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Neurohistology

300l, MBBS

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1. **Write an essay on the histological importance of the eye in relation to their cellular functions.**

The eye is a complex and highly developed photosensitive organ that analyses the form, intensity, and color of light reflected from objects, providing the sense of sight. The eyes are located in protective areas of the skull, the orbits, which also contain cushions of adipose tissue. Each eyeball includes a tough, fibrous globe to maintain its shape, a system of transparent tissues that refract light to focus the image, a layer of photosensitive cells, and a system of neurons whose function it is to collect, process, and transmit visual information to the brain.

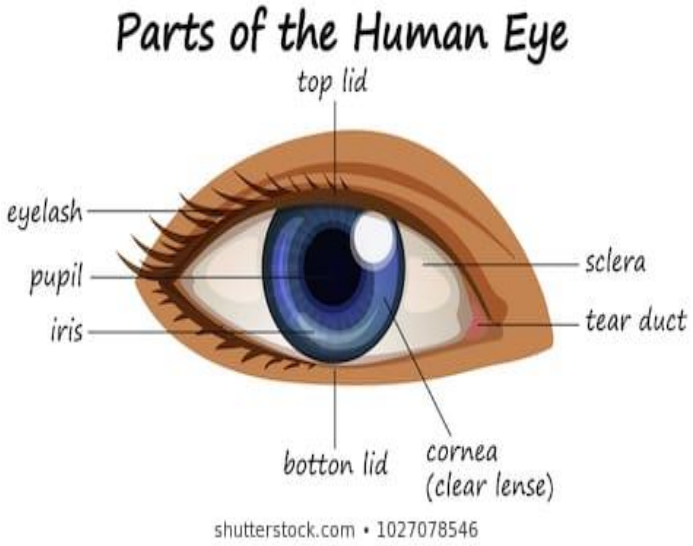

Diagram of External structures of the eye.

Layers of the eyes and their cellular functions

The external structure include

1. Eyelid
2. Eye lashes

3. Conjunctiva
4. Accessory gland

Each eye is composed of three concentric tunics or layers

1. A tough external layer consisting of the sclera and the cornea;

2. A more vascular middle layer consisting of the choroid, ciliary body, and iris;

3. an inner sensory layer, the retina, which consists of an outer pigmented epithelium and an inner retina proper

1. Fibrous Layer

It is the tough external layer of the eye consisting of

a. Sclera: The fibrous, external layer of the eyeball protects the more delicate internal structures and provides sites for muscle insertion. It is continuous with the cornea anteriorly and the optic sheath posteriorly. It consists of dense connective tissues made up of type 1 collage fibers which are oriented in different directions. This irregular arrangement of collagen fibers is what gives the sclera the whitish color as opposed the transparent nature of the cornea.

   It is made up of 4 layers

   - Episclera: The outermost layer of the sclera. It is connected to the deep fascia of the eye by thin collagen fibers. At the corneoscleral junction the tendon capsule contacts the stroma of the conjunctiva.
   - Stroma:
   - Lamina Fusca: brownish in color due to the presence of pigment cells. It is continuous with the suprachoroidal and superciliary lamina of uveal tract
   - Endothelium

b. Cornea: is colorless, transparent, and completely avascular. The cornea consists of five layers

   - An external non-keratinized stratified squamous epithelium; they are regenerative and helps to replace cells that are lost due to wear and tear

- An anterior limiting membrane (Bowman's membrane, the basement membrane of the stratified epithelium). It is made up of type 1 collagen, laminin and other heparin sulfate proteoglycans
- Stroma: largest layer and it’s made up of type 1 collagen arranged in uniform parallel direction. Stroma maintains transparency which is achieved by the regular arrangement and is maintained by keratocytes
- A posterior limiting membrane (Descemet's membrane, the basement membrane of the endothelium) made up of type 4 collagen fibers
- An inner simple squamous corneal endothelium: these cells do not regenerate and they possess pump which helped maintain fluid balance and prevents swelling of stroma because of the close proximity of the cornea and the aqueous humor

