CHAPTER 1

Basic Anatomy

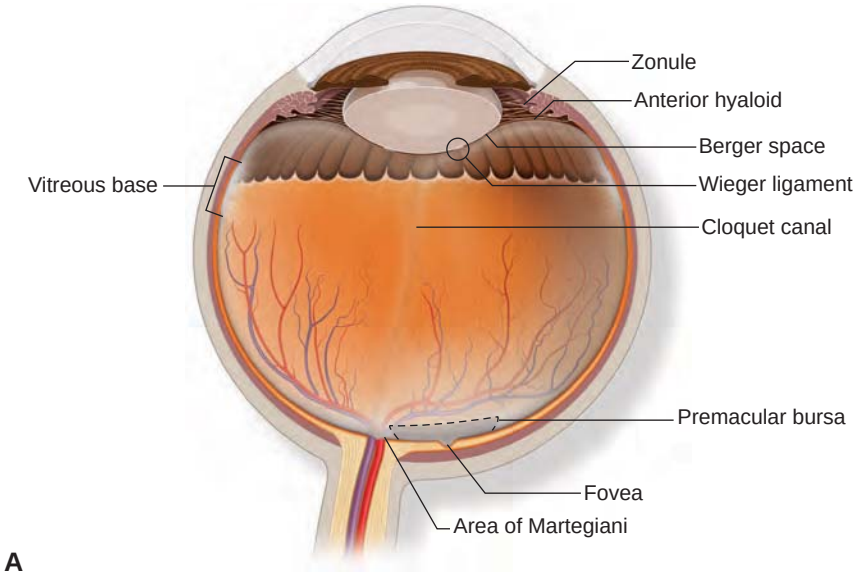
Highlights

- Spectral-domain optical coherence tomography is a noninvasive, high-resolution imaging technique that allows discernment of individual retinal layers which directly correlate with the layers seen in cross-sectional histologic preparations.
- The retinal pigment epithelium has many functions that are critical to retinal function, including absorbing light, forming the outer blood–ocular barrier, maintaining a fluid-free subretinal space, phagocytosing rod and cone outer segments, and recycling visual pigment.
- The choroid has the highest rate of blood flow per unit weight of any tissue in the body, supplying most of the metabolic needs of the retina.

Vitreous

The vitreous is a transparent gel composed principally of water, collagen, and hyaluronic acid. It occupies 80% of the volume of the eye. The vitreous body is divided into 2 main topographic areas: the central, or core, vitreous and the peripheral, or cortical, vitreous. Ultrastructurally, the vitreous gel is made up of collagen fibrils separated by hydrated hyaluronic acid molecules, which act as fillers between adjacent collagen fibrils.

The anterior surface of the vitreous body, called the *anterior cortical gel,* is made up of a condensation of collagenous fibers that attach to the posterior lens capsule, forming the Wieger ligament (Fig 1-1). The retrolental indentation of the anterior vitreous is called the *patellar fossa.* The potential space between the peripheral posterior lens and the anterior cortical gel bordered by the Wieger ligament is called the *Berger space.* In the vitreous base, the collagen fibers are particularly dense; they are firmly attached to the anterior retina and posterior pars plana, creating a ringlike area that extends approximately 2 mm anterior and 3–4 mm posterior to the ora serrata. The vitreous is not only attached at its base; it is also firmly attached to the posterior lens capsule, retinal vessels, optic nerve, and fovea. The densely packed collagen fibrils in the cortical vitreous form the cortical gel. Posteriorly, fibers course in a direction roughly parallel to the inner surface of the retina, forming the preretinal tract. The vitreous attaches to the retinal surface, specifically the internal limiting membrane, via the adhesion molecules fibronectin and laminin. There is no basement membrane between the vitreous base and lens, an area called the *annular gap,* which is a ringlike zone important for diffusion between the aqueous and vitreous



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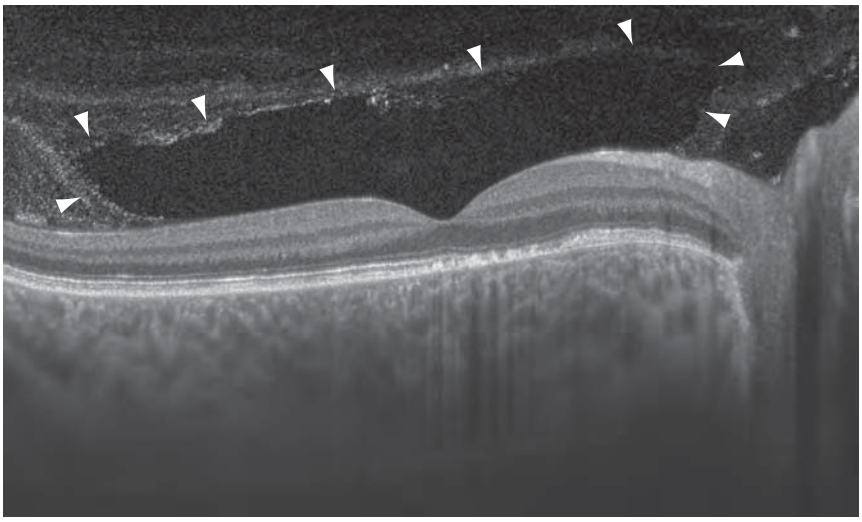

B

Figure 1-1 Cross section of vitreous anatomy. **A,** Diagram of the eye with emphasis on the anatomical features of the vitreous. The vitreous is most firmly attached to the retina at the vitreous base, and it also has adhesions at the optic nerve, along vessels, at the fovea, and to the posterior lens capsule. A prominent area of liquefaction of the premacular vitreous gel is called the *premacular bursa,* or *precortical vitreous pocket*. **B,** Swept-source optical coherence tomography image of the posterior vitreous and macular region demonstrates the signal void in the vitreous cavity in front of the macula that represents the premacular bursa *(arrowheads)*. Note also the very thick macular choroid and photoreceptor disruption in the central macula, extending nasally. *(Part A illustration by Mark M. Miller; part B courtesy of SriniVas Sadda, MD.)*

compartments. The space known as the *premacular bursa,* or *precortical vitreous pocket* (see Fig 1-1), which is anterior to the posterior attachment of the vitreous to the macula, is believed to decrease the tractional forces generated during ocular motion. The vitreous inserts on the edges of the optic nerve head, creating a funnel-shaped void of vitreous. This void is the opening of the Cloquet canal and is referred to as the *area of Martegiani.* The anatomy of the vitreous is difficult to delineate in vivo; however, the vitreous appears to contain interconnected cisterns and canals, most notably the ciliobursal canal that connects the ciliary body and macula.

