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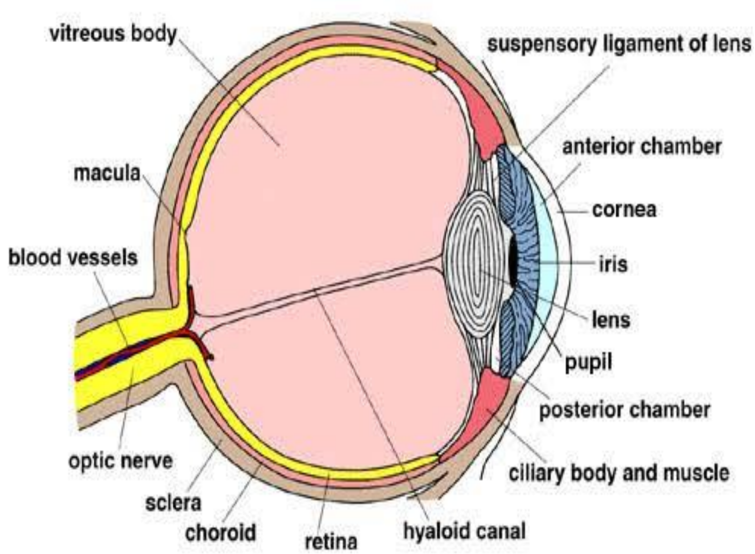
# QUESTION 1

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

The eye is a complex and highly developed photosensitive organ that analyses the form, intensity, and colour of light reflected from objects, providing the sense of sight. The eyes are located in protective areas of the skull, the orbits, which also contain cushions of adipose tissue. Each eyeball includes a tough, fibrous globe to maintain its shape, a system of transparent tissues that refract light to focus the image, a layer of photosensitive cells, and a system of neurons whose function it is to collect, process, and transmit visual information to the brain.



