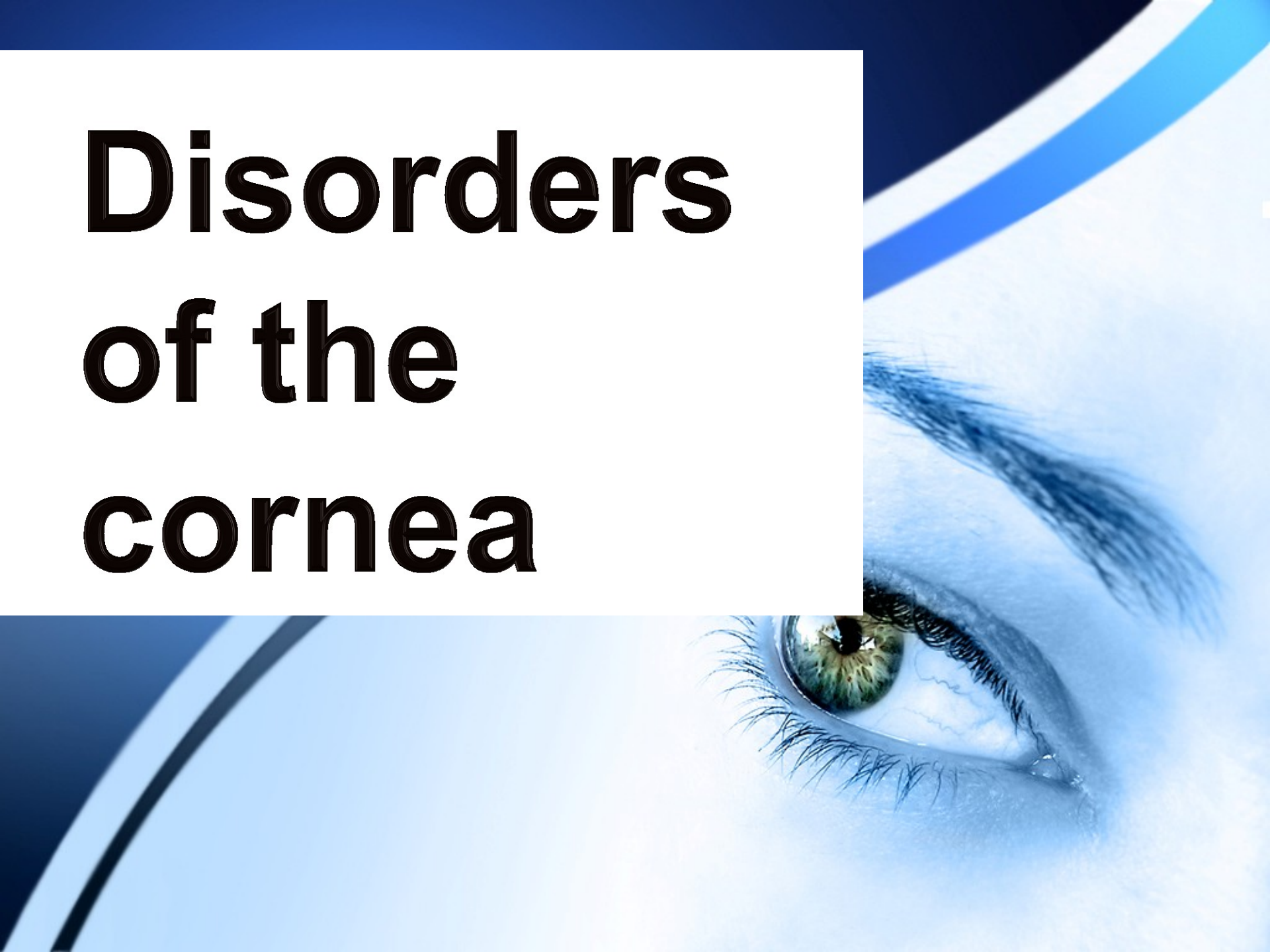
Disorders of the cornea



Cornea

- It is the transparent front part of the eye, that covers the iris, pupil and anterior chamber.
- The refractive power of the cornea is approximately 43 Dioptres (= two thirds of the total optical power)
- It is clear, protective outer layer of the eye.
- Is separated from the sclera by the corneal limbus.
- It serves as a barrier againts dirt, germs, and other particles that can harm the eye.

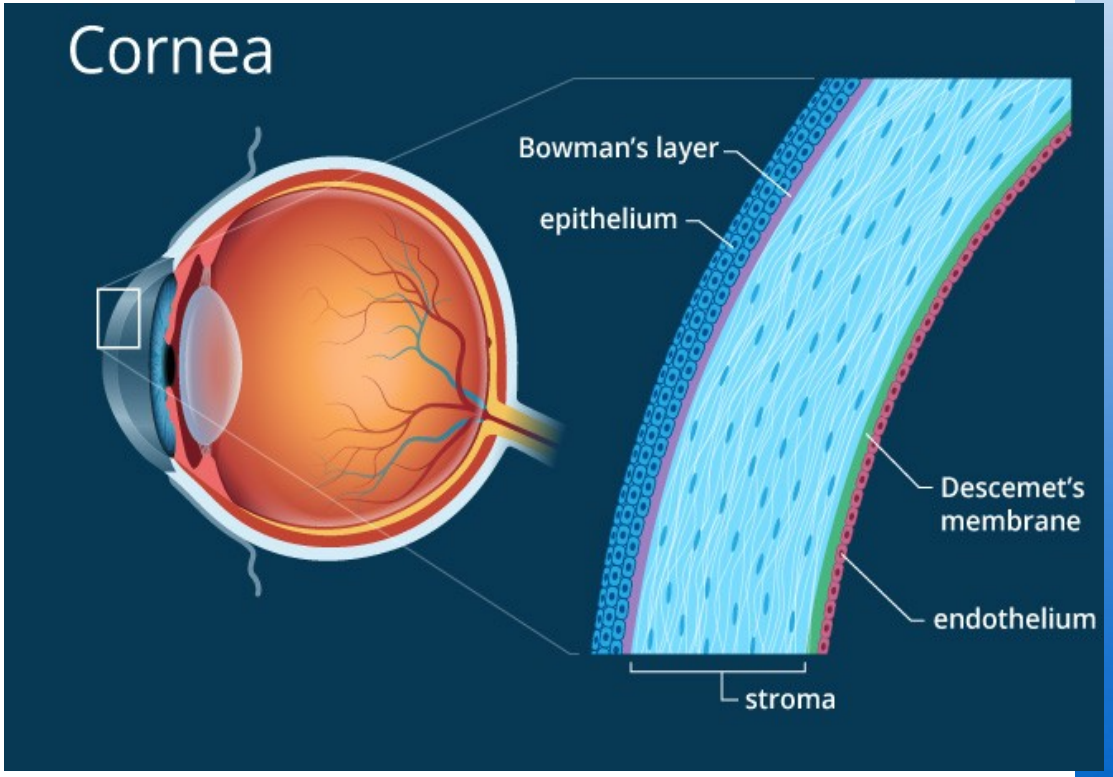
Cornea

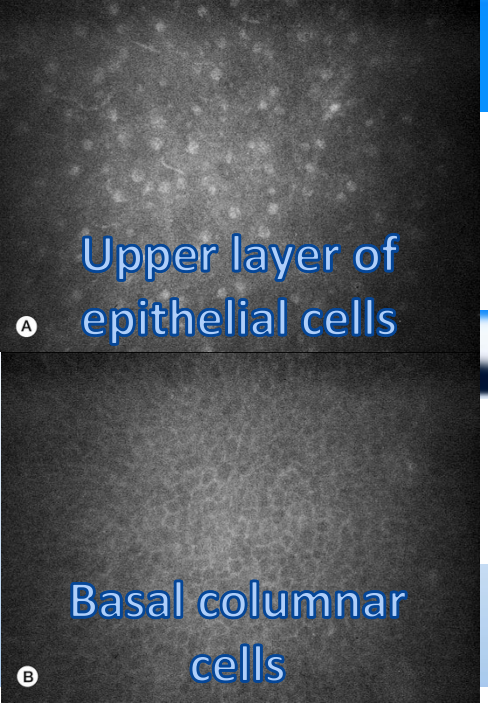
- Is one of the most sensitive tissues of the body
- Has unmyelinated nerve endings sensitive to touch, temperature and chemicals - a touch of the cornea causes an involuntary reflex to close the eyelid!
- The optical components is concerned with producing a reduced inverted image on the retina.
- Hasn´t got blood vessels – receives nutrients via diffusion from the tear fluid though the outside surface and the aqueous humour though the inside surface

Anatomy of Cornea

- **the cornea consists of the five following layers:**

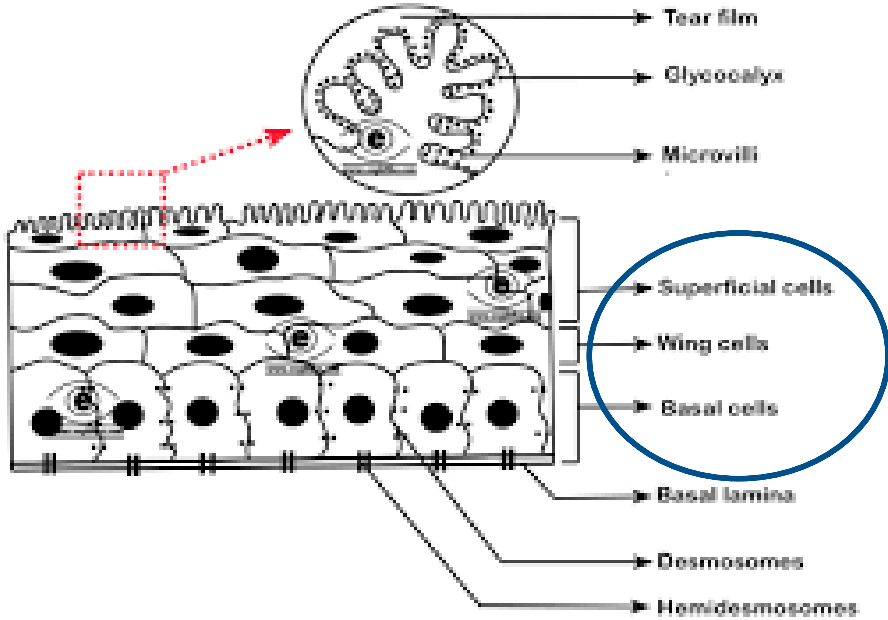
1. **Epithelium**
2. **Bowman´s membrane**
1. **Stroma**
2. **Descemet´s membrane**
5. **Endothelium**





Cornea

Epithelium



- The most superficial layer of cornea, this layer absorbs oxygen and nutrients from tears
- It is multicellular layer of fast-growing and easily regenerated cells (non-keratinized)
- Consists of three types of cells:
- A single layer of basal columnar cells which is attached by hemidesmosomes to the epithelial basement membrane
- Two to three rows of wing cells which have thin extension
- Two layers of long and thin surface cells joined by bridges.

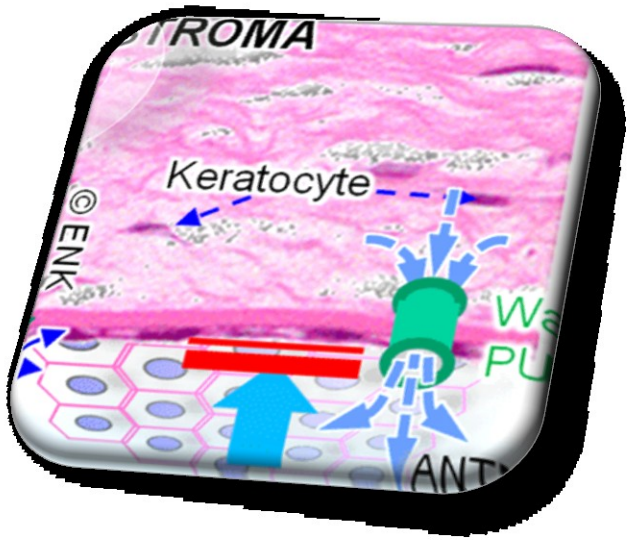
Cornea

Bowman s membrane

- Also known as the anterior limiting membrane
- It is a tough layer composed of collagen, acellular, condensed region ot the apical stroma
- 14 um thick

Cornea

Stroma

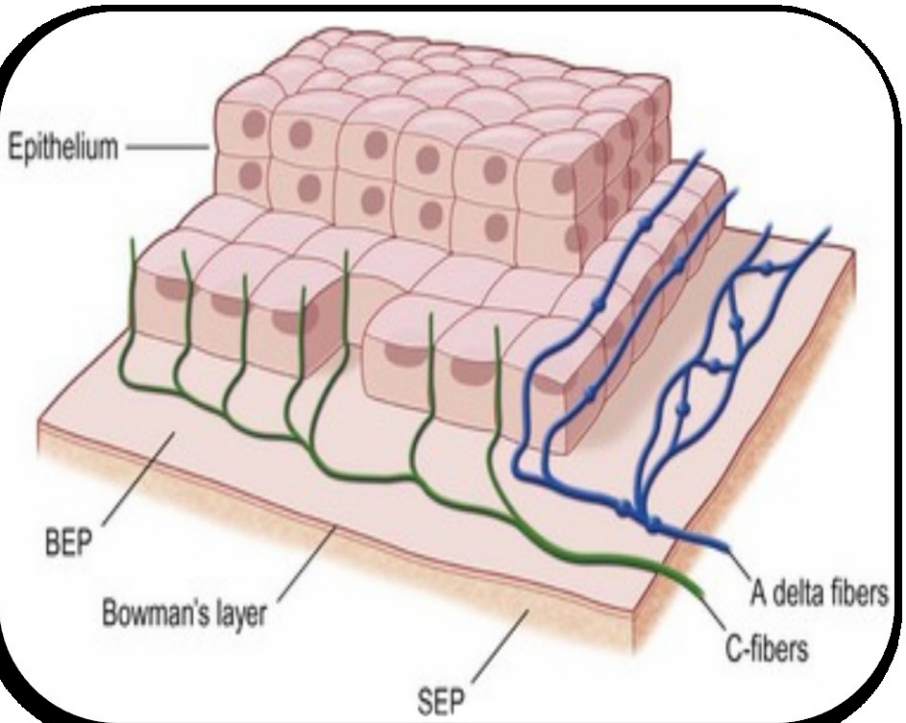


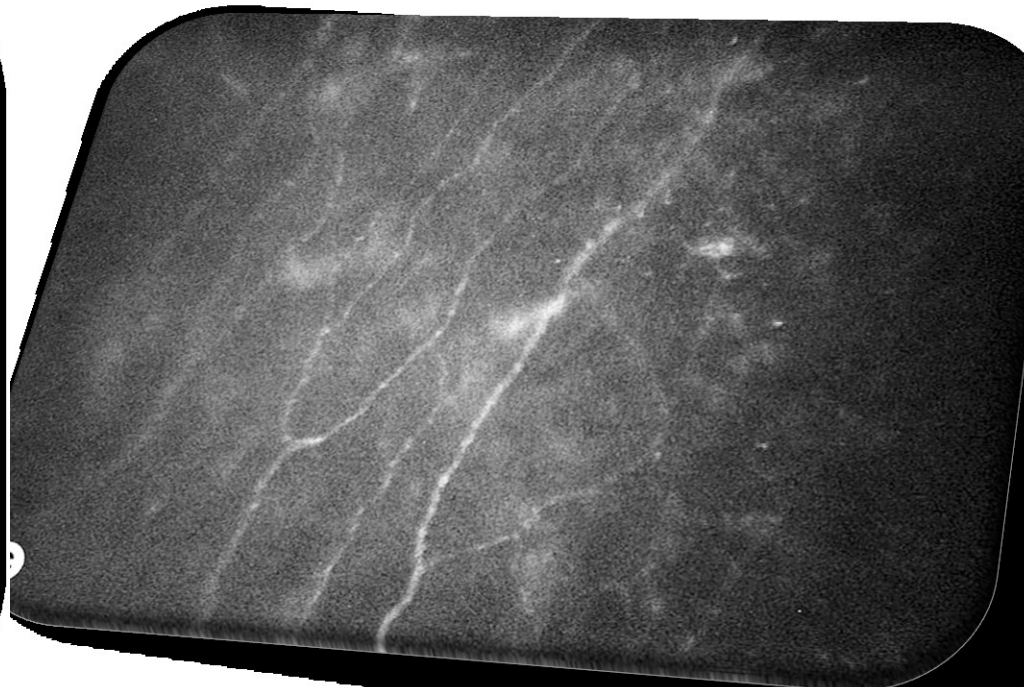
- The stroma makes up about 90 % of corneal thicknes.
- It is composed of regularly arranged collagen fibrils producing by fibroblasts (keratocytes), collagen fibril and ground substance.
- Consist of 200 layers of mainly type I collagen fibrils
- It is made up mostly of water and proteins that give it an elastic but solid form.

Cornea

Stroma

- Subbasal plexus of senzory nerve – first branch of trigeminal nerv

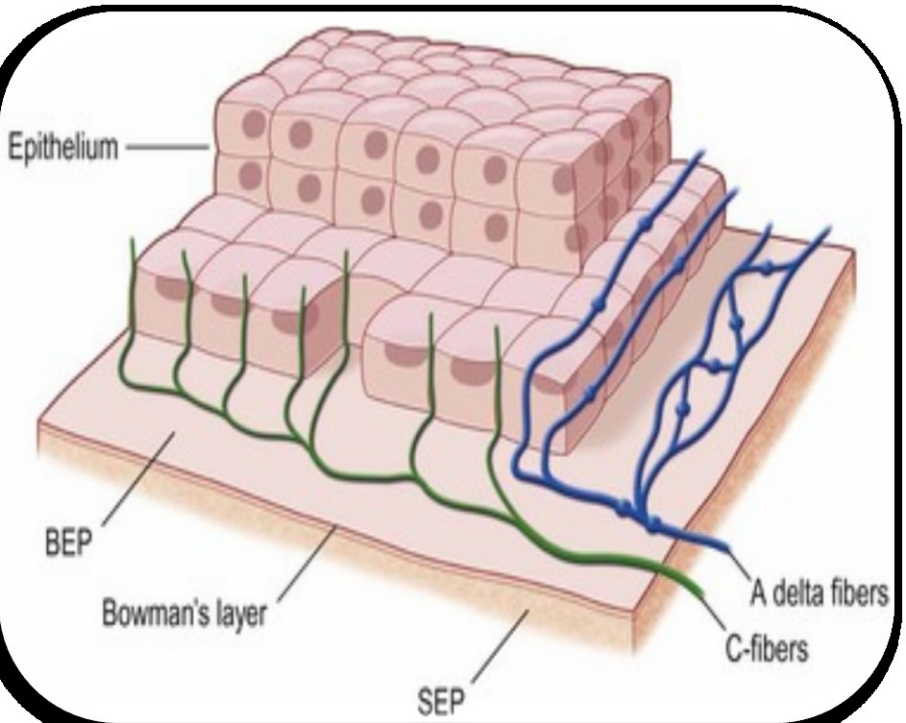


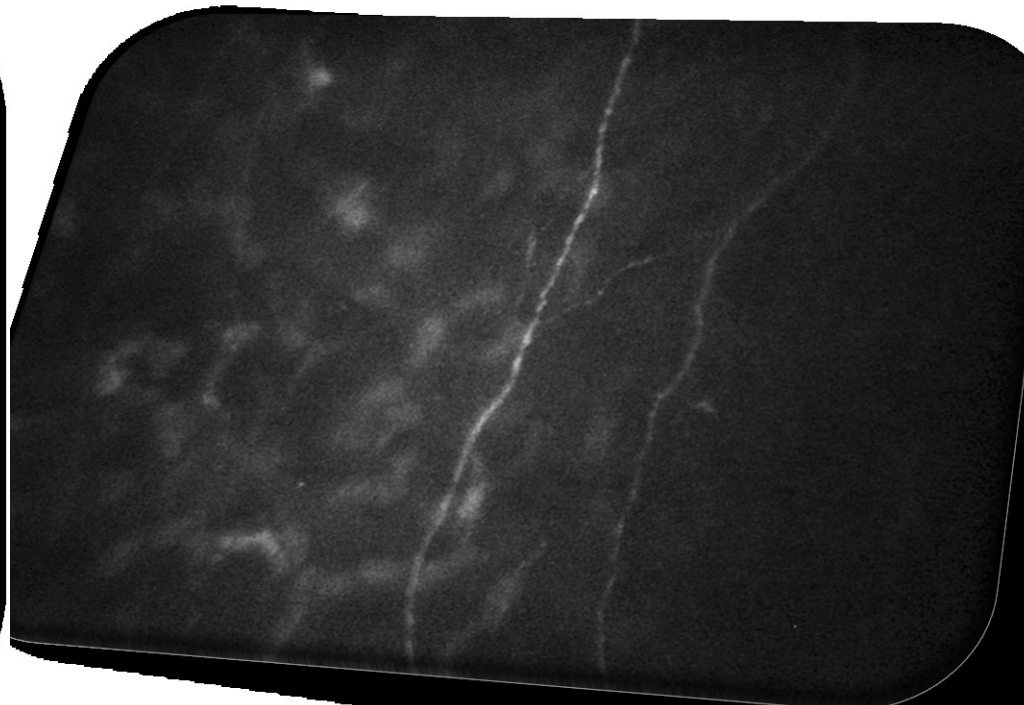


Cornea

Stroma

- Upper layer of stroma with keratocytes and subepitelial branches of senzory nerves





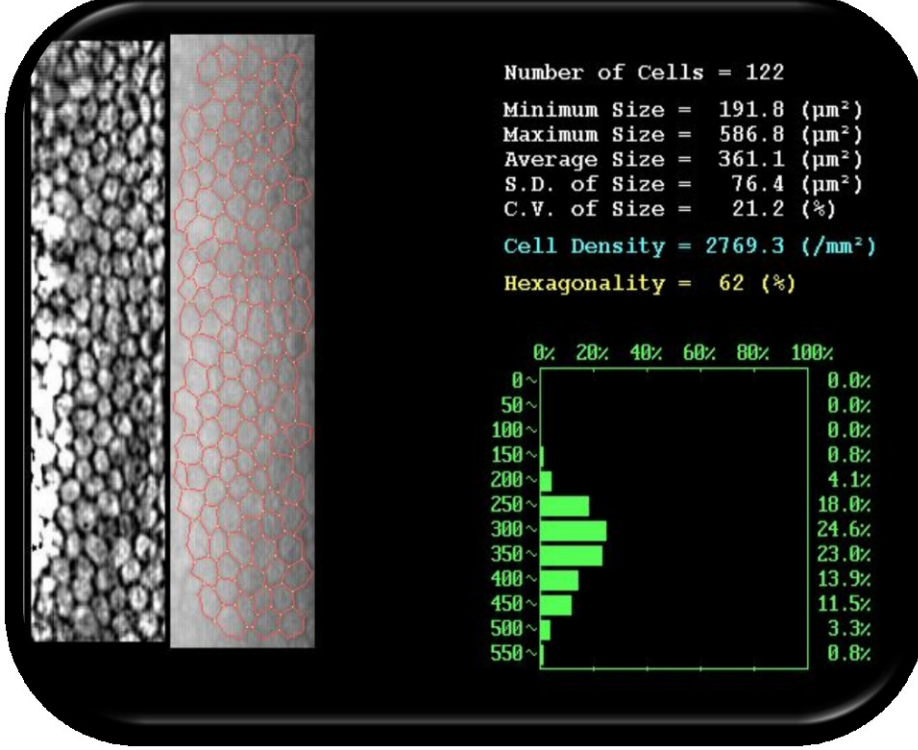
Cornea

Descemet s membrane

- Also known as the posterior limiting membrane
- It is a thin acellular layer that serves as the modified basement membrane of the corneal endothelium
- Is around 5-20 um thick

Cornea

Endothelium



- Single layer of hexagonal cells
- Cannot regenerate!
- Fyziological cells density 2500 cells/mm sq.
- Endotelial dysfunction results in stromal edema
- Regulates fluid and solute transport between the aqueous and corneal stromal compartments

Anatomy of Cornea

- Transparent optical part of the eyeball - impermeable barrier
- Refractive medium (43 D)
- Diameter 11.5 mm x 12.6 mm
- Central thickness of 560 µm (microns) peripheral thickness of 600 – 1000 µm
- Endothelial cell density (2600 / mm^2)
- Water content 76-80%

Anatomy of Cornea

- **Innervation: n. nasociliaris (nn. ciliares longi) V. cranial nerve**
- **Immunology: privileged status is due to avascularity, the lack of lymphatic drainage, a small proportion of antigen presenting cells and the secretion of imunosupresive cytokines (apoptosis of lymphocytes)**
- **The phenomenon ACAID (anterior chamber associated immune deviation)**