The vitreous also contains hyalocytes, which arise from bone marrow–derived stem cells. Oxygen is derived through diffusion from the choroidal and retinal circulation. Hyalocytes consume most of this, limiting the amount of oxygen that reaches the lens and anterior segment. However, the vitreous has high ascorbate levels, which protect against oxidative damage (eg, to the lens).

Worst JGF, Los LI. *Cisternal Anatomy of the Vitreous.* Kugler; 1995.

Neurosensory Retina

Retinal Topography

The central area of the retina, or macula (sometimes called the *area centralis*), measures approximately 5.5 mm in diameter and is centered between the optic nerve head and the temporal vascular arcades (Fig 1-2, Table 1-1). On histologic examination, this area features 2 or more layers of ganglion cells, accounting for half of all ganglion cells in the retina. Oxygenated carotenoids, in particular lutein and zeaxanthin, accumulate within the central macula and contribute to its yellow color.

The central 1.5 mm of the macula, which is called the *fovea* (or *fovea centralis*), is specialized for high spatial acuity and color vision. The fovea has a margin; a downward slope; and a floor known as the *foveola,* a 0.35-mm-diameter region where the cones are

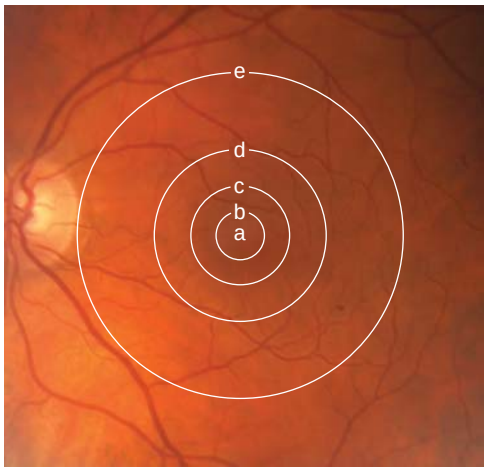

Figure 1-2 Anatomical macula, also known as the *area centralis* or *posterior pole.* The anatomical fovea and foveola are contained within the center of the anatomical macula. The borders of anatomical areas are indicated by letters: a = umbo; b = foveola; c = fovea; zone between c and d = parafoveal macula; zone between d and e = perifoveal macula; e = macula. *(Courtesy of Hermann D. Schubert, MD.)*

Table 1-1 Anatomical Terminology of the Macula (Area Centralis)

Term	Synonym	Histologic Definition	Clinical Observation and Size
Macula	Posterior pole Area centralis	Contains 2 or more ganglion cell layers	Area 5.5 mm in diameter centered between vascular arcades and optic nerve head; approx. 4.0 mm temporal and 0.8 mm inferior to center of optic nerve head
Perifovea		From the outer limit of the macula to the outermost limit of the parafovea	Ring 1.5 mm wide surrounding the parafovea
Parafovea		Margin, where the ganglion cell layer, inner nuclear layer, and outer plexiform (Henle fiber) layer are thickest (ie, the retina is thickest)	Ring 0.5 mm wide surrounding the fovea
Fovea	Fovea centralis	A depression in the inner retina; has a margin, slope, and floor, the photoreceptor layer of which consists entirely of cones	A concave central retinal depression seen on slit-lamp examination; 1.5 mm in diameter (approx. 1 disc diameter, or 5°)
Foveola		The floor of the fovea features cones only, arranged in the shape of a circle, where the inner nuclear layer and ganglion cell layer are laterally displaced	0.35 mm in diameter, usually smaller than the foveal avascular zone
Umbo	Fixation light reflex	Small (150–200 μm) depression at center of floor of foveola; features elongated cones	Observed point corresponding to the normal light reflex but not solely responsible for this light reflex

slender, elongated, and densely packed. At the very center of the foveola is a small depression, 150–200 μm in diameter, known as the *umbo.* Within the fovea is a region devoid of retinal vessels, the *foveal avascular zone (FAZ)*. The diameter of the FAZ ranges from 250 to 600 μm or greater. The geometric center of the FAZ is often taken to be the center of the macula and thus the point of fixation; it is an important landmark in fluorescein angiography. Surrounding the fovea is the *parafovea,* a 0.5-mm-wide ring where the ganglion cell layer, inner nuclear layer, and outer plexiform layer (also known as *Henle fiber layer*) are thickest. Surrounding this zone is the *perifovea,* a ring approximately 1.5 mm wide. Thus, the umbo forms the center of the macula, and the periphery of the perifovea forms its margin.

The retina outside the macula, sometimes referred to as the *extra-areal periphery,* is commonly divided into a few concentric regions, starting with the *near periphery,* a 1.5-mm ring peripheral to the temporal major vascular arcades. The *equatorial retina* is the retina around the equator, and the region anterior to the equatorial retina is called the *peripheral retina.* In the far periphery, the border between the retina and the pars plana is called the *ora serrata* (Fig 1-3). The posterior border of the vitreous base is typically located between the ora serrata and the equator of the eye. This region is where most retinal tears occur.

