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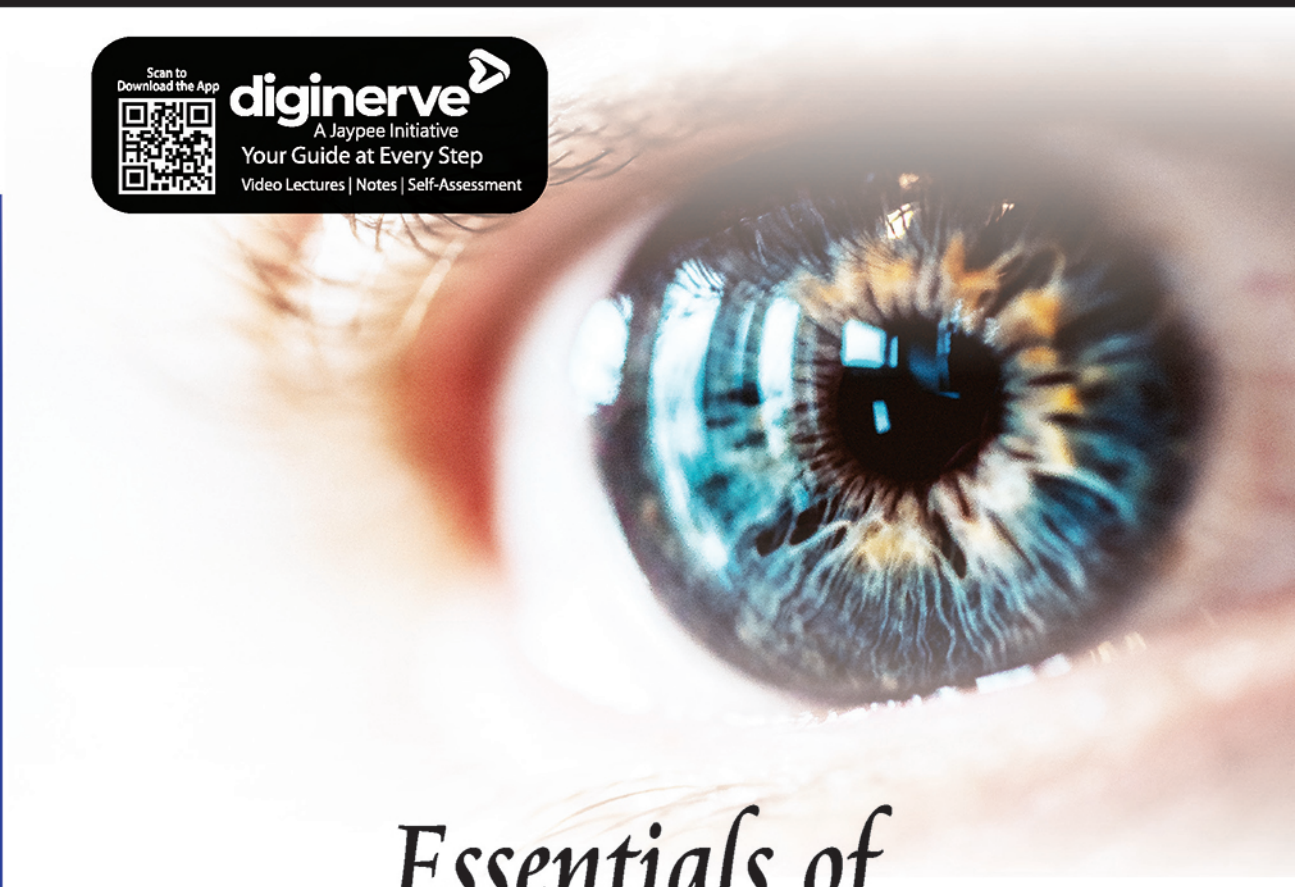

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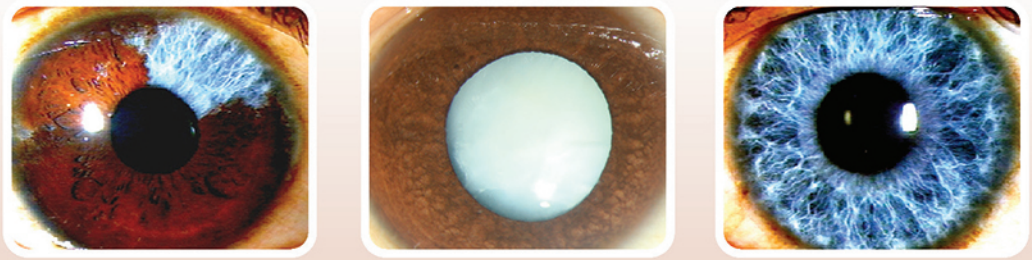

As per the Competency Based Medical Education Curriculum (NMC)

Samar K Basak

8th Edition

JAYPEE

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2

CHAPTER

Physiology of the Eye

CORNEA

The cornea is a transparent tissue, anterior surface of which is bathed with tears, and endothelial surface is bathed in aqueous humor.

