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Ophthalmology PG Exam Notes

1st Edition

CORNEA

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I notes
(Ophthalmology PG Exam Notes)

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This is a compilation effort from my preparation notes and other sources, thus any contributions or comments are welcomed in the effort to improve this book. Therefore, feel free to e-mail me at
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I notes

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Thank you GOD

This manual is collection of the notes I made, found in books or internet while studying for the Final MD exams for ophthalmology.

I have segregated topics just like book chapters to find them back easily. Though these all might be far less then other preparation notes available, I am proud of what I have made and I feel nice to present them to my upcoming ophthalmology friends.

Good luck!

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Therapeutic Lamellar Keratoplasty
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Refractive Surgery
Patient Evaluation and Selection
Topographic Analysis
Incisional Corneal Surgery
Onlays and Inlays
Photoablation
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Evaluation of the Cornea and External Eye

Examination of the Lids

- History of Patient
- Dermatologic Examination
- Eyelid Position: ectropion and entropion, Floppy Eyelid Syndrome
- Tear Meniscus and Puncta
- Anterior Eyelid: A ***collarette***, which forms in areas of inflammation or hyperkeratinization, is simply mucous debris, Lice, Demodex
- Posterior Eyelid
- **Meibomian Gland Expression**: normal diameter of each dome is **0.5-0.7 mm**, The volume of lipid is increased if any of the lipid domes are 0.8 mm or larger; this finding is sufficient to diagnose ***seborrheic meibomian gland dysfunction*** →viscosity and opacity of the expressed lipid are important signs
- After instilling lissamine green, rose Bengal or fluorescein onto the ocular surface, a visible line of demarcation, called the **Marx line**, is often apparent on the lid margin. This line is thought to represent the ***mucocutaneous junction***, and anterior displacement relative to the meibomian gland orifices may correlate with gland dysfunction.
- **Meibomian Gland Imagery**: The most obvious change seen with transillumination is gland dropout. Dropout is associated with obstructive meibomian gland dysfunction and is not associated with infectious blepharitis, allergic phenomenon, or seborrheic meibomian gland dysfunction.

Tear Film Evaluation

- General Inspection: Alterations in the eyelid structure
- **Inferior marginal tear strip**: normally about **0.5 mm** in width and has a concave upper aspect. If this strip is thin **(<0.25mm)** or discontinuous, it is evidence of deficient aqueous tear volume.
- **Tear Stability**:
    - The interval between the last complete blink and the appearance of the first random dry spot is the break-up time (**BUT**). Normally **10-30 seconds**. Values of

less than **10 seconds** are considered abnormal. Seen in aqueous tear deficient and in evaporative dry eye.

- **Noninvasive BUT** that employs reflective devices with a grid projected onto the corneal surface.
- **Video-recorded BUT**: Values below **7 seconds** are considered abnormal and reflective of the presence of dry eye disease.
- **Ocular Protection Index (OPI): OPI = BUT/IBI**. Values **below 1** are characteristic of tear film instability and dry eye disease. Blink rate, which is calculated by dividing 60 by the number of observed blinks per second. *(IBI: Inter-Blink Interval)*

- **Tear Production**
  - **Schirmer's test**: ***Schirmer's II (with anesthesia)*** has been purported to measure **'basal'** tear secretion, i.e. nonstimulated tears. Values **below 5.5 mm** of wetting are diagnostic of aqueous tear deficiency.
  - A **Schirmer's I (without anesthesia)** has become the generally accepted method for assessing aqueous tear production.
  - Without anesthesia, wetting of less than 15 mm indicates dry eyes, and less than 5 mm indicates very severe dry eyes.
  - **The phenol red test**: phenol red impregnated cotton thread is inserted over the inferior lid margin into the temporal conjunctival sac. At the end of **15 seconds**, the dye, which is pH sensitive, turns color ***from yellow to orange***, indicating the length of the thread wetted by tears. This test has been reported to be less uncomfortable and more specific in the diagnosis of aqueous tear-deficient dry eye disease.

- **Tear Composition and Characteristics**
  - **tear lysozyme** levels are decreased in aqueous tear-deficient dry eye disease
  - **tear protein lactoferrin**: Touch MicroAssay,
  - **Tear ferning**: normally there is crystalline pattern of tear mucin. In aqueous tear deficiency, this pattern resembles ferns

    Ocular Ferning Test: Crystallization of a drop of tear fluid on a glass slide at room temperature. (DES display type III and IV pattern)
  - **Tear osmolarity**: **single diagnostic test with the highest accuracy** in identifying patients with dry eye disease. **Cutoff- 316mOsm** (DEWS Report)

- **Meibomian Gland Structure and Excreta**
    - Expression of Meibum
    - transillumination of the eyelid
- **Tear Clearance Tests**
    - **Dye dilution studies**: concentration of the dye is measured over time.
    - **Fluorescein Clearance Test [FCT]:**
    - This **tear function index (TFI)** is the ratio of the value of the Schirmer's test over the tear clearance rate. The use of the TFI in the diagnosis of dry eye disease is reported to demonstrate a specificity of 91% and a sensitivity of 79%.
- **Staining of the Ocular Surface**
    - Fluorescein, which stains damaged epithelial cells, is best visualized on the corneal surface.
    - Staining of the conjunctiva is seen when there are disruptions in the protective mucin coating; RB and LG are used.
- **Tests of visual function**
    - **tear stability analysis system (TSAS)**, serial videokeratographic images are collected each second between blinks.
    - **functional visual acuity (FVA)** device has been developed which measures visual acuity by way of rapid presentation of optotypes.

Corneal Diagnostic Techniques

- **Corneal Staining**
    - **Fluorescein and rose Bengal:** both dyes can stain living cells, rose Bengal does so more effectively and is intrinsically toxic. healthy preocular tear film will block rose Bengal staining of healthy and damaged cells. Cell degeneration or death increases membrane permeability to both dyes, but rose Bengal diffusion into the stroma is limited. *Fluorescein stains BM of epithelial defect, while RB stains dead epithelial cells even without epithelial defect.*
    - **Lissamine green**: better tolerated than rose Bengal.
- **Pachymetry**

  - **thinnest** part of the cornea is usually located about ***1.5 mm temporal to the center*** of the cornea
  - Mean thickness is 515 µm in the central cornea.
  - cornea with a ***central thickness greater than the thickness in the midperipheral*** should be considered suspicious for endothelial dysfunction centrally or thinning in the midperiphery
  - If the intraocular pressure is normal, epithelial edema develops when the stroma has **swollen about 40%,** to a corneal **thickness greater than 700 µm**.
  - corneal striae become visible at 4–8%, folds are seen at 11–12% swelling, and loss of transparency can occur at greater than 20% swelling.
  - Techniques for measuring CCT include optical pachymetry, ultrasound pachymetry, confocal microscopy, ultrasound biomicroscopy, optical ray path analysis or scanning slit corneal topography, and optical coherence tomography.

- **Aesthesiometry**
  - **cotton-tipped swab**
  - **Cochet-Bonnet aesthesiometer**: **6.0 cm**-long adjustable **nylon monofilament**, Measurements are taken by advancing nylon filament smoothly and perpendicularly toward the center of the cornea. Contact is detected by the slightest bend of the nylon; ***sensitivity*** is measured as the length of the filament that gives a 50% positive response from a minimum of four stimuli. The **normal cutoff is 4.5 cm**, and measurements below this are compatible with decreased sensation.
  - jet of warm saline
  - noncontact air puff technique
  - Ocular sensitivity is greatest in the central cornea except in elderly patients, in whom the peripheral cornea is the most sensitive.

Keratometry and Topography

- 1619, **Father Christopher Scheiner** observed that shiny glass spheres of different radii produced reflected images of different sizes
- **Ramsden** later added a magnification system and also introduced the doubling device

- **1854**, **Helmholtz** extended this work and constructed a complex instrument that he called an **ophthalmometer**.
- **1881**, **Javal and Schiotz** introduced a simplified ophthalmometer → **keratometer**
- P = 0.3375/r
- **Principle**:
    - Anterior corneal surface to behave like a convex mirror and reflect light. The optical design of the keratometer allows the examiner to measure the size of the reflected image and thereby determine the radius of curvature of the anterior corneal surface.
- **Limitations**:
    - assumes that the mires are measuring an area directly over the pupil.
    - assumption that the cornea has a sphero-cylindrical surface with a single radius of curvature in each meridian and a major and minor axis separated by 90 degrees.
    - no information about areas central or peripheral to the points measured
    - only analyzes approximately 6% of the corneal surface
- Series of instrument developments that began with the **keratoscope**, followed by the **photokeratoscope**, and finally the **videokeratoscope** →now called the **corneal topographer**.

Keratoscopy

- **Cuignet** first described the technique of keratoscopy in the 1820
- **Henry Goode** described the first keratoscope in 1847
- **Antonio Placido** was the first to photograph the corneal reflections of a series of illuminated concentric rings in the 1880s.
- In 1896, **Gullstrand** was the first to quantitatively analyze photokeratoscopic images of the cornea.
- evaluate about 70% of the total corneal area (limited by the optics of the reflecting system itself)

- Types
    - **flat-target keratoscope**: rings of the target are located in the same plane
    - **Collimating keratoscope**: rings in different planes along the interior of a column and in this way are able to maximize the amount of corneal surface that can reflect the target mires
- Limitation
    - to produce an obviously distorted image, the cornea must be quite distorted itself
    - astigmatism of at least 3 diopters (D) must be present to be detected by traditional keratoscopy.

Videokeratoscopy = Topography

- Klyce in 1984: union of rapid computer analysis and digital video
- Two approaches are in general use currently: the Placido disk or reflection-based topographers, and the scanning slit-based tomographers.
    - **Placido disk-based topographers**:
        - vast majority of the older units
        - transilluminated cone acting as a modified Placido ring
        - Most systems can be divided into ‘near-design’ and ‘distant-design.’
        - sensitive to disruptions in the tear film
    - **Slit scanning tomography**
        - elevation of each surface can be measured directly with slit beam technology
        - The **PAR CTS** (PAR Technology, New Hartford, NY) was the first ‘topography system’ to produce a true topographic map, using elevation data from the corneal surface.
        - **Bausch & Lomb Orbscan**: Orbscan is a hybrid system – both a topographer and a tomographer – that uses Placido disk technology to display conventional corneal topography. Is is ***limited in its ability to reliably measure the postoperative posterior cornea***, the Oculus Pentacam had greater success in this area.

    - **Oculus Pentacam** uses a scanning slit but with ***Scheimpflug optics***, which increases the depth of focus. In doing so, simultaneous imaging of the cornea, lens, and iris is possible; this permits corneal, anterior chamber, and lens geometry to be imaged and analyzed.
    - **Zeimer Galilei**, also a ***Scheimpflug imaging*** device, has similar advantages with regard to image registration and measurement of the posterior corneal surface.

- **The main uses of corneal topography**
    - **Preoperative evaluation** to rule out certain corneal abnormalities, establish refractive stability, determine whether the patient's corneal shape will allow surgery to be performed safely, and determine whether the surgical outcome is likely to allow acceptable visual performance.
    - **Operative assessment** to determine surgical parameters, plan complicated 're-op' cases, and input data for customized ablations.
    - **Postoperative evaluation** to monitor the surgeon's and laser's performance.
    - **Aid in the calculation of IOLs** for patients who have undergone refractive surgery.
- **Presentation Methods**
    - **Color-coded maps**: The 'warmer' colors represent higher dioptric powers (steeper curvatures), while the 'cooler' colors are used to represent the lower dioptric powers (flatter curvatures). Similar color-coded maps can be used to present changes in elevation.
- topographies of fellow eyes tend to be mirror images of each other: ***enantiomorphs***
- The Universal Standard Scale has been adopted by the ANSI standard on corneal topography.
- **Axial = sagital Curvature Maps**: The cornea has a prolate shape, so power is higher in the center than in the periphery.
- **Refractive Power Map**: normal cornea will have a higher calculated power peripherally than in the center. This is due to the natural residual spherical aberration of the cornea.
- **Instantaneous or Tangential Power Map**: not recommended for routine clinical use, extremely useful in the demonstration and measurement of the optical zone size in modern refractive surgery as they emphasize transition zone power changes
- **Difference Maps**: Progression of keratoconus

- **Elevation Maps**: Commonly, the best-fitting sphere or toroidal surface is subtracted from the elevation data. Posterior elevation values can be used to distinguish normal and keratoconic corneas, but posterior elevations are not sensitive enough a measure to separately classify forme fruste keratoconus and normal corneas.
- **Pachymetric Maps**: thinnest areas of the corneal stroma are generally inferotemporal to the fixation-reflex
    - Simulated Keratometry: power derived from the corneal topography.
    - Surface Regularity Index (SRI): irregularity of the corneal topography over the pupil, correlated to potential visual acuity
    - I-S index: introduced by Rabinowitz and McDonnell
    - Contact lens warpage can mimic mild keratoconus and needs to be ruled out

Specular Microscopy

- images light reflected from an optical interface.
- confocal or nonconfocal /contact or noncontact.
- first direct visualization of the endothelium was demonstrated by **Vogt** in 1918
- in 1968, **David Maurice** described the first laboratory specular microscope that could be used to study excised living corneas
- Optical Principles:
    - Light striking a surface can be **reflected, transmitted, or absorbed** or Combination of 3
    - primary importance in clinical specular microscopy is the light that is reflected specularly
    - four zones of reflection can be seen → **Zone 3 is the endothelial region**
- **Instrumentation**
    - Konan NonCon Robo Series (Torrance, CA)
    - sequential images (Tomey, Inc., Phoenix, AZ)
    - live view (HAI Labs, Inc., Lexington, MA)

- **Qualitative Specular Microscopy**
    - Epithelium:
    - Endothelium (miscellaneous bright and dark structures) → Guttae are excrescences of Descemet's membrane. Guttae, however, can also be seen in the far periphery of young individuals. In this case, they are called **Hassall-Henle warts.**
    - Endothelium: morphometry
- **Quantitative Specular Microscopy**
    - endothelial cell density (**ECD**) (measured as cells/mm2), **mean cell area** (measured as µm2/cell), coefficient of variation (**CV**) (standard deviation of cell areas/mean cell area), and **pleomorphism** (usually measured as a percentage of 6, <6 or >6-sided cells).
    - The variable-frame analysis is more accurate than fixed-frame analysis because only whole cells are counted and it is not necessary to include portions of cells located on the frame boundary.
    - Cell density alone is not the most sensitive measure of endothelial health, as the endothelium functions even at low ECDs (under 500 cells/mm2).
    - **polymegathism** (variation in cell area as determined by the CV) and **pleomorphism** (variation in cell shape as represented by the percentage of hexagonal cells) are a more ***sensitive measure of the endothelium under stress***.
    - The corners method
    - The Center method (Konan Medical USA)
    - the center-flex method
- **Clinical Applications**
    - The ECD at which corneal edema occurs is quite variable, but has been estimated to be between **300 and 700 cells** per mm2.
    - Difference between two eyes: greater than **280** cells per mm2 is abnormal
    - A cornea with a **CV greater than 0.40 or the presence of less than 50% hexagonal cells** should be considered abnormal and at increased risk for postoperative edema.
    - age-related cell loss is approximately **0.5% per year**.
    - Combined surgery is considered **if CCT>600 and Specular <1000**

- The most striking abnormality in keratoconus, however, is elongation of endothelial cells
- FDA-approved Artisan/Verisyse phakic intraocular lens (IOL) has found acceptable mean cell loss rates of **1.8% per year** after insertion to correct high myopia.
- ***Cell loss after PKP:*** *10% after 2 week, 33% at 3 months, 50 % at 1 year*
- ***Cell loss after EK:*** *34% cell loss after 6 months, and 38% at 1 year*
- vitreous contact mechanically injures the endothelium and interferes with its physiologic function.

