuals with hyperopia.
- Transient apposition of the pupillary margin of the iris to the anterior surface of the lens may result in obstruction to the flow of aqueous humor through the pupillary aperture (pupillary block).

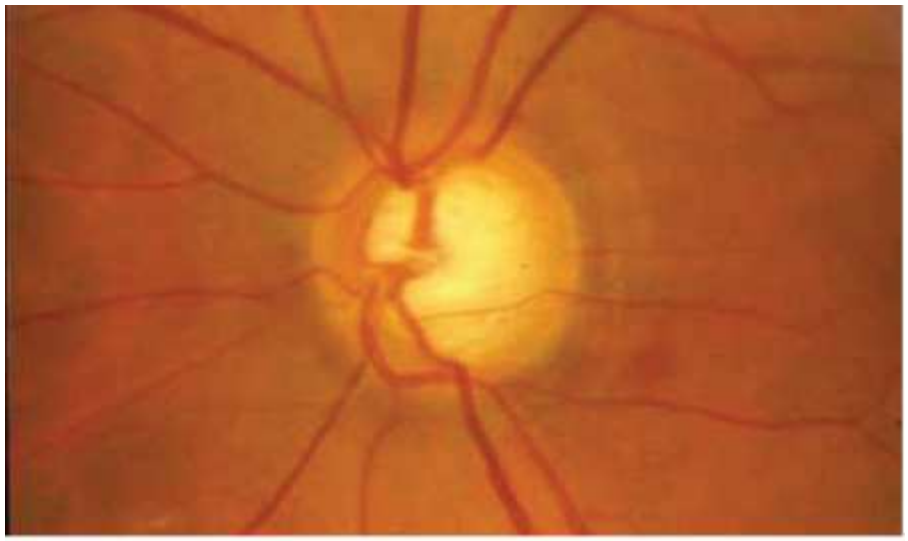
Glaucoma

- Continued production of aqueous humor by the ciliary body thus elevates pressure in the posterior chamber and may bow the iris periphery forward (iris bombé), apposing it to the trabecular meshwork.
- Unremitting elevation in intraocular pressure in primary angle-closure glaucoma can damage the lens epithelium.
- This leads to minute anterior subcapsular opacities that are visible by slit-lamp examination (glaukomflecken)

Glaucoma

- Secondary angle-closure glaucoma
- Neovascular glaucoma
- With chronic retinal ischemia, there is upregulation of VEGF and other proangiogenic factors.
- The appearance of VEGF in the aqueous humor is thought to induce the development of thin, clinically transparent fibrovascular membranes over the surface of the iris.
- Contraction of myofibroblastic elements in these membranes leads to occlusion of the trabecular meshwork by the iris

Glaucoma



The basic visual field loss is a nerve fiber bundle defect (baring the blind spot) with nasal step and peripheral nasal depression. Note the optic cupping.

Glaucoma

- A subset of patients have normal tension glaucoma.
- There is a diffuse loss of ganglion cells and thinning of the retinal nerve fiber layer.
- In advanced cases, the optic nerve is both cupped and atrophic, a combination unique to glaucoma.
- Elevated intraocular pressure in infants and children can lead to diffuse enlargement of the eye (buphthalmos) or enlargement of the cornea (megalocornea).
- After the eye reaches its adult size, prolonged elevation of intraocular pressure can lead to focal thinning of the sclera, and uveal tissue may line ectatic sclera (staphyloma).

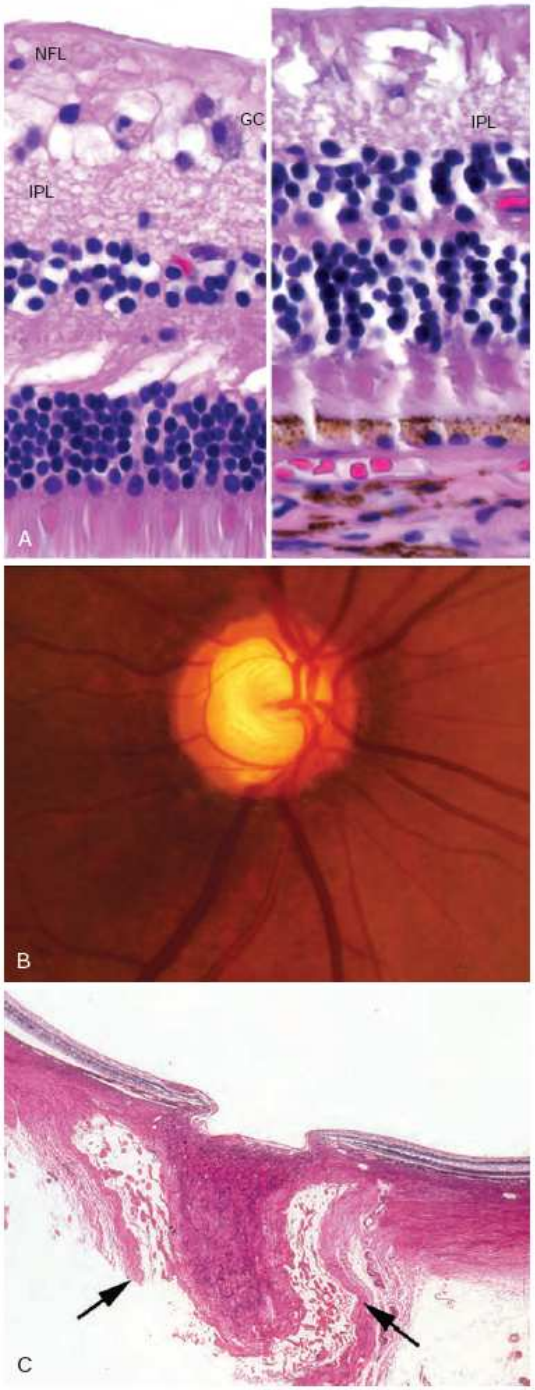


Figure 29-26 The retina and optic nerve in glaucoma. **A,** *Left panel*, normal retina; *right panel*, the retina in long-standing glaucoma (same magnification). The full thickness of the glaucomatous retina is captured *(right)*, a reflection of the thinning of the retina in glaucoma. In the glaucomatous retina, the areas corresponding to the nerve fiber layer (NFL) and ganglion cell layer (GC) are atrophic; the inner plexiform layer (IPL) is labeled for reference. Note also that the outer nuclear layer of the glaucomatous retina is aligned with the inner nuclear layer of the normal retina due to the thinning of the retina in glaucoma. See Figure 29-16 for orientation. **B,** Glaucomatous optic nerve cupping results in part from loss of retinal ganglion cells, the axons of which populate the optic nerve. **C,** The *arrows* point to the dura of the optic nerve. Notice the wide subdural space, a result of atrophy of the optic nerve. There is a striking degree of cupping on the surface of the nerve as a consequence of long-standing glaucoma.

Glaucoma therapy

- From the anterior chamber, the fluid into Schlemm's canal and into scleral venous plexuses.
- Prostaglandin analogs increase uveo-scleral flow of aqueous humor.
- Some also increase trabecular outflow.
- β-blockers diminish aqueous humor production by ciliary body.
- α-blockers diminish aqueous humor production and diminish trabecular outflow.
- Sympathomimetics increase outflow

Glaucoma therapy

- Parasympathomimetics pilocarpine) contract the ciliary muscle, tighten trabecular mesh network, and lead to greater outflow.
- Carbonic anhydrase inhibitors diminish aqueous humor secretion in the ciliary body.
- Laser iridotomy or trabeculectomy employed to remove syndechiae between iris and trabecular mesh network.
- Goal is to lower intra-ocular pressure below 20 mmHg to preserve optic nerve.

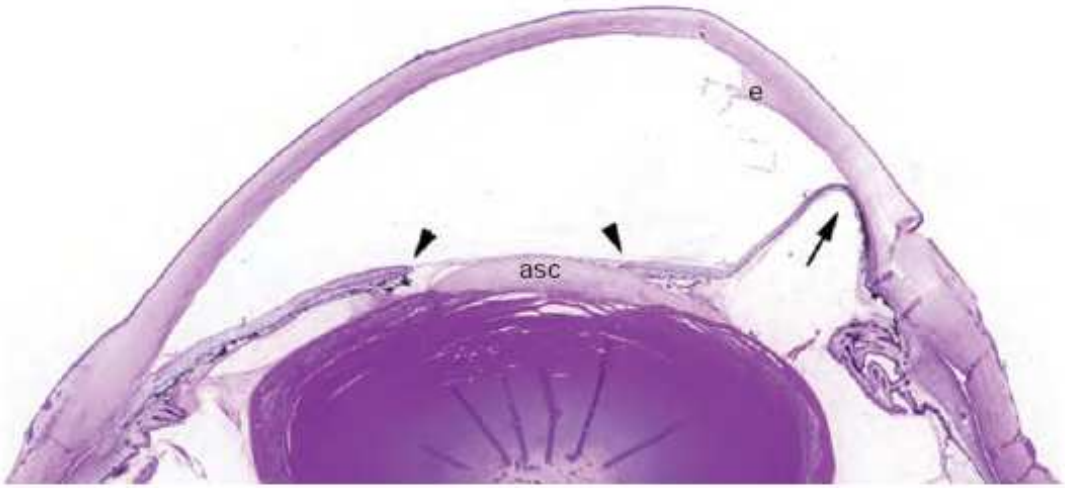


Figure 29-12 Sequelae of anterior segment inflammation. This eye was removed for complications of chronic corneal inflammation (not visible at this magnification). The exudate (e) present in the anterior chamber would have been visualized with a slit lamp as an optical "flare." The iris is adherent focally to the cornea, obstructing the trabecular meshwork (anterior synechia, *arrow*), and to the lens (posterior synechiae, *arrowheads*). An anterior subcapsular cataract (asc) has formed. The radial folds in the lens are artifacts.

Intraocular inflammation

- Vessels in the ciliary body and iris become leaky, allowing cells and exudate to accumulate in the anterior chamber.
- At times the inflammatory cells may adhere to the corneal endothelium, forming clinically visible keratic precipitates.
- Aggregates of macrophages on the endothelium in sarcoid produce characteristic “mutton fat” keratic precipitates.
- The presence of exudate in the anterior chamber can facilitate the formation of adhesions.

Intraocular inflammation

- Anterior synechiae form between the iris and the trabecular meshwork or cornea.
- Prolonged contact between the iris and the anterior surface of the lens can deprive lens epithelium of contact with aqueous humor and can induce fibrous metaplasia of the lens epithelium (anterior subcapsular cataract)
- Posterior synechiae form between the iris and anterior surface of the lens.

Intraocular inflammation

- Endophthalmitis is inflammation within the vitreous humor.
- The retina lines the vitreous cavity, and suppurative inflammation in the vitreous humor is poorly tolerated by the retina
- A few hours may be sufficient to cause irreversible retinal injury.
- Exogenous (trauma) or endogenous (hematogenous) origin
- Panophthalmitis is inflammation within the eye that involves the retina, choroid, and sclera and extends into the orbit

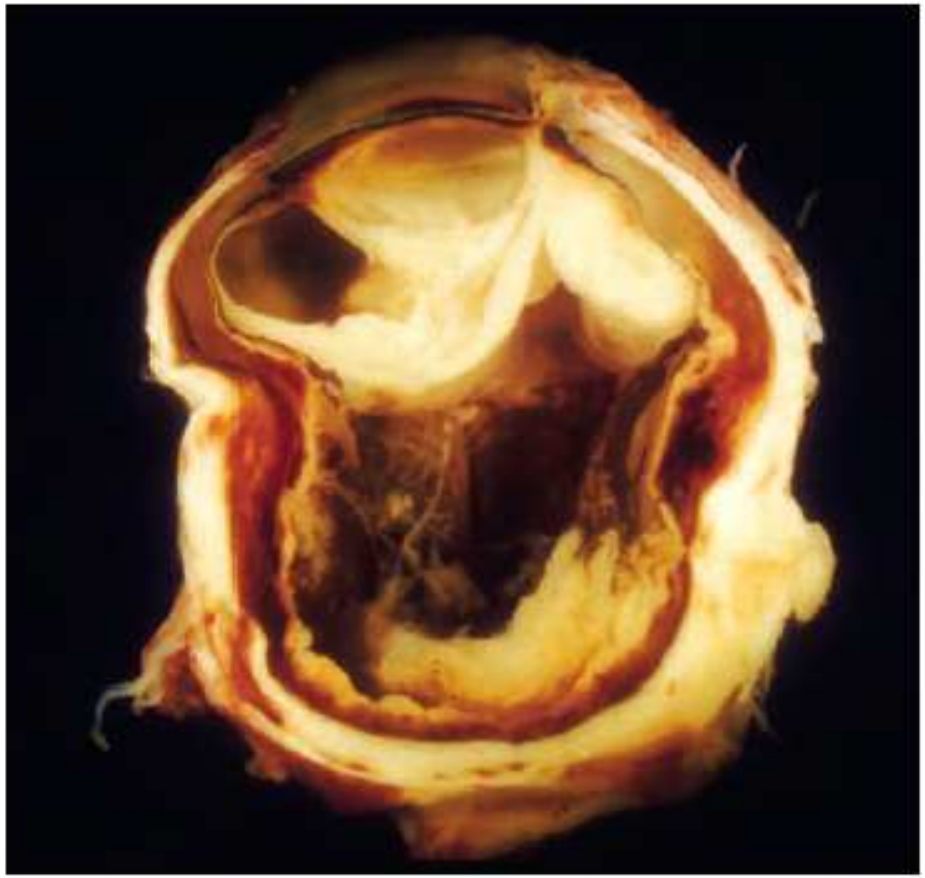


Figure 29-13 Exogenous panophthalmitis. This eye was removed after a foreign body injury. Note the suppurative inflammation behind the lens that is drawn up to the right of the lens to the cornea, the site of the wound. The central portion of the vitreous humor was extracted surgically (by vitrectomy). Note the adhesions to the surface of the eye at the 8 o'clock position, indicating that the intraocular inflammation has spread through the sclera into the orbit: panophthalmitis. (From Folberg R: The eye. In Spencer WH (ed): Ophthalmic Pathology—An Atlas and Textbook, 4th ed. Philadelphia, WB Saunders, 1985.)

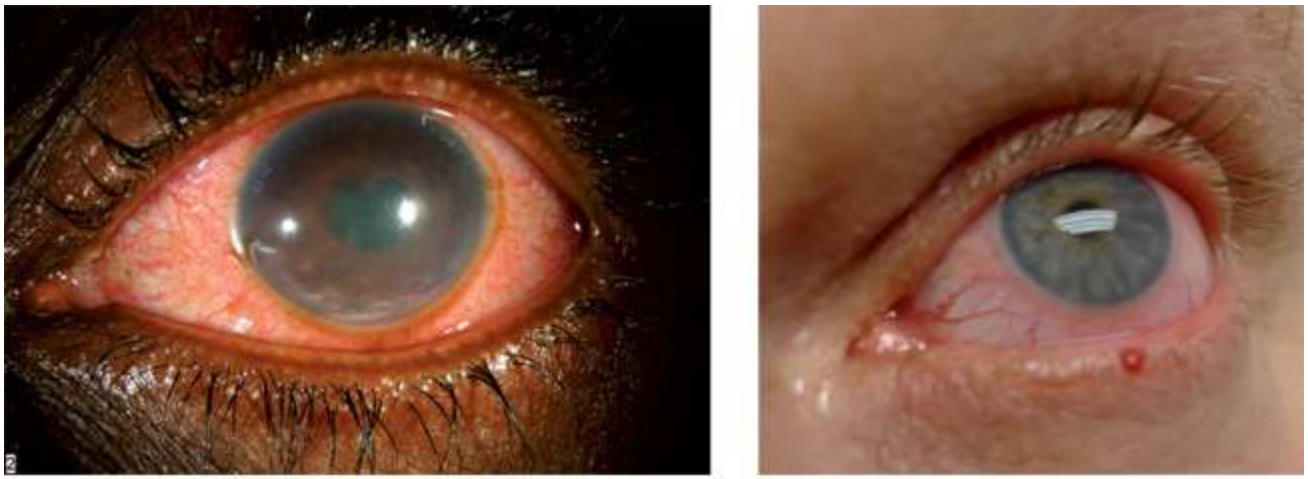
Uvea

- Uveitis is most commonly idiopathic.
- Trauma, infection (including parasites), allergy, sarcoidosis, and autoimmune conditions must be considered.
- Anterior uveitis is usually unilateral and acute in onset.
- Juvenile rheumatoid arthritis as an example
- Typical symptoms include pain, photophobia, and blurred vision.
- Circumcorneal redness with minimal palpebral conjunctival injection or discharge.
- The pupil may be small or irregular due to the formation of posterior synechiae.

Uveitis

- Keratic precipitates are usually evident on the corneal endothelium in patients with active inflammation.
- Keratic precipitates are usually located inferiorly in a wedge-shaped region (Arlt's triangle).
- May also be localized to an area of prior or active keratitis
- Herpes simplex infection commonly
- May lead to increased intraocular pressure.

Uveitis



Left: The episcleral vessels are dilated, the corneal endothelium is covered with inflammatory precipitates, and the iris is indistinct due to the anterior chamber cellular reaction. There is a mixed hypopyon and hyphema within the inferior anterior chamber. The pupil has scarred in places to the lens by posterior synechiae, which causes the irregular appearance of the pupil. Right: Note the ciliary flush.

Plate 13 Accessed 07/01/2010

Uveitis

- Iris nodules may be present at the iris margin (Koeppe nodules), within the iris stroma (Busacca nodules), or in the anterior chamber angle (Berlin's nodules).
- Atrophy of the iris can occur in the setting of herpes simplex or herpes zoster virus infection
- Decreased sensation occurs in herpes simplex or herpes zoster infection or leprosy.
- Keratic precipitates or iris nodules, may indicate an infectious cause of uveitis
- Usually sarcoidosis, sympathetic ophthalmia, or lens-induced uveitis.

