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To all the readers of **JAYPEE HIGHLIGHTS MEDICAL PUBLISHERS**, whose support and interest for what we write is the main stimulus for the major commitment we have made to continuously serve ophthalmologist all over the world.

To Mr. Jitendar P. Vij for his perseverance and support.

#### PREFACE

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It is a pleasure to introduce Retinal and Vitreoretinal Diseases and Surgery by Samuel Boyd, MD, Rafael Cortez, MD and Nelson Sabates, MD. This volume contains chapters written by global leaders in the field, and has both breadth and depth in covering clinically relevant and important topics. In forty-one chapters the editors have selected authors with particular areas of expertise, and areas of interest not only to vitreoretinal surgeons, but also to medical retina specialists, comprehensivists and trainees.

With 718 pages of content and 1000 color images and illustrations this book provides not only the fundamentals but the focus needed for the clinician to care for patients with both straightforward and complex retinal disease.

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# Section 1 Diagnostic Systems in Retina

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## The Normal Retina

SAMUEL BOYD, MD

In vertebrate embryonic development, the retina and the optic nerve originate as outgrowths of the developing brain, so the retina is considered part of the central nervous system (CNS). It is the only part of the CNS that can be imaged directly.

The retina ranges in thickness from about 100-500  $\mu$ m. It is a composite of numerous cellular and synaptic layers which can be grossly split into an outer epithelial layer (referred to as the retinal epithelium or retinal pigment epithelium) and an inner sensory layer (referred to as the sensory retina or neuroretina). The retina is one of the most metabolically active tissues in the body. Its major function is to convert light energy into chemical and electrical energy so that vision can occur (if a functional brain is present).

The retina is a complex, layered structure with several layers of neurons intercon-

nected by synapses. The only neurons that are directly sensitive to light are the photoreceptor cells. These are mainly of two types: the rods and cones. Rods function mainly in dim light, while cones support daytime vision. A third, much rarer type of photoreceptor, the photosensitive ganglion cell, is important for reflexive responses to bright daylight.

Neural signals from the rods and cones undergo complex processing by other neurons of the retina. The output takes the form of action potentials in retinal ganglion cells whose axons form the optic nerve. Several important features of visual perception can be traced to the retinal encoding and processing of light.

#### **Functional Anatomy**

The vital structures of the retina are conveniently arranged for us in distinct

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layers. These are clearly shown in Figure 1. The order of retinal layers starting from outer to inner layers (that is, from choroid to vitreous) is as follows: Retinal pigment epithelium, Photoreceptor outer segments, Photoreceptor inner segments, Outer or external limiting membrane, Outer or external nuclear layer, Outer or external plexiform layer, Inner nuclear layer, Inner plexiform layer, Ganglion cell layer, Nerve fiber layer, Internal limiting membrane.

The outermost layers next to the choriocapillaris are Bruchs membrane and the retinal pigment epithelium (RPE). Bruch's membrane allows passage of nutrients from the choriocapillaris to the retina, while acting as a barrier to invasion of the retina by its vessels. The RPE are supporting cells for the neural portion of the retina and are important for photopigment regeneration. The RPE is dark with melanin, which decreases light scatter within the eye. The rod and cone layer contains the outer and inner segments of the rods and cones photoreceptors. The outer limiting membrane orders these from the outer nuclear layer (ONL) - the cell bodies of rods and cones. Next, we see the outer plexiform layer (OPL), with the rods and cones axons horizontal cell dendrites, and bipolar dendrites. The inner nuclear layer (INL) contains the nuclei of the horizontal and bipolar cells. The inner plexiform layer (IPL) neatly contains the axons of the bipolar cells (the amacrines), and the dendrites of the ganglion cells. The layer of ganglion cells (GCL), is covered by the layer of the optic nerve fibers - fibers from ganglion cells traversing the retina to leave the eyeball at the optic disk. Finally, the internal limiting membrane forms the border between the retina and the vitreous.

There are two distinct vascular systems in the ocular fundus: retinal and choroidal. The retinal vasculature is identified in Figure 1C as (U) and (V). The choroidal vasculature is identified in Figure 1C as W. Between them lies the retinal pigment epithelium (RPE), Fig. 1-C-X, an opaque monolayer of cells anterior to the choroid that normally largely obscures its vasculature from ophthalmoscopic view. Pathologic alteration of the structure and pigmentation of the RPE affects the pattern of choroidal fluorescence perceptible during angiographic studies. Familiarity with the anatomy and interaction of these anatomic layers is the key to accurate interpretation of fluorescein angiograms, an examination which is vital to the diagnosis of retinal diseases.

The photoreceptor cells (rods and cones), Figure 1C-K and T, are supplied with nutrients from the choroid (Figure 1C-W) through the retinal pigment epithelium (Figure 1C-X).