Confocal Microscopy

- The optical sectioning ability of confocal microscopy allows images to be obtained from different depths within a thick tissue specimen, thereby eliminating the need for processing and sectioning procedures.
- **principle of Lukosz**, which states that resolution may be improved at the expense of field of view.
- In 1955, **Marvin Minsky** developed the first confocal microscope for studying neural networks in the living brain
- Because both condenser and objective lenses had the same focal point, the microscope was termed '**confocal**.'
- Because the illumination and detection of light through conjugate pinholes occurs in tandem, this microscope was named the ***tandem scanning confocal microscope (TSCM)***.
- There are three main confocal imaging systems used clinically:
    1. the TSCM
    2. the HRT III (a scanning laser system)
    3. the Confoscan 4 (a scanning slit system)

High-Resolution Ultrasound

- University of Toronto: UBM
- frequency range of 25–100 MHz
- resolution ranging from 20 to 100 μm
- penetration to the 4–15-mm range.
- For diagnosis of: Corneal edema, DMD, IOL malposition, Imaging the anterior segment behind corneal opacities, Corneal dystrophies, Peripheral corneal degenerations, Keratoconus, Corneal Tumors, post- Keratoplasty, Refractive surgery,

ASOCT

- **Fujimoto, Huang**, and colleagues
- The ***optical delay of the reflected light is determined by interferometry*** to generate a ranging measurement called the axial scan (A-scan)
- The original OCT technology is now classified as time-domain OCT (**TD-OCT**), in which the **reference mirror is moved through a range of delay**, and the resulting inference patterns between the sample and reference beams are processed into an axial image.
- new technology called Fourier-domain OCT (**FD-OCT**) has been developed. In FD-OCT, the **reference mirror is stationary and the A-scan is generated by Fourier transformation of spectral interference** patterns between the sample and reference reflections.
- ***5 pachymetric parameters for Keratoconus Screening:***
    1. minimum – median thickness < −63 μm
    2. I − S < −31 μm
    3. IT − SN < −48 μm
    4. Minimum corneal thickness is less than 492 μm.
    5. The thinnest region of the cornea is outside of the central 2-mm area.
- Keratoconus Screening, Refractive Surgery Evaluation, Corneal Power Calculation, Corneal Opacities, Cornea Transplant, Phakic Intraocular Lenses

DD in Cornea

Congenital Corneal Opacities

- 3-6 per 100000
- **STUMPED classification (Waring)**
    - Sclerocornea
    - Tears in Descemet's membrane: Congenital glaucoma, Birth trauma
    - Ulcer: Herpes simplex virus, Bacterial, Neurotropic
    - Metabolic (rarely present at birth): Mucopolysaccharidoses, Mucolipidoses, Tyrosinosis
    - Posterior corneal defect: Peters' anomaly, Posterior keratoconus, Staphyloma
    - Endothelial dystrophy: Congenital hereditary, Posterior polymorphous corneal dystrophy, Stromal: congenital stromal corneal dystrophy
    - Dermoid

- **Sclerocornea**
    - scleralization of the peripheral or the entire part of the cornea
    - sporadically, familial or autosomal dominant
    - bilateral but commonly asymmetric
    - opacification of the cornea is smooth, white, and vascular; it appears to be an extension of the sclera without limbal landmarks
    - **four groups (Waring et al)**
        1. Isolated peripheral sclerocornea
        2. Sclerocornea plana: <38D, High Hyperopia, Shallow AC, Pseudoptosis
        3. Sclerocornea associated with anterior chamber cleavage anomalies: Peter's

4. Total sclerocornea: the **most common** form causing congenital corneal opacity,

- **Histopathology in sclerocornea**
  1. Corneal stroma resembles sclera morphologically
  2. Precise arrangement of stromal lamellae absent
  3. Irregular arrangement of collagen fibers; variable in diameter
  4. Collagen fibrils thickened (up to 1500 Å in diameter); resemble scleral fibrils
  5. Diameter of collagen fibrils decreases in posterior stroma
  6. Changes in posterior cornea may resemble those seen in Peters' anomaly

- somatic abnormalities such as mental retardation, anomalies of the skin, facies, ears, cerebellum, and testes.
- DD: arcus juvenilis, interstitial keratitis, Peters' anomaly, and microcornea

- **Congenital glaucoma**
  - epiphora, photophobia, and blepharospasm
  - first signs are elevated intraocular pressure, corneal enlargement and clouding, and optic nerve cupping
  - increased corneal diameter
  - tears in Descemet's membrane can be single or multiple, and appear as elliptical, glassy, parallel ridges on the posterior cornea, either peripherally or across the visual axis. In congenital glaucoma these breaks have a random distribution, most commonly ***horizontal or concentric to the limbus***, in contrast to the ***oblique and vertical orientation of the breaks in Descemet's membrane seen in birth trauma***

- **Birth trauma**

- **Left eyes** seem to be affected more commonly than right eyes because neonates usually present in the **left-occiput-anterior position**
- The Descemet's tears in birth trauma are usually **unilateral, central** and, in contrast to congenital glaucoma, line up in a **vertical or oblique** pattern, presumably because the tip of the forceps has slipped over the rim of the orbit and compressed the globe vertically, stretching it horizontally to create the tears.
- corneal edema usually clears within weeks to months.
- high residual corneal astigmatism, which may range from 4 to 9 diopters, requires urgent correction and amblyopia treatment.

- **HSV Infection**
  - **80% HSV type 2** and 20% by type 1.
  - primary ocular infection that can later become recurrent
  - CNS involvement are common and are associated with significant mortality
  - usually apparent within 2 days to 2 weeks
  - **macrodendrites, geographic epithelial defects, and punctate keratopathy**.
  - An **oral ACV-cesarean combination** provides maximal protection for the neonate.
  - The treatment for neonatal HSV keratitis or conjunctivitis is **intravenous aciclovir**.

- **Congenital rubella**
  - Congenital rubella infection, however, causes microphthalmia, cataract, retinitis, iridocyclitis, corneal clouding, strabismus, nystagmus, nasolacrimal duct obstruction, and viral dacryoadenitis.

- **Bacterial corneal ulcers**
  - exceedingly rare in the neonate
  - Gonorrheal ophthalmia neonatorum usually presents as a unilateral conjunctivitis with an incubation period of a few hours to 2–3 days.
  - Ophthalmia neonatorum caused by Chlamydia: systemic erythromycin

- Congenital syphilis is not a cause of congenital corneal opacification.

- **Neurotrophic keratitis**
  - Familial dysautonomia (Riley–Day syndrome)

- **Metabolic diseases**: They are all autosomally recessive, with the exception of mucopolysaccharidosis type II (**Hunter's** syndrome), which is X-linked recessive.
  - ***Mucopolysaccharidosis***
    - **Hurler's syndrome** (MPS I-H) or gargoylism is caused by a deficiency of alfa-l-iduronidase and the gene involved with this error is mapped to 4p16.3. **Corneal clouding is significant** and helps differentiate this disease from Hunter's syndrome.
    - Hurler's, Scheie's, Morquio's, and Maroteaux-Lamy syndromes all demonstrate progressive corneal clouding. Hunter's and Sanfilippo's syndromes do not demonstrate clouding grossly, but may have slit lamp evidence of clouding at a later age.
  - ***Mucolipidosis***
    - Episodic ocular pain is an important symptom in mucolipidosis type IV. It is caused by corneal epithelial cytoplasmic accumulation of abnormal material with subsequent corneal surface irregularities.
  - Cystinosis: AR, needle-like cystine crystals in the cornea and conjunctiva is usually seen by 1 year of age.
  - Fabry's disease: sphingolipidosis caused by a lack of alfa-galactosidase A
  - Tyrosinemia: type II (**Richner-Hanhart syndrome**) is a rare congenital error of metabolism characterized by a triad of dendriform keratitis, hyperkeratotic lesions of the palms and soles, and mental retardation.

- **Peters' anomaly:**
  - Sporadic, AR, AD
  - central corneal opacity with corresponding defects in the posterior stroma, Descemet's membrane, and the endothelium.

- Synechiae frequently extend from the ***iris collarette to the edge of the posterior corneal*** defect
- **glaucoma 50-80%** → incomplete development of angle
- bilaterally 80%, asymmetric
- **Type I:** Corneal opacity + iridocorneal adhesions
  - systemic abnormalities are uncommon
- **Type II:** Corneal opacity + iridocorneal adhesions + lens abnormality (position or transparency)
  - **Peters'-plus syndrome**: Peters' anomaly + short stature, brachymorphy, mental retardation, abnormal ears, and, in some patients, cleft lip and palate
  - **Krause-Kivlin syndrome**: Peters' anomaly + facial abnormalities, disproportionate short stature, retarded skeletal maturation and developmental delay (probably inherited in an autosomal recessive manner)
- **Histopathology of Peters' anomaly**
  - Central concave defect in the posterior corneal stroma (posterior ulcer)
  - Disorderly stromal lamellae in ulcer bed
  - Absence of corneal endothelium and Descemet's membrane in the posterior ulcer
  - Corresponding area of central corneal edema and opacification
  - Keratolenticular adhesions to posterior cornea in some cases
  - Iridocorneal adhesions to margin of ulcer in some cases
  - Bowman's layer thickened or absent
- **differential diagnosis:** Von Hippel's internal corneal ulcer, sclerocornea, dermoid, CHED, and PPCD
- **proposed causes**: incomplete central migration of corneogenic mesenchyme (i.e., neural crest cells), accounting for posterior endothelial and stromal defects

- **Posterior keratoconus**

- very uncommon, mildest variant of Peters' anomaly
- nonprogressive and usually sporadic
- unilateral/ bilateral
- Descemet's excrescences can also be present in or just outside of the area of involvement. The corneal endothelium and Descemet's membrane are present.

- **Congenital anterior staphyloma**
  - protuberant congenital corneal opacity.
  - secondary to an intrauterine infection or related to a developmental abnormality such as a severe type of Peters' anomaly

- **CHED**
  - 1960 by **Maumenee**
  - **CHED 1**: **AD**, 20p11.2-q11, clouding is slowly progressive over 1–10 years. presents with photophobia and epiphora and the subsequent development of corneal clouding.
  - **CHED 2**: **AR**, 20p13 (Solute Carrier Family), previously referred to as Maumenee cornea dystrophy. ***bilateral corneal clouding at birth*** or shortly thereafter. The corneal changes are stable and do not progress or regress. There are no associated symptoms, such as epiphora or photophobia, but patients often develop nystagmus.
  - **DD**: CSCD, congenital glaucoma, PPCD, Peters' anomaly, and inborn errors of metabolism, especially the mucopolysaccharidoses

- **PPCD**
  - bilateral, nonprogressive, asymptomatic disease that rarely requires penetrating keratoplasty.
  - One form may present with congenital corneal edema, It is important to differentiate PPCD from CHED, because the treatment is different

- **CSCD**
  - **decorin** gene on chromosome 12
  - anterior stroma demonstrates a diffuse, flaky-feathery opacification caused by corneal lamellar irregularities

- **Congenital Dermoids**
  - solid benign congenital tumors → **choristomas**
  - yellowish-white, solid, vascularized, elevated nodules straddling the corneal limbus.
  - Sporadic, genetically mapped to chromosome Xq24-qter
  - **grade 1:** small, usually measuring 5 mm in diameter or less, single, limbal or epibulbar, 1/3 Goldenhar's syndrome → epibulbar dermoids, preauricular appendages, and pretragal fistulas.
  - **grade 2**: larger, covering part of or the entire corneal surface, with varible depth, generally does not involve Descemet's membrane or the corneal endothelium. It is the most important type in the differential of congenital corneal opacities.
  - **grade 3**: entire anterior segment, Microphthalmos is common, and posterior segment abnormalities
  - **Mx**: limbal dermoids are more of cosmetic problem → cut flush with the corneal surface, but it may recur. Penetrating keratoplasty for central dermoids if they are 7 mm or less. Larger central dermoids require a two-stage procedure: first the tumor is excised and a large lamellar graft is placed in the bed; once that is healed, a smaller central penetrating keratoplasty is performed

- **Corneal Keloids**
  - ***fibrous tissue proliferations*** that represent the exuberant response of embryonic connective tissue to injury.
  - white, sometimes protuberant, glistening, masses
  - presence of myofibroblasts in these lesions, differentiating them from Salzmann's nodules.
  - can be associated with Lowe's syndrome

Peripheral Corneal Disease

- portion located between the central 50% of the cornea and the limbus.
- thickest region of the cornea, which is directly adjacent to the corneal limbus and internal angle structures

- **Congenital/Developmental/Inherited Disorders:**
    - **Lattice dystrophy type II** is associated with systemic amyloidosis and primarily involves the peripheral cornea.
    - **Wilson's disease**: orangey-brown ring in the periphery of the cornea, Kayser–Fleischer ring consists of copper which is deposited in Descemet's membrane.
    - **Sclerocornea and cornea plana**:
    - **posterior embryotoxon**: a thickened, prominent Schwalbe's line, which is more anteriorly located than normal. 15% of the normal eyes. When it is associated with other peripheral corneal abnormalities, including multiple peripheral iris strands, it is termed Axenfeld–Rieger anomaly

- **Inflammatory/Autoimmune Disorders**
    - **rheumatoid arthritis**: KCS, sclerosing keratitis, peripheral corneal furrow
    - **Polyarteritis nodosa**: eye in 20% of cases, bilateral peripheral keratitis
    - **Wegener's granulomatosis**: Two forms of the ocular disease have been described: a severe progressive disease, which has a 1-year mortality of 82% if untreated; and a limited, less severe form.
    - **Marginal keratitis:** ocular hypersensitivity reactions to toxins produced by bacteria that commonly colonize the eyelids
    - **Phlyctenulosis** is an inflammatory disorder which is similar to marginal keratitis but involves a more severe reaction
    - **Mooren's ulcer** produces a painful progressive peripheral ulceration of the cornea.

- **vascular pannus**: blood vessels and fibrous connective tissue from the limbus grow onto the peripheral cornea
- **Superior limbal keratoconjunctivitis (SLK):** inflammatory disorder of unknown etiology which is associated with a peripheral corneal pannus, a punctuate keratopathy, a thickened superior conjunctiva which is chemotic and hyperemic, and a filamentary keratitis.

- **Neoplastic Disorders**
  - Pterygium:
  - pyogenic granuloma
  - Dermoid tumors
  - squamous metaplasia
  - carcinoma in situ or intraepithelial neoplasia (CIN)

- **Degenerative Disorders**
  - Corneal arcus
  - Lipid keratopathy: primary & secondary
  - White limbal girdle of Vogt: type 1 & 2
  - **Calcific band keratopathy**: intraocular inflammation, trauma, multiple eye surgeries, elevated serum calcium, or other systemic disorders. The deposition initially begins in the peripheral cornea, with a clear margin separating the deposit from the limbus. The clear interval is thought to represent the anatomic limit of Bowman's layer. Throughout the band are clear, small holes that give a ‘Swiss cheese’ appearance. The holes occur at sites where corneal nerves penetrate Bowman's layer.
  - **Calcific degeneration**: the calcium may be associated with a fibrovascular pannus or may occur deep in the corneal stroma, as opposed to calcific band keratopathy in which the calcium deposition is confined to the region of Bowman's membrane.
  - Corneal epithelial stem cell deficiencies
  - Terrien's marginal degeneration

- Pellucid marginal degeneration
- **Furrow degeneration**: elderly, not a true thinning but rather an optical illusion
- Dellen: areas of thinning or excavation. The overlying epithelium is usually intact,

- **Infectious Disorders**
  - Microbial keratitis
  - Herpes

Corneal Ulcer

Always search for →

1. infectious agent
2. local host factors
3. exogenous risk factors
4. endogenous factors: autoimmune disease, inflammatory, immunocompromised

Corneal Edema

1. **Primary endothelial failure**: FECD, CHED, PPCD, ICE
2. **Secondary endothelial failure**: Trauma, chemical, hypoxia
3. **Normal endothelium**: increased IOP
4. **Epithelial failure**: Epithelial Defect

- **Ancillary tests**
  - Pachymetry
  - Specular microscopy

- In vivo confocal microscopy
- Anterior segment optical coherence tomography

- **Treatment**
  - Treatment of inflammation and the underlying cause of inflammation
  - decreasing the pressure can improve or resolve corneal edema and prevent further damage to endothelial cells. Inhibition of corneal carbonic anhydrase pumps by topical CAIs may lead to decreased fluid flow from stroma to aqueous and progression to corneal edema.
  - Hypertonic agents
  - Bandage contact lens
  - **Anterior stromal cautery**: Application of light burns to Bowman's layer using a thermal cautery (**Salleras procedure**)
  - Conjunctival flap
  - Amniotic membrane
  - Excimer laser
  - Penetrating keratoplasty
  - Endothelial keratoplasty

Corneal Deposits

- **three depths**: superficial, stromal, and deep stromal.
- **three categories**: pigmented, nonpigmented, and refractile/crystalline.