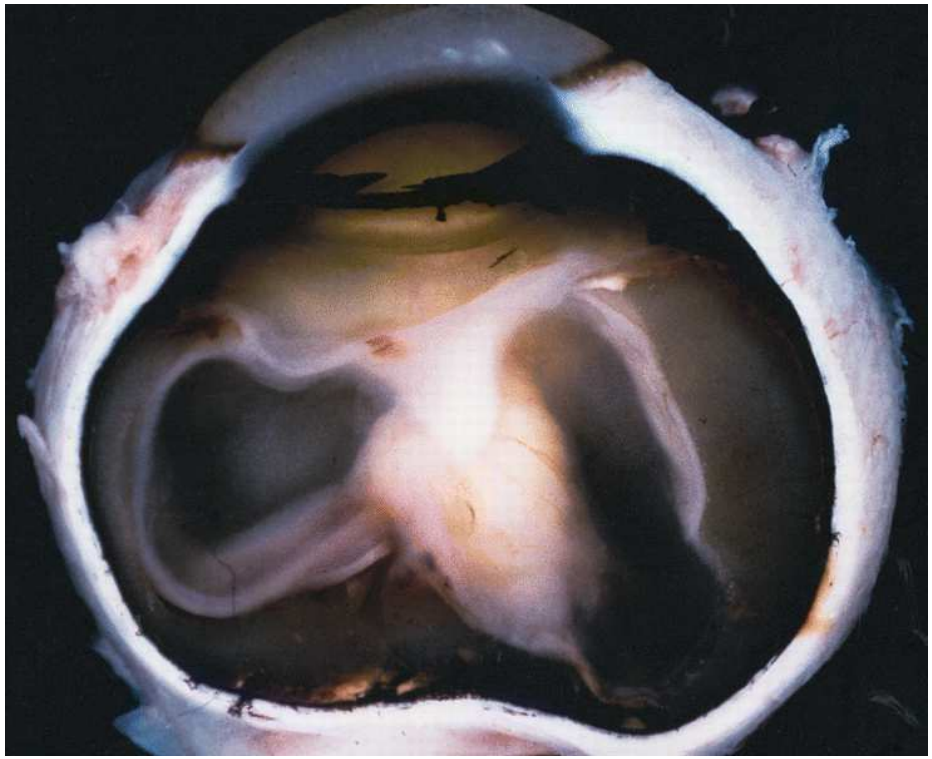
Uveitis

- Granulomatous uveitis is a common complication of sarcoidosis.
- In the anterior segment it gives rise to an exudate that evolves into “mutton-fat” keratic precipitates.
- In the posterior segment, sarcoid may involve the choroid and retina.
- Thus, granulomas may be seen in the choroid.
- Retinal pathology is characterized by perivascular inflammation
- Ophthalmoscopic sign of “candle wax drippings.

Uveitis

- Retinal toxoplasmosis is usually accompanied by uveitis and even scleritis.
- Individuals with AIDS may develop cytomegalovirus retinitis and uveal infection such as Pneumocystis or mycobacterial choroiditis.
- In agricultural communities in more humid parts of the developing world, leptospirosis is common.
- Toxocara canis may lead to endophthalmitis.

Toxocara canis endophthalmitis

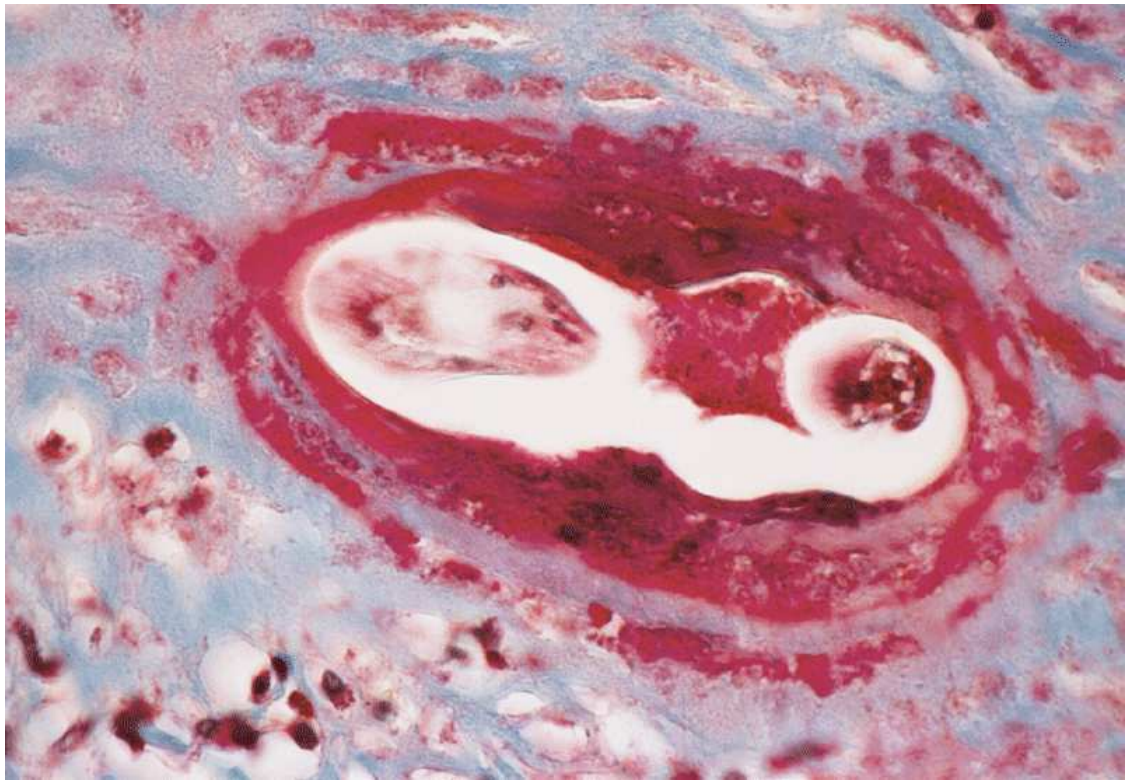


Whitish sclerotic vitreous mass causing traction total retinal detachment.

Fig. PL-05A

McLean, IW, Burnier, MN, Zimmerman, LE, Jakobiec, FA. , “Tumors of the eye and ocular adnexa.” Atlas of Tumor Pathology,.Third Series, Fascicle 12. Armed Forces Institute of Pathology, Washington, D.C. 1994.

Toxocara canis endophthalmitis



Higher power magnification of vitreous mass in plate V showing a larva surrounded by acidophilic material (Splendore-Hoeppli phenomenon) and scattered eosinophils.

Fig. PL-06A

McLean, IW, Burnier, MN, Zimmerman, LE, Jakobiec, FA. , “Tumors of the eye and ocular adnexa.” Atlas of Tumor Pathology,.Third Series, Fascicle 12. Armed Forces Institute of Pathology, Washington, D.C. 1994.

Uveitis

- Particularly severe anterior chamber inflammation may result in layering of inflammatory cells in the inferior angle (hypopyon).
- In North America and Europe the usual cause is HLA-B27–associated uveitis (ankylosing spondylitis).
- In Asia, Behçet's disease is common.

Uveitis

- The hallmark of intermediate uveitis is vitreous inflammation.
- Late teens or early adult years.
- Men are affected more than are women.
- Floaters and blurred vision are common.
- Pain, photophobia, and redness are usually absent or minimal.
- Mild anterior chamber inflammation may be present.

Uveitis

- Sarcoidosis and multiple sclerosis account for 10–20% of cases
- Syphilis and tuberculosis should be excluded in all patients.

Uveitis

- The most common complications include:
- Macular edema
- Retinal vasculitis
- Neovascularization of the optic disk.
- Symptoms of posterior uveitis typically include:
- Floaters
- Loss of visual field or scotomas
- Decreased vision
- Retinal detachment occurs infrequently.

Uveitis

- Sympathetic ophthalmia is an example of noninfectious uveitis limited to the eye.
- May follow trauma
- Characterized by bilateral diffuse granulomatous inflammation typically affecting all components of the uvea (panuveitis).
- Eosinophils in infiltrate
- Few plasma cells
- Retinal antigens sequestered from the immune system may gain access to lymphatics in the conjunctiva and thus set up a delayed hypersensitivity reaction that affects both eyes

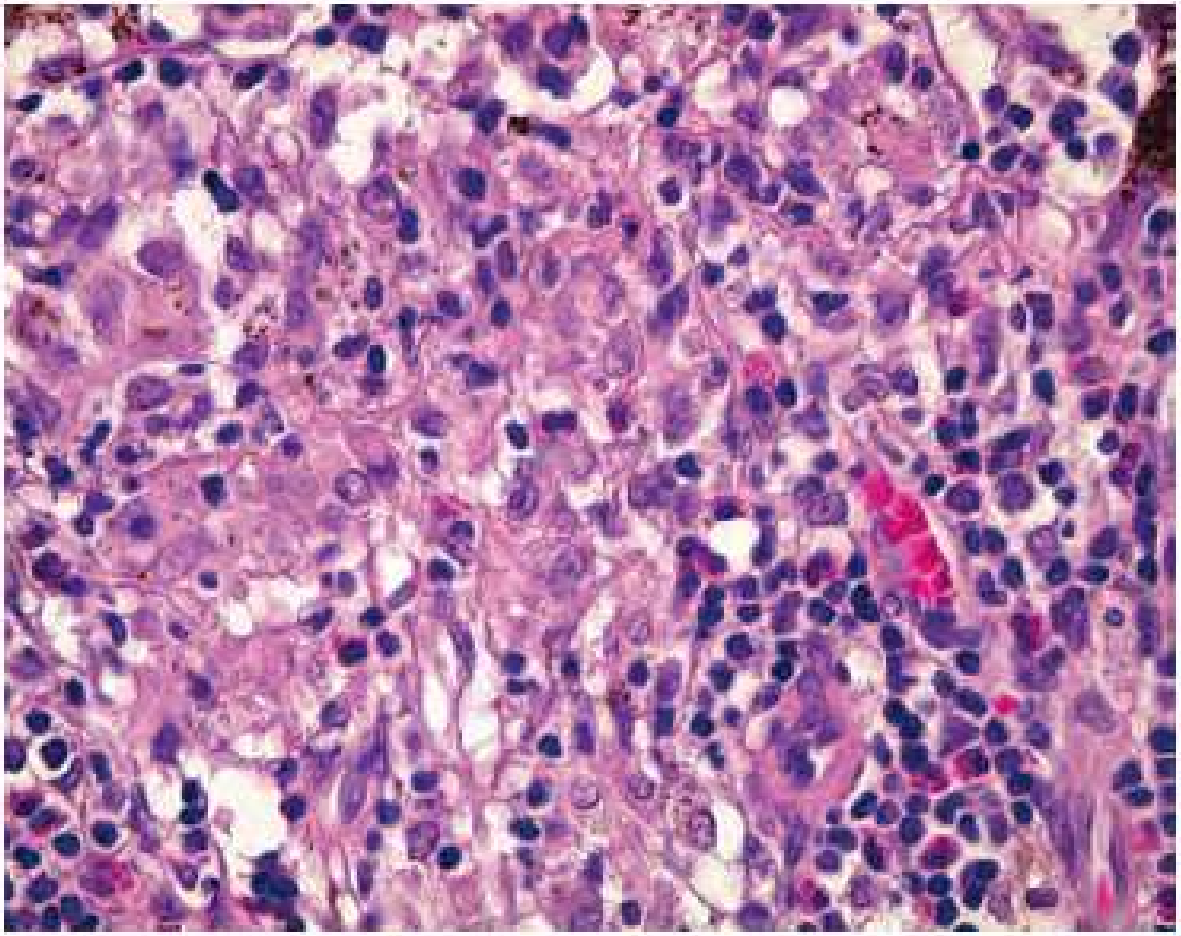


Figure 29-14 Sympathetic ophthalmia. The granulomatous inflammation depicted here was identified diffusely throughout the uvea. The uveal granulomas may contain melanin pigment and may be accompanied by eosinophils.

Intra-ocular melanoma

- 10% of European population have uveal nevi.
- Rarely progress to melanoma.
- Peak incidence in 7th decade.
- May arise in anterior (iris) or posterior (ciliary body or choroid) uveal tract.
- Hematogenous spread (no lymphatics in uvea).
- Liver prime metastatic site.
- 85% have GNAQ or GNA11 gain of function mutations
- Encode G-protein coupled receptors.
- Loss of BAP1 for progression to melanoma

Intraocular melanoma

- Two types of cells noted:
- Spindle cells are fusiform in shape
- Epithelioid cells are spherical and have greater cytologic atypia.
- Large numbers of tumor-infiltrating lymphocytesmay be seen in some cases.
- Commonly seen is the presence of looping slit-like spaces lined by laminin that surround packets of tumor cells.
- These spaces (which are not blood vessels) connect to blood vessels and serve as extravascular conduits for the transport of plasma and possibly blood. (vasculogenic mimicry)

Intra-ocular melanoma

- Iris melanoma (best prognosis)
- Ciliary body melanoma (worst prognosis)
- May be treated with plaque brachytherapy (^{125}I) or charged particle (protons, α-particles) therapy in an attempt to avoid enucleation.
- Large tumors are enucleated.

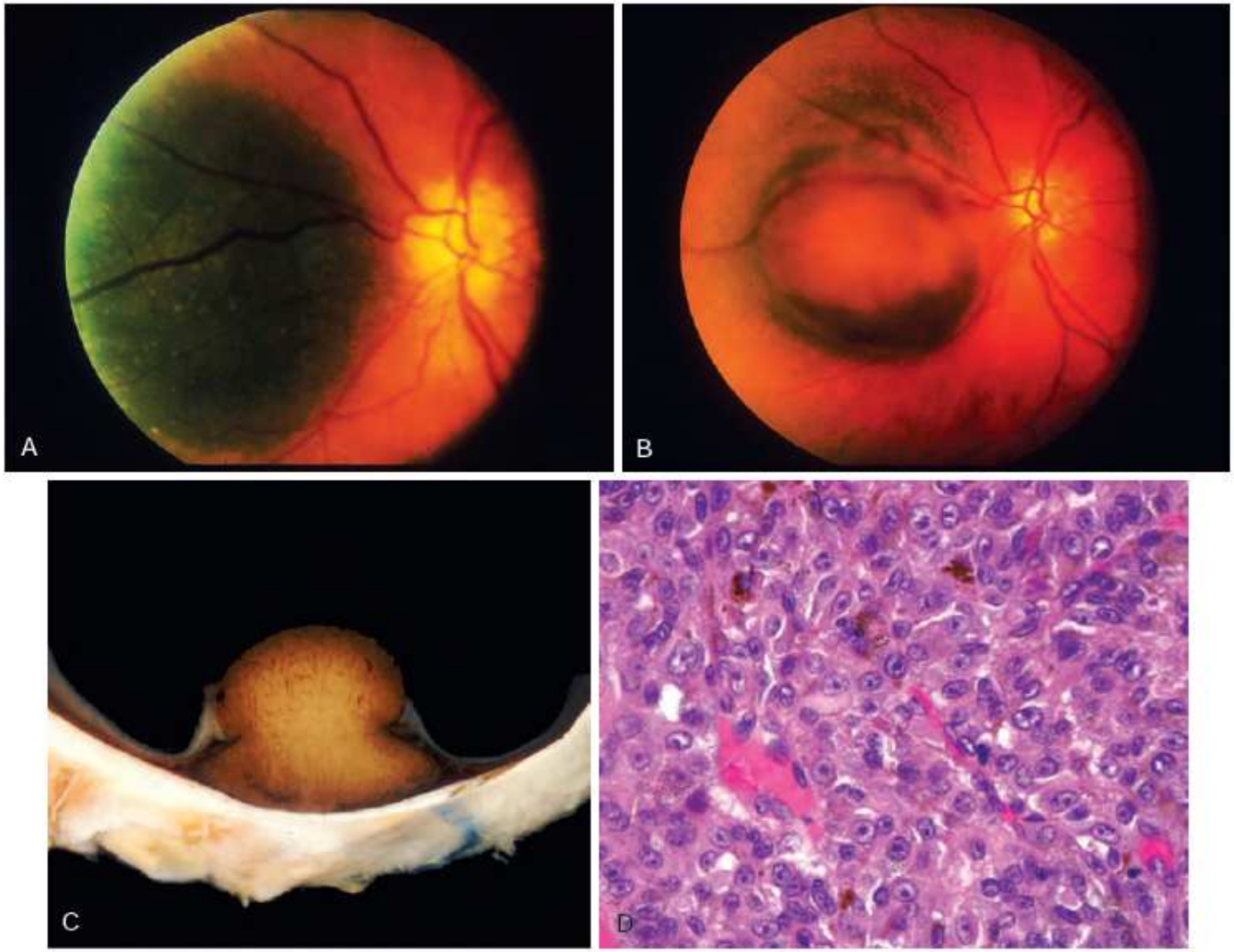
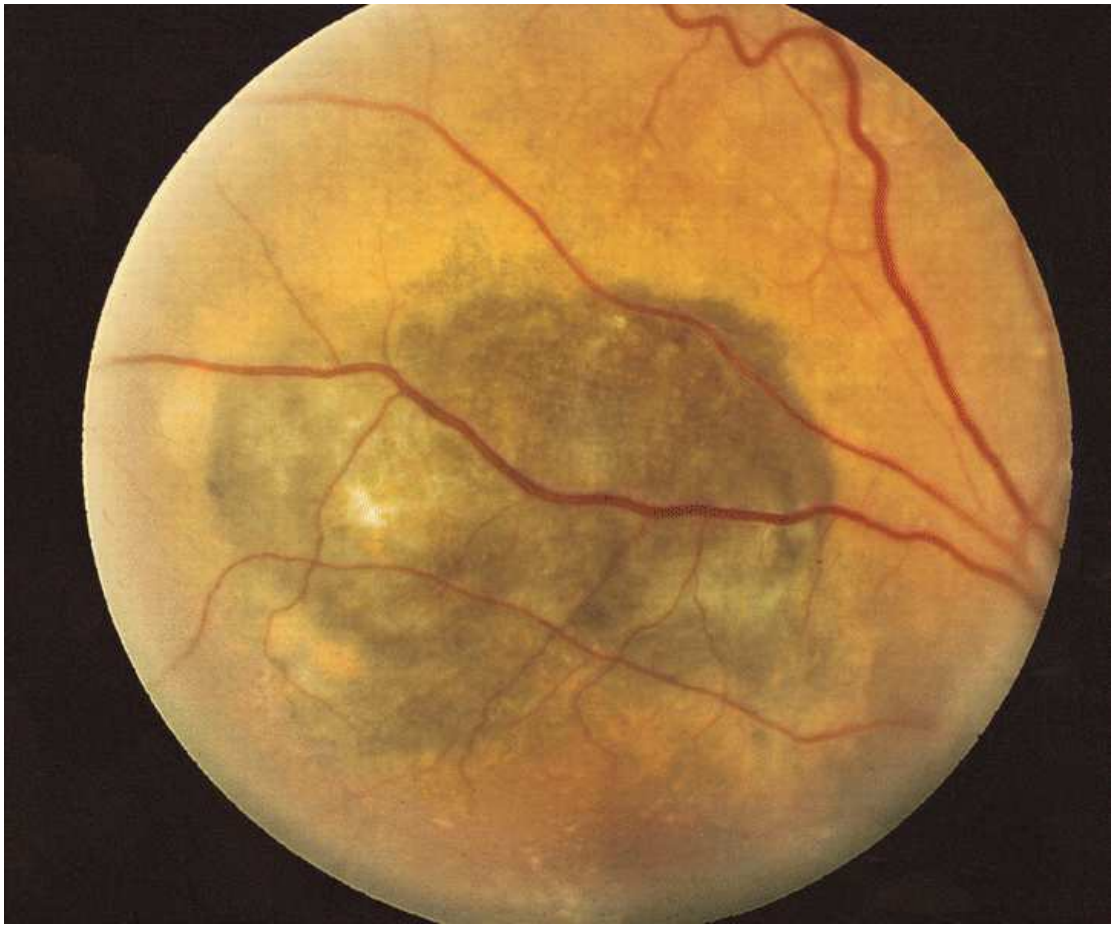


