**Name**: Ayenor E. Christabel

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**Department**: Medicine and Surgery

**Course:** Ana 305 – Neurohistology

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

**Definition**

 The Human Eye is an organ that reacts to light and allows vision. It can also be defined as a complex and highly developed photosensitive organ that permits an accurate analysis of the form, light intensity, and colour reflected from objects.

**Parts of the eye and their Histological Importance**

 Each eye is composed of three concentric layers, which are:

1. An external layer, that consists of the sclera and the cornea
2. A middle layer, consists of choroid, ciliary body and iris
3. An inner layer consists of lens, vitreous, retina which consists of an outer pigment epithelium and an inner retina proper.
4. An External Layer

i.) **Sclera**:- This is the white part of the eye. The sclera is made up of dense connective tissue made of mainly type 1 collagen fibres. It is the lack of parallel orientation of the fibres that give the sclera its white appearance. The Four layers of the sclera from the external to internal are:

* **Episcleral**, This is the outermost layer and it comprises of loose, fibrous, elastic connective tissue.
* **Stroma**, This comprises of collagen fibres and fibroblasts.
* **Lamina fusca**
* **Endothelium,** This is a specialized, flattened, single layer of cells. The endothelium governs fluid and solute across the posterior surface of the cornea.

**Histological Importance of the Sclera:**

* Presence of dense connective tissue in the sclera, allows the sclera to support the eyeball.

ii.) **Cornea**:- This is the transparent front layer of the eye that covers the iris, pupil and anterior chamber. It consists of type 1 collagen fibres oriented in a uniform parallel direction to maintain transparency. The cornea helps to focus light to produce a clear image on the retina and acts as a protective layer for the eye. It consists of five layers:

* **Corneal epithelium**; This is a non-keratinized stratified squamous epithelium, a regenerating multicellular layer which interacts directly with the tear film. Its kept moist with tears.
* **Bowman Layer**; This is also known as the Anterior limiting membrane. It is a layer of subepithelial basement membrane protecting the underlying stroma. It is composed of type 1 collagen fibres.
* **Stroma (Substantia Propria)**,This is the largest layer of the cornea. It’s a thick, transparent middle layer consisting of collagen fibres which are arranged in a regular pattern. Its function is to maintain transparency.
* **Descemet’s membrane**, This is also known as the Posterior limiting membrane. It’s an acellular layer made up of type IV collagen that serves as a modified basement membrane of the corneal endothelium.
* **Corneal endothelium**; This is a simple squamous or low cuboidal monolayer of mitochondria-rich cells. These cells are responsible for regulating fluid and solute transport between the aqueous and corneal stromal compartments. The cells here don’t regenerate, they stretch to compensate for dead cells which reduces the overall cell density of the endothelium which affects fluid regulation.
1. Middle Layer
2. **Choroid**; This consists of a dense network of blood vessels supplying nourishment to structures of the eye, housed in loose connective tissue. Presence of the
* Haller’s layer- outermost layer of the choroid consisting of larger diameter blood vessels
* Sattler’s layer - layer of medium diameter blood vessels
* Choriocapillaris – layer of capillaries
* Brunch Membrane, an extracellular matrix layer situated between the retina and choroid.

The function of the Choroid is to provide nourishment to the outer layers of the retina through the blood vessels

1. **Ciliary Body**; This is the tissue that divides the posterior chamber and vitreous body. It consists of the ciliary muscle and the ciliary epithelium. The ciliary muscle controls the structure of the lens, which is vital for accommodation. The ciliary epithelium produces aqueous humour which fills the anterior compartment of the eye.
2. **Iris**; The visible surface of the iris consists of loose connective tissue and includes blood vessels. The angle formed by the iris and cornea contains connective tissue with endothelial channels called the trabecular meshwork, which drains aqueous humor in the anterior chamber into the venous canal of Schlemm. It is responsible for controlling the diameter and size of the pupil and thus the amount of light reaching the retina.

 Consists of a.) Stromal layer with pigmented, fibrovascular tissue

 b.) Pigmented epithelial cells beneath the stroma

The pigmented layer of cells blocks rays of light and ensures that light must move through the pupil to reach the retina.

1. Inner Layer
2. **Lens**:- This separates the aqueous and vitreous chambers. The lens itself lacks nerves, blood vessels or connective tissue. It consists of an outer capsule, lens epithelium and the lens fibres. The lens capsule forms the outermost layer of the lens and the lens fibres from the bulk of the interior of the lens.
* Lens Capsule: This is a smooth transparent basement membrane that completely surrounds the lens. The capsule is elastic and is composed of Type IV collagen and sulphated glycosaminoglycans
* Lens Epithelium: The is a simple cuboidal epithelium. The cells of the epithelium regulate most of the homeostatic functions of the lens. The activity of the Na+/K+ ATPases keep water and current flowing through the lens from the poles and exiting through the equatorial regions.
* Lens Fibres: The lens fibers form the bulk of the lens. They are long, thin, transparent cells, they stretch lengthwise from the posterior to the anterior poles. The tightly packed layers of lens fibers ae referred to as laminae. They are linked together via gap junctions.

