PATHOLOGICAL RESPONSES OF THE CORNEA

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ANATOMICAL REGIONS OF THE CORNEA

- For discussing pathological responses of the cornea; the cornea is divided into 4 anatomical regions:

1. Epithelium
2. Subepithelial zone
   a. Epithelial basement membrane
   b. Bowman's layer
   c. Superficial stroma
3. Stroma
4. Endothelium and Descemet membrane.

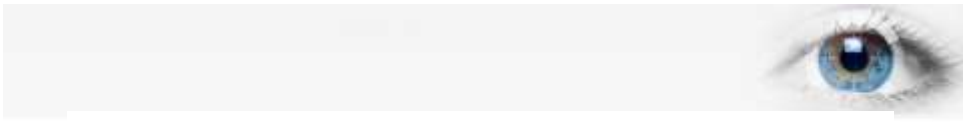
PATHOLOGICAL RESPONSES

- A spectrum of pathological processes can disrupt the structure of these 4 zones and interfere with corneal function

- The responses of the cornea to these insults can be grouped into 6 categories with some overlap among them

PATHOLOGICAL RESPONSES

- Defects and their repair
- Fibrosis and vascularization
- Edema and cysts
- Inflammation and immune responses
- Deposits
- Proliferation



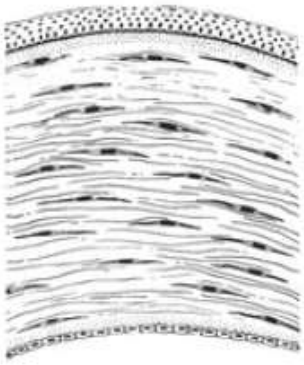
Four zones of cornea

Epithelium

Subepithelial zone

Stroma

Descemet membrane
endothelium



Six types of pathologic responses

Defects

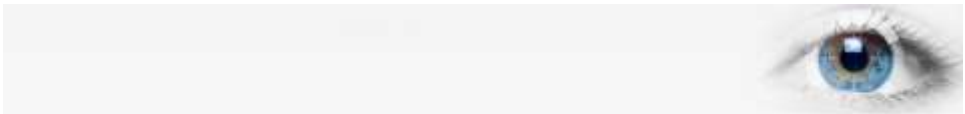
Fibrosis
vascularization

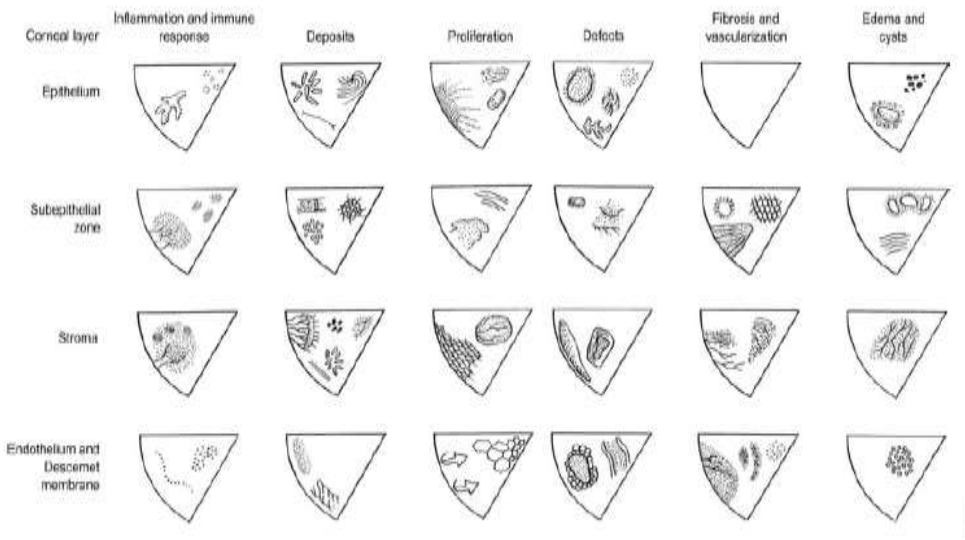
Edema
cysts

Inflammation
immune response

Deposits

Proliferation

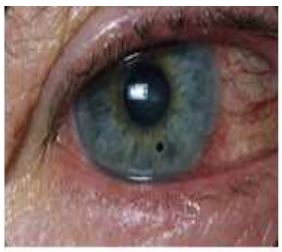




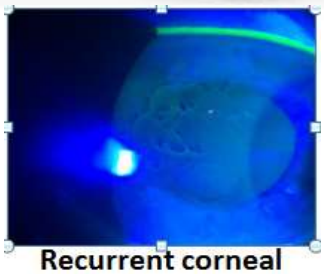
EPITHELIUM

❑ **DEFECTS**

Neurotrophic keratopathy (Herpes simplex)

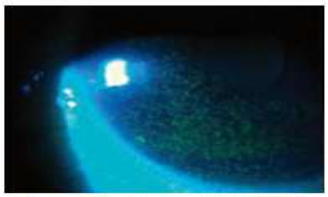


Focal corneal F.B.



