

ONYEMA FAVOUR

CHINAZAM

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NEUROHISTOLOGY

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

The Eye

The eyes are peripheral organs for vision and are located in the bony orbit. It is an organ that reacts to light and allows vision. The human eye can differentiate between about 10 million colours and it is a part of the sensory nervous system. 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 is to collect, process and transmit visual information to the brain.

The External structures of the eye are

- i. **Eyelashes**: This consists of the hair and hair follicle located on the thin skin of the eyelid. Its primary role is to protect and maintain the health of the lid margin. It is anchored by a root hair plexus to the eyelid. It aids in reflex action of eyelid to close when a foreign particle enters it. (Epithelia)
- ii. **Eyelids**: It consists of Corneified Stratified Squamous Epidermis, which is made up of basal cells, melanocytes, Langerhans cells, keratinocytes etc. Its dermis forms the support layer of the skin, which contains elastin, collagen, fibroblasts, nerves, vessels, Meibomian glands (tarsal glands that secrete sebum into eyelashes), Glands of Zeis (sebaceous glands that empty into space between conjunctiva and cornea), Glands of Moll (small sweat glands in dermis that open in a row near the base of eyelashes). The last layer here is the Subcutaneous layer, which lies on the orbicularis muscle.
- iii. **Muscles and accessory glands**: This includes orbicularis oculi muscle, lacrimal glands and other glands in dermis of eyelids. Levator palpebrae superioris and superior tarsal muscle are also included.
- iv. **Conjunctiva**:

This is a tissue that lines the inside of the eyelids and covers the sclera of the eye. It is composed of unkeratinized, stratified

Squamous epithelium with goblet cells and stratified columnar epithelium. It is highly vascularized with many microvessels. It is divided into three parts;

- a. Palpebral or tarsal conjunctiva that lines the eyelids
- b. Bulbar or ocular conjunctiva which covers the eyeball (anterior sclera) and is tightly bound to the underlying sclera by Tenon's capsule with thickness of 33 microns.
- c. Fornix Conjunctiva: It forms the junction between the bulbar and palpebral conjunctiva. It is loose and flexible.

The ophthalmic artery supplies it. The epithelial layer of the conjunctiva contains blood vessels, fibrous tissue and lymphatic channels. Lacrimal glands in conjunctiva produce aqueous portion of tears. Other cells present are melanocytes, T and B lymphocytes.

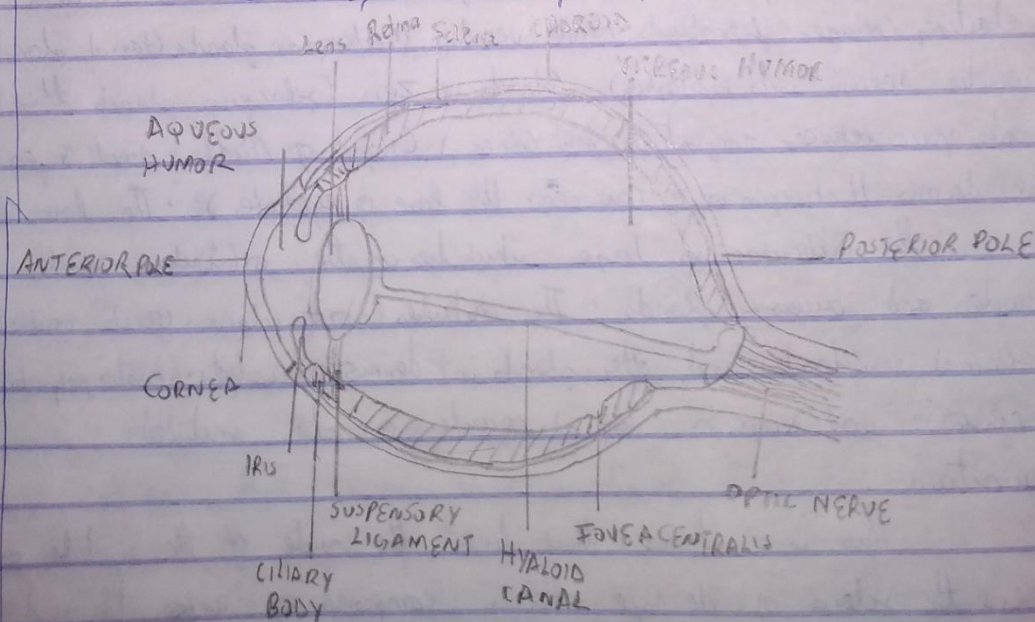
Function: The conjunctiva helps lubricate eye by producing mucus and tears. It prevents entrance of microbes into the eye and contributes to immune system.