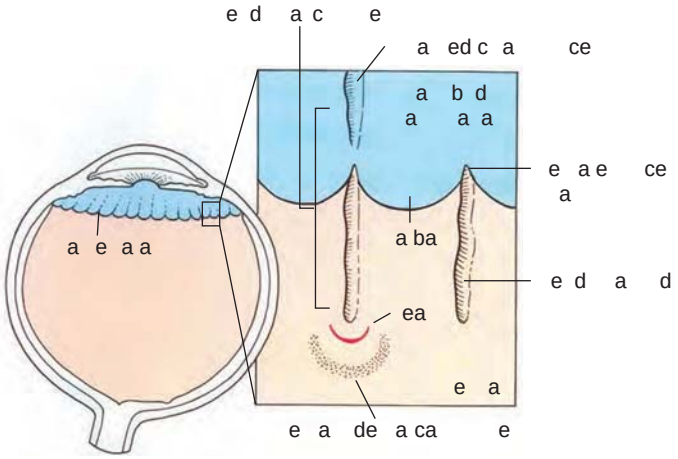

Figure 1-3 Schematic of the ora serrata, detail of which shows an ora bay, dentate process, and meridional folds (pleats of redundant retina). Tears may occur at the posterior end of such folds. Pigmentary demarcation lines may be a marker of chronicity. *(Used with permission from Federman JL, Gouras P, Schubert H, et al.* Retina and Vitreous. *Mosby; 1998. Podos SM, Yanoff M, eds.* Textbook of Ophthalmology; *vol 9.)*

Jetties of retinal tissue, called *dentate processes*, extend anteriorly into the pars plana. These processes are more prominent nasally. *Ora bays* are posterior extensions of the pars plana toward the retina. On occasion, dentate processes may wrap around a portion of an ora bay to form an enclosed ora bay. A *meridional fold* is a radially oriented, prominent thickening of retinal tissue that extends into the pars plana. When aligned with a ciliary process, such folds are known as a *meridional complex*.

Polyak SL. *The Retina.* University of Chicago Press; 1941.

Retinal Layers and Neurosensory Elements

The layers of the retina can be seen in cross-sectional histologic preparations, and most layers can be identified with spectral-domain optical coherence tomography (SD-OCT) (see Chapter 2, Activity 2-1), a noninvasive high-resolution imaging technique. The layers of the retina as seen in histologic sections and in corresponding OCT cross-sectional images are shown in Figure 1-4.

To reach the photoreceptors—retinal rods and cones—light must travel through the full thickness of the retina. The density and distribution of photoreceptors vary with their topographic location. In the fovea, the cones, which are predominantly red- and green-sensitive, are densely packed; their density exceeds 140,000 cones/mm^2. The foveola has no rods; the fovea contains only photoreceptors and processes of Müller cells. The number of cone photoreceptors decreases rapidly in areas farther from the center, even though 90% of cones overall reside outside the foveal region. The rods have their greatest density in a zone lying approximately 4 mm from the foveal center, or 12° from fixation, where they reach a peak density of about 160,000 rods/mm^2. The density of rods also decreases toward the periphery. A small area of high rod concentration (176,000 rods/mm^2) has