  (see tables in prints)
- **Epithelial iron lines**: Iron lines can be seen in the palpebral fissure **(Hudson-Stahli),** at the head of a pterygium (**Stocker**), surrounding the cone in keratoconus (**Fleischer**), at the head of a filtering bleb (**Ferry**), adjacent to areas of corneal elevation such as

Salzmann's nodular degeneration, anterior to the sutures in keratoplasty (**Mannis**), and after keratorefractive surgery.

- **Coat's white ring** is a superficial ring of iron deposition that remains after a metallic foreign body is removed. Small white opacities may be seen inside the ring. These rings develop when a rust ring from an iron foreign body is not entirely removed.

Red Eye

- Redness is not a symptom, but a nonspecific sign. The three major processes responsible for the majority of cases are subconjunctival hemorrhages, inflammation, and vascular abnormalities.

Eye Banking

- first formally organized eye bank established in New York in 1944
- **The FDA required testing includes**:
    1. HIV 1-2 antibody
    2. Hepatitis B & C antibody
    3. Syphilis testing
    4. HIV & HCV NAT testing (nucleactic acid DNA/MNA)

- The Uniform Anatomical Gift Act (UAGA) of 1968 stated that a signed and witnessed donor card was sufficient legal permission for organ or tissue removal after death.
- ***CMV, HSV is not contraindications***
- Eye malignancy like RB, Anterior segment Carcinoma like Adenocarcinoma etc. are contraindication. *Systemic malignancies are **not** contraindications **except lymphoma/ leukemia**.*

- **Primary Graft Failure**: currently believed to be about **1%**. Causes include pre-existing corneal endothelial abnormalities, damage during recovery or storage, and surgical trauma.

Corneal Storage Media

- First corneal preservation was done by **Magitot** in 1911. He stored cornea in **Hemolyzed blood serum** at 5-7deg.centigrade and Cornea was viable for 2 days. (JAMA)
- BASE MEDIA
    - **Tissue-culture199-**aminoacids, salts, buffer & energy to support life.
    - **Minimum Essential Media(MEM) with Earles salt**- matches natural salts & buffers of human tissue, electrolytes similar to aqueous
- BUFFER: **HEPES**(N-2-hydroxyethyl-piperazine-N-2ethane-sulfonic acid)
    - used for cultivation of sensitive mammalian cells
    - provides optimal physiological PH in the range7-7.2
- ANTIBIOTIC: Gentamicin only /& Streptomycin
- DEXTRAN
    - Polysaccharide, negatively charged.
    - Prevents tissue swelling.
    - Used alone does not provide sufficient tissue stability & viability for extended storage.
- CHONDROTIN SULFATE
    - Polysaccharide, negatively charged
    - Endothelial integrity & acts as osmotic agent. Superior to dextran. Longer storage time
- ENRICHED
    - Various salts, amino acids essential &non-essential, vitamins, phosphates & antioxidants to enhance cell & tissue viability & health during storage.

- ATP precursors → Provide energy for pumping function.
- Anti-Oxidants →Neutralize metabolic waste, maintain DNS synthesis
- Vitamins →Provides additional nutritional cell supplements.
- Sodium Pyruvate & Glucose → Energy supply
- Color Phenol Red-->Visual aid for pH indication.
- *CHECK MEDIA*
    - The cornea which is stored in MKmedia, Dexol, optisolGS.
    - The following parameters to be checked before using
    - Intact seal, Expiry date, Turbity, Colour (rose red),precipitates & FB.
    - COLOUR CHANGE INDICATES
        - Yellow-- Bacterial contamination.
        - Red--- Unacceptable Ph.
        - Cloudy—Contamination

- STORAGE TYPES
    - **SHORT-4deg.C(days)**
        - Moist chamber(1day)
            - Filatov & Castroviejo.
            - Whole globe is stored in a sterile jar having saline Humidification at Temp of 4 degrees C.
            - Popular until 1970.
        - M.K. Media (4days)
            - Tc199
            - Dextran 40 1%
            - PH 7.0-7.5

- Osmolality 295-355
- gentamycin sulphate 75-150 micro gm/ml
- HEPES as buffer.
- Phenol red as indicator.

- **INTERMEDIATE-14days- 4deg.C(wks)**
  - K-Sol
    - Tc 199, MEM & Earles media, HEPES, Gentamicin, Chondroin sulphate 2.5%
    - 1988 proprionibacteria contamination
  - Dexol
    - MEM
    - 1.35%Chondrotin Sulphate
    - 1mM Sodium pyruvate,
    - 1mM non- essential amino acids
    - Antioxidants
    - 1% dextran40.
  - Optisol GS
    - Introduced in 1991
    - MEM
    - 1.35% Chondrotin Sulphate
    - 1mM Sodium pyruvate
    - 1 mM non-essential aminoacids
    - Antioxidants
    - 1%dextran40, ATP, Iron, cholestrol,
    - L-hydroxyproline, Vitamins

- 2 antibiotics- Gentamycin, Streptomycin

- Procell
  - MEM,1.35%chondrotin sulphate,1mM sodium pyruvate1mM,Non-essential aminoacids,Antioxidants,Dextran40,
  - Humen insulin10mic.g/ml & Human epidermal growth factor(hEGF10ng/ml) to improve long term endothelial survival after PKP.
- Eusol-C
  - Store at 4deg.C
  - Storage time 14 days
  - SIMILAR TO DEXOL
  - Dextran, Sodium Piruvate, Glucose, Essential & non-essential aminoacids, mineral salts, Vitamins, Gentamin, hepes buffer, Bicarbonate, Phenol Red.

- **LONG(months)**
  - Organ culture
    - 1936, by Archer & Trevor-Roper.
    - Being used since1974.
    - Refrigeration not required.
    - Complicated, expensive & well trained microbiologist.
    - Contents: Eagles media, Earles salt without L-glutamine,L-glutamine1%final conc, Decomlemented calf serum10%final conc. Penicilllin 100 units/ml,, Gentamicin100microgram/ml. Amphoterician B 0.25% microgram/ml.
    -
  - European Organ culture-120days(37deg.C)
    - 31-37deg.C, EMEM, MEM, IMDM ,
    - HEPES, NaHCO3,Peni,Strep,Ampo-B,

- BOVINE SERUM 2-10ML,Dextran4-10%

- Eurosol-31deg.C-28days(New)
  - Duration of storage 28days.
  - Temp 31deg.C.
  - Better than the European culture media.
  - Maintains intact endothelium, epithelium & Keratocyte
- Cryopreservation-Unlimited-(-80degC)
  - Kaufman & Capella.1954
  - Cornea is stored in Liquid Nitrogen with **Dimethyl Sulfoxide (DMSO).**
  - DMSO, Prevents intracellular damage by ice crystals.
  - Not a procedure used.Holds a lot of research interest.
- *GLYCERINE PRESERVATION*
  - Patch graft or Lamellar Keraoplasty.
  - Corneo-scleral button.
  - 100%glycerine.
  - Enothelium is nonviable
  - Use with in 1 year.
  - Stored at room temp.

Diseases of the Lid

Anatomic Abnormalities

- **Entropion**
- **Ectropion**
- **Trichiasis and Distichiasis**
- **Floppy Eyelid Syndrome**
    - primarily a disorder of sleeping position
    - ocular irritation, mucous discharge, and papillary conjunctivitis.
    - histopathologic features of the floppy eyelid syndrome point primarily to a **marked reduction in eyelid tarsal elastin**
    - Identification of sleep apnea and institution of CPAP to allow a supine sleep position is paramount
- **Lid Imbrication Syndrome**
    - **abnormality of lid apposition in which the upper lid overrides the lower**, thereby allowing the lower lashes and keratinized epithelium to rub chronically against the upper eyelid marginal tarsal conjunctiva.
- **Lagophthalmos**
- **Eyelid Retraction**

Blepharitis

- Numerous classifications
    - **Fuchs**
        - blepharitis squamosa, which is characterized by small, dry scales
        - blepharitis ulcerosa, characterized by marginal crusting covering frank ulceration

- **Duke-Elder and MacFaul**
  - squamous blepharitis, which they described as a superficial, nondestructive dermatitis with eczema-like inflammation
  - Follicular blepharitis characterized as a deeply seated, purulent process
- **McCulley**
  1. staphylococcal disease
  2. seborrheic blepharitis
  3. both staphylococcal and seborrheic diseases
  4. meibomian seborrhea
  5. Seborrheic with secondary meibomitis
  6. Primary meibomitis (also known as meibomian keratoconjunctivitis)
  7. blepharitis associated with other conditions such as psoriasis and atopy.
- **practical standpoint of McCulley's**
  - anterior blepharitis (comprising the first three)
  - posterior blepharitis (comprising the remaining meibomian-related groups).

- **four principal arms of therapy for all of the categories of blepharitis**
  1. lid hygiene
  2. topical antibiotics
  3. systemic antibiotics (specifically tetracycline)
  4. corticosteroids

Meibomian Gland Dysfunction

- term first suggested by **Korb and Henriquez.**

- The meibomian gland secretion, which is distinct from sebum has been termed meibum by Nicolaides et al.
- **Meibography** is a technique that uses transillumination biomicroscopy of the everted eyelid with infrared photography
- Meibomian gland dysfunction →increases tear electrolytes uniformly

  lacrimal gland disease → sodium ions rise disproportionately in secretion at low flow rates
- The lipid layer is about 40–100 nm thick.
- Blinking is important for the excretion of meibomian lipid.
- **Meibometry** is used to measure the amount of lipid on the lid margin by determining the degree of translucency induced on plastic tape applied to the lid margin.
- **Tear film break-up time** is reduced in meibomian gland dysfunction.
- **Classification**
  - **McCulley et al. (1982)**
  - **Mathers et al. (1991)**
    - Seborrheic:
    - Obstructive:
    - Obstructive with sicca:
    - Sicca:
  - **Bron et al. (1991)**
    - Reduced number (congenital deficiency)
    - Replacement (trichiasis, metaplasia)
    - Hyposecretion
    - Obstructive meibomitis subdivided into focal, primary, secondary to local disease or systemic disease, and chalazia
    - Hypersecretory (seborrhea)
    - Neoplastic
    - Suppurative

- **Diagnosis**
    - burning, irritation, itching, red eyes, and decreased or fluctuating vision
    - The lid margin is often rounded with thickening, erythema, hyperkeratinization, vascularization, telangiectasia, or notching.
    - An increase or reduction in the number of orifices may be seen.
    - orifices are frequently less well defined or may show pouting
    - secretion instead of being clear, it is turbid, granular, or toothpaste-like
    - meibography → narrowing or occlusion of the glandular orifices and glandular distortion or dilation
    - meibometer: lipid imprint is then analyzed using a density measuring device
- **Associated Conditions**
    - lacrimal insufficiency
    - Rosacea
    - Giant papillary conjunctivitis (GPC)
    - Contact lens intolerance
    - Chalazia
- **Histopathology**
    - Obstruction, hyperkeratinization
- **Lipid Composition**
    - neutral sterol and wax esters with lesser amounts of polar lipids, diesters, triesters, triglycerides, free fatty acids, and free sterols.
    - cholesterol esters are always present in patients with meibomian gland dysfuncton
    - Unlike meibomian gland secretion, ***sebum*** *contains more triglycerides and free fatty acids and considerably less sterol esters. Squalene is present in sebum and absent in meibomian gland secretion.* The wax ester proportion is similar in both secretions. Overall, sebum is much more polar and will contaminate the tear film when mixed with it.

- Three of the bacteria commonly isolated from eyelids, S. aureus, Corynebacterium species (CN-S), and P. acnes, produce lipases that can alter the composition of meibomian lipids.
- Tetracycline ***reduces lipase*** production in S. epidermidis, S. aureus, and P. acnes. It also decreases serum cholesterol in mice, has ***antichemotactic*** effects on neutrophils, and has activity against ***collagenase and other metalloproteinases***. Any of these properties may produce a marked therapeutic effect in many patients with meibomian gland dysfunction and rosacea.
- **Treatment**
    - lid hygiene
        - Warm compresses:
        - Lid massage:
        - Lid scrubs:
    - Systemic antibiotic therapy consists of oral tetracycline, 250 mg four times a day; **doxycycline, 50–100 mg twice a day**, or minocycline, 50 mg twice a day.
    - Topical therapy consists of antibiotics and anti-inflammatory drugs.
    - treatment of associated conditions.

Disorders of Tear Production

- 1995 National Eye Institute (NEI)/Industry Dry Eye Workshop: Dry eye is a disorder of the tear film due to tear deficiency or excessive evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort.
- **International Dry Eye WorkShop (DEWS)** in 2007: dry eye is defined as multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface
- **Lacrimal Functional Unit (LFU):** ocular surface (cornea, conjunctiva, accessory lacrimal and meibomian glands), the main lacrimal glands, the blink mechanism that spreads tears, and the sensory and motor nerves.
- **Pathophysiology**

1. **Tear hyperosmolarity** is regarded as the central mechanism causing ocular surface inflammation, damage, and symptoms, and the initiation of compensatory events in dry eye.

2. **Tear film instability** can arise secondary to hyperosmolarity, or can be the initiating event

   The core mechanisms responsible for dry eye disease are tear hyperosmolarity and tear film instability. The major causes of tear hyperosmolarity are reduced aqueous tear flow and/or increased tear evaporation. Tear hyperosmolarity induces cascades of inflammatory events that result in damage to the surface epithelium, nerve endings, and ultimately tear film instability. This instability exacerbates ocular surface hyperosmolarity and completes the vicious circle. Tear film instability can also be initiated by other etiologies, including xerophthalmia, ocular allergy, topical preservative use, and contact lens wear.

- **Dry Eye Diseases DED** → aqueous tear-deficient dry eye (ADDE) and evaporative dry eye (EDE)

- **aqueous tear-deficient dry eye (ADDE)**
  - Sjögren's syndrome dry eye (SSDE)
  - Non-Sjögren's syndrome dry eye (NSSDE)
    - Primary lacrimal gland deficiencies
      - Age-related dry eye (ARDE)
      - Congenital alacrima:
    - Secondary lacrimal gland deficiencies
      - Lacrimal gland infiltration:
      - Obstruction of the lacrimal gland ducts
    - Reflex hyposecretion
      - Reflex sensory block: DM, Neurotrophic Keratitis
      - Reflex motor block
- **Evaporative dry eye (EDE)**
  - Intrinsic causes
    - Meibomian gland dysfunction
    - Disorders of lid aperture and lid/globe congruity or dynamic
    - Low blink rate
  - Extrinsic causes
    - Ocular surface disease
    - Contact lens wear

- **Diagnosis:**

- ***History***: foreign body sensation, burning, stinging, itching, dryness, soreness, heaviness of the lids, photophobia, and ocular fatigue. An important clue is exacerbation of symptoms by certain activities or environmental conditions.
- ***Physical examination***
  - **dynamics of blinking**: a) frequency of blinking; b) variation of blink intervals; c) size of the palpebral aperature, and d) adequacy of lid closure.
  - **Malposition of the lids**: a) entropion; b) ectropion; c) eversion of the lacrimal puncta; d) cicatrical malposition; e) dermatochalasis; and f) swelling of the lacrimal gland.
- ***Diagnostic tests***
  - **Tear film stability:**
    - tear breakup time (TBUT) test:
    - noninvasive breakup time, or NIBUT: It involves projecting a target onto the convex mirror surface of the tear film and recording the time following a blink for the image to break up. The test has been performed using custom-built devices such as **Tearscope** or keratometry devices.
    - arbitrary cutoff time of 10 s for both fluorescein-added and noninvasive techniques appears quite specific
    - Ocular Ferning Test
    - Impression cytology
  - **Diagnostic dye staining:**
    - **Fluorescein sodium**: dye diffuses rapidly in the intercellular spaces and staining indicates increased epithelial permeability
    - **Rose Bengal**: more sensitive for staining the conjunctiva; however, it is not tolerated as well and frequently causes irritation, stains devitalized epithelial cells as well as epithelial cells that lack a healthy layer of protective mucin coating.
    - **Lissamine green B** is similar to rose Bengal in its staining characteristics, and produces much less irritation after topical administration than rose Bengal

- **Van Bijsterveld** reported a grading scale that evaluates the intensity of staining based on a scale of 0–3 in three areas: nasal conjunctiva, temporal conjunctiva, and cornea.