Figure 29-15 Uveal melanoma. **A,** Fundus photograph from an individual with a relatively flat pigmented lesion of the choroid near the optic disc. **B,** Fundus photograph of the same individual several years later; the tumor has grown and has ruptured through the Bruch membrane. **C,** Gross photograph of a choroidal melanoma that has ruptured the Bruch membrane. The overlying retina is detached. **D,** Epithelioid melanoma cells associated with an adverse outcome. (**A** to **C,** From Folberg R: Pathology of the Eye—an Interactive CD-ROM Program. Philadelphia, Mosby, 1996.)

Malignant melanoma



Pigmented choroidal lesion noted. Irregular borders.

Fig. PL-10A

McLean, IW, Burnier, MN, Zimmerman, LE, Jakobiec, FA. , “Tumors of the eye and ocular adnexa.” Atlas of Tumor Pathology,.Third Series, Fascicle 12. Armed Forces Institute of Pathology, Washington, D.C. 1994.

Retina

- The neurosensory retina, like the optic nerve, is an embryologic derivative of the diencephalon. The retina therefore responds to injury by means of gliosis.
- As in the brain, there are no lymphatics.
- Hemorrhages in the nerve fiber layer of the retina are oriented horizontally and appear as streaks or “flames”
- The external retinal layers are oriented perpendicular to the retinal surface, and hemorrhages in these outer layers appear as dots (the tips of cylinders).

Retina

- Exudates tend to accumulate in the outer plexiform layer of the retina, especially in the macula
- Separation of the neurosensory retina from the retinal pigment epitelium defines a retinal detachment
- Rhegmatogenous retinal detachment is associated with a full thickness retinal defect.
- May be complicated by proliferative vitreoretinopathy, the formation of epiretinal or subretinal membranes by retinal glial cells (Müller cells) or retinal pigment epithelium cells.

Retina

- Non-rhegmatogenous retinal detachment does not involve a retinal break
- May complicate retinal vascular disorders associated with significant exudation
- Malignant hypertension
- Choroidal tumors

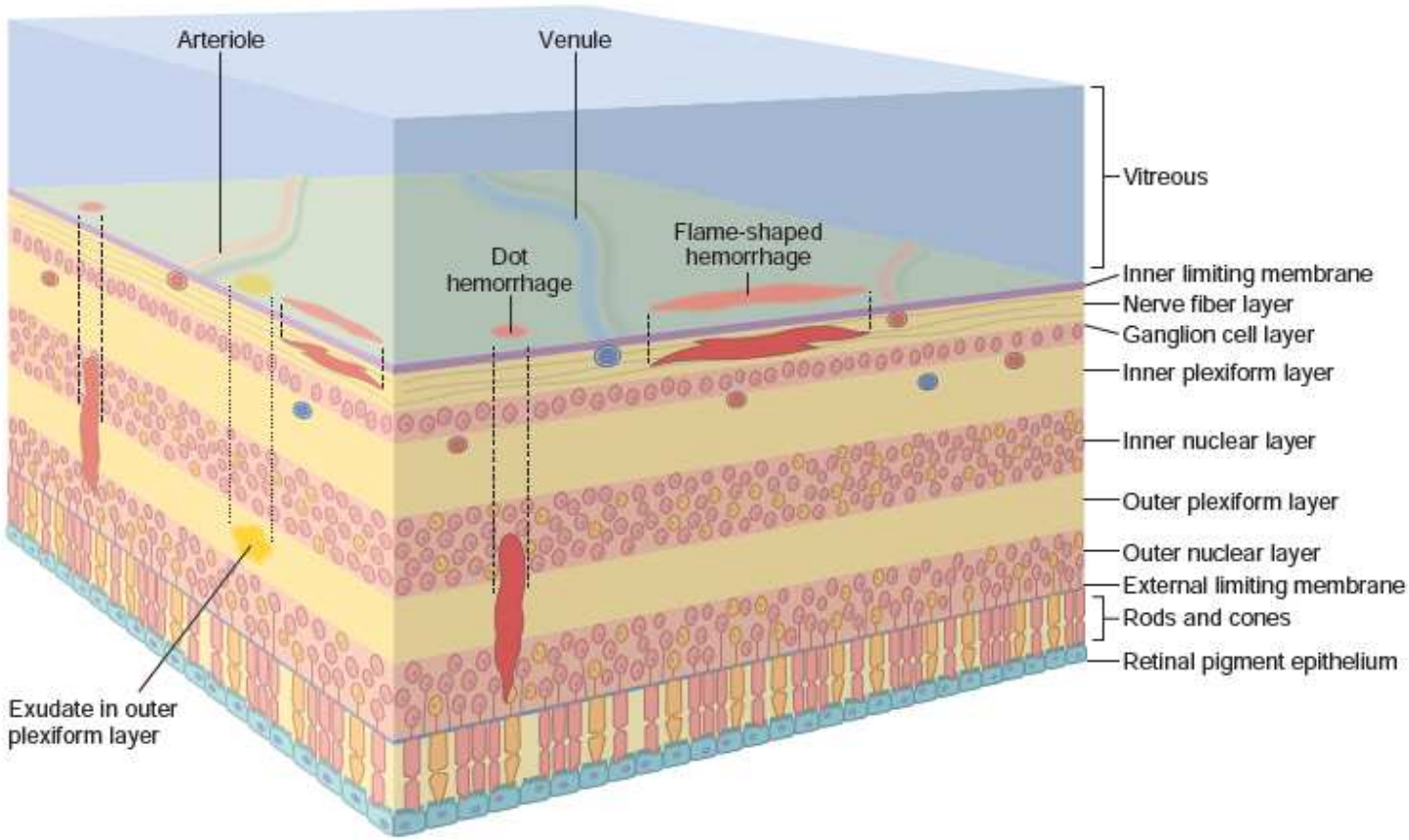


Figure 29-16 Clinicopathologic correlations of retinal hemorrhages and exudates. The location of the hemorrhage within the retina determines its appearance by ophthalmoscopy. The retinal nerve fiber layer is oriented parallel to the internal limiting membrane, and hemorrhages of this layer appear to be flame-shaped ophthalmoscopically. The deeper retinal layers are oriented perpendicular to the internal limiting membrane and hemorrhages in this location appear as cross-sections of a cylinder or "dot" hemorrhages. Exudates that originate from leaky retinal vessels accumulate in the outer plexiform layer.

Vitreous

- The adult vitreous humor is avascular.
- Incomplete regression of fetal vasculature persists as a retrolental mass (persistent hyperplastic primary vitreous).
- The vitreous humor can be opacified by hemorrhage from trauma or retinal neovascularization.
- With age the vitreous humor may liquefy and collapse, creating the visual sensation of “floaters.”
- With age, the posterior face of the vitreous humor, the posterior hyaloid, may separate from the neurosensory retina (posterior vitreous detachment)

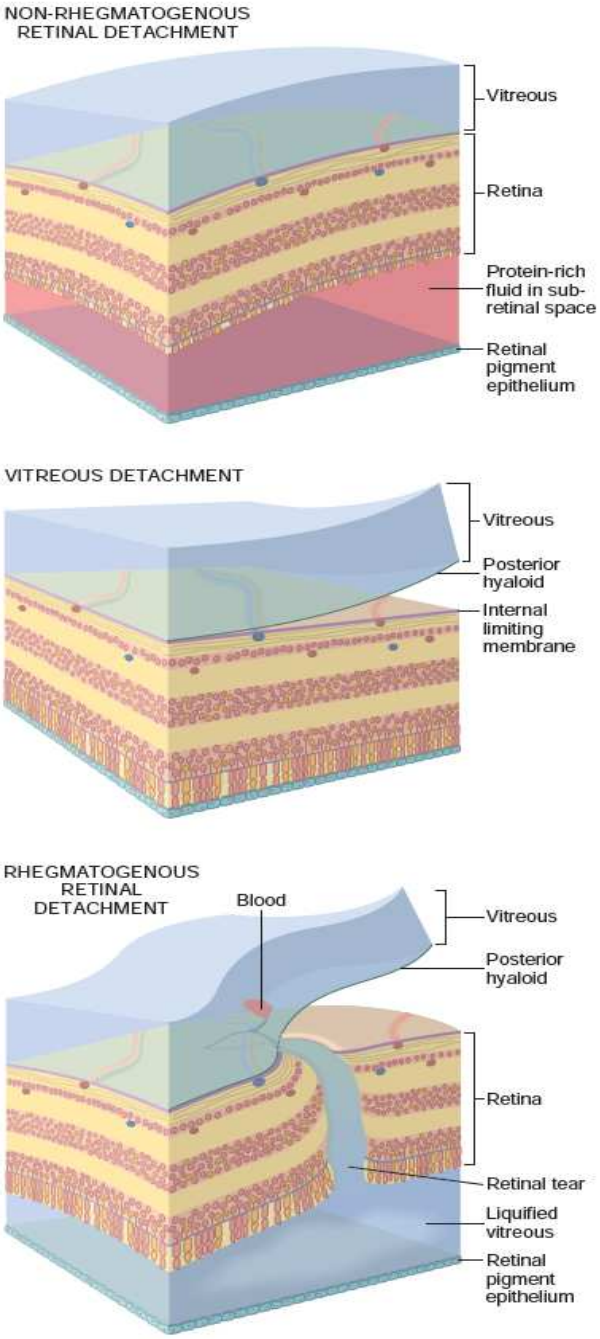


Figure 29-17 Retinal detachment is defined as the separation of the neurosensory retina from the RPE. Retinal detachments are classified broadly into non-rhegmatogenous (without a retinal break) and rhegmatogenous (with a retinal break) types. *Top*, In non-rhegmatogenous retinal detachment the subretinal space is filled with protein-rich exudate. Note that the outer segments of the photoreceptors are missing (see Fig. 29-16 for orientation of layers). This indicates a chronic retinal detachment, a finding that can be seen in both non-rhegmatogenous and rhegmatogenous detachments. *Middle*, Posterior vitreous detachment involves the separation of the posterior hyaloid from the internal limiting membrane of the retina and is a normal occurrence in the aging eye. *Bottom*, If during a posterior vitreous detachment the posterior hyaloid does not separate cleanly from the internal limiting membrane of the retina, the vitreous humor will exert traction on the retina, which will be torn at this point. Liquefied vitreous humor seeps through the retinal defect, and the retina is separated from the RPE. The photoreceptor outer segments are intact, illustrating an acute detachment.

Retina

- Retinal arterioles and veins share a common adventitial sheath.
- In pronounced retinal arteriolosclerosis the arteriole may compress the vein at points where both vessels cross.
- Venous stasis distal to arteriolar-venous crossing may precipitate occlusions of the retinal vein branches.
- Damage to choroidal vessels may produce focal choroidal infarcts (Elschnig spots).

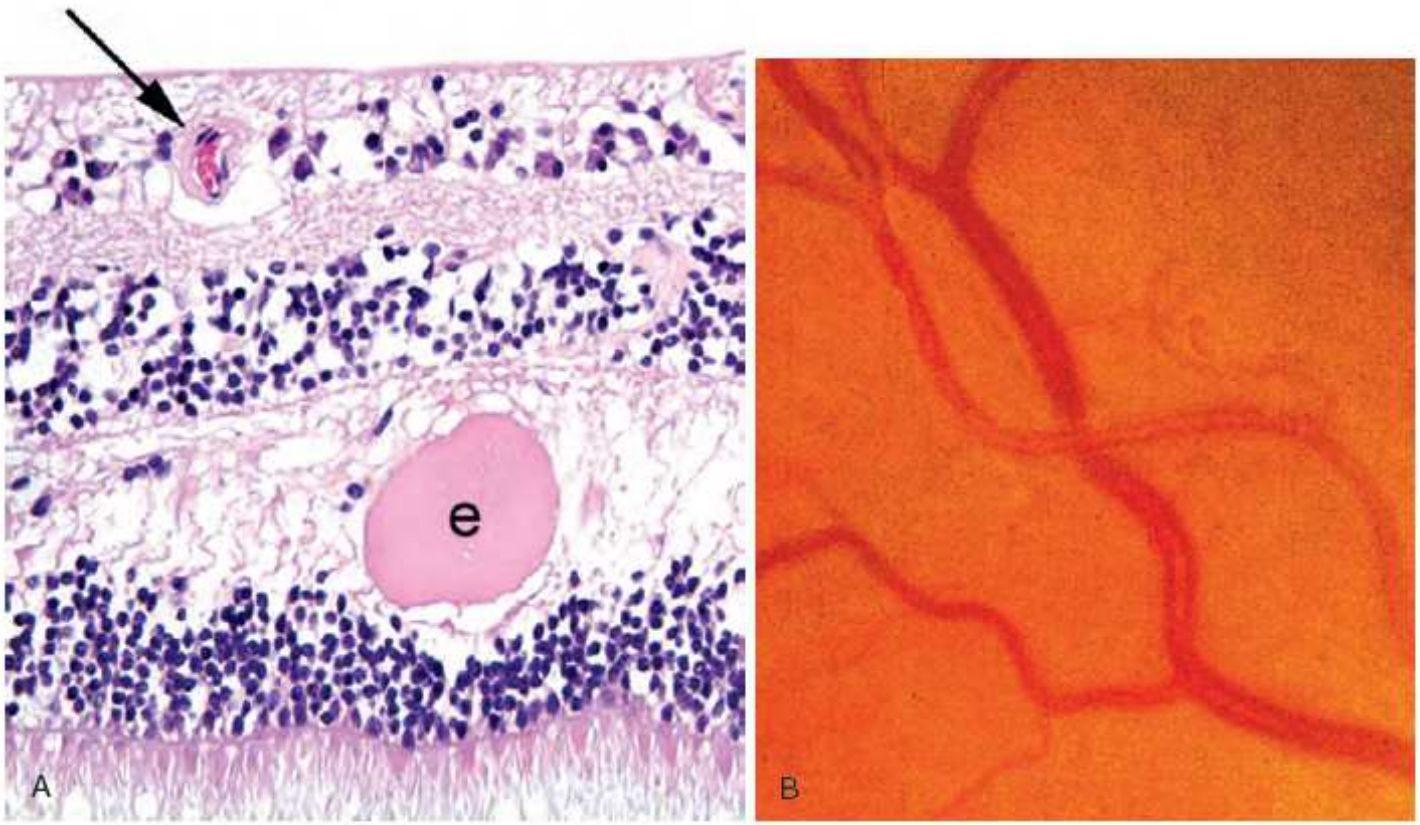


Figure 29-18 The retina in hypertension. **A,** The wall of the retinal arteriole *(arrow)* is thick. Note the exudate (e) in the retinal outer plexiform layer. **B,** The fundus in hypertension. The diameter of the arterioles is reduced, and the color of the blood column appears to be less saturated (copper wire–like). If the wall of the vessel were thicker still, the degree of red color would diminish such that the vessels might appear clinically to have a "silver wire" appearance. In this fundus photograph, note that the vein is compressed where the sclerotic arteriole crosses over it. (**B,** Courtesy Dr. Thomas A. Weingeist, Department of Ophthalmology and Visual Science, University of Iowa, Iowa City, Ia.)