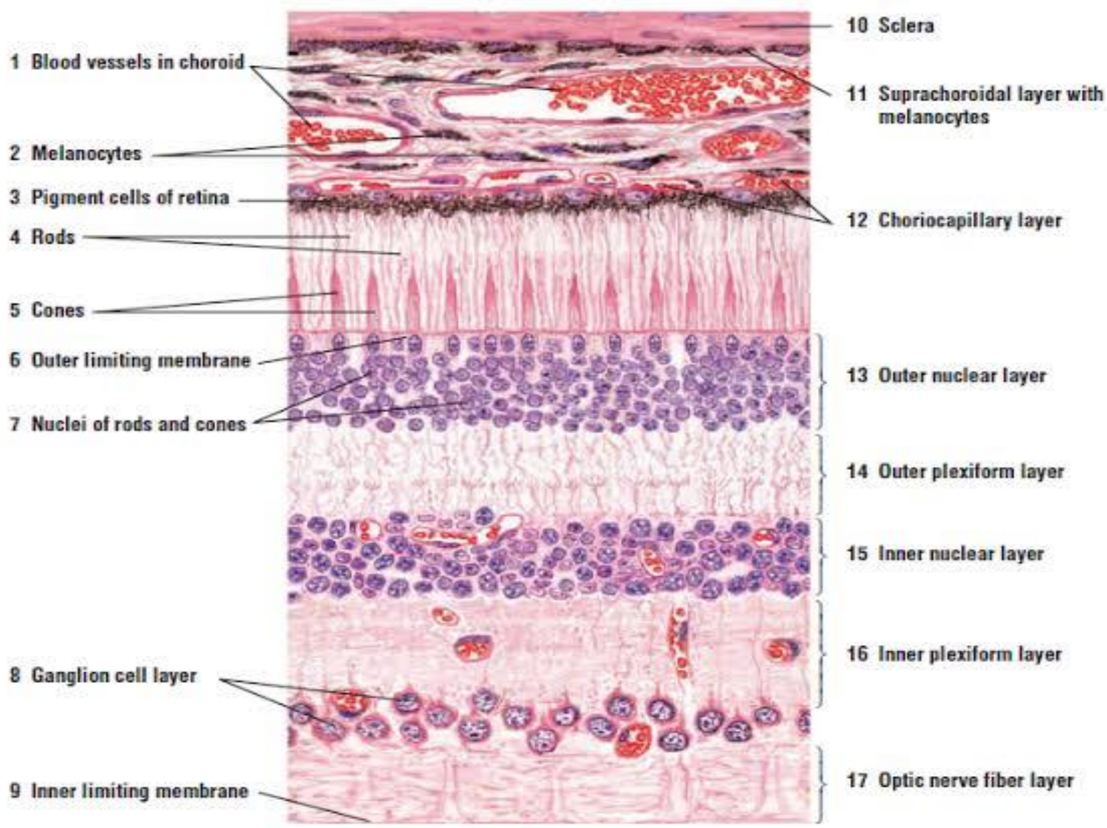

## CHAMBERS OF THE EYE

1. **Anterior chamber:** This is the aqueous humour-filled space between the corneal endothelium and the iris.
2. **Posterior chamber:** This is a narrow space behind the peripheral part of the iris and in front of the suspensory ligament of the lens.

3. **Vitreous chamber:** This is the largest of the three chambers and is located behind the lens and in front of the optic nerve. It is occupied by vitreous humour which supports the lens and maintains the shape of the vitreous chamber.

## LAYERS OF THE EYE

1. A tough, outer, fibrous layer consisting of the cornea and sclera.
2. The uvea; a middle vascular layer consisting of the choroid, the ciliary body and the iris.
3. An inner sensory layer; the retina which includes the outer pigmented epithelium and the inner neural retina.




## FIBROUS LAYER

### The Sclera "white of the eye"

The opaque white posterior five-sixths of the external layer is the sclera. The sclera consists of tough, dense connective tissue made up of mainly type I collagen fibers which intersect in various directions while remaining parallel to the surface of the organ. It has a diameter of approximately 22 mm in adults, averages 0.5 mm in thickness and is relatively avascular.

## The Cornea

The anterior one-sixth of the external layer of the eye is the cornea. It is colourless, transparent, and completely avascular. A section of the cornea shows that it consists of five layers:

i. **Corneal epithelium:** Non-keratinized, stratifies squamous epithelium. It has 5-6 cell layers and comprises about 10% of corneal thickness. It is a fast growing, regenerating multicellular layer that interacts directly with the tear film.
ii. **An anterior limiting membrane or Bowman's membrane:** The corneal epithelium rests on this basement membrane. It protects the underlying stroma and is composed of type I collagen, laminin and several other heparin sulphate proteoglycans.
iii. **Stroma:** This is the largest layer of the cornea. It 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.
iv. **Descemet's membrane:** This is an acellular layer made up of type IV collagen that serves as a modified basement membrane of the corneal endothelium.
v. **Corneal endothelium:** A one cell thick layer made up of either simple squamous or cuboidal cells. Cells in this region have pumps that maintain fluid balance and prevent swelling of the stroma.

The cornea receives nutrition from vessels around its periphery. The cornea has a rich nerve supply. The nerve fibres, which are non-myelinated, form a plexus deep to the corneal epithelium, and in the stroma. Free nerve endings are present in the epithelium.

## Limbus

Encircling the cornea is the corneoscleral junction, or limbus, a transitional area where the transparent stroma merges with the opaque sclera. This region does have microvasculature which, along with aqueous humour in the anterior chamber, provides metabolites for the corneal cells by diffusion. Stem cells for the stratified epithelium are concentrated at the limbus, from which rapidly dividing transit amplifying cells move centripetally into the corneal epithelium. A circular channel called the sinus venosus sclerae (or canal of Schlemm) is located in the sclera just behind the corneoscleral junction and it allows for slow, continuous drainage of aqueous humour from the anterior cavity.

