**THE EYE AND ITS HISTOLOGICAL IMPORTANCE.**

 The eye is a highly developed photosensitive organ whose function is to analyze the form, intensity and color of light reflected from objects in the environment and providing a sense of sight. A histological understanding of the layers of the eye is essential for appreciating disease pathophysiology and also understanding certain therapeutic approaches. From an anatomical perspective, the eye can be viewed as a series of overlapping layers of tissue.

 The eye consists externally of a rough, fibrous globe that maintains its overall shape. The internal structures of the eye consist of three layers of tissue arranged concentrically:

* The sclera and cornea make 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.

EXTERIOR LAYER

* SCLERA: The sclera is dense connective tissue made up of mainly type 1 collagen fibers parallel to the organ surface but intersecting in various directions with its microvasculature present near the outer surface. The lack of fibers gives the sclera its white appearance, as opposed to the transparent nature of the cornea.

 **Histological Importance:** The sclera supports the eye shape, protecting its delicate internal structures. It also serves as the site of attachment of the extrinsic eye muscles.

* CORNEA: The cornea consists of type 1 collagen fibers oriented in a uniform parallel direction to maintain transparency. It consists of five layers: epithelium (non-keratinized stratified squamous epithelium), Bowman layer (basement membrane of epithelium), stroma (also called substantia propria), Descemet's membrane, corneal endothelium.

 In short form, it is composed of two layers of epithelium with organized connective tissue in between. Of the five layers, two layers take more importance namely: Stroma and Endothelium.

 The stroma is the largest layer of the cornea and has collagen fibers arranged in a regular pattern .Cells called keratocytes maintain the integrity of this layer. The uniform orthogonal array of collagen fibrils contributes to the transparency of this avascular tissue.

 The corneal endothelium is a one cell thick layer made of either simple squamous or cuboidal cells. Cells in this region do not regenerate and have sodium/potassium pumps in the basolateral membranes largely responsible for regulating the proper hydration state of the corneal stroma to provide maximal transparency and optimal light refraction.

 **Histological Importance**: The cornea protects the anterior surface of the eye and refracts incoming light into the eye

MIDDLE LAYER/UVEA

* IRIS: It consists of a stromal layer with pigmented, fibrovascular tissue and pigmented 2 layered epithelia cells beneath the stroma continuous with the covering of the ciliary process (explained below). The pigmented layer of cells blocks rays of light and ensures that light must move through he pupil to reach the retina.

 The sphincter papillae and dilator papillae muscles connect to the stroma. The angle formed by the cornea and iris contains connective tissue with endothelial channels called the trabecular meshwork, which drains aqueous humor into the scleral venous sinus, from which it enters venules of the sclera.

 **Histological Importance:** The iris controls pupil diameter and thus the amount of light entering the eye.

* CILIARY BODY: It consists of ciliary smooth muscle and ciliary processes.

The ciliary muscle makes up most of the ciliary body’s stroma and consists of three groups of smooth muscle fibers. Contraction of these muscles affects the shape of the lens and is important in visual accommodation.

 The ciliary processes are a radially arranged series of about 75 ridges extending from the ciliary body. They provide a large surface area covered by a double layer of low columnar cells, the ciliary epithelium. Cells of this dual epithelium have extensive basolateral folds with sodium/potassium ATPase activity and are specialized for secretion of aqueous humor.

 **Histological Importance:** The ciliary body holds the suspensary ligaments that attach to the lens and change lens shape for far and near vision.

* CHOROID: It consists of a dense network of blood vessels supplying nourishment to structures of the eye, housed in loose connective tissue. Two layers make up the choroid: the inner choroido-capillary lamina that has a rich microvasculature important for nutrition of the outer retinal layers and the Bruch’s membrane, a thin extracellular sheet composed of collagen and elastic fibers surrounding the adjacent microvasculature and basal lamina of the retina’s pigmented layer.

