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## **Histology of the Eye**

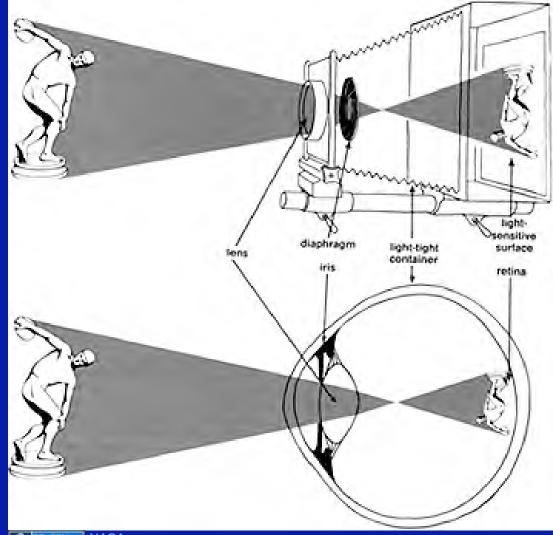
Michael Hortsch, Ph.D. Department of Cell and Developmental Biology University of Michigan

Winter 2009



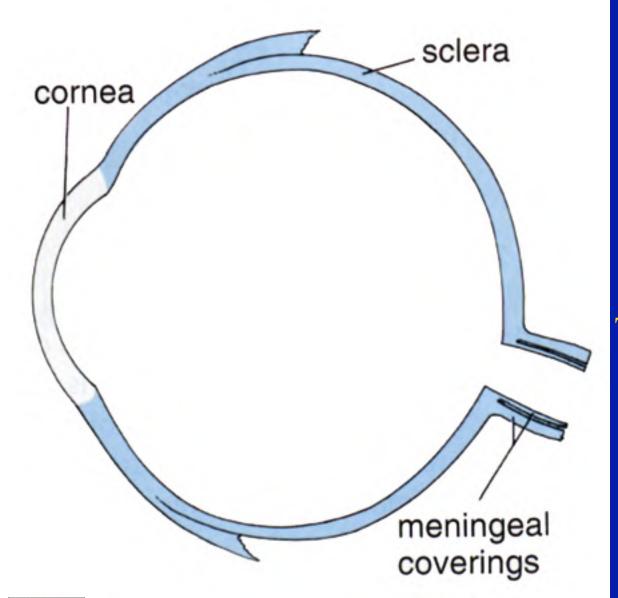
## **Objectives Eye Histology:**

- 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



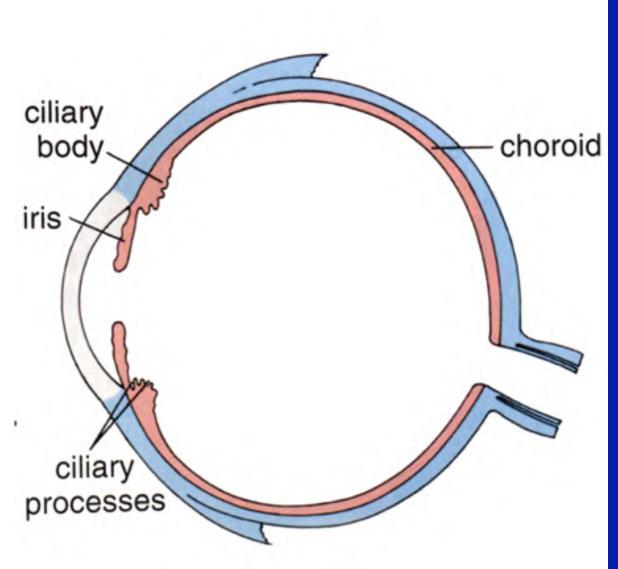
The overall function and design of the eye is similar to that of a camera.

PD-GOV NASA



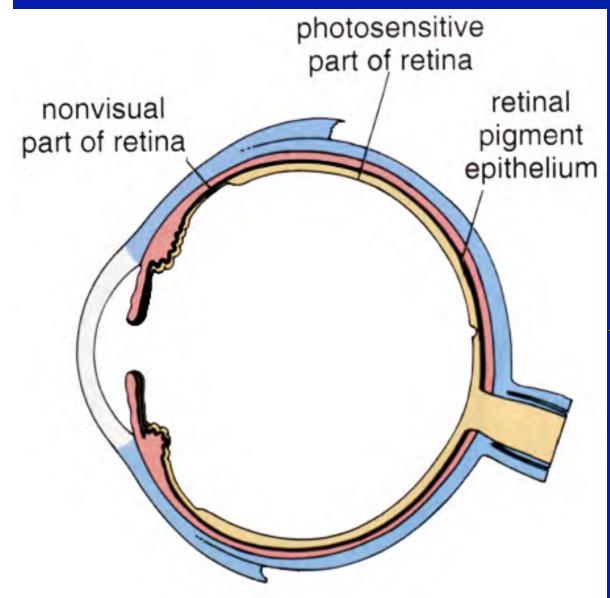
The eye consists of three major concentric layers: The outer sclera/cornea.

Williams and Wilkins, Fig. 24.1a Williams and Wilkins, Fig. 24.1a



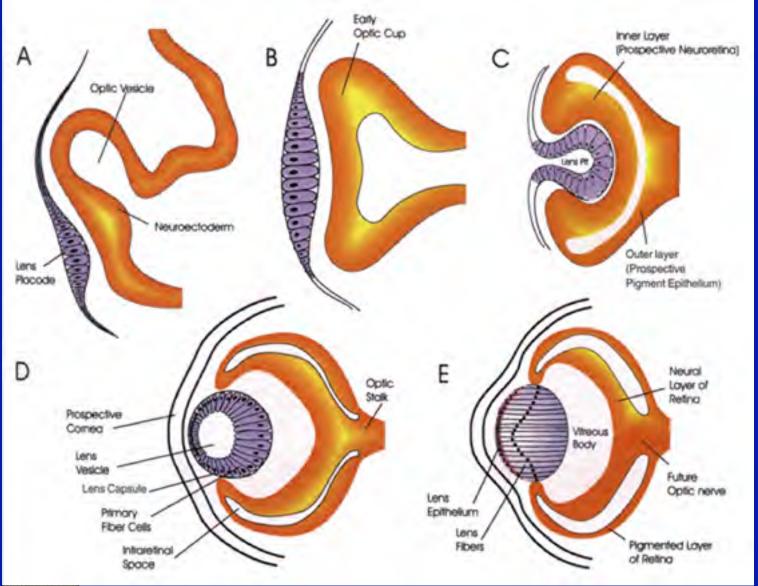
### The outer sclera/cornea and the the vascular or uveal layer.

**PD-INEL** Histology – A Text and Atlas by M.H. Ross and W. Pawlina; 5<sup>th</sup> edition, 2006, Lippincott Williams and Wilkins, Fig. 24.1b



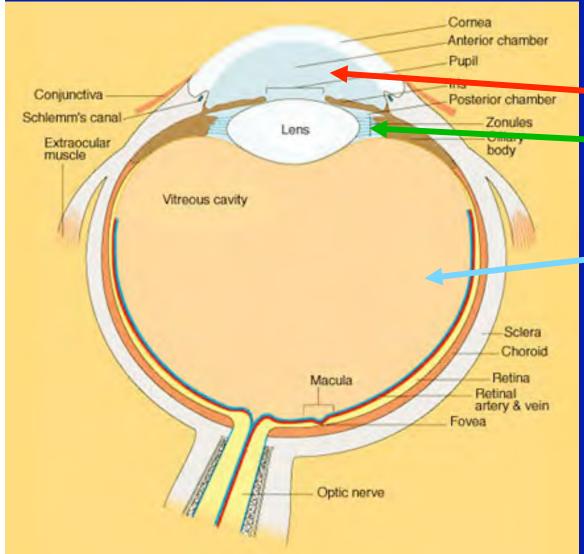
The outer sclera/cornea, the vascular or uveal layer and the inner retinal layer.

**EXAMPLE INTEL** Histology – A Text and Atlas by M.H. Ross and W. Pawlina; 5<sup>th</sup> edition, 2006, Lippincott Williams and Wilkins, Fig. 24.1c



Ales Cvekl and Joram Piatigorsky at Laboratory of Molecular and Developmental Biology, National Eye Institute

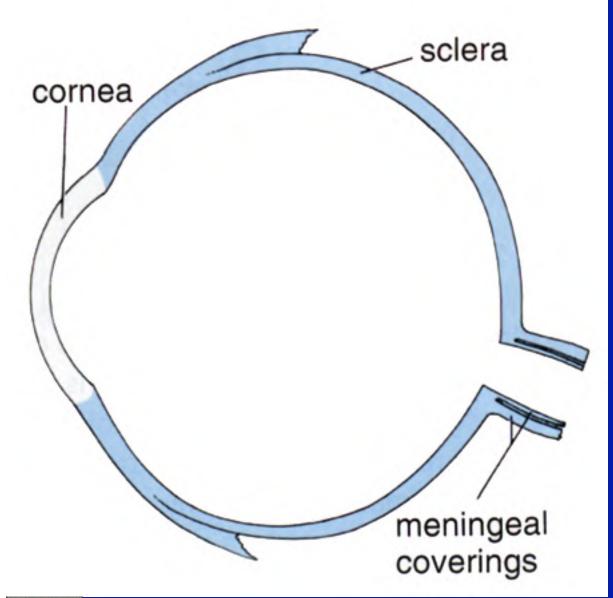
This layered structure is the direct result of the inductive mechanism during eye development in the embryo.



Churchill Livingstone Modified from Fig 21.3

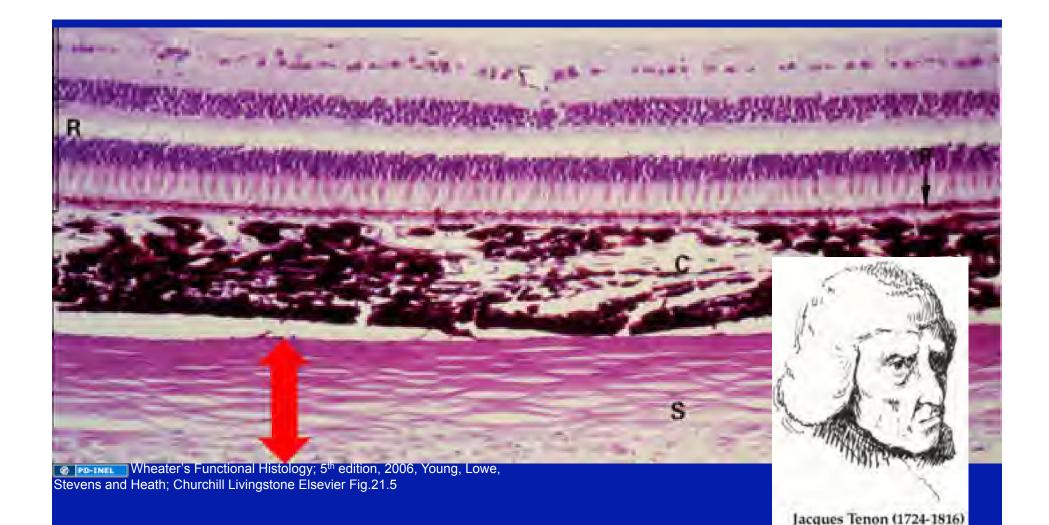
The <u>anterior</u> and <u>posterior chambers</u> are filled with <u>aqueous humor</u>. The <u>vitreous chamber</u> is filled with the gelantinous <u>vitreous body</u>.

