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List of Abbreviations

ABO	Blood group system
ACAID	Anterior chamber associated immune deviation
Al ₂ O ₃	Aluminum Oxide
BCL	bandage contact lens
BCVA	Best corrected visual acuity
BIOM	binocular indirect ophthalmomicroscope
BSS	balanced salt solution
CLAU	Conjunctival- limbal autograft
CP	Cicatricial pemphigoid
CRP	C-reactive protein
DALK	Deep anterior lamellar keratoplasty
DLEK	Deep lamellar endothelial keratoplasty
DMAEK	Descemet's membrane automated endothelial keratoplasty
DMEK	Descemet's membrane endothelial keratoplasty
DOTS	Directly observed treatment short course
DSAEK	Descemet's stripping automated endothelial keratoplasty
DSEK	Descemet's stripping endothelial keratoplasty
ERG	Electroretinogram
FDA	Food and Drug Administration
HSV	Herpes simplex virus
IE	Infectious endophthalmitis
IEK	IntraLase enabled keratoplasty
IOP	Intraocular pressure
IPN	Interpenetrating Polymer Network
KLAL	Keratolimbal allograft
KPro	Keratoprosthesis
LASIK	laser-assisted in situ keratomileusis

MRSA	Methicillin-resistant Staphylococcus aureus
Nd:YAG	neodymium-doped yttrium aluminium garnet
OCP	ocular cicatricial pemphigoid
OOKP	osteodonto-keratoprotheses
PDMS	poly(dimethylsiloxane)
PHEMA	Poly(2-hydroxyethyl methacrylate)
PKP	Penetrating keratoplasty
PMMA	Polymethyl methacrylate
PTFE	poly(tetrafluoroethylene)
PVP	poly(vinylpyrrolidone)
QALY	Quality-adjusted life years
RGP	rigid gas permeable
RPM	Retroprosthetic membrane
rTPA	recombinant Tissue Plasminogen Activator
SJS	Stevens Jonhson Syndrome
TKP	Temporary keratoprosthesis
VEP	visual evoked potential
WHO	World Health Organization

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The Anatomy & Physiology of the Cornea

The cornea is the most anterior part of the eye, in front of the iris and pupil. It is the most densely innervated tissue of the body.

The transparent cornea appears, from the front, to be oval, as the sclera encroaches on the superior and inferior aspects. The anterior horizontal diameter is 12 mm, and the anterior vertical diameter is 11 mm. If viewed from behind, the cornea appears circular, with horizontal and vertical diameters of 11.7mm. In profile, the cornea has an elliptic rather than a spheric shape, the curvature being steeper in the center and flatter near the periphery. The radius of curvature of the central cornea at the anterior surface is 7.8 mm and at the posterior surface is 6.5 mm. The central corneal thickness is 0.53 mm, whereas the corneal periphery is 0.71 mm.⁽¹⁾

The cornea is avascular and the branches of the anterior ciliary arteries stop at the limbus where they form arcades that supply the peripheral cornea.⁽²⁾ Therefore, the peripheral and central cornea are very distinct in terms of physiology and pathology.

Five layers can be distinguished in the human cornea: the epithelium, Bowman's membrane, the lamellar stroma, Descemet's membrane and the endothelium.

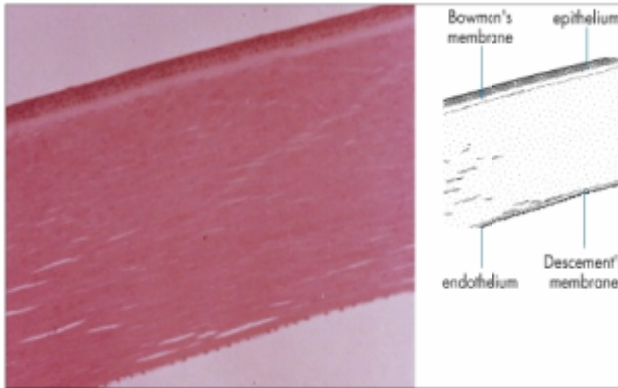


Fig (1): Light micrograph of normal cornea.⁽³⁾

The epithelium is covered with a tear film of 7 μm thickness, which is optically important in smoothing out microirregularities of the anterior epithelial surface. Without this film, degradation of visual images results. The tear-air interface, together with the underlying cornea, provides roughly two thirds of the total refractive power of the eye. The mucinous portion of tears, which forms the undercoat of the tear film and is produced by the conjunctival goblet cells, interacts closely with the corneal epithelial cell glycocalyx to allow hydrophilic spreading of the tear film with each eyelid blink. Studies suggest that part of this mucinous layer may also be secreted by the corneal epithelial cells. ⁽⁴⁾ Loss of the glycocalyx from injury or disease results in loss of stability of the tear film. The tear film also helps protect the corneal surface

from microbial invasion, as well as from chemical, toxic, or foreign body damage. Thus, the ocular surface tear film and the corneal epithelium share an intimate mutual relationship, both anatomically and physiologically.

