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Histology of the Eye

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Objectives Eye Histology:

• Introduce the three concentric layers of the eye and their subcompartments

• Understand the organization of the three chambers of the eye

• Know the cellular layers of the cornea and about the conjunctiva and associated glands

• Recognize the importance of the blood supply system in the choroid layer

• Understand aqueous humor production and drainage

• Study the anchoring of the lens by ciliary processes and zonule fibers

• Comprehend the counteracting muscular systems of the iris and the ciliary body

• Learn about the structure and growth of the lens

• Discuss the layered structure of the retina and its cellular components

• Know about the blood supply of the retina and its other special histological features
The overall function and design of the eye is similar to that of a camera.
The eye consists of three major concentric layers: The outer sclera/cornea.
The outer sclera/cornea and the vascular or uveal layer.
The outer sclera/cornea, the vascular or uveal layer and the inner retinal layer.
This layered structure is the direct result of the inductive mechanism during eye development in the embryo.
The anterior and posterior chambers are filled with aqueous humor. The vitreous chamber is filled with the gelatinous vitreous body.

Aqueous humor consists of:
- Water and salts (isotonic)
- <0.1% proteins

Vitreous body consists of:
- Water and salts (99%)
- Collagen (mainly randomly-oriented collagen II fibers)
- Glycosaminoglycans (specifically hyaluronan)
The outer sclera/cornea layer
The outer **scleral layer** (Tenon’s capsule) is made up of dense irregular connective tissue and is continuous with the anterior corneal layer. It maintains the overall shape of the eye.
The cornea covers the anterior portion of the eye and consists of several cellular and acellular layers. The cornea does not contain any blood vessels and corneal cells are supplied with nutrients by diffusion from the tear fluid and the aqueous humor.
The anterior cellular layer of the cornea is a stratified, squamous, non-keratinized epithelium. It contains numerous sensory nerve endings. Underneath is a thin acellular, collagenous layer, called Bowman’s membrane.
The bulk of the cornea is made up of the stromal layer, which contains a number of fibroblasts that are embedded in a collagen-glycoprotein matrix.
The stroma consists of about 200 perpendicularly-oriented layers of parallel collagen fibers (type 1 collagen).
Between the corneal stroma and the covering corneal endothelium is Descemet’s membrane, a fine collagenous (collagen IV) filament network.
The posterior, internal aspect of the cornea is covered by a cellular endothelial layer. Because of its ion transport activity, it keeps the stroma dehydrated. The corneal endothelium has a low capacity to regenerate after injury.
The conjunctiva is continuous with the outer corneal epithelium and is a 2 layer stratified, columnar epithelium with many goblet cells.

An allergic reaction or infection of the conjunctiva can lead to an inflammation known as conjunctivitis (pink eye).
Several types of glands are associated with the eyelid and the conjunctiva.

The major and minor lacrimal glands are pure serous-secreting compound acinar glands.

The glands of Moll are apocrine sweat glands, which secrete IgA and anti-microbial products.

The Meibomian glands and the eyelash-associated glands of Zeis are sebaceous glands. Sebum secretion prevents the evaporation of tear fluid.
### Summary of Glands Associated with the Eye:

<table>
<thead>
<tr>
<th>Name of gland(s)</th>
<th>Type of gland</th>
<th>Mode of secretion</th>
<th>Secretion product</th>
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</thead>
<tbody>
<tr>
<td>Goblet cells (of the conjunctiva)</td>
<td>Monocellular gland</td>
<td>Merocrine</td>
<td>Mucous</td>
</tr>
<tr>
<td><strong>Lacrimal Glands</strong>*:</td>
<td></td>
<td></td>
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<tr>
<td>Gland of Krause</td>
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<tr>
<td>Orbital and palpebral glands</td>
<td>Serous</td>
<td>Merocrine</td>
<td>Serous</td>
</tr>
<tr>
<td>Glands of Wolfring or Ciaccio</td>
<td>Apocrine</td>
<td>Merocrine</td>
<td>Serous</td>
</tr>
<tr>
<td><em>We will not require you to discriminate between different lacrimal glands</em></td>
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<tr>
<td>Glands of Moll</td>
<td>Apocrine</td>
<td>Merocrine</td>
<td>Serous</td>
</tr>
<tr>
<td>Meibomian glands (at tarsal plate)</td>
<td>Sebaceous</td>
<td>Holocrine</td>
<td>Sebum</td>
</tr>
<tr>
<td>Glands of Zeis (at eyelashes)</td>
<td>Sebaceous</td>
<td>Holocrine</td>
<td>Sebum</td>
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Emily F. Wolfring from “Geschichte der Augenheilkunde” by Julius Hirschberg; 3rd Book, Vol. 7, Chapter 23, Page 262 Fig 16 (1915) Leipzig, Verlag von Wilhelm Engelmann
Heinrich Melborn the Younger from “Die Universität Helmstedt 1576-1810” by Hans Haase and Günter Schöne, Jacobi-Verlag Bremen/Wolfenbüttel 1976; Abb. 80
Giuseppe V Ciaccio from “In memoria di Giuseppe Vincenzo Ciaccio nel X anniversario della sua morte” By Giuseppe Sergi, Antonio Della Valle Turin/Turino Published by Bona, 1912
The middle vascular or uveal layer.
The choroid covering the posterior part of the eye is a component of the middle, vascular layer and together with the ciliary body and the iris is also referred to as the uveal tract.
The choroid is a loose connective tissue and besides fibroblasts, macrophages and other connective tissue-type cells contains many melanocytes. Towards the retina it is covered by Bruch’s membrane (or glassy membrane).
The choroid layer is highly vascularized, providing one of two blood and nutrient supply sources to the overlying retinal layer.

Especially the region close to the retina contains a dense capillary network and is referred to as the choriocapillary layer (or Ruysch’s membrane).
The ciliary processes/body together with the choroid layer and the iris is part of the uveal layer.
The ciliary body is lined by two cuboidal/columnar epithelial cell layers, a surface non-pigmented layer, which is an extension of the posterior retinal cell layer, and a deeper pigmented epithelial layer, which is an extension of the posterior pigment cell layer.

These two epithelia are derivatives of the two layers of the optic cup and therefore are part of the retinal layer.
Aqueous humor is produced by the non-pigmented epithelial layer of the ciliary body, flows from the posterior into the anterior chamber and is drained at the limbus by the trabecular meshwork.
Diagram of the trabecular meshwork at the limbus and the canal of Schlemm, which are not directly connected. The aqueous humor is ultimately reabsorbed by small veins in the sclera. A blockage of aqueous humor drainage will result in an increase of intraocular pressure (glaucoma) and eventually in neuronal degeneration.
Trabecular meshwork and canal of Schlemm
Between all individuals the number of melanocytes in the iris stroma is fairly similar. Rather the variations in the amount of melanin pigment in each melanocyte determine eye color. This is due to genetic variabilities in the expression of melanocyte proteins, such as tyrosinase, melanocortin receptor and others.
Also light is reflected from the pigmented epithelial layer covering the posterior side of the iris. Both epithelial linings of the back side of the iris are heavily pigmented.
The **sphincter pupillae** and the **dilator pupillae muscle** regulate the opening and closing of the iris.

The sphincter/constrictor pupillae muscle is formed by a ring of smooth muscle. The dilator pupillae muscle is made of a myoepithelium, adjacent to the pigmented double epithelium.
The sphincter or constrictor pupillae muscle forms a circle at the pupillary margin and is under parasympathetic control. The dilator pupillae muscle is under sympathetic system control.
The Zonule fibers, which anchor the lens, are attached to the ciliary processes. These radially-oriented fibers form the Zonule of Zinn.
The lens is positioned behind the iris and between the ciliary processes.

Scanning electron micrograph of a lens anchored by zonule fibers to the ciliary processes.
The ciliary smooth muscles regulate the thickness of the lens, a process called accommodation.

The ciliary muscles are mainly under parasympathetic control.
The lens is formed from the embryonic lens vesicle.
The anterior side of the lens is covered by a simple epithelium. The basal side is facing anterior and is covered by a basement membrane/capsule, the apical side is anchoring the posterior lens fibers.
At the margin of the lens epithelial cells are transformed into lens fibers, which are filled with crystallin proteins and lose most of their intracellular organelles.