Aqueous humor consists of: Water and salts (isotonic) <0.1% proteins Vitreous body consists of: Water and salts (99%) Collagen (mainly randomlyoriented collagen II fibers) Glycosaminoglycans (specifically hyaluronan)



The outer sclera/cornea layer

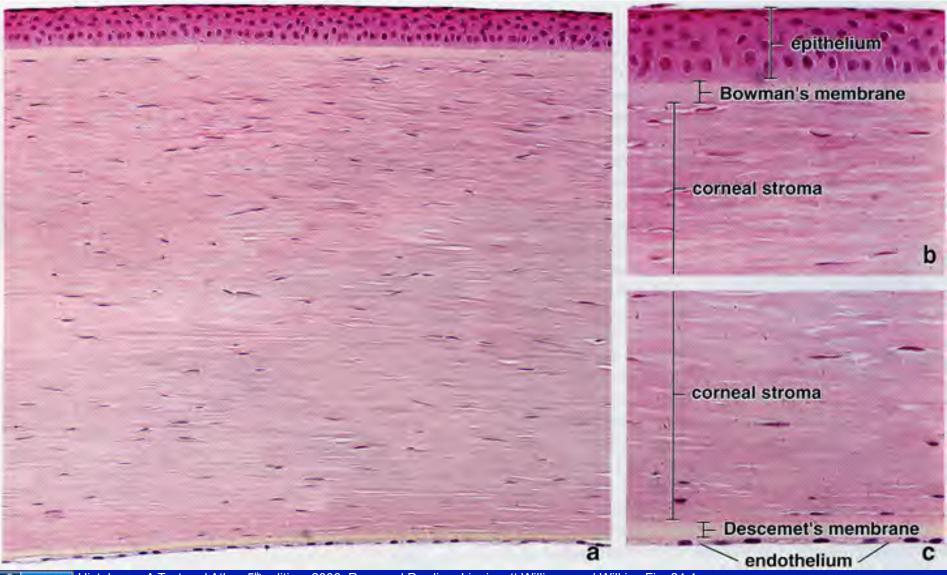
edition, 2006, Lippincott Williams and Wilkins, Fig. 24.1a



The outer <u>scleral layer</u> (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.

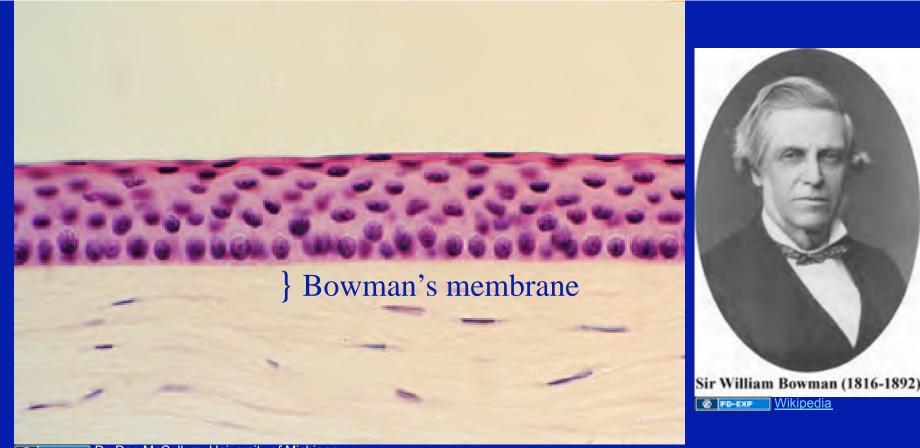
@ PD-EXP

Dovne's Hall of Fame



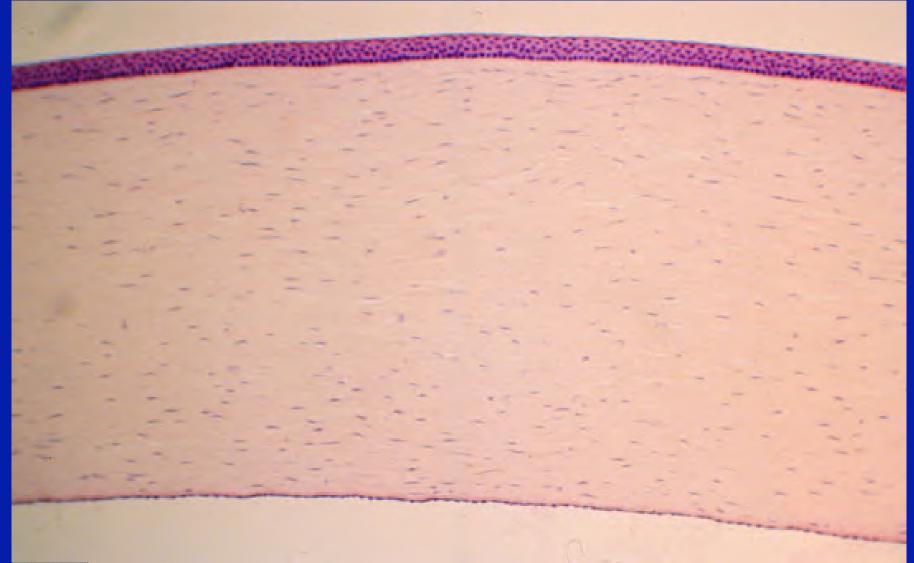
Internet Bistology – A Text and Atlas; 5th edition, 2006, Ross and Pawlina, Lippincott Williams and Wilkins Fig. 24.4

The <u>cornea</u> 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.



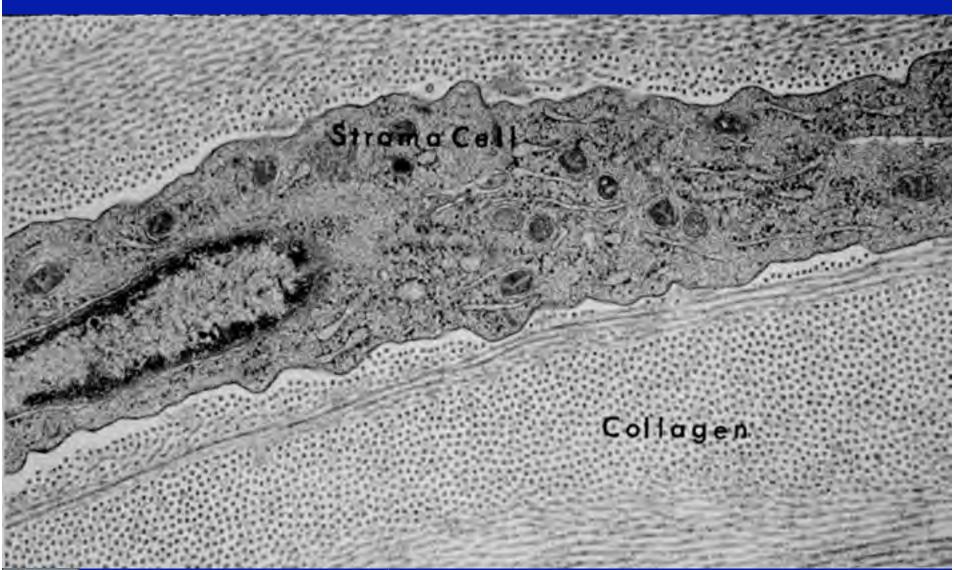
Dr. Don McCullum, University of Michigan

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 <u>Bowman's membrane</u>



Dr. Don McCullum, University of Michigan

The bulk of the cornea is made up of the <u>stromal layer</u>, which contains a number of fibroblasts that are embedded in a collagen-glycoprotein matrix.

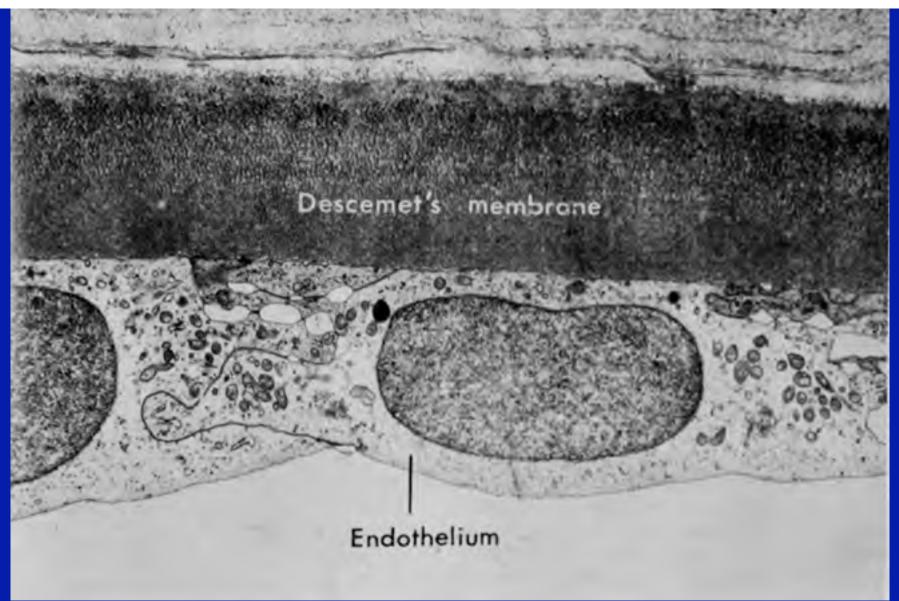


Cell and Tissue Biology – A Textbook of Histology; 6th edition; 1988; Weiss, Urban & Schwarzenberg Fig. 36-17

The stroma consists of about 200 perpendicularly-oriented layers of parallel collagen fibers (type 1 collagen).