Recurrent corneal erosion

Corneal abrasion



Punctate epithelial keratopathy

EPITHELIUM

** 4 factors are required to re-establish normal epithelial integrity

- Normal basement membrane
- Vitamin A
- Normal tear film
- Intact sensory innervation

EPITHELIUM

- **FIBROSIS AND VASCULARIZATION**

- Do not occur due to lack of connective tissue

EPITHELIUM

- **EDEMA AND CYSTS**

Microcystic edema, bullae (either due to endothelial dysfunction or epithelium hypoxia and trauma)

Cysts in epithelial basement membrane dystrophy

EPITHELIUM

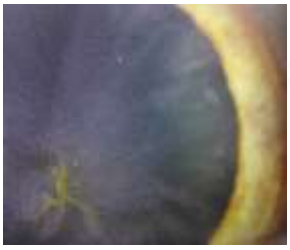
❑ INFLAMMATION AND IMMUNE RESPONSES

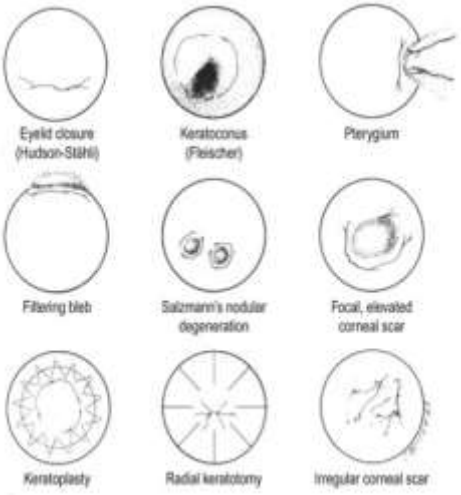
- Zoster dendrite
- Thygeson's superficial punctate keratitis
- In corneal allograft rejection (Epithelium attacked by sensitized cytotocic T lymphocytes

EPITHELIUM

❑ DEPOSITS

- Elements (Iron is the most common)



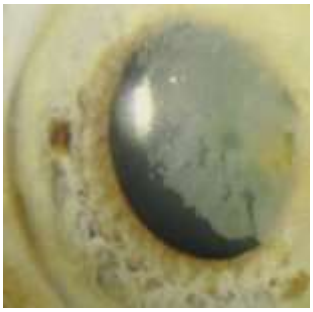


- Drugs like Amiodarone or chloroquine
- Crystals

EPITHELIUM

❑ PROLIFERATION

- Corneal intraepithelial neoplasia
- Epithelium filling in a defect (eg.Facet)
- Keratinization
- Epithelial ingrowth under LASIK flap



SUBEPITHELIAL ZONE

❑ DEFECTS

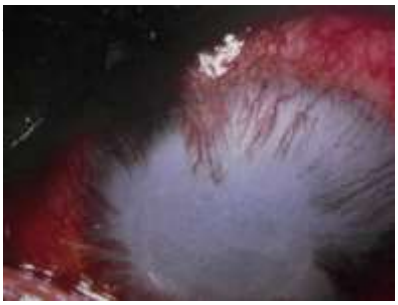
- Foreign body
- Keratoconus

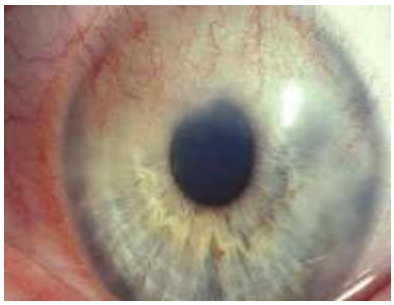
A defect in Bowman's layer fills with fibroblasts and connective tissue, creating a permanent scar

SUBEPITHELIAL ZONE

❑ FIBROSIS AND VASCULARIZATION

- Neither the epithelial basement membrane nor Bowman's layer can become fibrotic or vascularized.
- Fibrous or vascular tissues can spread between the two layers as either an avascular or vascular pannus