Clinical Anatomy:

Leptospirosis: infection with Leptospira that causes conjunctival suffusion which is characterized by chemosis and redness of the eye.

Internal Structures of the Eye

This consists of three layers of tissue arranged concentrically



- The three layers include
- i The Sclera and Cornea (outer fibrous coat)
 - ii The Uvea (middle vascular coat subdivided into choroid, ciliary body and iris)
 - iii The Retina (innermost layer)

I The Outer Fibrous Coat of Sclera and Cornea

a Sclera

This is the white of the eye. The Sclera is a dense connective tissue made up of mainly type 1 collagen fibers oriented in different directions which gives it the white appearance. The sclera consists of white fibrous tissue, elastic fibers, fibroblast and some pigments. The Sclera has four layers from external to internal which are:

- i Episcclera: It is the external surface or fascial sheath of the sclera. It is connected to the Tenon capsule by thin collagen fibers.
- ii Stroma
- iii Lamina Fusca (suprachoroid lamina); delicate connective tissue in perichoroid space
- iv Endothelium

It is important to note that the Sclera consists of five-sixths of the external or outer coat of the eye and has a thickness of about 0.5mm. It is relatively avascular and is a sphere of diameter of about 22mm in adults. It thickens posteriorly to about 1mm and joins with the epineurium covering the optic nerve. Tendons of the Extraocular muscles insert into the anterior areas of the Sclera. Posteriorly the Sclera becomes perforated and is called Lamina cribrosa through which bundles of optic nerve fibers pass.

Function

- i Sclera along with cornea form Fibrous tunic that protects the eye
- ii It resists intraocular pressure and maintains shape of eyeball
- iii It provides attachment for muscles and its smooth external surface allows for easy eye movement

Clinical Anatomy: Trauma to Sclera reduces vision quality

Yellowing of the Sclera is noticed in Jaundice, the sclera may turn blue in kidney and liver failure, Sclera may have blue tint in Osteogenesis Imperfecta.

b Cornea:

This is the anterior one-sixth of the eye ball which is continuous with the sclera at the Corneoscleral junction (Sclerocorneal junction or limbus). The cornea is a colorless, transparent avascular disc which is convex. It consists of type I collagen fibers oriented in a uniform parallel direction to maintain transparency. It has a very rich nerve supply. The Cornea consists of five layers.

- i Corneal Epithelium: This is non-keratinized Stratified Squamous Epithelium. Basal cells are columnar, middle layer cells are polygonal and apical cells are squamous. Cells are arranged. This epithelium is fast growing, regenerating multilayered layer which interacts directly with the tear film (consists of aqueous, mucus and oily secretions). Apical features include microvilli or plasma folds that maintain tear film.
- ii Bowman Layer: It is also called Anterior limiting lamina. It is composed of fine type I collagen fibres, laminin, heparan sulfate proteoglycans etc. It protects underlying stroma.
- iii Corneal Stroma: This is the largest layer of the cornea. It is also called Substantia Propria. It is made up of type I collagen fibres arranged in regular pattern in a ground substance containing sulphated glycosaminoglycans. Keratocytes (Corneal corpuscles or Fibroblasts) maintain the integrity of this layer. The transparency of the cornea is due to the regular arrangement of fibres and also because the fibres and ground substance have the same refractive index.
- iv Descemet's membrane: It is also referred to as Posterior limiting lamina. It is a thin homogenous acellular layer made of type IV collagen that serves as a modified basement membrane. This membrane, at the margin of the cornea, becomes continuous with fibres that form a network in the angle irido-corneal angle of which some fibres pass onto the iris as the Pectinate ligament.

v Corneal Endothelium: This is located on the posterior surface of the cornea. It is lined a single layer of either simple squamous or cuboidal cells. This layer is one cell thick and is in contact with the aqueous humor of the anterior chamber. Cells in this region do not regenerate and have pumps that maintain fluid balance and prevent swelling of the stroma.