#### Choroid

The choroid composed of is connective tissue and vessels that nourish the RPE (Figure 1C-X) and outer retina (Figure 1C-H). The inner layer is the choriocapillaris (Figure 1C-Y). The choroidal circulation is completely independent of the retinal circulation. It is supplied by the long and short posterior and recurrent anterior ciliary arteries and is

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Α

**Figure 1:** Anatomy of the Normal Retina and Choroid. Anatomy of the normal retina and choroid is displayed. (A) The posterior fundus view shows optic nerve (D), retinal arteries and veins of the parafoveal arcade (E), fovea (F), and visible choroidal vasculature (G) beneath the normal retina. From the oblique cross section (B), an area of the retina and choroid is magnified in (C) to show the direct relationship between clinical ophthalmoscopic fundus view above and its corresponding cellular pathology. Overall layers of the retina (H) include ganglion cell layer (I), layer of intermediary neurons (J), and photoreceptor layer (K). Detailed elements of the retina include inner limiting membrane (L), nerve fiber layer (M), ganglion cells (N), inner plexiform layer (O), inner nuclear layer (P), outer plexiform layer (Q), receptor nuclear layer (R), outer limiting membrane (S), and rods and cones (T)(photoreceptor cells). Retinal arteries (U) and retinal veins (V) run through the nerve fiber layer (M) beneath the inner limiting membrane (L), supplying all cells of the neural retina, except the photoreceptor cells. The photoreceptor cells are supplied by active transport from the choroid (W) through the retinal pigment epithelium (X). The choroid consists of the choriocapillaris (Y) supplied by the larger choroidal vessels (Z). Bruch's membrane (BR) lies between the pigment.

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drained by the four mid-peripheral vortex veins (Figure 1C-W). The choroidal capillary system, the choriocapillaris, is located innermost (Figure 1C-Y), its basement membrane forming the outer layer of Bruch's membrane. It has a lobular pattern, with central arterioles feeding capillary beds drained by peripheral venules.

The walls of the choroidal capillaries are extremely thin, with multiple fenestrations permitting passive fluid transport from the capillary lumen to the surrounding extravascular space. During fluorescein angiography studies, the fluorescein molecule is sufficiently small to pass readily and rapidly out of the choriocapillaris, but it does not pass through the overlying retinal pigment epithelium (Figure 1C-X).

#### Retinal Pigment Epithelium

The retinal pigment epithelium (RPE) (Figure 1C-X), is single layer а of pigmented cuboidal cells which are attached to the photoreceptors (Figure 1C-K-T) and whose basal portions lie on Bruch's membrane (Figure 1C-BR). It serves important metabolic functions for the overlying photoreceptors (Figure 1C-K-T) and forms a structural barrier between the sensory retina and choroid that, under normal circumstances, fluorescein dye will not cross.

Because of the presence of pigmented cells, the RPE serves as an optical barrier. Pigment density is not uniform across the whole retina. It is more intense in the macular region, where pigment epithelial cells are tall, columnar, and densely packed, and least in regions anterior to the equator, where these cells are flatter and have a sparsity of pigment granules.

#### Retina

The most important characteristics of the retina are its functional architecture and its light transmission and absorption properties. The retina is a thin transparent tissue perfused by vessels from the central retinal artery and, in about 30% of eyes, by an additional cilioretinal artery. The cilioretinal artery, when present, fills at the same time as the choroid. Unlike the choroid, the retinal capillaries are not fenestrated, and there is virtually no extracellular space between the densely packed retinal cells. As a result, the retinal vasculature constitutes a "closed system" that stands out in stark optical contrast to the surrounding tissue, especially in fluorescein angiography.

The outer nuclear and plexiform retinal layers of the retina (Figure 1C-Q) have a high concentration of yellow xanthophyll pigment, particularly in the macula, which is about two disc diameters in size surrounding (but not including) the fovea (Figure 2). The fovea centralis, which lies at 3.5 mm lateral to the optic disc, is specialized for fine visual perception. In the fovea, the cells are all cones. The axons of the receptor cells pass directly to the inner side of the outer plexiform layer, where they connect with dendrites of horizontal and bipolar cells, extending from the inner nuclear layer. Selective absorption of blue light by this pigment produces a relatively darker macular background in fluorescein angiography. The retina receives its blood supply from two sources: the choriocapillaris and the central retinal artery. The choriocapillaris is a layer of capillaries intimately attached to the outer surface of Bruchs membrane. The choriocapillaris supplies the outer third of the retina, including the outer plexiform and outer nuclear layers, the photoreceptors, the pigment epithelium and all of the fovea. The remaining inner two thirds of the retina is supplied by branches of the central retinal artery.

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**Figure 2:** Schematic Representation of the Retina and Related Structures. The retina terminates anteriorly at the ora serrata approximately 7-8 mm posterior to the corneoscleral limbus (A). The macula is clinically an area of altered light reflex which lies 3.5 mm lateral and 1 mm inferior to the edge of the optic nerve (B). The vitreous is a gel of approximately 4.3 ml and is attached anteriorly to the posterior lens capsule, posteriorly to the peripapillary zone and extends centrally to the attachment with the pars plana and anterior retina (C). (*Art from Jaypee-Highlights Medical Publishers*).