- **Corneal sensation**
  - cotton swab
  - Cochet–Bonnet esthesiometer
- **Tear film composition**
  - Osmolarity: well-validated cutoff value of 316 mmol/L for dry eye disease.
  - Tear protein analysis:
    - tear lysozyme: sensitivity and specificity >95%
    - Lactoferrin: Lactocard→ relative indicator of lacrimal gland function
- **Aqueous tear flow and turnover**
  - **Schirmer test:** Van Bijsterveld selected 5.5 mm strip wetting in 5 minutes for the Schirmer test without anesthesia to diagnose aqueous tear deficiency.
  - **phenol red-impregnated thread test (PRT):** cutoff value of 10 mm at 15 seconds, the sensitivity and specificity of the PRT have been shown to be 56% and 69%.
- **Delayed tear clearance:** increased tear cytokine concentration, which may contribute to chronic inflammation
  - fluorescein clearance test (FCT): detect the amount of residual fluorescein by Schirmer strip or use a fluorophotometer
- **Other noninvasive methods**
  - **Tear meniscus height (meniscometry):** meniscus radius of curvature <0.25 mm suggests a dry eye condition.
  - **Interferometry** of the tear film lipid layer is useful in screening and evaluating dry eye.

- **Systemic Work-Up**: anti-SS-A, anti-SS-B, rheumatoid factor, ANA, ESR, CRP

- **Management**
  - **Tear supplementation: lubricants**
    - electrolytes, surfactants, and various types of viscosity agent
    - Osmolarity: 181 to 354 mmol/L
    - Compatible solutes are small nonionic molecules (e.g., glycerin) Optive and Refresh Endura (with 0.9% and 1% glycerin)
    - Colloid osmolality (which relates to macromolecule concentration)
    - **Viscosity** agents: Macromolecular complexes → carboxymethylcellulose, polyvinyl alcohol, polyethylene glycol, propylene glycol, hydroxypropyl-guar (HP-guar), and lipids such as those that make up castor oil or mineral oil.
    - **Lipid-containing** artificial tear products such as Refresh Endura (with castor oil) and Soothe XP (with mineral oil) are intended to reduce tear evaporation by restoring the lipid layer of the tear film; this may be particularly useful in patients with MGD.
    - **HP-guar** (in products such as Systane) is believed to form a bioadhesive gel when exposed to ocular pH, increasing aqueous retention and protecting the ocular surface by mimicking the mucous layer of the tear film.
    - **two main types of preservative:**

1. ***Detergent*** preservatives act by altering bacterial cell membrane permeability.
    - BAK
2. ***Oxidative*** preservatives penetrate the bacterial cell membrane and act by interfering with intracellular processes. They are sometimes referred to as 'vanishing' preservatives because they dissipate on contact with the eye and are therefore less likely than detergents to cause ocular damage.
    - Stabilized oxychloro complex

  - **Tear retention**
    - **Punctal occlusion**: Punctal and intracanalicular plugs, argon laser,

2 types: absorbable are made of collagen or polymers and last for variable periods (3 days to 6 months). The nonabsorbable 'permanent' plugs include the Freeman style, which consists of a surface collar resting on the punctal opening, a neck, and a wider base, and are made of silicone or hydrophilic acrylic.

- **Moisture chamber spectacles:**
- **Contact lenses**: Boston scleral lens, Mini-scleral lens (**Jupiter Lens**)

- **Tarsorrhaphy**
- **Tear stimulation**: secretagogues
  - diquafosol (P2Y2 receptor agonists)
  - Orally administered cholinergic agonists, in particular pilocarpine and cevilemine
- **Biological tear substitutes**
  - **Serum**: Concentrations between 20% and 100% o
  - Salivary gland autotransplantation
- **Anti-inflammatory therapy**
  - ***Ciclosporin***
    1. Decreases proinflammatory cytokines (e.g., conjunctival IL-6 levels)
    2. Decreases activated lymphocytes in the conjunctiva
    3. Decreases conjunctival inflammatory and apoptotic markers
    4. increases conjunctival goblet cell numbers.
    - 0.05% and 1%, 2%
  - ***Corticosteroids***: inhibition of the activity of transcription factors such as activator protein-1 (AP-1) and nuclear factor κB (NFκB), that are involved in the activation of proinflammatory genes
    - loteprednol etabonate 0.5%
    - androgenic steroids

        - ***Tetracyclines***: antibacterial, anti-inflammatory, inhibits MMPs and IL1 production and protease inhibitory properties.
        - ***Essential fatty acids***: a higher omega-6:omega-3 ratio was associated with a significantly greater DED risk. omega-3 fatty acids (e.g., EPA found in fish oil) inhibit the synthesis of these lipid mediators and block the production of IL-1 and TNF-alfa.
    - **Topical vitamin A** (retinol)
        - Reversal of squamous metaplasia
        - Increased production of type I collagen
        - Promotes regeneration of conjunctival goblet cells and can re-establish intracellular conjunction of conjunctival epithelium
    - **Mucolytics**: Inhalational acetylcysteine is diluted to concentrations of 5–20% (most commonly 10%) for off-label use as a topical ophthalmic agent.

- **Treatment Guidelines**
    - In 2007 the Management and Therapy Subcommittee of the International Dry Eye WorkShop (DEWS) adopted a modified form of the ITF (International Task Force) severity grading. **(DELPHI Panel)**
    - ITF- ciclosporin at level 2 & Plugs at level 3
    - DEWS- ciclosporin & Plugs at level 2

Conjunctival Tumors

Squamous Neoplasms of the Conjunctiva

Read OSSN article form DOS

Conjunctivitis

- The conjunctival epithelium is contiguous with the corneal epithelium and also lines the lacrimal passages and glands, a fact that has significant clinical implications.
- The substantia propria is composed of a superficial adenoid layer and a deeper fibrous layer.
    - The **adenoid** layer: **lymphoid** tissue from which follicles are formed. Within the lymphoid tissue are germinal centers with lymphoblasts in the center.
    - The **fibrous** layer: connective tissue, which attaches to the tarsal plate and contributes to the characteristic appearance of **papillae**.
- **Conjunctival injection**: superficial bright red blood vessels, most conspicuous in the fornices and fade toward the corneoscleral limbus
- **Conjunctival hyperemia**: secondary to dilation of the conjunctival blood vessels without accompanying exudation or cellular infiltration. Due to environmental factors including smoke, smog or chemical fumes, wind, ultraviolet radiation, and prolonged topical instillation of vasoconstrictors.
- **Conjunctivitis:** inflammation of the conjunctiva and is characterized by cellular infiltration and exudation in addition to vascular dilation.
- **Chemosis**: accumulation of fluid within or beneath the conjunctiva, is frequently present.
- **Morphologic responses**
    - **Papillae**: where the conjunctiva is attached to the underlying tissue by anchoring septae, folds or projections of hypertrophic epithelium that contain a central fibrovascular core whose blood vessels arborize on reaching the surface. Micropappile < 1 mm

      giant papillae > 1 mm: vernal conjunctivitis, atopic keratoconjunctivitis, and as a foreign body reaction to suture material, contact lenses, or prostheses.
    - **Follicles**: yellowish-white, discrete, round elevations of conjunctiva produced by a lymphocytic response. Unlike a papilla, the central portion of the follicle is avascular. 0.5–2.0 mm in diameter.

Acute follicular conjunctivitis: Adenovirus, Inclusion conjunctivitis, Herpesviruses

Chronic follicular conjunctivitis: Chlamydial infections, Molluscum contagiosum, Moraxella

- **Membranes**: primarily of fibrin that has attached to the epithelial conjunctival surface. True membranes leave a raw surface and cause bleeding when peeled off, which differentiates them from pseudomembranes.

  C. diphtheria, ß-hemolytic streptococci, adenoviral, HSV, vernal conjunctivitis, inclusion conjunctivitis, and Candida. Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)

- **Cicatrizing changes**: Scar formation ensues only when there is destruction of stromal tissue.

- **Conjunctival granulomas**: affect the stroma.

- **Conjunctival exudates** may be classified as: (1) purulent or hyperacute; (2) mucopurulent or catarrhal; and (3) watery.

- **Anatomic localization**:

  - **Upper tarsal**: trachoma, contact lens wearers, patients wearing prostheses, or from exposed suture material.

  - **upper palpebral**: SLK, FES

  - **upper pretarsal**: VKC, AKC (can be in lower lid)

  - **lower tarsal**: toxic papillary conjunctivitis and the 'mucus-fishing syndrome.' The follicular response in inclusion conjunctivitis is more pronounced inferiorly than superiorly.

Bacterial Conjunctivitis

- Disruption of the host's defense mechanisms are predisposing factors for the development of bacterial conjunctivitis:

- **Risk factors**

  - Dry eye

  - Exposure

  - Nutritional deficiency/malabsorption
  - Local or systemic immune deficiency often after topical and systemic immunosuppressive therapy

- An organism may be isolated in as many as 90% of normal subjects, with more than one organism found in up to 35%. In most subjects, ***the flora is composed of aerobic staphylococci (>60%) (mostly Staphylococcus epidermidis), diphtheroids (>35%), and the anaerobe Propionibacterium acnes***, but the spectrum of bacteria and sensitivity to antibiotics varies among major age groups.
- **Manifestations**
  - Discharge
  - Membranes and pseudomembranes
  - Papillae and follicles
- **Classification**
  - **Hyperacute**: lid edema, marked conjunctival hyperemia, chemosis, and copious amounts of purulent discharge. **N. gonorrhoeae and N. meningitidis**.
    - Treatment
      - ***Systemic treatment is mandatory for patients with Neisseria conjunctivitis***; concomitant topical antibiotic therapy is optional.
      - single-dose intramuscular (IM) regimen of 1 g of ceftriaxone
      - To treat N. gonorrhoeae conjunctivitis in the newborn, 25–50 mg/kg intravenous (IV) or IM ceftriaxone administered in a single dose not exceeding 125 mg is currently recommended
  - **Acute conjunctivitis**: velvety papillary reaction, 10-14 days
    - **S. aureus**, the most frequent cause
    - **H. influenzae** (nonencapsulated) is the most common cause of bacterial conjunctivitis in young children
    - Treatment
      - topical antibiotic therapy hastens resolution, improves microbiologic cure, and may reduce morbidity, especially in culture-proven cases
  - **Chronic conjunctivitis:**

- foreign body sensation, mild stickiness and matting of the lashes, and minimal discharge.
- **S. aureus and M. lacunata**
- short-term topical therapy is often ineffective.
- Long-term therapy is required and, if there is concomitant blepharitis, the therapeutic regimen should include lid hygiene, lid margin cleansing with a mild baby shampoo diluted 50% with water, and the nightly application of an antibiotic ointment with good Gram-positive coverage, such as bacitracin, to the lid margins.
- Adjunctive oral therapy with 100 mg doxycycline one to two times a day.

Viral Conjunctivitis

- **Hallmark**: **follicular reaction** of the conjunctiva
- **RNA**: benign forms of conjunctivitis
  - Picornaviruses: most common causes of acute hemorrhagic conjunctivitis (AHC).
  - Paramyxoviruses: measles, Newcastle disease, and mumps

    Measles: Catarrhal conjunctivitis, superficial keratitis, and photophobia are the most common clinical features in healthy individuals. Keratitis is usually severe in patients with vitamin A deficiency.

    Newcastle disease is limited to poultry workers and laboratory personnel.

    Mumps is an acute viral infection characterized by swelling (more commonly bilateral) of the parotid salivary glands.
  - Togaviruses: Rubella (German measles)
  - Flaviviruses: Yellow fever
- **DNA**: associated with **vision-threatening forms** of inflammation
  - ***Adenoviruses***: MCC of viral conjunctivitis. six subgenera (A–F). **D is most common.**
    1. Pharyngoconjunctival fever (PCF) is characterized by pharyngitis, follicular conjunctivitis, fever, and adenopathy (preauricular and cervical).

2. Epidemic keratoconjunctivitis (EKC) is the severest ocular disease caused by adenoviruses. 8,19,37
3. Acute nonspecific follicular conjunctivitis may be caused by many serotypes of adenovirus, including those classically associated with PCF and EKC.
4. Chronic conjunctivitis is the least common form of adenovirus conjunctivitis.

   Stages: 0 to 5

   Treatment: preventing the transmission and complications. Cold compresses, Pseudomembranes and membranes should be removed, topical antiinflammatory agent- Steroids/ NSAIDs.

- ***Herpes simplex virus (HSV)***
  - usually a benign condition except in neonates when the herpetic infection can be associated with fatal disease and should be promptly treated.
  - commonly diagnosed in dendritic/geographic ulcers, disciform keratitis, and keratouveitis
  - Treatment of HSV conjunctivitis in the neonate is mandatory and should include both topical antiviral and intravenous acyclovir. A pediatric consultation should be obtained.

- Varicella-zoster virus (VZV)
- Molluscum contagiosum is a human host-specific poxvirus.

Chlamydial Infections

- In humans the largest burden of ocular disease is caused by C. trachomatis.
  - Serovars **A, B,Ba and C** are associated with **trachoma**.
  - Serovars **D-K** are causative of adult or neonatal **inclusion conjunctivitis** as well as urogenital diseases.
  - serovars **L1-3** are associated with **lymphogranuloma venereum**.

- It uses the cellular machinery of the host to provide it with energy for metabolic activity.
- The RB is the classic metabolically active intracellular form. In contrast, the EB exists only in an extracellular form. This form is metabolically inactive, possessing a rigid cell wall which is relatively impermeable to stimuli in its extracellular environment.
- **EB → IB → RB → binary fission of RB and increase in number → release**

- **Trachoma**
- third most common cause of blindness worldwide after cataract and glaucoma.
- Transmission: directly from eye to eye, fomites, flies, eye make-up, low socioeconomic status, lack of water, and poor hygiene
- WHO classification: **FISTO**
    - Trachomatous inflammation – follicular (TF): the presence of five or more follicles in the upper tarsal conjunctiva. Follicles must be at least 0.5 mm in diameter to be considered.
    - Trachomatous inflammation – intense (TI): pronounced inflammatory thickening of the tarsal conjunctiva that obscures more than half of the normal deep tarsal vessels.
    - Trachomatous scarring (TS): the presence of scarring in the tarsal conjunctiva.
    - Trachomatous trichiasis (TT): at least one eyelash rubs on the eyeball. Evidence of recent removal of inturned eyelashes should also be graded as trichiasis.
    - Corneal opacity (CO): easily visible corneal opacity over the pupil.
- The follicles around the limbus may eventually break down, and necrosis of the tissue can occur with subsequent scarring. These scars are referred to as **Herbert's pits**.
- Linear or stellate scarring on the upper tarsus can coalesce and form an '**Arlt's line**', which is suggestive of prior trachoma infection
- **Pathophysiology**
    - following the initial infection with ocular C. trachomatis, a hypersensitive state occurs such that subsequent infections results in more intense inflammation
    - Candidate antigens for inducing this hypersensitive state include the **60 kDa chlamydial heat shock protein**, the major outer membrane protein surface antigen, and lipopolysaccharide from the bacterial cell membrane,

  - reduced interferon (IFN), interleukin (IL)-2, and increased IL-4 secretion have been found to exist in subjects who progress to develop significant scarring

- **Treatment:**
  - TF/ TI → e/o azithromycin BD for 6 weeks = single dose 1000 mg oral azithromycin = 2-week course of oral tetracycline 250 mg four times daily or doxycycline 100 mg twice daily
  - TS/ TT → conservative, with ocular lubricants as well as close observation, managing trichiasis in order to avoid subsequent bacterial ulcers and corneal scarring
  - TO → manage the disability and to restore vision.
- **WHO's GET 2020 program** (Global Elimination of Trachoma by the year 2020) has adopted the so called **'SAFE'** strategy (Surgery for entropion/trichiasis, Antibiotics for infectious trachoma, Facial cleanliness to reduce transmission, and Environmental improvements such as access to clean water and control of disease-spreading flies)
- The currently accepted WHO guidelines include community-wide antibiotic treatment if there is ***>10% active trachoma in children aged 1-9 years***. This treatment should be reinstituted annually for 3 years, with reassessment at that time.

- **Neonatial inclusion conjunctivitis (NIC)**
- also known as ophthalmia neonatorum
- **0.4% and 5%**
- C. trachomatis is the single most common etiologic agent, accounting for up to 40% of cases. Other causes include Neisseria gonorrhoeae, other bacterial infections, herpes simplex virus (HSV), and chemical toxins
- NIC is associated with serovars **D-K**
- first manifestation is often bilateral conjunctival hyperemia, occurring **5-14 days** after birth. Other typical yet nonspecific signs include mucoid or mucopurulent discharge, lid edema, pseudomembranes, ***papillary reaction and not a follicular reaction,*** all occurring within the same timeframe
- Because of the systemic risk, the treatment for NIC should include **systemic antibiotics**. The current recommended therapy is oral erythromycin 50 mg/kg/day in four divided doses for 10–14 days.