Function

- i Corneal epithelium aid in retaining tear film over surface of cornea.
- ii Bowman's membrane gives great stability and strength to cornea.
- iii Corneal stroma provides transparency of the cornea and is responsible for two-thirds of the refractive properties of the eye.
- iv Endothelial cells in cornea are adapted for transport of ions and pump out excessive fluid from cornea thus ensuring its transparency.

Clinical Significance

- i Corneal abrasion: medical condition involving loss of epithelial layer of cornea due to trauma.
- ii Keratitis: Inflammation of the cornea.

II The Uvea (Middle Vascular Coat)

This is deep to the sclera and consists of the Iris, Ciliary Body and Choroid.

a Iris:

This is the most anterior part of the vascular coat of the eyeball. It forms a diaphragm placed immediately in front of the lens. It is continuous with the ciliary body at its periphery and at its center is an aperture called Pupil which regulates the amount of light passing into the eye.

The iris consists of a stromal layer with pigmented fibrovascular tissue and pigmented epithelial cells beneath the stroma. Blood vessels and smooth muscle fibers are embedded in

the stroma. Some muscle fibers, like Sphincter, arranged circularly around the pupil and contract it while the dilator pupillae run radially. The pigmented layer of cells blocks rays of light and ensures that light must move through pupil to reach the retina. Trabecular meshwork, formed by angle between iris and cornea that contains connective tissue with endothelial channels, aids in draining aqueous humor in the anterior chamber into the venous canal of Schlemm.

Function

It forms the pupil which regulates amount of light that enters the eye.

Clinical Significance

Glaucoma: Damage to optic nerve that increase the intra-ocular pressure thereby impeding the draining of aqueous humor by the Trabecular Meshwork.

Iritis: A type of uveitis that involves inflammation of the Iris.

b. Ciliary Body:

It is an anterior continuation of the choroid. It is a tissue ring like in shape that divides the posterior chamber and vitreous body. It is connected to the lens by the suspensory ligament. It is continuous with the periphery of the iris. It consists of ciliary muscle, vascular tissue, connective tissue and ciliary epithelium. Ciliary muscle via lens zonules and suspensory ligament, aid in alterations in the convexity of the lens (Accommodation).

Ciliary epithelium is a double layered epithelium where the outer layer is pigmented while the inner layer is non-pigmented. The cells of the inner surface has ciliary processes (short processes) toward the lens on the anterior part. These cells of the inner surface also produce aqueous humor.

Function

- i Ciliary muscle aids in accommodation.
- ii Ciliary epithelium produces aqueous humor which fills the anterior compartment of the eye.

Clinical Significance

- i Glaucoma: The medication taken when treating this affects the ciliary body.

Choroid:

This consists of choroid proper, suprachoroid lamina and basal lamina (membrane of Bruch).

i Choroid proper:

This consists of a dense network of blood vessels (supplying nourishment to structures of the eye) supported by connective tissue in which many pigmented cells are present giving the choroid a dark color (which darkens the interior of the eyeball). This dark color prevents reflection of light within the eyeball that helps to sharpen images on the retina. The choriocapillary is located in the innermost part of the choroid and supplies the retina.

- ii Suprachoroid lamina: It separates the choroid proper from the sclera. It is also called Lamina Fusca - It is non-vascular and made up of delicate connective tissue containing collagen, elastic fibers and pigment. Nerve fibres are present.

- ii Basal lamina: It is an extracellular matrix layer between the retina and choroid. It contains elastic and collagen fibers. It provides a smooth rounded surface on which pigment cells and receptors of retina can be arranged in precise orientation.

Function:

- i It supplies nutrients to retina and aids in modulation of intraocular pressure.
- ii Its dark pigment prevents reflection of light within the eyeball and sharpens images on the retina.

- i Age-related Macular Degeneration: Later stage of the disease results in choroidal thinning
- ii High myopia: Increased or severe degree of short sightedness

III Innermost Layer.