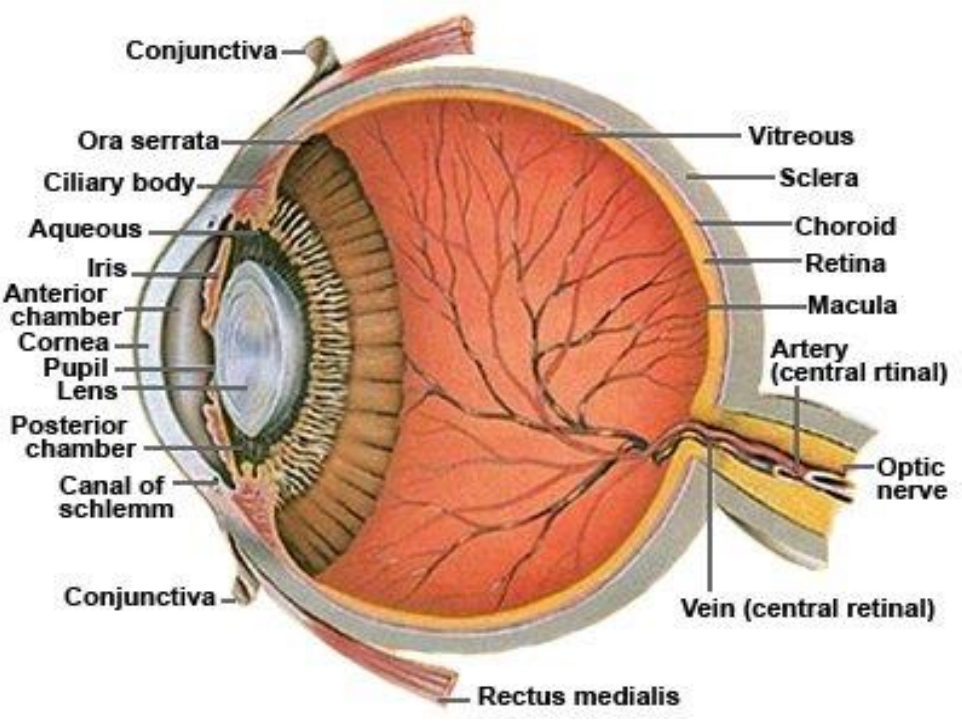

Diagram of the internal structure of the eyes.

2. Vascular Layer

The eye's more vascular middle layer, also known as the uvea, consists of three parts, from posterior to anterior:

- The choroid
- The ciliary body
- The iris

The Choroid:

Is a highly vascular tunic in the posterior two-thirds of the eye, with loose, well-vascularized connective tissue rich in collagen and elastic fibers, fibroblasts, melanocytes, macrophages, lymphocytes, mast cells, and plasma cells. The abundant melanocytes give the layer its characteristic black color and block light from entering the eye except through the pupil. The Choroid along with the iris and ciliary body, the choroid forms the uveal tract.

Structures in the choroid is generally divided into 4 layers

- The outer part of the choroid bound to the sclera is the suprachoroidal lamina
- Sattler's layer: layer of middle diameter blood vessels
- The inner region is richer than the outer layer in microvasculature and is called the choriocapillary lamina.
- A thin (2–4 m) amorphous hyaline sheet known as Bruch's membrane separates the choriocapillary layer from the retina

Ciliary body:

The ciliary body, an anterior expansion of the choroid at the level of the lens, it is a thickened ring of tissue lying just inside the anterior portion of the sclera. In transverse section the ciliary body is roughly a triangle, with its long base contacting the sclera, another side in contact with the vitreous body, and the third facing the posterior chamber The ciliary body has a stroma of loose connective tissue, rich in microvasculature, elastic fibers, and melanocytes, surrounding much smooth muscle.