Retina

- Exudate from damaged retinal arterioles typically accumulates in the outer plexiform layer of the retina
- Macular star is a spoke-like arrangement of exudate in the macula that results from exudate accumulating in the outer plexiform layer of the macula that is oriented obliquely instead of perpendicular to the retinal surface
- Thickening of the basement membrane of the epithelium of the pars plicata of the ciliary body is a reliable histologic marker of diabetes mellitus in the eye.

Retina

- Nonproliferative diabetic retinopathy
- The basement membrane of retinal blood vessels is thickened. The number of pericytes relative to endothelial cells diminishes.
- Microaneurysms are an important manifestation of diabetic microangiopathy
- May see macular edema
- May see exudates
- May have micro-occlusions

Retina

- Proliferative diabetic retinopathy
- Neovascularization either of the optic nerve head or of the retinal surface
- Retinal neovascularization if the newly formed vessels breach the internal limiting membrane of the retina.
- The web of newly formed vessels is referred to as a neovascular membrane.
- Composed of angiogenic vessels with or without a substantial supportive fibrous or glial stroma
- The neovascular membranes extend along the potential plane between the retinal internal limiting membrane and the posterior hyaloid.

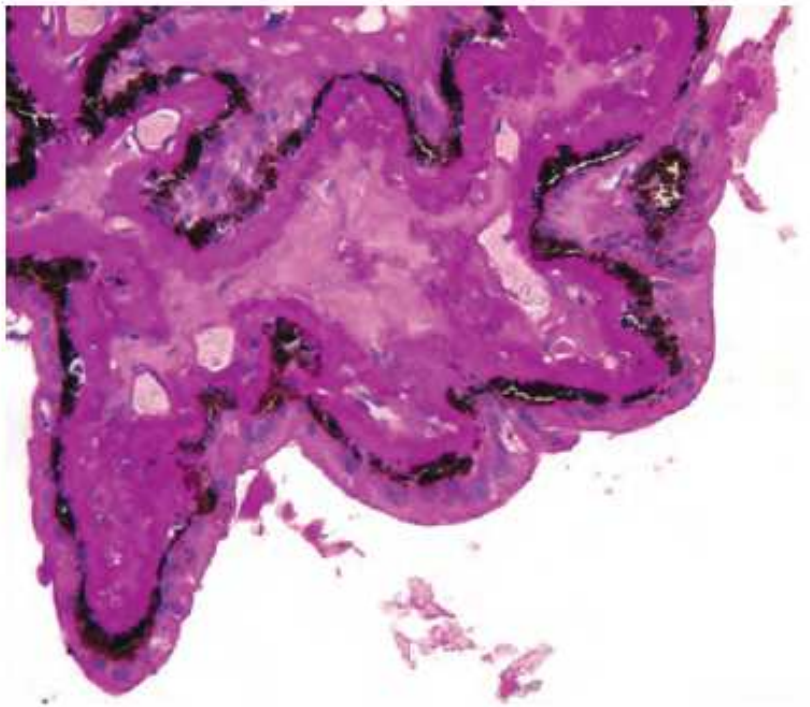


Figure 29-20 The ciliary body in chronic diabetes mellitus, periodic acid–Schiff stain. Note the massive thickening of the basement membrane of the ciliary body epithelia, reminiscent of changes in the mesangium of the renal glomerulus.

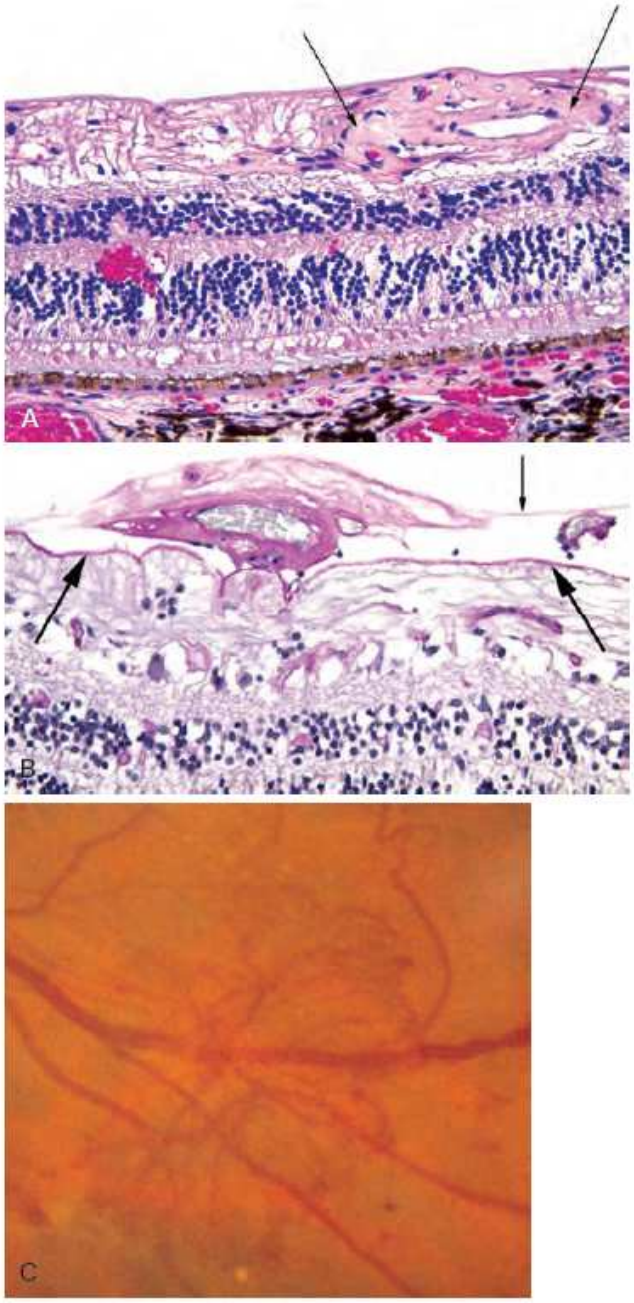


Figure 29-21 The retina in diabetes mellitus (see Fig. 29-16 for a schematic of retinal structure). **A,** A tangle of abnormal vessels lies just beneath the internal limiting membrane of the retina on the right half of the photomicrograph *(between arrows)*. This is an example of intraretinal angiogenesis known as intraretinal microangiopathy (IRMA). Note the retinal hemorrhage in the outer plexiform layer in the *left half*. The ganglion cell layer and the nerve fiber layer—the axons of the ganglion cells—are absent. The rarefied space beneath internal limiting membrane to the *left* of the focus of IRMA consists largely of elements of retinal glial (Müller) cells. Absence of the ganglion cell and nerve fiber layers is a hallmark of glaucoma. The chronic diabetes mellitus in this individual was complicated by iris neovascularization and secondary angle-closure glaucoma (neovascular glaucoma). **B,** In this section stained by periodic acid–Schiff, the internal limiting membrane is indicated by the *thick arrows* and the posterior hyaloid of the vitreous by the *thin arrow*. In the potential space between these two landmarks, the vessels to the left of the *thin arrow* are invested with a fibrous-glial stroma and would appear ophthalmoscopically as a white neovascular membrane. The thin-walled vessel to the right of the *thin arrow* is not invested with connective tissue. A posterior vitreous detachment in an eye such as this might exert traction on these new vessels and precipitate a massive vitreous hemorrhage. **C,** Ophthalmoscopic view of retinal neovascularization (known clinically as neovascularization "elsewhere" in contrast with neovascularization of the optic disc) creating a neovascular membrane.

Retina

- Retinopathy of Prematurity (Retrolental Fibroplasia)
- At term, the temporal (lateral) aspect of the retinal periphery is incompletely vascularized whereas the medial aspect is vascularized.
- In premature or low-birth-weight infants treated with oxygen, immature retinal vessels in the temporal retinal periphery constrict, rendering the retinal tissue distal to this zone ischemic.

Retina

- Sickle hemoglobinopathy
- Low oxygen tension within the blood vessels in the retinal periphery results in red cell sickling and microvascular occlusions.
- Nonproliferative (intraretinal angiopathic changes)
- SS and SC genotypes
- Subretinal hemorrhages
- Resolution give rise salmon patches, iridescent
- spots, and black sunburst lesions
- Proliferative (retinal neovascularization)
- Vasculitis
- “Sea fans” appearance

Retina

- Emboli to the central retinal artery can originate from thrombi in the heart or from ulcerated atheromatous plaques in the carotid arteries.
- Fragments of atherosclerotic plaques can lodge within the retinal circulation (Hollenhorst plaques).
- Total occlusion of a branch of retinal artery can produce a segmental infarct of the retina.
- Central retinal artery occlusion
- The fovea and foveola are physiologically thin
- The normal orange-red of the choroid is not only visible but also highlighted by the surrounding opaque retina (cherry-red spot)
- Retinal vein occlusion may occur without ischemia

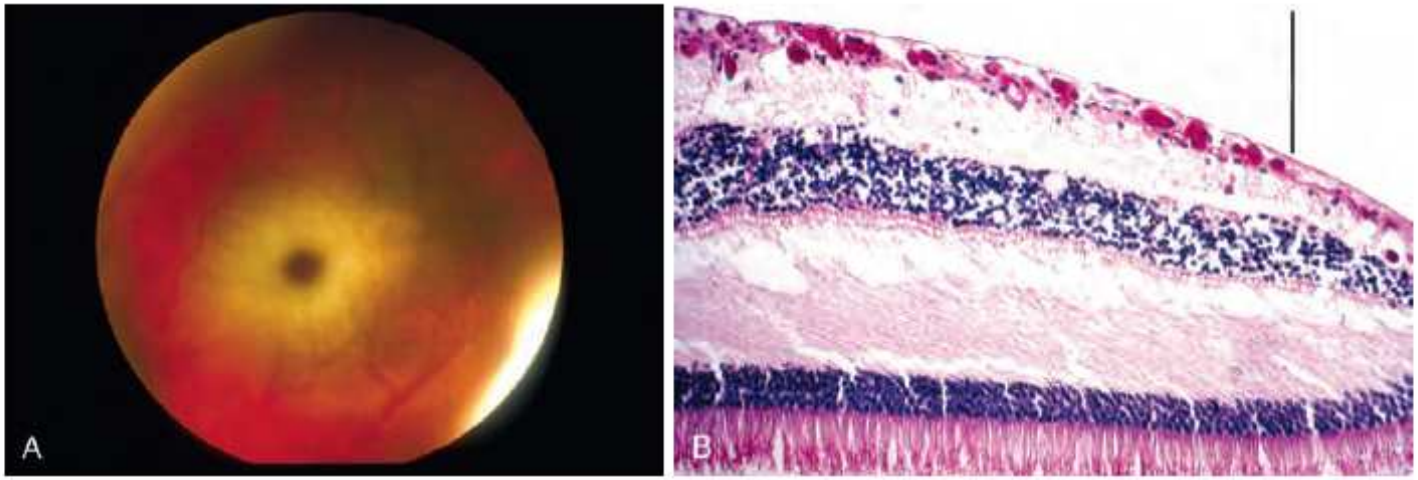


Figure 29-22 The cherry-red spot in Tay-Sachs disease. **A,** Fundus photograph of the cherry-red spot in Tay-Sachs disease. **B,** Photomicrograph of the macula in an individual with Tay-Sachs disease, stained with periodic acid–Schiff to highlight the accumulation of ganglioside material in the retinal ganglion cells. The presence of ganglion cells filled with gangliosides outside the fovea blocks the transmission of the normal orange-red color of the choroid, but absence of ganglion cells within the fovea (to the right of the *vertical bar*) permits the normal orange-red color to be visualized, accounting for the so-called cherry-red spot. (**A,** Courtesy Dr. Thomas A. Weingeist, Department of Ophthalmology and Visual Science, University of Iowa, Iowa City, Ia.; **B**, from the teaching collection of the Armed Forces Institute of Pathology.)

Retina

- Accumulation of mitochondria at the swollen ends of damaged axons creates the histologic illusion of cells (cytoid bodies).
- Secondary to ischemia
- Represent nerve fiber layer infarct and pre-capillary arterial occlusion
- Collections of cytoid bodies populate the nerve fiber layer infarct (“cotton-wool spots”).
- May be first indication of hypertension (50%)
- May be first indication of diabetes mellitus (20%)
- Cytomegalovirus infection in immunosuppressed

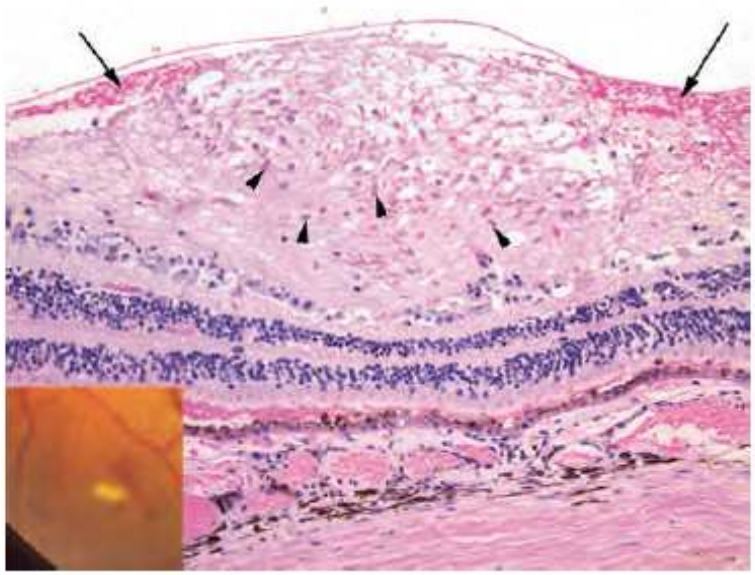
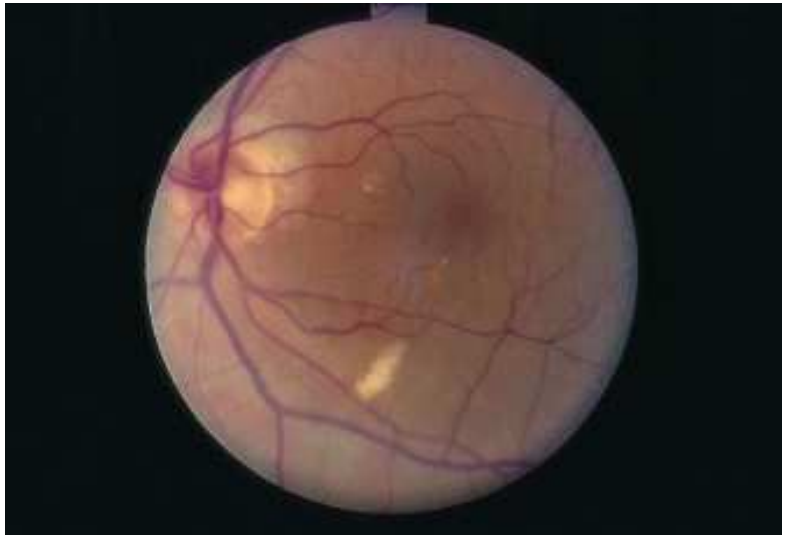
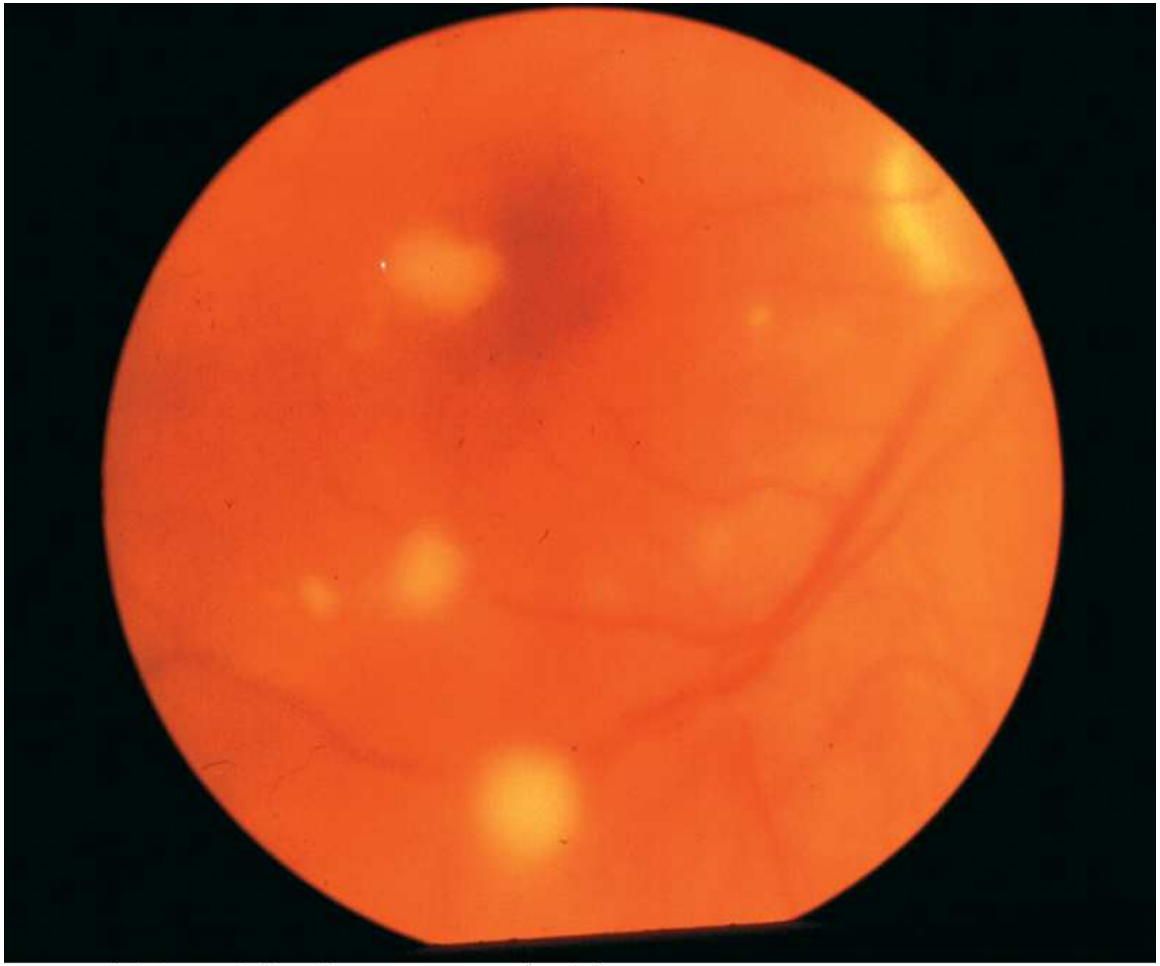


Figure 29-19 Nerve fiber layer infarct. A "cotton-wool spot" is illustrated in the *inset*, adjacent to a flame-shaped (nerve fiber layer) hemorrhage. The histology of a cotton-wool spot—an infarct of the nerve fiber layer of the retina—is illustrated in the photomicrograph. A focal swelling of the nerve fiber layer is occupied by numerous red to pink cytoid bodies *(arrowheads)*. Hemorrhage *(arrows)* surrounding the nerve fiber layer infarct as illustrated here is a variable and inconsistent finding. (Fundus photograph, Courtesy Dr. Thomas A. Weingeist, Department of Ophthalmology and Visual Science, University of Iowa, Iowa City, Ia.)



https://eyewiki.aato.org/Cotton_Wool_Spos



Candida retinitis. The typical rounded white exudates are caused by seeding from the bloodstream. (Picture courtesy of Dr. William Driebe, University of Florida College of Medicine.)