Functions of Cornea

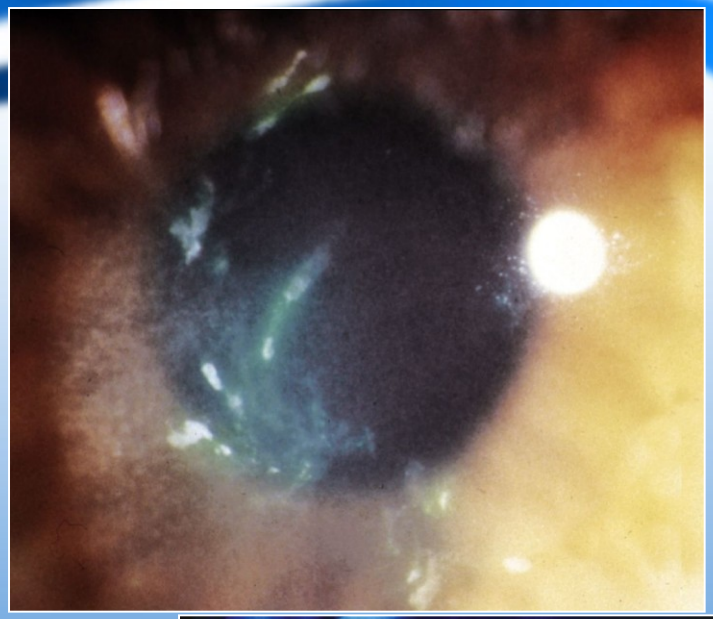
- Most refractive tissue (43D)
- Transparency is defined by the arrangement of fibrils
- Endothelial pump: ability of endothelium actively suck water- Na / K ATP pump
- Decrease in endothelial cells below 500 / mm^2 leads to irreversible changes

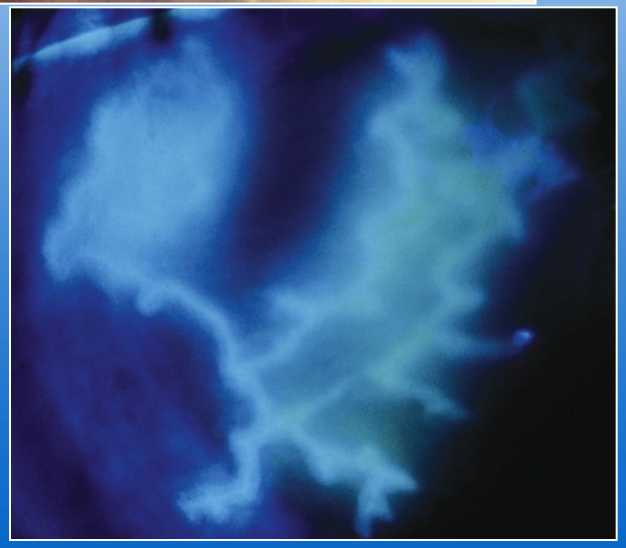
Basic examination methods

1. Anamnesis
2. Slit lamp biomicroscopy
3. Visual acuity
4. Laboratory test (microbiology, cytology, serology, PCR)

Special examination methods

Staining





Fluorescein:

is a water-soluble dye that stains in areas of missing epithelium

Bengal rose

Special examination methods

1. BUT (tear break up time):

Is i clinical test used to assess for evaporative dry eye disease. Fluorescein is instillater into tear film and the patient is asked not to blink, test is recorded as th number of seconds that elapse between tha last blink and the apperean of the first dry spot in the tear film. **Under 10 seconds** is considered **normal**

2. Schirmer test:

Determines whether the eye produces enough tears to keep it moist. Paper strips are inserted into the fornix inferiior for several minutes to measuer the production of tears. Results:

NORMAL is **over than 15 mm** wetting of the paper after 5 minutes X **severe DED** is less than 4 mm

Special examination methods

1. Pachymetry (ultrasound, optic):

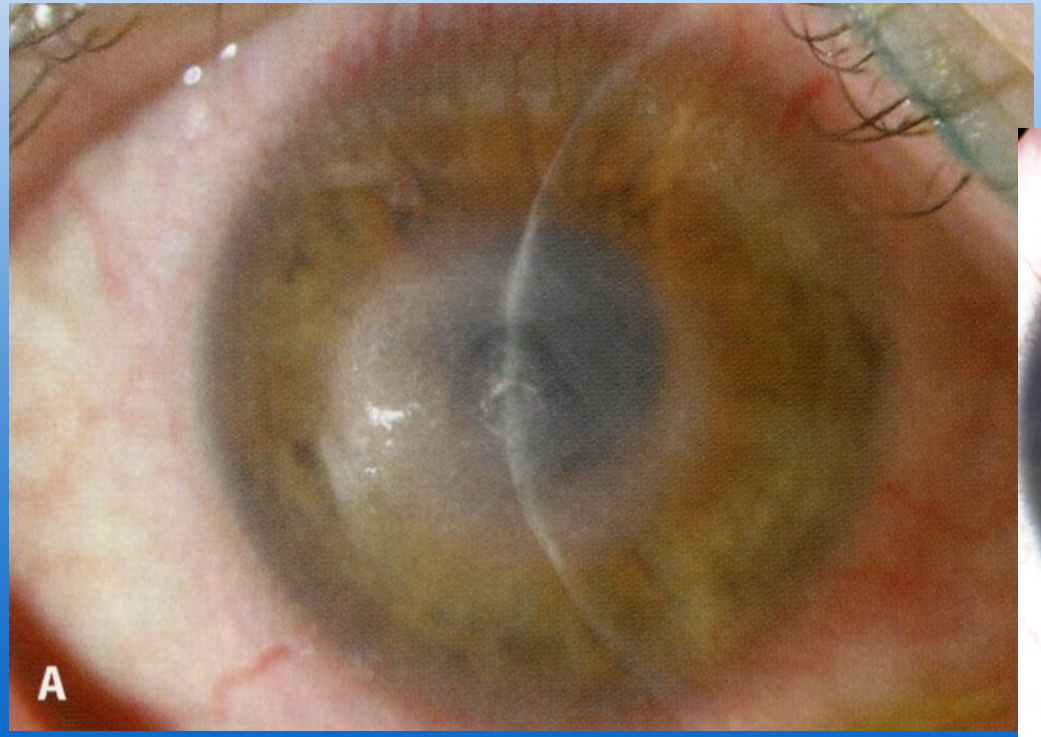
= a medical device used to measure the thickness of the cornea

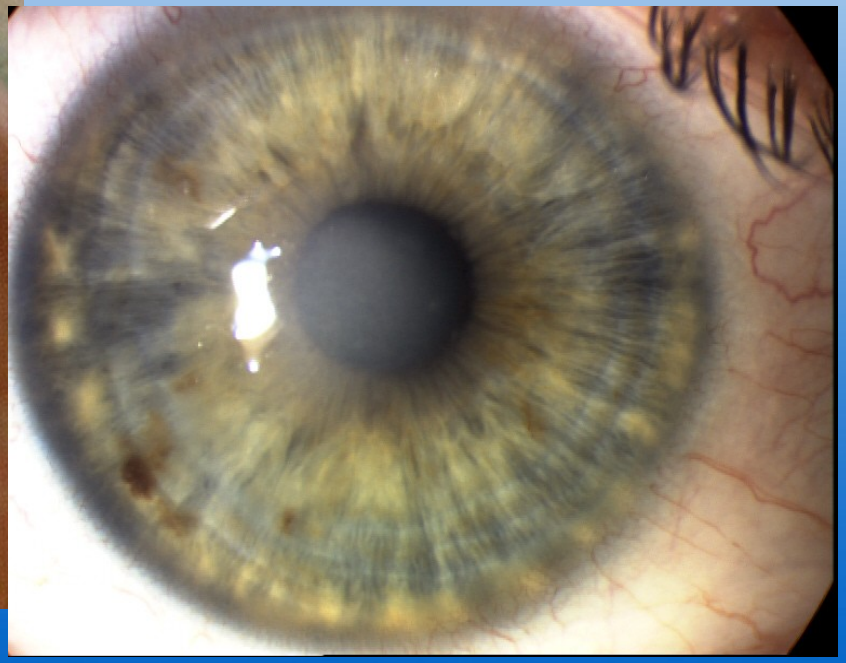
2. Esteziometry (cotton buds, estesiometr):

= testing of the sensitivity of the cornea

Special examination methods

Photodocumentation



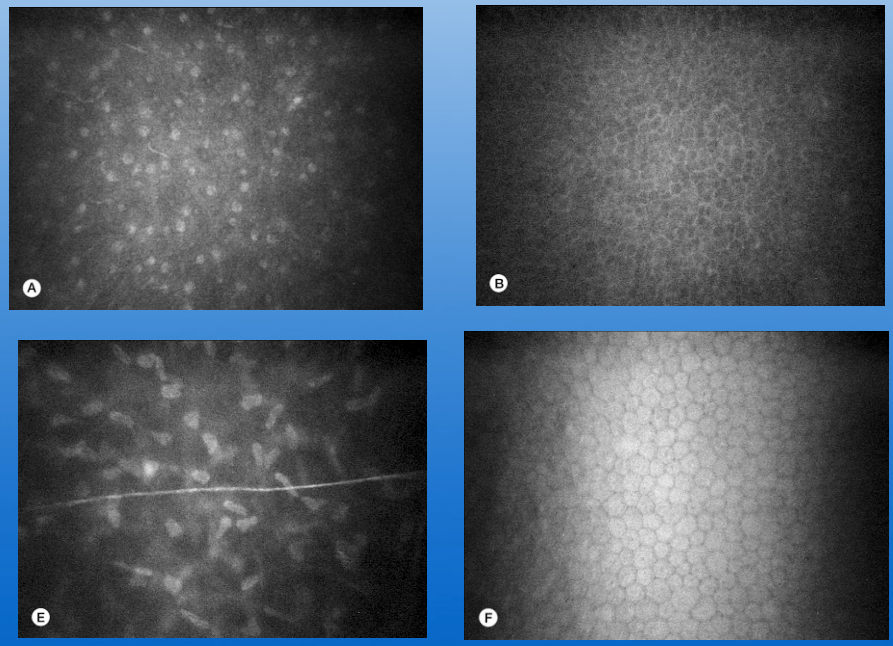


Special examination methods

Confocal microscopy

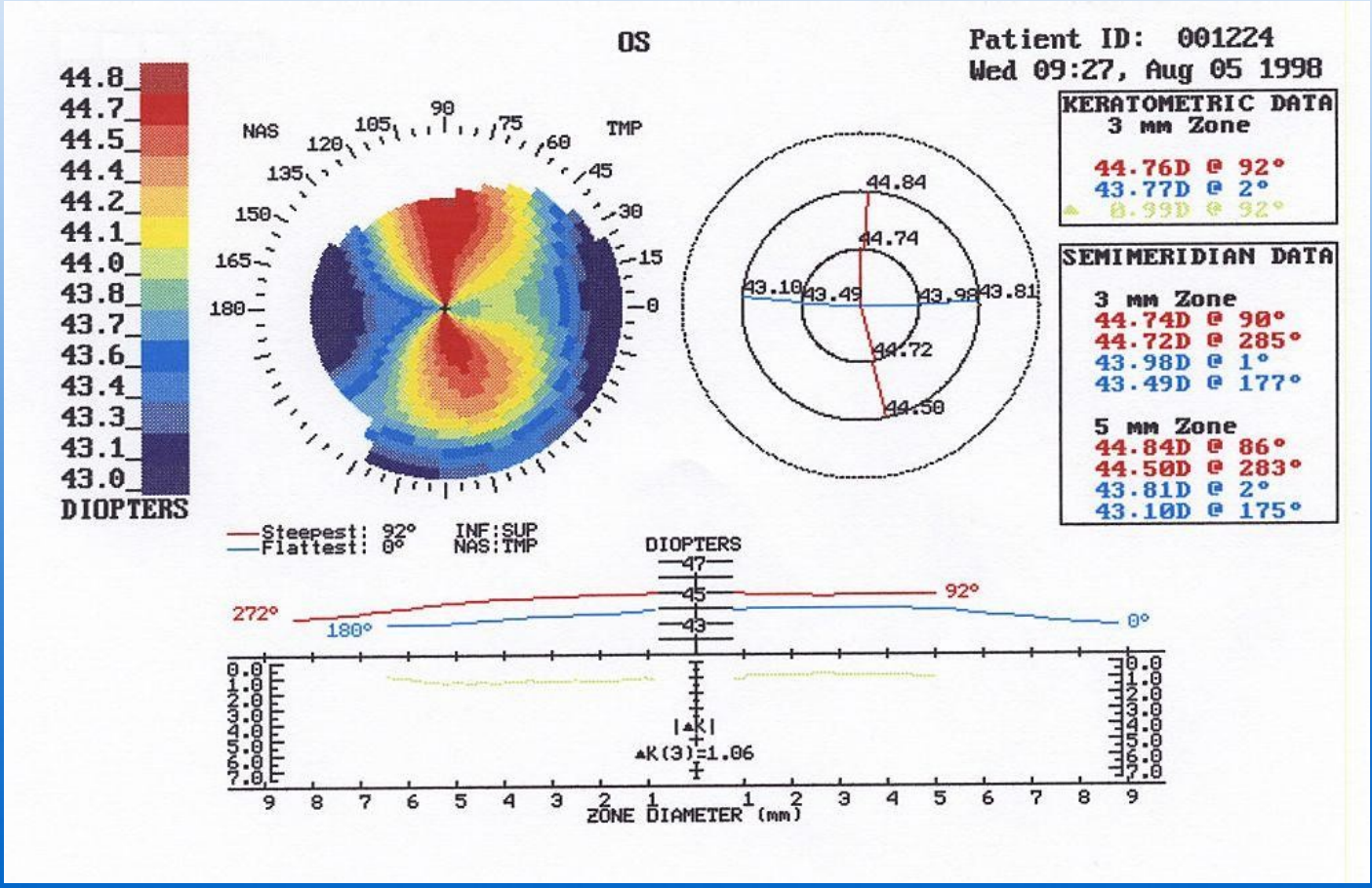
in vivo „histology" examnation

Non invasive, non contact



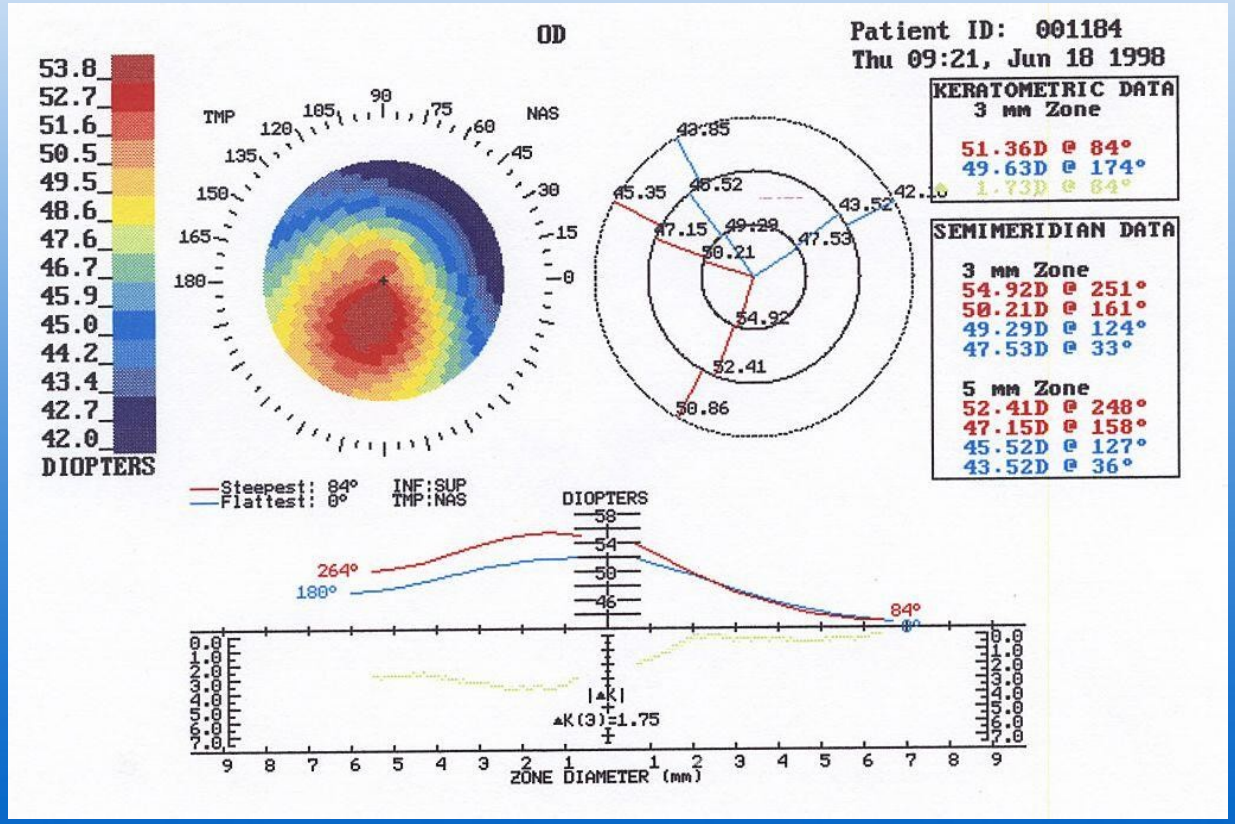
Special examination methods

Corneal topography



Special examination methods

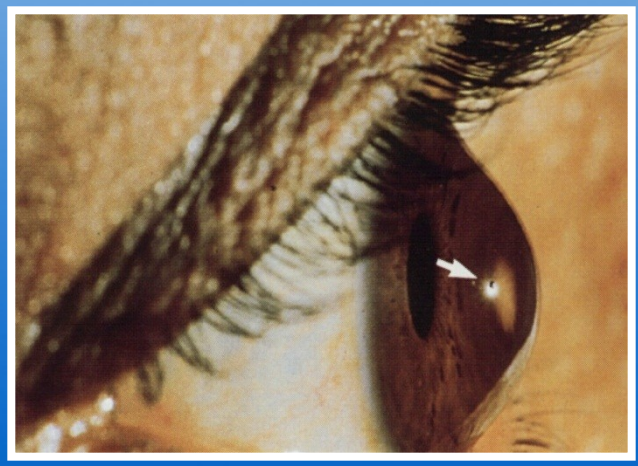
Corneal topography



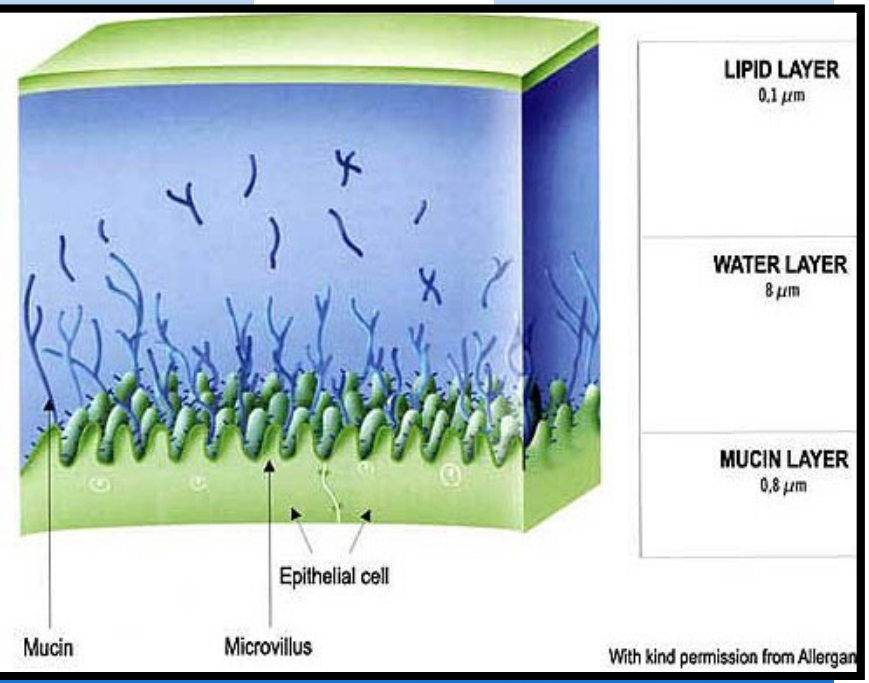
Keratoconus

flat curvature = blue

steep = red



First refractive layer
tear film



Lipid (outer layer) which is secreted by the meibomian glands

Functions: retarded evaporisation of the aqueus layer.

Assist in the vertical stability of the tear film

Aqueous (middle layer) is secreted by lacrimal glands

To supply atmospheric oxygen to the avascular corneal epithelium

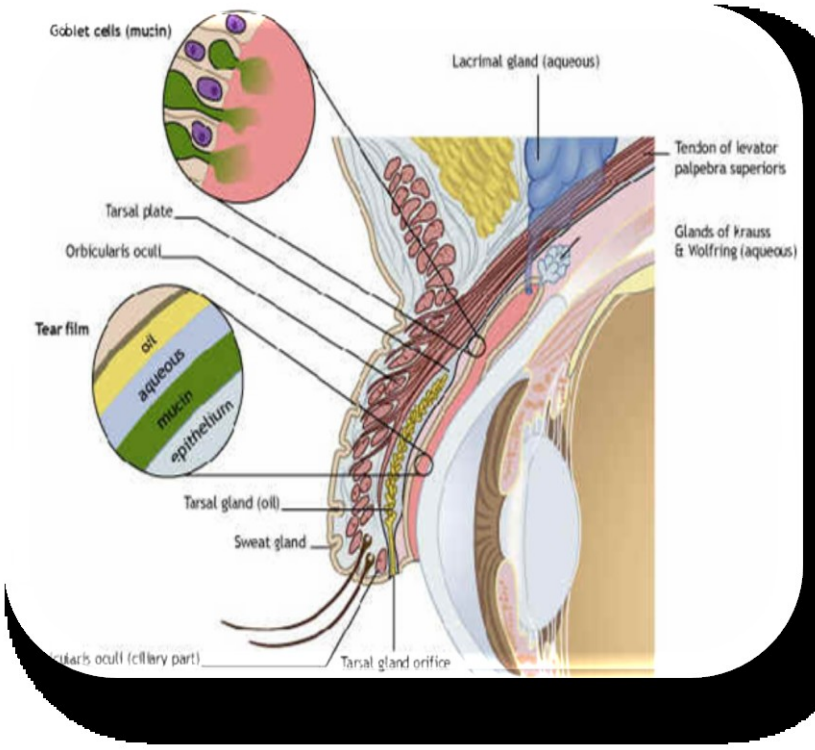
To wash away debris

Mucin (inner layer) is secreted by conjunctival globet cells

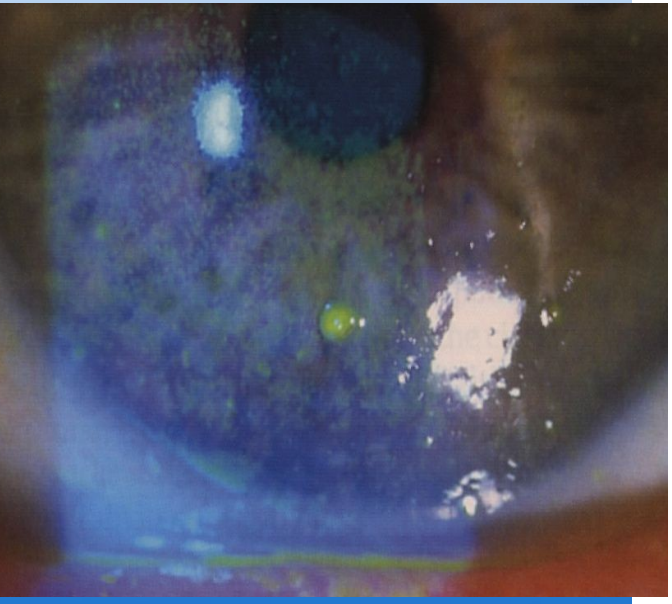
Converts hydophobic to a hydrophyllic surface

Tear film

- Lipid layer: thinnest accesory conjunctival glandulas
- Water middle layer: thickenest 95% from glandula lacrimalis and 5% Krause and Wolfring gll., lactoferin, immunoglobulins, lysozym, albumin.
- Mucin inner layer: goblet conjunctival cells - mucin



Tear film disorders

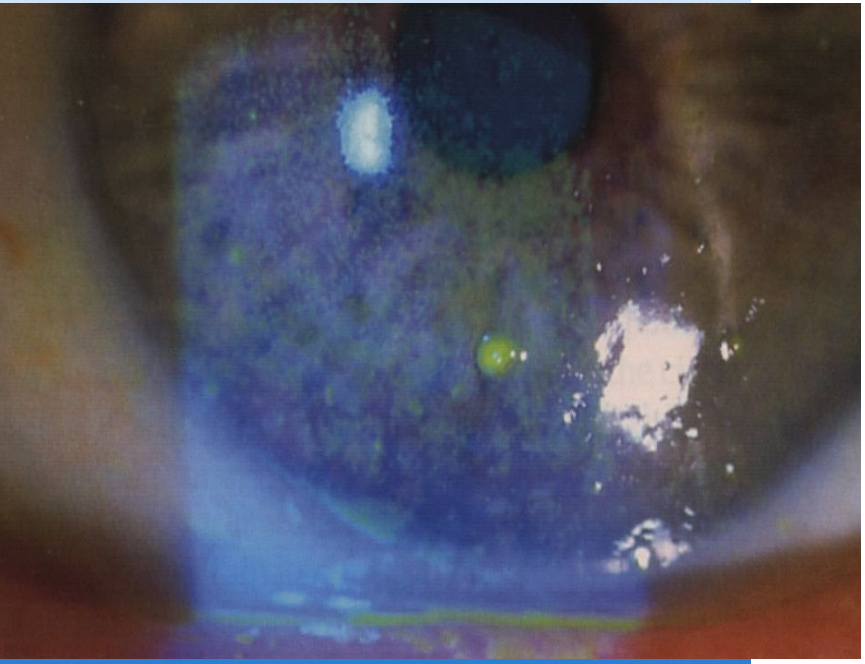


DRY EYE DISEASE

Can occur form conditions such as:

- Aging
- Dehydratation
- Corneal ulcers
- Vitamin A deficiency
- Sjogren syndrome
- Sekundary tearing deficiency (associated with disorders as lymphoma, leukemia, RA..)