## UVEA

## The Choroid

The choroid consists of:

(a) the choroid proper

(b) the suprachoroid lamina that separates the choroid proper from the sclera

(c) the basal lamina (membrane of Bruch) which intervenes between the choroid proper and the retina

**The choroid proper** is made up of an outer vascular lamina containing small arteries and veins, and lymphatics; and an inner capillary lamina (or choroidocapillaris). The connective tissue supporting the vessels of the vascular lamina is the choroidal stroma. This stroma contains many pigmented cells, giving the choroid a dark colour. This colour darkens the interior of the eyeball. The pigment also prevents reflection of light within the eyeball.

**The suprachoroid lamina** is also called the lamina fusca. It is non-vascular. It is made up of delicate connective tissue containing collagen, elastic fibres, and branching cells containing pigment. A plexus of nerve fibres is present. Some neurons may be seen in the plexus.

**The membrane of Bruch** is an extracellular matrix layer united on the outside to the capillary layer (of the choroid proper); and on the inside to the basement membrane of pigment cells of the retina. Nutrients passing from the capillary layer to the outer layers of the retina have to pass through this membrane.

## The Ciliary Body

The ciliary body represents an anterior continuation of the choroid. It is a ring-like structure continuous with the periphery of the iris. It is connected to the lens by the suspensory ligament. It consists of the ciliary muscle and ciliary epithelium. The ciliary muscle controls the structure of the lens which is vital for accommodation. The ciliary epithelium produces aqueous humour which fills the anterior compartment of the eye.

## The Iris

The iris is the most anterior part of the vascular coat of the eyeball. It forms a diaphragm placed immediately in front of the lens. At its periphery it is continuous with the ciliary body. In its centre, there is an aperture the pupil. The iris is composed of a stroma of connective tissue containing numerous pigment cells, and in which are embedded blood vessels and smooth muscle. Some smooth muscle fibres are arranged circularly around the pupil and constrict it; they form the sphincter pupillae. Other fibres run radially and form the dilator pupillae. The posterior surface of the iris is lined by a double layer of epithelium continuous with that over the ciliary body. The pupil regulates the amount of light passing into the eye. In bright light the pupil contracts, and in dim light it dilates so that the optimum amount of light required for proper vision reaches the retina.

## The Lens

The lens is a transparent biconvex structure immediately behind the iris, used to focus light on the retina. Derived from an invagination of the embryonic surface epithelium (ectoderm), the lens is a unique avascular tissue. It is highly elastic, a feature that is lost with age as lens tissue hardens. The lens has three principal components:

I. **Lens capsule:** The lens is covered by a thick (10–20 m), homogeneous capsule rich in proteoglycans and type IV collagen.
II. **Lens epithelium:** Subcapsular lens epithelium consists of a single layer of cuboidal epithelial cells and is present only on the anterior surface of the lens. The basal ends of the epithelial cells attach to the lens capsule and their apical surfaces have interdigitations that bind the epithelium to the internal lens fibers. At the posterior edge of this epithelium, near the equator of the lens, the cells divide to provide new cells that differentiate as lens fibers.
III. **Lens fibers:** Lens fibers are highly elongated and appear as thin, flattened structures. Developing from stem cells in the lens epithelium, the differentiating lens fibers eventually lose their nuclei and other organelles, fill the cytoplasm with a group of proteins called crystallins, and become very long. Mature lens fibers are typically 7–10 mm long, 8–10 m wide, and 2 m thick. The fibers are densely packed together forming a perfectly transparent tissue highly specialized for light refraction.

The lens is held in place by a radially oriented group of fibers, the elastic ciliary zonule, which inserts on both the lens capsule and on the ciliary body. This system is important in the process known as accommodation, which permits focusing on near and far objects by changing the curvature of the lens.