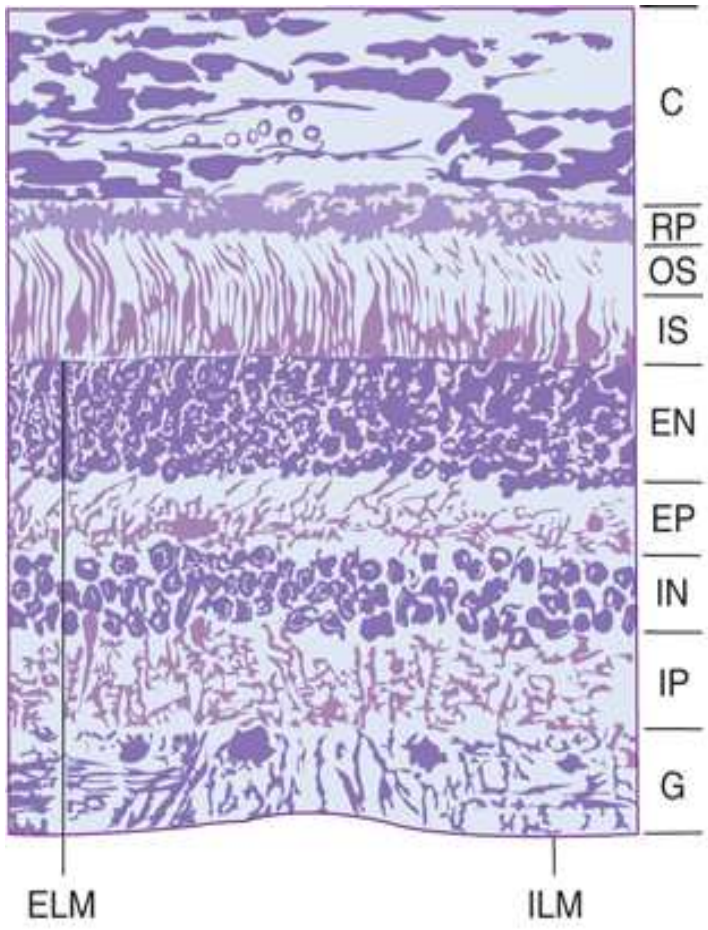
Retina

- Pigmented epithelium is a single layer of polygonal cells (photoreceptors) that absorbs light and prevents reflection that would distort vision.
- Photoreceptor cells maintain a roughly constant length by continuously generating new outer segments from their base while simultaneously releasing mature outer segments engulfed by the retinal pigment epithelium.
- Post-mitotic retinal pigment epithelial cells phagocytose an immense amount of material over a lifetime, disposing of photoreceptor cell waste while retaining useful content.

Retina

- Rods embedded in pigmented epithelium
- Store and release vitamin A (rhodopsin precursor)
- Peripheral regions of retina
- Dim or dark light vision
- Cones present centrally
- Color vision as well as acuity
- Cylindrical outer segment contains membrane bound discs (lamellae).
- Outer segment connected to mitochondrion rich inner segment by a thin neck.

Retina and choroid



Source: Waxman SG: *Clinical Neuroanatomy, 26th Edition*: http://www.accessmedicine.com

Light enters from the bottom and traverses the following layers: internal limiting membrane (ILM), ganglion cell layer (G), internal plexiform layer (IP), internal nuclear layer (IN) (bipolar neurons), external plexiform layer (EP), external nuclear layer (EN) (nuclei of rods and cones), external limiting membrane (ELM), inner segments of rods (IS) (narrow lines) and cones (triangular dark structures), outer segments of rods and cones (OS), retinal pigment epithelium (RP), and choroid (C). x655.

Fig. 15-2 Accessed 07/01/2010

Retina

- Inverted.
- Light must pass through optic nerve fibers, ganglion cells, and bipolar neurons to reach photoreceptors.
- Pigmented epithelium blocks light reflection.
- At the fovea, light strikes the photoreceptors directly.
- Cones are bunched and principally located in the fovea; outer segment is tapered.
- Lamellae are infoldings of plasma membrane.
- Rods, periphery.
- One cone, one bipolar cell
- Many rods, one bipolar cell.
- Rods function in dim light and not to color.
- Cones respond to bright light, color, shape.

Retinal processing

- Light rays excite photoreceptors.
- Photoreceptors excite bipolar cells and horizontal cells.
- Horizontal cells provide lateral communication.
- Bipolar cells excite ganglion cells and amacrine cells.
- Only ganglion cells (tonically active) generate action potentials.
- All others generate receptor potentials.

Retinal processing

- Darkness causes Na^+ channels to open.
- Light activates rhodopsin (associated with G-Protein in the disk membrane).
- 11-cis-retinal becomes trans-retinal.
- Opsin is released.
- Phosphodiesterase activated.
- Phsophodiesterase breaks down cGMP.

Retinal processing

- Without cGMP, the cell polarizes; Na^{+}-Ca^{2+} ion channel closes.
- Glutamine not released from cell.
- In the dark, trans-retinal is converted to 11-cis-retinal through retinal isomerase.
- Requires ATP.
- cGMP produced, opens ion channels.
- Rod cell depolarizes and releases glutamine.

Retinal processing

- Ganglion cells are either ON or OFF.
- ON and OFF midget and parasol ganglion cells sample complete population of cones sensitive to red and green light.
- Midget ganglion cells do not sample in a random fashion.
- OFF midget ganglion cells are sensitive to blue light input.

Retinal processing

- Photoreceptors are clustered.
- Bulk of retinal receptors respond to dark.
- Sight is not presented in pixel form but as light and dark contrast.
- The characteristic response of ganglion cells (green, red, blue) is one of color opponency.

Color blindness

- Opsin proteins absorb colors, responsible for color vision.
- Normal vision is trichromatic.
- Red and green opsins adjacent on X-chromosome.
- Share 98% sequence identity.
- Usually one red followed by one or more green.
- 8% of white men have abnormal arrangement.
- Unequal crossing over is the cause.

Retinitis pigmentosa

- Inability to produce functional protein for photoreceptor function
- Loss of night and peripheral vision
- Later, loss of color vision as well as acuity
- Cone-rod dystrophy
- Loss of color vision and acuity
- Later, loss of night and peripheral vision
- Both involve failure of microglia to dispose of outer segments is a cause of retinitis pigmentosa.
- C3-C3R dependent clearing

Retinitis pigmentosa

- Mutations in the RHO (rhodopsin) gene are the most common cause of autosomal dominant form
- 15% of autosomal recessive form have mutations in USH2A gene
- Usherin is a component of basement membranes in retina and inner ear
- Mutations in the RPGR and RP2 genes account for most cases of X-linked form
- Affect tubulin folding

WHAT TO EXPECT WITH RETINITIS PIGMENTOSA:

Symptoms depend on whether **rods** or **cones** are initially involved:

Rods: In most forms of RP, rods are affected first, causing **loss of peripheral vision** and **loss of night vision**. Vision becomes more constricted over time.

Cones: If and when the disease progresses and cones become affected, **visual acuity**, **color perception**, and **central vision** are diminished.

Typically diagnosed in children and young adults.

Rate of progression and degree of visual loss varies.

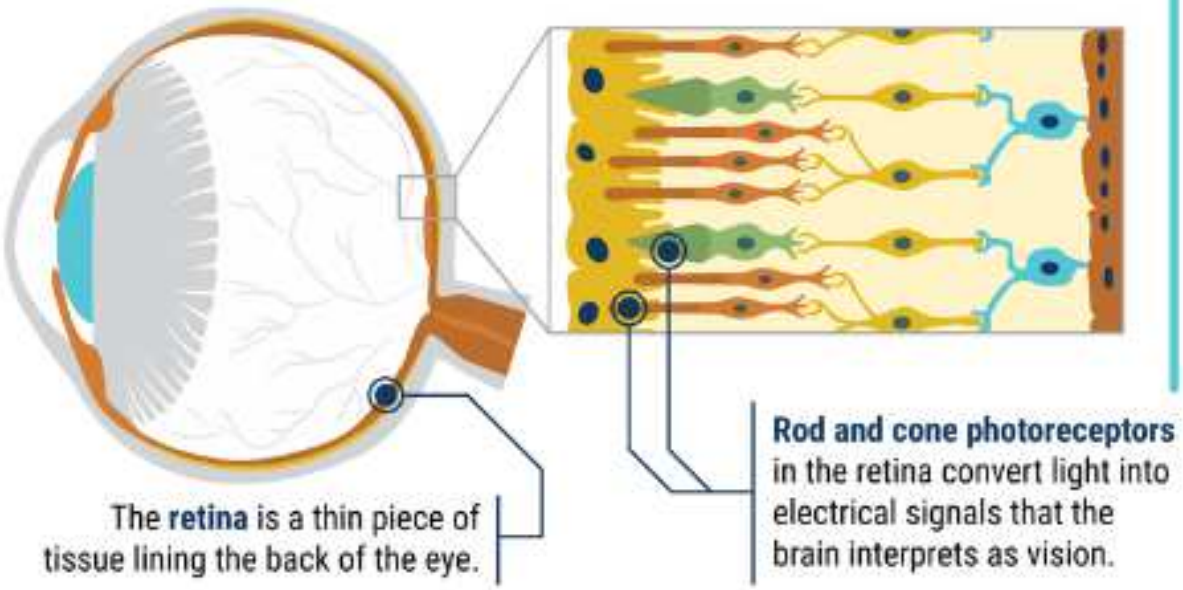
Many people with RP are legally blind by age 40.

Central visual field reduced by varying degrees.

https://www.fightingblindness.org/diseases/retinitis-pigmentosa

WHAT IS RETINITIS PIGMENTOSA?

Retinitis pigmentosa (RP) refers to a group of inherited retinal diseases, often leading to legal and sometimes complete blindness. Forms of RP and related diseases include Usher syndrome, Leber congenital amaurosis, and Bardet-Biedl syndrome, among others. An estimated 100,000 people in the U.S. have RP.



https://www.fightingblindness.org/diseases/retinitis-pigmentosa

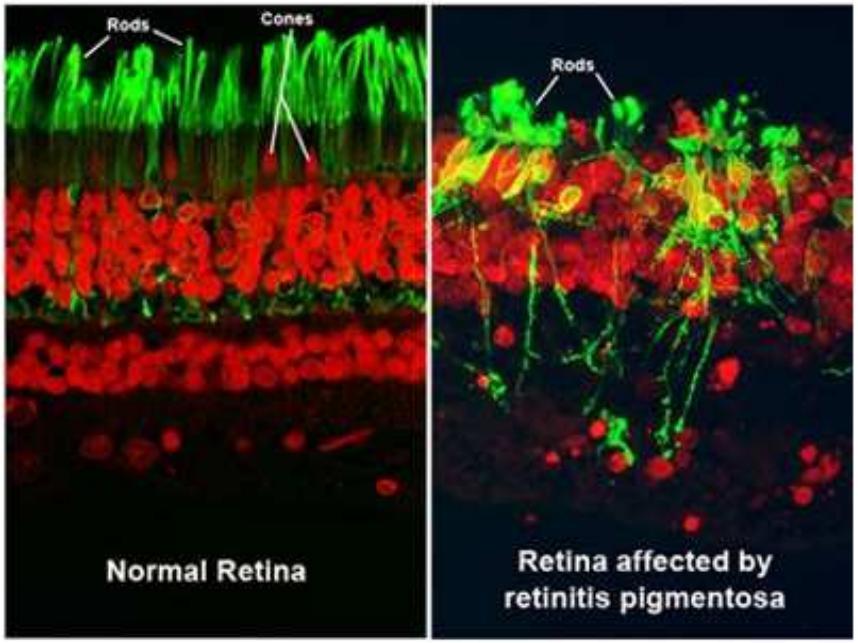
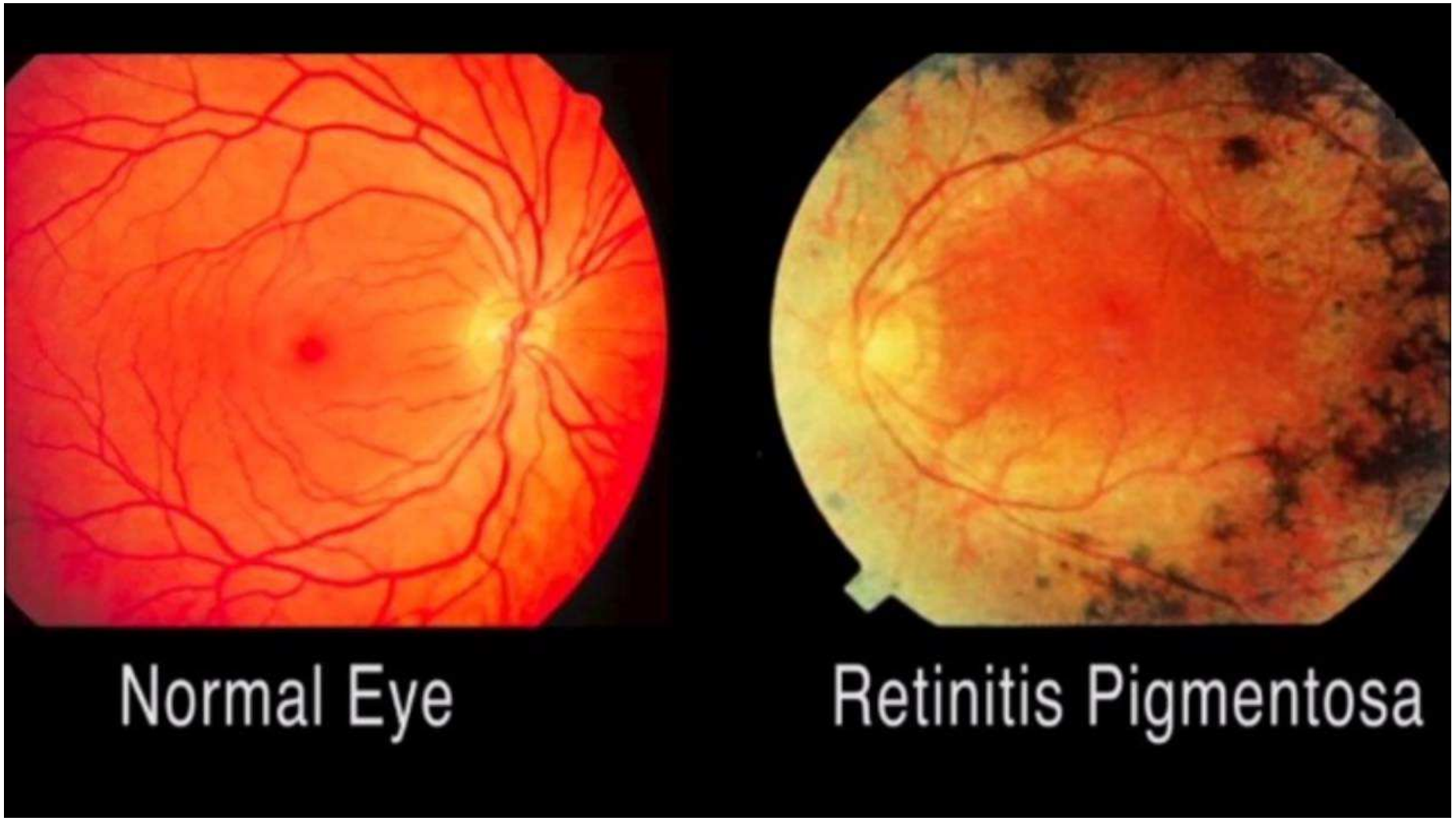


Image courtesy of Robert N. Fariss, Ph.D., chief of the NEI Biological Imaging Core, and Ann H. Milam, Ph.D., former professor in the Department of Ophthalmology at the University of Washington.



