

Mbala Margaret Ojiji

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Medicine and Surgery

300L

1.

Histological Importance of the Eye

The eyes are highly developed photosensitive organs used for analyzing the form, intensity and color of light reflected from objects and providing the sense of sight. The eye is formed by three layers, or tunics. Each of these three layers contributes with parts that have structural / nutritive functions and parts that form the optic and photoreceptive apparatus of the eye.

From the outside to the inside of the eyeball the three tunics are the

- A. **Fibrous tunic/layer:** which forms a capsule enclosing and protecting the other components of the eye. It is subdivided into the sclera, with primarily structural functions, and the cornea, which is part of the optic apparatus.
- B. **Vascular tunic/layer:** which forms the choroid, ciliary body and iris. This tunic is also called the uveal tract. The choroid has primarily nutritive functions. The ciliary body generates the aqueous humor of the eye, but the ciliary muscle also functions in the optic apparatus. The iris is part of the optic apparatus in which it functions a contractile diaphragm, i.e. the aperture of the eye.
- C. **Neural tunic/layer:** consists of the retina. The retina proper forms the photoreceptive layer of the eye. As a double-layered epithelium, the retina

also covers the ciliary process and the posterior surface of the iris, where it has both nutritive and structural functions.

A. Fibrous Tunic

- **Sclera:** mainly dense connective tissue with flat bundles of collagen I and networks of elastic fibers. Melanocytes are present in deep parts of the sclera in addition to the usual complement of connective tissue cells. This aids protection of the delicate internal structures. Distended by the intraocular pressure, the sclera maintains the shape of the eyeball. It is also the site of attachment of the ocular muscles. Anteriorly, the sclera forms a slight protrusion into the eyeball before it merges with the cornea - the scleral spur, which provides a point of insertion for part of the ciliary muscle.

- **Cornea:** The cornea forms the anterior surface of the eye in an area largely corresponding to the pigmented iris, which is visible behind the cornea. It is transparent and completely avascular. A section of cornea shows five distinct layers; three cellular layers, which are separated from each other by two thin, acellular layers. Blood vessels are not normally found in the cornea, and the cells are not pigmented. These layers are:

An exterior stratified squamous epithelium which is nonkeratinized with 5-6 cell layers thick. It comprises about 10% of the corneal thickness. The basal cells have a high proliferative capacity important for renewal and repair of the corneal surface. The flattened surface cells have microvilli protruding into a protective tear film of lipid, glycoprotein and water. As another protective adaptation, the corneal epithelium also has one of the richest sensory supplies of any tissue.

Anterior limiting membrane (Bowman's membrane). The basement membrane of the external stratified epithelium rests on the first acellular layer, the anterior limiting lamina or Bowman's membrane. It separates the epithelium from the corneal stroma and consists of densely packed collagen fibrils embedded in ground substance. Due to this, it contributes to the stability and strength of the cornea, helping to protect against infection of the underlying stroma.

The Stroma or substantia propria, makes up 90% of the corneal thickness and consists of 200 - 250 layers of regularly organized

collagen fibrils (mainly tropocollagen type I, but also types III, V and VI). Collagen fibres within each layer will run parallel to each other but at large angles to collagen fibres in the next layer. The regular arrangement of the collagen fibres and their small diameter (20 - 60 nm) account for the transparency of the cornea. Between the collagen laminae are cytoplasmic extensions of flattened fibroblast like cells called keratocytes.

Descemet's membrane. The posterior endothelium and the corneal stroma are separated from each other by the posterior limiting lamina or Descemet's membrane, which corresponds to the basement membrane of the posterior endothelium (i.e. it is a thick basement membrane which bounds the posterior surface of the stroma. This membrane supports the internal simple squamous endothelium).

Inner simple squamous endothelium. This endothelium maintains Descemet's membrane and includes most metabolically active cells of the cornea. Na^+/K^+ ATPase pumps in the basolateral membranes of these cells are largely responsible for regulating the proper hydration state of the corneal stroma to provide maximum transparency and optimal light refraction.

- **Limbus:** encircling the cornea is the limbus, a transitional area where the transparent cornea merges with the opaque sclera. Here Bowman's membrane ends and the surface epithelium become stratified as the conjunctiva that covers the anterior part of the sclera and lines the eyelids. At the limbus, Descemet's membrane and its simple epithelium are replaced by trabecular meshwork. These penetrate the stroma and allow slow continuous drainage of aqueous humor from the anterior chamber. This fluid moves from this chamber into an adjacent larger space of the scleral venous sinus, or canal of Schlemm.