- **Adult Inclusion Conjunctivitis**
- D-K, 5-14 days

- **Lymphogranuloma Venereum**
- L1-3
- Parinaud's oculoglandular syndrome, a condition in which patients present with a severe papillary conjunctivitis as well as massive tender posterior cervical and preauricular lymphadenopathy.

Ophthalmia Neonatorum

1. Chemical: 1-36 hours
2. Neisseria gonorrhoeae: 1-2 days
3. Bacterial (Staphylococcus, Streptococcus, Haemophilus): 2-5 days
4. Viral: 3-15 days
5. Chlamydia: 5-14 days

Parinaud's Oculoglandular Syndrome

- The most common bacterial cause, **Bartonella henselae**, is particularly difficult to culture.

Allergic Conjunctivitis

- Ocular allergy may be classified into **five categories** -

1. seasonal and perennial allergic conjunctivitis
2. vernal keratoconjunctivitis
3. atopic keratoconjunctivitis
4. giant papillary conjunctivitis
5. contact allergic conjunctivitis

- **Immunopathophysiology**
    - **Mast cells**, the primary inflammatory cells involved in ocular allergy, normally reside within the vascular stroma (**substantia propria**), but can be present within the conjunctival epithelium in pathologic situations.
    - early-phase response (EPR) and a dose related late-phase response (LPR)
    - two components of mast cell activation. The first is the release of preformed mediators, including histamine. The second is the synthesis of arachidonic acid and the subsequent metabolic cascade, resulting in the production of prostaglandins and leukotrienes

- **Seasonal allergic conjunctivitis (SAC)**
    - the most common form of ocular allergy
    - Tree and flower pollen in the spring, grass pollen in the late spring and early summer, and ragweed during the late summer and early fall
    - **hallmark** symptom, **ocular itching**.
    - **clear, ropy discharge** is characteristic
    - nasal and pulmonary symptoms, as the same allergens could trigger rhinitis and asthma
    - Skin testing, both prick and intradermal methods, is the most widely accepted method for allergy testing.
- **Perennial allergic conjunctivitis (PAC)**
    - a year-round variant of seasonal allergic conjunctivitis
    - 79% of these patients have seasonal exacerbations

    - most common aeroallergens implicated in PAC are found indoors, and include animal dander, dust mites, and feathers.

- **Treatment**
    - Avoiding known allergen triggers is critical.
    - itch-rub cycle: Encouraging patients to stop rubbing their eyes
    - Over-the-counter topical decongestants containing vasoconstrictors with or without antihistamines
    - The more potent **topical antihistamines**, levocabastine hydrochloride 0.05% and emedastine difumarate 0.05%, selectively block H1 receptors.
    - The **dual-acting medications**, including olopatadine hydrochloride 0.1% and 0.2%, azelastine hydrochloride 0.05%, ketotifen fumarate 0.025% (available over the counter), and epinastine hydrochloride 0.05%, have **antihistamine and mast cell stabilizing** properties
    - Traditional **mast cell stabilizers** include sodium cromoglycate 4% and lodoxamide tromethamine 0.1%.
    - Ketorolac tromethamine 0.5% and diclofenac are **NSAIDs**, which decrease the activity of cyclooxygenase, an enzyme responsible for arachidonic acid metabolism. This, in turn, reduces prostaglandin production, most notably the highly pruritic PGE2 and PGI2.
    - Topical corticosteroids are highly effective therapy for ocular allergy, blocking most allergic inflammatory cascades
    - Oral antihistamines are seldom used to treat isolated seasonal or perennial allergic conjunctivitis

- **Vernal Keratoconjunctivitis**
    - chronic, bilateral, conjunctival inflammatory condition found in individuals predisposed by their atopic background
    - onset: 2-10 year → lasts till puberty
    - Young males in dry, hot climates
    - family history of atopy is found in 40–60%

- Symptoms: Severe itching and photophobia, foreign body sensation, ptosis, thick mucus discharge, and blepharospasm
- Signs:
    1. papillary response, principally of the limbus or upper tarsus, classic 'cobblestone' papillae.
    2. Limbal papillae tend to be gelatinous and confluent → **Horner-Trantas dots**, which are collections of epithelial cells and eosinophils
    3. punctate epithelial keratitis → frank epithelial erosion → shield ulcer (due to its shape) → subepithelial ring-like scar
- Pathophysiology:
    1. epithelium contains large numbers of mast cells (mast cells predominantly of the type containing the neutral proteases tryptase and chymase) and eosinophils
    2. Basophils are found in the epithelium, and may indicate that one form of a delayed-type hypersensitivity reaction is occurring
    3. substantia propria contains elevated numbers of mast cells
- Diagnosis: intense photophobia, ptosis, and the characteristic finding of giant papillae.
- DD: AKC
- Treatment
    1. avoidance of allergens
    2. Hyposensitization in VKC has limitations (due to multiple allergens)
    3. short-term, high-dose pulse regimen of topical steroids
    4. Cromolyn sodium, a mast cell stabilizer, has repeatedly been shown to be effective in VKC
    5. Topical calcineurin inhibitors of ciclosporin A (CsA) and tacrolimus have been demonstrated effective in the treatment of VKC
    6. Climatotherapy
    7. Cryoablation of upper tarsal cobblestones is reported to render short-term improvement

- **Atopic Keratoconjunctivitis**
    - bilateral, chronic inflammation of the conjunctiva and lids associated with atopic dermatitis
    - 15% to 67.5% of patients with atopic dermatitis have ocular involvement
    - Male: female = 2.4: 1
    - Symptoms: Itching >> watering, mucus discharge, redness, blurring of vision, photophobia, and pain
    - Signs
        1. periocular skin often shows a scaling, flaking dermatitis with a reddened base
        2. Lateral canthal ulceration, cracking, and madarosis
        3. lid margins may show loss of cilia, meibomianitis, keratinization, and punctal ectropion
        4. ***In contrast to VKC, the papillary hypertrophy of AKC is more prominent in the inferior conjunctival fornix.***
        5. perilimbal, gelatinous hyperplasia
        6. Punctate epithelial keratopathy → Persistent epithelial defects → scarring → microbial ulceration → neovascularization
    - Pathophysiology
        1. both type I and type IV hypersensitivity
        2. conjunctival epithelium containing Mast cells (tryptase) and eosinophils
        3. increase in the CD4:CD8 ratio →
        4. substantia propria: increased number of mast cells, Eosinophils (never found normally), Increased fibroblasts
    - Treatment
        1. opical application of a vasoconstrictor–antihistamine combination
        2. topical administration of steroids

3. Mast cell stabilizers two to four times daily is recommended year-round
4. Ciclosporin A and tacrolimus, both orally and topically, have been shown effective in treating AKC

Giant Papillary Conjunctivitis

- noninfectious inflammatory disorder involving the superior tarsal conjunctiva.
- currently defined **as papillae greater than 0.3 mm** in diameter
- **average length of time**: ***soft*** contact lenses → **8 months**, ***hard*** contact lenses → **8 years**
- mild irritation, scant mucous discharge, and occasionally mild itching
- slow, progressive character → ropy, whitish, mucoid discharge
- **Allansmith** has divided the superior tarsal surface into three zones.
    - Zone 1 is located proximally along the uppermost edge of the tarsal plate;
    - Zone 2 is upper tarsal plate
    - zone 3 is located distally adjacent to the lid margin.
- Papillae with **soft** contact lens → **zone 1 to 3**
- Papillae with **RGP** contact lens → **zone 3**
- **Pathophysiology**:
    - combined effect of ***mechanical trauma and the subsequent immune response*** to antigens in the form of contact lens surface deposits
- **Treatment:**
    - Discontinuation of offending irritant if appropriate
    - Modifying the patient's contact lens care routine and wearing schedule
    - appropriate surfactant cleaner and a 'rub' routine becomes mandatory
    - Reducing contact lens wearing time
    - Treat if any meibomian gland disease

- Histamine antagonists and receptor blocking agent
- Topical corticosteroids have not proved particularly effective
- **Suprofen**, an NSAID, has been studied topically in contact lens-associated GPC.
- **Cromolyn sodium** has been studied extensively and has been shown to promote resolution of early giant papillary conjunctivitis when combined with meticulous lens hygiene.

Cicatricial Pemphigoid

- chronic cicatrizing autoimmune disease of the mucous membranes and skin.
- OCP affects primarily the **conjunctiva and the mucosae**, including oral, nasal, and esophageal, in lesser frequency
- average age at onset of OCP is **65 years**
- ***Scarring*** (**Brusting-Perry dermatitis**) occurs in approximately 25% of cases, and ***cicatrizing conjunctivitis*** develops in 70–75%
- **Histology**: the conjunctival lesions show submucosal scarring, chronic inflammation, perivasculitis, and squamous metaplasia of the epithelium, with loss of goblet cells; mast cell participation in the inflammation is surprisingly great.
- **Pathogenesis**
  - autoimmune disease with a genetic predisposition and probably a **'second-hit'** environmental requirement to trigger the onset
  - increase in frequency in the HLA-DR4 and HLA-DQw3
  - ***second-hit → microbial or chemical***
  - **β4 subunit of α6β4 integrin**, 205 kilodalton (kDa) protein molecule in the BMZ of the conjunctiva → ***the target of attack***
- The **diagnosis** is confirmed by the demonstration of one or more immunoreactants at the epithelial BMZ. Additional confirmation can be sought from immunoblot analysis of patient serum, an identifying autoantibody that binds to the 205-kDa protein band from conjunctival or epidermal lysates: anti-β4 antibody.
- **Ocular Manifestations**

- chronic, recurrent unilateral conjunctivitis.

  Stages:

  1. Subepithelial fibrosis
  2. fornix foreshortening
  3. Symblepharon
  4. end-stage disease, is characterized by ankyloblepharon and surface keratinization

- **Therapy**
  - **Sicca syndrome:** lubricants without preservatives, Punctal occlusion, Topical retinoid (0.01% tretinoin) ointment
  - **Chronic blepharitis and meibomitis**: vigorous warm compresses and lid hygiene, oral doxycycline, 100 mg BD
  - **Immunomodulatory therapy** (minimum 2 years)
    - prednisone 1 mg/kg/day, and cyclophosphamide 2 mg/kg/day.
    - Methotrexate (15–25 mg once weekly) and mycophenolate mofetil (1–3 g/day) are used for cases that are less active and are not rapidly progressing.
    - Dapsone and prednisone can also be used for such cases; the initial daily dose of dapsone employed is 1 mg/kg/day
    - intravenous immunoglobulin (IVIG) alone and especially in combination with rituximab therapy
    - surgical treatment: tarsectomy for correction of entropion, strip peritomy to provide an avascular barrier against corneal neovascularization, superficial keratectomy for removal of corneal vascular and scar tissue, and fornix incision for release of symblepharon.

EM, SJS & TEN

- across-the-spectrum manifestations of the same clinical entity, affecting the skin and mucous membranes.

- ***international classification*** was adopted in 1993
- **Ferdinand von Hebra**, in 1866, first described erythema multiforme
- Incidence: 4.2 per million person-years
- M:F = 1:1.5/2
- Drugs and infections are the most frequent identifiable precipitating factors
- ***Clinical Features:***
- **Eye findings**
- ***Acute eye findings***
    - nonspecific conjunctivitis: may precede the skin eruption
    - may be catarrhal or pseudomembranous
    - severe anterior uveitis
    - corneal ulceration (uncommon)
- ***Chronic eye findings***
    - Scarring, symblepharon formation, and cicatrization of the conjunctiva
    - entropion formation, trichiasis, and instability of the tear film
    - corneal scarring, neovascularization, and, in severe cases, keratinization
    - Keratin not only on the corneal surface but also along the posterior lid margin.
    - Subepithelial fibrosis of the conjunctiva
    - Cicatrization of the lacrimal ducts
    - destruction of the conjunctival goblet cells
- **Diagnostic criteria for bullous skin diseases**
    - **Erythema multiforme minor**

1. Target (iris) lesions (typical or atypical)
2. Individual lesions less than 3 cm in diameter
3. No or minimal mucous membrane involvement

4. Less than 20% of body area involved in reaction
5. Biopsy specimen compatible with erythema multiforme minor

- **Stevens-Johnson syndrome (erythema multiforme major)**

1. Less than 20% of body area involved in first 48 hours
2. Greater than 10% body area involvement
3. Target (iris) lesions (typical or atypical)
4. Individual lesions <3 cm in diameter (lesions may coalesce)
5. Mucous membrane involvement (at least two areas)
6. Fever
7. Biopsy specimen compatible with erythema multiforme major

- **Toxic epidermal necrolysis**

1. Bullae and/or erosions over 20% of body area
2. Bullae develop on erythematous base
3. Occurs on non-sun-exposed skin
4. Skin peels off in >3 cm sheets
5. Mucous membrane involvement frequent
6. Tender skin within 48 hours of onset of rash
7. Fever
8. Biopsy specimen compatible with toxic epidermal necrolysis

- ***Incidence of ocular complications***: average of 24% had ocular manifestations during their hospitalization
- ***DD***
  - ***Ocular disorders***: cicatricial pemphigoid, chronic keratoconjunctivitis caused by bacteria or viruses, medications, allergies, chemical burns, avitaminosis A, and trachoma, drug reaction.
  - ***Dermatologic***: SSSS, urticarial viral exanthema, drug reaction, toxic shock syndrome, Kawasaki disease, Leiner disease, erythroderma secondary to other causes, contact dermatitis, thermal burns, or poisonings

- **Etiology**
    - Drug-related cases
    - certain infections
    - malignancy
- **Pathogenesis**
    - immune-mediated responses to certain drugs and infectious organisms
    - keratinocyte death occurs from extensive apoptosis
    - suicidal interaction between Fas and Fas ligand
    - soluble FasL is secreted by peripheral blood mononuclear cells
    - Cytokines released by T lymphocytes, macrophages, or keratinocytes may enhance the expression of Fas and FasL on keratinocytes or enhance skin recruitment of lymphocytes by up-regulating adhesion molecules
    - SJS: significantly increased incidence of HLA-B12, HLA-Aw33, and DRw53
    - HSV EM: HLA-DQw3
    - TEN: HLA-B12
    - ocular lesions of SJS: HLA-B44
- **Histopathology**
    - Skin: lymphocytic infiltrate at the dermal–epidermal junction with a characteristic vacuolization of epidermal cells and necrotic keratinocytes within the epidermis
    - Eye: nonspecific inflammatory response is seen in the acute phases. In chronic phase, absence of the mucus-producing goblet cells as sequel of cicatrization.
- **Management**
    - ***Systemic***: specialized nursing and medical care, fluid balance, respiratory function, nutritional requirements, and wound care
    - ***Ophthalmic***:
    - Acute: ocular surface hygiene, preservative-free artificial tear, Cycloplegics, topical steroids (controversial), Lamellar or penetrating keratoplasty
    - Chronic stage

1. restore eyelid and forniceal anatomy and function: Epilation, cryotherapy, argon laser treatment, electrolysis, or blepharotomy for trichiasis
2. supply tear function: artificial tear supplementation, 10% N-acetylcysteine, tarsorrhaphy
3. restore ocular surface: Keratolimbal allograft (keratoepithelioplasty), Topical transretinoic acid can be used to reverse conjunctival transdifferentiation seen after ocular surface injury.

- **Prognosis**
  - AIDS patients who develop erythema multiforme do not have a worse prognosis. Elderly patients have a worse prognosis, and children have the best.