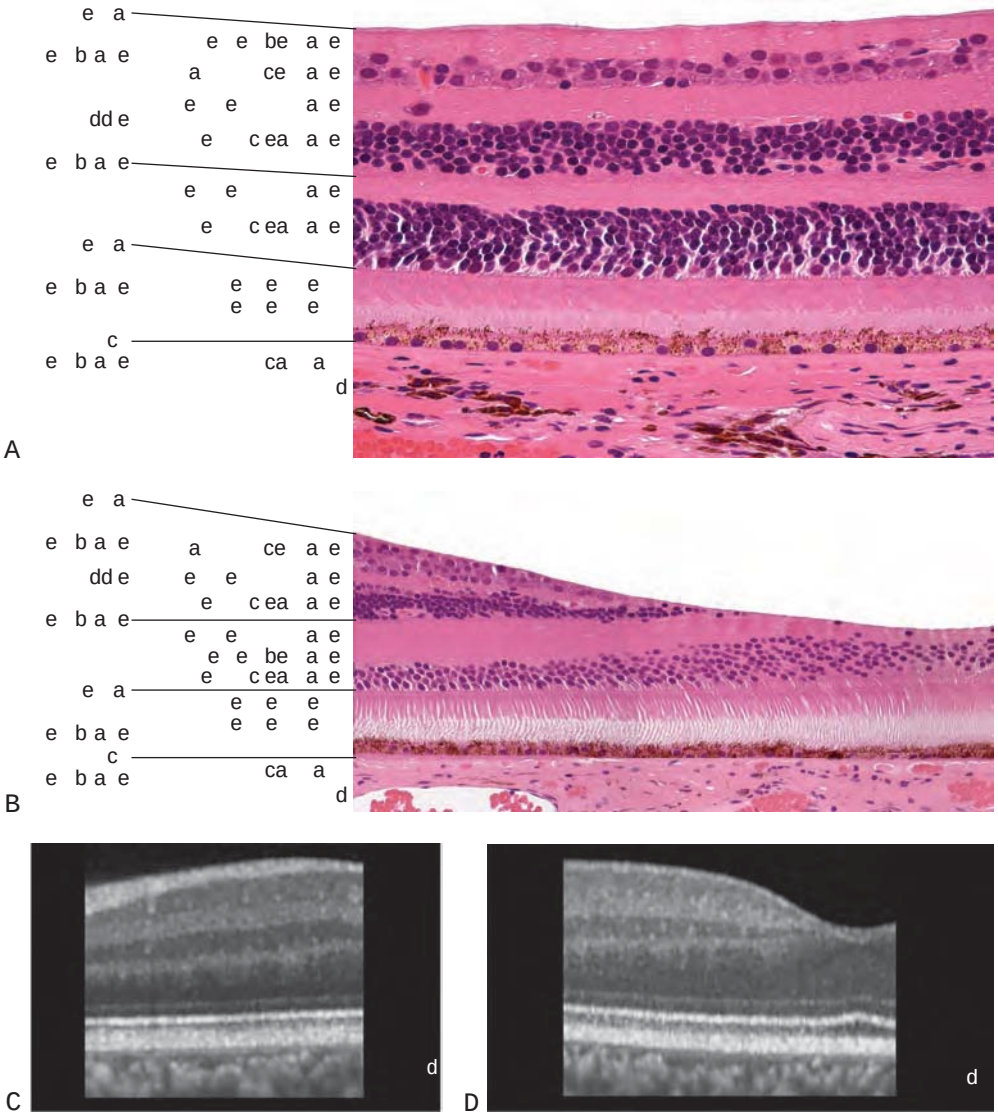

Figure 1-4 Cross-sectional images of peripheral macular **(A, C)** and foveal **(B, D)** retina. **A, B,** Photomicrographs (hematoxylin-eosin stain) of retina and choroid *(labeled)*. In the fovea **(B),** the inner cellular layers are laterally displaced, and there is an increased density of pigment in the retinal pigment epithelium (RPE). Note that on the right edge of the image, the inner cellular layers are laterally displaced. This allows incident light to fall directly onto the photoreceptors, avoiding the inner retinal layers, thereby reducing the potential for scattering of light. **C, D,** Corresponding spectral-domain optical coherence tomography cross-sectional images of macular and foveal retina. Layers labeled from inner to outer retina, following the path of incident light: internal limiting membrane (ILM), nerve fiber layer (NFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), external limiting membrane (ELM), ellipsoid zone (EZ), RPE, and choroid. *(Parts A and B courtesy of Ralph Eagle, MD; parts C and D courtesy of Hannah J. Yu, BS, and Charles C. Wykoff, MD, PhD.)*

been found in the superior macula. The arrangement of rods and cones can be visualized with noninvasive adaptive optics imaging (Fig 1-5).

Each photoreceptor cell consists of an outer segment and an inner segment. The light-sensitive molecules in rods and cones are derived from vitamin A and are contained in the disc membranes of the photoreceptor outer segments (Fig 1-6). The discs are attached to a cilium, which is rooted through neurotubules in the ellipsoid and myoid of the inner segment. The ellipsoid, which is adjacent to the cilium, contains mitochondria and is

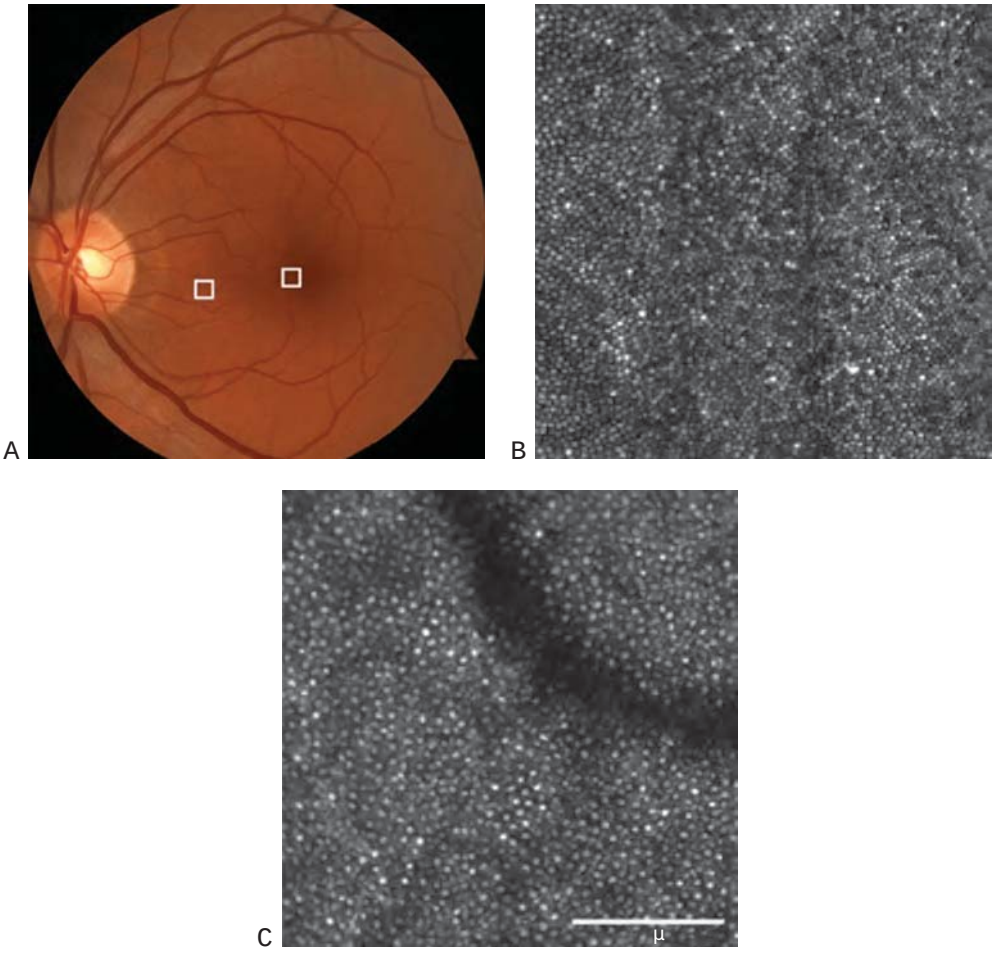

Figure 1-5 Comparison of a conventional fundus photograph and confocal adaptive optics scanning laser ophthalmoscope (AOSLO) images of a healthy left-eye macula. **A,** In the fundus photograph, the white box that is closer to the fovea is 0.5° from fixation and represents a 300 × 300–μm area of macula. **B,** The corresponding AOSLO image of the retina within that white box shows cones that are smaller and very tightly packed; no rods are visible. **C,** AOSLO image corresponding to the white box in **A** that is closer to the optic nerve and 7° from fixation and also represents a 300 × 300–μm area of macula. The image shows cones that are larger and less densely packed; intervening rods are starting to become visible. *(Courtesy of Mina M. Chung, MD, and Hongxin Song, MD, PhD.)*