## RETINA

The retina consists of two major layers:

i. The inner one, the neural retina, is a 10- layered structure. It contains the neurons and photoreceptors. This layer's visual region extends anterior only as far as the ora serrata, but it continues as a cuboidal epithelium lining the surface of the ciliary body and posterior iris.
ii. The outer pigmented layer is an epithelium resting on Bruch's membrane just inside the choroid. This pigmented, cuboidal epithelium also lines the ciliary body and posterior iris, contributing to the double epithelium described with those structures. The pigmented epithelium consists of low columnar cells with basal nuclei. The cells have well-developed functional complexes, gap junctions, and numerous invaginations of the basal membranes associated with mitochondria. The apical ends of the cells extend processes and sheath-like projections that surround the tips of the photoreceptors. Melanin granules are numerous in the extensions and apical cytoplasm. This cellular region also contains numerous phagocytic vacuoles and secondary lysosomes, peroxisomes, and abundant smooth ER, with specialized regions in these cells for isomerization of all-trans-retinal (derived from vitamin A) and its transport to the photoreceptors. The diverse functions of the cells in the retinal pigmented epithelium include the following:

a) serve as an important part of the blood-retina barrier
b) absorb light passing through the retina to prevent its reflection
c) phagocytose shed components from the adjacent rods and cones

d) remove free radicals
e) isomerize and regenerate the retinoids used as chromophores by the rods and cones.

## ACCESSORY STRUCTURES OF THE EYE

### Conjunctiva

The conjunctiva is a thin, transparent mucosa that covers the exposed, anterior portion of the sclera (ocular conjunctiva) and continues as the lining on the internal surface of the eyelids (palpebral conjunctiva). It consists of a stratified columnar epithelium, with numerous small cells resembling goblet cells, supported by a thin lamina propria of loose vascular connective tissue. At the free margin of the eyelid the palpebral conjunctiva becomes continuous with skin; and at the margin of the cornea the ocular conjunctiva becomes continuous with the anterior epithelium of the cornea. When the eyelids are closed the conjunctiva forms a closed conjunctival sac. The line along which palpebral conjunctiva is reflected onto the eyeball is called the conjunctival fornix: superior, or inferior. The ducts of the lacrimal gland open into the lateral part of the superior conjunctival fornix. Lacrimal fluid keeps the conjunctiva moist. Accessory lacrimal glands are present near the superior conjunctival fornix (glands of Krause).

### Eyelids

Eyelids are pliable structures containing skin, muscle, and conjunctiva that protect the eyes. The skin is present only on the external surface. It is loose and elastic, lacking fat, and has very small hair follicles and fine hair, except at the distal edge of the eyelid, where large follicles forming eyelashes are present. Associated with the follicles of eyelashes are sebaceous glands and modified apocrine sweat glands.

Deep to the skin are fascicles of striated muscle that make up the orbicularis oculi and levator palpebrae muscles which fold the eyelids. Adjacent to the conjunctiva is a dense fibroelastic plate of connective tissue called the tarsus which provides support for the other tissues of the eyelids. This tissue also contains a series of 20–25 large sebaceous glands, each with many acini secreting into a long central duct that opens among the eyelashes at the eyelid's distal margin. Oils in the sebum produced by these tarsal glands, commonly called Meibomian glands, form a surface layer on the tear film, reducing its rate of evaporation, and help lubricate the ocular surface.

### Lacrimal glands

The lacrimal glands produce fluid continuously for the tear film that moisturizes and lubricates the cornea and conjunctiva and supplies oxygen to the corneal epithelial cells. Tear fluid also contains various metabolites, electrolytes, and proteins, including lysozyme, an enzyme that hydrolyzes the cell walls of certain species of bacteria, facilitating their destruction. The main lacrimal glands are located in the upper temporal portion of the orbit and have several lobes that drain separately through excretory ducts into the superior fornix, the conjunctiva-lined recess between the eyelids and the eye. After moving across the ocular surface, the fluid secreted by these glands collects in other parts of the bilateral lacrimal apparatus: flowing into two small round openings (0.5 mm in diameter) to canaliculi at the medial margins of the upper and lower eyelids and then passing into the lacrimal sac and finally draining into the nasal cavity via the nasolacrimal duct. The canaliculi are lined by stratified squamous epithelium, but the more distal sac and duct are lined by pseudostratified ciliated epithelium like that of the nasal cavity.

## GENERAL 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 cornea serves a protective role and is responsible for two-thirds of the refractive properties of the eye. The remaining one-third 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 send these impulses to the brain via the optic nerve.