This consists of Lens, Vitreous and Retina

- a Lens: This is a transparent biconvex avascular structure. It separates the aqueous and vitreous chambers. It is suspended between the iris and the vitreous by the zonules which connect the lens with the ciliary body. It is surrounded by an elastic capsule which is semi-permeable. It consists of three parts
 - i Lens Capsule: This is a transparent homogeneous and highly elastic collagenous basement membrane. It is made up of Type IV collagen and glycoproteins. It is secreted by lens epithelium
 - ii Lens Epithelium: This also called cortex. The cells here are cuboidal but become longer towards the periphery. They contain Na^+/K^+ ATPase and generate ATP to meet energy demand of the lens. Lens epithelium end up becoming lens fibres and have high mitotic activity as they migrate towards the equator.
 - iii Lens Substance: This is the inner layer which is also called the Nucleus. It consists of lens fibres. lens fibres develop from lens epithelium and are mostly composed of soluble proteins called Crystallins.

Function:

- i One-third of refraction is performed by the lens
- ii It changes the focal distance of the eye.
- iii It focuses light rays that pass through it.

Clinical Significance

- i Cataract: This is the opacification of the normally crystalline lens which leads to gradual painless blurring of vision

Vitreous: a jelly like pore made of type II collagen separated

the retina and the lens. It contains 99% water, bound to hyaluronic acid and collagen.

Function

- i It holds eye in spherical shape.
- ii It helps absorb shock to the eye.

Clinical Significance

- i Vitreous detachment: The vitreous pulls away from the retina.

c Retina:

This is the inner coat of the eyeball and lines its posterior three-fourth surface. It is the nervous tissue of the eye where photons of light are converted to neurochemical energy via action potentials. It contains photo-receptors (rods and cones) which are essential for vision. Retina has a portion called Fovea centralis or macula where the vision is most acute and the area only contains cones which are bare. The blind spot (optic disc) on the retina is the spot where optic nerve leaves the eye and there are no photoreceptor cells.

Following the path of light there are 10 distinct layers found in the retina which include

- i Inner or Internal Limiting Membrane: This is a basement membrane elaborated by Müller cells. These cells (gliaocytes) and the basement membrane demarcates the vitreous anteriorly from the retina posteriorly. This is the innermost layer.
- ii Nerve Fibre Layer or Layer of Optic Nerve Fibers: It is made up of axons of retinal ganglion cells and the astroglia which support them. These fibres or axons converge on the optic disc where they pass through foramina of the Lamina cribrosa to enter the optic nerve.
- iii Ganglionic Layer or Layer of Ganglion Cells: This layer contains nuclei of retinal ganglion cells. It contains the cell bodies of ganglion cells whose dendrites enter the internal plexiform layer to synapse with processes of bipolar cells and of amacrine cells. Each ganglion

cell gives off an axon that forms a fiber of the optic nerve.

- iv) **Internal Plexiform Layer:** It is also called the Inner Synaptic Zone. It consists of synapsing nerve fibres. This layer has axons of amacrine, bipolar and glial cells and dendrites of retinal ganglion cells. The axons of bipolar cells synapse with dendrites of ganglion cells and then both processes synapse with processes of amacrine cells. This layer contains some horizontally placed internal plexiform cells.
- v) **Internal / Inner Nuclear Layer:** This layer contains the cell bodies and nuclei of amacrine, bipolar, glial and horizontal cells. The bipolar cell gives off dendrites that enter external plexiform layer to synapse with axons of rods and cones and axons enter internal plexiform layer. The bipolar cells are oriented perpendicular to the layers of the retina. The horizontal cells give off processes that run parallel to the retinal surface. (they are oriented parallel to the layers of retina). The amacrine cells also lie horizontally in the retina. Their processes enter the inner plexiform layer while the processes of horizontal cells enter the outer plexiform layer.
- vi) **Outer or External Plexiform:** This layer contains synaptic processes of rod and cone cells. It is also called Outer synaptic zone and it only consists of nerve fibres that form a plexus. The axons of rods and cones synapse here with dendrites of bipolar neurons and horizontal cells.
- vii) **External or Outer Nuclear layer:** It contains cell bodies and nuclei of rod cells and of cone cells. These cells are photoreceptors that convert the stimulus of light into nervous impulses. This layer is darkly stained.
- iii) **Outer Limiting Membrane:** This is below a pink linear marking. It results because of zona adherens of Muller cells with the cell bodies of photoreceptor cells. This layer of Muller cells and rod and cone junctions serves to separate the photosensitive regions of the retina from the areas that transmit electrical signals.