Ciliary bodies are made up of

i. Ciliary muscles: The ciliary muscle has small fascicles of muscle that insert on the sclera and are arranged in such a way that their contraction in response to parasympathetic nerves decreases the internal diameter of the ciliary body ring,

reducing tension on the fibers that run from this body to the lens. This allows the lens to become more rounded and better focus light from nearby objects onto the retina. The ciliary muscles are therefore important in visual accommodation.

ii. Ciliary Epithelium: The surfaces of the ciliary body that face the vitreous body, posterior chamber, and lens are covered by a double layer of low columnar epithelial cells, the ciliary epithelium, formed from the rim of the embryonic optic cup. The epithelial cells directly covering the ciliary stroma are rich in melanin and correspond to the anterior projection of the pigmented retina epithelium. The surface layer of cells lacks melanin and is contiguous with the sensory layer of the retina.

Iris:

The iris is the most anterior extension of the uvea (middle layer) that partially covers the lens, leaving a round opening in the center called the pupil. The anterior surface of the iris, exposed to the anterior chamber, is not covered by epithelium, but consists of an irregular, discontinuous layer of fibroblasts and melanocytes, densely packed and with interdigitating processes.

The iris consists of two layers

i. The front pigmented fibrovascular layer known as stroma
ii. Pigmented epithelial cells

i. The stroma: connected to a sphincter muscle (sphincter pupillae) which contract the pupil in a circular motion and a set of dilator muscle (dilator pupillae) which pulls the iris radially to enlarge the pupil, pulling it in folds.

ii. Pigmented epithelial cells: This layer lies below the stroma layer. These pigment cells prevent light rays from moving through the iris and ensure that they enter the eyes through the pupils. It is two cells thick. The outer edge of the iris known as the root is attached to the sclera and the anterior ciliary body. The angle formed by the iris and the cornea contains connective tissues with endothelial channels called trabecular meshwork which drains aqueous humor.

The iris is divided into two major regions

i. The papillary zone is the inner region whose edge form the boundary of the pupil
ii. The Ciliary zone is the rest of the iris that extends to its origin at the ciliary body.

3. Inner sensory layer

It consists of;

i. Lens
ii. Retina

Lens

The lens is a transparent biconvex structure immediately behind the iris, used to focus light on the retina. Derived from an invagination of the embryonic surface epithelium (ectoderm), the lens is a unique avascular tissue. Accommodation, which is the refocusing of light to better view near object is achieved by the lens. It is highly elastic, a feature that is lost with age as lens tissue hardens. The lens has three principal components.

i. LENS CAPSULE: The lens is covered by a thick (10–20 m), homogeneous capsule rich in proteoglycans and type IV collagen. Originally the basement membrane of embryonic surface ectoderm, the lens capsule protects the underlying cells and provides the place of attachment for zonular fibers
ii. LENS EPITHELIUM: Subcapsular lens epithelium consists of a single layer of simple cuboidal epithelial cells and is present only on the anterior surface of the lens. The basal ends of the epithelial cells attach to the lens capsule and their apical surfaces have interdigitations that bind the epithelium to the internal lens fibers. At the posterior edge of this epithelium, near the equator of the lens, the cells divide to provide new cells that differentiate as lens fibers. This process allows for growth of the lens and continues at a slow, decreasing rate near the equator of the lens throughout adult life. It maintains the homeostatic function of the lens through Na^+/K^+-AT Pase pump. They also provide lens fibers.
iii. LENS FIBERS Lens fibers are highly elongated and appear as thin, flattened structures. Developing from stem cells in the lens epithelium, the differentiating lens fibers eventually lose their nuclei and other organelles, fill the cytoplasm with

a group of proteins called crystallins, and become very long. Mature lens fibers are typically 7–10 mm long, 8–10 m wide, and 2 m thick. The fibers are densely packed together forming a perfectly transparent tissue highly specialized for light refraction. The lens is held in place by a radially oriented group of fibers, the elastic ciliary zonule, which inserts on both the lens capsule and on the ciliary body

Retina

The retina, the inner layer of the eye, is derived from the embryonic optic cup.