The uvea of the eye is crucial mediator of nutrition and gas exchange, as blood vessels course through the ciliary body and iris, while the choriocapillaris help support the retina.

## CLINICAL ANATOMY

Aqueous humour is produced continuously. If its drainage from the anterior chamber is impeded, typically by obstruction of the trabecular meshwork or scleral venous sinus, intraocular pressure can increase, causing the condition called glaucoma. Untreated glaucoma can cause pressing of the vitreous body against the retina, affecting visual function and possibly leading to neuropathy in that tissue.

# QUESTION 2

***Coronavirus can penetrate the body through the eye and implicate the immune system. Briefly discuss the layers of the retina for information penetration.***

The retina is the innermost layer of the eye that is responsible for the visual processing that turns light energy from photons into three-dimensional images. It is a layered structure with ten distinct layers of neurons interconnected by synapses. These cells are subdivided into 3 basic cell types:

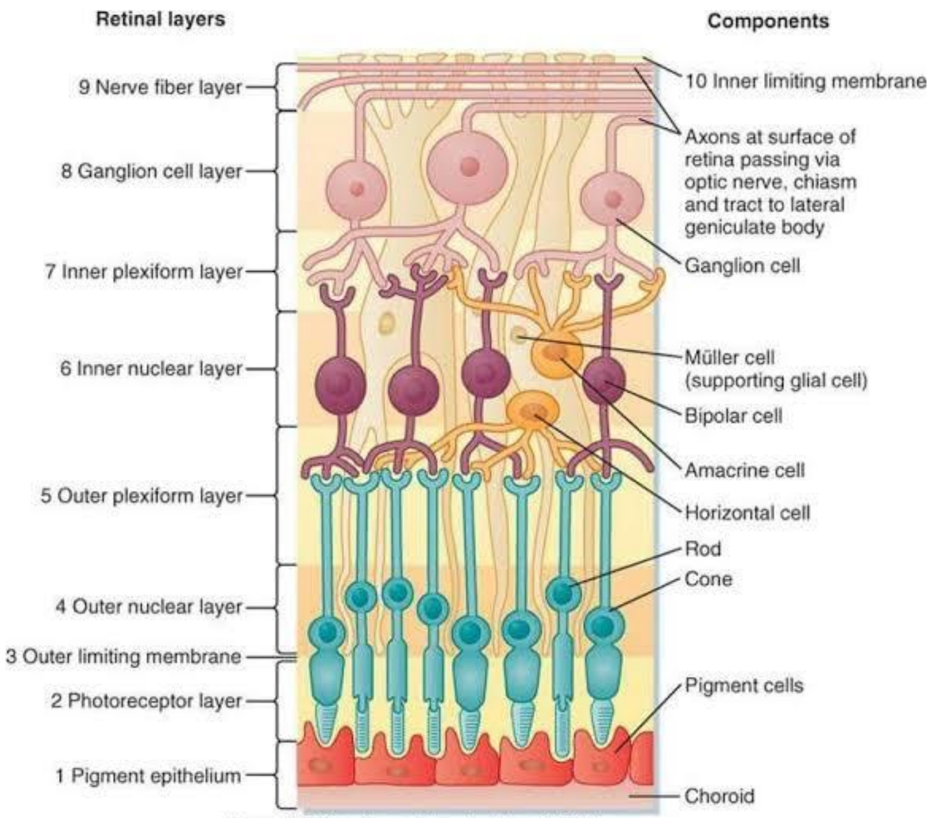
I. Photoreceptor cells- Rod cells and cone cells
II. Neuronal cells- Bipolar neurons, Ganglion cells, Amacrine cells, Horizontal cells
III. Glial cells- Cells of Muller