Michigan Medical Histology Slide Collection

Between the corneal stroma and the covering <u>corneal endothelium</u> is <u>Descemet's membrane</u>, a fine collagenous (collagen IV) filament network.



Concise Histology" by Fawcett and Jensh, 1997, Chapman & Hall Fig 24-4 (courtesy of T. Kuwabara)

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.



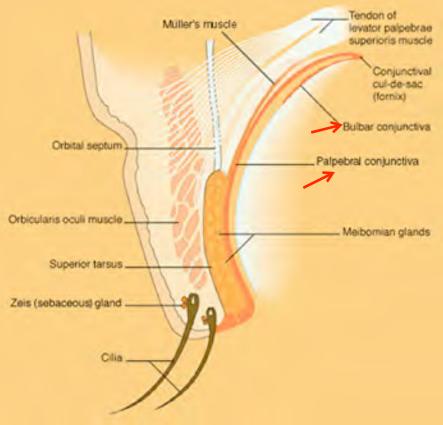
The <u>conjunctiva</u> is continuous with the outer corneal epithelium and is a 2 layer stratified, columnar epithelium with many goblet cells.

Anatomy and Physiology of The Eye by Dr. Thomas Caceci

The area of the conjunctiva that surrounds the cornea is called <u>bulbar conjunctiva</u> and the region that covers the inner side of the eyelids is referred to as <u>palpebral</u> <u>conjunctiva</u>.



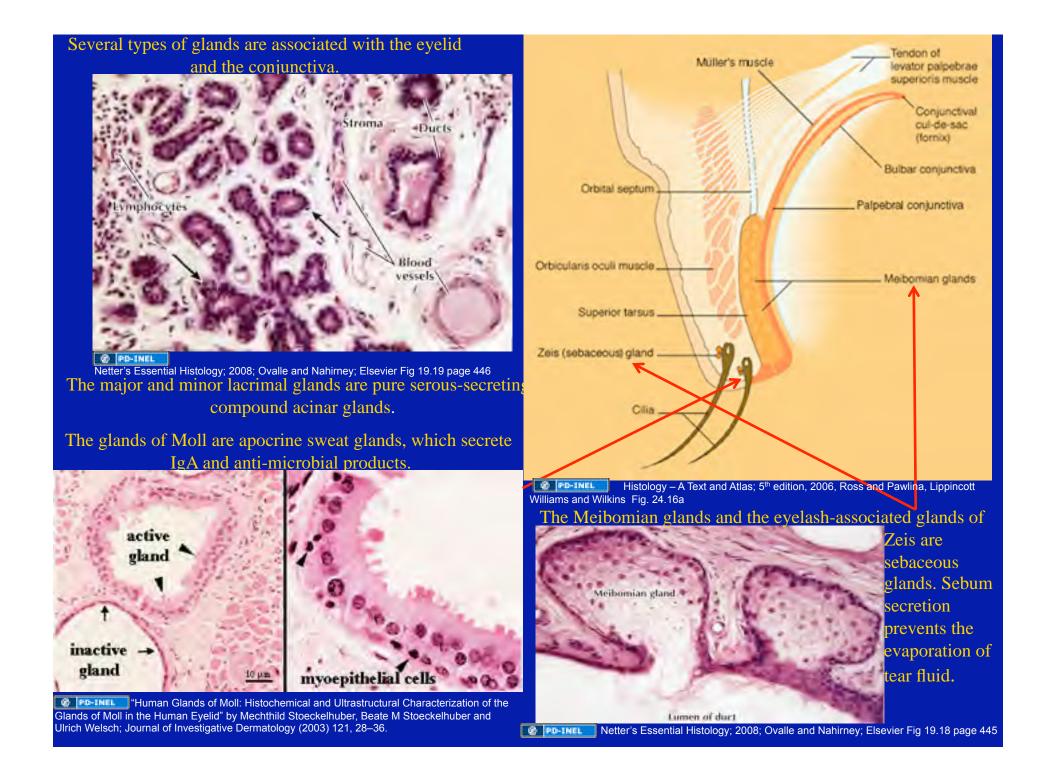
An allergic reaction or infection of the conjunctiva can lead to an inflammation known as conjunctivitis (pink eye).



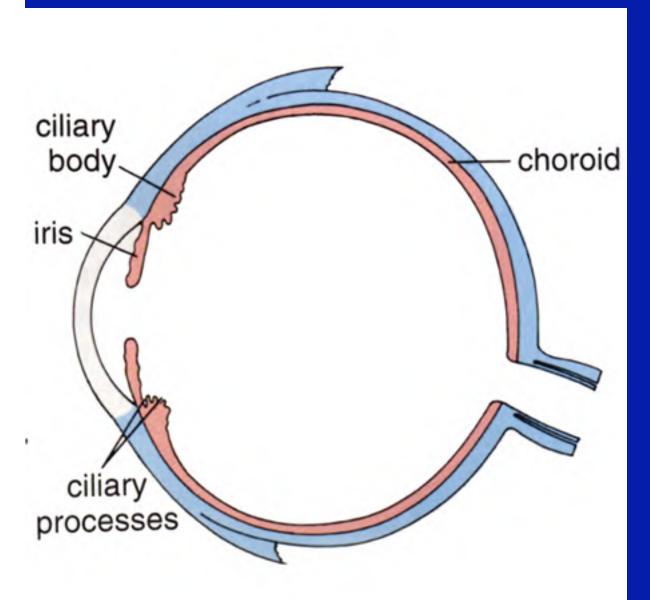
Pawlina, Lippincott Williams and Wilkins Fig. 24.16a



Wikipedia Wikipedia

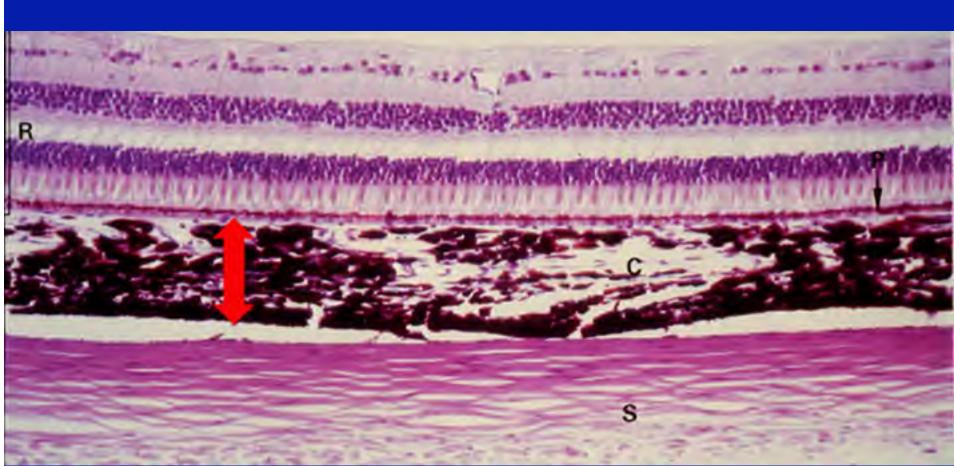


Summary of Glands Associated with the Eye:				
Name of gland(s)	Type of gland o	Mode f secretion	Secretion product	5.4
Goblet cells (of the conjunctiva)	Monocellular gland	Merocrine	Mucous	Karl Friedrich Theodor Krause
Lacrimal Glands*: Gland of Krause Orbital and palpebral glands c Glands of Wolfring or Ciaccio *We will not require you to discriminate betw	Serous ompound acinar ween different lacri		Serous	(1797-1565)
Glands of Moll	Apocrine sweat glands	Merocrine	Serous a	useppe Vincenzo Claccio (1824-1901) Émilj F. von Wolfring (1838-1906)
Meibomian glands (at tarsal plate) Glands of Zeis (at eyelashes)	Sebaceous	Holocrine	Sebum	
Karl F.T. Krause from http://www.mrcophth.com/ophthalmologyhalloffam Emily F. Wolfring from "Geschichte der Augenheilkunde" by Julius Hirso Verlag von Wilhelm Engelmann Heinrich Meibom the Younger from "Die Universität Helmstedt 1576-18 Wolfenbüttel 1976; Abb. 80 Eduard Zeis from Der Hautarzt (1989) Vol. 40(1) 45-52 '150 Jahre "Har (1807-1868)' by G. Sebastian Giuseppe V Ciaccio from "In memoria di Giuseppe Vincenzo Ciaccio ne Turin/Turino Published by Bona, 1912	chberg; <sup>3rd</sup> Book, Vol. 7, Chap 10" by Hans Haase and Günt ndbuch der plastischen Chirur	er Schöne, Jacobi-Verlag gie" - Erinnerungen an Ed	Bremen/ luard Zeis	Sincick Meibon, the Younger (16.88-1700) Eduard Zeis (1807-1868)



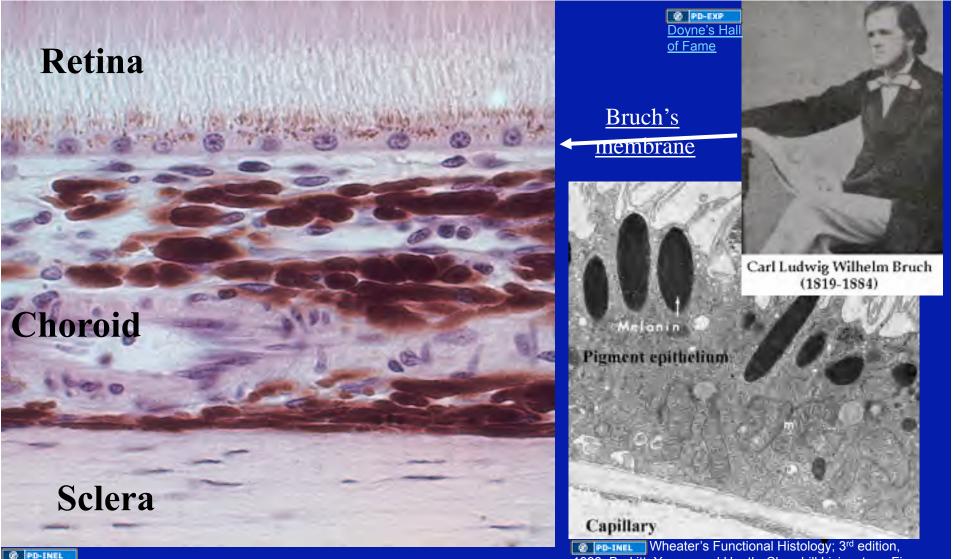
# The middle vascular or uveal layer.

edition, 2006, Lippincott Williams and Wilkins, Fig. 24.1b



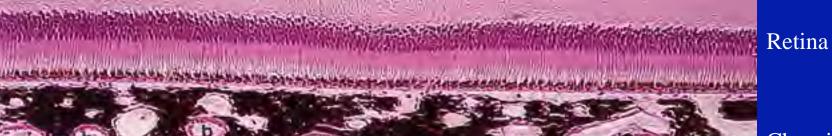
Wheater's Functional Histology; 3<sup>rd</sup> edition, 1993, Burkitt, Young, and Heath; Churchill Livingstone Fig 21.5

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.