SUBEPITHELIAL ZONE

- **Subepithelial avascular fibrosis:**

- Advanced Fuchs endothelial dystrophy
- Salzmann's nodular degeneration

- **Subepithelial vascular fibrosis** (Leukocytes, proliferating endothelial cells and fibroblats):

- After mild inflammation (hyopxia in CL wearers)
- Chronic inflammation (Trachomatous pannus)
- Severe inflammation (Alkali burns)

SUBEPITHELIAL ZONE

- **EDEMA AND CYSTS** (from endothelial dysfunction)
  - Basement membrane folds
  - Subepithelial bullae

- **INFLAMMATION AND IMMUNE RESPONSES** (Superficial infiltarate)
  - Phlyctenulosis
  - Severe infection or trauma
  - Adenovirus punctate keratitis
  - Allogaft rejection after PKP

SUBEPITHELIAL ZONE

- **DEPOSITS**
  - Calcium (band keratopathy)
  - Amyloid (Reis-Bucklers' dystrphy)

- **PROLIFERATION** (The basal corneal epithelial cells can secrete exuberant amounts of basement membrane)
  - Maps and fingerprints in epithelial basement membrane dystrophy
  - Salzmann's degeneration
  - Manifestation of systemic disease (DM)

STROMA

❑ DEFECTS

❖Acute:

- Accidental or surgical trauma (Repair according to principles of normal corneal wound healing
- Ulceration due to microbial invasion (Repair requires clearance of organisms and control of inflammation)

STROMA

❑ DEFECTS

❖Chronic :

- Stromal thinning without ulceration (Keratoconus, Keratoglobus, Pellucid marginal degeneration and terrien marginal degeneration)
- Sterile stromal ulceration (Alkali burns)
- Congenital posterior corneal defects

STROMA

❑ FIBROSIS AND VASCULARIZATION

3 basic phases for stromal wound healing

1- **Destructive phase:** removal of Abnormal tissues by PMN leukocytes and macrophages

-- If not present …. melting then perforation

2- **Synthetic phase:** Synthesis of new collagen and proteoglycans by stromal fibroblasts

-- If inhibited by drugs (steroids) or diseases(RA)… delayed healing

-- If proceeds uncontrolled…Visually significant scar

3- **Remodeling phase:** Clearance of initial scar

STROMA

❖ STROMAL FIBROSIS

Pattern of scarring is not diagnostic but some processes leave characteristic scar

- **Bacterial and fungal keratitis:** Local sharply demarcated scar
- **Alkali burns:** Diffuse opaque scar
- **Syphilitic interstitial keratitis:** Deep stromal scars with ghost vessels and lipid deposits

STROMA

❖ STROMAL VASCULARIZATION

Source

- Superficial conjunctival vessels
- Deep scleral vessels
- Iris vessels

In inflammatory conditions, the pattern follows the leukocytic infiltrate.

STROMA

❑ EDEMA AND CYSTS

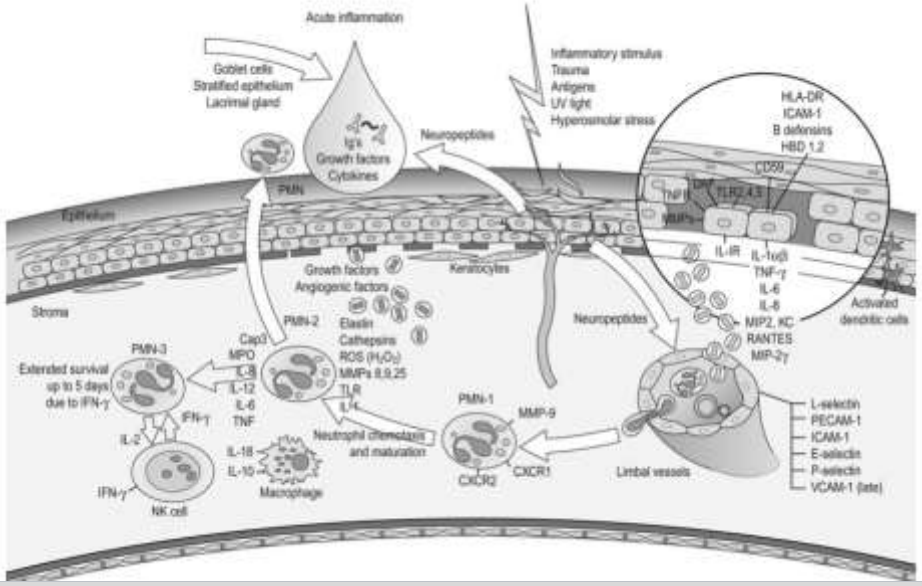
- Edema of the corneal stroma occurs when its water content rises above the normal 78%.
- In most cases, corneal stromal edema results from disruption of endothelial or epithelial pump functions and manifests as an increase in corneal thickness.
- Causes: Surgical trauma, Fuchs endothelial dystrohy and acute angle closure glaucoma.

