NEUROHISTOLOGY ASSIGNMENT

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QUESTION 1

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

The eyes are the peripheral organs for vision. Each eyeball is like a camera which has a lens that creates images which fall on a light sensitive membrane called the **RETINA.** Cells in the retina convert light images into nervous impulses that pass through the optic nerve and other parts of the visual pathway, to reach visual areas in the cerebral, where vision is perceived.

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

The eye can be seen as a series of overlapping tissue.

The internal structures of the eye consist of three (3) layers of tissue arranged concentrically:

A. The outermost layer: made up of the sclera and the cornea

B. The middle layer, the uvea, which is a vascular layer: subdivided into the iris, ciliary body and choroid

C. The innermost layer: made up of nervous tissues

A. Outermost Layer: Sclera and Cornea:

i. The Sclera (White of the eye): it is a dense connective tissue made

of mainly type 1 collagen fibers, oriented in different directions.

It is the tough opaque aspect of the eyeball.

The lack of parallel orientation of collagen fibers gives the sclera its white appearance as opposed to transparent nature

The collagen of the sclera and cornea are continuous

It is lined by thin non-keratinized stratified squamous epithelium and it is relatively avascular

The sclera is divided into four (4) layers: 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.

ii. The cornea (transparent front layer of the eye): it controls and focuses the entry of light into the eyes and it is avascular.

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:

- 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: The tissue that divides the posterior chamber and vitreous body

- Consists of 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:

- 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, Retina:

1. Lens: separates the aqueous and vitreous chambers

- Consists of an outer capsule, 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 body: a jelly-like space made of type II collagen separating the retina and the lens.

It occupies the large vitreous chamber behind the lens

It consists of transparent, gellike connective tissue that is 99% water (vitreous humour), with collagen fibrils hyaluronate, contained within an external lamina called the vitreous membrane.

The only cells in the vitreous body are called hyalocytes, which synthesize the 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

Moreover, the retina itself is divided into various layers as follows:

Retinal pigment epithelium: 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.

- Outer limiting membrane: 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.
- Outer nuclear layer: This layer consists of nuclei of rod and cone cells.
- Outer plexiform layer: This layer contains synaptic processes of rod and cone cells.
- Inner nuclear layer: This layer contains the cell body of glial, amacrine, bipolar, and horizontal cells
- Inner plexiform layer: This layer relays information from cells of the inner nuclear layer. Thus, this layer has axons of amacrine, bipolar, and glial cells and dendrites of retinal ganglion cells.
- Ganglion cell layer: This layer contains nuclei of retinal ganglion cells.
- Nerve fiber layer: This layer contains axons of retinal ganglion cells and the astroglia which support them. Collectively, these axons constitute the optic nerve.
- Internal limiting membrane: A thin layer of Muller glial cells and basement membrane which demarcates the vitreous anteriorly from the retina posteriorly.

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 anatomy

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.

QUESTION 2

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

Introduction

The retina is a layer of photoreceptors cells and glial cells within the eye that captures incoming photons and transmits them along neuronal pathways as both electrical and chemical signals for the brain to perceive a visual picture.

The retina is located in the posterior segment and forms the innermost boundary among the other major layers of the eye that include the vascular choroid and the fibrous sclera.

Disease manifestations can occur in the retina at different stages of life, many of which severely compromise visual ability and consequently the quality of life.

Layers of the Retina

The retina, more specifically, subdivides into ten distinct layers that are described in order from the innermost layers closer to the pupil to the layers further towards the posterior and periphery of the eyeball:

- **Inner Limiting Membrane** – the innermost layer of the retina that forms a smooth boundary against the vitreous humor which fills the vitreous chamber of the eye. The peripheral boundary of this layer consists of Müller glial cells, which function to maintain retinal homeostasis by upholding retinal lamination and by supporting other cells.
- **Retinal Nerve Fiber Layer** – the layer composed of retinal ganglion cell axons mixed with astrocytes and the processes of the Muller cells.