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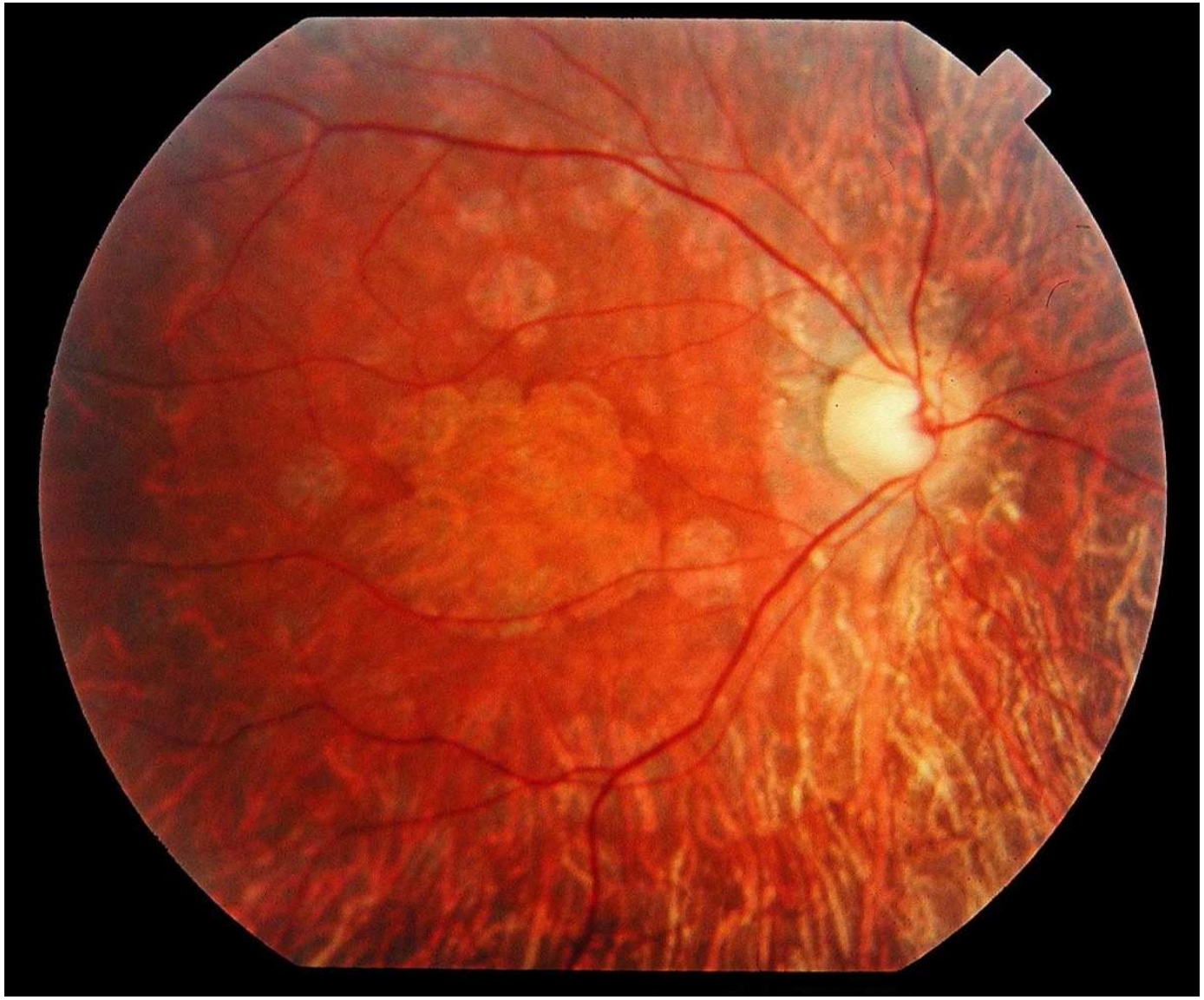


Cone-rod dystrophy

https://media.springernature.com/full/springer-static/image/art%3A10.1186%2F1750-1172-2-7/MediaObjects/13023_2006_Article_58_Fig3_HTML.jpg

Macular degeneration

- Age-related macular degeneration (AMD) is the most common cause of irreversible visual loss in the United States.
- Dry form (Geographic atrophy)
- 85 to 90%
- It is characterized by a buildup of yellowish deposits (drusen) beneath Bruch membrane and vision loss that worsens slowly over time.
- The most advanced stage is known as geographic atrophy
- Areas of the macula atrophy, resulting in severe vision loss.

Macular degeneration

- Dry age-related macular degeneration typically affects vision in both eyes,
- Dry form responds to vitamin therapy.
- May progress to wet form.
- Pegcetacoplan, a Complement inhibitor (C3), slows growth of geographic atrophy

Macular degeneration

- Wet form
- 10 to 15%
- Characterized choroidal neovasularization underneath the macula. Penetrate Bruch membrane.
- C3 gene at 19p13.3
- ARMS2 and HTRA1 genes at 10q26.13
- Intraocular injections or systemic infusions of VEGF inhibitor to treat wet form.

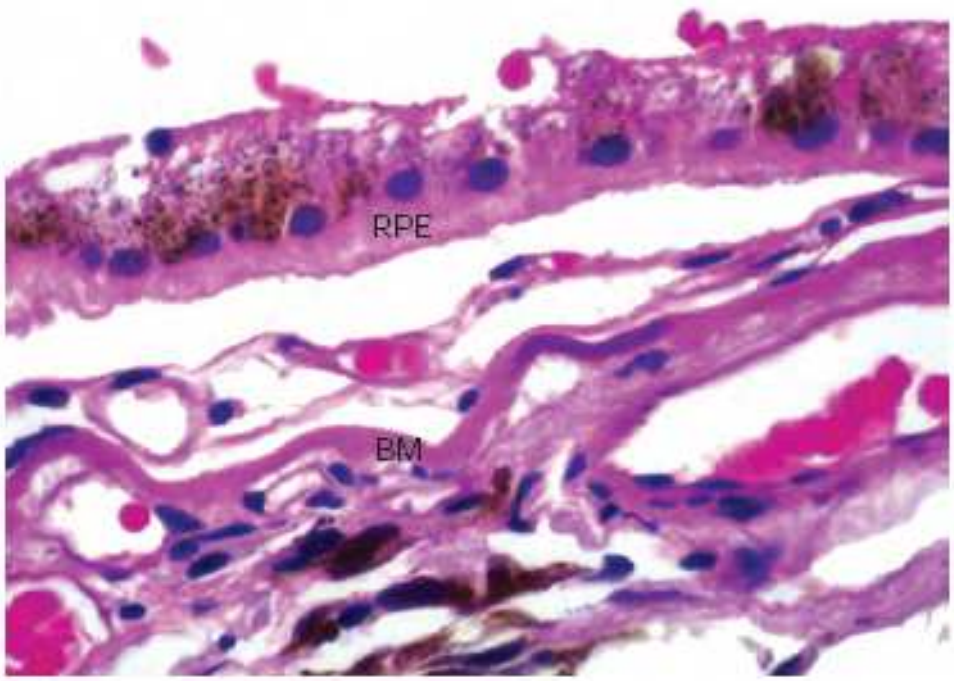


Figure 29-23 "Wet" age-related macular degeneration. A neovascular membrane is positioned between the RPE and Bruch membrane (BM). Note the blue discoloration of Bruch membrane to the right of the label, indicating focal calcification.

Retinoblastoma

- Neuronal origin.
- 70% sporadic.
- Bi-allelic loss of Rb gene
- Usually, one germline mutation and one somatic mutation
- Retinocytoma is a benign lesion that is a precursor of retinoblastoma and is noted in those with heritable disease.
- Bi-allelic germline mutation associated with bilateral disease as well as pinealoblastoma.
- Loss of light reflex; “red” eye

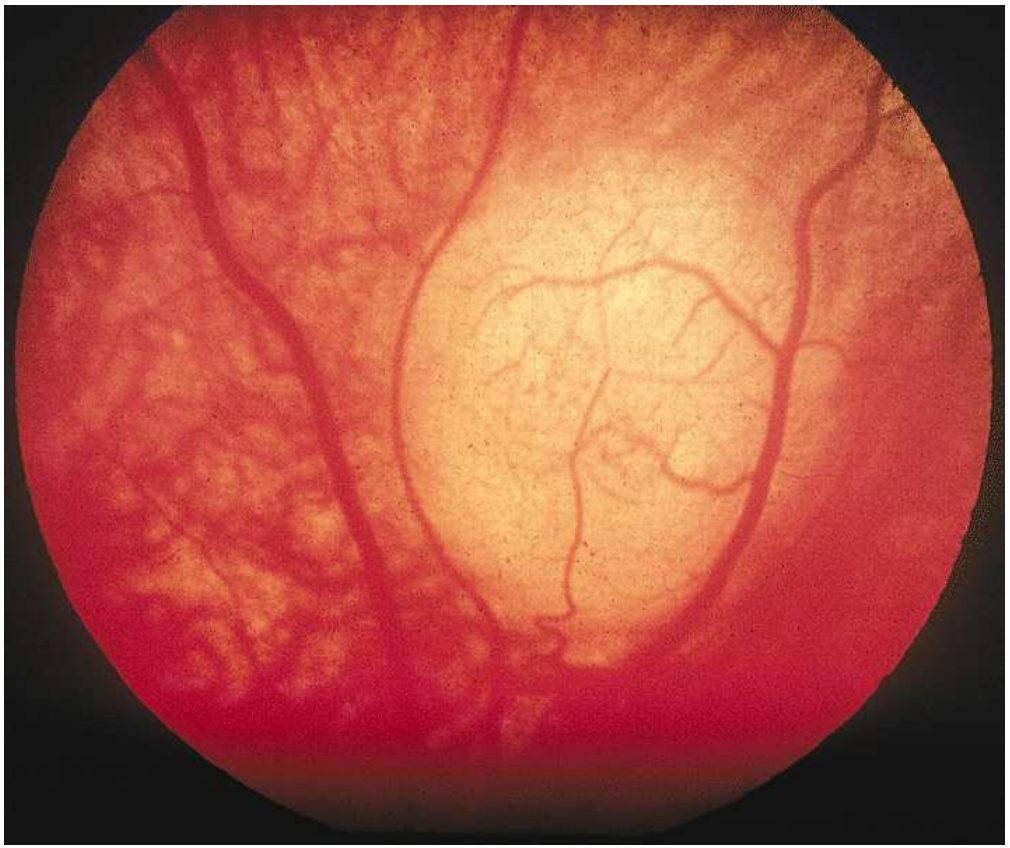
Retinoblastoma

- Tumors may contain both undifferentiated and differentiated elements.
- The former appear as collections of small, round cells with hyperchromatic nuclei.
- In well-differentiated tumors there are Flexner-Wintersteiner rosettes and fleurettes reflecting photoreceptor differentiation.
- Tumor cells found about blood vessels in areas of necrosis (tumor highly dependent upon blood supply)
- Focal areas of dystrophic calcification

Retinoblastoma

- Carboplatin, vincristine, etoposide chemotherapy in attempt to reduce tumor burden and salvage eye
- May follow with laser ablation.
- Enucleation if eye not salvageable.
- Spread is usually to brain and bone marrow.
- Risk of osteosarcoma and melanoma as secondary cancers

Retinoblastoma

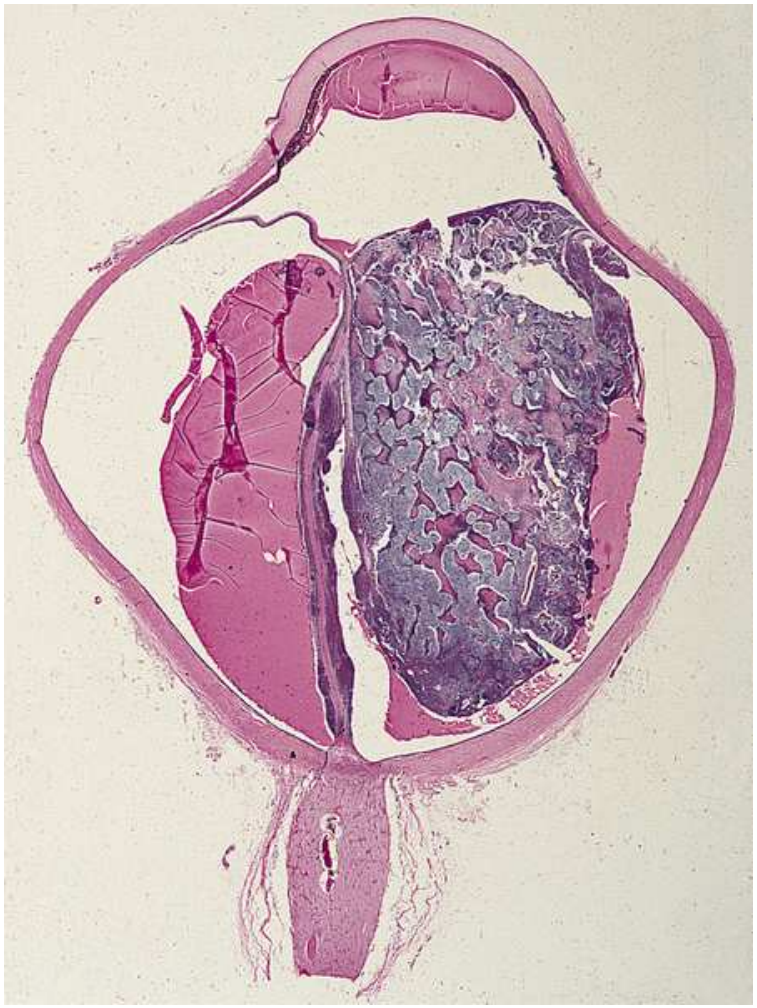


Fundus photograph of retinal tumor that has grown into the subretinal space. Retinal blood vessels pass over the tumor.

Fig. PL-04A

McLean, IW, Burnier, MN, Zimmerman, LE, Jakobiec, FA., “Tumors of the eye and ocular adnexa.” Atlas of Tumor Pathology,Third Series, Fascicle 12. Armed Forces Institute of Pathology, Washington, D.C. 1994.

Retinoblastoma



Total retinal detachment and collapse of the anterior chamber caused by a partially necrotic tumor with viable cells surrounding blood vessels in a sleeve pattern. There is no invasion of choroid, sclera, or optic nerve.

Fig. PL-04C

McLean, IW, Burnier, MN, Zimmerman, LE, Jakobiec, FA. , “Tumors of the eye and ocular adnexa.” Atlas of Tumor Pathology,.Third Series, Fascicle 12. Armed Forces Institute of Pathology, Washington, D.C. 1994.

Retinoblastoma

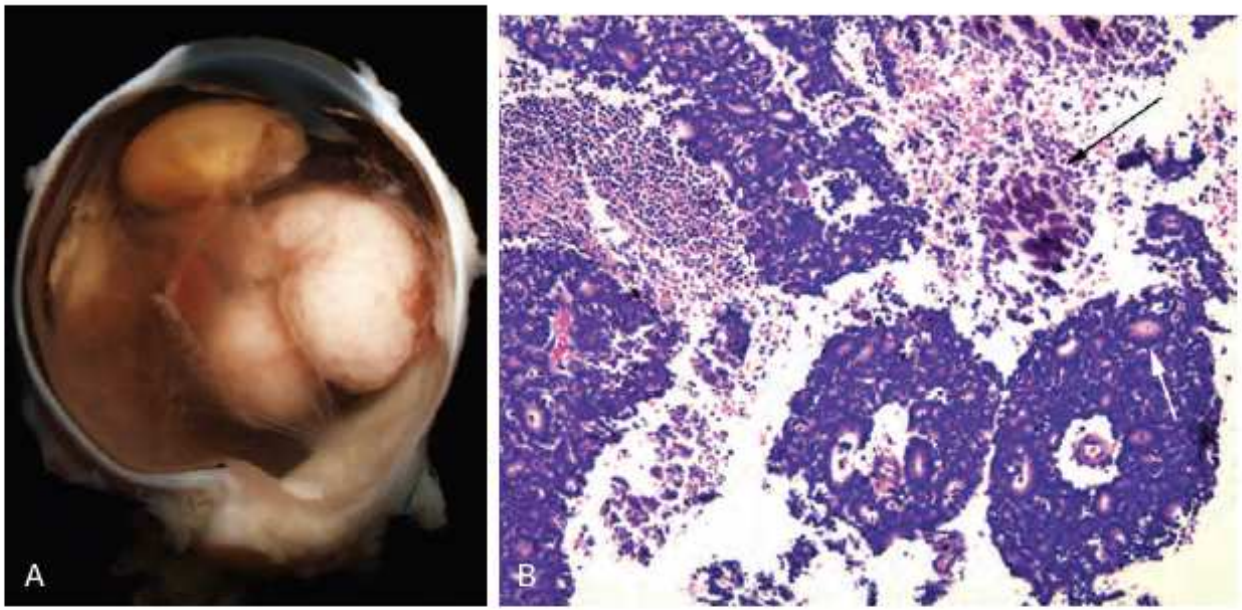
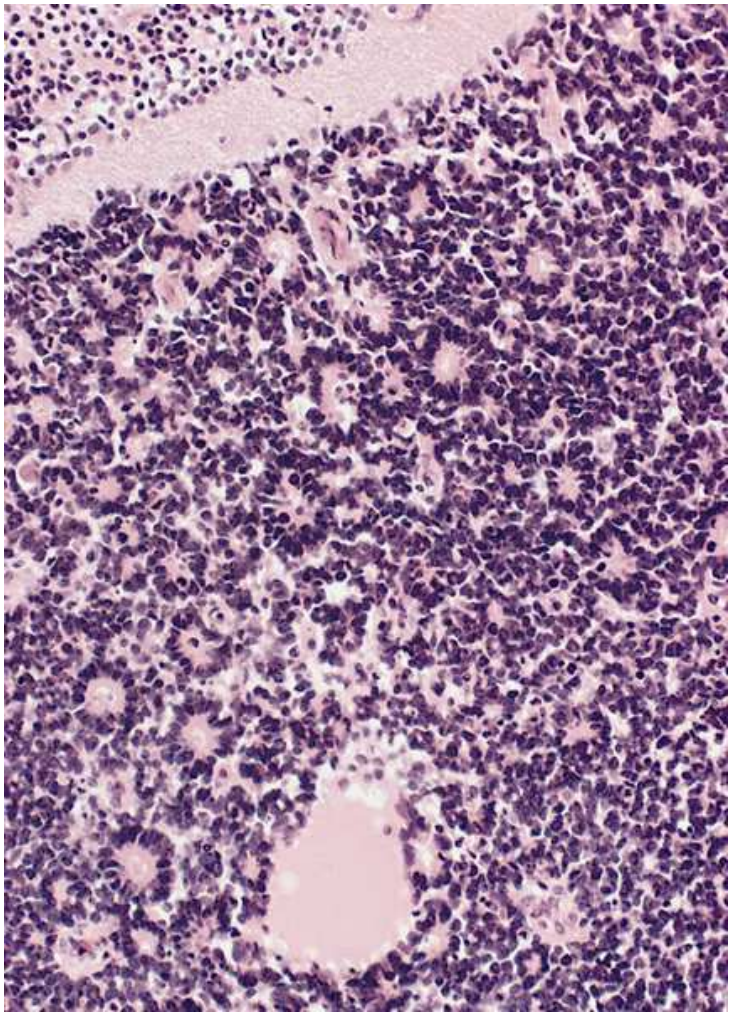


Figure 29-24 Retinoblastoma. **A,** Gross photograph of retinoblastoma. **B,** Tumor cells appear viable when in proximity to blood vessels, but necrosis is seen as the distance from the vessel increases. Dystrophic calcification *(dark arrow)* is present in the zones of tumor necrosis. Flexner-Wintersteiner rosettes—arrangements of a single layer of tumor cells around an apparent "lumen"—are seen throughout the tumor, and one such rosette is indicated by the *white arrow*.