STROMA

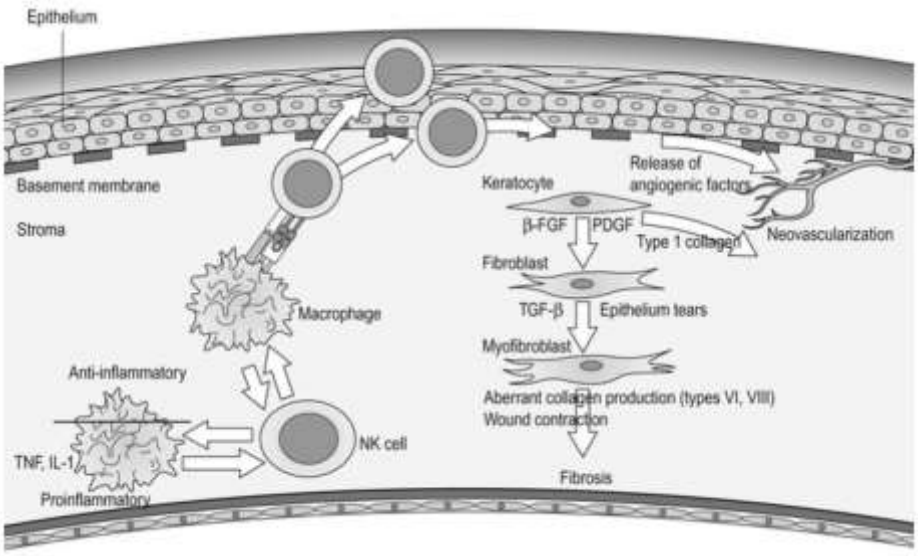
❑ INFLAMMATION AND IMMUNE RESPONSES

- leukocytes migrate along stromal lamellae and congregate with varying density. Bacteria, particularly Gram-negative bacteria such as *Pseudomonas aeruginosa*, cause severe stromal suppuration and destruction due to the secretion of proteolytic enzymes from both the PMNs and the bacteria
- Immune-based stromal inflammation is more complicated and can result from deposition of antigen–antibody complexes and complement-mediated hypersensitivity(e.g.RA)
- Herpes simplex immune stromal keratitis is probably mediated by deposition of viral antigens into the stroma and subsequent immune complex hypersensitivity with migration of PMNs and lymphocytes.

ACUTE INFLAMMATION



CHRONIC INFLAMMATION



STROMA

❑ DEPOSITS

- **Topical and systemic drugs** Gold can accumulate in the cytoplasm of keratocytes and appear as myriad, fine, round, ash-like particles (ocular chrysiasis).
- **Ocular diseases**

- Retained foreign bodies(wood, nylon suture)
- Lipid dposits from blood vessels
- Corneal arcus
- Blood staining in hyphoema

STROMA

❑ **DEPOSITS**

- **Systemic diseases**
- Mucopolysaccharidosis
- Globulin crystals in multiple myeloma
- Lipid deposits in disorders of HDL
- **In stromal dystrophies and degenerations**
- Amyloid in lattice dystrophy or polymorphic amyloid degeneration
- Phospholipids in granular dystrophy
- Glycosaminoglycans in macular dystrophy
- lipid in Schnyder central crystalline dystrophy

STROMA

❑ **PROLIFERATION (Usually in peripheral cornea)**

- Congenital: Dermoid choristomas
- The acquired type includes connective tissue elements of the stroma that proliferate at a surgical or accidental wound without vascularization.

ENDOTHELIUM AND DESCEMET MEMBRANE

❑ DEFECTS

- Normal adult endothelial cell density is approximately 2500 cells/mm2 and normal cell size is approximately 250 µm.

- Defects in the endothelium can occur alone or in combination with defects in the Descemet membrane. In either case, aqueous humor rushes through the defect into the corneal stroma, producing stromal and epithelial edema that persists until a functioning endothelial monolayer re-establishes itself.