B. Vascular tunic/ Uvea

- **Choroid:** It consists of loose, well vascularized connective tissue and contains numerous melanocytes. This forms a characteristic black layer in the choroid and prevents light from entering the eye except through the pupil. Two layers make up the choroid; the *inner choroido-capillary lamina* (which has a rich microvasculature important for nutrition of the outer retinal layers) and *Bruch's*

membrane(a thin extracellular sheet which is composed of collagen and elastic fibres surrounding the adjacent microvasculature and basal lamina of the retina's pigmented layer.

- **Ciliary Body:** The ciliary body is an inward/anterior extension of the uvea at the level of the lens which lies posterior to the limbus.

Structures associated to the ciliary body include:

A small amount of loose connective tissue similar to that of the choroid is located between smooth muscle cells which form the bulk of the ciliary body. They form three bundles, the ***ciliary muscle***. Contraction of these muscles affect the shape of the lens and is important in visual accommodation.

Ciliary processes are short extensions of the ciliary body towards the lens. The inner surface of the ciliary body and its processes are lined by two layers of columnar cells which belong to the retina - the ciliary epithelium formed by the pars ciliaris of the retina. The outer cell layer is pigmented, whereas the inner cell layer, i.e. the layer that faces the posterior chamber of the eye, is nonpigmented.

The ciliary processes contain a dense network of capillaries. The cells of the inner layer of the ciliary epithelium generate *the aqueous humor* of the eye. i.e. they transport the plasma filtrate generated by the capillaries in the ciliary processes into the posterior chamber of the eye. Tight junctions between the cells form the blood - aqueous humor barrier.

Ciliary Zonule is system of fibers. These fibers, which consist of fibrillin, extend from the ciliary processes towards the lens and form the suspensory ligament of the lens. These fibres are also called zonule fibres. Two of the bundles of the ciliary muscles attach to the sclera and stretch the ciliary body when they contract, thereby regulating the tension of the zonule fibres. The reduced tension will result in a thickening of the lens which focusses the lens on close objects, a process called accommodation as discussed earlier.

- **Iris:** The posterior surface of the iris is covered by the retina. The inner layer of the retina, i.e. the layer facing the posterior chamber, is called the *posterior epithelium* of the iris. Both layers of the retina are pigmented, but pigmentation is heavier in the inner layer. In the

region of the central opening of the iris, the *pupil*, the retina extends for a very short distance onto the anterior surface of the iris. The iridial stroma consists of a vascularized loose connective tissue rich in melanocytes in addition to macrophages and fibrocytes, which are all surrounded by a loose meshwork of fine collagen fibers. The anterior surface of the iris is not covered by an epithelium - instead of we find a condensation of fibrocytes and melanocytes, the *anterior border layer* of the iris.

The iris forms the aperture of the eye. Myoepithelial cells in the outer (or anterior) layer of the retina, i.e. the layer adjacent to the stroma of the iris, have radially oriented muscular extensions. These extensions form a flat sheet immediately beneath the anterior layer of the retina, the dilator pupillae muscle. Embedded in the central portion of the iridial stroma are smooth muscle cells which form the annular sphincter pupillae muscle. In humans, this muscle surrounds the pupil as a less than 1 mm wide and only 0.2 mm thick band. The two muscles regulate the size of the pupil.

Pupillary constriction, which is mediated by the sphincter pupillae muscle, is clinically referred to as miosis - dilation, mediated by the dilator pupillae muscle, as mydriasis.

The pigmentation of cells in the stroma and anterior border layer of the iris determines the color of the eyes. If cells are heavily pigmented the eyes appear brown. If pigmentation is low the eyes appear blue. Intermediate levels create shades of green and grey.

- **Lens**: this is a transparent biconvex structure suspended immediately behind the iris, which focuses light on the retina. The posterior surface of the iris is covered by the retina. The inner layer of the retina, i.e. the layer facing the posterior chamber, is called the posterior epithelium of the iris. Both layers of the retina are pigmented, but pigmentation is heavier in the inner layer. In the region of the central opening of the iris, the pupil, the retina extends for a very short distance onto the anterior surface of the iris. The iridial stroma consists of a vascularized loose connective tissue rich in melanocytes in addition to macrophages and fibrocytes, which are all surrounded by a loose meshwork of fine collagen fibers. The anterior

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- **Vitreous body:** occupies the large vitreous chamber behind the lens. It consists of transparent, gel like connective tissue that is 99% water, with collagen fibres and hyaluronate, contained within an external lamina called the vitreous membrane. The only cells present are small mesenchymal cells near the membrane called hyalocytes; which synthesize the hyaluronate, collagen and few macrophages.

C. Neural Tunic

Retina: Similar to the retinal lining of the iris and ciliary body, the outer layer of the light sensitive retina forms a single layer of cuboidal cells - the pigment epithelium. The inner layer of the retina contains the photoreceptors, the first neurons which process the sensory information, and the neurons which convey the pre-processed sensory information to the central nervous system.