Indiana University School of Medicine, Department of Anatomy and Cell Biology, ANAT D502 Wheater's Functional Histology; 3<sup>rd</sup> edition, 1993, Burkitt, Young, and Heath; Churchill Livingstone Fig 21.5

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 <u>Bruch's membrane (or glassy membrane)</u>.



### Choroid

### Sclera



Source: Color Atlas of Basic Histology; 1993; Berman; Appelton and Lange Fig 20-11 The choroid layer is highly vascularized, providing one of two blood and nutrient supply sources to the overlying retinal layer.

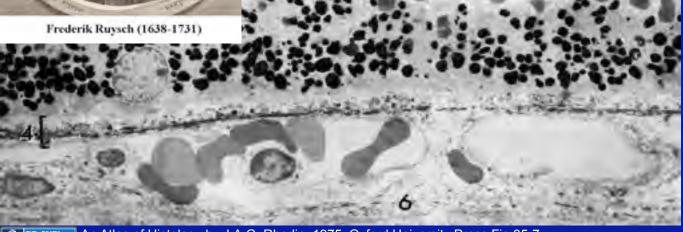
Especially the region close to the retina contains a dense capillary network and is referred to as the <u>choriocapillary layer</u> (or Ruysch's

membrane).

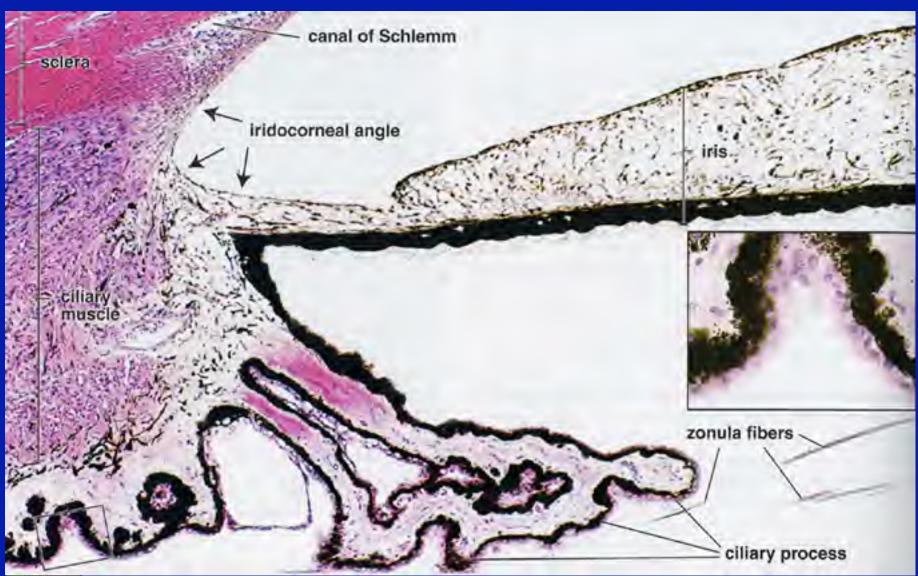
## Pigment epithelium of the retina

Bruch's membrane

Choriocapillary layer

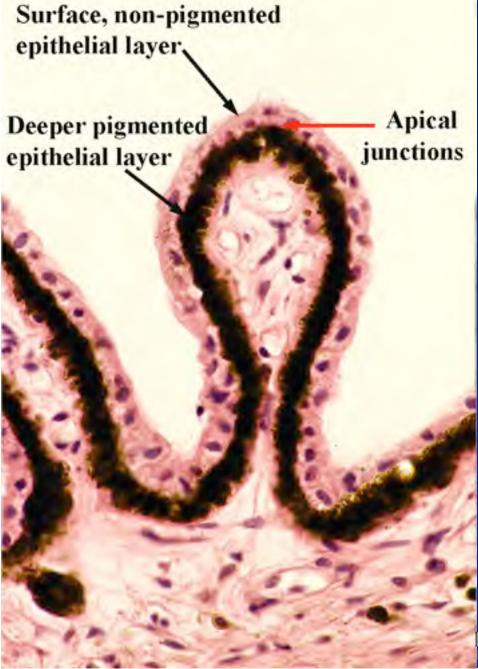


FD-INEL An Atlas of Histology by J.A.G. Rhodin; 1975, Oxford University Press Fig 35-7



😰 📭 INEL Histology – A Text and Atlas; 5th edition, 2006, Ross and Pawlina, Lippincott Williams and Wilkins Fig. 24.7

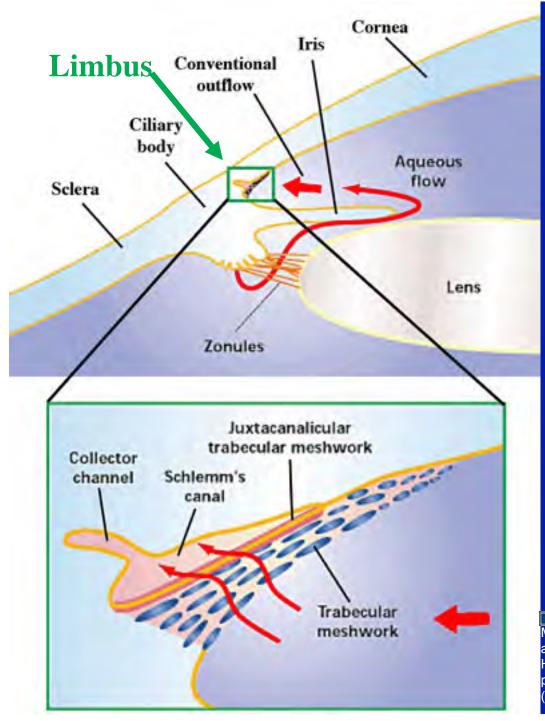
The ciliary processes/body together with the choroid layer and the iris is part of the uveal layer



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**.

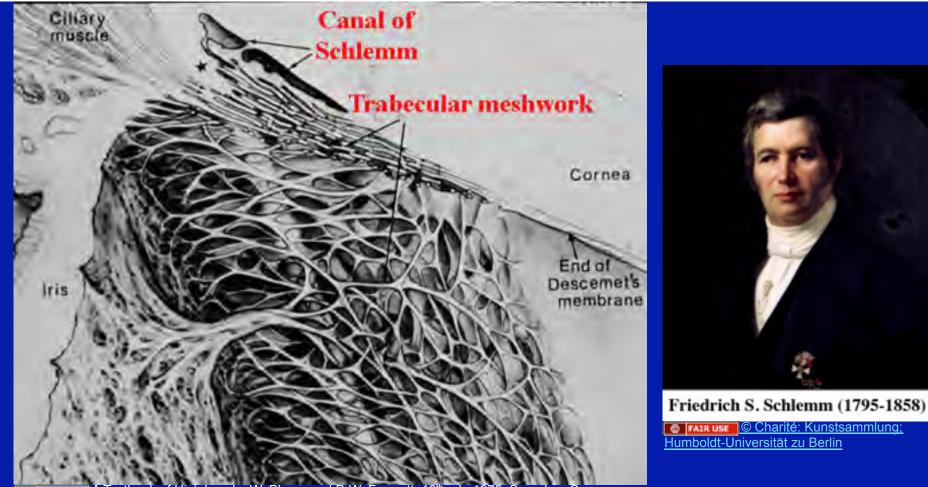
Dr. Don McCullum, University of Michigan



Aqueous humor is produced by the nonpigmented epithelial layer of the ciliary body, flows from the posterior into the anterior chamber and is drained at the <u>limbus</u> by the <u>trabecular meshwork</u>.

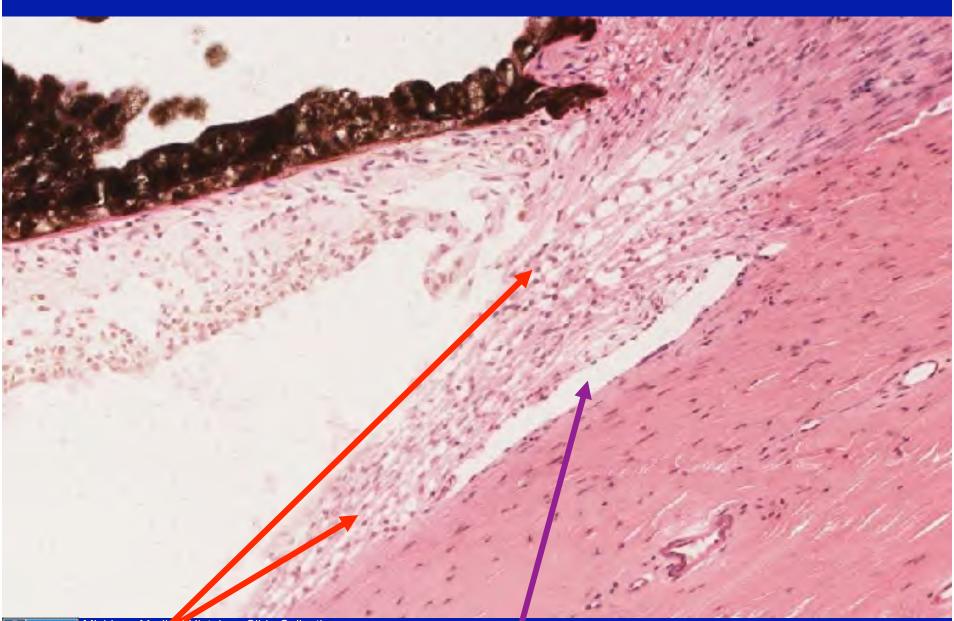
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Modified from Basic Histology – Text & Atlas by Junqueira, Carneiro and Kelley; 8<sup>th</sup> edition, 1995; Appelton &Lange Fig. 24-9; Ham: Histology 6th ed Lippincott, 1969); "Eyeing a new route along an old pathway" by Stanislav I. Tomarev, Nature Medicine 7, 294 - 295 (2001)



A Textbook of Histology by W. Bloom and D.W. Fawcett, 10th ed., 1975, Saunders Comp. Fig. 35-11 page 928 (after M.Y. Hogan et al., Histology of the Human Eye, Saunders, 1971)

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 degenration.