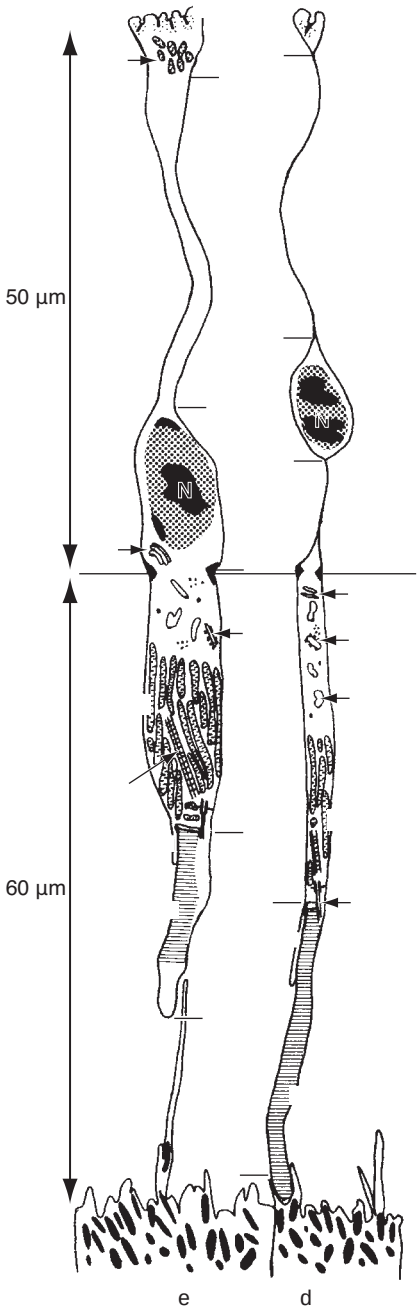

Figure 1-6 Schematic of a cone cell *(left)* and a rod cell *(right)* in the peripheral retina. In the diagram, light enters from the top; the pigmented epithelium is on the distal side. C = cilium; CP = cone cell pedicle; DM = membranous discs; ELM = external limiting membrane; G = Golgi apparatus; IF = inner fiber; IS = inner segment; M = mitochondria; MV = microvilli of pigment epithelial cells; N = nucleus; OF = outer fiber; OS = outer segment; P = perikaryon; PC = processus calycoides; PE = pigment epithelium; R = free ribosomes; RER = rough endoplasmic reticulum; RF = rootlet fiber; S = rod cell spherule; SER = smooth endoplasmic reticulum. *(Adapted with permission from Springer Nature. Krebs W, Krebs I.* Primate Retina and Choroid. Atlas of Fine Structure in Man and Monkey. *1991.)*

responsible for the cone shape. The myoid, which is closer to the photoreceptor nucleus, contains endoplasmic reticulum. The mitochondria, cilia, and inner discs together form the *inner-outer segment junction,* which provides evidence of the origin of the photoreceptor as a modified sensory cilium prone to the full range of ciliopathies. Rod outer segments may contain up to 1000 discs stacked like coins. These discs are renewed in and shed from the outer retina and are phagocytosed by the retinal pigment epithelium (RPE) for processing and recycling of components.

Cone photoreceptors have a 1-to-1 synapse with a type of bipolar cell known as a *midget bipolar cell.* Other types of bipolar cells also synapse with each cone. Conversely, more than 1 rod—and sometimes more than 100 rods—converge on each bipolar cell. Bipolar cells, the first neurons of the visual pathway, synapse with ganglion cells, the second neurons of the visual pathway, in the inner plexiform layer (IPL). The ganglion cells summate responses from bipolar and amacrine cells and develop action potentials that are conducted to the dorsolateral geniculate nucleus and the third neuron in the brain. Amacrine cells in the inner portion of the inner nuclear layer (INL) help process signals by responding to specific alterations in retinal stimuli, such as sudden changes in light intensity or the presence of certain sizes of stimuli. The INL is composed of horizontal cells, bipolar cells, and amacrine cells. In the nerve fiber layer (NFL), axons of the ganglion cell layer (GCL) course along the inner portion of the retina to form the optic nerve, a brain tract. The internal limiting membrane (ILM), which is not a true membrane but is formed by the footplates of Müller cells, is attached to the posterior cortical gel of the vitreous (Fig 1-7).

Two additional intraretinal "membranes" identified by histologists, the external limiting membrane (ELM) and the middle limiting membrane (MLM), are actually junctional systems, not true membranes. At the outer extent of the Müller cells, zonular attachments between photoreceptors and Müller cells form the ELM, a structure visible with both light microscopy and OCT. Thus, the Müller cells, whose nuclei reside in the INL, course through almost the entire thickness of the retina. The inner third of the outer plexiform layer (OPL) has a linear density in which synaptic and desmosomal connections occur between the photoreceptor inner fibers and the processes of the bipolar cells. This linear density, which is also apparent with OCT, is the junctional system that has been called the MLM.

