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

Broadly, from an anatomical perspective, the eye can be viewed as a series of overlapping layers of tissue. External structures of the eye include the eyelashes, lids, muscles, accessory glands, and conjunctiva. The internal structures of the eye consist of three layers of tissue arranged concentrically:

* The sclera and cornea make up the exterior layers.
* The uvea is the vascular layer in the middle, subdivided into the iris, ciliary body, and choroid.
* The retina constitutes the innermost layer and is made up of nervous tissue.

All of these layers can further subdivide and undergo histological classification.

**Structure**

**"External Structures of the Eye":**

1. *Conjunctiva*: lines the inner part of the eyelids. The tarsal plate lies beneath the conjunctiva and contains meibomian glands, which secrete an oily substance to decrease the evaporation of the tear film.

2. *Tear film:* The tear film consists of aqueous, mucus, and oily secretions.

3. *Accessory glands:* Apocrine glands of Moll, meibomian glands, lacrimal glands.

4. *Muscles:*Orbicularis oculi, levator palpebrae superioris, superior tarsal muscle.

5. *Eyelid:* The eyelid, likewise known as the cover of the eye, a mobile layer made up of skin and also muscular tissue and also covers the eyeball.

**"Internal Structures of the Eye":** The innermost structures of the eye are organized in the three layers as follows

**(A)- *"Outermost Layer: Sclera and Cornea":***

1. **"*The sclera (white of the eye)"***:

* The sclera is dense connective tissue made of mainly type 1 collagen fibers, oriented in different directions. The lack of parallel orientation of collagen fibers gives the sclera its white appearance, as opposed to the transparent nature of the cornea. However, the collagen of the sclera and cornea are continuous.
* The four layers of the sclera from external to internal are episclera, stroma, lamina fusca, and endothelium.
* The episclera is the external surface of the sclera. It is connected to the Tenon capsule by thin collagen fibers. At the corneoscleral junction, also known as the limbus, the Tenon capsule contacts stroma of the conjunctiva.

2. **"*Cornea (transparent front layer of the eye)":***

* Consists of type I collagen fibers oriented in a uniform parallel direction to maintain transparency
* Consists of five layers: epithelium (non-keratinized, stratified squamous epithelium), Bowman layer, stroma (also called substantia propria), Descemet’s membrane, corneal endothelium.
* **Epithelium**: fast growing, regenerating multicellular layer which interacts directly with the tear film.
* **Bowman layer**: This is a layer of subepithelial basement membrane protecting the underlying stroma. It is composed of type 1 collagen, laminin, and several other heparan sulfate proteoglycans.
* **Stroma**: The largest layer of the cornea, the stroma has collagen fibers arranged in a regular pattern. Keratocytes maintain the integrity of this layer. The function of this layer is to maintain transparency, which occurs by the regular arrangement, and lattice structure of the fibrils, whereby scatter from individual fibrils gets canceled by destructive interference, and the spacing of less than 200 nm allows for transparency.
* **Descemet’s membrane**: an acellular layer made of type IV collagen that serves as a modified basement membrane of the corneal endothelium
* **Corneal endothelium**: a one cell thick layer made of either simple squamous or cuboidal cells. Cells in this region do not regenerate and have pumps that maintain fluid balance and prevent swelling of the stroma. When corneal endothelial cells are lost, neighbouring cells stretch to attempt to compensate these losses.

**(B)- "Middle Layer: Uvea (Iris, Ciliary Body, And Choroid)":**

*1.* ***"Iris":*** It covers part of the lens leaving a round central pupil. It con

* Consists of (1) stromal layer with pigmented, fibrovascular tissue and (2) pigmented epithelial cells beneath the stroma. Fibroblasts, melanocytes and myoepithelial cells are also present.
* The sphincter pupillae and dilator pupillae muscles connect to the stroma
* The pigmented layer of cells blocks rays of light and ensures that light must move through the pupil to reach the retina
* 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. From here, fluid drains into episcleral veins.

*2.* ***"Ciliary Body"****:* The tissue that divides the posterior chamber and vitreous body

* Consists of the ciliary muscle and the ciliary epithelium and lies posterior to the limbus.
* The ciliary muscle, via the lens zonules, controls the structure of the lens, which is vital for accommodation. Zonules are connective tissue fibers composed of fibrillin 1 and 2 that connect the ciliary muscle and lens.
* The ciliary epithelium produces aqueous humor which fills the anterior compartment of the eye.