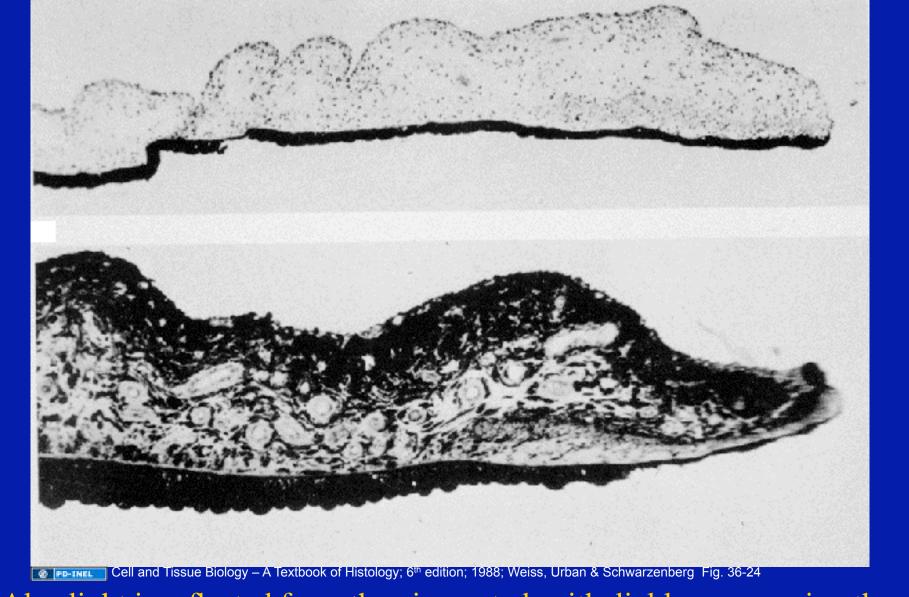
Michigan Medical Histology Slide Collection

Trabecular meshwork and canal of Schlemm

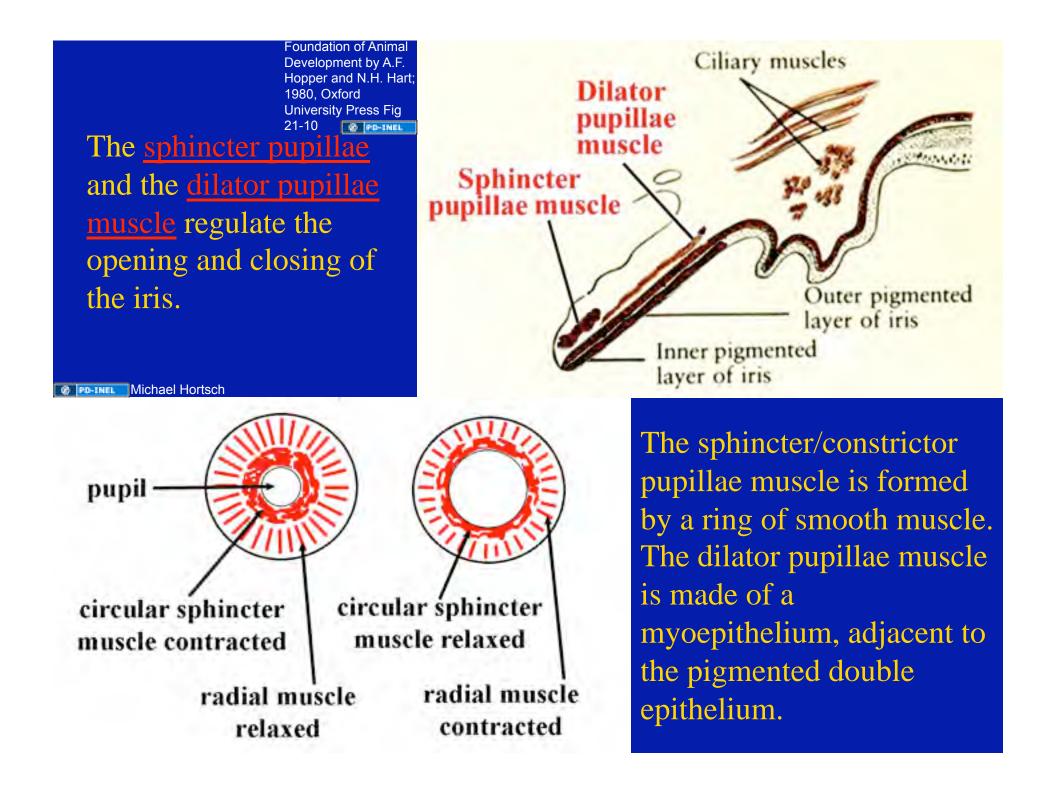


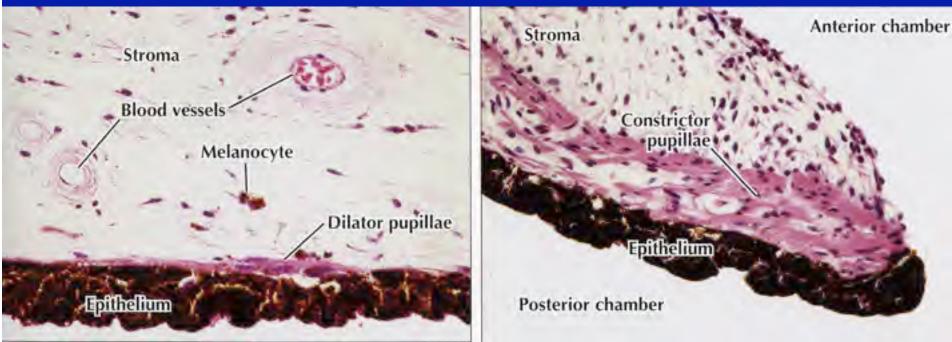
<sup>(</sup>All images) Look into My Eyes, <u>flickr</u>

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.



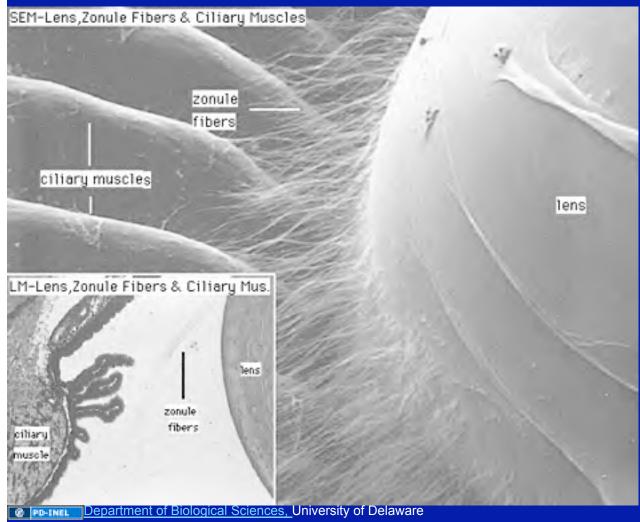
Also light is reflected from the pigmented epithelial layer covering the posterior side of the iris. Both epithelial linings of the back side of the iris are heavily pigmented.





RE-INEL Netter's Essential Histology; 2008; Ovalle and Nahirney; Elsevier Fig 19.4 page 431

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.



ORIGINAL IMAGE: Basic Histology – Text & Atlas; 10<sup>th</sup> edition, 2003; Junqueira and Carneiro, Lange McGraw-Hill Fig 24-5 (Reproduced with permission from MJ Hogan et al: Histology of the Human Eye. Saunders, 1971) The <u>Zonule fibers</u>, which anchor the lens, are attached to the ciliary processes. These radially-oriented fibers form the Zonule of Zinn.



Wikipedia Johann G

Re-INIL Japanese slide set (Humio Mizoguti, Department of Anatomy, Kobe University School of Medicine, Slide No. 995

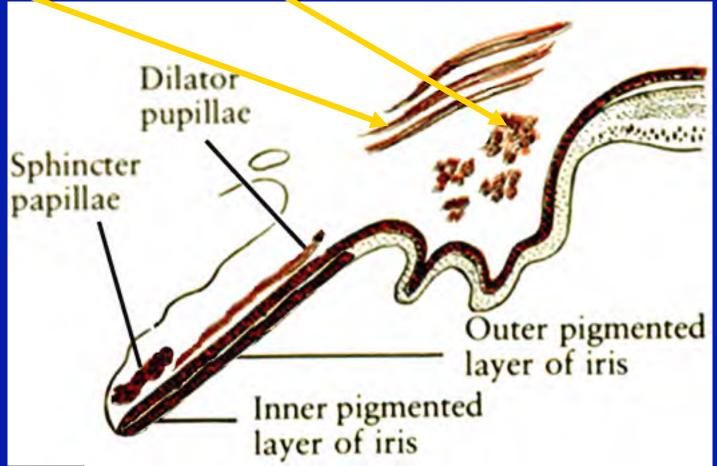
Scanning electron micrograph of a lens anchored by zonule fibers to the ciliary processes

The lens is positioned behind the iris and between the ciliary processes.



