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**QUESTION**

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

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

**SOLUTION**

1. THE EYE

The eye is a complex and highly developed photosensitive organ that permits an accurate analysis of the form, light intensity and color reflected from objects and providing the sense of sight. It is a microcosm - a very compendium of all tissues. True cell-tissues, connective tissues in several forms, muscular, vascular and nervous tissue are all presented here; and there is not another part of the whole human body which offers such facilities for direct clinical observation, and for the anatomical investigation of the minute tissue changes produced by disease.

Broadly, from an anatomical perspective, the eye can be viewed as a series of overlapping layers of tissue protected within the oribits of the skull which also contains adipose cushions. A histological understanding of the layers of the eye is essential for appreciating disease pathophysiology and also understanding certain therapeutic approaches.

The eye has both external and internal structures.

External structures of the eye include the eyelashes, lids, muscles, accessory glands, and conjunctiva.

The internal structures of the eye consist of three layers/tunics of tissue arranged concentrically:

* A tough external **fibrous layer** consisting of sclera and the transparent cornea
* A middle **vascular layer** that includes the choroid, ciliary body and iris
* An inner sensory layer, the retina, which communicates with the cerebrum through the posterior optic nerve.

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

**"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. It protects the more delicate internal structures and provides sites for muscle insertion. 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, 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.

The supportive framework/ tissue of the sclera, usually composed of connective tissue is it’s stroma.

The lamina fusca is the layer of thin pigmented connective tissue on the inner surface of the sclera of the eye.

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

The cornea 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.

Corneal 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, neighboring cells stretch to attempt to compensate these losses.

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

1. "Iris":

The iris consists of (1) stromal layer with pigmented, fibrovascular tissue and (2) pigmented epithelial cells beneath the stroma

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":

This is the tissue that divides the posterior chamber and vitreous body. It consists of:

a.) The ciliary muscle and the ciliary epithelium

- The ciliary muscle, via the lens zonules, controls the structure of the lens, which is vital for accommodation. Zonules are connective tissue fibers that connect the ciliary muscle and lens.

- The ciliary epithelium produces aqueous humor which fills the anterior compartment of the eye.

3. "Choroid":

This 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: Retina":**

1. Retina: The nervous tissue of the eye where photons of light convert to neurochemical energy via action potentials.

**FUNCTIONS**

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 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. 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 retina, which then send these impulses to the brain, via the optic nerve.

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 help support the retina. This abundant blood supply is implicated in uveitis, as inflammatory mediators enter the eye through this vascular network.

**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.

**"Age-related macular degeneration"**: A progressive eye disease causing damage to the macula or central portion of the retina. Accumulation of drusen, or lipid-laden deposits in Bruch’s membrane of the retina, is associated with disease severity.

**"Fuchs Dystrophy"**: A disease of the corneal endothelium, that causes accumulation of excess edema in the corneal stroma. Progression of the disease often causes blisters in the eye, also referred to as bullous keratopathy.

**"Floaters"**: The sensation of floaters is due to changes that occur in the jelly-like vitreous layer of the eye.

**"Retinal detachment"**: It occurs when the outer pigment epithelial layer separates from the inner neurosensory layer consisting of rods and cones; this is a vision-threatening condition as the neurosensory layer is unable to receive nutrients from the underlying choriocapillaris and retinal pigment epithelium.

2. **THE RETINA**

An understanding of the histology of the retina is essential to consider for complete insight into diseases involving a vital sensory component in the eye.

The retina is the innermost layer of the wall of the eye. It is in immediate contact with the vitreal cavity on one side and with the choroid (of the uveal layer) on the other side.

The retina consists of two fundamentally distinct layers, the neural retina (often called simply "the retina") and the pigmented epithelium. These two layers derive, respectively, from the front and back ectodermal surfaces of the embryonic optic cup.

Cells comprising the neural retina give the appearance of several layers. The layers from the closest to the front anterior of the head towards the posterior of the head are as follows:

1. Inner limiting membrane

2. Nerve fiber layer (NFL)

3. Ganglion cell layer

4. Inner plexiform layer

5. Inner nuclear layer

6. Outer plexiform layer

7. Outer nuclear layer

8. External limiting membrane

9. The layer of rods and cones

The innermost layer is the **inner limiting membrane,** a basal lamina separating nervous tissue of the retina from connective tissue of the vitreous humor.

**The layer of nerve fibers** contains axons from ganglion cells which travel across the retina to the optic nerve and hence past the optic chiasm into the optic tract and into lateral geniculate nucleus of the thalamus.

**The ganglion cell layer** contains the cell bodies of ganglion cells, the cells whose axons project to the brain.

**The inner plexiform layer** contains dendrites of ganglion cells synapsing with axons of bipolar cells.

**The inner nuclear layer** contains the cell bodies of bipolar cells

**The outer plexiform layer** contains dendrites of bipolar cells synapsing with axons of photoreceptor cells.

**The outer nuclear layer** contains the cell bodies of receptor cells(rods and cones).

Between the outer nuclear layer and the receptor layer is the site of the **outer limiting membrane,** a basal lamina bounding the neural retina. The outer segments (rods and cones) of the receptor cells penetrate the outer membrane to contact the pigmented epithelium.

**The receptor layer** contains the photoreceptive outer segments (rods and cones) of receptor cells.

The (tenth) layer, the **pigmented epithelium** is the outermost layer of the retina, consisting of cuboidal epithelial cells derived from the outer layer of the embryonic optic cup. The dense melanin pigment of this layer absorbs light not captured by photoreceptors. The cells of the pigmented epithelium also contribute to the maintenance of photoreceptors, "recycling" membranes that are shed from rod and cone outer segments.

**Clinical note:** Although cells of the pigmented epithelium are intimately associated with outer segments (rods and cones) of receptor cells, this surface where the neural retina contacts the pigmented epithelium is inherently extremely fragile and is the site where retinal detachment can occur.