*3.* ***"Choroid":***

* Consists of a dense network of blood vessels supplying nourishment to structures of the eye, housed in loose connective tissue. The choriocapillary layer is located in the innermost part of the choroid and supplies the retina
* The Bruch membrane is an extracellular matrix layer situated between the retina and choroid and has significance in age-related macular degeneration, where an accumulation of lipid deposits prevent diffusion of nutrients to the retina.

**(C)- "Innermost layer: Lens, Vitreous, And Retina":**

1. **Lens**: separates the aqueous and vitreous chambers. It’s a thick biconvex structure

* Consists of an outer capsule composed of proteoglycans and type IV collagen, a middle layer called cortex, and an inner layer called the nucleus.
* The capsule is the basement membrane of the lens epithelium which lies below
* New lens cells differentiate from the lens epithelium and are incorporated peripherally, pushing older lens cells towards the middle.

2. **Vitreous**: a jelly-like space made of type II collagen separating the retina and the lens. Cells here are called hyaluronates, which synthesize hyaluronate and collagen, and a few macrophages.

3. **Retina**: nervous tissue of the eye where photons of light convert to neurochemical energy via action potentials. It is subdivided into two major layers:

* Outer pigmented layer: is a simple cuboidal epithelium attached to Bruch’s membrane and the choroido-capillary lamina of the choroid. This heavily pigmented layer forms the other part of the dual epithelium covering the ciliary body and posterior iris.
* Inner neural layer: is thick and stratified with various neurons and photoreceptors. Although its neural structure and visual function extend anterior only as far as the ora serratathis layer continues as part of the dual cuboidal epithelium that covers the surface of the ciliary body and posterior iris. This layer is further subdivided into 9 layers:
* *Outer limiting membrane*
* *Inner/outer segment layer*
* *Outer plexiform layer*
* *Outer nuclear layer*
* *Inner nuclear layer*
* *Inner plexiform layer*
* *Ganglion cell layer*
* *Nerve fiber layer*
* *Internal limiting membrane*

Retinal pigment epithelium is made of cuboidal cells containing melanin which absorbs light. These cells also establish a blood-retina barrier through tight junctions. "Rod and cone cells": the layer of cells with photoreceptors and glial cells. Rods are located peripherally and are more sensitive to light and motion than cones. Cones have higher visual acuity and specificity for color vision.

**Function/ histological importance**

The layers of the eye perform distinct functions which coalesce to create a unified, perceptual experience. The essential role of the external eye structures is to protect the delicate tissue of the internal eye. The eyelid prevents foreign bodies from entering the inner eye and helps refresh and distribute the tear film by blinking. Eyelashes are finely sensitive to touch and warn the eye of possible debris and particles that may cause injury.

Internal parts of the eye have primarily structural and visual functions. The **sclera** supports eye shape, protects delicate internal structures and acts as the site for extrinsic eye muscle attachment. The **cornea** serves a protective role and is responsible for two-thirds of the refractive properties of the eye. The remaining one-third of refraction is performed by the **lens**, which is functionally adjustable through the action of the zonular fibers and ciliary muscles.

The **uvea** of the eye is a crucial mediator of nutrition and gas exchange, as blood vessels course through the ciliary body and iris, while the choriocapillaris in the posterior eye **(choroid)** help support the retina. This abundant blood supply is implicated in uveitis, as inflammatory mediators enter the eye through this vascular network. The **ciliary body** also holds suspensory ligaments that attach to the lens and change lens shape for far and near vision. Its epithelium secretes aqueous humor. The **iris** controls pupil diameter and thus the amount of light entering the eye.

At the end of the visual process, as rays of light bend through the cornea and lens, photon energy is converted to neurochemical action potentials by cells of the **neural layer of the retina**, which then send these impulses to the brain, via the optic nerve. **The pigmented layer** absorbs extraneous light and provides vitamin A for photoreceptor cells.

**Clinical Significance**

Several of the most common diseases of the eye are manifestations of pathology within specific histological layers. Below are examples of common eye conditions, and the layers of the eye implicated.