ix Layer of Rods and Cones: Each rod cell or cone cell can be regarded as a modified neuron and consists of a cell body or peripheral (external) process and a central (internal) process. The peripheral process of rod cells are called rods while that of cone cells are called cones due to the shape of their peripheral processes.

The Layer of Rods and Cones contains the peripheral processes of rods and cones^{cell}. Each rod is about $50 \mu\text{m}$ in length and about $2 \mu\text{m}$ in thickness while each cone is about $40 \mu\text{m}$ in length and about $3-5 \mu\text{m}$ in thickness. There are about 7 million cones and more than 100 million rods in each retina. The outer or peripheral segment of rods and cones contain photosensitive pigments that are concerned with conversion of light into nerve impulses. The pigment in rods is rhodopsin and that in cones is iodopsin. Cones are responsible for photopic vision (vision in bright light), sharp vision and for discrimination of color. Cones are of three types; red sensitive, green sensitive and blue sensitive.

Rods however are responsible for scotopic vision (vision in poor light) and motion across the field of vision.

x Pigment Cell Layer or Retinal Pigment Epithelium: It is the outermost layer of retina and is separated from choroid by Bruch's membrane. It contains a single layer of low cuboidal cells containing melanin pigment which absorbs light. Pigments from these cells enter the layer of rods and cones. It contains pigment cells which have microvilli that interact with processes of rods and cones. These pigment cells absorb excess light, play a role in regular spacing of rods and cones etc. It forms tight junction with endothelial cells of capillaries to form Blood-Retina Barrier.

Function

- i) Retina translates an optical image into neural impulses
- ii) Cones are responsible for photopic vision, sharp vision and discrimination of color
- iii) Cones have higher visual acuity and specificity for color vision

- iv Rods are more sensitive to light and motion
- v Rods are responsible for scotopic vision and motion across field of vision
- vi Pigment cells aid absorption of excessive light and avoidance of back reflection
- vii Pigment cells have phagocytic role and play a role in regular spacing of rods and cones
- viii Pigment cells provide mechanical support to rods and cones and produce melanin
- ix Muller cells are supporting cells of the retina
- x Pigment epithelium forms Blood-Retina Barrier

Clinical Significance

- i Retinitis Pigmentosa: This is a group of genetic, systemic and ocular diseases of unknown etiology characterized by degeneration of retinal pigment epithelium. Symptoms include loss of night vision and peripheral vision that leads to total blindness
- ii Retinoblastoma: This is the most common malignant ocular tumour in children.