Retinoblastoma



Flexner-Wintersteiner rosettes.

Fig. 23-23L

Lack, EE., “Tumors of the Adrenal Gland and Extra-Adrenal Paraganglia.” Atlas of Tumor Pathology, Third Series, Fascicle 19. Armed Forces Institute of Pathology, Washington, D.C. 1997.

Primary intraocular lymphoma

- Older individuals
- Mimic uveitis clinically.
- Most are diffuse large B cell lymphomas.
- Spread to the brain via the optic nerve.

Optic nerve

- Anterior ischemic optic neuropathy (AION)
- Zones of relative ischemia may surround segmental infarcts of the optic nerve.
- Optic nerve function in these poorly perfused but not infarcted zones may recover.
- The optic nerve does not regenerate, and visual loss from infarction is permanent.
- Result from inflammation of the vessels that supply the optic nerve or from embolic or thrombotic events.
- Bilateral total infarcts of the optic nerve resulting in total blindness have been reported in temporal arteritis.

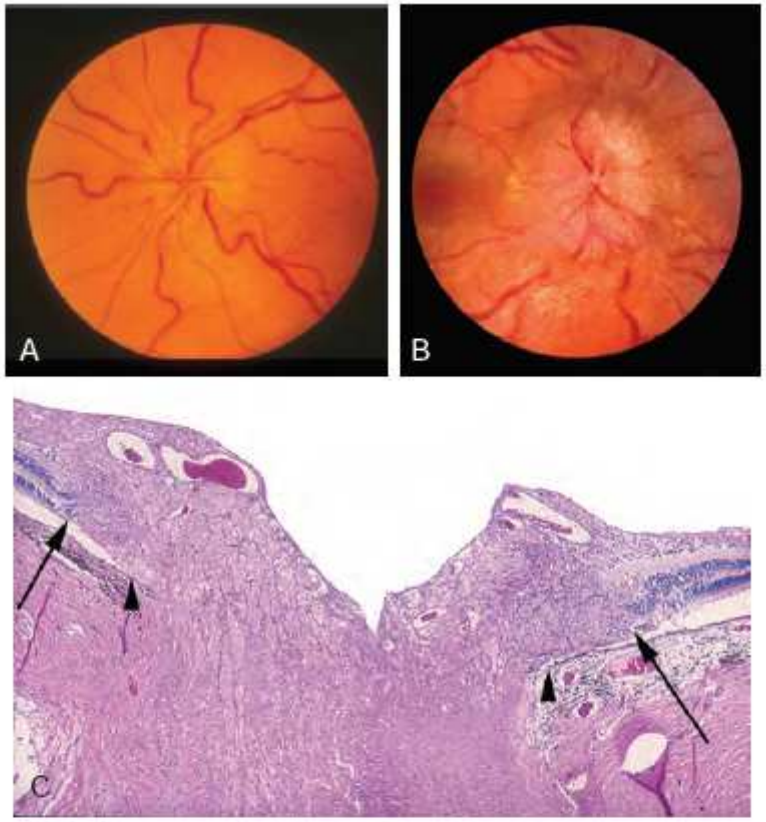


Figure 29-25 The optic nerve in anterior ischemic optic neuropathy (AION) and papilledema. **A,** In the acute phases of AION the optic nerve may be swollen, but it is relatively pale because of decreased perfusion. **B,** In papilledema secondary to increased intracranial pressure, the optic nerve is typically swollen and hyperemic. **C,** Normally, the termination of Bruch membrane *(arrowhead)* is aligned with the beginning of the neurosensory retina, as indicated by the presence of stratified nuclei *(arrow)*, but in papilledema the optic nerve is swollen, and the retina is displaced laterally. This is the histologic explanation for the blurred margins of the optic nerve head seen clinically in this condition. (**A** and **B,** Courtesy Dr. Sohan S. Hayreh, Department of Ophthalmology and Visual Science, University of Iowa, Iowa City, Ia.; **C,** from the teaching collection of the Armed Forces Institute of Pathology.)

Papilledema

- Consequence of compression of the nerve (unilateral) or from elevations of cerebrospinal fluid pressure surrounding the nerve (bilateral).
- The concentric increase in pressure encircling the nerve contributes to venous stasis and also interferes with axoplasmic transport, leading to nerve head swelling.
- Not usually associated with visual loss.

Optic neuropathy

- May be inherited or may be secondary to vitamin B1, folic acid, and B12 deficiencies or toxins such as methanol.
- If the nerve fibers that originate from the macula are affected then central visual acuity is lost.

Optic neuropathy

- Methanol toxicity preferentially affects the retina, where degeneration of retinal ganglion cells may cause blindness.
- Selective bilateral necrosis of the putamen and focal white-matter necrosis also occur when the exposure is severe.
- Formic acid metabolites interfere with oxidative phosphorylation.

Optic neuropathy

- Leber hereditary optic neuropathy
- Mutations MT-ND1,MT-ND4, MT-ND4L, MT-ND6 affect NADH regeneration
- Men 9:1
- 10-30 years of age
- May have cardiac conduction abnormalities
- Optic neuritis refers to demyelinization of the optic nerve.
- Multiple sclerosis is principal cause.

Phthisis bulbi

- Trauma, intraocular inflammation, chronic retinal detachment, and many other conditions can give rise to an eye that is both small (atrophic) and internally disorganized.
- Congenitally small eyes (microphthalmic) are generally not disorganized internally
- Phthisic eyes are disorganized internally

Phthisis bulbi

- Typically show the following changes:
- The presence of exudate or blood between the ciliary body and sclera and the choroid and sclera (ciliochoroidal effusion)
- The presence of a membrane extending across the eye from one aspect of the ciliary body to the other (cyclitic membrane)
- Chronic retinal detachment
- Optic nerve atrophy
- Intraocular bone (osseous metaplasia of the retinal pigment epithelium).
- A thickened sclera, especially posteriorly.

Phthisis bulbi

- Ciliochoroidal effusion is typically associated with the physiologic state of low intraocular pressure (hypotony).
- The normal pull of the extraocular muscles on a hypotonous eye may render the appearance of the eye as square rather than round.

Vision

- Axons leave the retinal ganglion cells leave the retina via the optic papilla and are myelinated proximal to the lamina cribosa.
- Axons from the nasal half of the retina cross in the optic chiasm.
- Those from the temporal half are uncrossed.
- Some optic fibers enter the supra-chiasmatic nucleus of the hypothalamus and connect with the pineal gland.

Vision

- The right visual field projects to the left half of the brain; the left visual field, to the right half.
- During passage through the lens, the image is reversed.
- Vision is a crossed sensation.
- Upper visual field projects to the lower retina.
- The axons synapse in the lateral geniculate nucleus.
- Axons, heaviy myelinated, then project to Area 17 (the primary visual cortex) which occupies the wall of the calcarine sulcus.
- The lateral geniculate body is binocular.
- Retinal representation is posterior-anterior.

Loop of Meyer

- The neurons of the lateral part of the lateral geniculate body which receive input from the lower retina, project via the loop of Meyer to the lower lip of the calcarine sulcus.
- The loop forms as optic radiations from the lateral part of the lateral geniculate are pulled forward by the growth of the temporal horn.
- The loop of Meyer loops around from the inferior horn of the lateral ventricle.
- Damage to the temporal lobe (and loop of Meyer) may cause a contrateral loss of the upper quadrant of the visual vield.

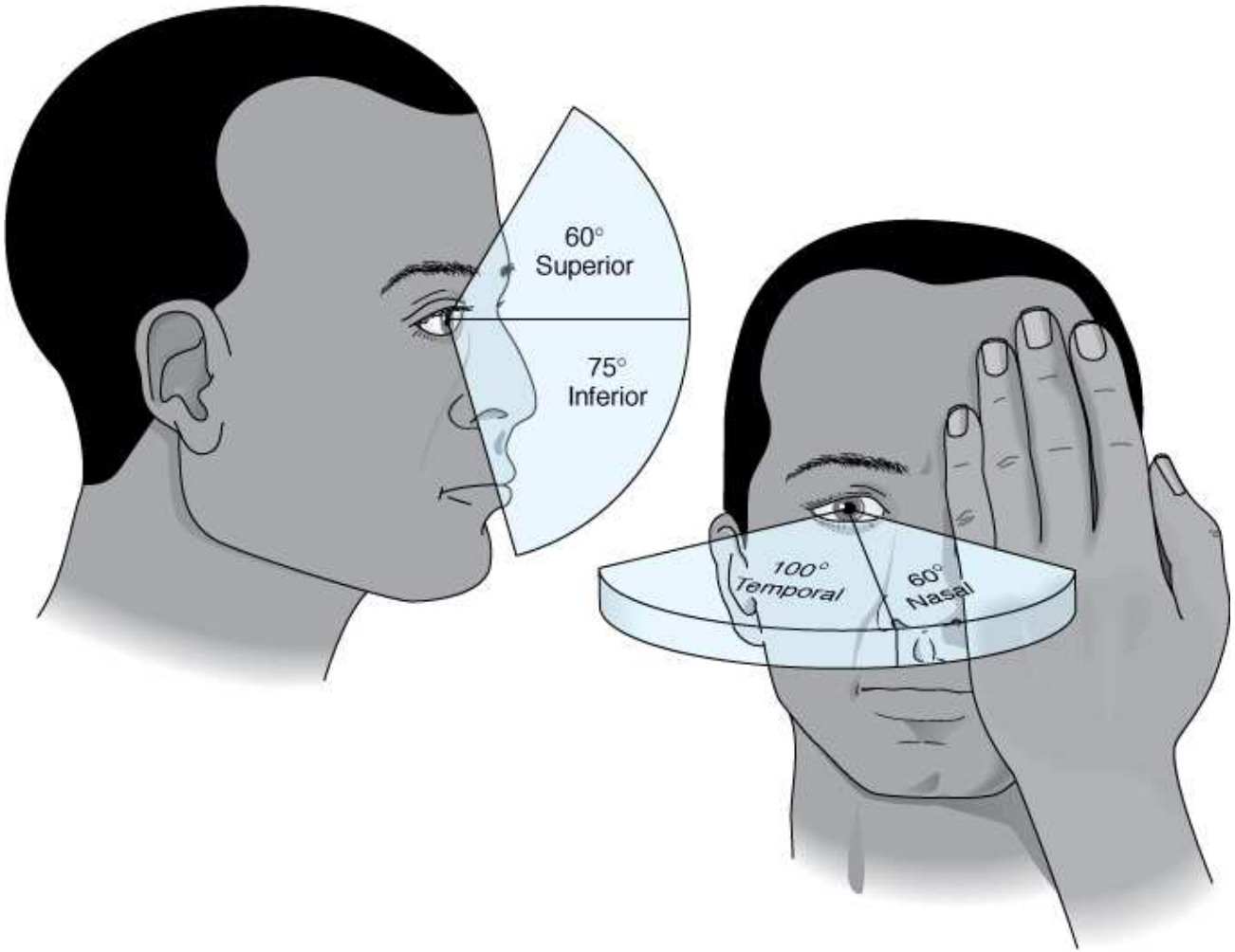
Receptive fields

- Ganglion cells, lateral geniculate cells, and cells in layer IV of cortical area 17 have circular fields with an excitatory center and an inhibitory surround or an inhibitory center and an excitatory surround.
- There is no preferred orientation of a linear stimulus.
- Simple cells respond best to a linear stimulus with a particular orientation in a specific part of the cell's receptive field.

Receptive fields

- Complex cells respond to linear stimuli with a particular orientation.
- They are less selective in terms of location in the receptive field.
- They often respond maximally when the stimulus is moved laterally.

Visual Field



Source: Simon RP, Greenberg DA, Aminoff MJ:
Clinical Neurology, 7th Edition: http://www.accessmedicine.com