ENDOTHELIUM AND DESCEMET MEMBRANE

❑ DEFECTS In Endothelium

❖ Acute

After trauma or surgery

❖Chronic

Fuchs dystrophy

❑ DEFECTS In Descemet membrane

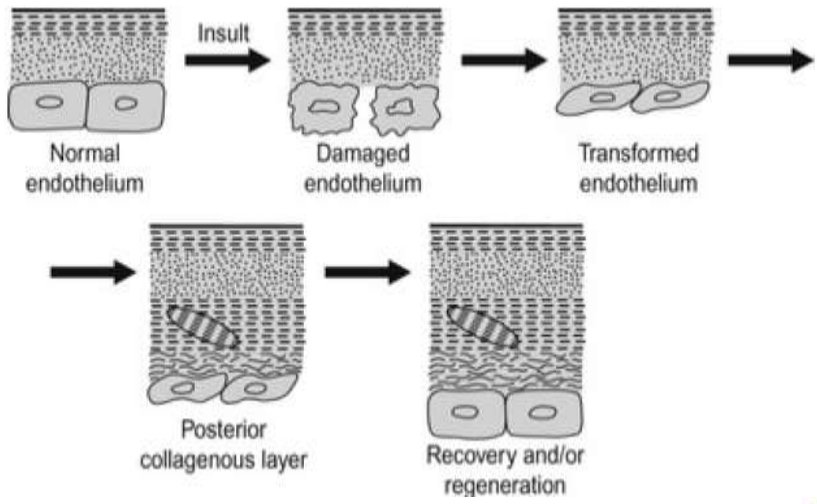
- Descemet membrane has less tensile strength than full-thickness stroma, and thus may break with corneal stretching (Infantile glaucoma)
- Congenital: Peters anomaly

ENDOTHELIUM AND DESCEMET MEMBRANE

❑ FIBROSIS AND VASCULARIZATION

- The endothelium and Descemet membrane contain no connective tissue and therefore do not develop classic fibrosis or vascularization.
- However, when the endothelium is damaged or diseased, it secretes a layer of abnormal fibrillar tissue (the posterior collagenous layer), which may lead to visual loss
- Endothelial cells, like stromal keratocytes, can transdifferentiate into epithelium-like cells (e.g. posterior polymorphous dystrophy (PPMD))

ENDOTHELIUM AND DESCEMET MEMBRANE



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ENDOTHELIUM AND DESCEMET MEMBRANE

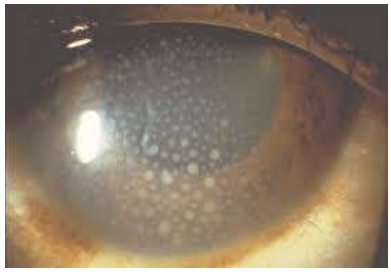
❑ EDEMA AND CYSTS

- Endothelial edema
- True cysts do not occur

ENDOTHELIUM AND DESCEMET MEMBRANE

❑ INFLAMMATION AND IMMUNE RESPONSES

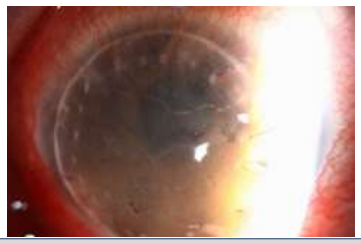
- The endothelium indirectly becomes involved in inflammatory processes in disorders such as microbial keratitis and iridocyclitis.
- Vasodilatory and chemotactic factors bring it into contact with leukocytes, forming keratic precipitates (KP).



ENDOTHELIUM AND DESCEMET MEMBRANE

❑ INFLAMMATION AND IMMUNE RESPONSES

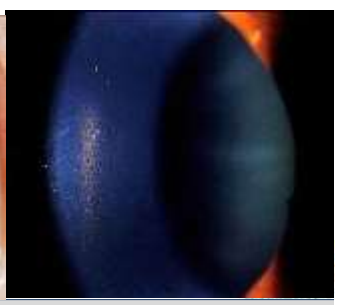
- The endothelium also becomes directly involved in inflammatory processes in disorders such as herpetic disease and allograft rejection reactions, in which antigens on the endothelial cell surface stimulate an immune reaction (e.g. endothelial rejection line (Khodadoust) on the donor)



ENDOTHELIUM AND DESCEMET MEMBRANE

❑ DEPOSITS

- Corneal arcus (Lipid)
- Wilson's disease (Cupper)
- Krukenberg's spindle (Melanin pigment)



ENDOTHELIUM AND DESCEMET MEMBRANE

❑PROLIFERATION

- Spread in ICE syndrome

the endothelium can proliferate over the surface of the trabecular meshwork, iris, and vitreous under specific circumstances, especially in children. (results in glaucoma)

- Hypertrophic cells