Retinal Vasculature and Oxygen Supply

The vascular supply of the retina comes from the retinal circulation for the inner retina and indirectly from the choroidal circulation for the avascular outer retina. The central retinal artery (a branch of the ophthalmic artery) enters the eye and divides into 4 branches, each supplying blood to a quadrant of the retina. These branches are located in the inner retina. A cilioretinal artery, derived from the ciliary circulation, supplies a portion of the inner retina in approximately one-third of human eyes (Fig 1-8). On a tissue level, the retina is supplied by up to 4 layers of vessels:

- *radial peripapillary capillary network,* located in the NFL and around the optic nerve head
- *superficial vascular plexus,* which includes the *superficial capillary plexus,* in the retinal GCL
- *deep capillary complex* with 2 capillary beds, one on either side of the INL

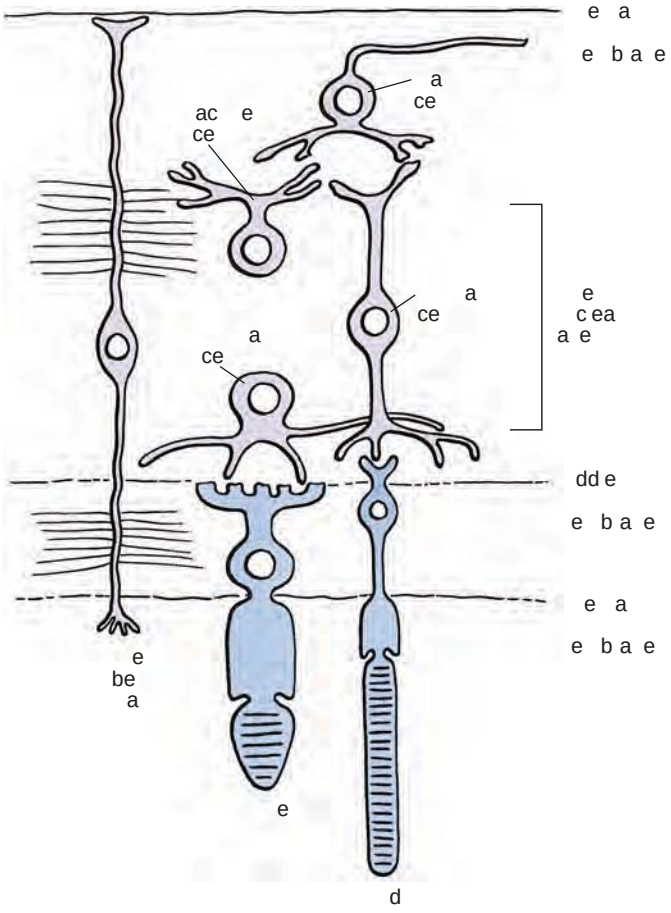

Figure 1-7 Schematic of the neuronal connections in the retina and participating cells. In the diagram, light enters from the top, at the ganglion cell layer. *(Redrawn from Federman JL, Gouras P, Schubert H, et al.* Retina and Vitreous. *Mosby; 1988. Podos SM, Yanoff M, eds.* Textbook of Ophthalmology; *vol 9. Illustration by Mark Miller.)*

Although the superficial layer of the deep capillary plexus is sometimes referred to as the *intermediate capillary plexus*, typically both layers are collectively referred to as the *deep capillary complex*. OCT angiography can visualize these distinct capillary layers. The retinal vasculature, including its capillaries, retains the blood–brain barrier with tight junctions between capillary endothelial cells. Blood from the capillaries is collected by the retinal venous system; it eventually leaves the eye through the central retinal vein by way of branch retinal veins.

The outer retinal layers, beginning with the OPL, derive their oxygen supply from the choroidal circulation. The exact boundary between the retinal vascular supply and the diffusion from the choriocapillaris varies according to the topographic location, retinal thickness, and amount of light present. For additional discussion, see the choroid section later in this chapter, as well as Part I, Anatomy, of BCSC Section 2, *Fundamentals and Principles of Ophthalmology*.

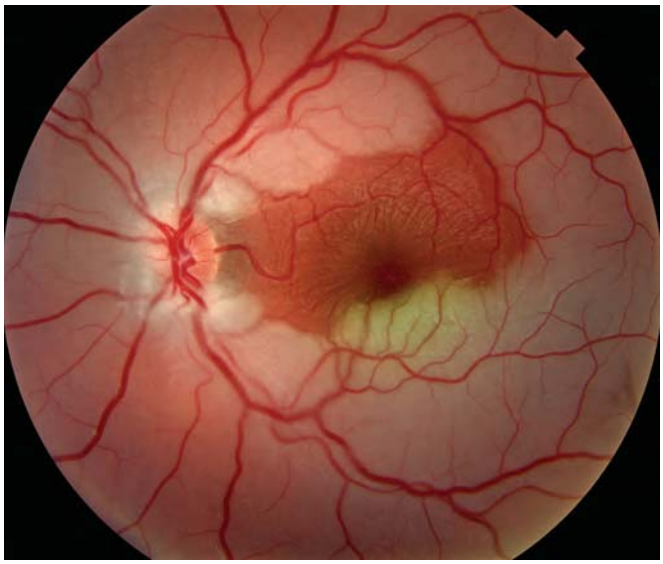

Figure 1-8 A central retinal artery occlusion in a young patient with a previously unknown patent foramen ovale. Presumably, an embolus from the systemic circulation passed through the patent foramen ovale and lodged in the central retinal artery, occluding its blood flow. Fortunately, a cilioretinal artery supplied part of the eye's retina. Note the retinal ischemic whitening in the distribution of the central retinal artery but preservation of the normal retinal transparency in the zone supplied by the cilioretinal artery. *(Used with permission from Ho IV, Spaide RF. Central retinal artery occlusion associated with a patent foramen ovale.* Retina. *2007;27(2):259–260. doi:10.1097/IAE.0b013e318030cc2)*

Retinal Pigment Epithelium

The RPE is a monolayer of pigmented, hexagonal cells derived from the outer layer of the optic cup. This layer is continuous with the pigment epithelium of the ciliary body and iris. In the macula, RPE cells are taller and denser than in the periphery. The lateral surfaces of adjacent cells are closely apposed and joined by tight junctional complexes (zonulae occludentes) near the apices, forming apical girdles and the outer blood–ocular barrier. Each RPE cell has an apex and base; the apical portion envelops the outer segments of the photoreceptor cells with villous processes (Fig 1-9). The basal surface of the cells shows a rich infolding of the plasma membrane. The basement membrane does not follow these infoldings. The cytoplasm of the typical RPE cell contains several melanosomes, each designed to absorb light. Melanosomes are spheroidal; their melanin is distributed on protein fibers.