The stroma consists of type I collagen fibers of uniform diameter, arranged in a regular lattice work within a ground substance.

The ground substance consists of acid mucopolysaccharides, chondroitin sulfate (type A and type C), and keratin sulfate.

Transparency

In the visible range of spectrum (380 nm to 760 nm), the cornea transmits almost 100% of the light energy.

This transparency is due to following factors:

- ***Anatomical factors:***
  - Avascularity of cornea
  - Absence of pigment in the cornea
  - Demyelinated nerve supply
  - Regular arrangement of the epithelial and endothelial cells
  - Regular arrangement of stromal collagen fibrils (lattice theory)
  - Paucity of cells in the stroma
  - Epithelial cells are non-keratinized
  - Anterior surface of the tear-film helps in forming a regular refracting surface.
- ***Relative dehydration (deturgescence) of the stroma which is maintained by:***
  - Epithelium, which is largely impermeable to water
  - ***Endothelial transport-pump system:*** The endothelial transport system pumps fluid from the corneal stroma to the aqueous by Na-K-ATPase mechanism.
  - Special intercellular junction in the endothelium is also responsible to control the fluid traffic.
- ***Intraocular pressure (IOP):*** It must be optimum to control fluid transport. An acute rise in IOP may result in corneal edema.

Nutrition and Permeability

- ***The peripheral cornea*** receives its nutrients via the bloodstream of perilimbal plexus.
- ***The central cornea*** is avascular and the nutrition depends on substances that enter either via the endothelium or via epithelium.
- ***Permeability:*** The tear film is permeable to water-soluble substances.
  - The corneal epithelium is readily permeable to lipid-soluble substances, as the cell membrane is composed of lipoprotein.
  - The stroma and the endothelium are permeable to water-soluble substances.

Metabolism

Cornea gets its oxygen mostly from the atmosphere. Cornea requires energy to maintain its deturgescence, and also for epithelial cell renewal.

Energy in the form of adenosine triphosphate (ATP), is provided by the metabolism of glucose.

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The epithelium and the endothelium are the sites of most metabolism.

The metabolic pathways are:

- ***Glycolysis*** (Embden-Meyerhof pathway) which requires no oxygen.
- ***Tricarboxylic acid cycle*** (Kreb's cycle), in presence of oxygen, mainly in the epithelium.
- ***Hexose monophosphate (HMP) shunt:*** About 65% of corneal metabolism occurs via glycolysis and the remainder by way of Kreb's cycle and HMP shunt.

Wound Healing

- ***Epithelium*** regenerates rapidly, large abrasion is being covered within 24 hours. This involves both epithelial migration, and proliferation of the surviving epithelial cells. After 6 weeks, epithelium adheres to its underlying basement membrane firmly.
- ***Injury to the Bowman's membrane*** causes scar formation.
- ***Stromal healing:*** By multiplication of undamaged keratocytes and migrated fibroblasts. New mucopolysaccharide synthesis begins after 24–48 hours, and established by 5th day. Stromal healing is not initiated until the defect is covered by epithelium.
- ***Endothelium:*** No multiplication occurs in human beings. The cells spread to cover the defect, by enlargement and migration.

LENS

The lens is a transparent crystalline structure, covered by a homogenous capsule, and has epithelium only beneath the anterior lens capsule.

Transparency

It transmits almost 80% of light energy. Its transparency is due to:

- Sparsity of cells
- Single layer of epithelial cells, which is not thick
- Close alignment of individual cells (the lens extracellular space is less than 5% of its total volume, so the ***zone of discontinuity*** is very small compared to the wavelength of light)
- Semipermeable character of the lens capsule
- Avascularity
- Its index of refraction ranges from about 1.406 at the center (nucleus) to about 1.386 in outer cortical layers, making it a gradient index lens.
- Pump mechanism of the lens fiber membranes, which maintains relative dehydration of the lens.
- ***Autoxidation:*** High concentration of reduced glutathione in the lens maintains the lens protein in a reduced state and ensures the integrity of the cell-membrane pump.