Toxic Conjunctivitis

- keratoconjunctivitis caused by topical atropine was described by **Von Graefe** in 1864
- **Toxicity versus Allergy**
  - Toxicity implies damage to the structure of the ocular tissues, or disturbance of function, with or without an accompanying inflammatory response. Allergic reactions may be of the anaphylactoid (type 1) or of the delayed (type IV) hypersensitivity type.
  - Follicles are generally not seen in allergy alone, and may be a key sign suggesting toxicity.
  - Allergic conjunctivitis is often associated with a mucous discharge that is typically thin and clear. A more purulent or mucopurulent discharge may be associated with toxicity.
  - TOXIC: oval epithelial defects located primarily in the inferonasal quadrants, with coarse surrounding keratitis, resembling a **'comet's impact' crater**
- **Diagnostic testing**
  - **type 1** hypersensitivity → intradermal skin test
  - **type IV** hypersensitivity → the patch test
- **Hurricane keratitis**

- postoperative corneal transplant patients as a result of the toxicity of topical medications.
- whorl-shaped punctate keratopathy develops as early as 1 week
- related to the intrinsic pattern of corneal epithelial repair, which appears to be a spiral or whorl-shaped epithelial slide

Superior Limbic Keratoconjunctivitis

- January 1963, **Frederick Theodore**
- Clinical features
  1. marked inflammation of the tarsal conjunctiva of the upper lid
  2. inflammation of the upper bulbar conjunctiva
  3. fine punctate staining of the cornea at the upper limbus and the adjacent conjunctiva above the limbus
  4. superior limbic proliferation
  5. filaments on the superior limbus or upper fourth of the cornea in about half of the patients.
- **Histopathology**: The superior palpebral conjunctiva shows goblet cell hypertrophy, while the bulbar conjunctiva, which is thickened and keratinized, shows very few goblet cells.
- **Origin and Pathogenesis**
  - The origin of SLK has not been determined: ***viral***, ***immunologic***
  - interesting associations: thyroid disease (**hyperthyroidism, is present in patients with SLK in at least 30%**), KCS
- **Treatment**
  - Conjunctival resection
  - therapeutic soft contact lenses
  - 0.5–1% silver nitrate
  - botulinum toxin injection of the orbicularis

- thermal cauterization
- topical vitamin A
- topical use of cromolyn sodium
- Supratarsal triamcinolone injection
- Liquid nitrogen cryotherapy: **Brymill E tip spray** (0.013-inch aperture) with a double freeze–thaw technique is another approach described by Frederick Fraunfelder
- N-acetylcysteine

- **DD**
  - **Theodore's SLK and CL-SLK**: **CL-SLK** is not always bilateral and has no relationship with thyroid disease. SLK is more commonly seen in females, while CL-SLK is not. CL-SLK also occurs in younger patients than does SLK. While vision with SLK is usually not decreased, it can be severely decreased in patients with CL-SLK, since corneal involvement is greater. Corneal filaments are usually not seen with CL-SLK, but they are frequently seen with SLK. A final distinction between the two is that contact lens keratoconjunctivitis often improves quickly after cessation of lens wear, whereas SLK goes on with remissions and recurrences for many years.

Ligneous Conjunctivitis

- protracted course of recurrent, membranous, conjunctival lesions, which has been associated with a ***systemic plasminogen deficiency***
- 1847, **Bouisson**
- **Borel** in 1933, assigned the name ligneous → meaning 'woody,' to this disorder because of the charateristic ***woodlike consistency of the membranes*** in severe cases
- median age of first clinical manifestation was **9.75 months**
- CF
  - chronic conjunctivitis
  - ligneous lesion appears as a highly vascularized, raised, friable lesion.
  - can be removed easily with forceps, although it tends to bleed
  - pain and photophobia, almost constant discomfort

  - more severe lesions extend beyond the lid margin, giving rise to one of the worst complications of the disorder, the cosmetic deformity

- **Pathophysiology**
  - *type I plasminogen deficiency*
- **Etiology**
  - type I plasminogen deficiency has been reported to cause any form of pseudomembranous disease.
- **Treatment**
  - Plasminogen substitution: Topical plasminogen preparations,
  - complete excisional biopsy of all ocular ligneous lesions
  - **systemic and topical FFP** and started on a corticosteroid and broad-spectrum antibiotic four times daily with topical ciclosporin A 2% twice daily.

Conjunctivochalasis

- redundant conjunctiva
- **Hughes** in 1942
- most often located between the eyeball and the lower eyelid.
- grading of the degree of CCh was found to have a high predictive value for diagnosis of KCS
- **Epidemiology**
  - changes related to the aging eye
- **Histopathology**
  - senile process related to conjunctival laxity
  - abnormalities in the extracellular components: **MMP-1 and MMP-3** were found to be overexpressed in the conjunctivochalasis fibroblasts. tissue inhibitors of metalloproteinases (**TIMPs**) expression remains unchanged, particularly TIMP-1 and TIMP-2. This ***change in the ratio of MMPs to TIMPs*** may facilitate the breakdown

of the extracellular matrix and result in the clinical changes observed in conjunctivochalasis.

- **CF**:
    - irritation in mild stages, marked tearing due to obstruction of the lower punctum in the moderate stage, and ocular surface exposure in more severe stages.
- **Diagnosis**
    - Rule out lid pathology
    - **LIPCOF classification**
        0. No persistent fold
        1. Single, small fold
        2. More than two folds and not higher than the tear meniscus
        3. Multiple folds and higher than the tear meniscus
    - **Meller's new grading system** for conjunctivochalasis
- **Treatment**
    - No treatment is recommended if the patient is asymptomatic
    - medical therapy: surface lubricants, antihistamines, and topical corticosteroids
    - Surgical management:

Developmental Abnormalities of Cornea

Anomalies of Size and Shape

- organogenesis (between the fourth and sixth gestational weeks)
- period of anterior segment differentiation (between the sixth and sixteenth gestational weeks)
- **Absence of the Cornea**
    - always accompanied by agenesis of various other anterior segment structures.
- **True cryptophthalmos**, otherwise known as complete cryptophthalmos or ablepharon, occurs when skin replaces the normal eyelid architecture and connects to the underlying globe, leaving the cornea and part of the conjunctiva unprotected and exposed.

  The term cryptophthalmos syndrome, also termed **Fraser syndrome**, has been used to describe patients who meet specific criteria as outlined by Thomas.
- **Pseudocryptophthalmos** (total ankyloblepharon) is a related condition in which the eyelids form but fail to separate, leaving a normal cornea and conjunctiva totally covered by skin. Unlike its true counterpart, both lashes and brows are present with an otherwise normal eye, and vision is restored by surgically creating a palpebral fissure.

- **cornea usually reaches adult size by 2 years of age.**
- **newborn cornea measures approximately 10 mm in horizontal, adult 12 mm**

- **Megalocornea**
    - horizontal diameter greater than or equal to **13 mm**
    - **XR** →Xq21, Xq12; nonprogressive, bilateral and symmetrical
    - steeper cornea usually results in **with-the-rule astigmatism** and **myopia**
    - pathognomonic biometric findings of X-linked megalocornea not present in congenital glaucoma or other forms of megalocornea: markedly increased anterior chamber depth, posterior lens and iris positioning, and a short vitreous length

- **Microcornea**
    - horizontal diameter **less than or equal to 10 mm** in an otherwise normal-sized globe

- nonprogressive, unilateral or bilateral
- Male = Female
- AD, AR, Sporadic
- Flatter than normal cornea →**hyperopia**
- rarely an isolated condition and can have many ocular and systemic anomalies associated with it
- 20% of patients with microcornea develop **glaucoma**, with angle closure being most common

- **Oval cornea**
  - **horizontal oval cornea**: exaggeration of scleral encroachment in the superior and inferior horizontal meridians. indicates the presence of some degree of sclerocornea and has no other associated findings.
  - **Vertical oval cornea** exists when the vertical diameter of the cornea exceeds the horizontal diameter. a/w iris coloboma, microcornea, intrauterine keratitis, Rieger's anomaly, and Turner's syndrome.

- **Astigmatism**
  - **with-the-rule astigmatism in the first decade** of life progressing to against-the-rule astigmatism in later years.

- **Sclerocornea (cornea plana)**
  - cornea is flat with a curvature of **less than 43 diopters** (D)
  - ranges from 30 to 35 D
  - The embryologic explanation for sclerocornea: **absence of the limbal anlage**, the structure responsible for both limbal differentiation and corneal curvature.
  - Bilateral & asymmetric, may be unilateral
  - AD, AR (chromosome 12), Sporadic
  - Male = Female

- Total or Peripheral
- Mx: Refraction, PK, Glaucoma Mx

- **Keratoglobus**
  - typically develops during the **first 20 years** of life
  - bilateral, noninflammatory, ectatic disorder in which the entire cornea becomes thinned and takes on a globular shape, with keratometry readings as high as 60–70 D.
  - strong association with Ehlers-Danlos syndrome **type VI**

- **Congenital Anterior Staphyloma**
  - bulging, opaque cornea lined posteriorly with uveal tissue protrudes through the palpebral fissure beyond the plane of the normal eyelids
  - result from the **abnormal migration of neural crest cells** into the developing cornea
  - cornea is vulnerable to perforation in utero and subsequently undergoes dermoid transformation to resemble the stratified squamous epithelium of skin
  - unlike cryptophthalmos, the **metaplastic change is limited to the cornea** and does not involve the conjunctiva or eyelids.

- **Keratectasia**
  - congenital anterior staphyloma **minus** the posterior uveal lining.

ARS and PA

- Axenfeld syndrome, which is Axenfeld anomaly with glaucoma.

- While the word ‘syndrome’ means systemic abnormalities in ‘Rieger syndrome,’ it means glaucoma when used in ‘Axenfeld syndrome.’
- **Divisions of Axenfeld-Rieger syndrome**

  PARR PAIS

Disease	Posterior embryotoxon	Angle abnormalities	Iris stroma abnormalities	Systemic abnormalities	Glaucoma risk
Posterior embryotoxon	+	–	–	–	–
Axenfeld anomaly	+	+	–	–	+
Rieger anomaly	+	+	+	–	+
Rieger syndrome	+	+	+	+	+

- **Axenfeld-Rieger Syndrome**
-

Noninflammatory Ectatic Disorders

- **Corneal ectasia following keratorefractive surgery**
  - **Randleman** et al. studied patients with **post-LASIK ectasia** and identified five main risk factors for this complication.
    1. Young age at the time of surgery
    2. abnormal preoperative topography,
    3. reduced residual stromal bed thickness
    4. decreased preoperative cornea thickness,
    5. High myopia

- **Pellucid marginal degeneration (PMD)**
    - **Schlaeppi** appropriately chose the name pellucid, meaning **clear**, to describe this thinning disorder. These corneas are generally clear and avascular, with no iron ring, infiltrate, or lipid deposition.
    - bilateral, peripheral corneal ectatic disorder characterized by a band of thinning **1-2 mm** in width, typically in the **inferior** cornea, extending from the **4 to the 8 o'clock** position.
    - In contrast to keratoconus, ***maximal corneal protrusion typically occurs just superior*** to, rather than within, the area of thinning
    - **shift in the axis of astigmatism** from against-the-rule, superiorly, to with-the-rule, near the point of maximal protrusion.
    - PMD and keratoconus can occur in the same eye
    - typical **crab-claw** illustrates the shift in astigmatism from the superior to the inferior cornea
    - poor candidates for refractive surgery because of the potential for an **undesirable outcome** and the risk that the surgical procedure might stimulate progressive ectasia.
    - present for treatment between the second and fifth decades of life with complaints of blurred vision resulting from irregular astigmatism.
    - **DD**:
        - The findings typical of **keratoconus**, specifically, protrusion within the area of corneal thinning, striae, and Fleischer's ring, are not seen in PMD.
        - **Terrien's marginal degeneration** can cause high astigmatism in a similar age group. However, in contrast to pellucid degeneration, this disorder has a male predilection. It commonly affects the cornea, superiorly as well as inferiorly, with vascularization and lipid deposition. When corneal protrusion occurs in Terrien's degeneration, it is usually within the area of thinning.
        - **Mooren's ulcer** is usually unilateral and is associated with marked inflammation and pain, an epithelial defect in the area of ulceration, undermining of the central edge of the ulcer, and vascularization up to the peripheral edge. Corneal changes in Mooren's ulcer are not confined to the inferior or superior cornea.
        - **Idiopathic furrow degeneration**, while bilateral and noninflammatory, occurs in the elderly within a corneal arcus.
    - Mx;

- Spectacles usually fail to adequately correct the high irregular astigmatism associated with typical cases of PMD. Large-diameter, rigid gas-permeable contact lenses can be tried. However, because of the contour abnormality, a stable long-term fit can be difficult to achieve. The hybrid lenses, such as the **SoftPerm** lens, have been used successfully in PMD. The newer generation of scleral lenses made from gas-permeable plastic may also be of benefit.
- **Large-diameter or eccentric penetrating keratoplasty** may be necessary to encompass the area of peripheral thinning.
- **thermokeratoplasty, crescentic lamellar keratoplasty, and crescentic or wedge excision**

- **Keratoglobus**
  - bilateral ectatic disorder that is usually nonprogressive or minimally progressive.
  - generalized thinning, most marked in the periphery
  - ***Acute hydrops occurs less frequently*** than in keratoconus; however, the opposite is true about corneal perforation and rupture. Keratoglobus patients are prone to ***corneal rupture*** after minimal trauma, even when there is no history of trauma.
  - **Associations**:
    - Unlike keratoconus, **keratoglobus is not associated with atopy, tapetoretinal degeneration, or hard contact lens wear**. Keratoglobus has been reported in association with ***inflammatory orbital pseudotumor, chronic marginal blepharitis, chronic eye rubbing, and in glaucoma*** following penetrating keratoplasty. Acquired keratoglobus has also been described in association with vernal keratoconjunctivitis and hyperthyroidism.
    - **no association with Down's syndrome**, keratoglobus has been reported in association with ***Rubinstein-Taybi syndrome***, in which intellectual impairment occurs
  - **Management:**
    - Spectacle correction is the first step
    - There may be a role for a rigid gas-permeable scleral lens
    - lamellar graft or epikeratoplasty

- **Posterior Keratoconus**
  - thinning results from an increase in the curvature of the posterior cornea

- **keratoconus posticus generalis** the entire posterior corneal surface has an increased curvature and the cornea typically remains clear.
- In the localized form, **keratoconus posticus circumscriptus**, there may be one, or occasionally more, central or paracentral areas of posterior excavation associated with variable amounts of stromal scarring
- relative lack of involvement of the anterior refractive surface explains why posterior keratoconus results in only mild to moderate reduction in visual function.
- developmental, usually **nonprogressive, noninflammatory, and unilateral**
- does not develop into keratoconus, despite the fact that anterior steepening can occur in a central or paracentral affected area.
- similarities between posterior keratoconus and Peters' anomaly. However, a difference is observed histopathologically. ***In Peters' anomaly the corneal endothelium and Descemet's membrane are either absent or markedly thinned***, which is not the case in posterior keratoconus.
-

Keratoconus

Kerato= Horn, cornea

Conus= cone

- Keratoconus is a noninflammatory , ectatic corneal condition characterized by central or paracentral stromal thinning , apical protrusion and irregular astigmatism
- British physician, **Jhon Nottingham** in 1854 did practical observations on conical cornea
- **50-230 / 100000** individuals
- M=F
- Starts at puberty, over a period of 10 to 20 years the process continues until the progression gradually stops
- **Familial incidence= 65%,** Autosomal dominant with variable penetrance
- **Pathophysiology:**
  - **Antioxidant deficiency**

- **Proteinase and antiproteinase imbalance**: up-regulation of degradative enzymes and the down-regulation of proteinase inhibitors could result in a degradation of the extracellular matrix of the stroma
- **Apoptosis**: Keratocytes from keratoconus corneas have been found to have four times the interleukin-1 binding sites, when compared to nonkeratoconus corneas. This may result in an increased sensitivity of the keratocytes in keratoconus to the effects of interleukin-1. Interleukin-1 has also been shown to induce apoptosis or controlled cell death of stromal keratocytes in vitro.
- **Contact lens wear** is another form of corneal microtrauma: 17.5% to 26.5%
- **ectodermal disease**, then associations with atopic disease and tapetoretinal degenerations

- **Pathology**:
  - **Breaks in the epithelial layer** can be associated with epithelium growing posteriorly into Bowman's layer and collagen growing anteriorly into the epithelium, forming Z-shaped interruptions at the level of Bowman's layer. These Z-shaped areas are typical of keratoconus.
  - **Fleischer ring** found at the base of the cone
  - **normal-sized collagen fibers**; however, the number of collagen lamellae was abnormally low. The number found within the cone was less than half (41%) the number outside of the cone.
  - **Endothelial cell pleomorphism** and polymegathism occur in keratoconus
- **CF**:
  - Late teens
  - Blurring of vision
  - Shadowing around images
  - Glare, halos, ocular irritation
  - Frequent changes in spectacle number
  - Contrast sensitivity measurement may, however, uncover visual dysfunction before Snellen visual acuity loss can be measured
  - Two types of cones have been described. The **round or nipple-shaped cone** is smaller in diameter, while the **larger oval or sagging cone** may extend to the limbus and is more prone to contact lens fitting problems.
- **Signs**:
  - Irregular astigmatism

- Striae occur in the posterior stroma, just anterior to Descemet's membrane.
- Red reflex - Oil droplet sign
- Scissoring reflex
- Vogt ‘s straie
- Fleischer’s ring
- Prominent corneal nerves
- Corneal topograph
- Progressive corneal thinning
- Munson’s sign
- **Central corneal scarring**: Factors predictive of incident corneal scarring include corneal curvature greater than 52 diopters (D), contact lens wear, corneal staining, and age less than 20 years.