The RPE contributes to retinal function in several ways; it

- absorbs light
- phagocytoses rod and cone outer segments
- participates in retinal and polyunsaturated fatty acid metabolism
- forms the outer blood–ocular barrier
- maintains a fluid-free subretinal space
- heals and forms scar tissue
- regenerates and recycles visual pigment

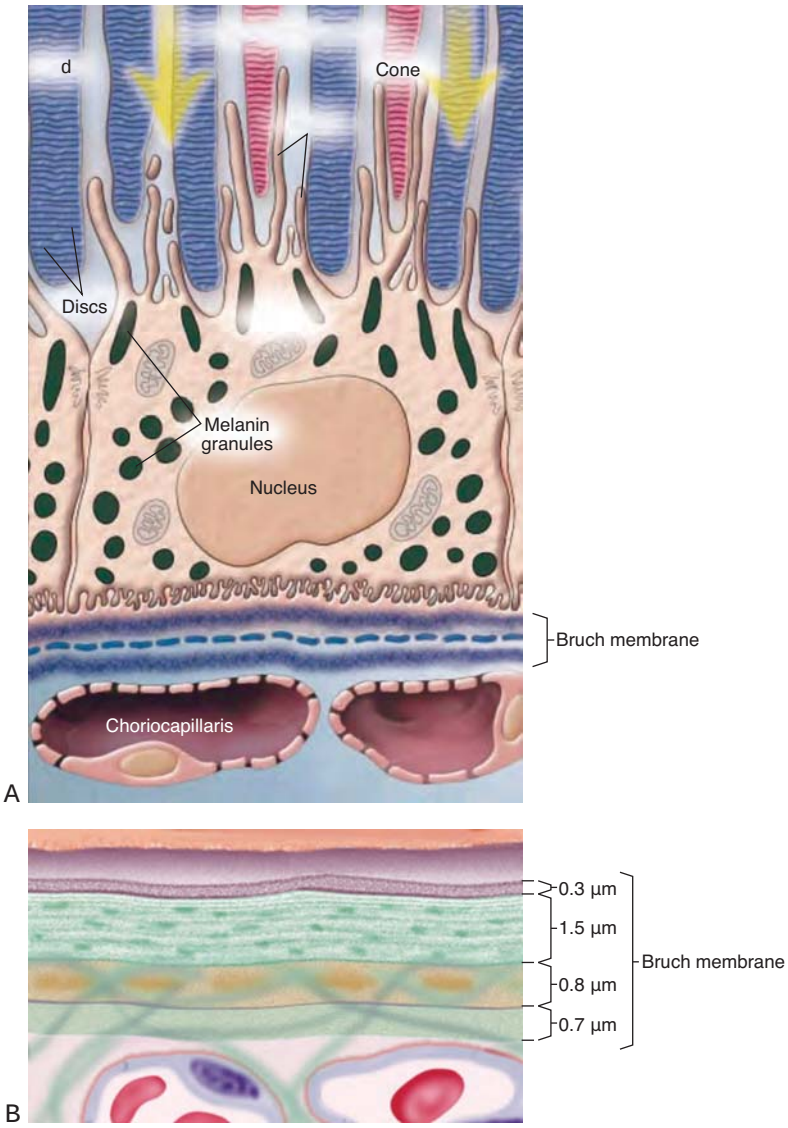

Figure 1-9 Illustrations of Bruch membrane. **A,** The RPE and its relationship to the photoreceptors and Bruch membrane. Note the interdigitations; villi from the RPE make contact with the outer segments of both rods and cones. **B,** The folded plasmalemma of the RPE rests on its smooth basement membrane (0.3 µm thick) bordering the inner collagenous zone (1.5 µm thick). The outer collagenous zone (0.7 µm thick) borders the elastic layer (0.8 µm thick) and is continuous with intercapillary bridges and the subcapillary fibrous tissue. APRP = apical process of the RPE. *(Part A courtesy of the University of Rochester; part B illustration by Daniel Casper, MD, PhD.)*

RPE cells serve a phagocytic function, continually ingesting the disc membranes shed by the outer segments of photoreceptor cells. Over the course of a lifetime, each RPE cell is thought to phagocytose billions of outer segments. This process of shedding, phagocytosis, and photoreceptor renewal follows a daily (circadian) rhythm. Rods shed discs at dawn,

and cones shed them at dusk. The ingested outer segments are digested gradually, broken down by enzymes from lysosomes.

Visual pigments contain 11-*cis*-retinaldehyde that is converted to 11-*trans*-retinaldehyde in the photoreceptor outer segments. Most of the regeneration of 11-*cis* to the 11-*trans* configuration occurs in the RPE and requires a highly efficient transfer of metabolites from the outer segments to the RPE cells and back. The interdigitation of the RPE and outer segments facilitates the regeneration by increasing the surface area of contact and allowing proximity. The visual pigments' biochemical cycle is discussed in more detail in BCSC Section 2, *Fundamentals and Principles of Ophthalmology.*

A variety of pathologic changes—caused by such factors as genetic defects, drugs, dietary insufficiency (of vitamin A), or senescence—can impair the process of phagocytosis and renewal. Physical separation of the retina from the RPE, which occurs when subretinal fluid (ie, retinal detachment) or blood is present, also disrupts the important exchange of metabolites.