New lens fibers are formed from epithelial cells throughout adult life.
Formation of lens fibers involves the destruction of internal cell organelles by “arrested apoptosis”. This EM micrograph displays this lack of cellular organelles in lens fiber cells.
Cataracts, clouding of the lens, are treated by a surgical replacement of the lens with an artificial lens.
The inner retinal layer.
The retina is the innermost, cellular layer of the eye. The retina itself has multiple layers, with the photosensitive components/cells at the outer aspect of the retina.
The **ora serrata** is the transition in the more anterior region of the eye where the photosensitive part of the retina epithelium connects with the non-photosensitive part, which constitutes the inner lining of the ciliary body and posterior part of the iris.

Cysts/lacunae/spaces of Blessig are often observed at the ora serrata and appear to be the result of tissue degeneration.
Pigment epithelium

External nuclear layer
- containing the nuclei of the photoreceptor cells

Inner nuclear layer
- containing the nuclei of bipolar cells

Ganglion cell layer

Outer plexiform layer

Inner plexiform layer

Optic nerve fibers

Outer limiting membrane

Photoreceptor layer
- containing outer and inner segments

Inner limiting membrane

Don McCullum, University of Michigan
The outer pigment epithelium is derived from the outer layer of the optic cup and constitutes a simple columnar epithelium.

The pigment epithelium cells contain many melanin granules.
The pigment epithelium cells ensheath the tips of the overlying photoreceptor cells and optically isolate them with their melanosomes. The pigment epithelium cells constantly remove the tips of the photoreceptor cell outer segments and recycle their components.
Since the junction between the pigment epithelium and the external segments of the photoreceptor cells is rather weak, this can lead to retinal detachment, a condition that ultimately results in the degeneration of the photoreceptor cells.
Ultrastructure of the two types of photoreceptor cells: **rod cells** and **cone cells**.

Rod and cone cells not only differ in the expression of their membrane-associated visual pigments: Rhodopsins ($\lambda_{\text{max}} \sim 495$ nm in rod cells) and Photopsins in cone cells ($\lambda_{\text{max}} \sim 420$ nm, $\lambda_{\text{max}} \sim 530$ nm and $\lambda_{\text{max}} \sim 560$ nm).
Rod and cone cells also exhibit distinct morphological differences. E.g., rod cells have internal photosensitive membrane discs and cone cells invaginations or their plasma membrane.
The retina proper has a layered structure and contains a number of different neuronal cells and glial cells, especially Müller glial cells.

Rods and cone cells do not directly connect with the CNS, but rather via bipolar neurons and ganglion cells. There are two synaptic layers in the retina, the inner and outer plexiform layer.
The retina proper has a layered structure and contains a number of different neuronal cells and glial cells, especially Müller glial cells. In some species Müller cells appear to have stem cell properties and after injury are able to differentiate into photoreceptor and other retinal cell types.
Among the different types of glial cells in the retina, Müller glial cells are of special interest. They span most of the retinal layer, from the external to the internal limiting membrane (these are not really membranes). In some species (e.g. fish) Müller cells appear to have stem cell properties and after injury are able to differentiate into photoreceptor and other retinal cell types.
At the **optic papilla** the optic nerve penetrates the retinal layer and leaves the eye, and the retinal blood supply enters and exits. This creates a **blind spot** in the retina.
The second blood supply system of the retina is the retinal artery and vein system, which enters and exits at the optic papilla.
The pattern of the retinal artery/vein system is unique for each person. In diabetic patients weakening of capillary tight junctions can result in hemorrhages and diabetic retinopathy. The arrow marks a normal, special area of the retina, which is devoid of retinal blood vessels.
The fovea centralis or macula is the region of the retina with the highest visual acuity.

Named after its discoverer the macula/fovea is also sometimes referred to as Sömmering’s yellow spot.
At the fovea the other overlying bipolar and ganglion cell layers are pushed to the side (rod cells located in surrounding retina, cone cells located in the center of the fovea)
The fovea contains no rod cells, but rather exclusively cone cells, which have an approximate 1 to 1 ratio with their connecting bipolar cells.
The most common form of blindness in older individuals is age-related macular degeneration (ARMD), which mainly affects the central region of the retina around the fovea.
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