**Beginning from the external surface, the following layers can be made out:**

1. **Retinal pigment epithelium:** This is a single layer of cuboidal epithelial cells containing pigment. This layer is closest to the choroid and provides nourishment and supportive functions to the neural retina. The pigment prevents light reflection throughout the globe of the eyeball.
2. **Layer of rods and cones:** The rods are processes of rod cells, and cones are processes of cone cells. The tips of the rods and cones are surrounded by processes of pigment cells.
3. **External limiting layer:** This layer separates the inner segment portions of the photoreceptors from their nuclei.
4. **Outer nuclear layer:** The outer nuclear layer contains the cell bodies and nuclei of rod cells and of cone cells.
5. **Outer plexiform layer:** This layer consists 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.
6. **Inner nuclear layer:** This layer contains nuclei and surrounding cell bodies of the amacrine cells, bipolar cells and horizontal cells.
7. **Inner plexiform layer:** This layer contains the synapse between the bipolar cell axons and the dendrites of the ganglion and amacrine cells.
8. **Ganglion cell layer:** This layer contains nuclei of ganglion cells, the axons of which become the optic nerve fibers and some displaced amacrine cells.
9. **Nerve fiber layer:** This layer consists of the ganglion cell bodies. The fibers converge on the optic disc where they pass through foramina of the lamina cribrosa to enter the optic nerve. There is a thin layer of Muller cell footplates existing between this layer and the inner limiting membrane.
10. **Inner limiting membrane:** This is the basement membrane elaborated by Muller cells.

These layers can be grouped into 4 main processing stages:

I. Photoreception
II. Transmission to bipolar cells
III. Transmission to ganglion cells
IV. Transmission along the optic nerve






## <u>ROD CELLS</u>

The human retina has approximately 120 million rod cells. They are extremely sensitive to light, responding to a single photon, and allow some vision even with light low levels, such as at dusk or night time. Rod cells are thin, elongated cells (50 m x 3 m), composed of two distinct segments. The outer segment is photosensitive; the inner segment contains the metabolic machinery for the cell's biosynthetic and energy-producing processes. The outer rod-shaped segment consists mainly of 600–1000 flattened membranous discs stacked like coins and surrounded by the plasma membrane. Between this outer segment and the cell's inner segment is a constriction, the connecting stalk, which is a modified cilium arising from a basal body. The inner segment is rich in glycogen and mitochondria near the base of this cilium. Abundant polyribosomes located inside the mitochondrial region produce proteins that are transported to the outer segment, where they are incorporated into the membranous discs. These proteins include the visual pigment rhodopsin (visual purple) which is bleached by light and initiates the visual stimulus.

## CONE CELLS

The human retina has 6 or 7 million cone cells, which are less sensitive to low light than rod cells and are specialized for colour vision in bright light. Three functional types of cone cells, not distinguishable morphologically, contain variations of the visual pigment iodopsin with maximal sensitivities in the red, blue, or green regions of the visible spectrum, which enables these cells to detect those colours in reflected light.

Cone cells are also elongated, with outer and inner segments, a modified cilium connecting stalk, and an accumulation of mitochondria and polyribosomes. The outer segments of cones differ from those of rods in their shorter, more conical form and in the structure of their stacked membranous disks, which in cones remain as continuous invaginations of the plasma membrane along one side. Also, newly synthesized membrane proteins are distributed uniformly throughout the outer segment of cones and although iodopsin turns over, the discs are shed much less frequently than in rods.

## BIPOLAR NEURONS

Bipolar neurons are second-order long-projection neurons that receive visual input from photoreceptors and projects their axons onto retinal ganglion cells. Thirteen different types of bipolar cells divide into rod bipolar cells and cone bipolar cells, depending on the cell from which cell they receive inputs. Each cone bipolar cell and rod bipolar cell is further subdivided depending on whether it depolarizes in response to light (ON-bipolar cells) or those that hyperpolarize (OFF-bipolar cells). Cone bipolar cells are either ON or OFF type whereas rod bipolar cells are only the ON type.

Rods specialize in scotopic vision and thus only need to determine whether or not photons are striking the retina quantitatively, thus ON bipolar cells are adequate for this binary function.

Cones cells provide information for the photopic vision that can differentiate fine details, movements and colours, and this require both ON and OFF bipolar cells to qualitatively differentiate incoming photons.