Fig. 4-8 Accessed 07/01/2010

Visual Field

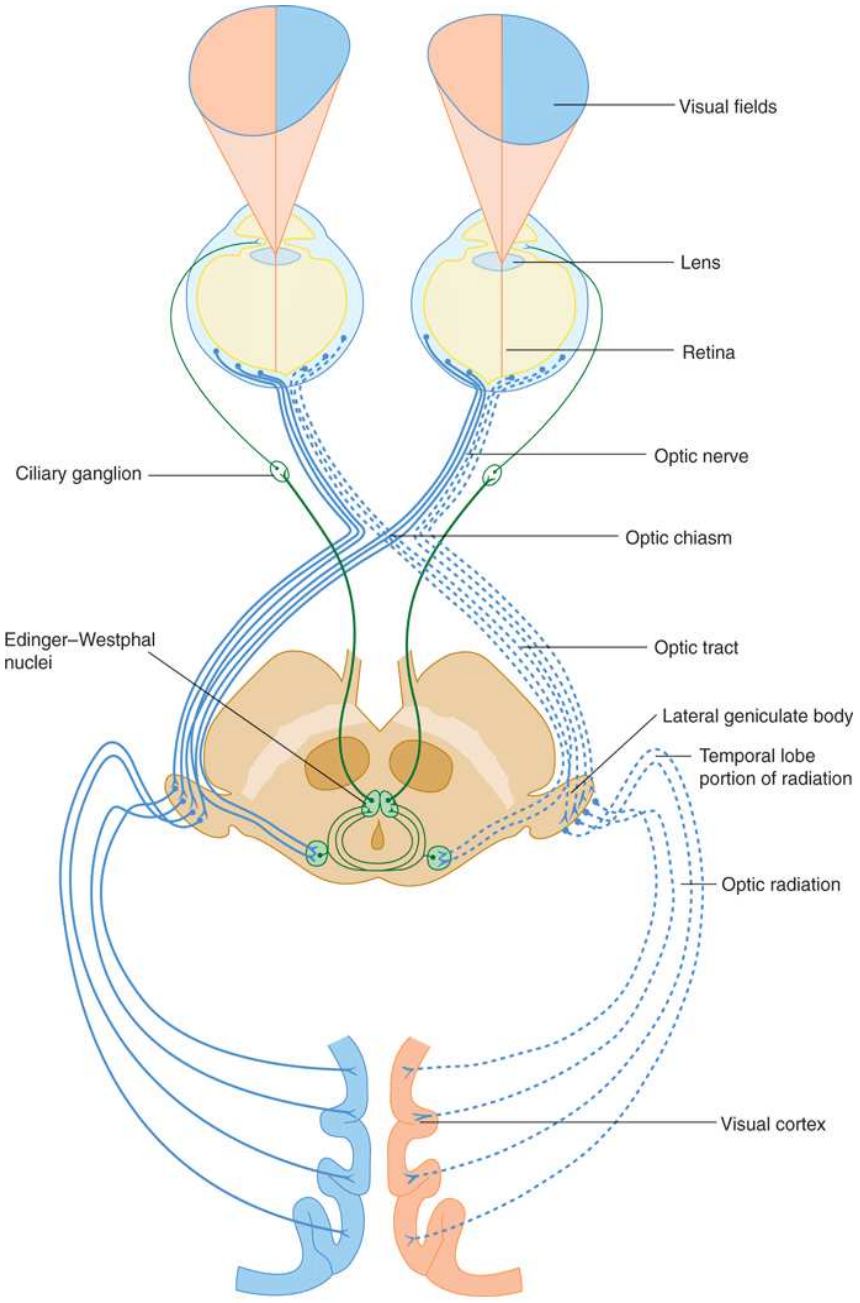


Fig. 15-14 Accessed 07/01/2010

Visual field defects

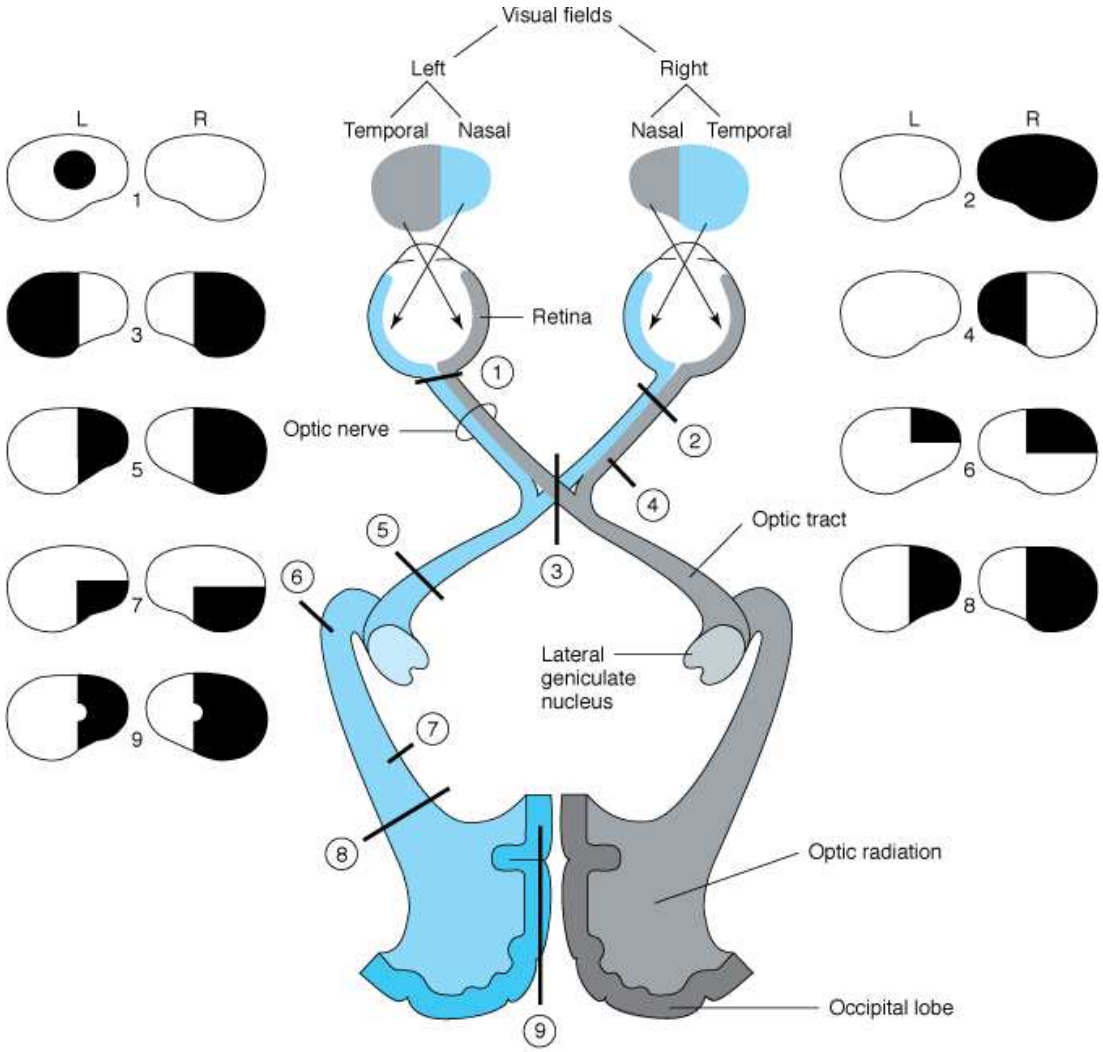


Fig. 4-7 Accessed 07/01/2010

Muscles of the eye

- The levator palpebrae superioris elevates the superior eyelid.
- Sympathetic fibers run with CN III.
- The superior obligue abducts, depresses, and medially rotates the eyeball.
- CN IV.
- The inferior oblique abducts, elevates, and laterally rotates the eyebal.
- CN III.

Muscles of the eye

- The superior rectus elevates, adducts, and rotates the eyeball medially.
- The inferior rectus depresses, adducts and rotates the eyeball medially.
- CN III.
- The medial rectus adducts the eyeball.
- CN III.
- The lateral rectus abducts the eyeball.
- CN VI.

Extra-ocular movements

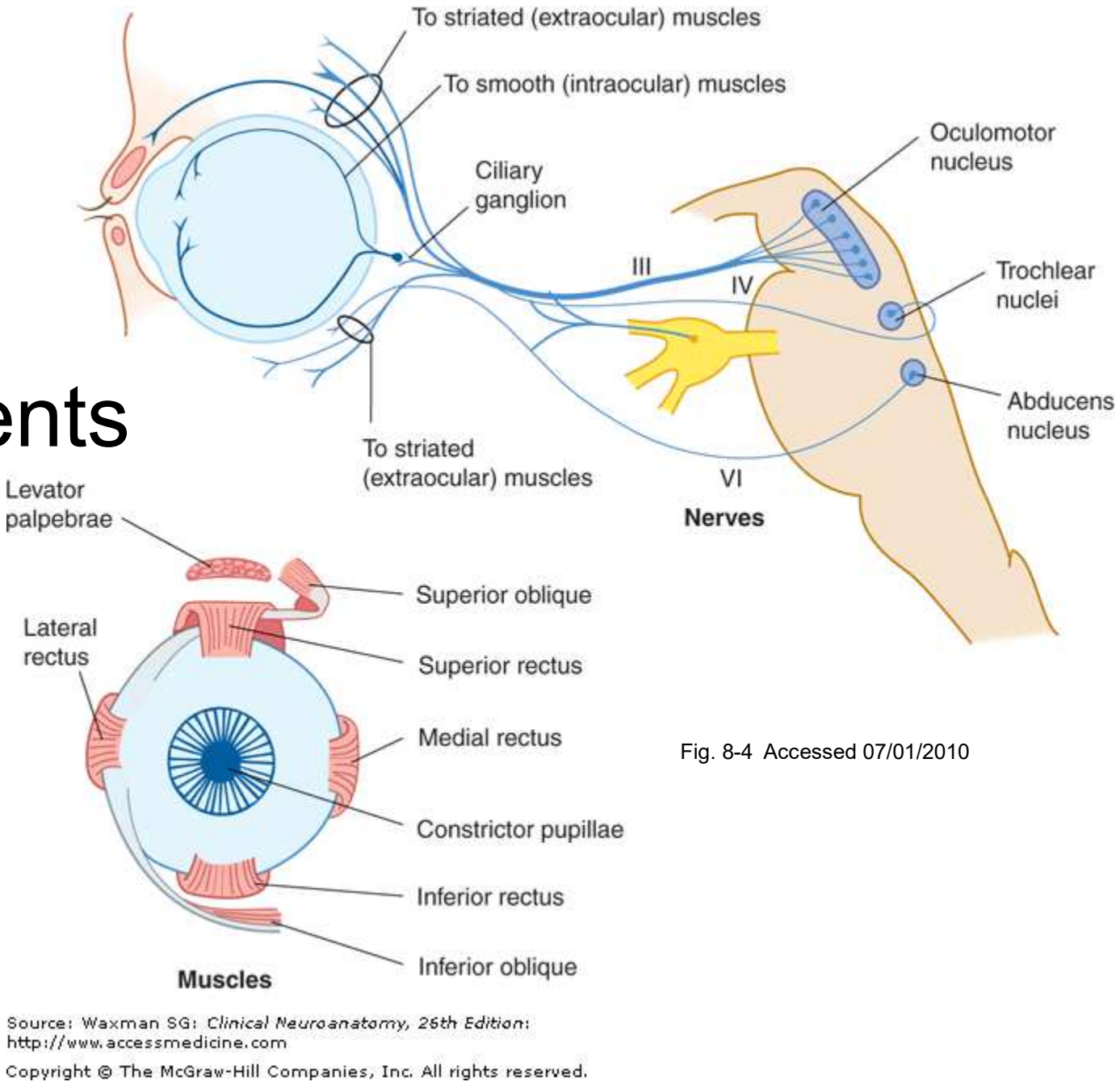


Fig. 8-4 Accessed 07/01/2010

Papillary muscles

- The constrictor pupillae muscle is smooth muscle innervated by postganglionic parasympathetic fibers from the ciliary ganglion.
- Preganglionic parasympathetic axons from the neurons are in the Edinger-Westphal nucleus of the oculomotor complex terminate in the ciliary ganglion.
- The dilator pupillae muscle is innervated by postganglionic sympathetic fibers from the superior cervical ganglion.

Papillary muscles

- The preganglionic neurons are in the intermediolateral cell column of T_1.
- Myoepithelial cells form a layer just anterior to the posterior pigmented epithelium in the dilator pupillae muscle.

Strabismus and amblyopia

- Strabismus is a deviation of the eye.
- It may reflect a problem with the muscles of the eye.
- Surgical correction may prevent permanent misalignment and the development of amblyopia.
- Amblyopia is a reduction in vision that develops in an otherwise normal eye.
- Amblyopia may be caused by suppression of retinal images (as a result of strabismus) and also by opacities of the cornea or lens.
- The underlying cause must be addressed.

Co-ordination of eye movement

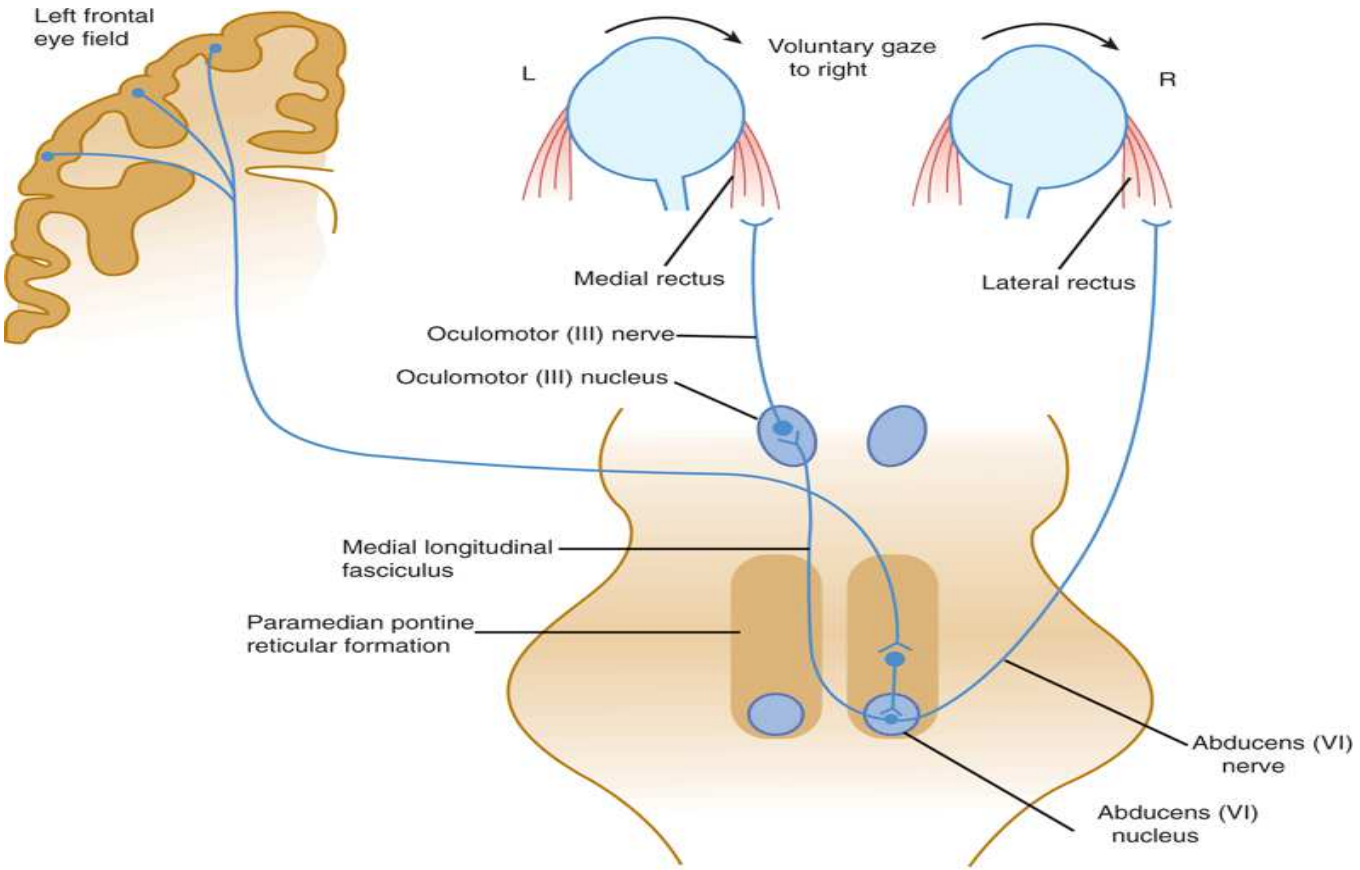
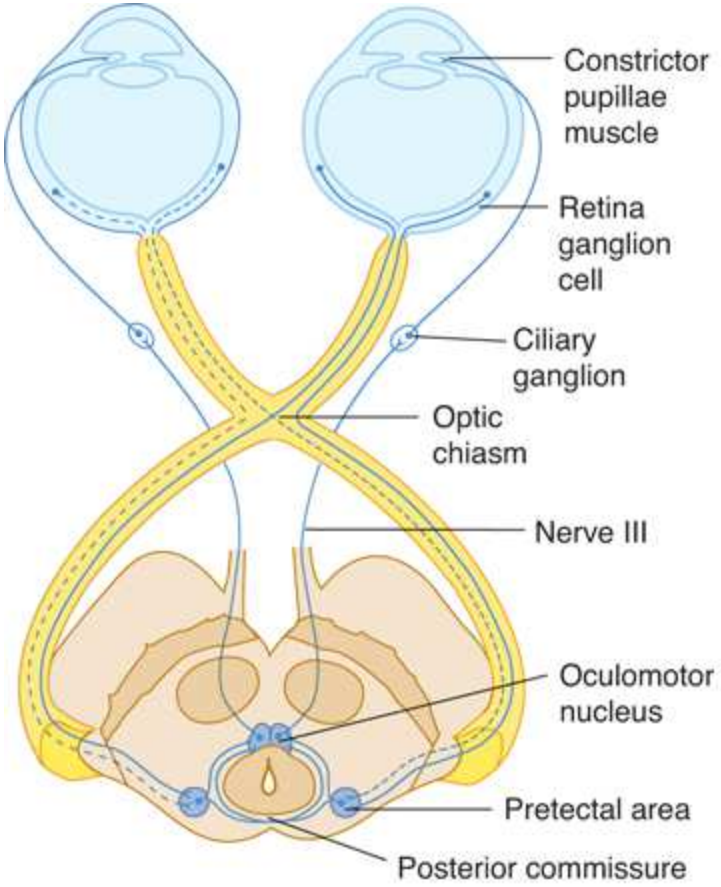


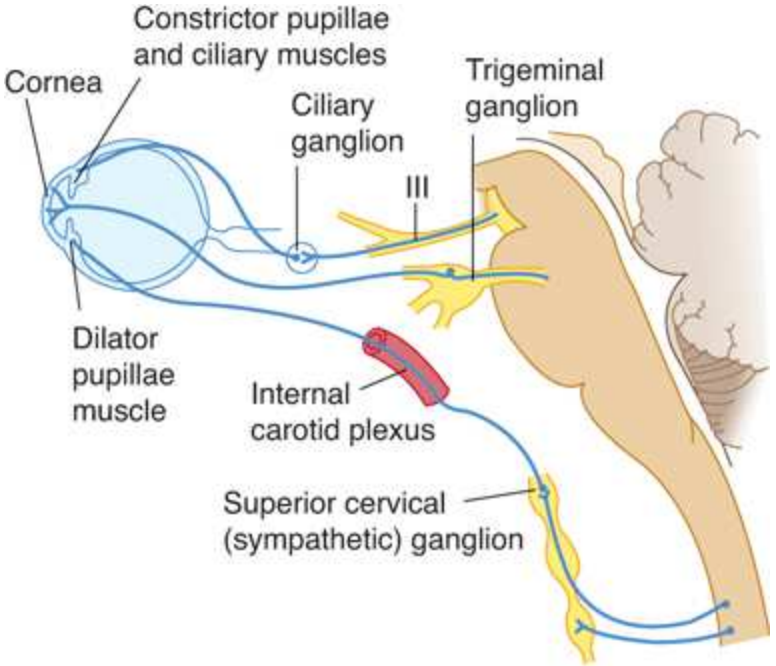
Fig. 8-7 Accessed 07/01/2010

Saccades

- Frontal eye field tonically active bilaterally.
- Activity on side causes contralateral saccade.
- Parietal eye field involved in reflexive saccades.
- Supplementary eye field involved in motor planning.
- Area 22 saccades to sound source.

Pupillary activity





Figs. 8-9 and 8-8 Accessed 07/01/2010

Pupil abnormalities

- Axons from the retina are the afferents to pupillary muscles.
- These axons terminate in the pretectal area and the superior colliculus.
- Unopposed action of the dilator pupillae muscle (innervated by sympathetics) leads to dilated pupil.
- Indicates damage involving the Edinger-Westphal nucleus.

Pupil abnormalities

- The afferent limb of the accommodation reflex passes through the lateral geniculate nucleus.
- The pretectal area serves as a relay in the efferent limb of the reflex.
- Ptosis occurs because of paralysis of Müller’s muscle.