Metabolism

The lens fibers are composed entirely of soluble and insoluble proteins.

- ***Water-soluble proteins (85%)*** are α-crystalline, β-heavy and β-light crystalline, and γ-crystalline; and they are found mainly in the lens cortex. Human lens protein is more labile than that of other species.
- ***Water-insoluble protein (15%):*** Albuminoid fraction and found mainly in the lens nucleus. With age insoluble protein increases. In strict physiological terms, the position of the lens within the eye is similar to a cell surrounded by extracellular fluid.
- ***The lens epithelium generates energy from carbohydrate metabolism:***
  - Anaerobic glycolysis by Embden-Meyerhof pathway—85%
  - Hexose monophosphate shunt
  - Kreb's cycle
  - Sorbitol pathway.

The lens epithelium maintains low concentration of sodium and water within the lens by active Na-K-ATPase pump system. Glycolysis provides the necessary ATP energy.

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Pathogenesis of Cataract

Any opacity in the lens or its capsule is called a cataract. Three basic mechanisms cause a cataract:

1. Damage to the lens capsule that changes its membranous properties
2. Change in the lens-fiber protein synthesis
3. Increased lens hydration.

When a ***cortical cataract*** forms, the sodium-extruding mechanisms fail.

With aging
↓
Lens capsule becomes more permeable
↓
Accumulation of Na-ions and water
↓
Increased hydration
↓
Disruption of lens-fiber membranes and formation of vacuoles
↓
Increased ratio of insoluble to soluble protein
↓
Cortical opacity formation

In Nuclear Cataract

Long-term effects of ultraviolet irradiation
↓
Photo-oxidation of aromatic amino acids
↓
Brown pigmentation and/or deposition of abnormal lipoproteins
↓
A marked reduction of reduced glutathione, and increased concentration of Ca^{2+}-ions
↓
Increased ratio of insoluble to soluble proteins
↓
Nuclear cataract formation

TEARS

Anterior surface of the eye is moistened by tears, secreted by the lacrimal gland and basic secretors, located in the margin of the eyelid and the conjunctiva. The basic secretors of the conjunctiva contribute 10% of the total mass of lacrimal gland.

Circulation of Tears

Lacrimal gland + accessory lacrimal glands + conjunctival glands secrete tears
↓
Along the surface of the eyeball
↓
Lower fornix
↓
Lacus lacrimalis around the caruncle
↓
Lacrimal puncta (70–80% via lower and 20–30% via upper)
↓
Lacrimal canaliculi into the lacrimal sac (by capillary action and negative pressure of lacrimal pump)
↓
Into the inferior meatus of the nose by lacrimal pump and also by gravity (contraction of orbicularis oculi, especially its Horner's fibers around the sac)

Composition of Tears

- Very much similar to blood plasma, slightly more dilute (98.2% of water)
- Relative lack of protein (0.6%)
- pH of tear is 7.35, but it may vary with disease ***(alkaline pH is found in vernal catarrh)***
- Osmotic pressure varies from that of blood (0.9% saline) to the equivalent of 1.4% saline (normal = 290–320 mOsmol)
- ***Protective substances*** present in tears are:
  - Immunoglobulins (IgA, IgG, and IgM)
  - Lymphocytes
  - Complements
  - Lactoferrin

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- ***Lysozyme (muramidase):*** A specific enzyme which is lethal to common bacteria, since it is mucolytic and dissolves the bacterial membrane.

Production

The average normal secretion of tears is 0.5–2.2 µL/min. The maximum capacity of conjunctival cul-de-sac is about 30 µL.

The lacrimal glands secrete continuously throughout the day, but not during sleep. Half of this secretion is lost from the surface by evaporation.

Reflex stimulation occurs in following situations:

- From irritative sensation of the cornea and the conjunctiva
- In yawning, coughing, sneezing or vomiting
- After psychic stimulation, as in weeping or laughing. This curious reflex is confined to human beings, and only develops in infants after 3–4 months.
- After exposure to bright lights
- Secretion can be stimulated by cholinergic drugs (e.g., pilocarpine) and inhibited by anticholinergic drugs (e.g., atropine).