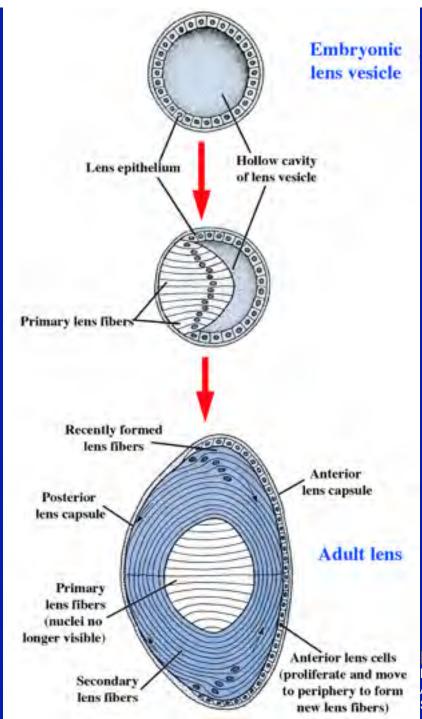
Department of Biological Sciences, University of Delaware @ PD-INEL

### Radially- and circularly-oriented ciliary smooth muscles



Foundation of Animal Development by A.F. Hopper and N.H. Hart; 1980, Oxford University Press Fig 21-10

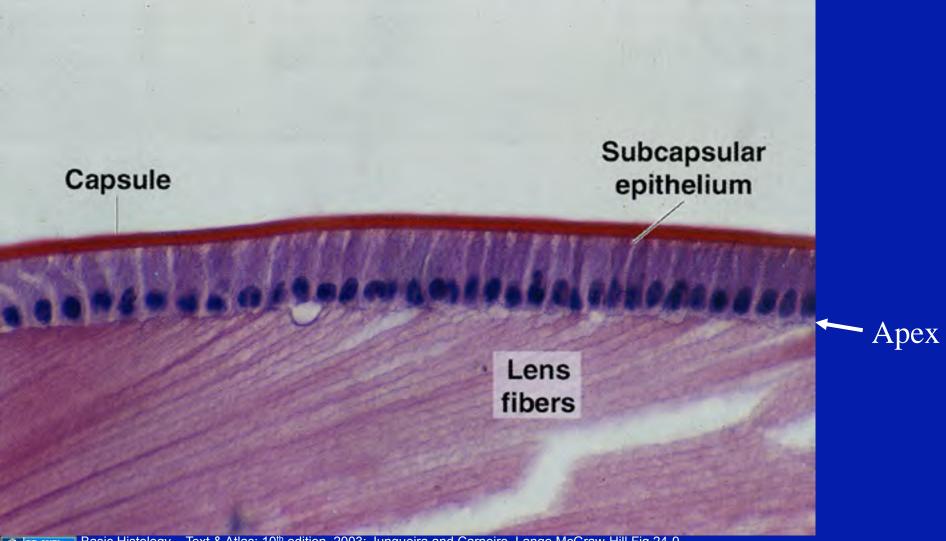
The ciliary smooth muscles regulate the thickness of the lens, a process called <u>accomodation</u>. The ciliary muscles are mainly under parasympathtic control.



# The lens is formed from the embryonic lens vesicle.

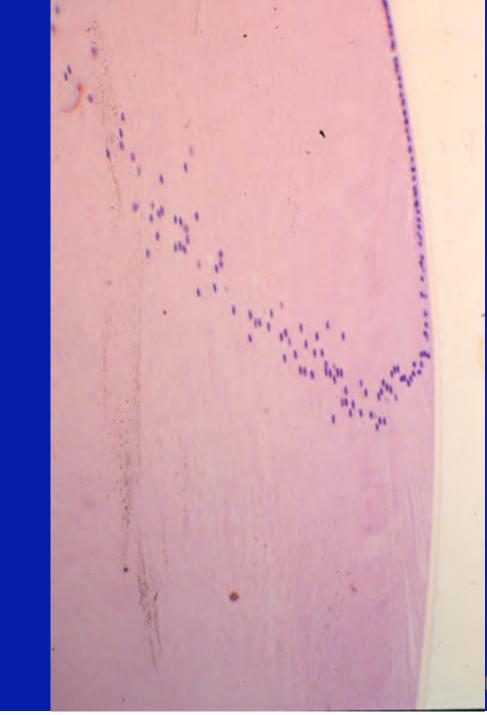
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Modified from Developmental Biology by S.F. Gilbert, 7th edition, Sinauer Assoc., Sunderland, MA, Originally after D. Paton and J.A. Craig, CIBA Clin. Symp. 1974, 26(3):2-32.



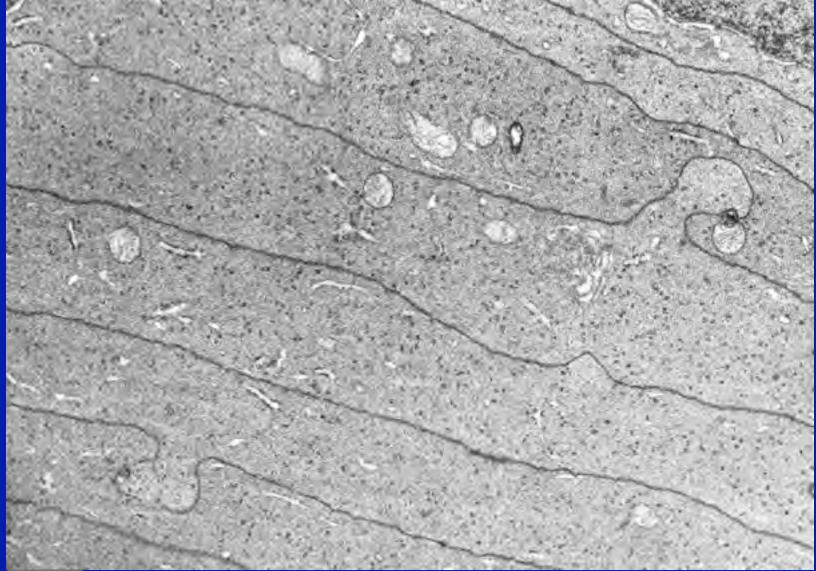
Text & Atlas; 10th edition, 2003; Junqueira and Carneiro, Lange McGraw-Hill Fig 24-9

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.

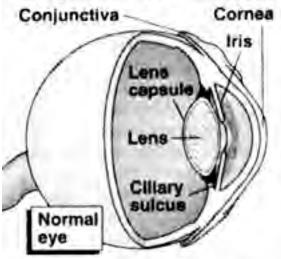
New lens fibers are formed from epithelial cells throughout adult life.



Concise Histology" by Fawcett and Jensh, 1997, Chapman & Hall Fig 24-9B (courtesy of T. Kuwabara)

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.

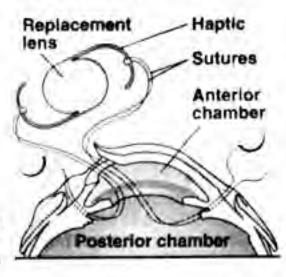
## **Replacing intraocular lenses**

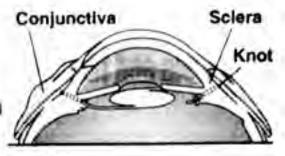


Sometimes intraocular lenses cause problems and need replacing. If a lens capsule has been removed, there are two procedures used to replace an old lens with a new one. One, shown here, is called transscieral fixation.

The plastic lens has two arms, or haptics, that anchor it in a pocket behind the iris called the ciliary sulcus. It is sewn in place with polypropylene thread. The knot of the suture is buried in the outer wall of the eye, or sclera. The suture is covered by the conjunctiva

In a normal, healthy eye (at left), the lens is surrounded by a capsule and situated just behind the ins. If this lens grows cloudy and impairs vision, it can be replaced by an artificial intraocular lens.



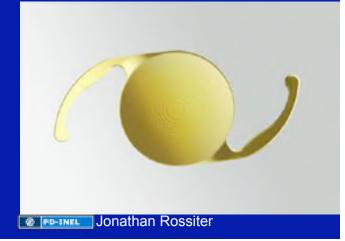


ho's counting: Since 1989, 115 medical articles have been published on secondary intraocular lens implants.

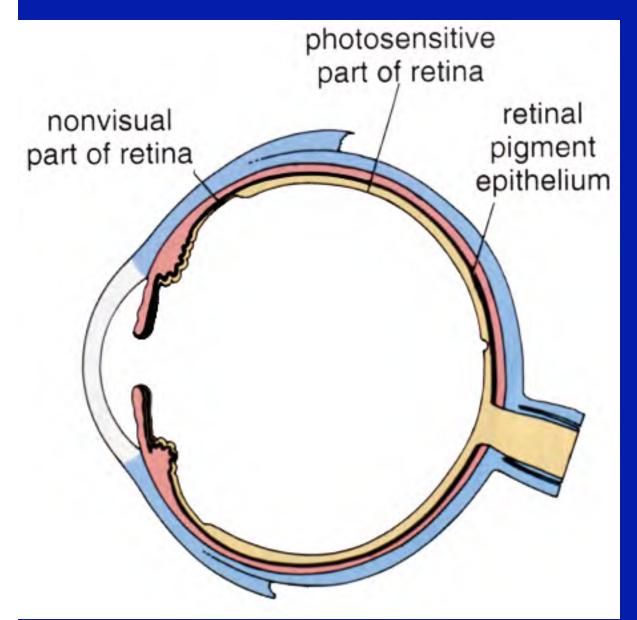


**INTL** <u>i4visior</u>

Cataracts, clouding of the lens, are treated by a surgical replacement of the lens with an artificial lens.

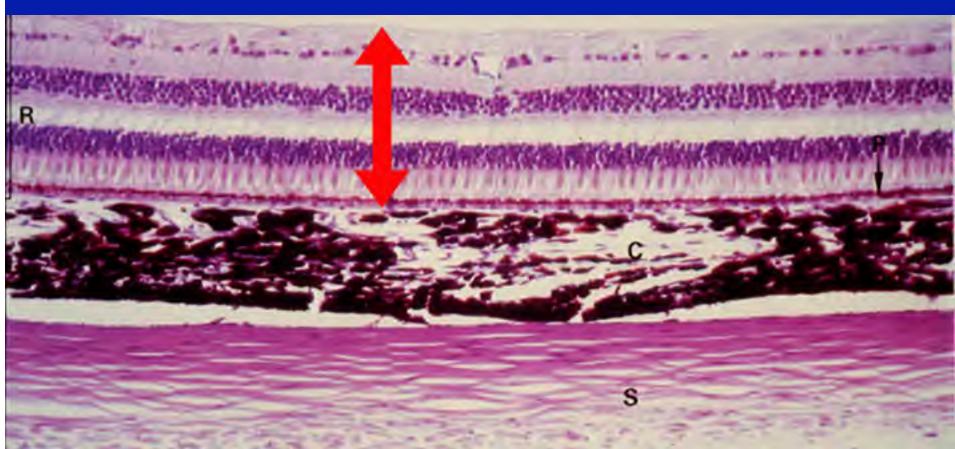


Ann Arbor News



### **EXAMPLE INFL** Histology – A Text and Atlas by M.H. Ross and W. Pawlina; 5<sup>th</sup> edition, 2006, Lippincott Williams and Wilkins, Fig. 24.1c

#### The inner retinal layer.



PP-INEL Wheater's Functional Histology; 3rd edition, 1993, Burkitt, Young, and Heath; Churchill Livingstone Fig 21.5

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.