Optic Nerves

Due to the origin of the retinae and optic nerves from the developing forebrain, the optic nerves (cranial nerves II) corresponds to fibre tracts connecting parts of the CNS - in this case the ganglion cells of the retina with neurons in the lateral geniculate nucleus of the thalamus and neurons in the superior colliculus and pretectum of the midbrain.

Ganglions cell axons run towards the optic disc where they turn towards the sclera. Numerous bundles (or fascicles) of axons pass through the choroid and openings in the sclera, the lamina cribosa. The axons become myelinated in this region. Collectively, the bundles form the optic nerve. Like other parts of the CNS, the optic nerve is surrounded by the three meninges - the outer dura mater, the middle arachnoid and the inner pia mater, which are separated from each other by subdural and subarachnoid spaces. At the eyeball, the dura fuses with the sclera while the arachnoid and pia mater merge with the choroid. Connective tissue septa, which arise from the pia mater, separate the fibre bundles in the optic nerve. The axons in the optic nerve are supported by astrocytes and oligodendrocytes. Microglia is also present.

Eyelid

The posterior (facing the eyeball) and anterior (facing the world) surfaces of the eyelid are also called conjunctival and cutaneous parts. The cutaneous part is covered by skin and contains sweat glands, sebaceous glands and, along the margins of the lid, 3-4 rows of hairs - the eyelashes. Modified apocrine sweat glands, the glands of Moll, empty into the follicles of the eyelashes. The eyelashes lack arrector pili muscles.

The inner, conjunctival part of the lids is lined by conjunctiva. Beneath the conjunctiva, large sebaceous glands are embedded in a plate of dense connective tissue containing many elastic fibres. The plate and the sebaceous glands within it are called the tarsal plate the tarsal glands (also Meibomian glands). Oils in the sebum produced by these glands form a surface layer on the tear film, reducing its rate of evaporation, and help lubricate the ocular surface. Extensive skeletal muscle bundles between the tarsal plate and the skin belong to the orbicularis oculi muscle which folds the eyelids.

Conjunctiva

The margins of the cornea merge with the conjunctiva. The conjunctiva extends over the 'white of the eye', which corresponds to the anterior part of the sclera, folds back and continues over the posterior part of the eyelid. At the opening formed by the eyelids, the conjunctive merges with the skin which covers the anterior surface of the eyelids.

The epithelium of the conjunctiva varies from stratified squamous (most of it) to stratified columnar (at the reflection from the sclera to the eyelid). It contains goblet cells. The conjunctival epithelium rest on the loose connective tissue of its lamina propria.

Lacrimal Glands

Produce fluid continuously for the tear film that moistens and lubricates the cornea and conjunctiva and supplies oxygen to the corneal epithelial cells.

2.

Layers of the Retina

The retina, the innermost tunic of the eye, develops with the two fundamental sublayers from the inner and outer layers of embryonic optic cup.

- **The outer pigmented layer:** this consists of cuboidal or low columnar cells with basal nuclei and surrounds the neural layer of the retina. This layer absorbs scattered light, with many tight junctions, the cells of this layer form the protective blood retina barrier, etc.
- **The inner neural layer:** this layer functions as an outpost of the CNS with glia and several interconnected neuronal subtypes in well-organized strata.

Now, between the vitreous body and the choroid, the retina can usually be seen to consist of nine neural layers of which are photosensitive and a pigmented layer which are derived from the inner and outer layers of the optic cup. Following the path of light, the layers are:

- **The inner limiting layer (ILL):** consists of terminal expansions of other Müller cell processes that cover the collagenous membrane of the vitreous body.
 - **The nerve fiber layer (NFL):** containing ganglionic cell axons that converge at the optic disc form the optic nerve
 - **The ganglionic layer (GL):** containing cell bodies of the ganglion cells and thicker near the retina's center than its periphery.
 - **The inner plexiform layer (IPL):** containing fibers and synapses of the ganglion cells and the bipolar neurons of the next layer
 - **The inner nuclear layer (INL):** with cell bodies of several types of bipolar neurons which begin to integrate signals from the rod and cone cells. The cells of the inner nuclear layer are concerned with the initial processing of the sensory input. The three major neuron types are horizontal, bipolar and amacrine cells. The inner nuclear layer also houses the perikarya of the Müller cells.
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- **The outer plexiform layer (OPL):** containing fibers and synapses of the bipolar neurons and rod and cone cells
 - **The outer nuclear layer (ONL):** with the cell bodies and nuclei of the photosensitive rod and cone cells.
 - **The Outer Limiting Layer (OLL):** a line formed by junctional complexes holding rod and cone cells to the intervening Müller cells.
 - **The rod and cone layer (RCL):** which contains the outer segments of these cells where the photoreceptors are located.
 - **The non-neural pigmented layer (PL):** which has several supportive functions important for the function and maintenance of the neural layer.