- **Investigations**:
  - The **keratometer** is an invaluable, widely available tool for measuring corneal curvature. Inability to superimpose the central keratometric rings suggests irregular corneal astigmatism, a hallmark of keratoconus.
  - **Keratoscopy or videokeratography**, based on the Placido disk, can provide qualitative contour information. In early keratoconus, a focal area of increased corneal curvature appears as an isolated area of smaller ring spacing and distortion. As the condition progresses, the ring spacing decreases overall and becomes increasingly irregular

- **Rabinowitz has suggested four quantitative videokeratographic indices** as an aid for screening patients for keratoconus. These indices include
  1. central corneal power value greater than 47.2 D
  2. inferior–superior dioptric asymmetry (I-S value) over 1.2
  3. Sim-K astigmatism greater than 1.5 D
  4. skewed radial axes (SRAX) greater than 21 degrees.

- **KISA% index:**
  - Uses 4 parameters →
  - keratometry; I-S value; the AST index, which quantifies the degree of regular corneal astigmatism (simulated flat and steep keratometry values, Sim K1 and Sim K2); and SRAX, which is an expression of irregular astigmatism.

- **keratoconus-prediction index(KPI) →Indices of Maeda and Klyce**

- derived from eight other quantitative videokeratographic indices.
- two simulated K values (steep and flat powers), differential sector index (DSI), center/surround index (CSI), opposite sector index (OSI), surface asymmetry index (SAI), analyzed area (AA), and the irregular astigmatism index (IAI).

- **Amsler-Krumeich classification**

- **Stage 1:**

  Eccentric steeping

  Myopia and astigmatism < 5.00 D

  Mean central K readings < 48.00 D

- **Stage 2:**

  Myopia and astigmatism from 5.00 to 8.00 D

  Mean central K readings < 53.00 D

  Absence of scarring

  Minimum corneal thickness >400 µm

- **Stage 3:**

  Myopia and astigmatism from 8.00 to 10.00 D

  Mean central K readings >53.00 D

  Absence of scarring

  Minimum corneal thickness 300 to 400 µm

- **Stage 4:**

  Refraction not measurable

  Mean central K readings >55.00 D

  Central corneal scarring

  Minimum corneal thickness 200 µm

- **Systemic Association:**
    - ATOPY
        - Asthma
        - Atopic keratoconjunctivitis
        - Hay fever
        - Eczema
    - CONNECTIVE TISSUE DISORDERS
        - Marfan's syndrome: An increased prevalence (38%[20] to 58%) of mitral valve prolapse has been found in keratoconus patients
        - EDS
        - Osteogenesis imperfecta
    - MISCELLANEOUS
        - Down's: 5.5% and 15%
            - structural or biochemical changes
            - habitual eye rubbing
        - Turner's syndrome
    - diabetes offered a protective effect regarding keratoconus. (also smoking?? As they cause C3R like effect)
- **Ocular Associations:**
    - RP
    - Infantile tapetoretinal degeneration (Leber's congenital amaurosis) is frequently complicated by keratoconus and cataract.
    - retinopathy of prematurity, progressive cone dystrophy, aniridia, iridoschisis, and essential iris atrophy
    - VKC: 26.8%.
    - 17% in a group of patients with floppy eyelid syndrome.
- **Cx**:
    - **High Refractive errors**: Intolerance to glasses
    - **Acute Hydrops** : Rupture Descemet's membrane →Aqueous influx → Corneal edema→ Sudden drop in vision / Opacity

Management

- The management of keratoconus begins with **spectacle correction**.
- Once glasses fail to provide adequate visual function, **contact lens fitting** is required. Contact lens wear improves visual function by creating a new anterior refractive surface. Contact lenses **do not prevent progression** of corneal ectasia. While they seem to be associated with the development of keratoconus in some cases, this important mode of therapy should never be withheld for fear of causing progressive disease.
    - **RGP**: three-point touch technique, remain the mainstay of contact lens treatment for keratoconus. apical clearance fitting technique is also commonly used.
    - Other options include soft toric lenses, standard bicurved hard lenses, custom-back toric lenses, piggyback systems, hybrid lenses made of combined hard lens with a soft skirt, scleral lenses, and mini-scleral lenses.
    - **Hybrid lenses**, such as the SoftPerm lens (CIBA Vision Corp., Duluth, GA) and the newer SynergEyes KC lens (SynergEyes, Inc., Carlsbad, CA) may be more comfortable for patients who cannot tolerate an RGP alone.
    - **Mini-scleral lenses** have a diameter of 14–17 mm compared to scleral lenses with a diameter of 20–24 mm.
- **Contact lens-intolerant** keratoconus patients without central scarring, who have mild or moderate disease, may be candidates for intrastromal ring segment insertion. The ideal candidates also have low spherical equivalents and average keratometry readings of less than 53 D.
    - **Ferrara rings** (Ferrara Ophthalmics, Belo Horizonte, Brazil) and **Intacs** (Addition Technology Inc, Des Plaines, IL, USA), commonly used ring segments, are made of rigid polymethyl methacrylate. Ferrara rings have a fixed inner diameter of 5.0 mm and a triangular anterior contour. Intacs have an inner diameter of 6.8 mm, a flat anterior surface, and are available in thicknesses of 0.25–0.45 mm, in 0.05 mm increments.
- C3R (read below as separate theory)

- While **penetrating keratoplasty** has traditionally been the surgery of choice, lamellar surgery is becoming more popular for patients with mild to moderate disease.
    - The iron ring, found at the base of the cone, should be used as a reference when planning graft size.
    - Postkeratoplasty myopia can be reduced by using the same-sized donor and host corneal buttons.

- **Lamellar Keratoplasty**
  - Deep anterior lamellar keratoplasty (DALK): host endothelium is preserved, thus reducing the risk of rejection. The risk of endophthalmitis is theoretically less because this is largely an extraocular procedure.
-

C3R

- **Collagen cross-linking (CXL or C3-R)** is the most recent addition to the surgical armamentarium and may slow or halt the progression of keratoconus by using a photo-oxidative treatment to increase the rigidity of the corneal stroma.
- Theo Seiler, MD, PhD, of Switzerland, was the first to suggest applying this principle to ophthalmology, more specifically cross-linking corneal collagen fibers.
  - The principal effects of cross-linking are localized to the **anterior 300 µm** of the stroma.
  - Riboflavin is a vitamin (vitamin B2), nontoxic and available as a drug. It has two important functions: the absorption of the UV-irradiation and as photosensitizer the generation of reactive oxygen species (singlet oxygen).
  - molecular weight (376 g/mol) → so epithelial debridement needed
  - **Lambert-Beer's-law**: 400 µm-thick cornea the concentration at the endothelium reaches a level where the absorption of the UV-light is high enough to protect endothelium and intraocular structures
  - two absorption maxima: 365 nm and 430 nm. 365 nm → higher energy, so it is used
  - with an irradiance of 3 mW/cm^2 an optimal irradiation time of 30 minutes was found
  - damage threshold for the endothelium of 4 mW/cm2 and it gets only 0.18 mW/cm2. no risk for lens and retina.
  - UVA-radiation source: UV-X (Fa. Peschke) → homogenous irradiance of 3 mW/cm^2 in a distance of 5 cm within a diameter of 8 mm of the central cornea

Effect and Evidence of Cross-linking

- cross-linked cornea is stiffer by factor 1.8 than normal cornea
- cornea´s shrinking temperature is raised from 63°C to 70°C.
- Cross-linked collagen shows significantly less tendency for swelling
- The diameter of collagen lamellas increases by 12% in the anterior stroma and by 4.5% in the posterior
- enhanced resistance against proteolytic enzymes
- Apoptosis of keratocytes in the anterior stroma is seen after cross-linking. new keratocytes move in from the limbus.

- **328.9% increase in corneal rigidity**

- **2.68 D reduction** in corneal power at 1 year postoperatively. Three years after the treatment, the BCVA improved one line in 58% of 33 eyes and remained stable in 29% of eyes
- most beneficial for patients with mild progressive keratoconus
- corneal stroma is greater than 400 µm thick

Avedro KXL:

The KXL System for ***Accelerated Cross-linking achieves speed by increasing the UVA power and reducing the exposure time***, thereby maintaining the same energy on the eye as standard cross-linking while reducing crosslinking time by an order of magnitude.

Avedro's new procedures made possible with its KXL System, can restore the strength of the cornea with a 5-minute treatment that accompanies LASIK, according to a company news release.

"Lasik Xtra helps patients avoid the risk of ectasia after LASIK, which has become a troublesome and unpredictable unpredictable problem," David Muller, PhD, President and Chief Executive Officer of Avedro, said in the news release. "In addition, our accelerated KXL procedure offers a much more acceptable treatment for patients with keratoconus and for those already suffering from post-LASIK ectasia."

Other uses of C3R

- **Athens Protocol**
- Corneal ulcer
- LASIK Xtra
    - Prophylaxis in myopic LASIK
    - Hyperopic LASIK (!!.. Yes this is to prevent regression..!!)
-

Iridocorneal Endothelial Syndrome

- The diagnosis of the ICE syndrome is considered when two of the three main clinical features are present **unilaterally**: ***typical iris changes, abnormal corneal endothelium, and PAS.***
- Coincidentally, the acronym ICE also signifies commonly used names of these conditions – Iris nevus syndrome, Chandler's syndrome, and Essential (progressive) iris atrophy.
- Etiology
    - Unknown
    - **membrane theory of Campbell**
        - Earliest stage of iris and anterior chamber angle involvement. Solitary peripheral anterior synechiae (PAS), but no pupil and iris abnormality.
        - Growth and extension of abnormal membrane from posterior corneal surface over the anterior chamber angle
        - contraction of membrane on iris surface, and early stretch-induced iris stromal atrophy in the quadrant opposite the membrane
        - Diffuse anterior chamber angle and iris involvement with abnormal membrane growth
- **Essential iris atrophy**
    - **Most common**
    - first presents typically in young adults, unilaterally, and in women > men
    - bare eccentricity of the pupil to severe corectopia
    - Iris atrophy and partial-thickness holes in the iris stroma appear on the side opposite the pupillary eccentricity
    - Glaucoma, iris atrophy, or nodules
    - Specular microscopy is an invaluable tool for early or confirmatory diagnosis. Although endothelial cell pleomorphism and a decrease in the percentage of hexagonal cells of the contralateral eye have been described, typical morphologic specular microscopic changes (ICE cells) are unilateral.
- **Chandler's syndrome**
    - blurred vision or seeing colored halos around lights.
    - Corneal edema was first described as occurring at a normal or slightly elevated intraocular pressure and, because of the abnormal endothelium, is the dominating clinical characteristic of this subtype of ICE syndrome

- The abnormal corneal endothelium, best seen with specular reflection, has a fine hammered silver appearance, which is finer in appearance than the guttata of Fuchs' endothelial dystrophy

- **Cogan-Reese syndrome**
  - the least common of the major variants of ICE syndrome
  - A hyaline membrane ('ectopic Descemet's membrane')
- **Iris nevus syndrome**
  - unilateral diffuse nevus of the iris and several other signs including loss of surface architecture of the iris resulting in a matted appearance, ectropion uvea, heterochromia, PAS, corneal edema, and unilateral glaucoma.
- **Differential Diagnosis**
  - Posterior polymorphous dystrophy
  - Axenfeld-Rieger syndrome
- **Management**
  - Medical treatment is generally ineffective
  - glaucoma develops it may be managed initially with aqueous suppressants. glaucoma filtering surgery is required
  - corneal edema may respond to lowering intraocular pressure. Hypertonic saline solutions and soft contact lenses may be helpful
  - Cataracts may develop de novo or subsequent to glaucoma or corneal surgery.

Corneal and Conjunctival Degenerations

- Degeneration of a tissue is defined as a deterioration and decrease in function.

- **Arcus senilis:**
  - Gerontoxon in geriatrics
  - arcus juvenilis or anterior embryotoxon in the young
  - lipid deposition in the peripheral cornea

- gray to yellow arc, first in the inferior cornea then the superior cornea
- sharp peripheral border ending at the edge of Bowman's layer with a lucent zone (***lucid interval of Vogt***) to the limbus
- Histopathologically, the arcus has an **hourglass appearance** as the opacity extends into the corneal stroma from these two layers.
- lipid particles are similar to a type found in human atherosclerotic lesions but accumulate in the absence of foam cells, unlike atherosclerotic lesions.
- limbal vasculature is part of a low-pressure perfusion system. The endothelium of these blood vessels act as tight junctions but in the presence of elevated circulating LDL may become dysfunctional. Lipid in the peripheral cornea likely originates from LDL, it is modified LDL and apo B sparse.
- ***affects men more than women***.
- Hyperlipoproteinemia types IIa and IIb are associated with premature corneal arcus formation
- Rare genetic disorders of high-density lipoprotein (HDL) metabolism causing corneal deposits include lecithin cholesterol acyltransferase ***(LCAT) deficiency, fish eye disease and Tangier disease***.

- **Lipid degeneration**
- ***primary lipid degeneration***
  - no prior history of the following: trauma, family history of similar conditions, corneal vascularization, and no known disorders of lipid metabolism.
  - due to increased vascular permeability of the limbal vessels. Alternatively, the etiology may be an altered metabolic activity of the keratocytes
  - more common in women than men, with a ratio of 70 : 30
- ***Secondary lipid degeneration***
  - associated with corneal neovascularization

- **Spheroidal degeneration (climatic droplet keratopathy)**
  - Bietti's nodular corneal degeneration, Labrador keratopathy, climatic droplet keratopathy, degeneratio corneae sphaerularis elaioides, corneal elastosis, fisherman's keratitis, keratinoid corneal degeneration, and chronic actinic keratopathy.
  - **Type 1** occurs bilaterally in the cornea without evidence of other ocular pathology

- **Type 2,** or secondary spheroidal degeneration, occurs in the cornea in association with other ocular pathology.
- **Type 3** is the conjunctival form of the degeneration and may occur with types 1 or 2
- clear to yellow-gold spherules are seen in the subepithelium, within Bowman's, or in the superficial corneal stroma. They measure from 0.1 to 0.4 m
- Etiology: ultraviolet radiation and microtrauma including sand, dust, wind, and drying.
- HP: hyaline-like material are found in the corneal stroma, Bowman's layer, and subepithelium. Bowman's layer is disrupted, and in advanced cases the epithelium is elevated and thinned. They have a histochemical staining characteristic similar to degenerative connective tissue, such as in pingueculae, but ***fail to stain for other components found in elastotic material from pingueculae***.

- **Climatic proteoglycan stromal keratopathy**
  -

- **Amyloid degeneration**
  - Primary localized
  - Primary systemic
  - Secondary localized
  - Secondary systemic

- **Salzmann's nodular degeneration**
  - degenerative process that follows episodes of keratitis.
  - history of phlyctenular disease but was also observed after vernal keratoconjunctivitis, trachoma, measles, scarlet fever, or interstitial keratitis
  - idiopathic or in association with practically any significant corneal inflammatory disease, especially meibomian gland dysfunction
  - Lubrication can be tried for mildly symptomatic lesions. Superficial keratectomy, by manual dissection or with phototherapeutic keratoablation, may be used for lesions near the visual axis. For lesions extending to the mid stroma, lamellar or

penetrating keratoplasty may be necessary. Recurrence is possible after keratoplasty. The recurrent lesions are often not clinically similar to the original lesion but are indistinguishable histologically.