The retina consists of two major layers.

i. The inner one, the neural retina, contains the neurons and photoreceptors. This layer's visual region extends anterior only as far as the ora serrata but it continues as a cuboidal epithelium lining the surface of the ciliary body and posterior iris. The outer pigmented layer is an epithelium resting on Bruch's membrane just inside the choroid. This pigmented cuboidal epithelium also lines the ciliary body and posterior iris, contributing to the double epithelium described with those structures.

ii. The outer pigmented layer is an epithelium resting on Bruch's membrane just inside the choroid. This pigmented; cuboidal epithelium also lines the ciliary body and posterior iris, contributing to the double epithelium described with those structures. The pigmented epithelium consists of low columnar cells with basal nuclei. The cells have well-developed junctional complexes, gap junctions, and numerous invaginations of the basal membranes associated with mitochondria. The diverse functions of the cells in the retinal pigmented epithelium include the following:

- ❖ Serve as an important part of the blood-retina barrier,
- ❖ Absorb light passing through the retina to prevent its reflection,
- ❖ Phagocytose shed components from the adjacent rods and cones,
- ❖ Remove free radicals, and
- ❖ Isomerizes and regenerate the retinoid used as chromospheres by the rods and cones.

The retina has 10 layers from the closest to the farthest from the vitreous body

1. Inner limiting membrane
2. Nerve fiber layer
3. Ganglion cell layer
4. Inner plexiform layer
5. Inner nuclear layer
6. Outer plexiform layer
7. Outer nuclear layer
8. Over limiting membrane
9. The rod and cone layer
10. Retinal pigment epithelium

2. Corona virus can penetrate the body through the eye and implicate the immune system, briefly discuss the layers of retina for information penetration.

The retina is the innermost, light sensitive layers of tissue of the eye of most vertebrates. The optics of the eye creates a focused two-dimensional image of the visual world on the retina, which translates that image into electrical neural impulses to the brain to create visual perception. On the retina is a central pit called fovea. It is surrounded by yellow spot called Macula. It produces the sharpest vision and it contains high concentration of cones within the macula with no retinal blood vessels. Cones are the light sensitive retinal receptors cells that provide detail vision and color discrimination. They function under bright light. Rods are light sensitive specialized retinal receptor that works on night vision. Rods function with movement and provide light/dark contrast. It makes up peripheral vision.