The RPE functions as a barrier to prevent diffusion of metabolites between the choroid and the subretinal space. Because of this, the environment of the photoreceptors is largely regulated by the selective transport properties of the RPE. The RPE has a high capacity for water transport, so in a healthy eye, fluid does not accumulate in the subretinal space. This RPE-mediated dehydration of the subretinal space also modulates the bonding properties of the interphotoreceptor matrix, which acts as a bridge between the RPE and photoreceptors and helps bond the neurosensory retina to the RPE. With deterioration or loss of the RPE, there is corresponding atrophy of the overlying photoreceptors and underlying choriocapillaris.

Bruch Membrane

The basal portion of the RPE is attached to Bruch membrane, which has 5 layers. Starting with the innermost, the layers are as follows (see Fig 1-9):

- basement membrane of the RPE
- inner collagenous zone
- middle layer of elastic fibers
- outer collagenous zone
- basement membrane of the endothelium of the choriocapillaris

Degeneration of Bruch membrane over time is associated with buildup of lipids and oxidatively damaged materials as well as calcification. In some disease states, extensive Bruch membrane calcification can lead to fractures, known as *angioid streaks.* In age-related macular degeneration, areas of calcification with microscopic breaks have also been found.

Choroid

The choroid nourishes the outer portion of the retina. Blood enters the choroid, which consists of 3 layers of vessels, through the posterior ciliary arteries (Fig 1-10). The outer layer

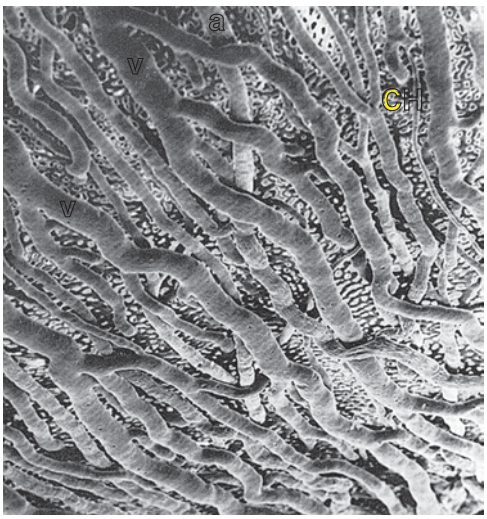

Figure 1-10 Scanning electron micrograph (70×) of the choroid. Vascular cast of the choroid from the posterior pole of a 62-year-old man, showing arteries (a), veins (v), and the choriocapillaris (CH). *(Courtesy of A. Fryczkowski, MD.)*

of large-caliber vessels, known as the *Haller layer,* is relatively thick. The vessels in this layer divide into smaller-diameter vessels and precapillary arterioles, which make up the middle layer, known as the *Sattler layer*. These smaller vessels distribute the blood throughout the choroid, reducing arterial pressure to the relatively low pressure found in the innermost layer, the *choriocapillaris.*

The choroid has a maximal thickness posteriorly. On histologic examination, it is 0.22 mm thick in the central macular region, becoming progressively thinner anteriorly; at the ora serrata, it is 0.1 mm thick. Subfoveal choroidal thickness, measured by SD-OCT in vivo in healthy volunteers with a mean age of 50 years, is approximately 287 μm. However, thickness changes with age and disease states of the eye. The presence of thin choroid (leptochoroid) and thick choroid (pachychoroid) may be associated with ocular diseases.

In the posterior pole, the choriocapillaris forms a plexus of capillaries, even though the capillaries themselves are not arranged strictly into lobules. The capillary arrangement becomes more irregular toward the periphery, where the capillaries are arranged more radially. Interspersed between the vessels of the choroid are loose connective tissue, fibroblasts, and melanocytes.

After passing through the choriocapillaris, the blood is collected in venules, which coalesce into collecting channels, or ampullae, of the vortex veins. Most eyes have 4 or 5 vortex veins, which exit the eye at or posterior to the equator. The vortex veins drain into the superior and inferior ophthalmic veins.

The choroid supplies the metabolic needs of the retina, which has one of the highest metabolic rates per gram of tissue in the body. In some estimates, the choroidal circulation supplies 90% of the oxygen consumed by the retina, primarily by the photoreceptors. The choroid also has the highest rate of blood flow per unit weight of any tissue in the body, and the venous blood exiting the choroid still has a very high oxygen tension. The RPE cells, which are anatomically closely associated with the choriocapillaris, are exposed to the highest oxygen tensions of any perfused tissue, increasing the risk of oxidative damage.

The rapid flow in the choroid also acts as a heat sink, removing thermal energy obtained by light absorption.

Mrejen S, Spaide RF. Optical coherence tomography: imaging of the choroid and beyond. *Surv Ophthalmol.* 2013;58(5):387–429.

Sclera

The sclera is composed of collagen and a few elastic fibers embedded in a matrix of proteoglycans. It terminates at the histologists' limbus. The sclera does not have uniform thickness. It is thinnest immediately behind the insertion of the rectus muscles, whereas it is thicker at the posterior pole, around the optic nerve head.

The sclera is normally permeable to the passage of molecules in both directions. Up to 40% of the aqueous leaves the eye via uveoscleral outflow, making the sclera an important path of fluid movement. Scleral permeability allows drugs to be delivered to the eye by means of injection into the sub-Tenon space. The sclera is a hydrophilic tissue and is therefore only variably permeable to hydrophobic or amphiphilic substances or medications. This characteristic is an important consideration for periocular injection of pharmacologic agents.

Hogan MJ, Alvarado JA, Weddell JE. *Histology of the Human Eye.* Saunders; 1971:chaps 5, 8, 9, 11.