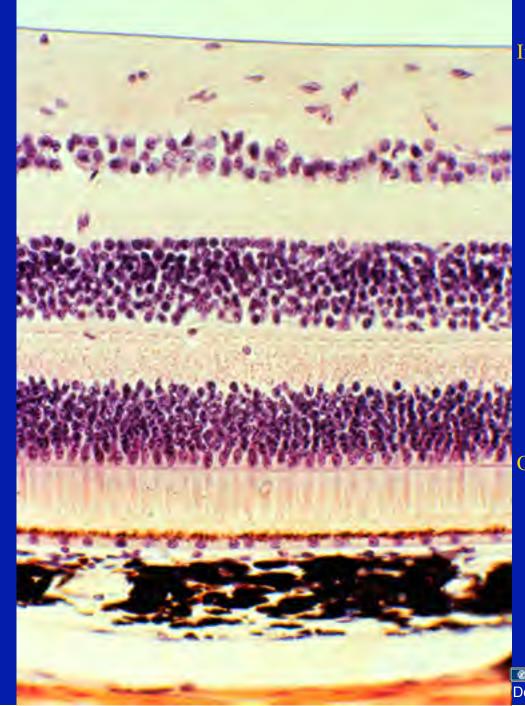
Cysts/lacunae/spaces of Blessig are often observed at the ora serrata and appear to be the result of tissue degeneration.

Robert Blessig (1830-1878)

by Hugh Myddleton Heyder 1954, Pg 113

Slide Collection Slide EYE-2\_20x

The <u>ora serrata</u> 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.



Inner limiting membrane Optic nerve fibers Ganglion cell layer Inner plexiform layer

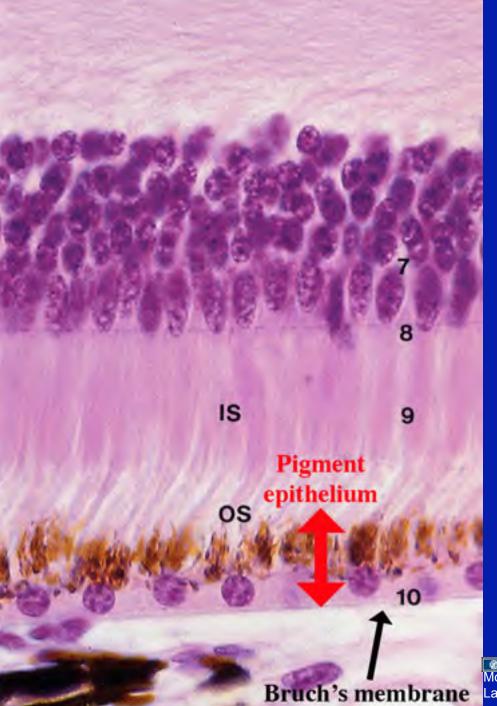
Inner nuclear layer containing the nuclei of bipolar cells

Outer plexiform layer

External nuclear layer containing the nuclei of the photoreceptor cells Outer limiting membrane

Photoreceptor layer containing outer and inner segments Pigment epithelium

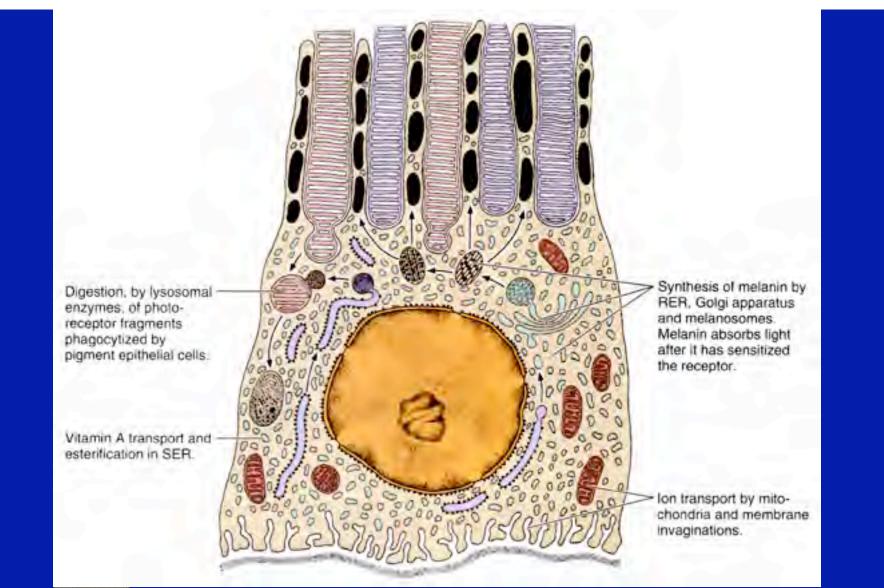
Don McCullum, University of Michigan



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.

Modified from Color Atlas of Basic Histology by I. Berman; 1993; Appelton and Lange, Fig. 20-10



Basic Histology – Text & Atlas; 10th edition, 2003; Junqueira and Carneiro, Lange McGraw-Hill Fig. 24-16

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.

## Pigment epithelium cells

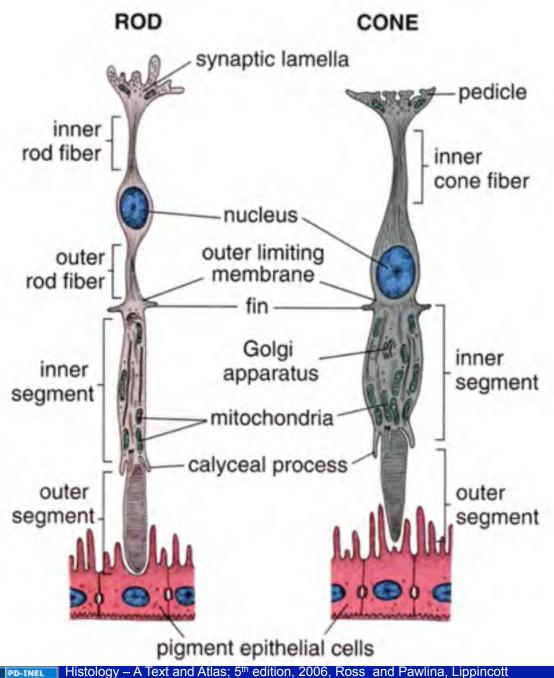
#### Bruch's membrane

#### Capillary

Cell and Tissue Biology – A Textbook of Histology; 6th edition; 1988; Weiss, Urban & Schwarzenberg Fig 36-33

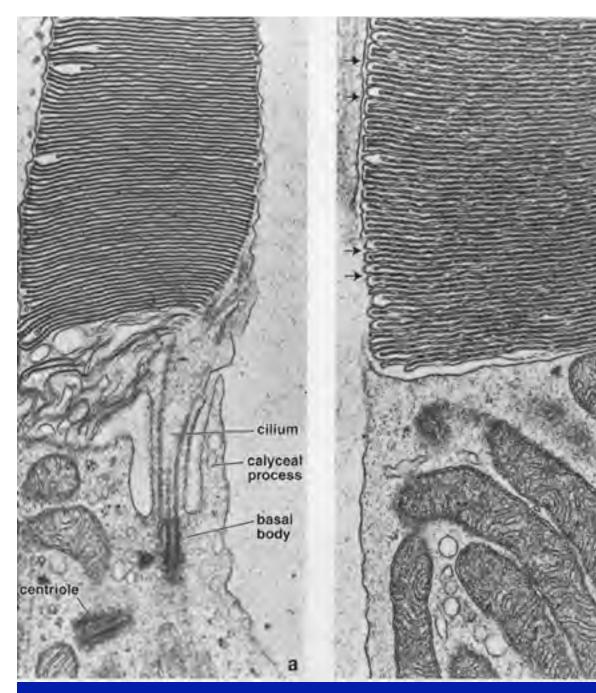
Since the junction between the pigment epithelium and the external segments of the photoreceptor cells is rather weak, this can lead to <u>retinal detachment</u>, a condition that ultimately results in the degeneration of the photoreceptor cells.





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 ( $\lambda$ max) ~495 nm in rod cells and Photopsins in cone cells ( $\lambda$ max ~420 nm,  $\lambda$ max ~530 nm and λmax ~560 nm).

Williams and Wilkins Fig. 24.11



Histology – A Text and Atlas; 5<sup>th</sup> edition, 2006, Ross and Pawlina, Lippincott Williams and Wilkins, Fig. 24.12

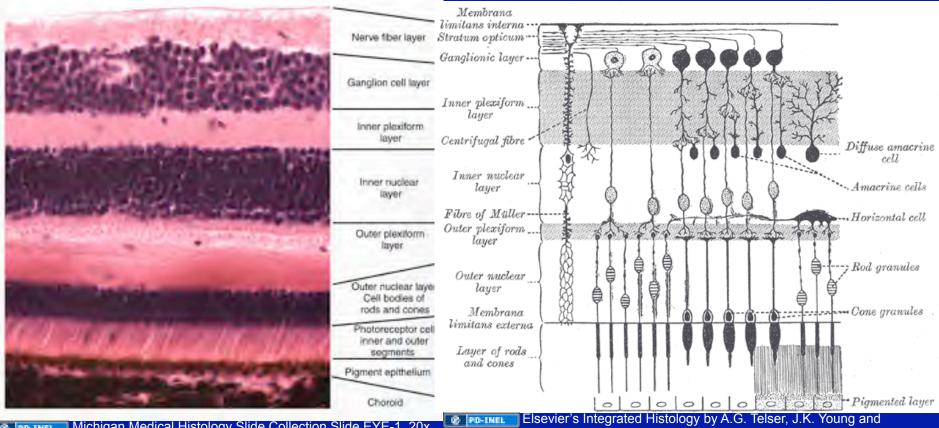
Rod and cone cells also exhibit distinct morphological differences. E.g., rod cells have internal photosensitive

internal photosensitive membrane discs and cone cells invaginations or their plasma membrane.

#### Rod cell

#### Cone cell

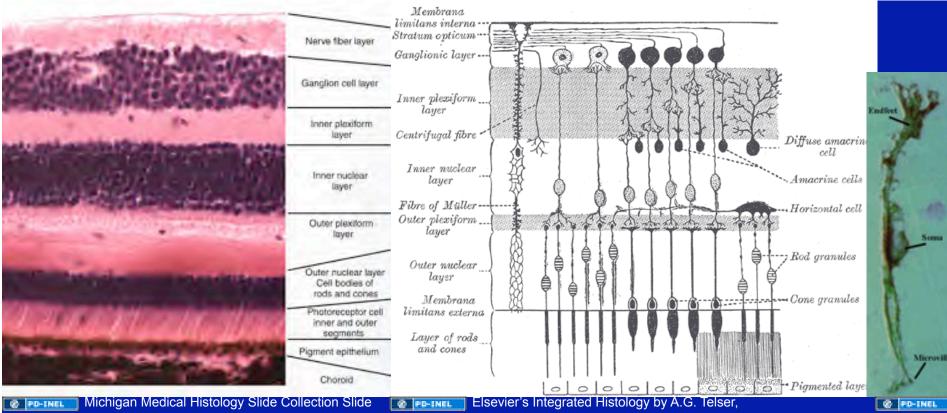
Rods and cone cells do not directly connect with the CNS, but rather via bipolar neurons and ganglion cells. There are two synaptic layers in the retina, the inner and outer plexiform layer.