Tear film disorders

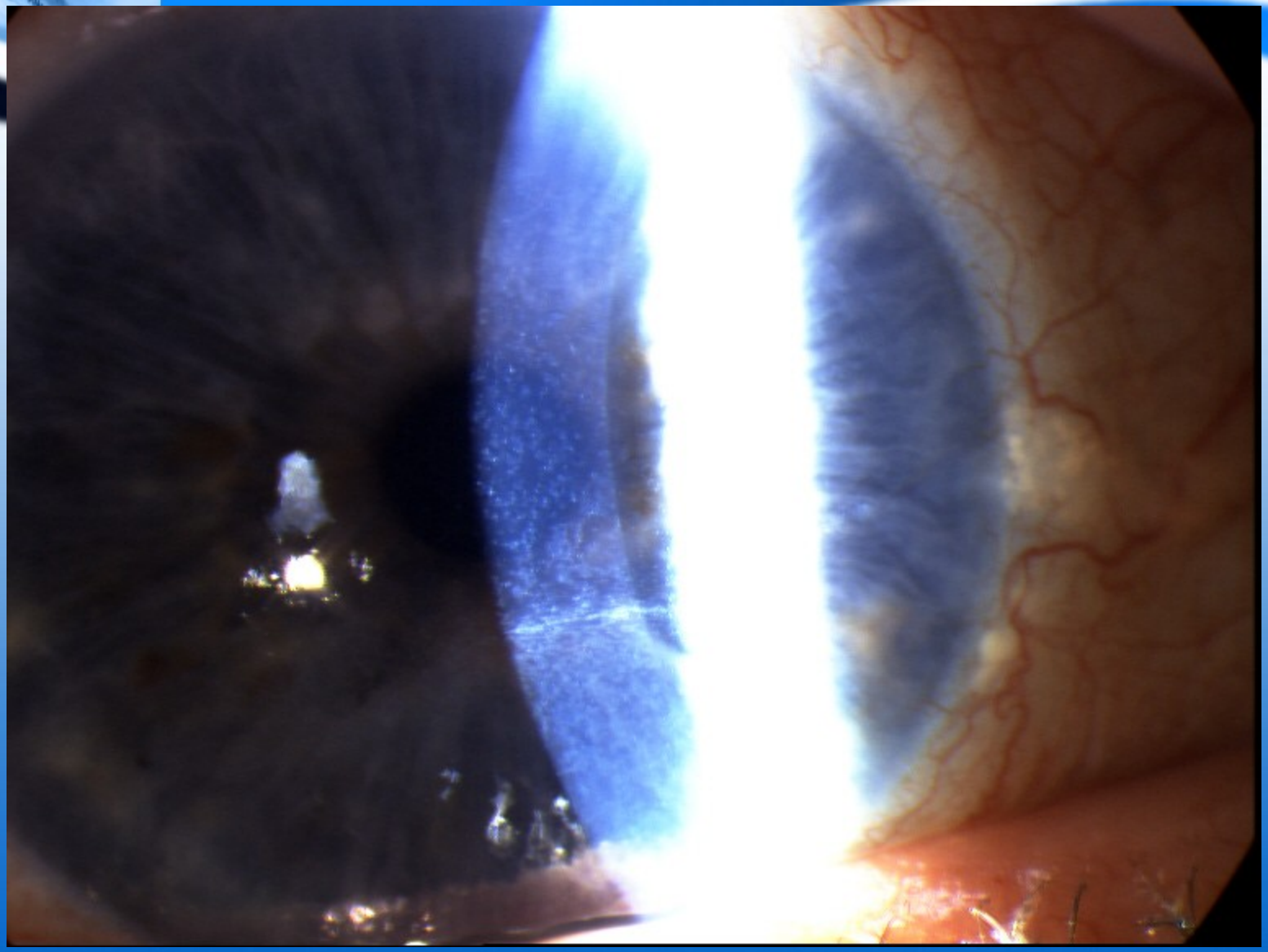


- Corneal epitelopathy
- Mucous plaques – white to grey elevated lesions of various size – makes corneal filaments which stain with fluorescein

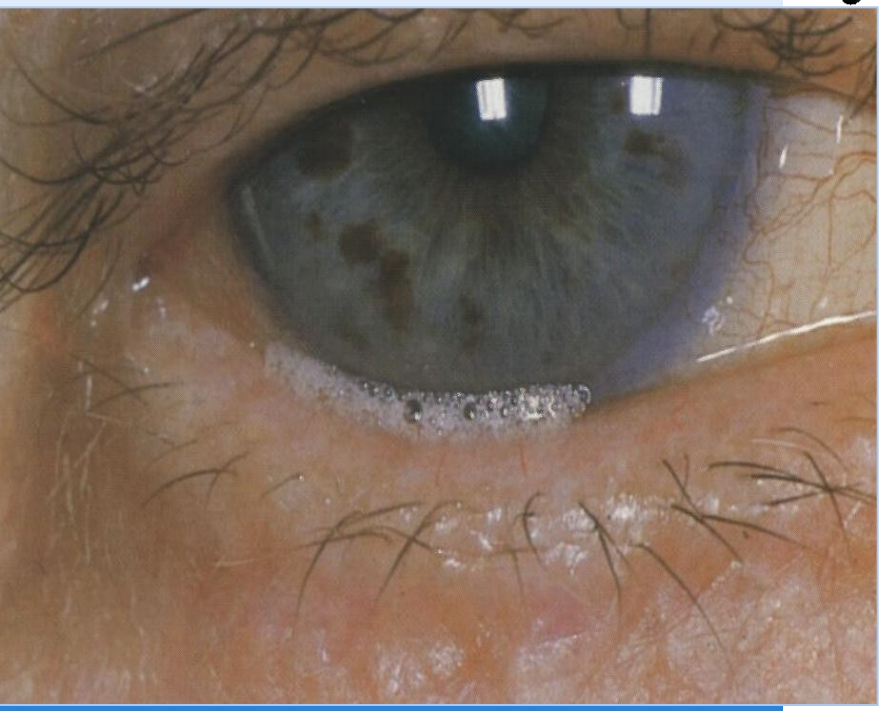
Therapy – tear substitutes (arteficial tears)

Punctate epithelial erosions (PEE) are evidence of ocular surface dryness. They represent areas of epithelial cell loss and therefore stain

Superficial punctate keratopathy



Meibomian glands abnormality



- Foam on the margin of the lid

Therapy: arteficial tears

Temporary punctal occlusion

Permanent punctal occlusison

Cornea

- **What are symptoms of cornea problems?**
- **Pain**
- **Blurred vision**
- **Tearing**
- **Redness**
- **Extreme sensitivity to light – fotofobia**
- **….**
- **What conditions can damage the cornea?**
- **Infections, degenerations, injuries…**

Cornea

- **The most common corneal disorders are the following:**
- **Corneal abrasion**
- **Corneal dystrophy**
- **Corneal ulcer**
- **Corneal neovascularisation**
- **Keratitis**
- **Keratoconus**

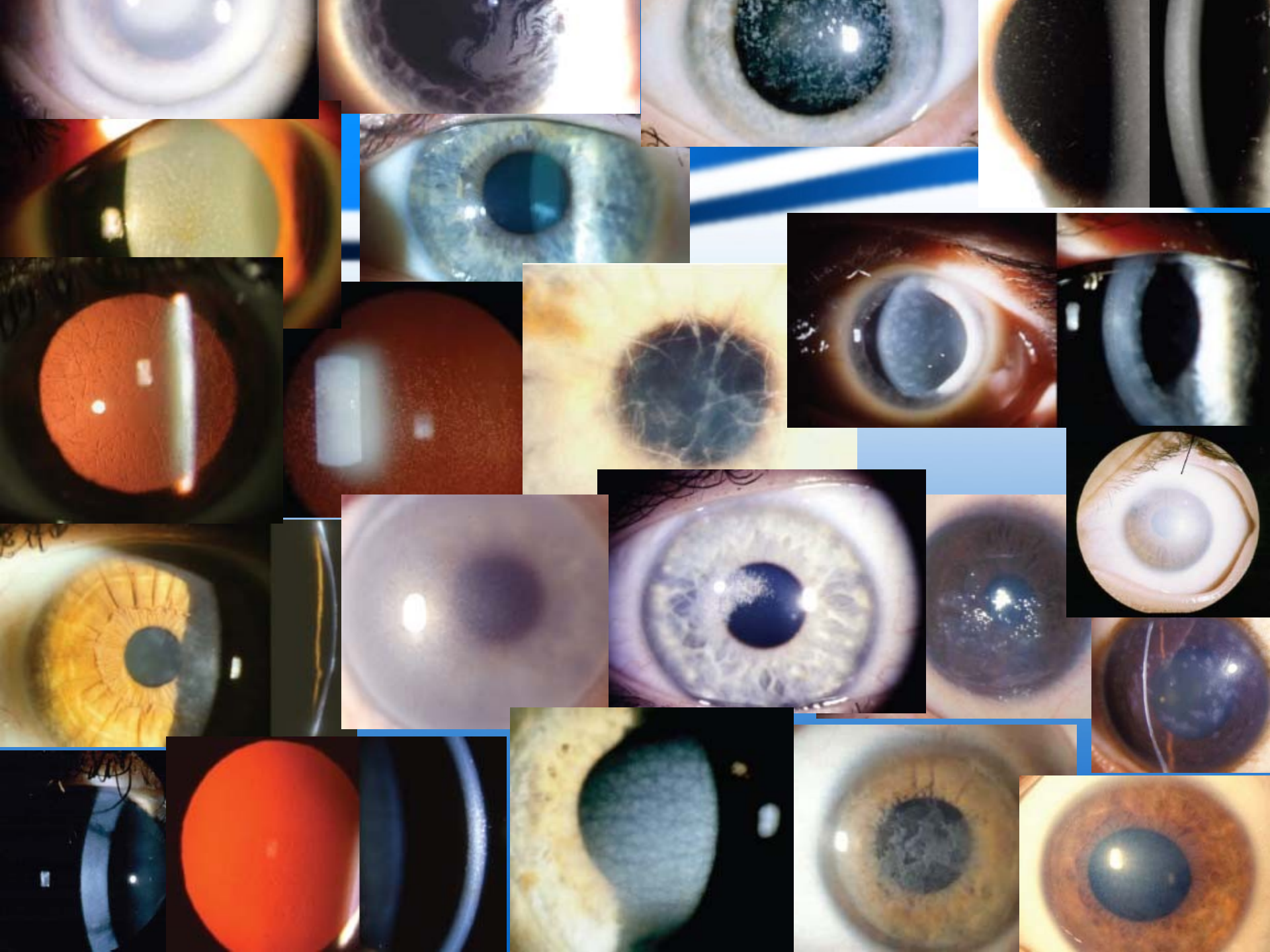
Corneal dystrophies - classification

- Hereditary disorders that progresivelly affect the central part of both corneas & are not associated with inflammation
- Progressive
- Bilateral opacifying

TABLE 2

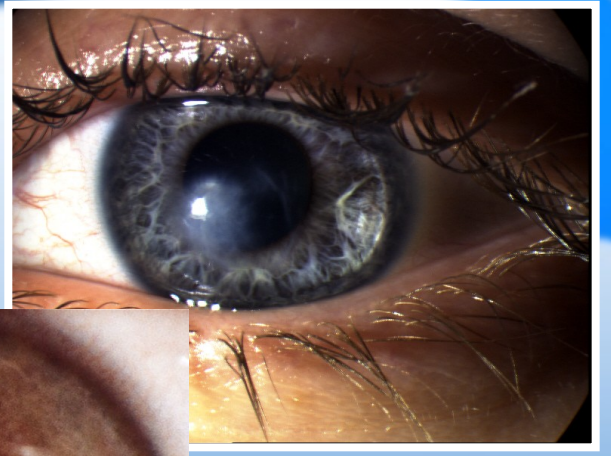
Corneal Dystrophies with Onset, Symptoms, and Signs to Aid in Differentiating and Diagnosis (Weiss et al, 2008)

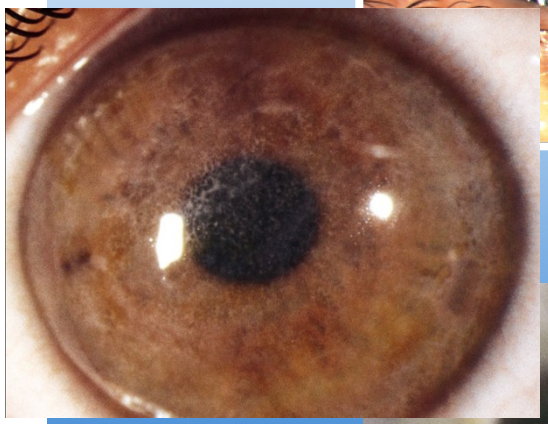
DYSTROPHY	Figure	Onset	Symptoms	Signs
EPITHELIAL AND SUBEITHELIAL				
Epithelial basement membrane dystrophy (EBMD)	1	Adult	Corneal erosions, mild visual reduction	Areas of thickened epithelium, round or oval opacities, lines
Epithelial recurrent erosion dystrophy (ERED)	2	1st decade of life	Painful erosions, burning, redness, photophobia	None, other than when erosions are present
Subepithelial mucinous corneal dystrophy (SMCD)	3	1st decade of life	Painful recurrent erosions	Bilateral subepithelial opacities and haze
Meesmann's corneal dystrophy (Stocker-Holt Variant)	4	Early childhood	Mild corneal erosions, some visual reduction	
Symptoms more severe in Stocker-Holt variant				
Lisch epithelial corneal dystrophy	5	Childhood	Asymptomatic or blurred vision if visual axis is affected	Localized gray opacities in various shapes: whorls, bands, flames, or feather shaped
Gelatinous drop-like corneal dystrophy	6	1st to 2nd decade	Decreased vision, photophobia, irritation, redness, tearing	Subepithelial lesions in bands or clusters that exhibit late staining, superficial vascularization is common
BOWMAN'S LAYER DYSTROPHIES				
Reis-Buckler's corneal dystrophy	7	Childhood	Visual impairment, painful recurrent erosions	Confluent irregular opacities at the level of Bowman's membrane and superficial stroma
Thiel-Benke corneal dystrophy	8	Childhood	Painful recurrent erosions with gradual visual impairment	Subepithelial reticular (honeycomb) opacities mainly in the central cornea. Can progress fully into stroma
Grayson – Wilbrandt corneal dystrophy	—	1st to 2nd decade	Mild visual reduction and mild recurrent erosions	Diffuse mottling / grayish opacities at Bowman's membrane that extend anteriorly into epithelium. Stroma may have refractile opacities
STROMAL DYSTROPHIES				
Lattice type 1 corneal dystrophy Lattice type 2 (less severe, later onset, (+) systemic signs)	9, 10	1st decade	Discomfort, pain, and visual impairment, recurrent erosions	Thin, branching, refractile lines and/or subepithelial dots at onset, ground glass haze develops later
Granular corneal dystrophy types 1 and 2	11, 12	Childhood	Glare, photophobia, recurrent erosions possible	Well-defined white opacities that appear as confluent granules. Type 2 can add snowflakes and lattice lines between granules
Macular corneal dystrophy	13	Childhood	Severe visual reduction, photophobia, painful recurrent erosions possible	Limbus-to-limbus stromal haze initially, later superficial, central, elevated white opacities
Schnyder corneal dystrophy	14, 15	Childhood to 3rd decade	Visual acuity decreases with age, glare increases	Initial signs include central haze and subepithelial crystals (up to age 23), Arcus lipoides between age 23 and 38, midperipheral panstromal haze after age 38
Congenital stromal corneal dystrophy	16	Congenital	Moderate to severe vision loss	Diffuse, bilateral corneal clouding with flake-like whitish opacities distributed throughout the cornea. Increased corneal thickness with pachymetry
Fleck corneal dystrophy	17	Congenital	Asymptomatic	Small, translucent, disc-shaped opacities or gray-white flaky opacities with clear stroma in between
Posterior amorphous corneal dystrophy	18	1st decade, possibly congenital	Mild visual reduction	Diffuse gray-white, sheet-like opacities mainly in the posterior stroma. Corneal thinning and flat topography are often present. Many other minor signs possible
Central cloudy dystrophy of Francois	19	1st decade	Mostly asymptomatic	Cloudy central polygonal or rounded stromal opacities

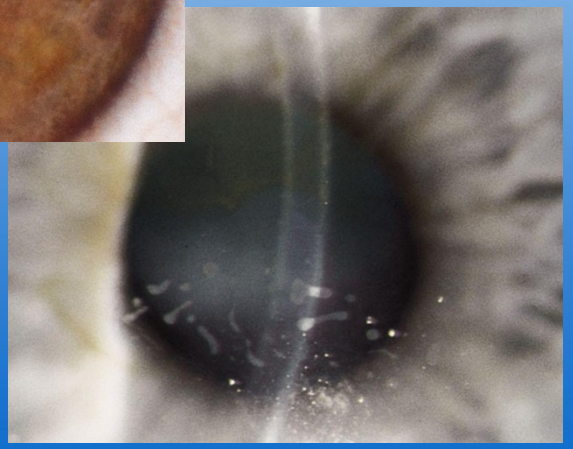


Corneal dystrophies - classification

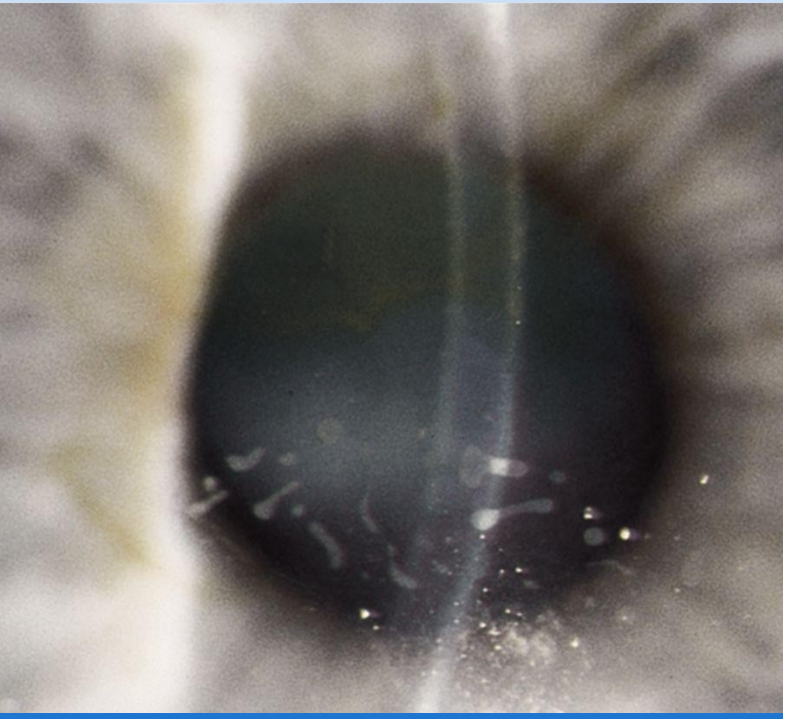
- Anterior dystrophies
  - Cogan´s
  - Reis-Bucklers´
- Stromal dystrophies
  - Latice
  - Macular
  - Granular
- Posterior dystrophies
  - Fuchs´endotelial





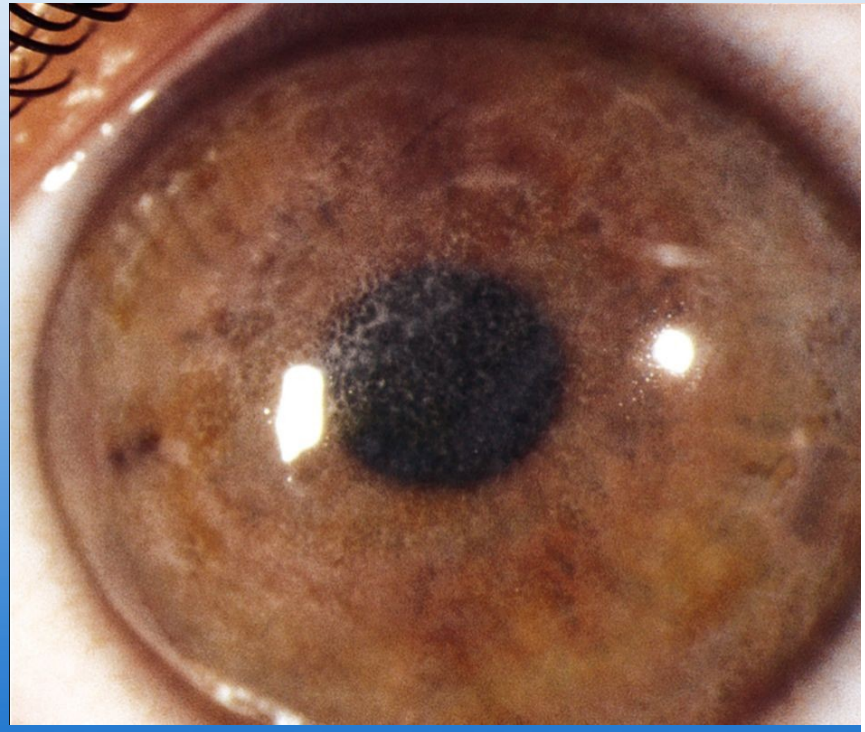


Cogan´s map-dot-fingerprint dystrophy



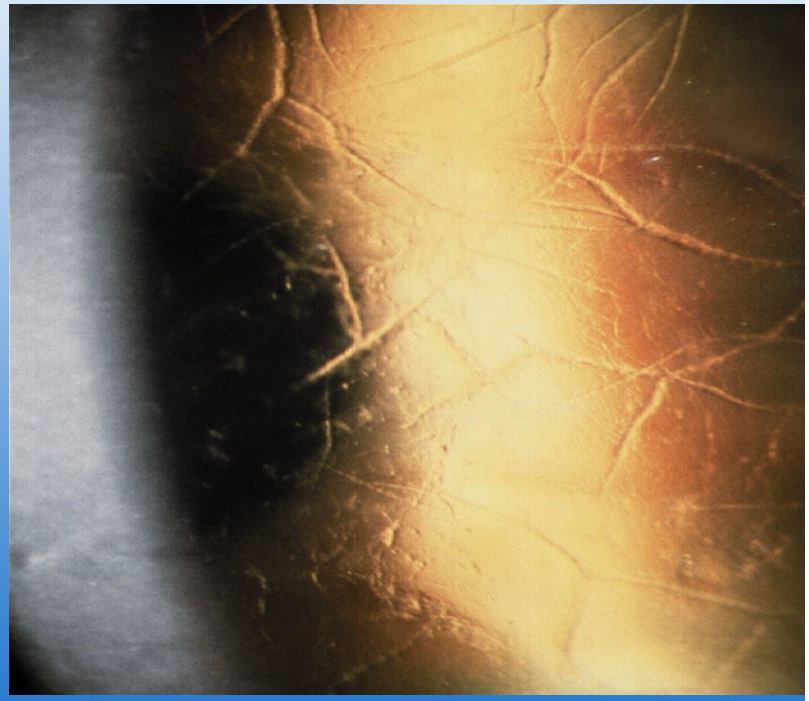
- Most common dystrophy of epitelial basement membrane
- Clinical features:
- recurrent corneal erosiones
- Usually after the age of 30.
- Bilateral microcysts
- Therapy: excimer laser terapeutic fotoablation