Precorneal Tear Film (Figs. 2.1 and 2.2) and its Functions

It is a relatively stagnant layer of tears that covers the corneal epithelium and consists of ***three layers***, each of which has separate functions.

1. ***The outer lipid layer:*** It is secreted by the Meibomian glands, glands of Zeis, and glands of Moll.

   Functions

   - To retard the evaporation of the aqueous layer of the tear film
   - To increase surface tension and vertical stability of the tear film to prevent overflow of tears
   - To lubricate the eyelids.
2. ***The middle aqueous layer:*** It is the main bulk of the tear film and secreted by the lacrimal and accessory lacrimal glands.

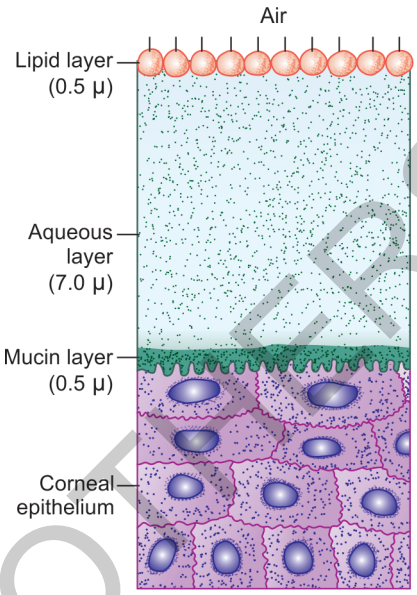

Fig. 2.1: Precorneal tear film (traditional view).

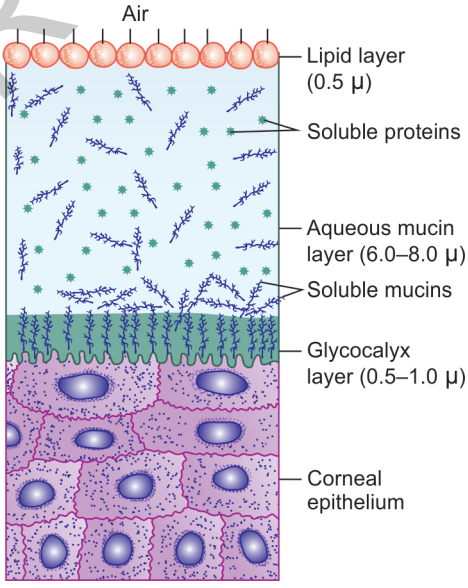

Fig. 2.2: Precorneal tear film (recent concept).

Functions

- To supply atmospheric oxygen to the corneal epithelium.
- It has antibacterial action due to presence of lysozyme and lactoferrin.
- To provide a smooth optical surface.

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- To wash away dust and debris from the conjunctiva and cornea.

3. ***The inner mucin layer:*** It is secreted by the conjunctival goblet cells, glands of Manz, and crypts of Henle.
   Functions
   - To convert the corneal epithelium from a ***hydrophobic*** to a ***hydrophilic*** surface.
   - To wet the microvilli of the corneal epithelium and thereby retains the precorneal tear film.

According to a recent concept

- ***Outer lipid layer:*** It contains both polar and nonpolar lipids. Polar lipids such as phospholipids and fatty acids lie adjacent to the aqueous mucin layer and ***nonpolar lipids*** such as cholesterol esters and triglycerides are present at the tear-air interface.
- ***Middle aqueous-mucin layer:*** Contains soluble mucins and proteins in additions to water and ions.
- ***Inner glycocalyx layer:*** Contains membrane-adherent mucin which is anchored at the cell membrane of numerous microvilli of the corneal epithelium.
- ***Glycocalyx/MUC1:*** It is secreted by the apical conjunctival and corneal epithelial cells. It provides hydrophilic surface.
- ***Mucin (MUC4 and 5AC):*** It is secreted by the conjunctival goblet cells. It adds viscosity to tears and protects the ocular surface during blinking.

AQUEOUS HUMOR

The internal structures of the eye are bathed and surrounded by the aqueous humor, a crystal clear fluid.

Functions

- It helps to maintain IOP
- It supplies nourishment to the cornea and the lens
- It maintains optical transparency
- It takes the place of the lymph that is absent within the eye.