The lens function is for accommodation, transparency and nourishment.

1. **Vitreous humour**:- This is a jelly-like space made of type II collagen separating the lens and the retina of the eyeball. It helps in the protection of the human eye, most importantly it helps it to hold its spherical shape. It also helps absorb shocks to the eye and keeps the retina properly connected to the back wall of the eye.
2. **Retina**:- This is a thin layer of tissue that lines the back of the eye on the inside. The Neural retina consists of several layers of neurons interconnected by synapses and is supported by an outer layer of pigmented epithelial cells. The primary-light sensing cells in the retina are the photoreceptor cells, which are called Rods and Cones and they are primarily responsible for detecting light. They send signals to the brain through retinal ganglion cells (RGCs) so the brain can form our perception of images. The retina can be divided into 10 layers including

**a.)** The inner limiting membrane **b.)**The Nerve fiber layer **c.)** The Ganglion cell layer

**d.)** The inner plexiform layer **e.)** The inner nuclear layer **f.)** The outer plexiform layer **g.)** The Outer nuclear layer **h.)** The Outer limiting membrane **i.)** The photoreceptor layer **j.)** The retinal pigmented epithelium monolayer (It is composed of retinal pigmented epithelial cells joined by tight junctions and represents the outer blood-retinal barrier. The inner blood-retinal barrier is made of endothelial cells joined by tight junctions and glial extensions surrounding all the retinal blood vessels)

Major cell types that form the various layers above within the human retina are:

1.) **Photoreceptors (Rods and Cones):-** They form the outer nuclear layer. They use the neurotransmitter, glutamate to communicate at the synapse with bipolar cells at the outer plexiform layer. The human eye contains about 130 million rods and about 7 million cones.

* Rod Cells; These are photoreceptor cells in the retina of the eye that can function in lower light than the other type of visual photoreceptor, cone cells. Rod cells are more sensitive than cone cells and are almost entirely responsible for night vision. The peripheral retina is Rod dominated. Absence of rods in the center of the fovea
* Cone cells; They respond differently to light of different wavelengths and are thus responsible for colour vision and function best in relatively bright light as opposed to rod cells. They are three cone types, that is, S-Cones, M cones, L-Cones. The central retina is cone dominated. The highest density of cones is at the center of the fovea, which is located at the center of the macula.
* Retinal Ganglion cells:- They form the Ganglion cell layer, this is the innermost layer furthest from the photoreceptors. They are stimulated by light even when all rods and cones are blocked.

2.) **Nerve cells or Neural cells**

* Bipolar cells:- They make up the inner nuclear layer, but the bipolar cell bodies are shallow to this layer. They synapse with Amacrine cells and Ganglion cells at the inner plexiform layer and they are responsible for transmitting an impulse to retinal ganglion cells. They are contained entirely within the retina, connecting the photoreceptors to the ganglion cells. These are vertically oriented (perpendicular to the retinal surface). There are nine types of bipolar cells. Bipolar cells are postsynaptic to rods and cones.
* Amacrine cells:- These are inhibitory cells which interact with bipolar cells and retinal ganglion cells. They modulate the excitation of the retinal ganglion cells through contact with ganglion cell dendrites or bipolar cell axon terminal bulbs, using the neurotransmitters GABA and glycine. Amacrine cells function within the inner plexiform layer, the second synaptic retinal layer where bipolar cells and retinal ganglion cells form synapses. There are about 40 different types of amacrine cells, most lacking axons. Like horizontal cells, amacrine cells are horizontally oriented and work laterally, affecting the output from bipolar cells. Each type of amacrine cell connects with a particular type of bipolar cell, and generally has a particular type of neurotransmitter.
* Horizontal cells:- They assist in operations such as contrast enhancement and preservation of spatial information. These are the final receivers and transmitters of the initial stimulus. They send the information they receive down their axons, which eventually form the optic nerve and project to higher brain centers. They connect bipolar cells with each other. Horizontal cells are the laterally interconnecting neurons in the outer plexiform layer of the retina. Horizontal cells are responsible for allowing eyes to adjust to see well under both bright-light and dim-light conditions. These are horizontally oriented (parallel to the retinal surface).
* Ganglion cells:- They have dendrites that synapse with bipolar cells. The axons of ganglion cells become the nerve fiber layer within the retina and then become optic nerve fibers terminating within the brain.