Reis-Bücklers´ dystrophy



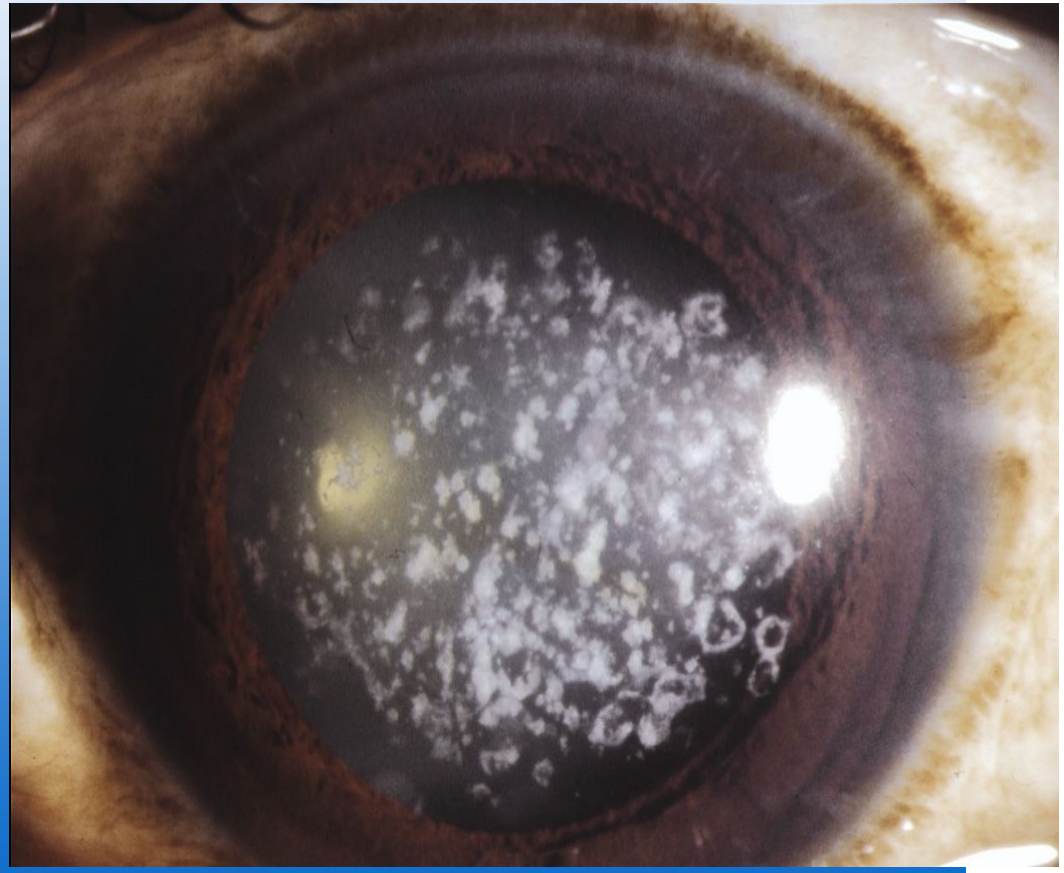
- Inheritance – autosomal dominant
- Progressive dystrophy with symptoms of recurrent corneal erosions
- Corneal sensation is reduced
- Honeycomb appearance

Lattice dystrophy



- Associated with systemic amyloidosis
- Type 1: first decade of life with recurent corneal erosions
- Network of branching spider like deposit of amyloid
- Therapy: Visual acuity is usually good, keratoplasty is rarely needed (anterior lamellar)

Granular dystrophy



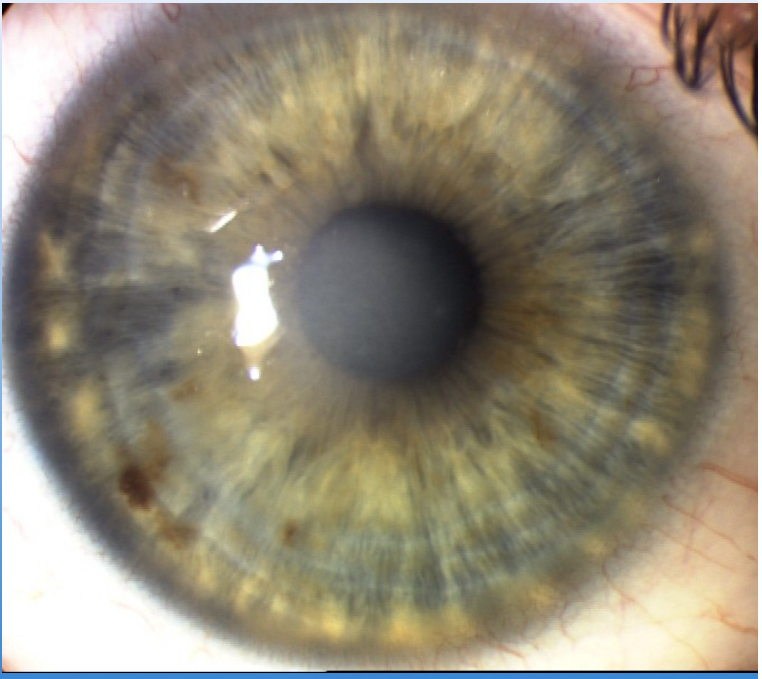
Autosomal dominant condition

„bread crumb“ white deposits in the stroma

Deposits are concentrated centrally and in the anterior stroma

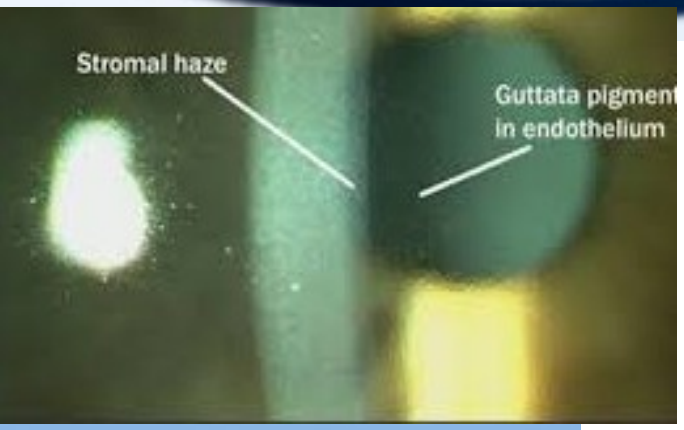
Visual impairment usually begins after the fifth decade of life

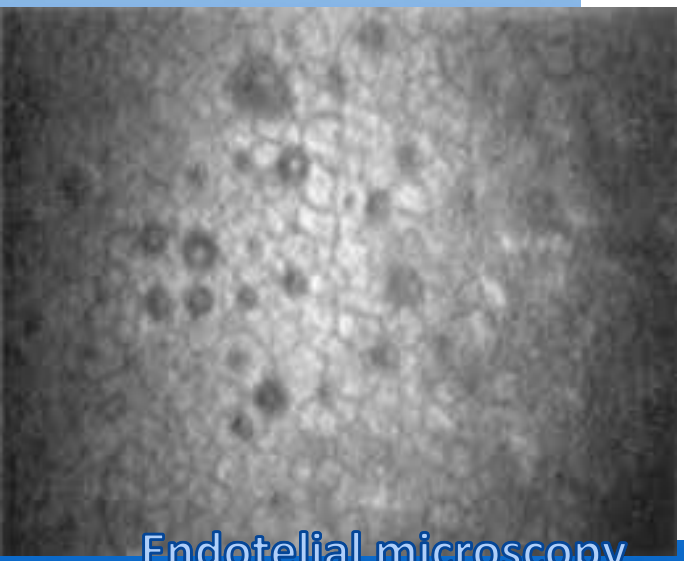
Fuchs´ endotelial dystrophy



- Slowly progressive
- Usually bilateral
- More common for women
- Inheritace autosomal dominant
- Sings: Endotelial protuberances, decompensations of endotelial cells result in oedema in the central stroma. When edema of the stroma increases, Bullous keratopathy develops
- Therapy: Descemet membrane endotelial keratoplasty (DMEK) (Deep posterior lamellar transplantation)

Fuchs´ endotelial dystrophy

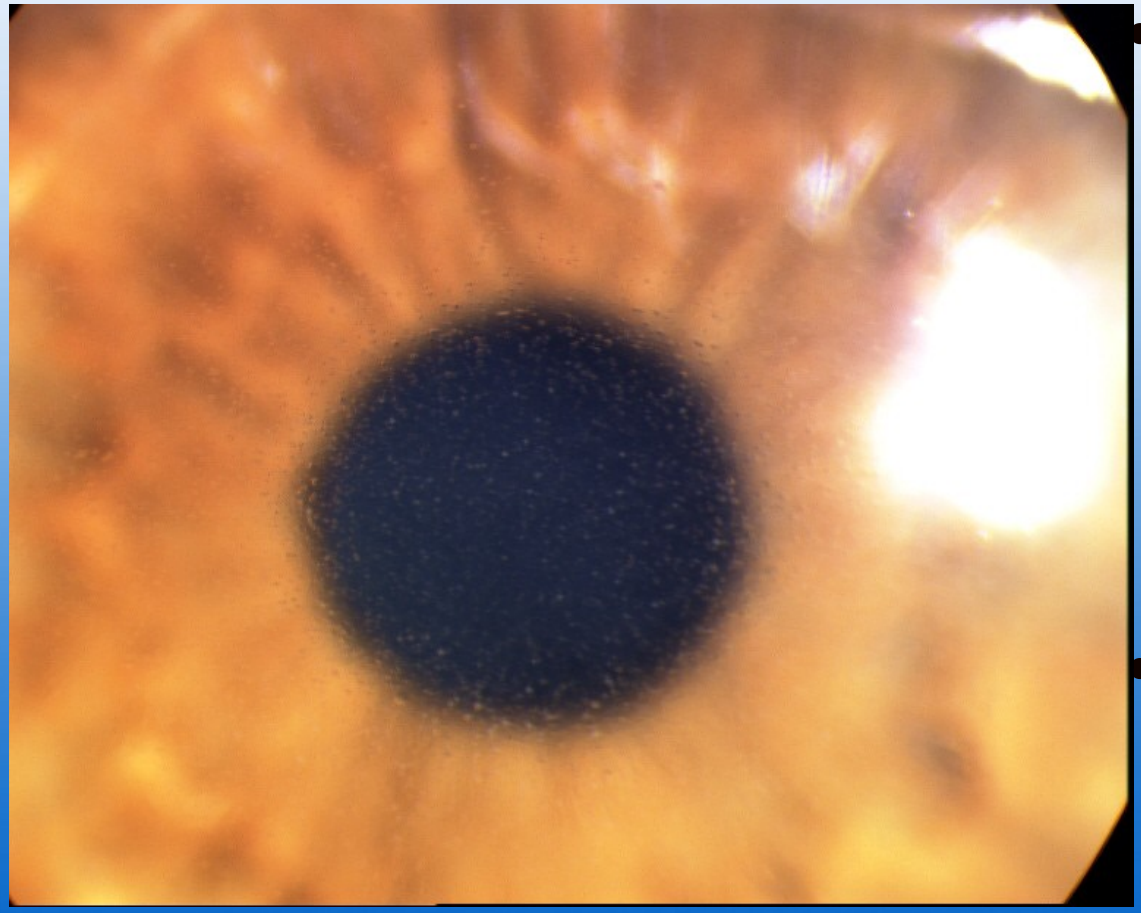




Endotelial microscopy

As a result of irregularities on the inner surface of the cornea, affected individuals may simply notice a reduction in the quality of vision or glare or haloes particularly when driving at night. Individuals with symptomatic Fuchs' dystrophy typically awaken with blurred vision which improves during the day. This occurs because the cornea is normally more swollen in the morning due to nocturnal fluid retention in the absence of normal evaporation due to the lids being closed. During waking hours this fluid evaporates once the eyes are open

Fuchs´ endotelial dystrophy



- Confluent guttata and thickening of Descemet°s membrane produce **a beaten metal appearance**
- Cornea guttata (are seen with red reflex)

Corneal ectasias

KERATOCONUS:

progressive, the cornea assume the cone shape

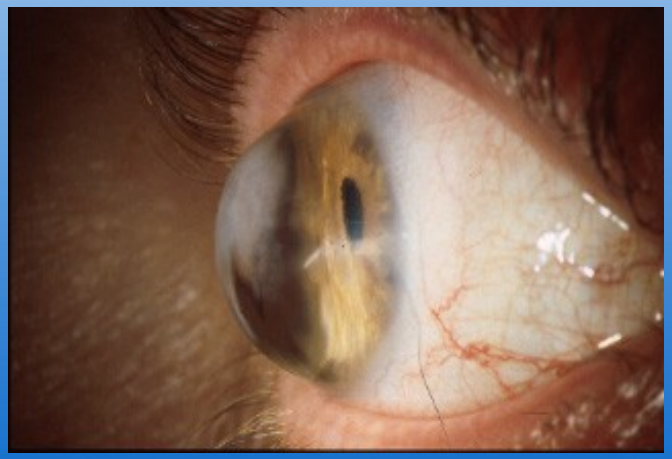
Treatment: rigid contact lenses, CLX, intrastromal ring, lamellar and penetrating keratoplasty

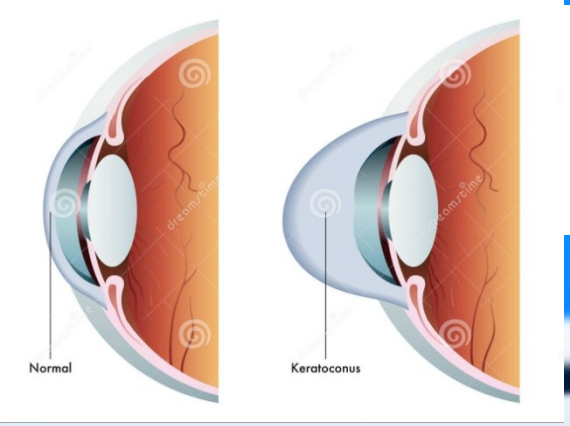
KERAGLOBUS:

the thinning of entire cornea

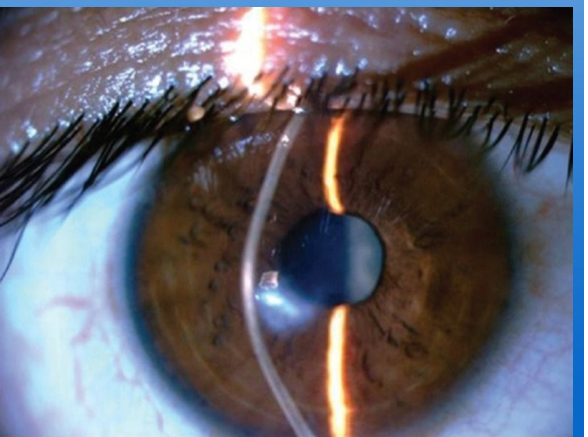
PELLUCID MARGINAL DEGENERATION:

thinning in the lower periphery of the cornea, perforation sometimes occurs



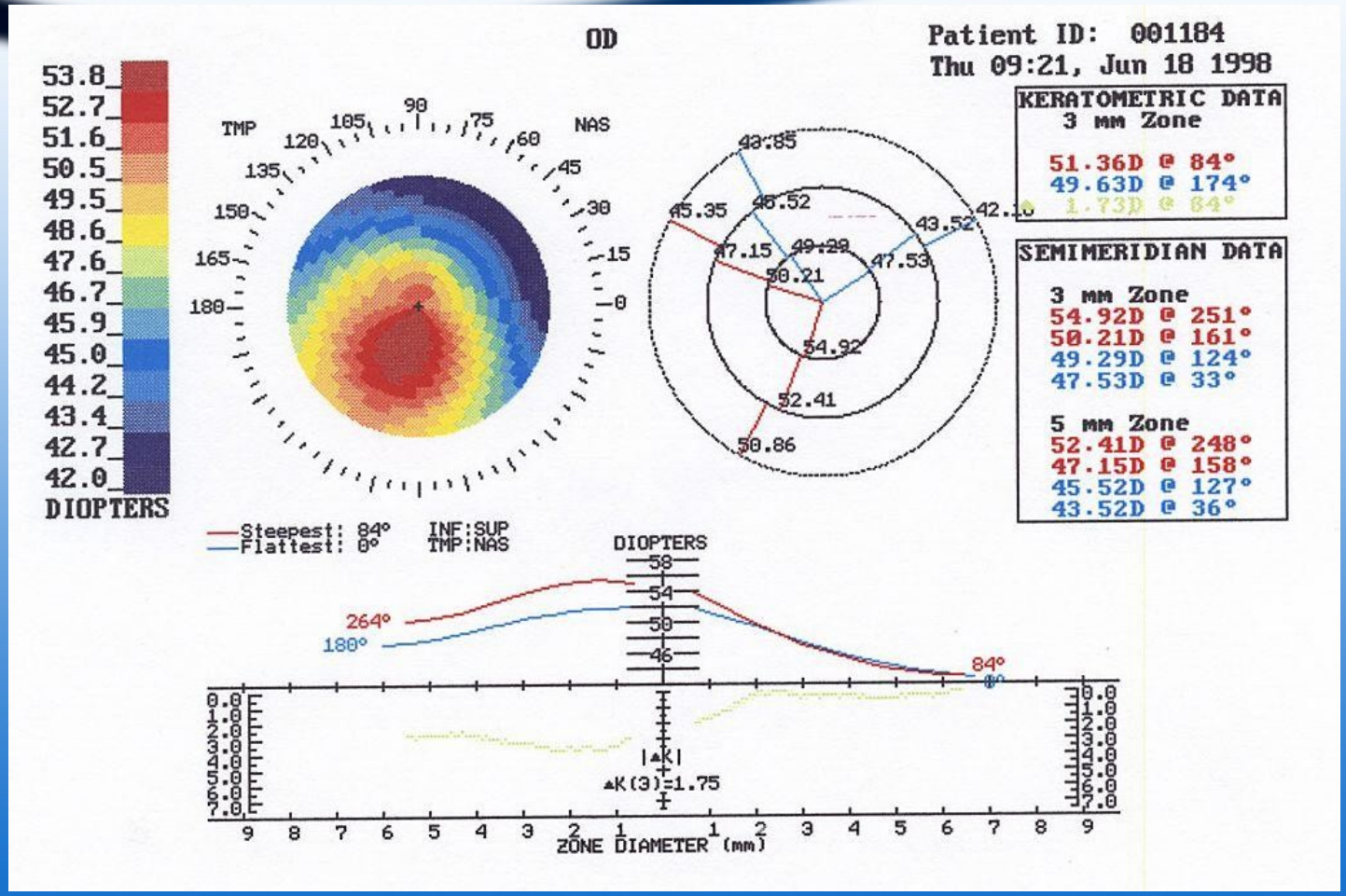


Keratoconus

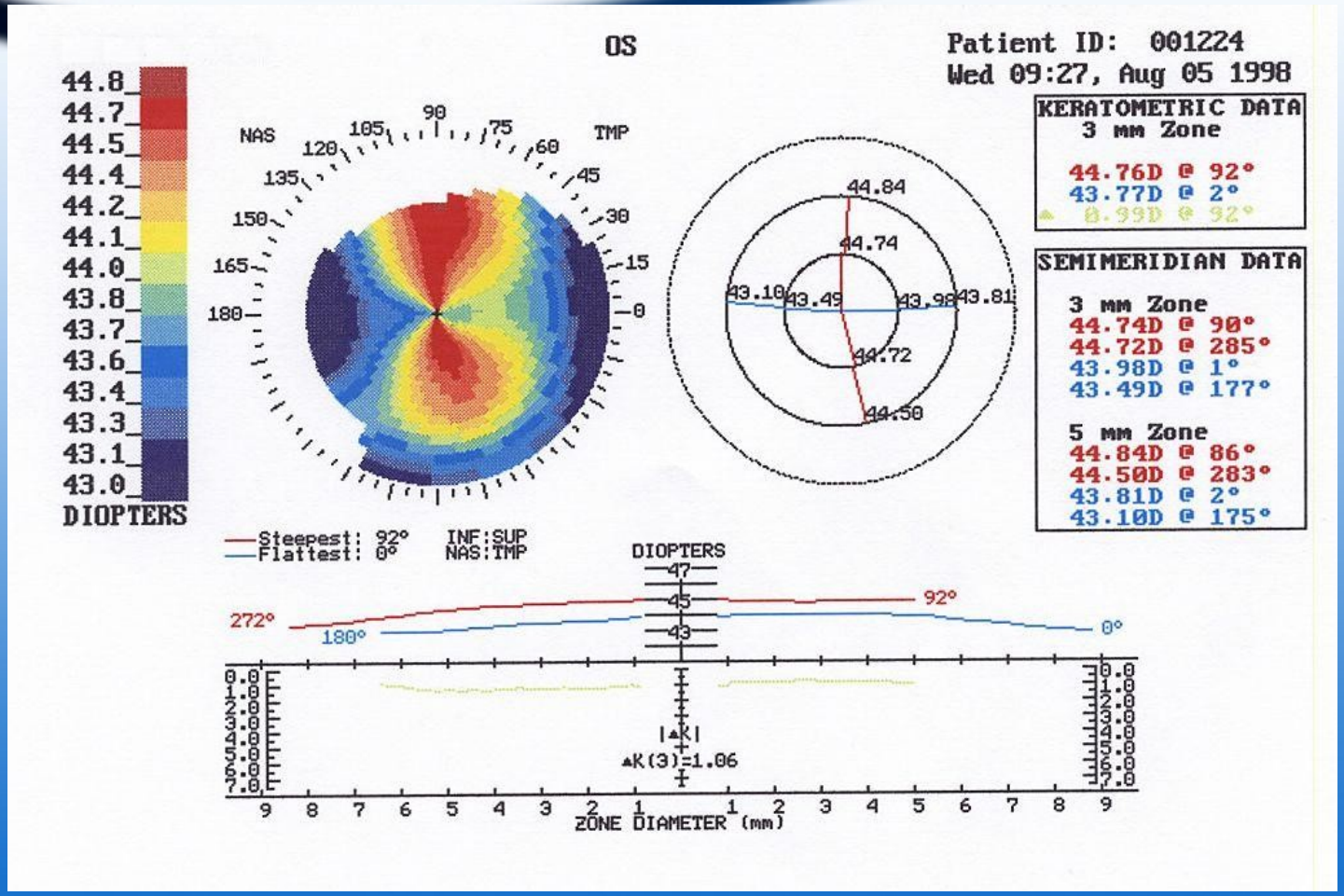


- Conical cornea
Progressive disorder
Central or paracentral
Irregular astigmatism
Both eyes affected in about 85% of cases
occurs with increased frequency in the following disorders: Down´s syndrome, Marfan´s syndrome, atopy, vernal disease, retinitis pigmentos, aniridia, ectopia lentis