Refractive index = 1.336

Composition

Water content	= 98.92%
Solid	= 1.08%

The composition of aqueous of the posterior chamber differs from the aqueous of the anterior chamber. Posterior chamber aqueous contains chloride and ascorbate in excess, than that of the anterior chamber aqueous. But there is deficiency of bicarbonates.

Solid Components

- ***Proteins:*** They are more dilute than plasma, due to blood-aqueous barrier. But when the protein concentration increased, a ***plasmoid aqueous*** results as in inflammation of anterior uvea (iridocyclitis), and also after surgery with newly-formed aqueous.
- ***Non-electrolytes:*** Examples, glucose, urea, uric acid, alcohol and creatinine (all are little less than those of plasma).
- ***Electrolytes:*** Na ions, K ions, chloride, and bicarbonates.
- ***Organic acids:*** Ascorbic acid is present in greater concentration than in plasma. Other acids present in aqueous are lactic acid and hyaluronic acid.
- ***Oxygen*** is present in aqueous in dissolved state.

Aqueous Humor Formation

Two mechanisms are involved: (1) Ultrafiltration and (2) Secretion.

Ultrafiltration

Capillary wall in the ciliary processes behaves as a crude semipermeable membrane. It retains most proteins, but allows smallest molecules to leave the bloodstream, and collects in the stroma of the ciliary processes, and then into the posterior chamber across the ciliary epithelium.

Secretion

By active secretion of the ciliary processes. Two mechanisms are involved:

1. ***Bicarbonate system*** mediated by carbonic anhydrase.

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2. ***Na-K-ATPase system*** for electrolytes. Once formed, the aqueous is modified by metabolic processes of the cornea and lens, and this chiefly results in a fall in glucose and bicarbonate concentration, but a rise in lactate levels.

Circulation of Aqueous Humor

Circulation is necessary both for metabolic process and to regulate the IOP.

Aqueous formed in the ciliary region → flows from posterior chamber through the pupil into the anterior chamber → angle of the anterior chamber → trabecular meshwork → Schlemm's canal → aqueous veins → episcleral venous plexus.

Normal flow rate of aqueous—2 µL/minute.

In addition, there is a second accessory exit ***(uveoscleral outflow)*** which may sometimes be of importance (as in ***buphthalmos or in retinal detachment or with some antiglaucoma medication)***. Aqueous formed in the ciliary body → suprachoroidal space → episcleral venous plexus.

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He is the recipient of ten Gold Medal Awards from All India Ophthalmological Society Conferences: eight other Gold Medal Oration honours as well as the prestigious Prof LP Agarwal Oration honour from the AIIMS, New Delhi, India. Internationally, he has received the "Best of Show" Video Award six times, Best Paper Award, and Best Poster Award four times in the American Academy of Ophthalmology (AAO) Conferences. He has also bagged the Best Video Award two times from ESCRS and "People's Choice" Best Video Award in ASCRS-2012. He was awarded an "Achievement Award" by the AAO in 2008 and by the APAO in 2011; Senior Achievement Award by the AAO in 2015 and Senior Scholar Award by the AAO in 2017.

Basak, an FRCS Examiner since 2008, has written six other books on ophthalmology including "Ophthalmology: Oral & Practical" (currently in its fifth edition) for undergraduate, postgraduate students and comprehensive ophthalmologists. He has over fifty publications in national and international peer-review indexed journals. He is the reviewer of eleven prestigious peer-review journals, including ophthalmology and cornea journal.

He is involved with teaching and training programs with ORBIS, SightLife and Visionaries—International, in India and South-East Asia regions (Phaco/SICS; and DSEK/DMEK/Boston KPro-1 Skill Transfer Course). He is a bulk Phaco surgeon performing approximately 2500 surgeries per year; and Keratoplasty (PK/DALK/DSEK/DMEK/Boston KPro) surgeon performing approximately 250 surgeries per year. He has been obsessed with DMEK in recent years, performing more than 200 DMEK per year and has performed more than 1300 DMEK in a short span of seven years.

In leisure time, he is busy with his unique hobby, "Ophtha-Philately" (Ophthalmology + Philately), collecting and studying 'Postage stamp only related to Ophthalmology.

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Printed in India

Available at all medical bookstores
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JAYPEE BROTHERS
Medical Publishers (P) Ltd.
EMCA House, 23/23-B, Ansari Road,
Daryaganj, New Delhi - 110 002, INDIA
www.jaypeebrothers.com

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OPHTHALMOLOGY

ISBN 978-93-5696-382-5

9 789356 963825