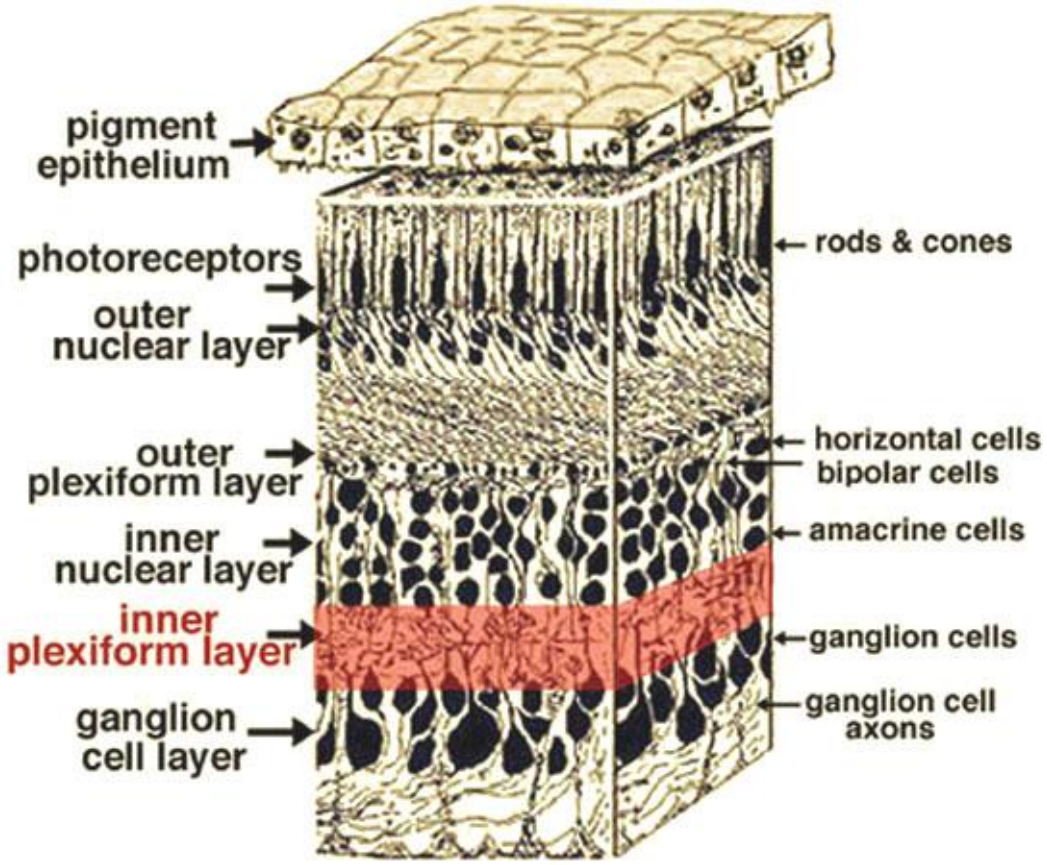

Fig. 7. 3-D block of retina with the inner plexiform layer highlighted (red).

The retina has 10 layers from the closest to the farthest.

1. Inner Limiting membrane: is the boundary between the retina and the vitreous body. It is formed by astrocytes and the foot plates of Muller cells together with basal lamina
2. Nerve fiber layer: layer of optic nerve fibers consisting of ganglion cells, axon fibers which course toward the optic nerve head
3. Ganglion cell layers: contains the nuclei of ganglion cell, the axons of which becomes the optic nerve fibers for messages. This layer contains the non-rod and non-cone photoreceptors. The photosensitive ganglion cells are important for reflective responses to bright day light
4. Inner plexiform layers: contains the synapses between dendrites of ganglion cells and amacrine cells and the axons of bipolar cells
5. Inner nuclear cells: this layer contains the cell body of glial, amacrine, bipolar cells and horizontal cells.
6. Outer plexiform layer: this layer contains the synaptic processes of rod and cone cells

7. Outer nuclear layer: this layer contains the cell bodies of the rods and cones
8. Outer limiting membrane: is a layer of Muller glial cells that separate the cell body from the inner segment of rods and cones
9. Rods and cone layer: also called the photoreceptive layer, this layer contains the inner and outer segment of the rods and cones. The inner and outer segments are connected to each other by cilium. The inner segments contain organelles while the outer segment contains light absorbing materials.
10. Retinal pigment epithelium: most external layer of the retina made up of a layer of simple cuboidal epithelial cells. This layer is closest to the choroid plexus and provides nourishments and supportive to the retina.

These layers above can be grouped into four main processing stages

1. Photoreception
2. Transmission of bipolar cells
3. Transmission of ganglion cells
4. Transmission along optic nerve

1. Photoreception

   Photoreceptors are the cells in the retina that respond to light. Their distinguishing feature is the presence of large amounts of tightly packed membrane that contains the photopigment rhodopsin. The tightly packing is needed to achieve a high photopigment density, which allows a large proportion of the light photons that reach the photoreceptors to be absorbed. In the retina of vertebrates, the rods and cones have a photopigment-bearing region (outer segment)

   Rods and cones are photoreceptive cells located in the retina of the eye. The outer segment contains the phototransduction apparatus.