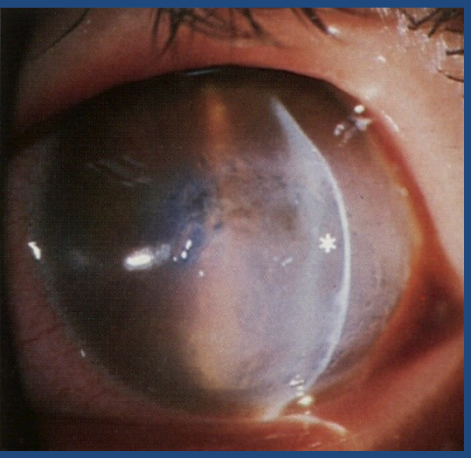
Keratoconus



Fyziological astigmatism

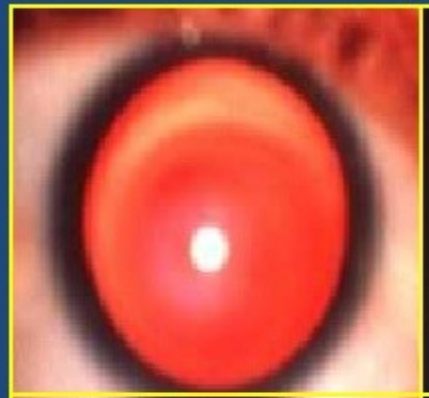


Keratoconus – acutus, subacutus



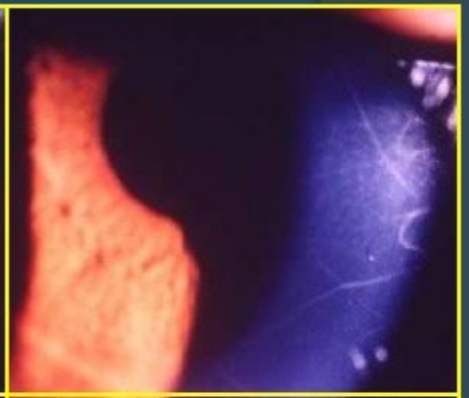
Signs of keratoconus

Bilateral in 85% but asymmetrical



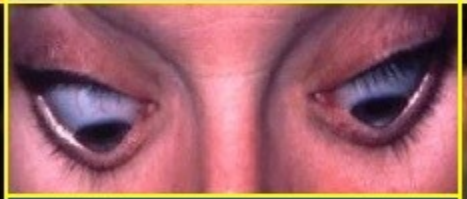
Oil droplet reflex

Vogt striae



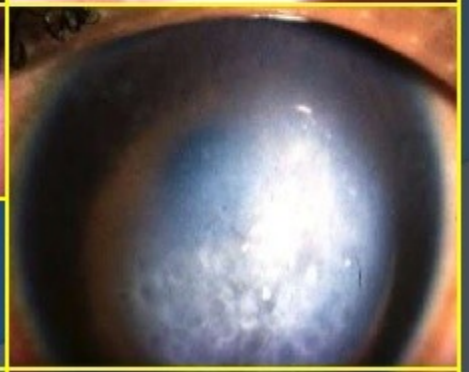
Prominent corneal nerves

Fleischer ring & scarring



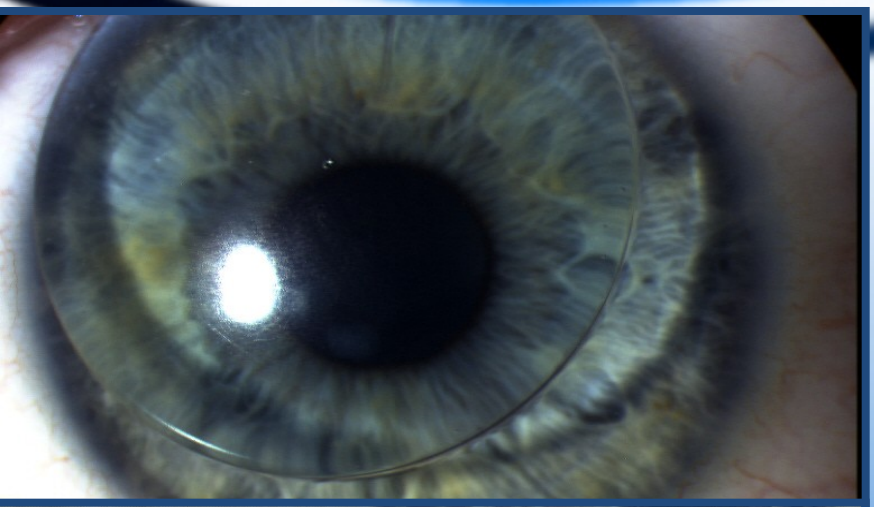
Bulging of lower lids on downgaze

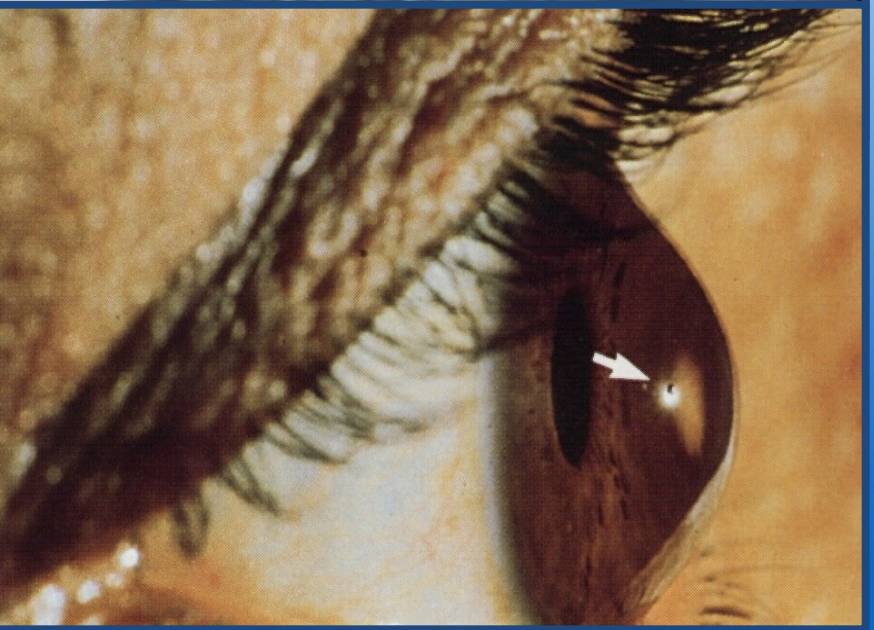
Munson sign



Acute hydrops

Keratoconus incipiens et progrediens

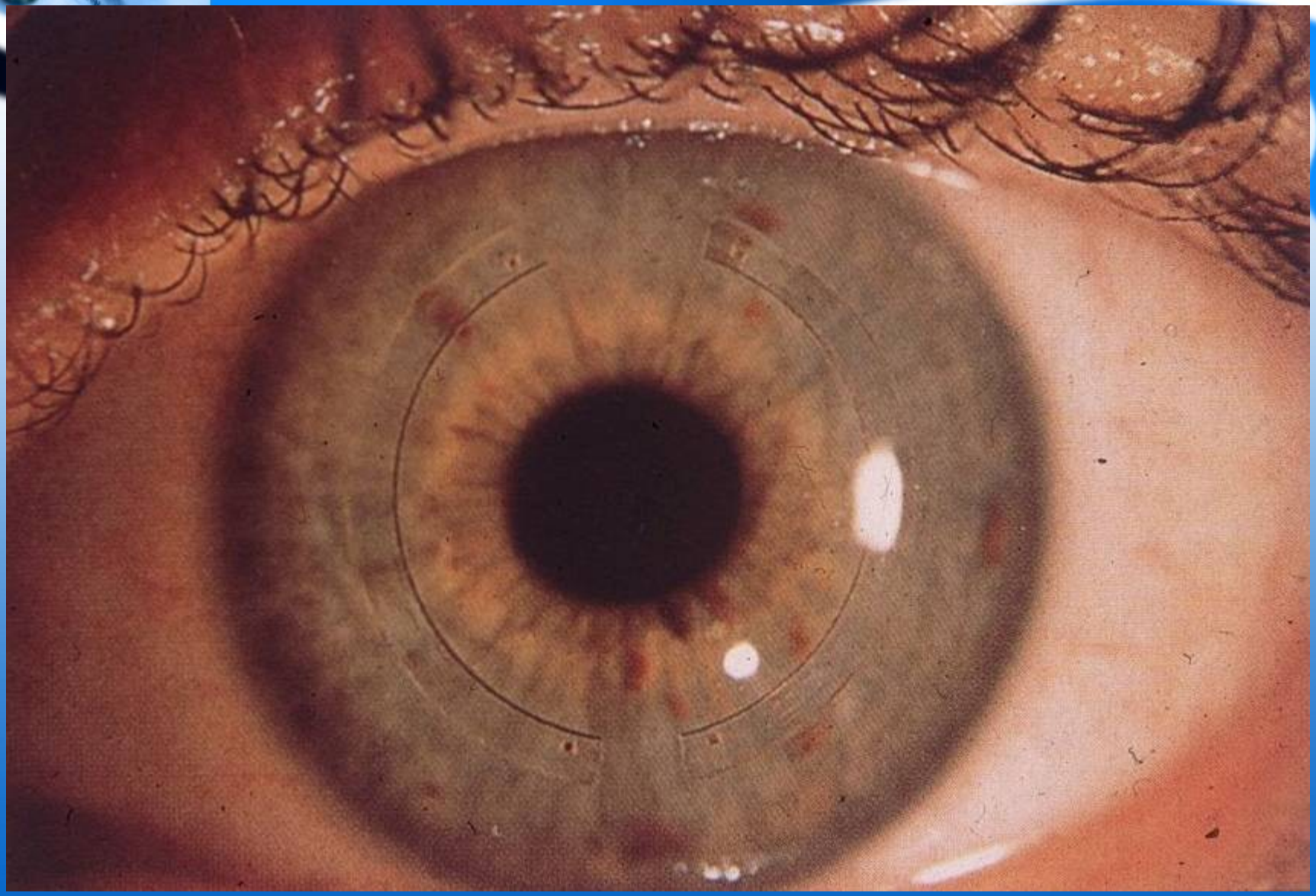




Management

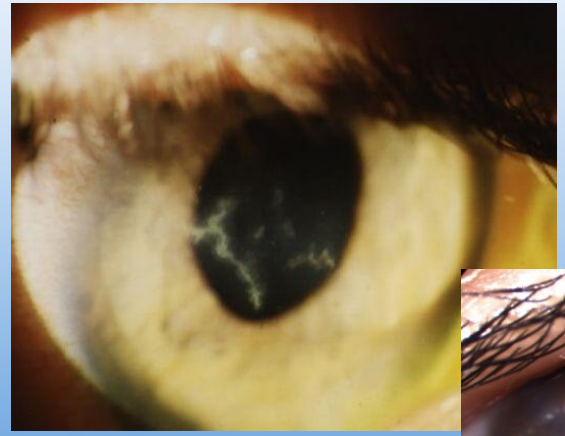
1. Spectacle correction in very early cases can correct regullar astigmatism
2. Contact lenses
3. Intrastromal corneal rings
4. Deep anterior lamellar keratoplasty
5. Penetrating keratoplasty

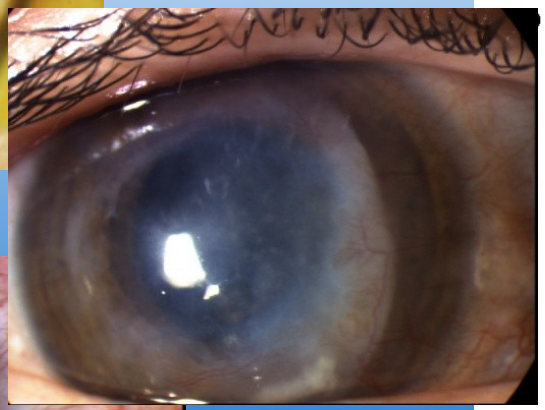
Intrastromal corneal rings

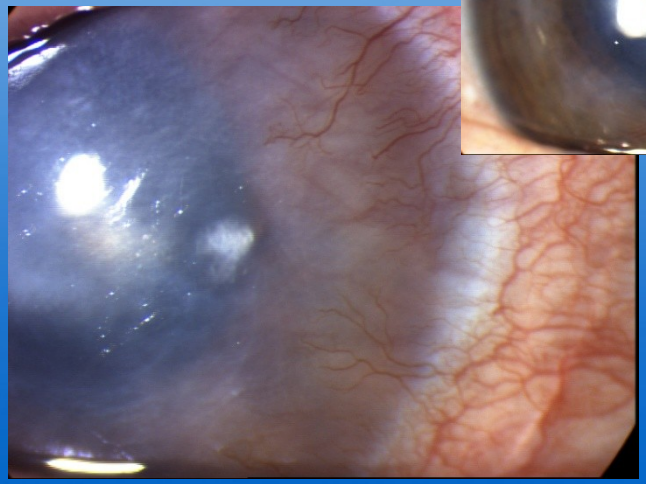


Infections of the cornea

What is the most common infection of the cornea and conjunctiva?



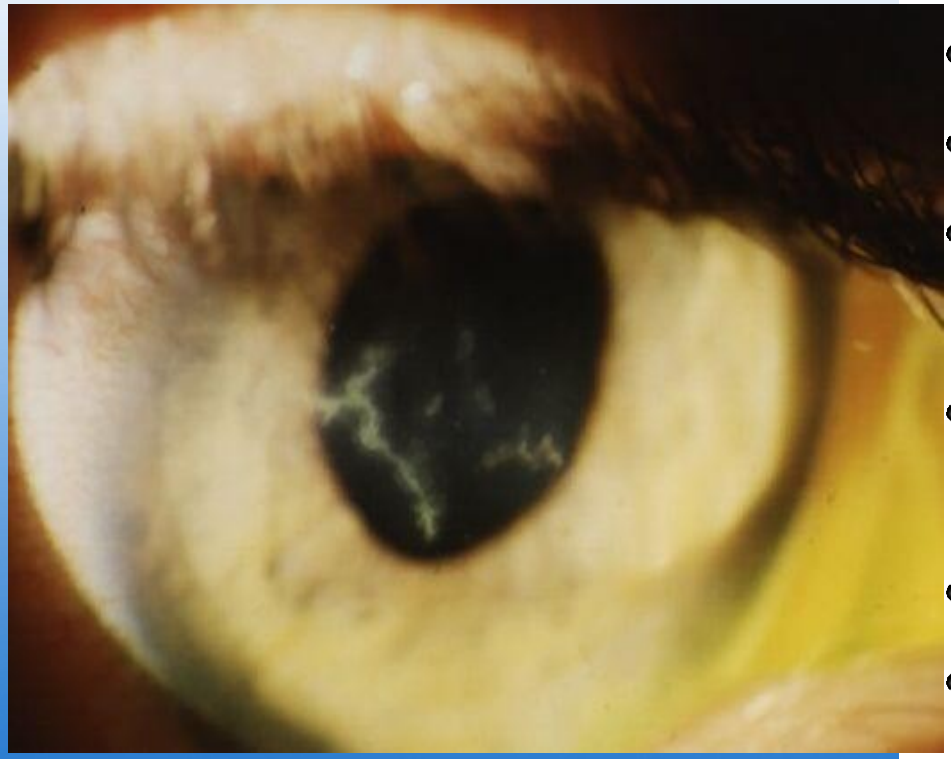




- Viral keratitis
- Bacterial keratitis
- Fungal keratitis
- Acanthamoeba keratitis

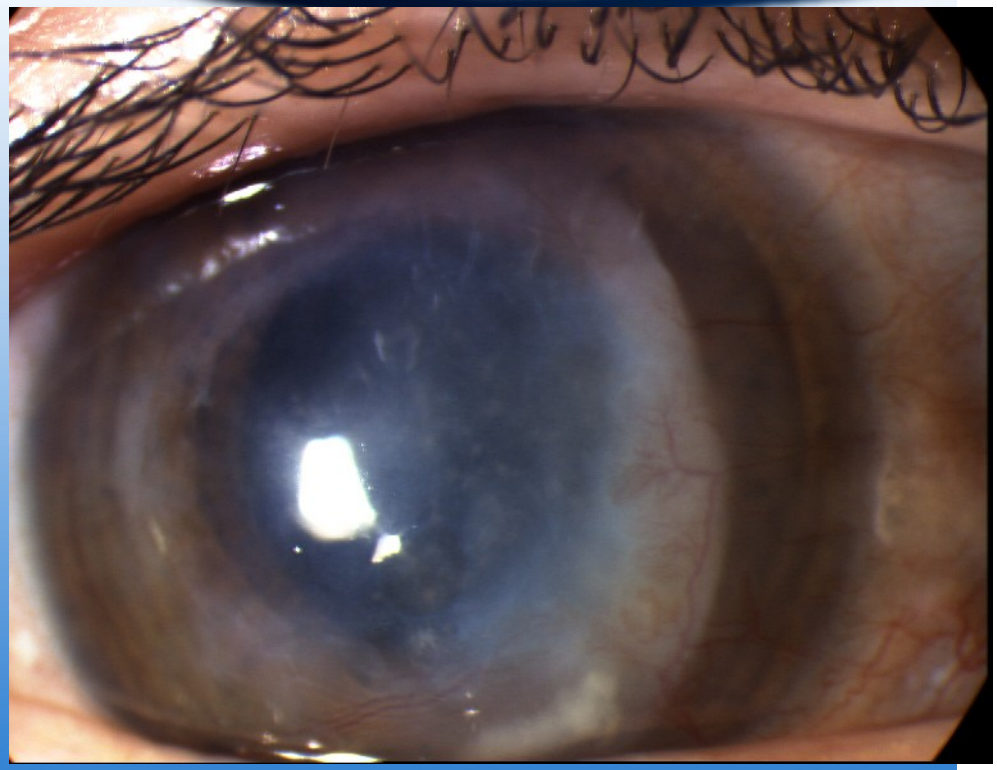
When damage to the cornea occurs, such as in a viral infection, the collagen used to repair the process is not regularly arranged, leading to an opaque patch (leukoma)

Viral keratitis



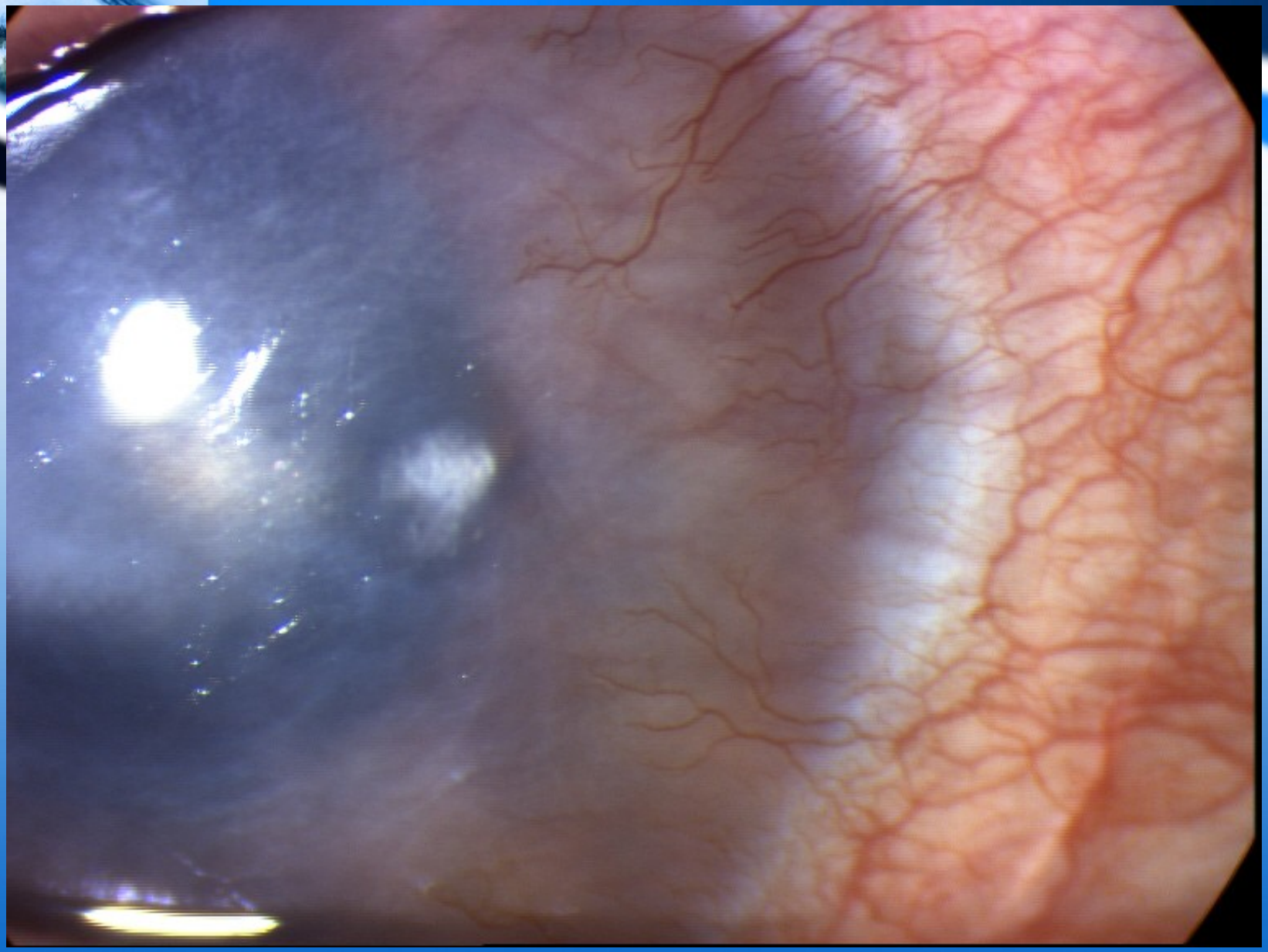
- Herpes simplex virus
- DNA neurotropic virus
- Primary infection
- Between 6 m and 5 years
- Associated with viral illness
- Recurrent infection
- Variety of dendritic shapes
- DIMINISHED CORNEAL SENSITIVITY !

Viral keratitis

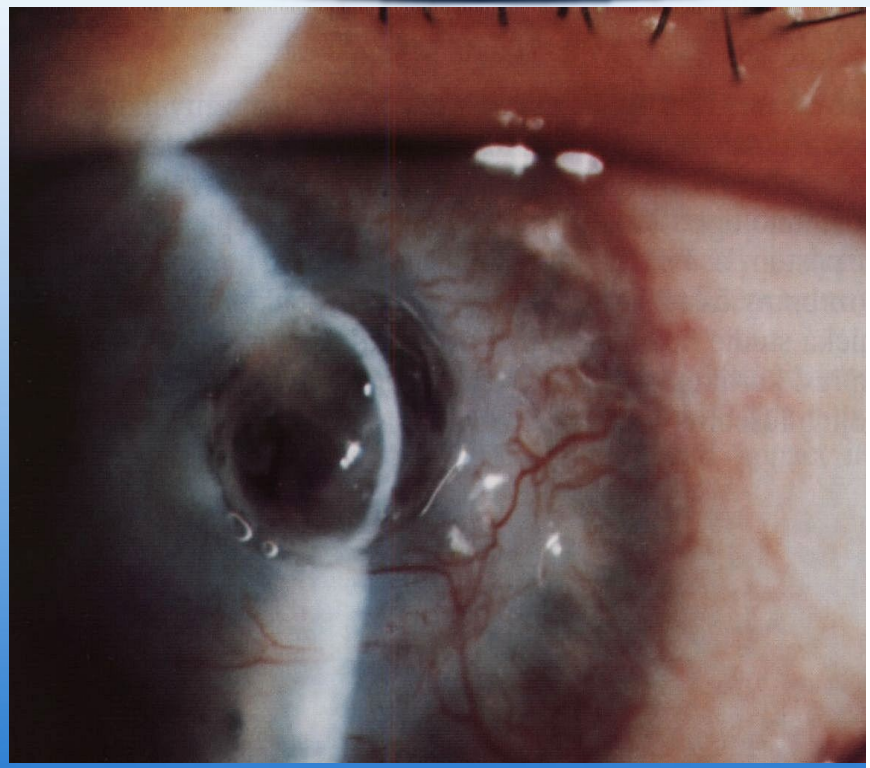


Disciform keratitis

- Aetiology:
- Herpes simplex virus
- Herpes zoster ophthalmicus
- Destruction of stromal nerves
- Viral infection of keratocytes
- Hypersensitivity reaction to viral antigen

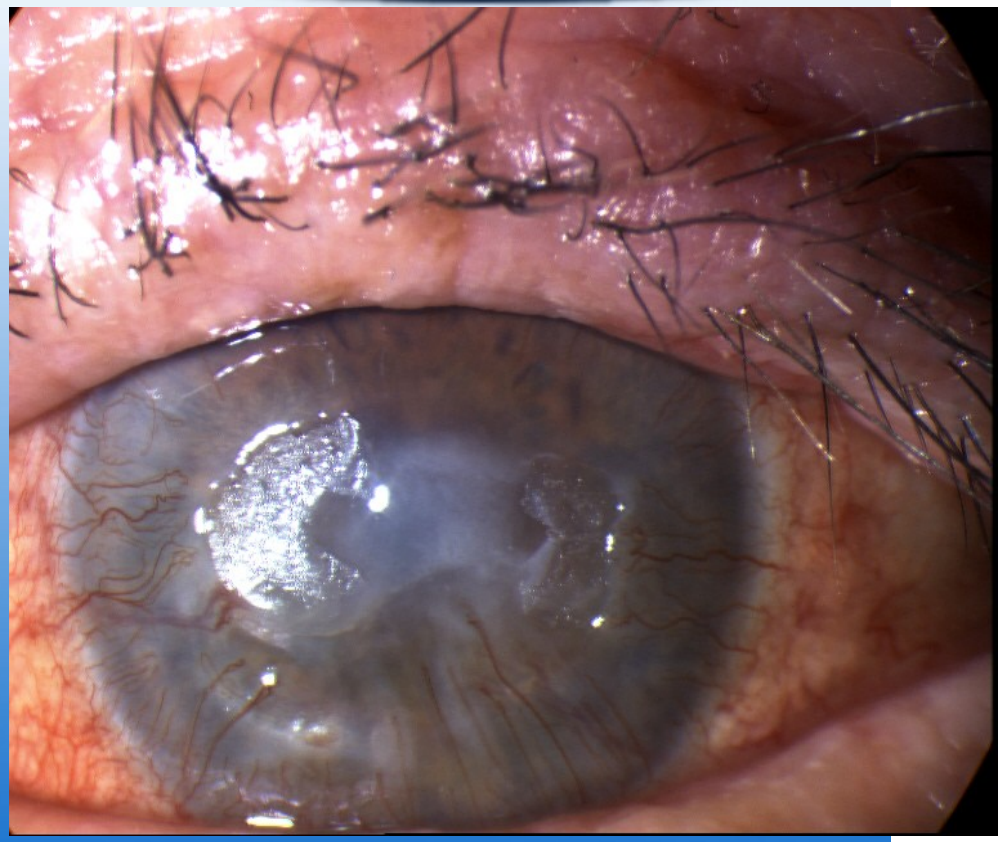


Descemetocele



- Elevation of Descemet´s membrane
- Neurotrophic keratitis
- Imminent perforation
- **Therapy**: Acute keratoplasty - Keratoplasty à chaud

Herpes zoster ophthalmicus



- Human HHV 3
Varicella and zoster are different conditions caused by the same virus
The virus is retained in the dorsal root ganglion
Ocular damage –
direct as the cellular infiltration
Indirect – by denervation and ischemia induced by vasculitis

Bacterial keratitis

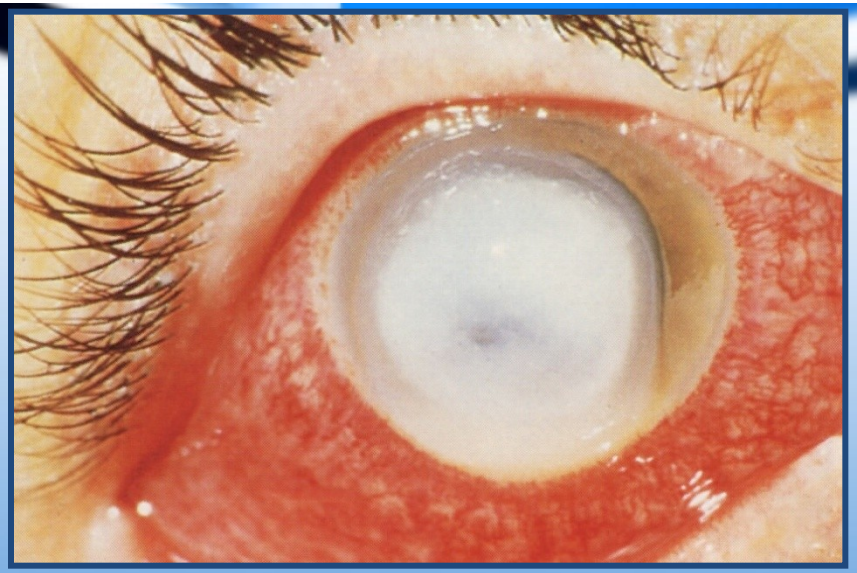
Risk factors:

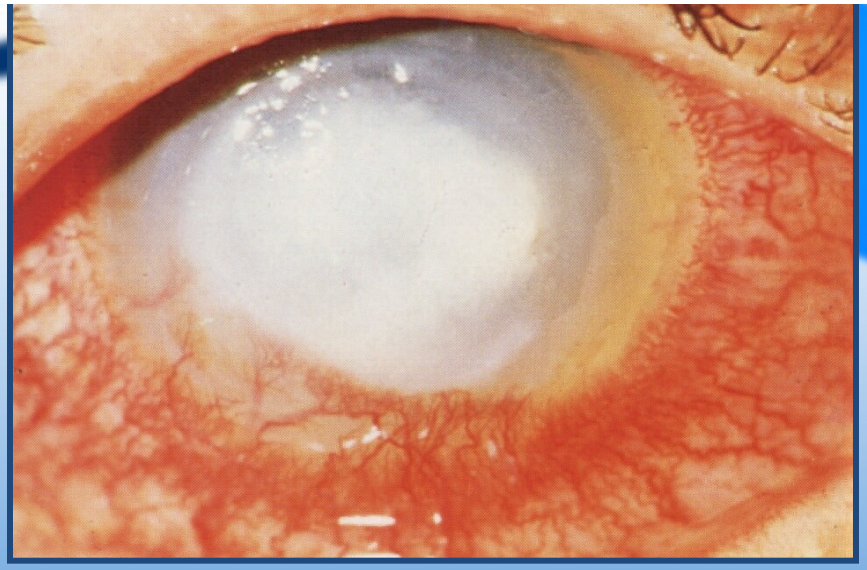
- Contact lens wear
- Pseudomonas aeruginosa
- Ocular surface disease
- Postherpetic cornea diseases, trauma, bullous keratopathy, corneal exposure, dry eye
- Signs and symptoms:
- Acutely painful red eye
- White spot in the cornea

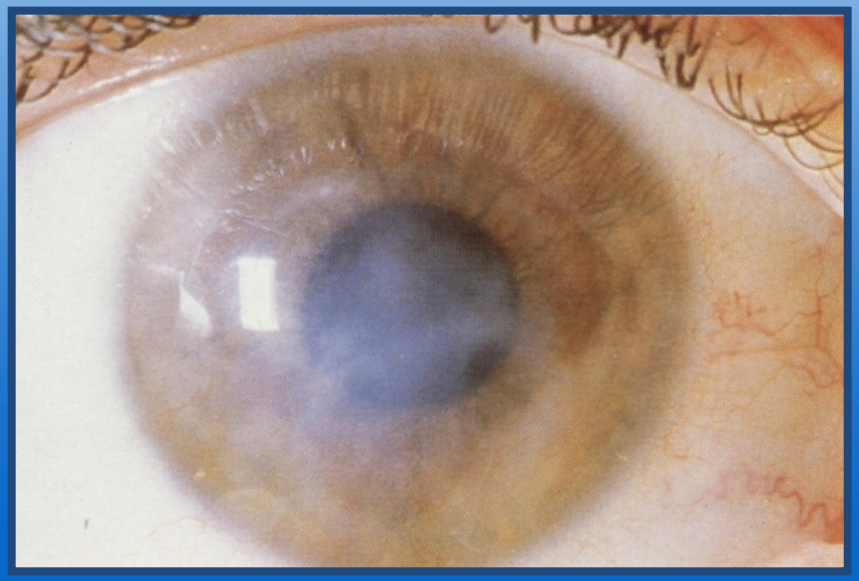
Aetiology and management

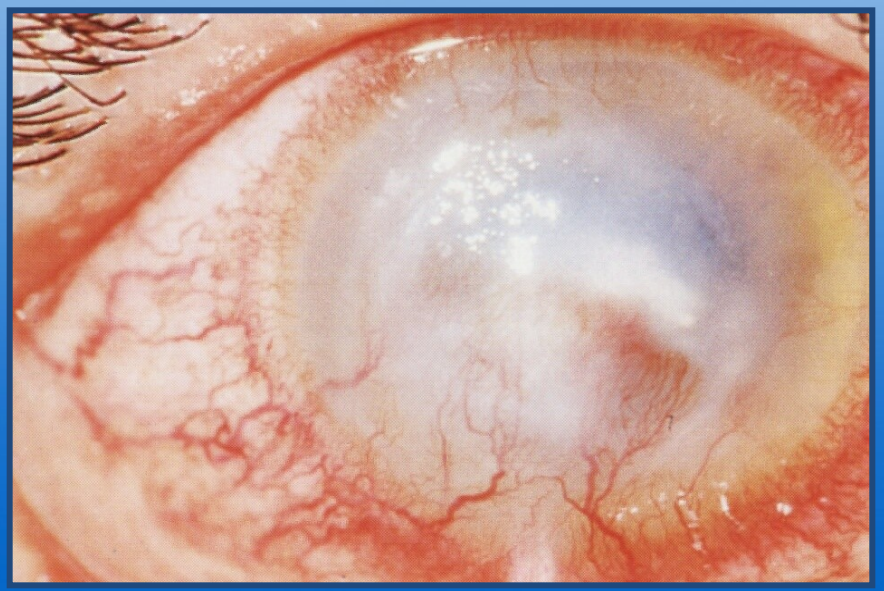
- **Aetiology :**
  - Staphylococcus aure
  - Pseudomonas sp.
  - Enterobacteriaceae
- **Management:**
  - Choice of antibiotics
    - Gentamycin
    - Cefuroxim
    - Ofloxacin
  - Topical instillation
  - Subconjunctival injection
  - Systemic antibiotics

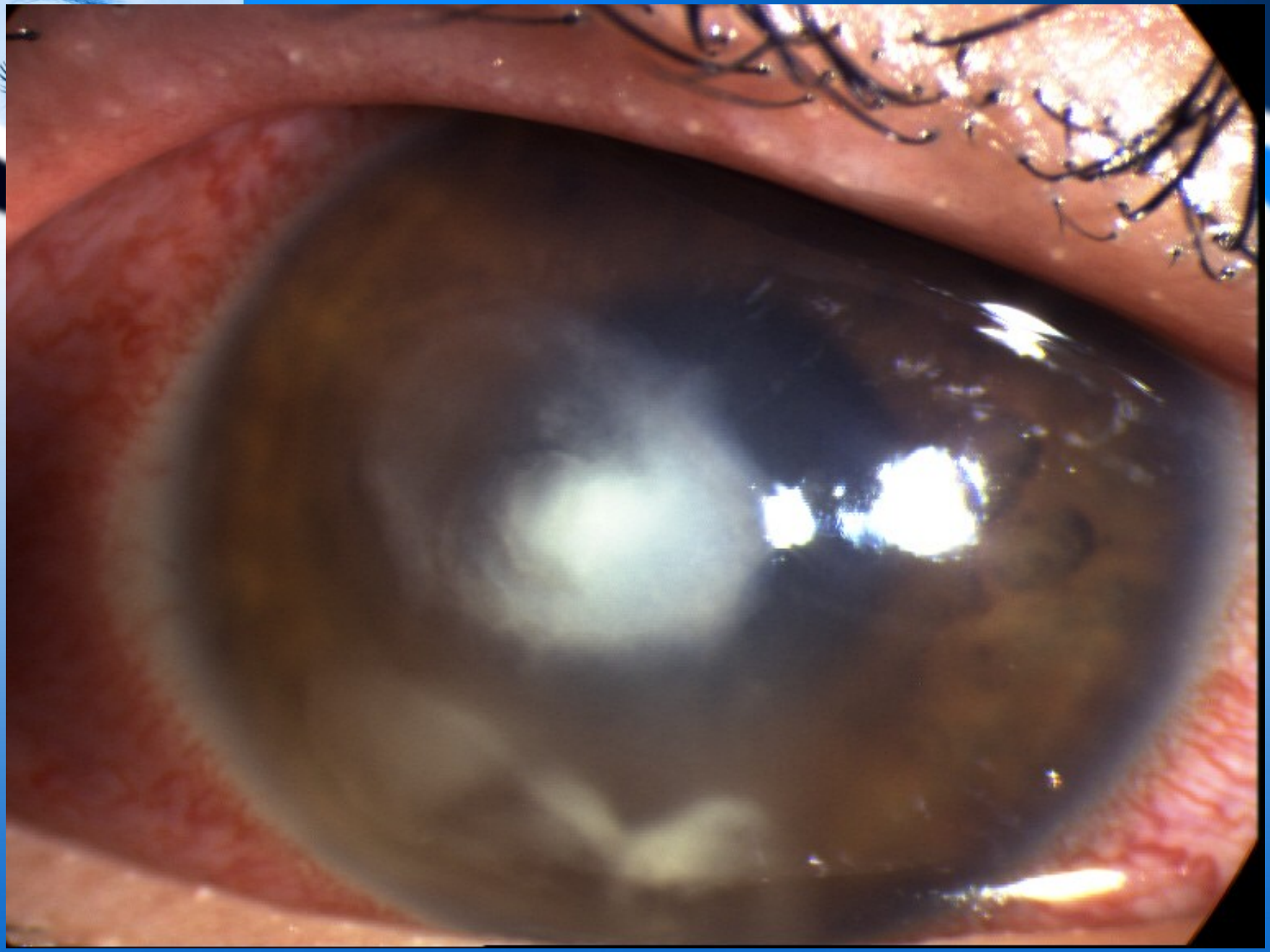
Pseudomonas Aeruginosa

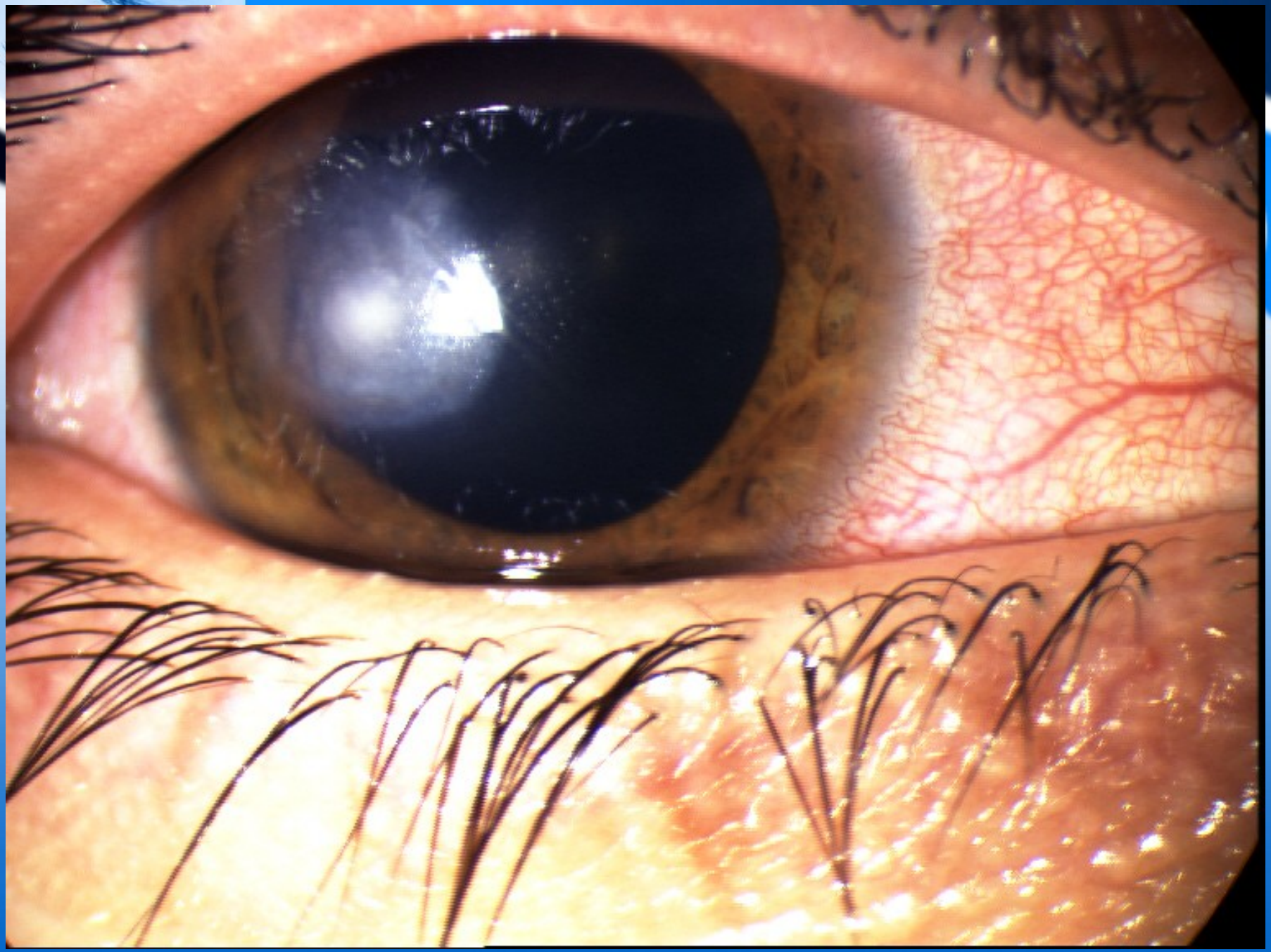


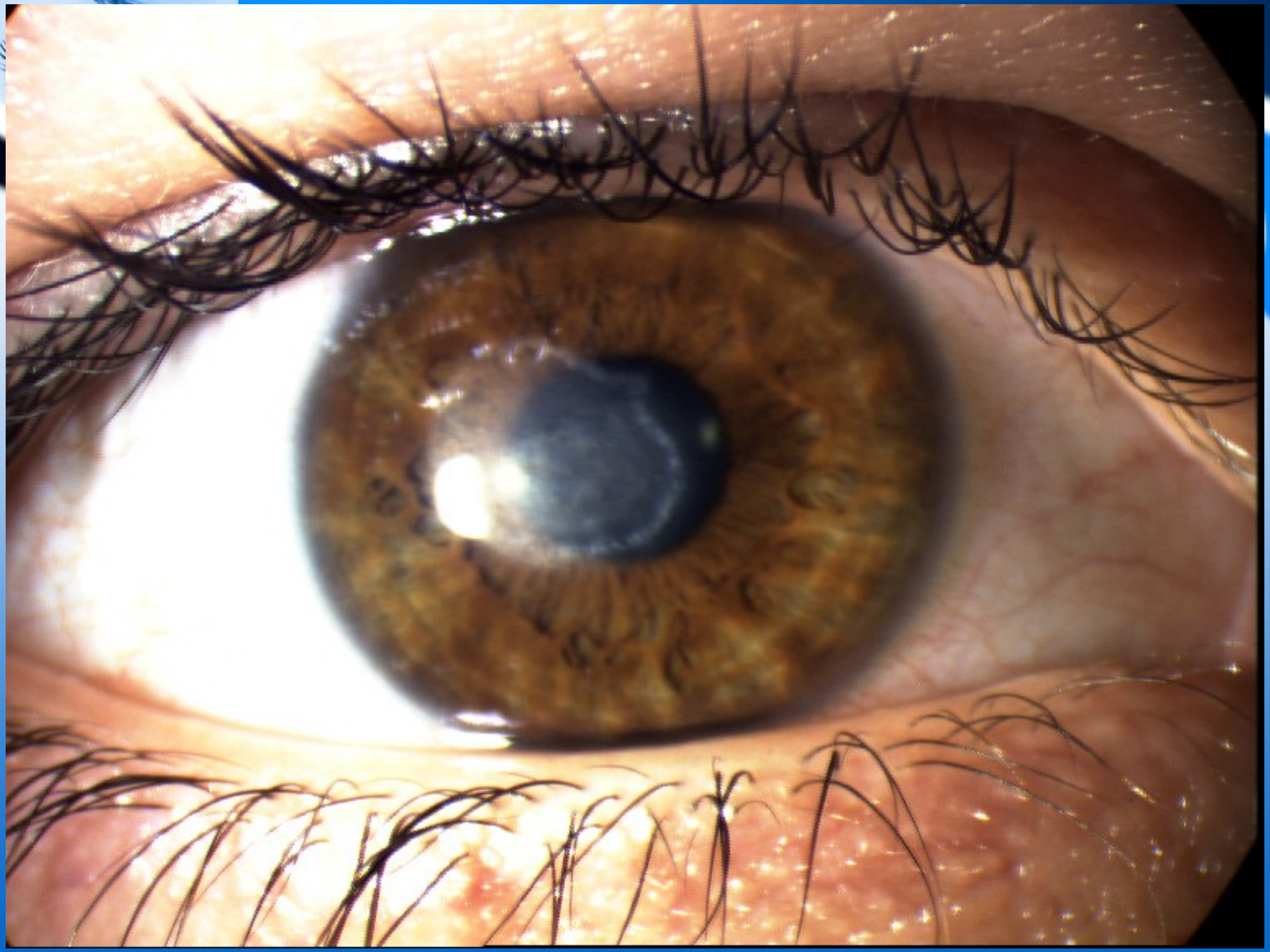




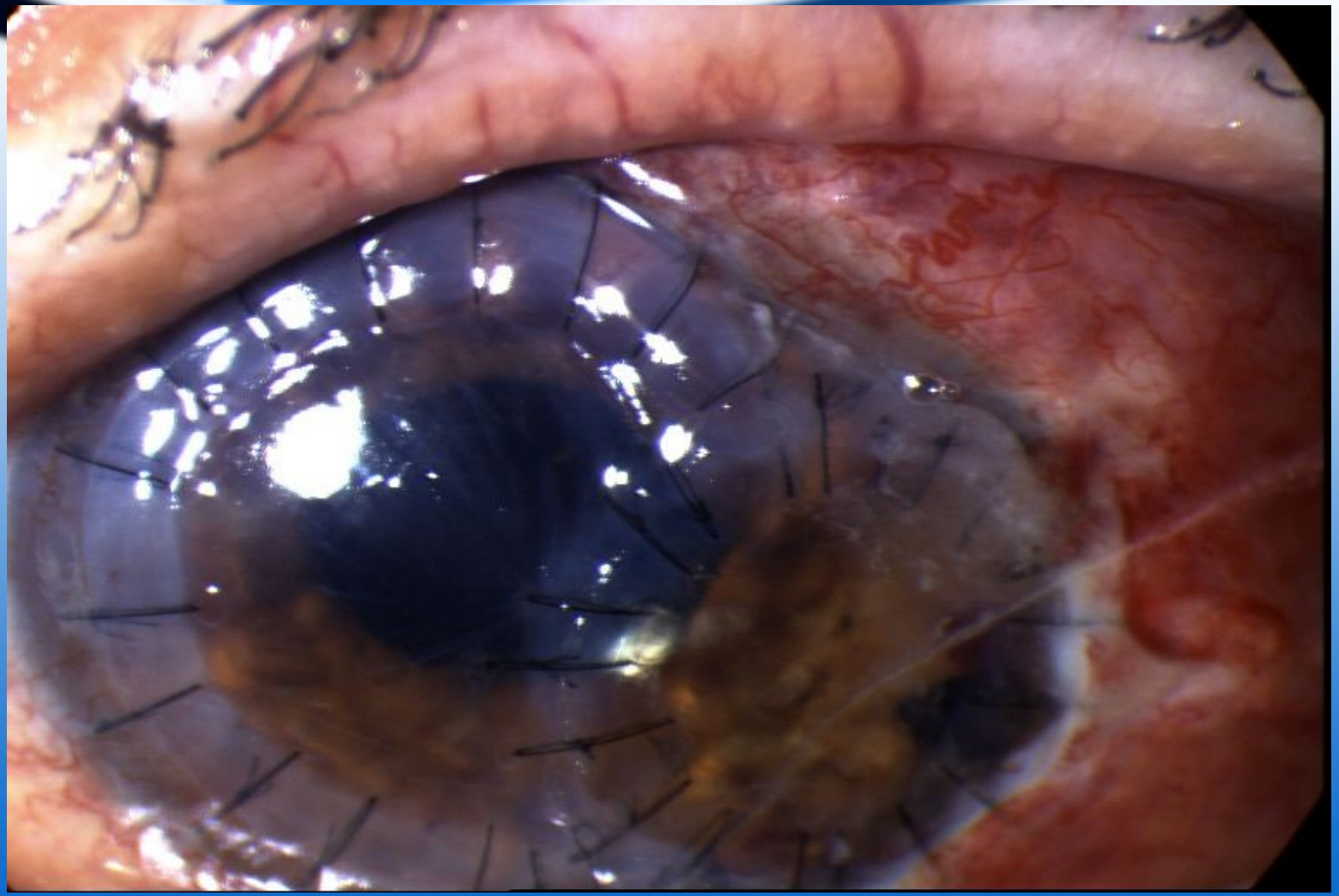




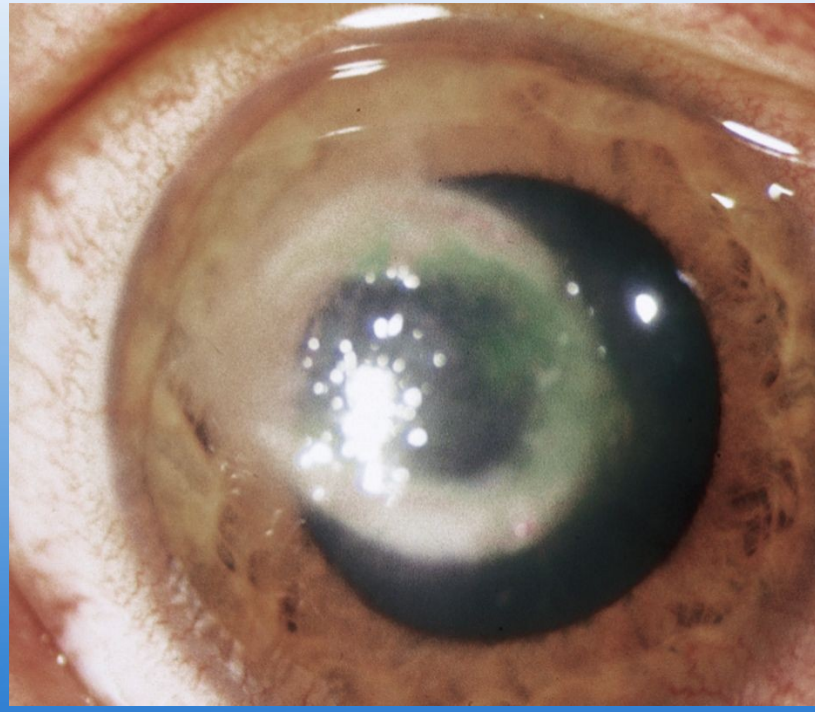




Keratitis neurotrophica

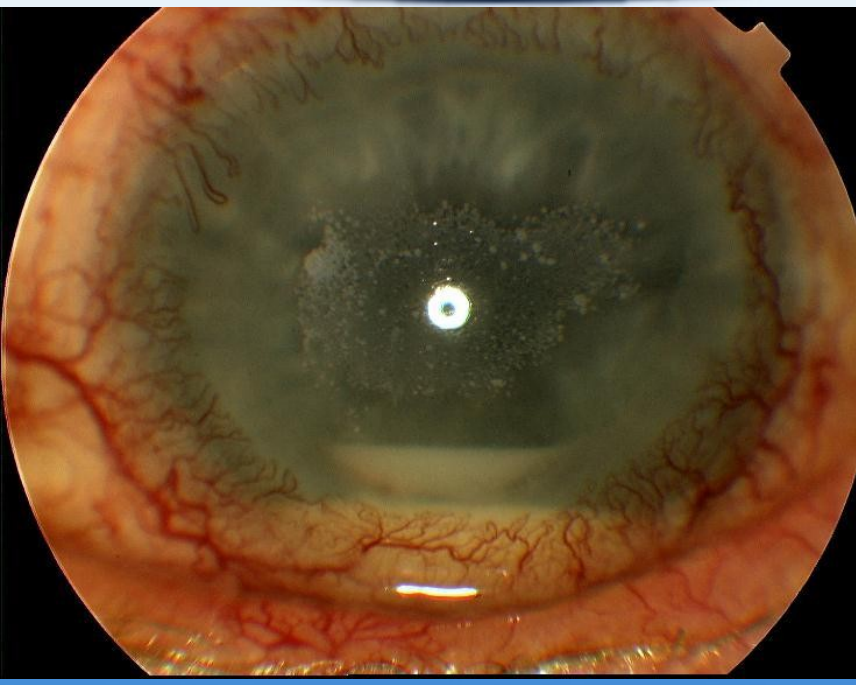


Ameba keratitis - protozoa



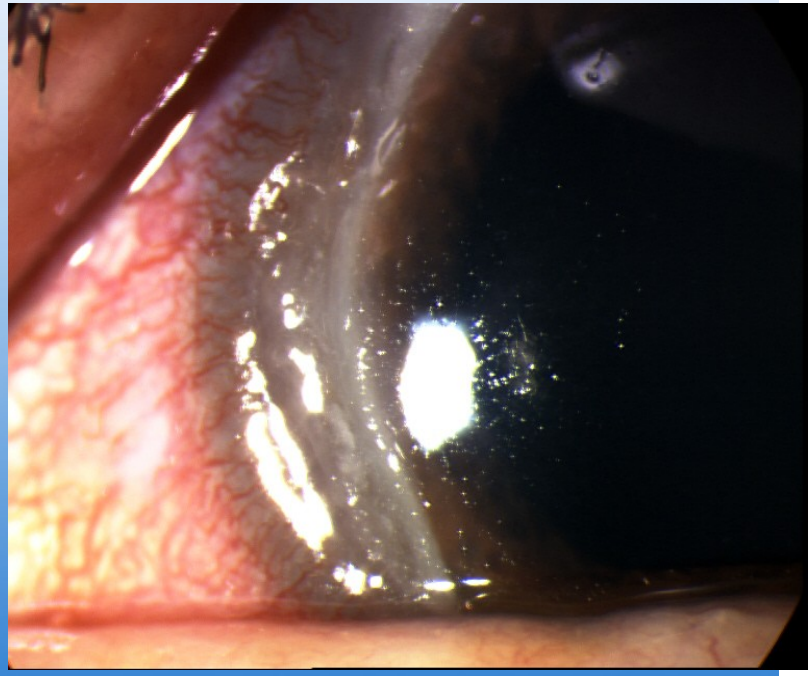
- **Pain** which is characteristically severe and disproportionate to the extent of ocular involvement
- The overlying epitelium may be intact
- Paracentral non supurative ring which may be associated with variable epitelial brakedown or pseudodendrite formation.