* ***"Chalazion"****:* A sterile lump often in the upper eyelid caused by obstruction of the meibomian oil glands.
* ***"Conjunctivitis":*** Inflammation of the transparent conjunctiva that may be caused by bacterial or viral infections, allergies, or exposure to certain chemicals.
* ***"Cataracts":***A sclerotic nuclear cataract is the most common and is due to opacification in the central nucleus of the lens. Cortical cataracts are due to opacifications in the cortex and have a distinct wedge-shaped appearance. Posterior subcapsular cataracts arise from behind the sac-like structure of the lens.
* ***"Glaucoma":*** Refers to optic nerve damage related to increased intraocular pressure. Drainage of aqueous humor through the trabecular meshwork is often implicated.

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

The **retina** is the innermost, light-sensitive layer of tissue of the [eye](https://en.wikipedia.org/wiki/Eye). Light striking the retina initiates a cascade of chemical and electrical events that ultimately trigger nerve impulses that are sent to various visual centres of the [brain](https://en.wikipedia.org/wiki/Brain) through the fibres of the [optic nerve](https://en.wikipedia.org/wiki/Optic_nerve).

Six major cell types form the various retinal layers:

* The primary light-sensing cells in the retina are the [photoreceptor cells](https://en.wikipedia.org/wiki/Photoreceptor_cell), which are of two types: [rods](https://en.wikipedia.org/wiki/Rod_cell) and [cones](https://en.wikipedia.org/wiki/Cone_cell). They form the outer nuclear layer and synapse with bipolar cells at the outer plexiform layer. Rods function mainly in dim light and provide black-and-white vision. Cones function in well-lit conditions and are responsible for the perception of colour, as well as high-acuity vision used for tasks such as reading.
* A third type of light-sensing cell, the [photosensitive ganglion cell](https://en.wikipedia.org/wiki/Intrinsically_photosensitive_retinal_ganglion_cells), is important for [entrainment](https://en.wikipedia.org/wiki/Entrainment_%28chronobiology%29) of circadian rhythms and reflexive responses such as the [pupillary light reflex](https://en.wikipedia.org/wiki/Pupillary_light_reflex). Neural signals from the rods and cones undergo processing by other neurons, whose output takes the form of [action potentials](https://en.wikipedia.org/wiki/Action_potential) in [retinal ganglion cells](https://en.wikipedia.org/wiki/Retinal_ganglion_cell) whose [axons](https://en.wikipedia.org/wiki/Axon) form the optic nerve.
* Bipolar cells make up the inner nuclear layer and synapse with the amacrine cells and ganglion cells at the inner plexiform layer.
* Amacrine cells are inhibitory cells which interact with bipolar and ganglion cells.
* Horizontal cells assist in operations such as contrast enhancement and preservation of spatial information.
* Muller cells are glial cells which support metabolism and homeostasis of the retina.

The vertebrate retina has ten distinct layers of [neurons](https://en.wikipedia.org/wiki/Neuron) interconnected by [synapses](https://en.wikipedia.org/wiki/Chemical_synapse), and is supported by an outer layer of pigmented epithelial cells. From closest to farthest from the vitreous body:

1. [**Inner limiting membrane**](https://en.wikipedia.org/wiki/Inner_limiting_membrane) – basement membrane elaborated by [Müller](https://en.wikipedia.org/wiki/Muller_glia) glial cells and basement membrane which demarcates the vitreous anteriorly from the retina posteriorly.
2. [**Nerve fibre layer**](https://en.wikipedia.org/wiki/Nerve_fiber_layer) – axons of the [ganglion cell](https://en.wikipedia.org/wiki/Retinal_ganglion_cell) bodies (note that a thin layer of Müller cell footplates exists between this layer and the inner limiting membrane).
3. [**Ganglion cell layer**](https://en.wikipedia.org/wiki/Ganglion_cell_layer) – contains nuclei of ganglion cells, the axons of which become the optic nerve fibres, and some displaced [amacrine cells](https://en.wikipedia.org/wiki/Retina_amacrine_cell).
4. [**Inner plexiform layer**](https://en.wikipedia.org/wiki/Inner_plexiform_layer) – contains the synapse between the [bipolar cell](https://en.wikipedia.org/wiki/Retina_bipolar_cell) axons and the dendrites of the [ganglion](https://en.wikipedia.org/wiki/Retinal_ganglion_cell) and amacrine cells.
5. [**Inner nuclear layer**](https://en.wikipedia.org/wiki/Inner_nuclear_layer) – contains the nuclei and surrounding cell bodies (perikarya) of the [amacrine cells](https://en.wikipedia.org/wiki/Amacrine_cells), [bipolar cells](https://en.wikipedia.org/wiki/Retina_bipolar_cell), and [horizontal cells](https://en.wikipedia.org/wiki/Retina_horizontal_cell).
6. [**Outer plexiform layer**](https://en.wikipedia.org/wiki/Outer_plexiform_layer)– projections of rods and cones ending in the rod spherule and cone pedicle, respectively. These make synapses with dendrites of bipolar cells and horizontal cells. In the [macular](https://en.wikipedia.org/wiki/Macula) region, this is known as the *Fiber layer of* [*Henle*](https://en.wikipedia.org/wiki/Friedrich_Gustav_Jakob_Henle).
7. [**Outer nuclear layer**](https://en.wikipedia.org/wiki/Outer_nuclear_layer) – cell bodies of rods and cones.
8. [**External limiting membrane**](https://en.wikipedia.org/wiki/External_limiting_membrane) – layer that separates the inner segment portions of the photoreceptors from their cell nuclei. A layer of Muller cells and rod/cone junctions which serves to separate the photosensitive regions of the retina from the areas that transmit the electrical signals.
9. **Inner segment / outer segment** **layer** – inner segments and outer segments of rods and cones. The outer segments contain a highly specialized light-sensing apparatus.
10. [**Retinal pigment epithelium**](https://en.wikipedia.org/wiki/Retinal_pigment_epithelium) – single layer of cuboidal epithelial cells. This layer is closest to the choroid, and provides nourishment and supportive functions to the neural retina, the black pigment melanin in the pigment layer prevent light reflection throughout the globe of the eyeball; this is extremely important for clear vision. Retinal pigmented epithelial cells are joined by tight junctions and represent the outer blood-retinal barrier (BRB). The inner BRB is made of endothelial cells joined by tight junctions and glial extensions surrounding all the retinal blood vessels.

These layers can be grouped into 4 main processing stages: photoreception; transmission to [bipolar cells](https://en.wikipedia.org/wiki/Retina_bipolar_cell); transmission to [ganglion cells](https://en.wikipedia.org/wiki/Retinal_ganglion_cell), which also contain photoreceptors, the [photosensitive ganglion cells](https://en.wikipedia.org/wiki/Photosensitive_ganglion_cell); and transmission along the optic nerve. At each synaptic stage there are also laterally connecting [horizontal](https://en.wikipedia.org/wiki/Retina_horizontal_cell) and [amacrine cells](https://en.wikipedia.org/wiki/Retina_amacrine_cell).

Virtually all of the junctions (synapses) between the retinal neurons are made in the two synaptic layers, and all visual information passes across at least two synapses, one in the outer plexiform layer and another in the inner plexiform layer, before it leaves the eye.

Processing of visual information occurs in both plexiform layers. The outer plexiform layer separates visual information into on and off channels and carries out a spatial type of analysis on the visual input. The output neurons of this layer, the on and off bipolar cells, demonstrate a center-surround antagonistic receptive field organization. The inner plexiform layer, on the other hand, is concerned more with the temporal aspects of light stimuli. Many cells receiving input in this layer respond with transient responses and respond better to moving stimuli than to static spots of light. The output Neurons of this layer, the ganglion cells, reflect either the processing of information in the outer plexiform layer, i.e., the cells respond in a sustained fashion to appropriately positioned stimuli, or the inner plexiform layer, i.e., the cells respond better to moving stimuli than to static ones.

Though the rod and cones are a [mosaic](https://en.wikipedia.org/wiki/Retinal_mosaic) of sorts, transmission from receptors, to bipolars, to [ganglion cells](https://en.wikipedia.org/wiki/Retinal_ganglion_cell) is not direct. Since there are about 150 million receptors and only 1 million optic nerve fibres, there must be convergence and thus mixing of signals. Moreover, the horizontal action of the [horizontal](https://en.wikipedia.org/wiki/Retina_horizontal_cell) and [amacrine cells](https://en.wikipedia.org/wiki/Retina_amacrine_cell) can allow one area of the retina to control another (e.g. one stimulus inhibiting another). This inhibition is key to lessening the sum of messages sent to the higher regions of the brain. The optic nerve carries the [ganglion cell](https://en.wikipedia.org/wiki/Retinal_ganglion_cell) [axons](https://en.wikipedia.org/wiki/Axon) to the brain.