   In vertebrate retina a series of biochemical stages that converts the isomerization of the retinal of the rhodopsin molecule from (11-cis to all *trans*) into an electrical signal within about one milliseconds of photon absorption, the altered rhodopsin molecules become excited, causing activation of a heterotrimeric G-protein (guanine nucleotide binding protein) called **transducin**. In the case of rhodopsin excitation, transducin activates an enzyme called phosphodiesterase which cleaves

a second messenger known as cGMP (3’5’-cyclic guanosine monophosphate) into 5’GMP.This process reduces the amount of cGMP in the cell.

In dark conditions, cGMP binds to sodium channels in the cell membrane, keeping the channels open and allowing sodium ion to enter the cell continuously. The constant influx of positive sodium ions maintains the cells in somewhat depolarized

In light conditions, cGMP does not bind to the channels to close and cuts off the inward flow of sodium ions. The reduction in influx of sodium ions causes the cell to become hyperpolarized.

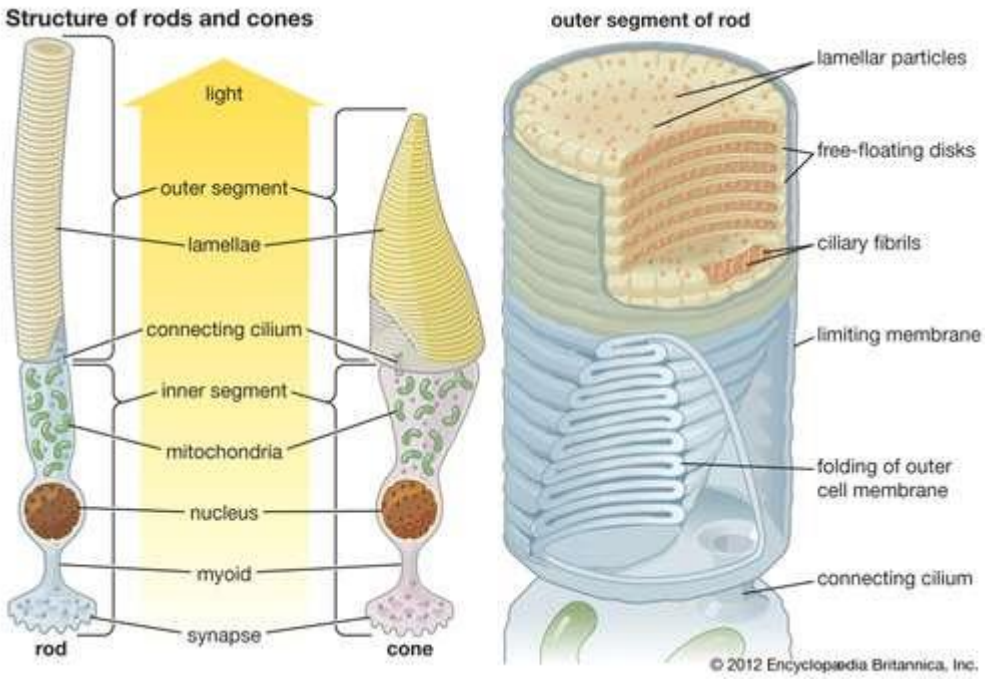

Diagram of a photoreceptor; rod and cone.

2. Transmission of bipolar cells

This process involves the inner nuclear layer and the inner plexiform layer. The bipolar neurons found in these layers form synapses with the synaptic processes of the rods and cones in the outer plexiform layer. The electrical impulse generated

through these synapses to the bipolar neurons. The impulses travel to the axon of bipolar neurons and are transmitted to the ganglion cells.

3. Transmission of ganglion cells

   This process involves the ganglion cell, nerve fibers, and inner plexiform layer of the retina. The retinal ganglion cells are found in these layers and they form synapses with the bipolar neurons. Impulses from bipolar neuron are transmitted to them

4. Transmission along optic nerve

   The ganglion cells of the ganglion cell layer send their axons through the nerve fiber layers and converge at a point nasal to the center of the retina, forming optic nerve. There are no photoreceptors present in this region where ganglion axon fibers feed into optic nerve