Fungal keratitis

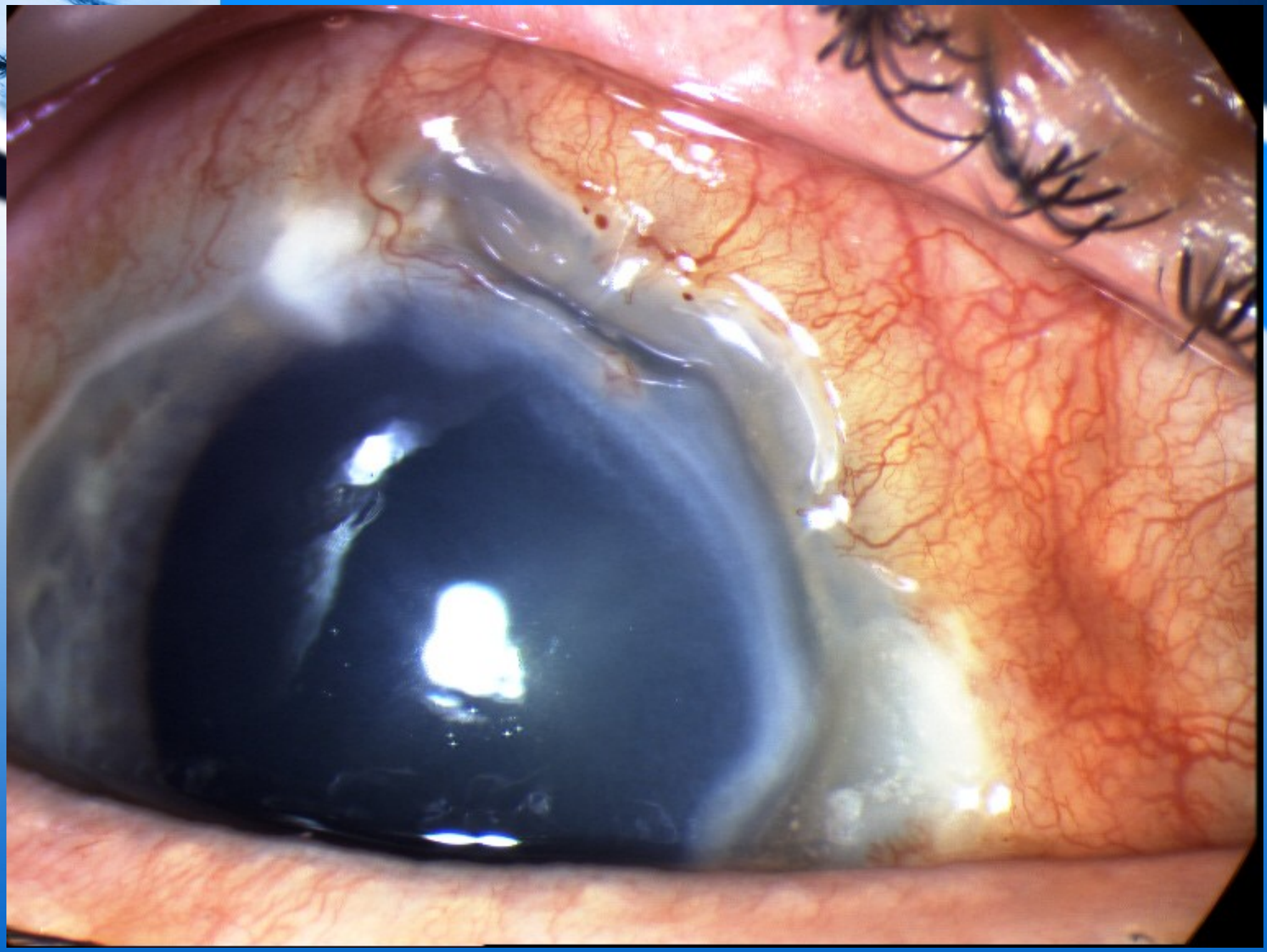


- Pre-existing chronic corneal ulcers
- Immunocompromisd patient
- Yellow-white ulcer with satelite infiltrations

Systemic eye diseases



- Keratitis in systemic collagen vascular disorders
- Periferal corneal melting
- - with inflammation
- - without inflammation
- Rheumatoid arthritis
- Systemic lupus erytematosus
- Polyarteritis nodosa
- Wegener´s granulomatosis



Surgery treatment

Transplantation of amniotic membrane
Transplantation of conjunctiva partial
Lamellar transplantation
Perforating keratoplasty
DMEK
Keratoprostheses (osteo – odonto)
Arteficial cornea
Phototherapeutic keratectomy (PTK)

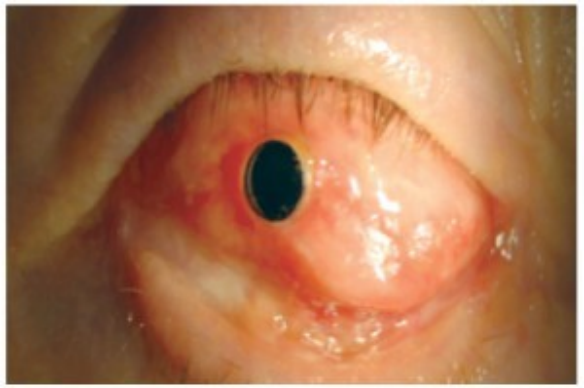
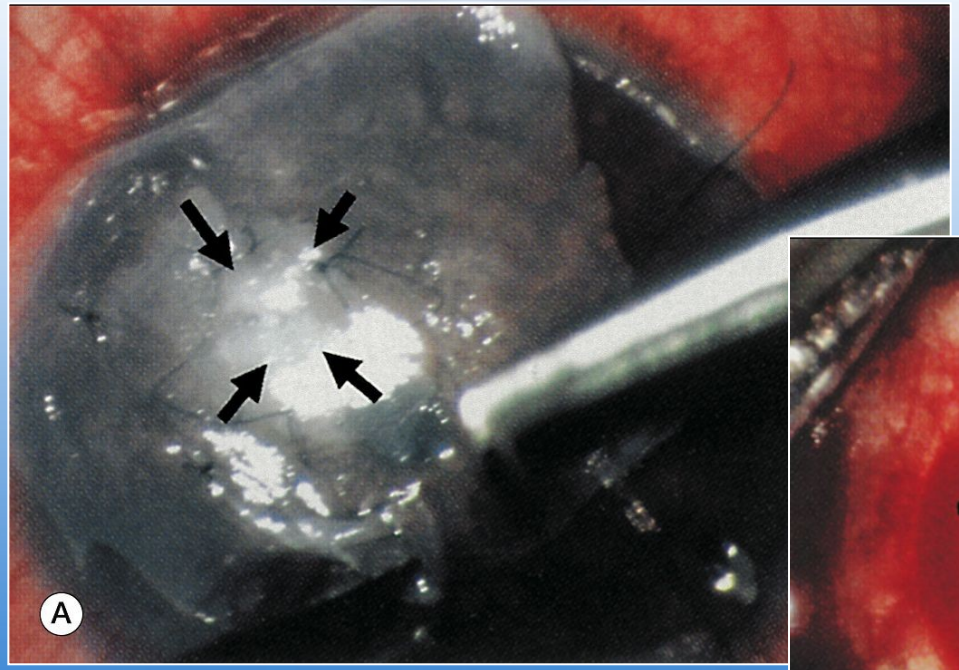
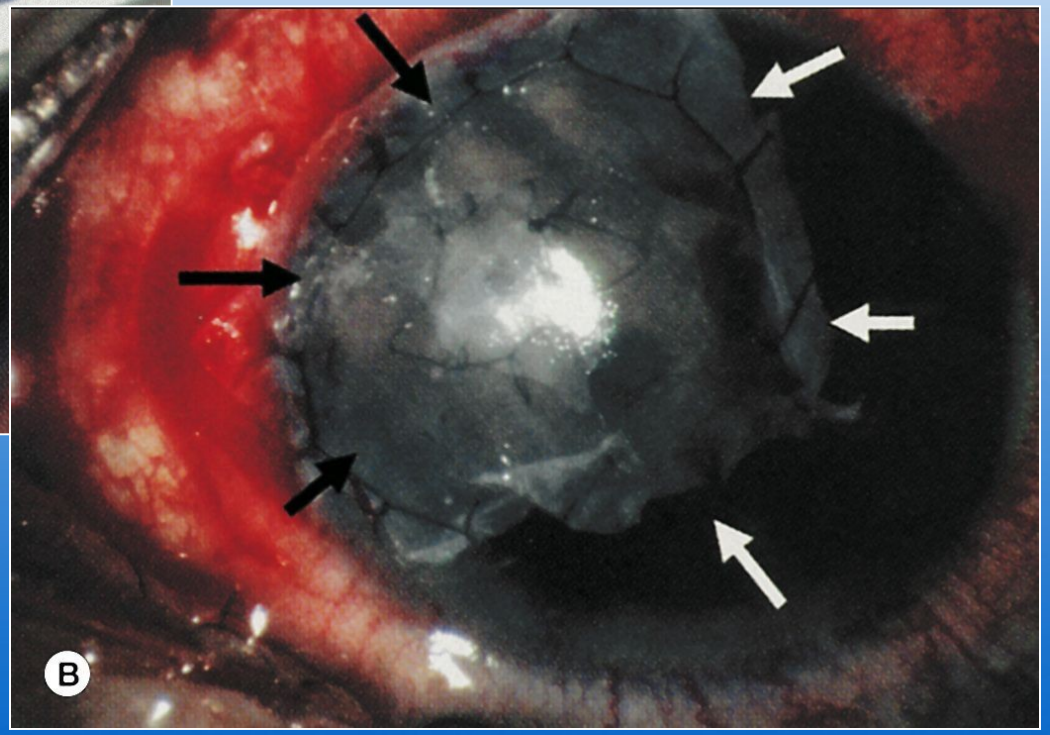


FIGURE 3 Modified Osteo-odonto-keratoprosthesis one year after implantation. *(Photo courtesy of Victor Perez, MD.)*

