CHAPTER 6 THE POSTERIOR SEGMENT OF THE EYE

The posterior segment consists of the following layers, from the outside to the inside:.

Sclera
Choroid
Pigment epithelium of the retina
Rods and cones (photoreceptors)
External limiting membrane
Outer nuclear layer (nuclei of rods and cones with bipolar cells)
Inner nuclear layer (nuclei of bipolar cells)
Inner plexiform layer (synapses of bipolar cells with ganglion cells)
Ganglion cell layer
Nerve fibre layer
Internal limiting membrane
Vitreous

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<u>The visual pathways include</u>:

A. <u>The retina</u>:	
1. rods and cones	
2. bipolar cells	
3. ganglion cells	} common to
	} visual
	} and
B. <u>Axons of the ganglion cells</u>:	} reflex
	} pupillary
1. nerve fibre layer of retina	} pathways
2. optic nerve	
3. optic chiasm	
4. optic tract	

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C. <u>Subcortical centres and relays</u>:	} reflex control
	} of eye movts,
1. superior colliculus	} pupillary
2. pretectal nuclei	} reflexes,
3. lateral geniculate nucleus	} cortical relay

D. <u>Cortical connections</u>:	} vision
	} and
1. optic radiation	} reflex
2. visual cortex(17)	} eye
3. visual association areas(18,19)	} movements
4. frontal eye fields	} voluntary eye
	} movements

If the rods and cones are considered analogous to the sensory organs for touch, pressure, temperature, etc. then the bipolar cells may be compared to the first-order sensory neurons of the dorsal root ganglia, and the retinal ganglion cells to the second-order sensory neurons whose cell bodies lie within the spinal cord or medulla.

THE RETINA

It is important to note that the photoreceptor cells are on the external side of the retina. The relationship of the retinal elements can be understood most readily by following the formation of the optic cup. As the single-cell layered optic vesicle 'invaginates' to form the two-cell layered optic cup, the initially superficial cells become the inner layer of the cup. The pigment epithelium develops from the outer layer of the cup, facing the photoreceptors across the now obliterated cavity of the optic vesicle. From the inner layer all the neurons of the retina differentiate.

Since the photoreceptor cells are on the external side of the retina, all layers internal to them must be transparent,if light is to reach and form a sharp image on them. Inversion of the retina allows close proximity between the photosensitive portion of the receptor cells and the opaque pigment epithelium layer which prevents scattering of light.

The absence of myelin sheaths around the axons of the retinal neurons contributes to retinal transparency. The axons of the retinal ganglion cells become myelinated as they leave the eye and enter the optic nerve. Not infrequently, myelination of a small area of retinal nerve fibres occurs as a congenital anomaly. A scotoma occurs at this point.

In the primate and avian eye the small optical disadvantage resulting from inversion is partly offset by peripheral displacement of all layers of the retina internal to the outer plexiform layer at the centre of the 'fovea centralis', the central area specialised for acute vision.

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The term 'fovea' is frequently misused to designate the 'foveola', an area 0.3 mm in diameter, where the receptor cells are all cones, thinner and taller than the cones found elsewhere in the retina. The inner processes of these cones turn away from the centre of the foveola to reach bipolar cells at the edges of the fovea, which is 1.5mm in diameter (equal in size to the optic disc). The retina reaches maximum thickness at the margins of the fovea, partly because of the displacement of the inner retinal layers from the foveola and partly because of the dense accumulation of ganglion cells required to provide the 1:1 ratio to receptor cells necessary for maximum visual acuity.

PHOTORECEPTION

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The highly specialised photoreceptor cells are divided into two types, the rods which are highly sensitive even at low levels of illumination, and the cones, less sensitive, but capable, at least in some species, of subserving colour vision and visual acuity. In man, cones only are present at the central 0.5 to 0.6mm area. In a 3 mm wide zone surrounding this rod-free area, rods and cones appear in about equal amounts, while peripheral to this the rods predominate.

The rod or cone proper is made up of an outer segment which contains the photoreceptive pigment, connected by a fine bridge (cilium) to thee inner segment which contains many mitochondria. The cell then extends to the external plexiform layer and synapses with bipolar cells.

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The photoreceptors have been studied extensively by electron microscopy. The rod outer segment has the appearance of a stack of discs orientated perpendicularly to the long axis of the rod. The discs contain the photosensitive pigment rhodopsin.

The term rhodopsin (from the Greek,rhoden,rose + opsis, sight) was coined to describe the colour of the photoreceptive pigment visible grossly in freshly excised frog retinas and has been found to be present in the rods of most vertebrates. Exposure to light bleaches rhodopsin to a colourless end product.

Autoradiography of the rod outer segment at intervals after feeding isotopically labelled amino acids has shown that the labelling begins at the internal end of the outer segment and moves externally. It appears that the outer segments are continuously being broken down at their external ends and regenerating adjacent to the inner segment. It has also been shown that the retinal pigment epithelium phagocytoses and digests the cast off portions of the outer segments.

Photochemistry

The reaction of an organism to light requires first the absorption of photons by some intracellular pigment. All of the known photosensitive pigments for vision in higher animals are derivatives of carotenoids, coloured non-saponifiable lipids.

Carotenoids in the tissues of vertebrates seemingly are derived exclusively from the diet. Dietary carotene in man is converted in the liver to vitamin A.

In the retina vitamin A is dehydrogenated to retinene, which after isomerisation, can combine with proteins called 'opsins' from the light sensitive molecules of the receptors.