Bipolar cells link the inner and outer layers of the retina by forming a synaptic connection with the rods and cones in the inner plexiform layer.

## RETINAL GANGLION CELLS

Retinal ganglion cells (RGCs) are the retina’s main output neuron, but also a third class of photoreceptors that are also photosensitive and help transmit both image-forming and non-image forming information that functions in the physiological processes of the circadian rhythm, modulation of melatonin release, and regulation of pupil size. RGCs receive both excitatory and inhibitory inputs from two types of intermediate neurons: amacrine cells and bipolar cells. Ganglion cells are of two main types. Those that synapse with only one bipolar neuron are mono-synaptic, while those that synapse with many bipolar neurons are polysynaptic.

Monosynaptic ganglion cells are also called midget ganglion cells. Each of them synapses with one midget bipolar neuron. We have seen that midget bipolars in turn receive impulses from a single cone. This arrangement is usual in the central region of the retina, and allows high resolution of vision to be attained.

Polysynaptic ganglion cells are of various types. Some of them synapse only with rod bipolars (rod ganglion cells). Others have very wide dendritic ramifications that may synapse with several hundred bipolar neurons (diffuse ganglion cells). This arrangement allows for summation of stimuli received through very large numbers of photoreceptors facilitating vision in poor light.

## HORIZONTAL NEURONS

Horizontal cells are involved in modulating information transfer between bipolar cells and photoreceptors and are involved with helping eyes adjust to both bright light and low light conditions. They have wide and diffuse horizontal projections and couple to their neighbours via gap junctions. Horizontal neurons are of two types, rod horizontals and cone horizontals, depending on whether they synapse predominantly with rods or cones. Each horizontal cell gives off one long process, and a number of short processes (7 in case of rod horizontal cells, and 10 in case of cone horizontal cells). The short processes are specific for the type of cell: those of rod horizontals synapse with a number of rod spherules, and those of cone horizontals synapse with cone pedicles. The long processes synapse with both rods and cones (which are situated some distance away from the cell body of the horizontal neuron). The long and short processes of horizontal cells cannot be distinguished as dendrites or axons, and each process probably conducts in both directions.

## AMACRINE NEURONS

The term amacrine is applied to neurons that have no true axon. Like the processes of horizontal cells those of amacrine neurons also conduct impulses in both directions. Each cell gives off one or two thick processes that divide further into a number of branches. Different types of amacrine neurons are recognised depending upon the pattern of branching. We have seen that the processes of amacrine neurons enter the internal plexiform layer where they may synapse with axons of several bipolar cells, and with the dendrites of several ganglion cells. They also synapse with other amacrine cells. At many places an amacrine process synapsing with a ganglion cell is accompanied by a bipolar cell axon. The two are referred to as a dyad. The amacrine cells are believed to play a very important role in the interaction between adjacent areas of the retina resulting in production of sharp images. They are also involved in the analysis of motion in the field of vision.

## CELLS OF MULLER

These cells, also known as retinal gliocytes, give off numerous protoplasmic processes that extend through almost the whole thickness of the retina. Externally, they extend to the junction of the layer of rods and cones with the external nuclear layer. Here the processes of adjoining gliocytes meet to form a thin external limiting membrane. Internally, the gliocytes extend to the internal surface of the retina where they form an internal limiting membrane. This membrane separates the retina from the vitreous. The retinal gliocytes are neuroglial in nature. They support the neurons of the retina and may ensheath them. They probably have a nutritive function as well. Some astrocytes are also present in relation to retinal neurons.

## CLINICAL ANATOMY

**Cone-rod dystrophy:** This is a rare genetic isolated inherited retinal disorder characterized by primary cone degeneration with significant secondary rod involvement. Typical presentation includes reduced visual acuity, central scotoma, photophobia, colour vision alteration followed by night blindness and loss of peripheral visual field.

**Glaucoma:** This refers to a group of eye diseases which result in damage of the optic nerve and cause vision loss. Ocular hypertension is the most important risk factor in most glaucomas.