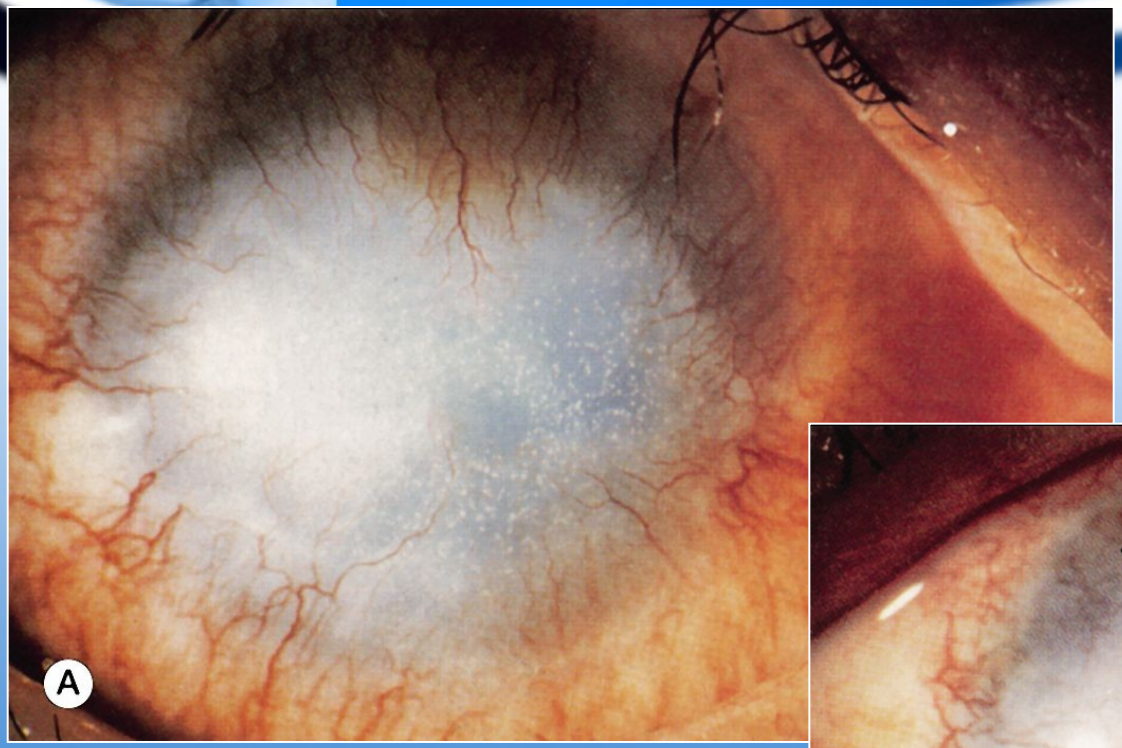
Surgery treatment

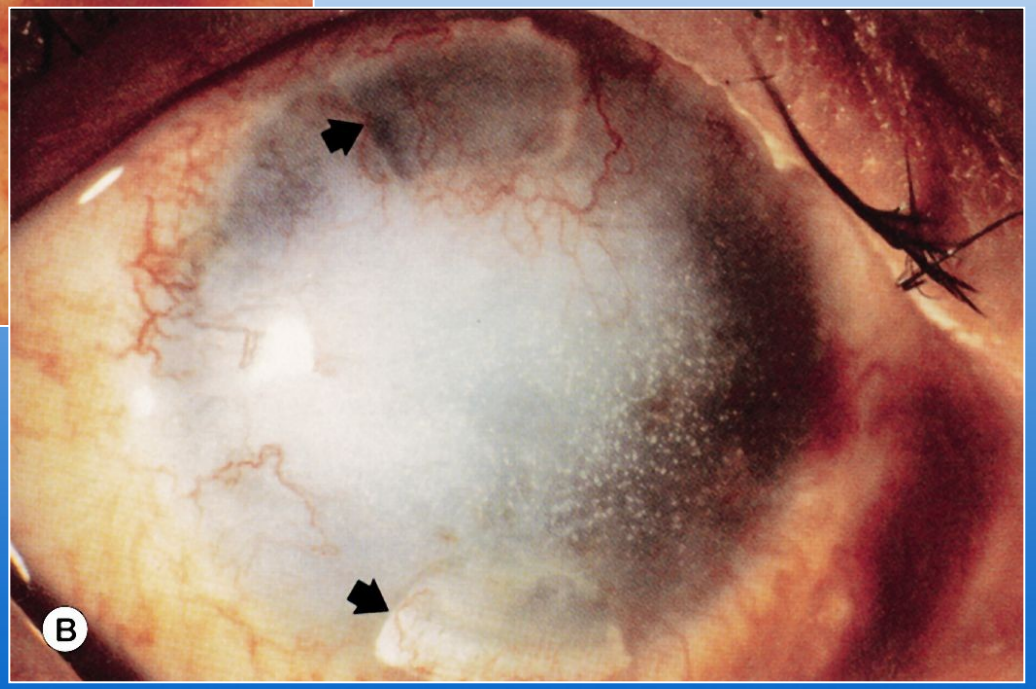




Amniotic membrane

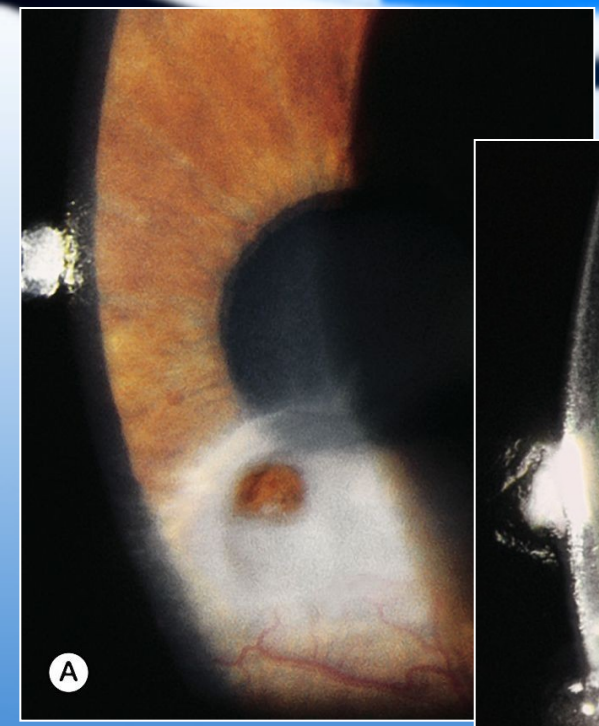
Surgery treatment

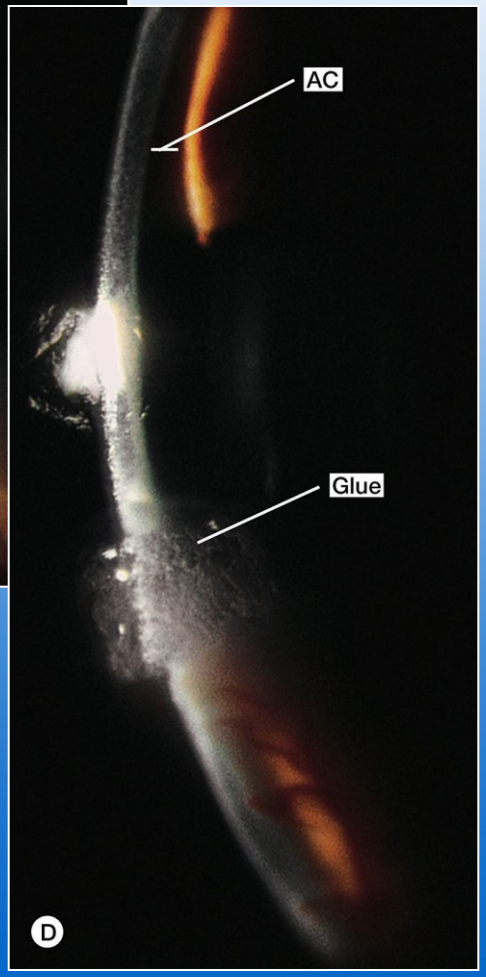


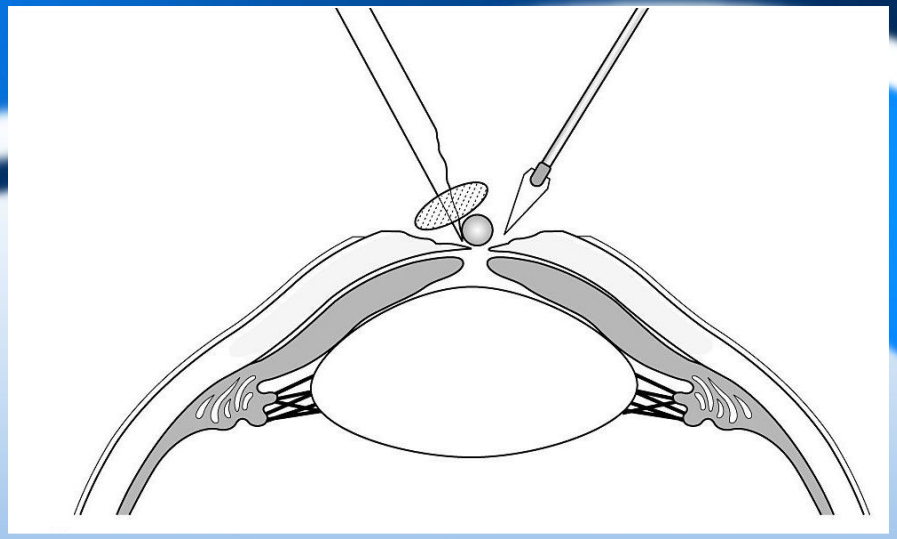


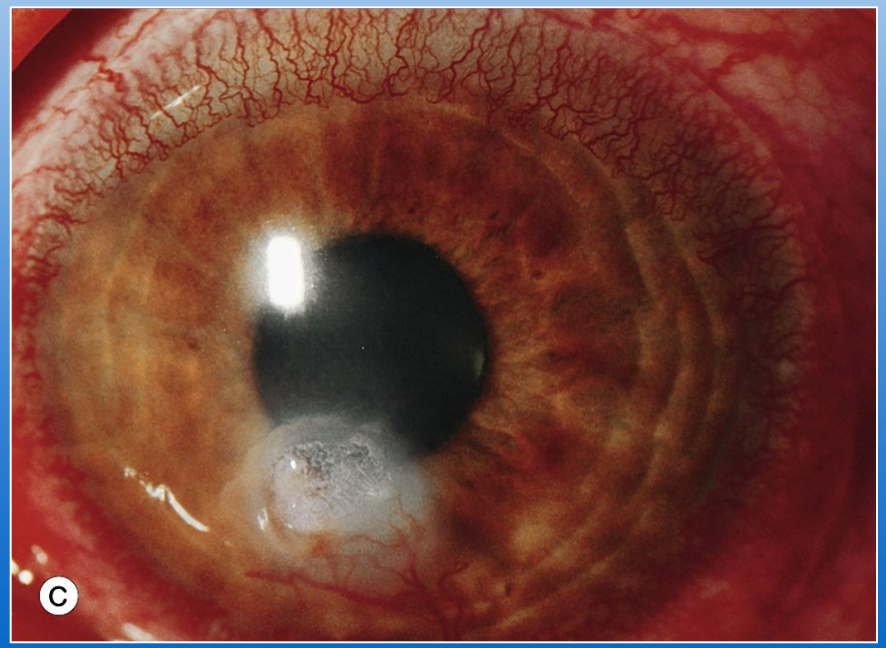
Conjunctiva transplantation

Surgery treatment

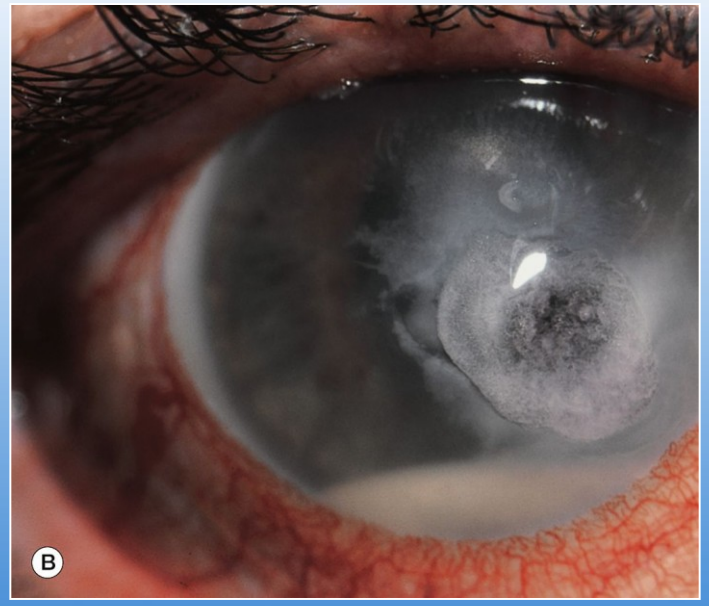


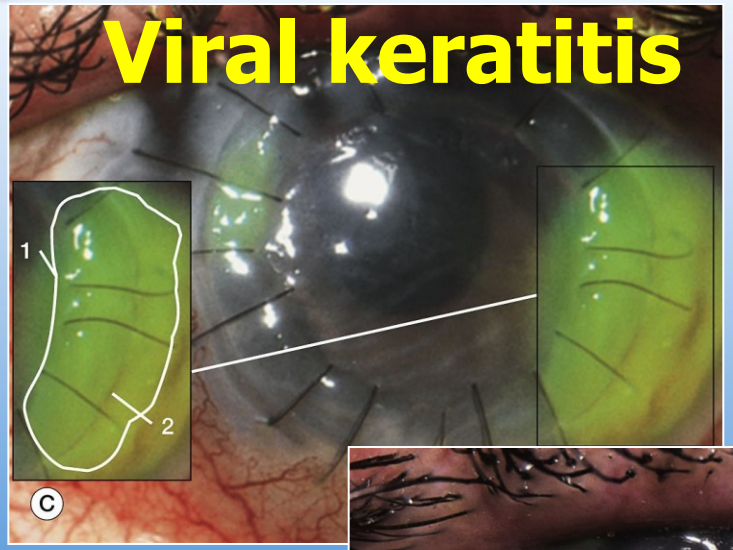


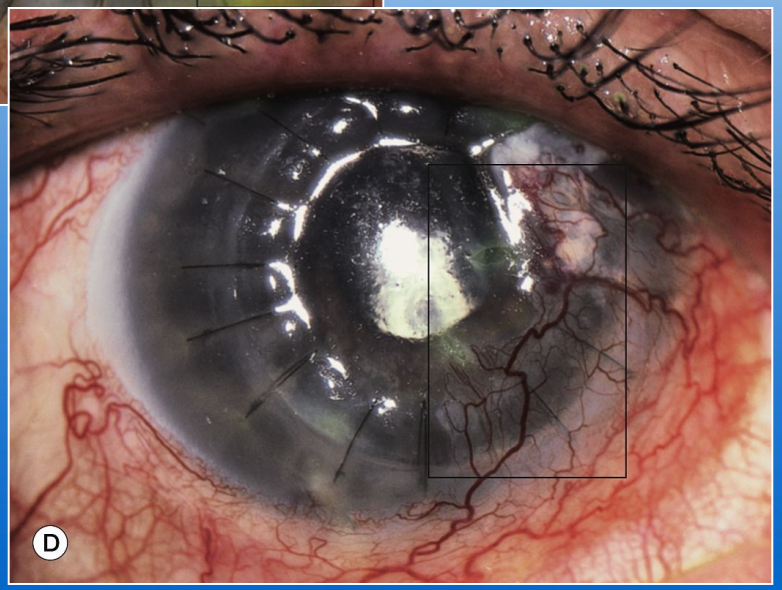




Surgery treatment

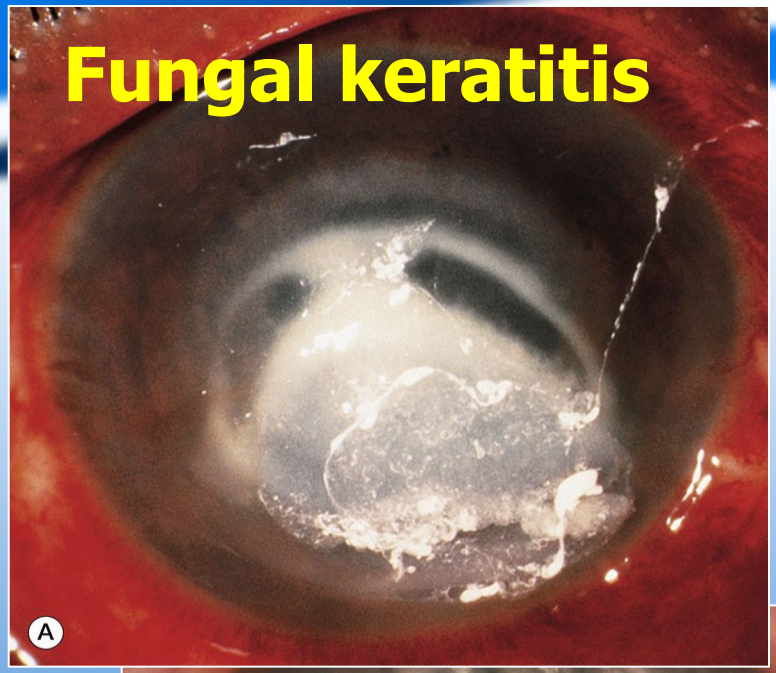


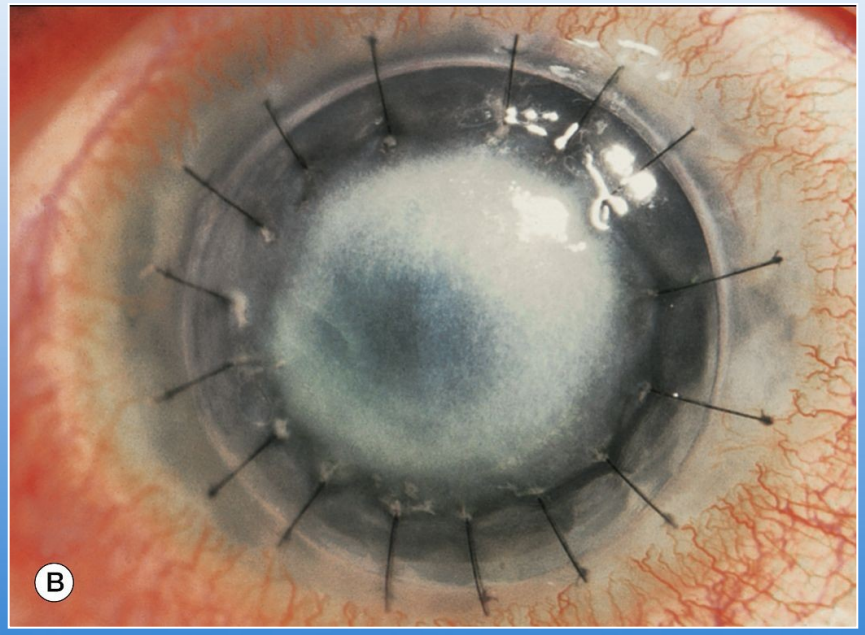


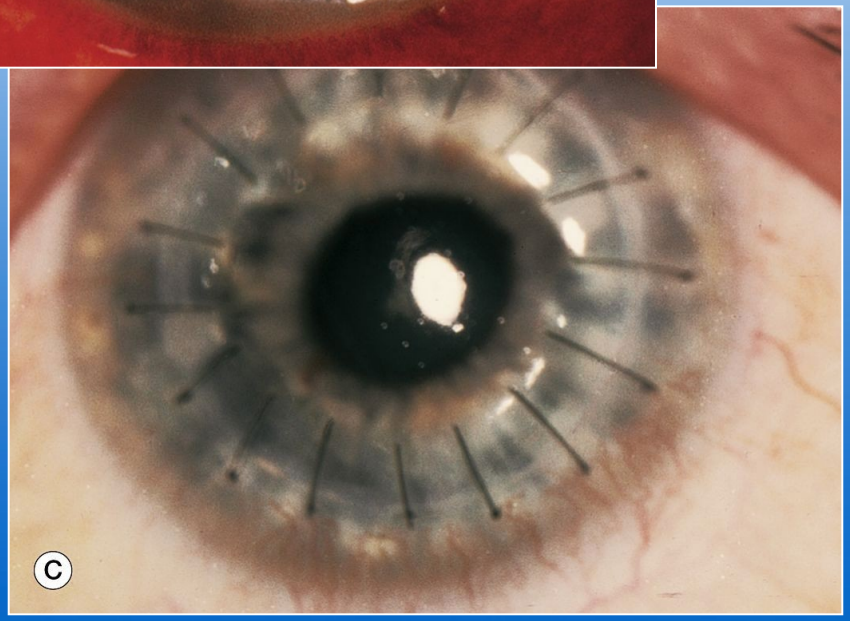


Penetrating keratoplasty

Surgery treatment

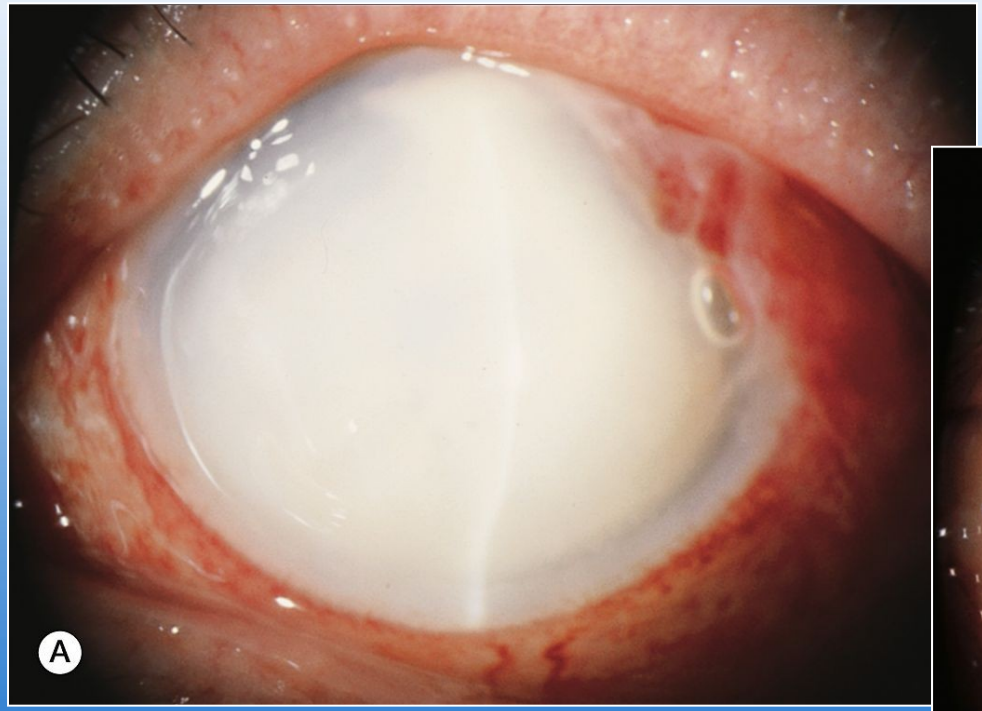


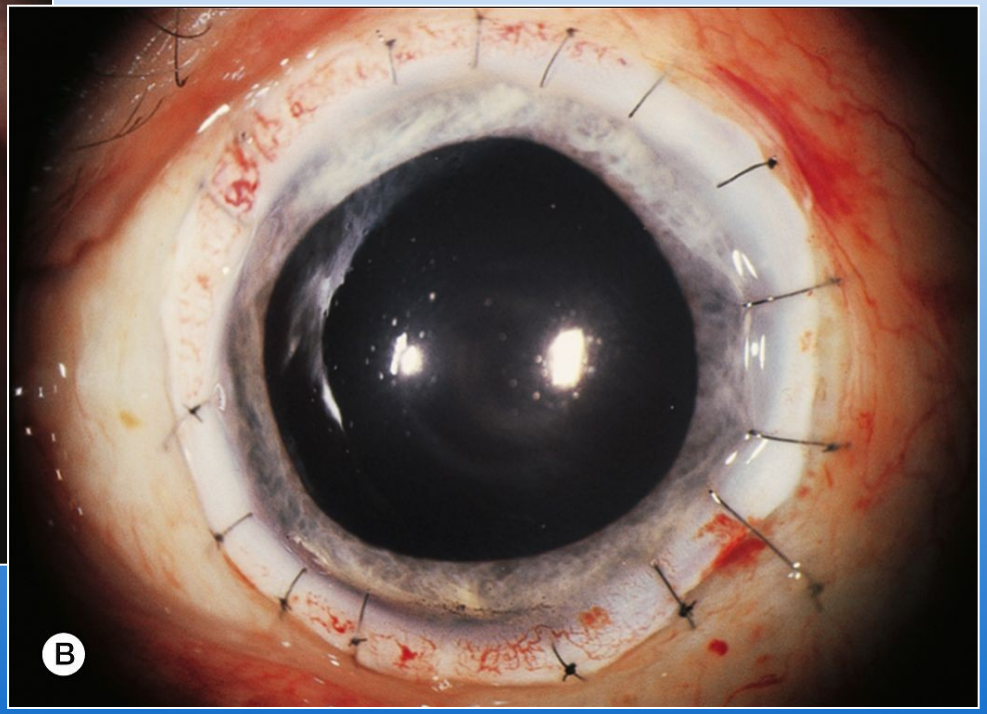




Penetrating keratoplasty

Surgery treatment



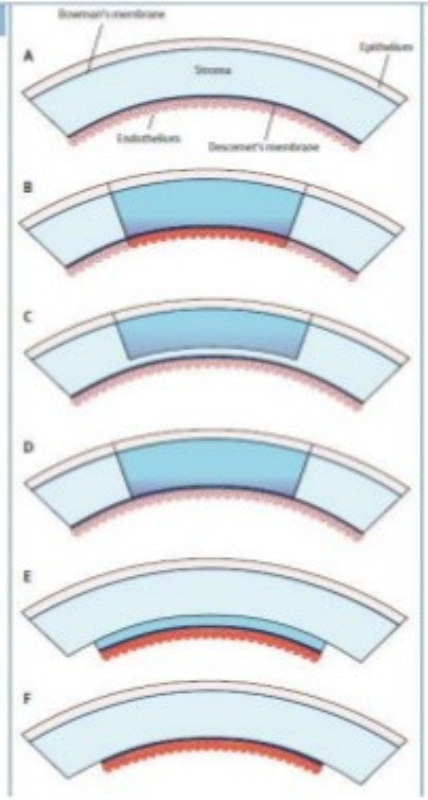


Bacterial sklerokeratitis

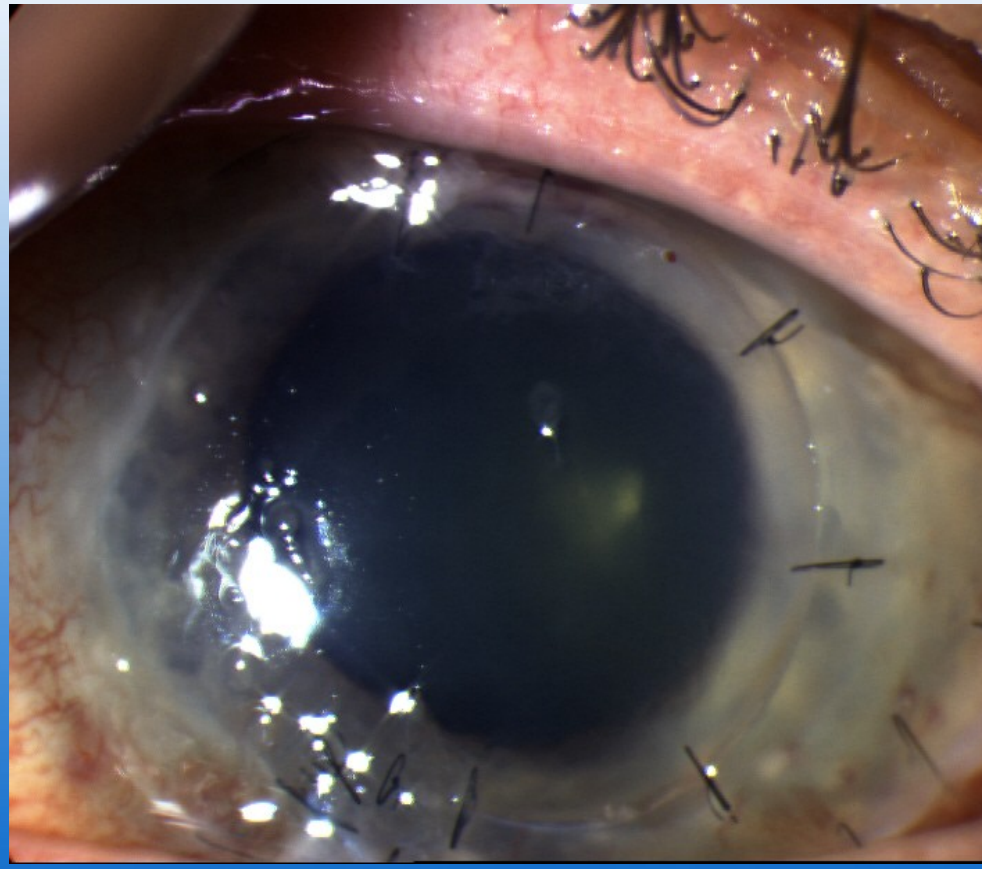
Corneal surgical techniques

TYPES OF CORNEAL TRANSPLANTS

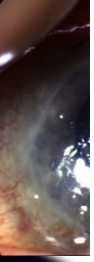
- Penetrating keratoplasty **(PK)**
- Lamellar keratoplasty **(LK) –**
- Anterior lamellar keratoplasty **(ALK)**
- Deep anterior lamellar keratoplasty **(DALK)**
- Posterior lamellar keratoplasty **(PLK)/** Endothelial keratoplasty **(EK)**
  - Descemet's stripping endothelial keratoplasty **(DSEK)**
  - Descemet membrane endothelial keratoplasty **(DMEK)**



Corneal surgical techniques



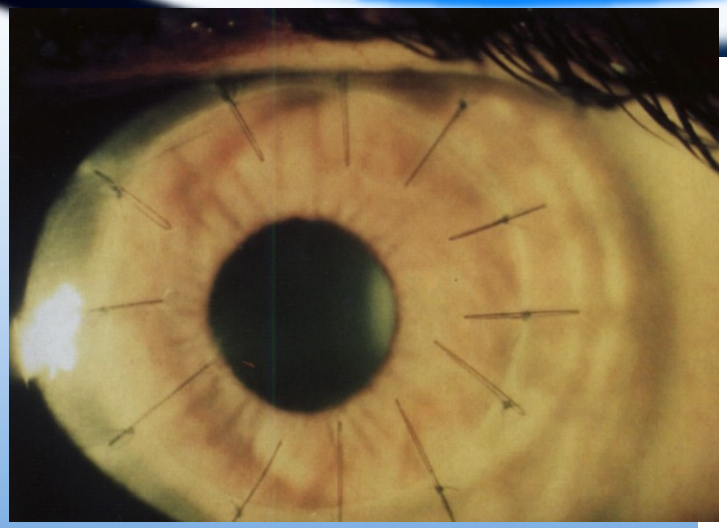
- **Deep anterior lamellar keratoplasty (partial thickness) = DALK**
- involves only the donor stroma, leaving the recipient's own Descemet membrane and endothelium for treating corneal pathologies in the circumstances of a normally **functioning endothelium.**

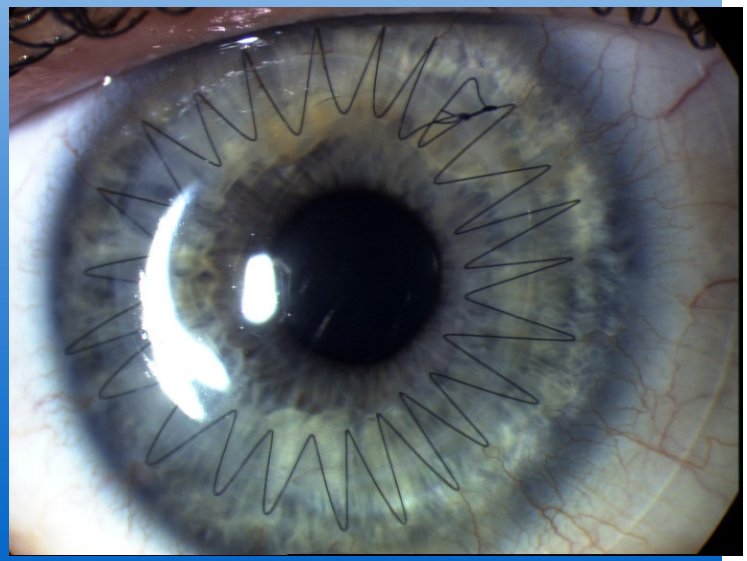


Corneal surgical techniques – indications of DALK

- Corneal ectasias
- Keratoconus:
- Pellucid marginal degeneration (PMD): DALK is a useful surgical alternative to PK in the management of PMD.
- Corneal scars:
- Corneal stromal dystrophies: Patients with Avellino, lattice and granular corneal dystrophies are good candidates for DALK
- DALK also has utility for correcting Bowman's membrane ReisBücklers' dystrophies and map-dot-fingerprint dystrophy with recurrent erosions.
- Ocular surface disease: Severe surface disease with limbal stem cell deficiency is a common presentation of trachomatous keratopahty, Stevens-Johnson syndrome, ocular cicatrical pemphigoid and chemical/thermal burns.
- DALK is also used for corneal degeneration such as in patients with Salzmann's nodular degeneration, climatic degeneration and band keratopathy.

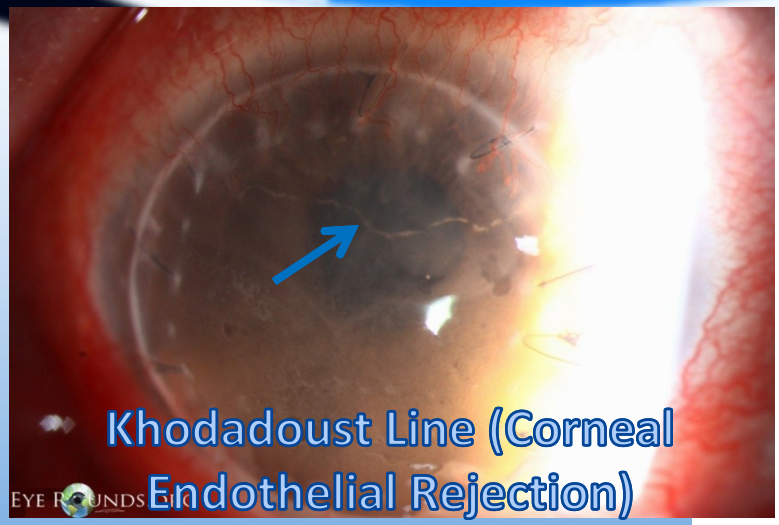
Penetrating keratoplasty - PKP

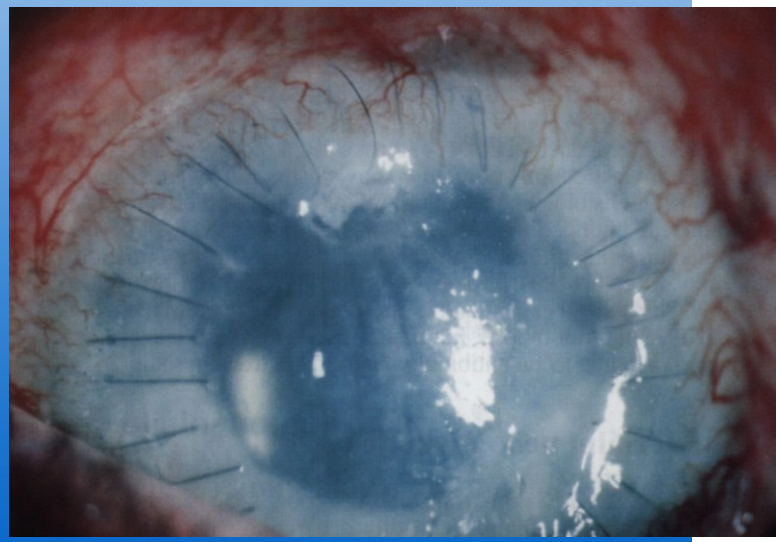




- Full thickness
- Indications:
- **Optical** –improvement of visual acuity by replacing opaque corneal tissue – most common indication is keratoconus, corneal dystrophies and degenerations and scars caused by trauma or inflammation
- **Tectonic** – penetrations of the cornea
- **Terapeutic** – removal of inflammed corneal tissue in eyes unresponsive to conventional antimicrobial therapy

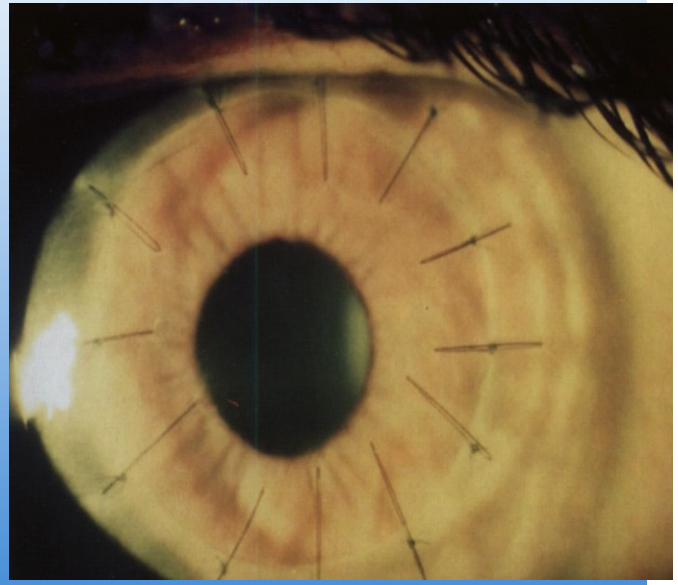
Penetrating keratoplasty - PKP





Determination of graft size
The graft size of more than 8,5 mm in diameter increases incidence of postoperative anterior synechiae formation and vascularisation
Ideal size is 7,5 – 8,0 mm
Graft smaller than 7,0 mm gives rise to astigmatism
Excision of donor cornea
Excision of host tissue
Fixation of donor tissue

Postoperative management



- Topical **steroids**
- Systemic steroids – first six weeks
- Suture removal after 12-15 months
- Graft failure:
- **Early** – endotelial dysfunction resulting from defective donor endotelium or surgical trauma at the time of operation
- **Late** – immune graft rejection – endotelial damage

Refractive eye surgery

Keratotomy - radial, hexagonal, arcuat
Intrastromal rings - myopia, astigmatism
Intracorneal lens

Refractive eye surgery

Laser technology:

LASIK, femto-LASIK (laser in situ keratomileusis) „light amplification by stimulated emission of radiation“ – laser is deviced that emits electromagnetic radiation

Surface ablation:

- PRK (photorefractive keratectomy), LASEK, Epi-LASEK

Photoablation - argon-fluoride laser (Ar-F)

Femtosecond laser – intrastromal

Refractive eye surgery

- RES techniques change the shape of the cornea in order to reduce the need for corrective lenses or otherwise improve the refractive state of the eye.
- In many of the techniques used today, reshaping of the cornea, is performed by photoablation using the excimer laser.

Refractive eye surgery

- If the corneal stroma develops visually significant opacity, irregularity or edema, a cornea of a deceased donor can be transplantated.
- Because there are no blood vessels in the cornea, there are also few problems with rejection of the new cornea.
- The synthetic cornea – keratoprosthesis

Thank You