3.) **Supporting cells of the retina**:- Glial cells are interspersed between and among the axons of the ganglion cells within the retina and optic nerve. These supporting cells of the retina include Muller cells, astrocytes, and microglial cells.

* Muller cells:- These are glial cells which support metabolism and homeostasis of the retina. They form a supporting matrix radially across the thickness of the retina and also form the inner and outer limiting membranes of the retina. Muller cell bodies sit in the inner nuclear layer and project irregularly thick and thin processes in either direction to the outer limiting membrane and to the inner limiting membrane. Muller cell processes insinuate themselves between cell bodies of the neurons in the nuclear layers and envelope groups of neural processes in the plexiform layers. Retinal neural processes are only allowed direct contact at their synapses.
* Astrocyte cell bodies and processes are almost entirely restricted to the nerve fiber layer of the retina.
* Microglial cells are of mesodermal origin. Unlike the Muller cells and astrocytes, they are not neuroglial.
1. **Corona virus can penetrate the body through eye and implicate the immune system , briefly discuss the layers of retina for information penetration.**

The layers of the retina are as follows from the innermost layer to the outermost layer:-

**a.)** The inner limiting membrane: The Inner Limiting Membrane (ILM) is the retina's inner surface bordering the vitreous humor and thereby forming a diffusion barrier between the neural retina and vitreous humor. The ILM contains laterally contacting Muller cell synaptic boutons and other basement membrane parts. It is formed by astrocytes and the footplates of Muller cells together with a basal lamina.

**b.)**The Nerve fiber layer: The nerve fiber layer is the second innermost layer of the retina from the vitreous. The nerve fiber layer is the layer of optic nerve fibers consisting of ganglion cell axon fibers, which course towards the optic nerve head.

**c.)** The Ganglion cell layer: This layer contains displaced amacrine cells. As a rule of thumb, smaller RGCs dendrites arborize in the inner plexiform layer while larger RGCs dendrites arborize in other layers. The ganglion cells layer contains the nuclei of ganglion cells, the axons of which become the optic nerve fibers for messages. Additionally, this layer also contains the non-rod and non-cone photoreceptors, the photosensitive ganglion cells, which are important for reflexive responses to bright daylight.

**d.)** The inner plexiform layer: The inner plexiform layer is an area comprised of a dense reticulum of fibrils formed by interlaced dendrites of RGCs and cells of the inner nuclear layer. The inner plexiform layer contains the synapses between dendrites of ganglion cells and amacrine cells and the axons of bipolar cells.

**e.)** The inner nuclear layer: This layer of the retina contains the cell bodies of bipolar cells, horizontal cells, and amacrine cells. The inner nuclear layer is thicker in the central area of the retina compared with peripheral retina because of a greater density of cone-connecting second-order neurons (cone bipolar cells) and smaller and more closely spaced horizontal cells and amacrine cells concerned with the cone pathways. There are also nuclei of the supporting Muller cells.

**f.)** The outer plexiform layer: This layer of the retina contains a neuronal synapse of between rods and cones with the footplate of horizontal cells. Capillaries are also found to be primarily running through the outer plexiform layer. It contains the rod and cone axons (projections of rods and cones ending in the rod spherule and cone pedicle), horizontal cell dendrites, and bipolar cells dendrites. Synapses among these structures occur within this layer. In the macular region, this layer is termed the **fiber layer of Henle**. The outer plexiform layer is also known as the **outer synaptic layer.**

**g.)** The Outer nuclear layer: This layer contains the rod and cone granules that sense photon, extensions from the rod, and cone cell bodies. In the peripheral retina, the rod cell bodies outnumber the cone cell bodies, whereas the reverse is true for the central retina.

**h.)** The Outer limiting membrane: This layer contains the bases of the rod and cone photoreceptors cell bodies. The Outer limiting membrane forms a barrier between the subretinal space, into which the inner and outer segments of rods and cones project to be in close association with the pigment epithelial layer behind the retina, and the neural retina proper.

**i.)** The photoreceptor layer

**j.)** The retinal pigmented epithelium monolayer (RPE monolayer): It is composed of retinal pigmented epithelial cells joined by tight junctions and represents the outer blood-retinal barrier. The inner blood-retinal barrier is made of endothelial cells joined by tight junctions and glial extensions surrounding all the retinal blood vessels. The retina is supported by the retinal pigment epithelium (RPE), which has many functions including vitamin A metabolism, maintenance of the blood-retina barrier, phagocytosis of photoreceptor outer segments, production of mucopolysaccharide matrix surrounding the outer segments of the retina, and active transport of materials into and out of the RPE.