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K.M. Baldwin; 2007 Mosby Elsevier Fig 6-27

The retina proper has a layered structure and contains a number of different neuronal cells and glial cells, especially Müller glial cells.



EYE-1 20x

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#### J.K. Young and K.M. Baldwin; 2007 Mosby Elsevier Fig 6-27

Müllerzelle einer Kaninchen-Netzhaut

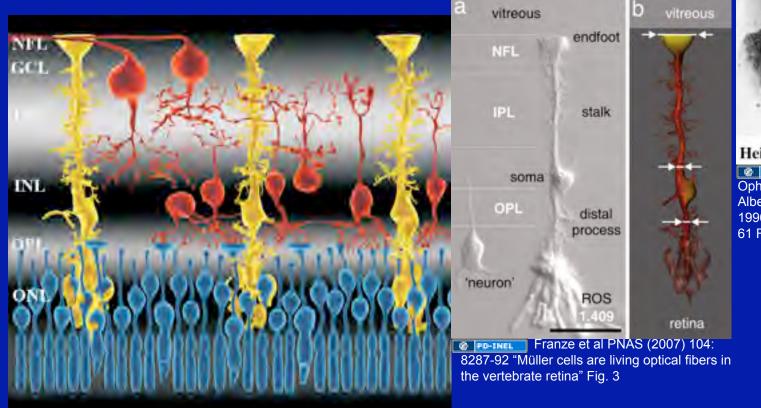
The retina proper has a layered structure and contains a number of different neuronal cells and glial cells, especially Müller glial cells. In some species Müller cells appear to have stem cell properties and after injury are able to differentiate into photoreceptor and other retinal cell types.



The History of Ophthalmology" by Daniel B. Albert and Diane D. Edwards, 1996, Heinrich Müller (1820-1864) Blackwell Science, page 61 Fig 4.28

## Müller cells Ganglion and bipolar cells

#### **Cone and rod cells**

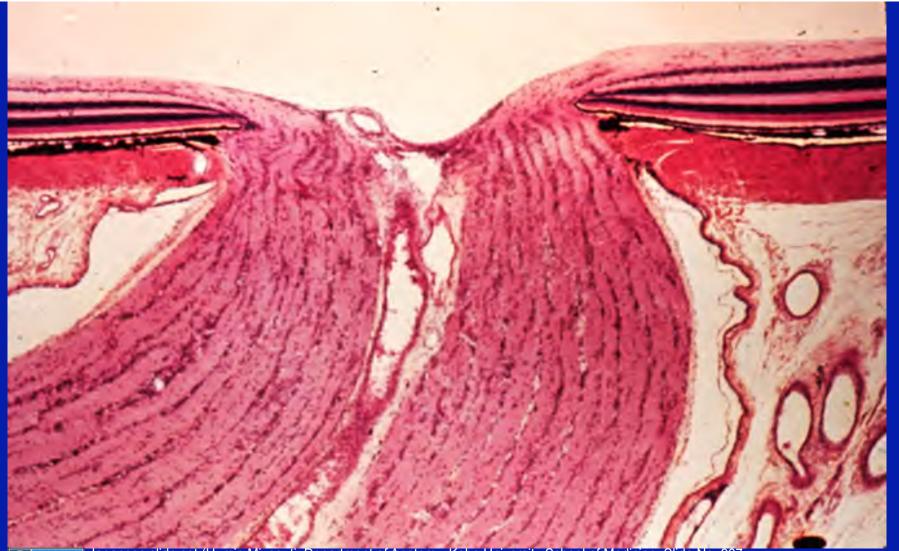




Heinrich Müller (1820-1864) Contract of The History of Ophthalmology" by Daniel B. Albert and Diane D. Edwards, 1996, Blackwell Science, page 61 Fig 4.28

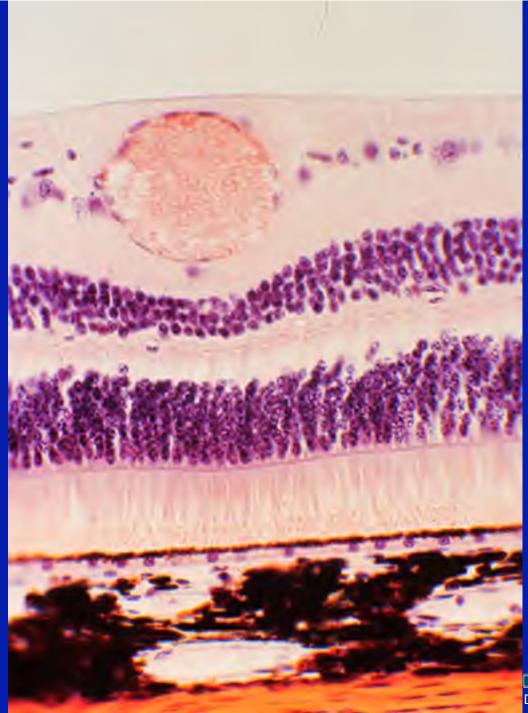
**IDENTIFIE** Lu et al. PNAS (2006) 103: 17759-64 "Viscoelastic properties of individual glial cells and neurons in the CNS" Fig. 7

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.



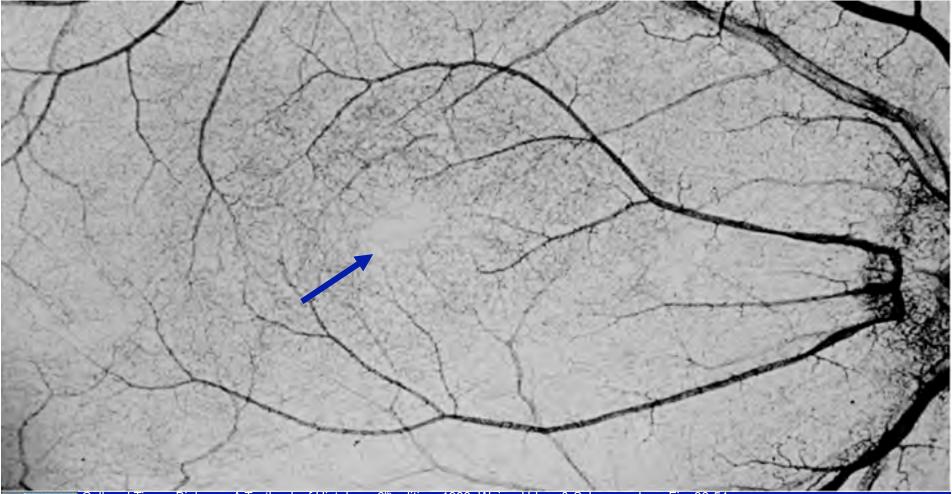
Dentre Japanese slide set (Humio Mizoguti, Department of Anatomy, Kobe University School of Medicine, Slide No. 987

At the <u>optic papilla</u> the optic nerve penetrates the retinal layer and leaves the eye, and the retinal blood supply enters and exits. This creates a <u>blind spot</u> 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.

Dr. Don McCullum, University of Michigan



Cell and Tissue Biology – A Textbook of Histology; 6<sup>th</sup> edition; 1988; Weiss, Urban & Schwarzenberg Fig. 36-54

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 <u>diabetic retinopathy</u>.

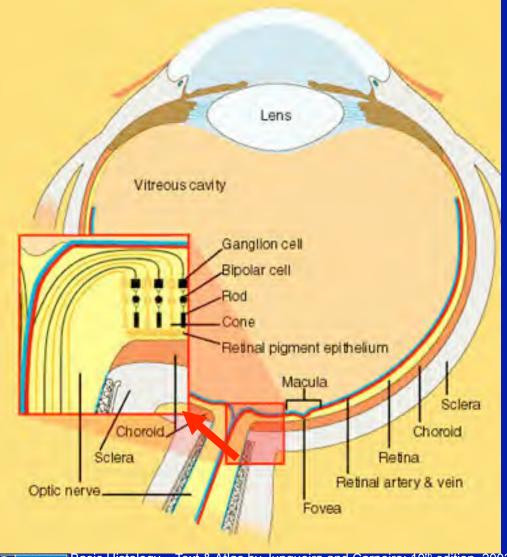
The arrow marks a normal, special area of the retina, which is devoid of retinal blood vessels.

The <u>fovea centralis</u> or <u>macula</u> 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.

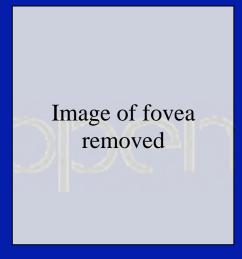


Samuel Thomas von Sömmering 1755-1830



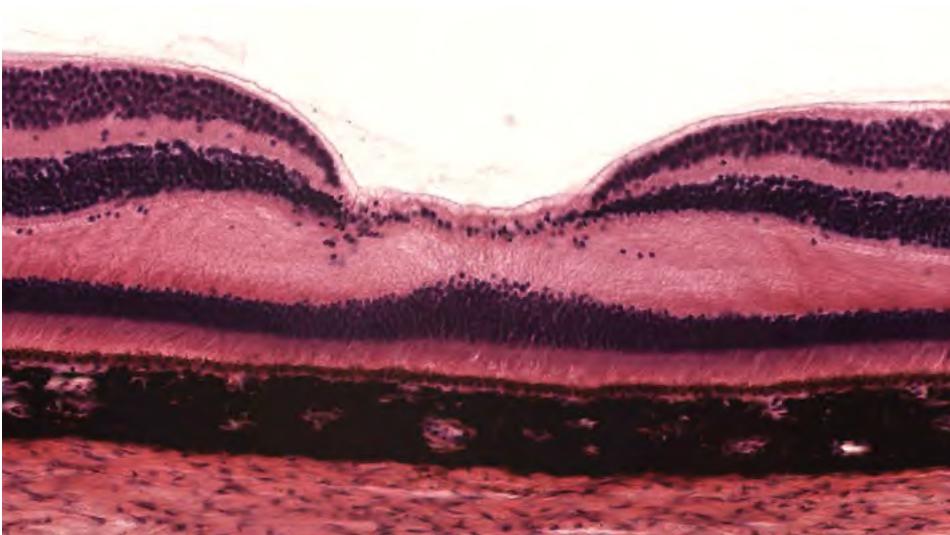
Lange McGraw-Hill Fig 24-2





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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



FD-INFL
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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 agerelated macular degeneration (ARMD), which mainly affects the central region of the retina around the fovea.

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