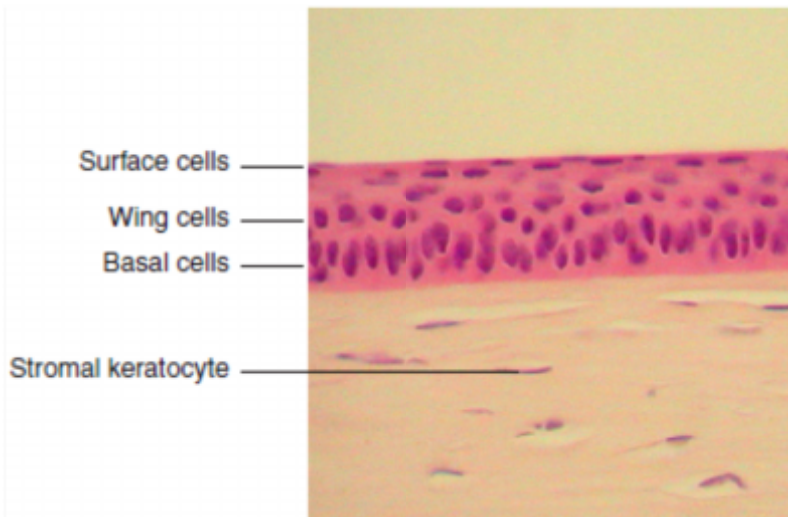


Fig (2): Light micrograph of corneal epithelium showing columnar basal cells, wing cells, and squamous surface cells of cornea; Bowman's layer and anterior stroma are also evident.⁽⁵⁾

The corneal epithelium is composed of two to three layers of superficial cells, two to three layers of wing cells and one layer of basal cells. The surface of the superficial epithelial cells is irregular due to the presence of microplacae (ridge-like folds of the plasmalemma) that interact with the overlying tear film. The cells of the corneal epithelium are renewed every 7–10 days from a pluripotent stem cell population, which resides in the palisades of Vogt at the corneoscleral limbus. The stem cells differentiate into transient amplifying cells when they

migrate to the central cornea.⁽⁶⁾ The corneal epithelium is extremely impermeable and stable due to the presence of cell junctions. It is also anchored very strongly to the basal lamina. The latter is secreted by the basal cells and mainly consists of type IV collagen.

Maintenance of the smooth corneal surface depends on replacement of the surface cells that constantly are being shed into the tear film. Cell proliferation occurs in the basal layer, basal cells move up to become wing cells, and wing cells move up to become surface cells. Only the cells in contact with the basement membrane have the ability to divide; the cells that are displaced into the wing cell layers lose this ability.⁽⁷⁾

Repair to corneal epithelial tissue proceeds quickly; minor abrasions heal within hours, and larger ones often heal overnight. If the basement membrane is damaged, however, complete healing with replacement of basement membrane and hemidesmosomes can take months.⁽⁸⁾

The second layer of the cornea is approximately 8-12 μm thick. Bowman's layer is a dense, fibrous sheet of interwoven collagen fibrils randomly arranged in a mucoprotein ground substance. The fibrils have a uniform diameter of about 25 nm, run in various directions, and are not ordered into bundles.

Bowman's layer sometimes is referred to as a "membrane," but it is more correctly a transition layer to the stroma rather than a true membrane. It differs from the stroma in that it is acellular and contains collagen fibrils of a smaller diameter. Bowman's layer is produced prenatally by the epithelium and is not believed to regenerate. Therefore, if injured, the layer usually is replaced by epithelial cells or stromal scar tissue. However, Bowman's layer is very resistant to damage by shearing, penetration, or infection. Corneal nerves passing through Bowman's layer typically lose their Schwann cell covering and pass into the epithelium as naked nerves.⁽⁹⁾

The corneal lamellar stroma (500- μ m-thick) provides structural integrity to the cornea. Stromal keratocytes secrete collagen and proteoglycans, which are ultimately fundamental for the transparency of the cornea and hydration. The stroma is separated from the epithelium by the Bowman's layer. The bulk of the stromal extracellular matrix consists of collagen fibrils arranged in 200–250 parallel lamellae that run from limbus to limbus. The stromal collagen fibrils are surrounded by proteoglycans consisting of keratan sulfate or chondroitin sulfate/dermatan sulfate side chains. These proteoglycans have an important structural function and help regulate hydration. Keratocytes are the predominant cell type in the stroma and

play a role in maintaining its organization. These stellar-shaped cells contact to each other by long cytoplasmatic extensions (morphologic and functional syncytium) and also interact with the corneal epithelium.