 **Histological Importance:** The choroid supplies nourishment to the retina and its pigment absorbs extraneous light. The Bruch’s membrane has significance in age-related macular degeneration, where an accumulation of lipid deposits prevent diffusion of nutrients to the retina.

INNERMOST LAYER

* LENS: It 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.
* VITREOUS: It is 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.
* RETINA: It is the nervous tissue of the eye where photons of light convert to neurochemical energy via action potentials. The outer pigmented layer of the retina is a simple cuboidal epithelium attached to Brusch’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. The inner retinal region, the neural layer, is thick and stratified with various neurons and photoreceptors.

 **Histological Importance:** The pigmented layer absorbs extraneous light and provides vitamin A for the photoreceptor cells. The neural layer detects incoming light rays and converts there light rays into nerve signals and transmits them to the brain.

CLINICAL CONSIDERATION

* Glaucoma: Refers to optic nerve damage related to increased intraocular pressure. Drainage of aqueous humor through the trabecular meshwork is often implicated.
* Floaters: The sensation of floaters is due to changes that occur in the jelly like vitreous layers of the eye.
* 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 s 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 sub capsular cataracts arise from behind the sac-like structure of the lens.
* Age related macular degeneration: A progressive eye disease causing damage to the macula or central portion of the retina.

**LAYERS OF THE RETINA FOR INFORMATION PENETRATION**

The retina is simply defined as the 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 serrata this 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:
1. Outer limiting membrane
2. Inner/outer segment layer
3. Outer plexiform layer
4. Outer nuclear layer
5. Inner nuclear layer
6. Inner plexiform layer
7. Ganglion cell layer
8. Nerve fiber layer
9. Internal limiting membrane

As explained above, the retina has ten distinct layers. From closest to farthest from the vitreous body:

* **Inner limiting membrane**: basement membrane elaborated by Müller cells.
* **Nerve fibre layer**: axons of the ganglion cell bodies, note that a thin layer of Müller cell footplates exists between this layer and the inner limiting membrane.
* **Ganglion cell layer**: contains nuclei of ganglion cells, the axons of which become the optic nerve fibres, and some displaced amacrine cells.
* **Inner plexiform layer**: contains the synapse between the bipolar cell axons and the dendrites of the ganglion and amacrine cells.
* **Inner nuclear layer**: contains the nuclei and surrounding cell bodies (perikarya) of the amacrine cells, bipolar cells, and horizontal cells.
* **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 region, this is known as the Fiber layer of Henle.
* **Outer nuclear layer**: cell bodies of rods and cones.
* **External limiting membrane**: layer that separates the inner segment portions of the photoreceptors from their cell nuclei.
* **Inner segment / outer segment layer**: inner segments and outer segments of rods and cones. The outer segments contain a highly specialized light-sensing apparatus.

**RETINAL PIGMENT EPITHELIUM**

It is a 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 prevents light reflection throughout the globe of the eyeball; this is extremely important for clear vision.

 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.

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

* Photoreceptors (rods and cones): form the outer nuclear layer and synapse with bipolar cells at the outer plexiform layer, Rods deal predominantly with peripheral and night vision, Cones deal mainly with central vision
* Bipolar cells - make up the inner nuclear layer :Synapse with amacrine cells and ganglion cells at the inner plexiform layer
* Amacrine cells :Inhibitory cells which interact with bipolar cells and retinal ganglion cells
* 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
* Horizontal cells: Assist in operations such as contrast enhancement and preservation of spatial information.
* Muller cells: glial cells which support metabolism and homeostasis of the retina.

These layers can be grouped into 4 main processing stages:

* Photoreception
* Transmission to bipolar cell
* Transmission to ganglion cells, which also contain photoreceptors, the photosensitive ganglion cells
* Transmission along the optic nerve. At each synaptic stage there are also laterally connecting horizontal and amacrine cells.
* 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.

 NOTE: Though the rod and cones are a mosaic of sorts, transmission from receptors, to bipolars, to ganglion cells 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 and amacrine cells 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 axons to the brain.