  The inner limiting membrane serves as the basal lamina for the cells of the retinal nerve fiber layer.
- **Ganglion Cell Layer** – the layer of ganglion cell bodies that project their axons, eventually to form the optic nerve.
- **Inner Plexiform Layer** – this layer is where the axons of bipolar cells synapse onto the ganglion cells. The dendrites of amacrine cells also synapse at this zone and function in modulating the electrical conduction between the bipolar cells and ganglion cells, preventing lateral potentiation.
- **Inner Nuclear Layer** – the layer composed of the cell bodies of bipolar cells, horizontal cells, and amacrine cells. Bipolar cells function as channels that transmit and encode various synaptic inputs from photoreceptor cells onto ganglion cells. Horizontal cells provide feedback modulation onto rod and cone cells.
- **Outer Plexiform Layer** – the region where projections from photoreceptor cells synapse with the dendrites of the cells residing in the inner nuclear layer.
- **Outer Nuclear Layer** – the layer containing the cell bodies of both rods and cones.
- **External Limiting Membrane** – the region that is composed of gap-junctions between photoreceptor cells and Muller cells; it separates the cell bodies of the rods and cones from their inner segments and

outer segments.

- **Photoreceptor Layer** – the region consisting of the inner segments and outer segments of rods and cones.

  The outer photoreceptor segments consist of membrane-bound discs that contain the light-sensitive pigments such as rhodopsin that are necessary for phototransduction.

  The inner segments house the abundance of mitochondria needed to meet the high metabolic demands of the photoreceptor cells.

- **Retinal Pigment Epithelium** – the outermost retinal layer that spans a width of a single cell located between the neural retina and the Bruch membrane, adjacent to the highly-vascularized choroid layer.

  The retinal pigment epithelium (RPE) contributes to the blood-retinal barrier in conjunction with the endothelium of the retinal vessels and has many functions including ion and water transport and secretion of growth factors and cytokines.

  The RPE cells intermingle with the outer segments of the rods and cones. This proximity allows for the recycling of all-*trans*-retinal back into 11-*cis*-retinal and its delivery back to the cones and rods to be used again for phototransduction.

  RPE cells are crucial in the support and maintenance of both photoreceptor cells and the underlying capillary endothelium.

Six major cell types form the various layers within the human retina:

1. Photoreceptors (rods and cones) - form the **outer nuclear layer**
    - Synapse with bipolar cells at the outer plexiform layer
    - Rods deal predominantly with peripheral and night vision
    - Cones deal mainly with central vision
2. Bipolar cells - make up the **inner nuclear layer**
    - Synapse with amacrine cells and ganglion cells at the inner plexiform layer
3. Amacrine cells
    - Inhibitory cells which interact with bipolar cells and retinal ganglion cells

4. Retinal ganglion cells - form the **ganglion cell layer** (innermost layer, furthest from the photoreceptors)
    - Axons tract towards the back of the eye and form the **optic nerve**
5. Horizontal cells
    - Assist in operations such as contrast enhancement and preservation of spatial information.
6. Muller cells
    - glial cells which support metabolism and homeostasis of the retina.

How Corona virus can penetrate the body through the eye:

Infectious droplets and body fluids can easily contaminate the human conjunctival epithelium.

Respiratory viruses such as coronavirus are capable of inducing ocular complications in infected patients, which then leads to respiratory infection.

Severe acute respiratory syndrome coronavirus (SARS-CoV2) is predominantly transmitted through direct or indirect contact with mucous membranes in the eyes, mouth, or nose.

Based on the ocular and nasal anatomy, a highly plausible path is via the lacrimal and nasolacrimal ducts (the tear ducts) and then into nose, trachea, and finally lung.

Regarding the mechanism of travel, two scenarios may be entertained that are not mutually exclusive.

In the first, the virus travels through reinfection and replication of adjoining cells by syncytial contact or by short-range diffusion.

In this model, travel is dependent on replication en route.

Alternately, the virions may travel in a replication-independent manner, perhaps propelled by the ciliary cells that line the lacrimal and respiratory mucosae to reach the lungs (Vira et al., 2007).

Reference

Vira Bitko, Alla Musiyenko, Sailen Barik (2007). Viral Infection of the Lungs through the Eyes. Journal of Virology. DOI: 10.1128/JVI.01437-06