<u>In rods</u>: retinene + rod opsin (scotopsin) = rhodopsin .

<u>In cones</u>: retinene + cone opsin (photopsin) = iodopsin.

The ability of iodopsin to absorb given wavelengths of light (i.e.the absorption spectrum) differs from that of rhodopsin, the difference being attributable to the specific opsin to which retinene is bound. Colour perception is believed to depend on the presence in the retina of three types of cones containing <u>dissimilar opsins</u>.

<u>The visual cycle</u>.

Much of the current concepts are a result of the work of the Nobel laureate, George Wald.

- Only the 11-cis isomer of retinene has the proper configuration for combination with the various opsins to form the visual pigments.

- On absorption of light energy by rhodopsin (or other visual pigment), its 11-cis retinene becomes isomerised into all-trans retinene which, no longer fitting the opsin, is released.

- Generation of the nerve impulse begins even before retinene has completely separated from the opsin (ie. before bleaching is completed). The isomerisation of retinene exposes a portion of opsin believed to enzymatically alter membrane potentials.

- Regeneration of rhodopsin occurs in darkness. Retinene, liberated in the trans configuration, must be isomerised to 11-cis retinene to recombine with opsin.

- Retinene not used to regenerate rhodopsin is enzymatically reduced to vitamin A and stored in the pigment epithelium as fatty acid esters of the vitamin.

. Comparable reactions involving iodopsin probably occur in cones. Iodopsin is regenerated more rapidly than rhodopsin.

<u>THE PIGMENT EPITHELIUM AND CHOROID</u>

These structures are intimately related to the outer segments of the photoreceptors.

The pigment epithelium is a single layer of cells. The cells are hexagonal and fixed to Bruch's membrane. Bruch's membrane is a collagenous/elastic membrane which serves to stabilise and support the retina. It separates the outer retina from the choroid. The cells of the pigment epithelium send fine processes internally to surround the tips of the rod and cone outer segments. The nucleus lies in the external part of the cell, while the pigment is concentrated in the inner portion. The cells in the foveal region are taller, and this explains the darker appearance of this area on ophthalmoscopy.

The pigment epithelium plays an important part in the photoreceptor cycle. Exposure to light leads to a prompt drop in rhodopsin in the retina concomitantly with increase in vitamin A in the retina and pigment epithelium. The rise in vitamin A in the retina is transient, but in the pigment epithelium it is sustained until a high plateau is reached. It appears that the retinene liberated from rhodopsin is being converted to vitamin A and migrating to the pigment epithelium. When the light is turned off rhodopsin in the retina rises (dark adaptation) while vitamin A in the pigment epithelium falls. Presumably vitamin A is moving back into the outer segments from the pigment epithelium.

The pigment epithelium cells are firmly bound by a cement substance to one another and to the underlying Bruch's membrane. They are not particularly adherent to the outer segments of the rods and cones, as indicated by the frequent occurrence of separation of the retina from the pigment epithelium which occurs clinically as <u>retinal detachment</u>.

The choroid serves as the blood supply to the retinal pigment epithelium and the visual receptors. The retinal capillary network extends no deeper than the inner nuclear layer. It is therefore appreciated that, following retinal detachment, the photoreceptors must receive nutrition by diffusion of metabolites across the subretinal fluid or by diffusion from the deeper retinal capillaries, thus these delicate and highly specialised cells are placed in jeopardy.

The <u>choroid</u> is composed of the following parts:

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1. <u>Bruch's membrane</u> - a 'structureless' membrane lying on the external surface of the pigment epithelium, made up of the basement membrane of the pigment epithelial cells plus the basement membrane of the endothelial cells of the choriocapillaris, between which collagenous and elastic fibres are found. Small localised thickenings of Bruch's membrane called drusen appear as white dots in the fundus. These suggest dysfunction of the retinal pigment epithelium.

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2. Immediately external to Bruch's membrane lies the <u>choriocapillaris</u>, a network of capillary vessels supplying the pigment epithelium and photoreceptors. These capillaries are unusual in that their lumens are

very wide (10-30 microns) and have 'pores' in their walls permitting rapid transfer of fluid and metabolites. The rate of flow of blood through the choriocapillaris is one of the highest in the body. The choriocapillaris is particularly dense at the macula and posterior pole. It is blood in the choriocapillaris that produces the 'red reflex' of the fundus, found on looking into the eye with an ophthalmoscope.

3. A layer of larger vessels lies external to the choriocapillaris.

Chromatophores are pigment-bearing cells scattered throughout the choroid external to the choriocapillaris. They are particularly large and numerous just beneath the sclera in a zone designated the suprachoroid.

FUNDUS BACKGROUND

The normal variations in the pigment epithelium and choroid described above result in several different ophthalmoscopic appearances:

1. Uniform stippled designates the uniform orange background covered with fine black stippling seen in the posterior pole of most eyes. The dense network of choroidal vessels provides the uniform orange-red background which is partially obscured by the pigment epithelial cells.

2.. A tessellated or tigroid appearance is found in the peripheral fundus of some individuals. Orange streaks alternate with patches of grey, the former being large choroidal vessels and the latter the heavily pigmented choroidal stroma between vessels. Presumably pigmentation in the pigment epithelium is relatively sparse, allowing visualisation of the underlying choroid.

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3. Albinotic fundi occur where both retinal and choroidal pigment is sparse, as in blonde individuals. The patches between the large choroidal vessels appear pale yellow or white, since there is little pigment to obscure the underlying sclera.