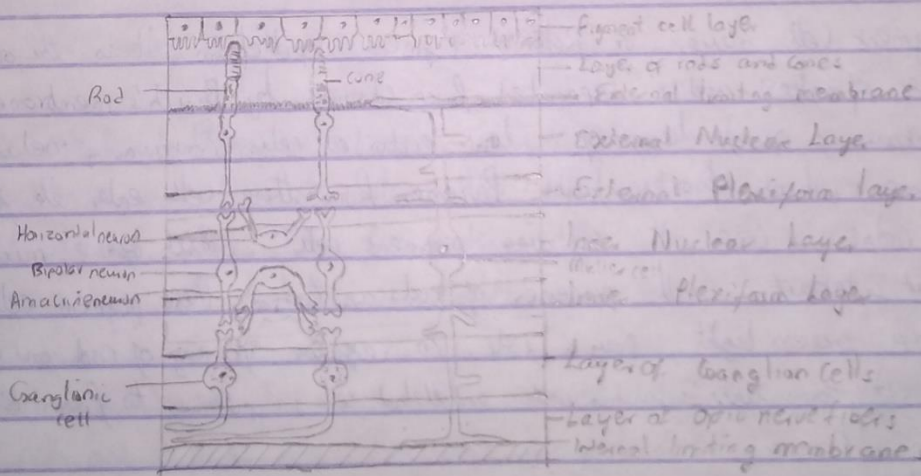


DIAGRAM SHOWING LAYERS OF RETINA

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

2. Coronavirus Disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus. Coronaviruses are a large family of viruses that are known to cause illness ranging from common cold to more severe disease such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The symptoms range from respiratory symptoms, fever, cough, shortness of breath, breathing difficulties to pneumonia, severe acute respiratory syndrome, kidney failure and even death in severe cases. It has been noted that the disease could be quite asymptomatic or may show symptoms after 14-21 days. The virus is a single stranded RNA virus that derives its name from the crownlike or club shaped projections on the viral envelope of the virus. It is said that the virus infiltrates the inflammatory cells through attachment to specific cellular receptor receptors.

The Coronavirus is spread through droplets released into the air when an infected person coughs or sneezes. It spreads through droplets of saliva or discharge from the nose of an infected person. A person can contract this disease by inhaling or swallowing these droplets or through the eyes.

Unprotected eyes were associated with increased risk of transmission of COVID 19 because when the fluid containing Corona virus is placed on the eye, the fluid can be taken up by the conjunctiva, sclera or cornea. This is why one-third of patients in 2019 hospitalized for COVID 19 were found to have symptoms consistent with conjunctivitis or other ocular diseases. When the virus reaches the eye, it might stay in the tear fluid and is collected by lacrimal duct and transported to inferior meatus of the nose and spread to other respiratory tracts and tissues from there.

The virus might however penetrate the layers of the eye from the outer fibrous coat to the uvea and lastly to the retina.

For the virus to fully penetrate and infect the retina, it must pass through the 10 distinct layers of the retina. The layers of the retina are as follows from outer to inner;

i) Pigment Cell Layer or Retinal Pigment Epithelium: This is the outermost layer and contains a single layer of cuboidal cells containing melanin. Pigment cells have phagocytic function and have an immunomodulatory role through secretion of soluble immunosuppressive factors. Pigment epithelial cells also form tight junctions with capillary endothelial cells to form the Blood-Retinal Barrier, which is an immune defense system.

ii) Layer of Rods and Cones: This layer contains peripheral processes of rod cell and cone cell. The cones are about 7 million while the rods are more than 100 million.

iii) Outer Limiting Membrane: This is a pink linear marking and it results because of zona adherens of Müller cells with the cell bodies of photoreceptor cells.

iv) External Nuclear Layer: It contains cell bodies and nuclei of rod cells and of cone cells. These cells are photoreceptors that convert the stimulus of light into nervous impulses.

v) External Plexiform Layer: It contains synaptic processes of rod and cone cells. It consists of nerve fibers that form a plexus. The axon of rods and cone cells synapse here with dendrites of bipolar neurons and horizontal cells.

vi) Internal Nuclear Layer: This layer contains the cell bodies and nuclei of amacrine, bipolar and horizontal cells. Dendrites of bipolar cell synapse with axons of rods and cones in External plexiform layer, while its axons enter internal plexiform layer.

Processes of amacrine cells enter the inner plexiform layer and processes of horizontal cell enter the outer plexiform layer.

vii. Internal Plexiform Layer: It consists of synapsing nerve fibres. This layer has axons of amacrine, bipolar and glial cells and dendrites of retinal ganglion cells. Axons of bipolar cells synapse with dendrites of ganglion cells and both processes then synapse with processes of amacrine cells.

viii. Layer of Ganglion Cells: This layer contains nuclei of retinal ganglion cells. It contains the cell bodies of ganglion cells. Each ganglion cell gives off an axon that forms a fibre of the optic nerve.

ix. Nerve Fibre Layer: It is made up of axons of retinal ganglion cells and astroglia which support them. These fibres converge on optic disc and enter the optic nerve through foramina of lamina cribrosa.

x. Internal Limiting Membrane: This is a basement membrane which is elaborated by Müller cells. This membrane demarcates the vitreous anteriorly from the retina. This is the last innermost layer.