The corneal stroma provides important structural integrity and comprises roughly 85% of the corneal thickness. The stroma differs from other collagenous structures in its transparency and biomechanical properties. These functional properties result from the precise organization of stromal fibers and extracellular matrix.⁽¹⁰⁾ The fibers are aligned in a parallel fashion within each lamella, and arranged at angles relative to fibers in adjacent lamellae. This network reduces forward light scatter and contributes to the mechanical strength of the cornea. The peripheral stroma is thicker than the central stroma and the collagen fibrils may change direction to run circumferentially as they approach the limbus.⁽¹¹⁾

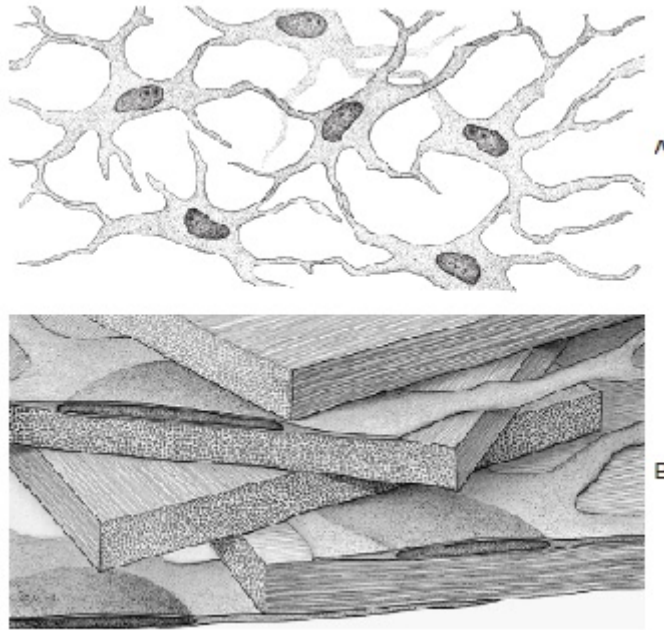


Fig (3): Diagram of corneal stroma. **A**, Fibroblasts. **B**, Lamellae. Collagen fibrils within a lamella are parallel to one another and run the full length of cornea. Successive lamellae run across cornea at an angle to one another fibrils. ⁽¹²⁾

Corneal shape and curvature are governed by the intrinsic biomechanical structure and extrinsic environment. Anterior corneal stromal rigidity in particular appears to be important in maintaining the corneal curvature. Organizational differences in the collagen bundles of the anterior stroma may contribute to a tighter cohesive strength in this area and may also explain why the anterior curvature resists change to stromal hydration much more than the posterior stroma, which tends to more easily develop folds. Stromal hydration also appears to affect the cornea's response to strain and shear forces. ⁽¹³⁾

Descemet's membrane is considered the basement membrane of the endothelium. It is produced constantly and therefore thickens throughout life, such that it has doubled by age 40 years. In children it is 5 μm thick and will increase to approximately 15 μm over a lifetime.

Descemet's membrane consists of two laminae. The anterior lamina, approximately 3 μm thick, exhibits a banded appearance and is a latticework of collagen fibrils secreted during embryonic development. The posterior lamina is nonbanded and homogeneous; it is the portion secreted by the endothelium throughout life. Although no elastic fibers are present, the collagen fibrils are arranged in such a way that Descemet's membrane exhibits an elastic property; if torn, the membrane will curl into the anterior chamber. Descemet's membrane is very resistant to trauma, proteolytic enzymes, and some pathologic conditions and can be regenerated if damaged.

The corneal endothelium is a monolayer, which appears as a honeycomb-like mosaic when viewed from the posterior side. The individual cells continue to flatten over time and stabilize at about 4 μm in thickness in adulthood. The posterior surface of the endothelium is devoid of villi, except in certain pathological conditions, in which it may develop epithelioid