-

- **Corneal keloids**
  - after trauma or in association with chronic ocular surface inflammation
  - in association with Lowe's syndrome & Rubinstein-Taybi syndrome.
  - Clinically similar to SND but usually seen in a younger age group than Salzmann's degeneration and occur more frequently in men.
  - superficial keratectomy or penetrating or lamellar keratoplasty may be performed for visually significant lesions.
  -
- **Terrien's marginal corneal degeneration**
  - peripheral inflammatory condition
  - 20 and 40 years of age.
  - **M:F = 3:1**
  - bilateral and symmetric
  - usually begins superonasally with fine punctate opacities in the anterior stroma with a lucent area to the limbus.
  - vascularization from the limbal arcades leading to the lesion differentiates it from arcus.
  - gutter similar to marginal furrow degeneration then forms between the opacity and limbus. The stroma progressively thins, usually over many years
  - Two types of Terrien's degeneration have been classified.
    - The more common quiescent type is seen in older patients. These patients may be asymptomatic for a long time because the lesion produces no pain.
    - Inflammatory Terrien's degeneration usually occurs in the younger age groups. These patients may have recurrent episodes of inflammation, episcleritis, or scleritis. This is treated with steroids.
  - **against-the-rule astigmatism**, which may be the presenting symptom

- HP: fibrillar degeneration of collagen, Epithelium may be normal, thick, or thinned; Bowman's layer is fragmented or absent. Breaks in Descemet's membrane may be seen in thinned areas

- **Limbal girdle (of Vogt)**
  - two types
  - crescentic yellow-to-white band found in the interpalpebral limbus
    - Type 1 appears as a white band that may contain holes. The central border is relatively sharp with no extensions. It is separated from the limbus by a ***narrow lucent area***. Type 1 is generally thought to represent ***early calcific band keratopathy***.
    - Type 2, however, is thought to be a **true** limbal girdle. This **chalky band** has no holes or clear interval to the limbus. Centrally, there are irregular linear extensions.
  - Histopathologically, the lesion is subepithelial and may have overlying epithelial atrophy. Destruction and calcification of Bowman's layer have been observed in type 1.

- **Band keratopathy**
  - Two forms
  - **Calcific band keratopathy**
  - deposition across the cornea at the level of Bowman's layer
  - causes
    1. Hypercalcemic states
    2. Chronic ocular disease
    3. Chemicals (eye drops and irritants)
    4. Inherited diseases
    5. Systemic diseases
    6. Idiopathic
  - sharply demarcated peripheral edge separated from the limbus by a lucent zone. This zone is due either to the lack of Bowman's layer at the periphery or from the buffering capacity of the limbal vessels, which prevent precipitation of calcium.

- HP: fine basophilic granules are first seen at the level of Bowman's layer. Calcium is deposited in the form of hydroxyapatite, a phosphate salt.
- Mx:
  - When the patient becomes symptomatic, the mainstay of treatment is the application of ethylenediaminetetraacetic acid (**EDTA**). Epithelial debridement & 0.05 molar concentration on saturated cellulose sponges.
  - excimer laser phototherapeutic keratectomy.

- **Calcareous degeneration**
- second type of calcific degeneration. Like band keratopathy, this degeneration occurs in diseased eyes. Unlike band keratopathy, calcareous degeneration involves the posterior stroma.
- S

- **Reticular degeneration of Koby**
  - fine white reticulum at the level of Bowman's layer. Overlying epithelium may have a brownish discoloration. This degeneration is most commonly reported in patients with chronic inflammation.

- **Iron lines**
  - most common iron line is the **Hudson-Stähli line**, which is located in the lower third of the cornea
  - Iron deposition in filtering bleb after glaucoma surgery was described by **Ferry** in 1968. It appears on the cornea just anterior to the filtering bleb. He related its incidence to the size of the filtering bleb. Iron may be seen at the advancing edge of a pterygium (**Stocker's line**) and at the base of the cone in keratoconus (**Fleischer ring**).
  - Histologically, iron, predominantly ferritin, is found intracellularly and extracellularly in the basal epithelial layer of the cornea, regardless of the type of iron line.
  - The most common theory attributes the deposition to localized trauma at the site of contour change or to a pooling of tears at this site

- **Coats' white ring**
  - 1 mm or less in diameter

- inferior portion of the cornea.

- **Hassall-Henle bodies**
  - Descemet's warts are excrescences of Descemet's membrane found in the peripheral cornea.

- **Crocodile shagreen**
  - corneal mosaic pattern resembling cobblestone or crocodile skin is seen in the anterior or posterior cornea.
  - Histopathologically, the stroma is thrown into folds, either at Bowman's layer in the anterior form or around Descemet's membrane in the posterior form.

- **Senile furrow:** Peripheral thinning is seen in the avascular zone between arcus senilis and the limbal vascular arcades

- **Cornea farinata:**
  - tiny opacities, found bilaterally in the posterior stroma near Descemet's membrane.
  - 'flour dust' appearance on retro-illumination

- **Dellen:**
  - Fuchs' dimples
  - Dellen may last only 24 to 48 hours and are found most commonly in the temporal peripheral cornea, usually adjacent to a paralimbal elevation.
  - saucer-like depressions in the corneal surface
  - Histopathologically, thinning of the corneal epithelium, Bowman's layer, and anterior stroma is seen. Treatment with ocular lubricants or pressure patching will accelerate the healing process.

- **Pingueculae**
  - elevated masses on the conjunctiva, gray-white to yellow in color

- interpalpebral zone, paralimbal, in the 3 and 9 o'clock positions.
- more often found nasally than temporally.
- HP: normal, atrophic, or hyperkeratotic conjunctival epithelium. The substantia propria shows basophilic degeneration on hematoxylin and eosin staining. This material stains for elastin but is not broken down by elastase. Thus it is termed elastotic degeneration.
- damage from ultraviolet radiation, Other possible causes of pingueculae include trauma, wind, sand, or drying
- Gaucher's disease can be associated with a pinguecula that is brownish in color.

- **Concretions:**
  - white to yellow spots found on the palpebral conjunctiva occasionally encased in clear cysts.
  - later stages of trachoma
  - chronic inflammation causes hyperplasia and invagination of the conjunctival epithelium.
  - They may be easily removed for patient comfort.

Corneal Dystrophy

- dys = wrong, difficult; trophe = nourishment
- dystrophy word was introduced in **1890** by **Arthur Groenouw** when he published his classic paper describing two patients with '***Noduli Corneae***.'
- group of inherited corneal diseases that are usually bilateral, symmetric, slowly progressive and not related to environmental or systemic factors.
  - Exceptions:
    1. Hereditary pattern is not present in most patients with→EBMD
    2. Unilateral corneal changes may be found→ PPCD
    3. Systemic changes are found→ macular dystrophy, in which the level of antigenic serum keratan sulfate correlates with the immunophenotypes of the disease.

- The first classification by Bücklers of corneal dystrophies described the differences between granular, macular, and lattice dystrophy.
- The most commonly used classification system is anatomically based.
- International Committee for Classification of Corneal Dystrophies (**IC3D**) was created in **2005** in order to revise the corneal dystrophy nomenclature and create a current and accurate corneal dystrophy classification system.
- four descriptive, evidential categories were created in the IC3D classification
    - Category 1. A well-defined corneal dystrophy in which the **gene has been mapped** and identified and specific mutations are known.
    - Category 2. A well-defined corneal dystrophy that has been mapped to one or more specific **chromosomal loci,** but the gene(s) remains to be identified.
    - Category 3: A clinically well-defined corneal dystrophy in which the disorder has **not yet been mapped to a chromosomal locus.**
    - Category 4. This category is reserved for a **suspected new**, or previously documented, corneal dystrophy, where the evidence for it being a distinct entity is not yet convincing.

Anterior Corneal Dystrophies

- **Meesmann's Juvenile Epithelial Dystrophy**
    - Least common
    - mutation in corneal **keratin (K3 or K12)**
    - seen in the first few years of life as intraepithelial microcysts or vesicles visible only at the slit lamp.
    - Vision is usually good in the first few years of life but may diminish gradually if the cysts increase in number and cause slight irregularity of the corneal surface.
    - *Recurrent erosion is not common*

- **Epithelial Basement Membrane Dystrophy**
    - map-dot-fingerprint, Cogan's microcystic dystrophy

- **most common** anterior corneal dystrophy and is classified as a corneal dystrophy because these changes occur more in some families
- **pathogenesis**: Epithelial cells produce abnormal multilaminar basement membrane, both in normal location and intraepithelially. As the intraepithelial basement membrane thickens, it blocks normal migration of epithelial cells toward the surface. Trapped epithelial cells degenerate to form intraepithelial microcysts that slowly migrate to the surface. Abnormal basement membrane produces map and fingerprint changes, and microcysts produce the dot pattern seen clinically.
- spontaneous recurrent corneal erosions and blurred vision. The erosions may be mild and transient, lasting minutes, or occasionally characterized by more severe pain.
- The treatment has been similar for recurrent corneal erosion, whether traumatic or dystrophic.
- anterior stromal reinforcement (puncture) seems to be the best way to treat recalcitrant recurrent erosions below the visual axis. It is effective in 80% of cases the first time it is done
- Epithelial debridement with diamond burr polishing works best for anterior basement membrane dystrophy in the visual axis causing either blurred vision or recurrent erosion.

Corneal Dystrophies of Bowman's Layer

- **Küchle** et al divided the anterior membrane dystrophies into two classifications: corneal dystrophy of Bowman's layer types I (CDB-I) and II.
- Type I is synonymous with Reis-Bücklers' original dystrophy and equivalent to what has been called the superficial variant of granular dystrophy. It has an autosomal dominant inheritance, recurrent corneal erosions beginning in childhood, and is marked by early and fairly marked visual loss.
- Corneal dystrophy of Bowman's layer type II (CDB-II), which many people have confused with the Reis-Bücklers' dystrophy, is honeycomb-shaped and should be known as Thiel-Behnke corneal dystrophy. Similar to CDB-I, CDB-II's inheritance is dominant, with recurrent erosions starting early in childhood, but visual acuity is reduced later in life than with CDB-I. The clinical appearance of these dystrophies is similar, and differentiation can be made only with light and, particularly, electron microscopy. Interestingly, *CDB-I stains positively with Masson's stain, whereas CDB-II is only equivocally positive to Masson's stain (honeycomb-shaped, Thiel-Behnke dystrophy).*

- Transmission electron microscopy differentiates these two dystrophies. In CDB-I, ultrastructural deposits of **rodlike bodies** are present, similar to those seen in granular dystrophy. These changes are not seen in CDB-II. Instead, **'curly' fibers** appear in the region of Bowman's membrane.
- they can be managed similarly to the therapy of recurrent erosion due to epithelial basement membrane dystrophy.
- Phototherapeutic keratectomy (PTK) with the excimer laser is now the treatment of choice when vision is disturbed sufficiently or painful erosions occur, despite recurrences after PTK.

Stromal Dystrophies

- **Granular corneal dystrophy type 1 (classic)**
  - 1890 by Groenouw
  - small, discrete, sharply demarcated, grayish-white opacities in the anterior central stroma
  - drop-shaped, crumb-shaped, and ring-shaped.
  - the stroma between the opacities remains clear.
  - As the condition advances, individual lesions increase in size and number and may coalesce. They frequently extend into the deeper and more peripheral stroma. However, 2–3 mm of the peripheral cornea usually remain free of deposits.
  - **autosomal dominant** trait and appears in the first or second decade of life
  - TGFBI gene-related dystrophy, 5q31 gene locus
  - **Histopathology**
    - Light microscopy demonstrates eosinophilic, rod, or trapezoidal-shaped **hyaline** deposits in the stroma and beneath the epithelium.
    - stain bright red with **Masson's trichrome** and stain weakly with **periodic acid-Schiff** (PAS)
  - **Management**
    - Recurrent epithelial erosions should be managed routinely with therapeutic contact lenses and artificial tears.

        - The traditional surgical approach has been penetrating keratoplasty, which is uncommonly performed before the fifth decade. If the opacities are extremely superficial, epithelial scraping, superficial keratectomy, or lamellar keratoplasty can be performed.
    - Granular dystrophy can recur in the grafts as early as 1 year after surgery,

- **Granular corneal dystrophy, type 2 (granular-lattice)**
    - **Avellino** corneal dystrophy
    - (1) anterior, stromal, discrete gray-white granular deposits; (2) mid to posterior stromal lattice lesions; and (3) anterior stromal haze.
    - foreign body sensation, pain, and photophobia, most likely secondary to recurring erosion.

- **Granular corneal dystrophy, type 3 (RBCD – Reis-Bücklers)**

- **Macular Dystrophy (MCD)**
    - **Fehr spotted dystrophy**
    - corneal opacities resulting from intracellular and extracellular deposits within the corneal stroma
    - **least common and the most severe**
    - progressive loss of vision as well as attacks of irritation and photophobia. Vision is usually severely affected by the time the patient reaches the twenties or thirties.
    - This opacification extends to the **periphery** and usually involves the **entire thickness** of the cornea by the second decade of life.
    - reduced central corneal thickness.
    - slit lamp examination demonstrates a ground-glasslike haze in the central and superficial stroma, which is best observed with oblique illumination. With progression of the dystrophy, small, multiple, gray-white, pleomorphic opacities with irregular borders are seen
    - **autosomal recessive**

- **chromosome 16**, Type I has no detectable antigenic keratan sulfate; type II has normal amounts of antigenic keratan sulfate; in type IA the serum lacks detectable antigenic keratan sulfate, but the keratocytes react with antibodies to keratan sulfate.
- **Histopathology**
  - accumulation of **glycosaminoglycans** between the stromal lamellae
  - stain with **Alcian blue, colloidal iron, metachromatic dyes, and PAS**
  - Light microscopy demonstrates degeneration of the basal epithelial cells, and focal epithelial thinning is seen over the accumulated material. Bowman's membrane may be irregular, thinned, or absent in some areas. Electron microscopy shows accumulation of mucopolysaccharide within stromal keratocytes, which are distended by numerous intracytoplasmic vacuoles with pyknotic nuclei.
- **Management**
  - Tinted cosmetic lenses can be used to reduce photophobia
  - Recurrent erosions are treated with therapeutic contact lenses or lubricant drops.
  - Phototherapeutic keratectomy
  - lamellar Keratoplasty
  - penetrating keratoplasty is the surgical modality of choice

- **Lattice Dystrophy**
  - ***Biber-Haab-Dimmer dystrophy***
  - bilateral, inherited, primary, localized corneal amyloidosis.
  - ovoid or round subepithelial opacities, anterior stromal white dots, and small refractile filamentary lines that may appear in the first decade of life
  - **Histopathology**
    - sources of the amyloid include leakage from serum, extracellular breakdown of corneal collagen, and, most probably, localized intracellular production

        - eosinophilic layer separating the epithelial basement membrane from Bowman's layer is present and is composed of **amyloid and collagen**
        - stain orange-red with **Congo red**, and also stain with **PAS, Masson's trichrome, and fluorochrome thioflavin T**.
        - When viewed with a polarizing filter, amyloid deposits demonstrate green birefringence
    - **autosomal dominant** mode of inheritance, and the disease results from mutations at 5q31 gene locus
    - **Management**
        - lamellar or penetrating Keratoplasty
        - recurs more frequently than does granular or macular dystrophy, and the recurrence can appear in the graft in as few as 3 years after Keratoplasty

- **Schnyder's Crystalline Dystrophy (SCD)**
    - Bilateral gray, disclike opacities are seen, primarily in the anterior stroma. These opacities are often central and also may include fine polychromatic cholesterol crystals in the anterior stroma
    -

- **Fleck Corneal Dystrophy (FCD)**

- **Central Cloudy Dystrophy of François (CCDF)**

- **Posterior Amorphous Corneal Dystrophy (PACD)**

- **Congenital Hereditary Stromal Dystrophy (CSCD)**

- **Pre-Descemet Corneal Dystrophy (PDCD)**

Descemet's Membrane and Endothelial Dystrophies

- **Posterior Polymorphous Corneal Dystrophy**
  - bilateral asymmetrical
  - asymptomatic to progressive
  - second or third decade of life
  - abnormalities in PPCD occur at the level of Descemet's membrane and endothelium and can be divided into three patterns:
    1. **vesicle-like lesions**: 0.10 to 1.00 mm, sharply demarcated large round areas that contain lighter thick ridges or cell aggregates
    2. **band lesions**: typically horizontal, have parallel scalloped edges, and do not taper toward the ends
    3. **diffuse opacities**: either small, macular, gray-white lesions or larger sinuous geographic lesions at the level of Descemet's membrane
  - **hallmark of PPCD is the vesicular lesion**
  - Corneal edema occurs infrequently and ranges from minimal stromal thickening to bullous keratopathy
  - PAS are also a characteristic feature of PPCD and an important prognostic indicator
  - Angle closure is thought to result from endothelial cell migration across the trabecular meshwork onto the iris, forming synechiae. The mechanism of open angle glaucoma has been suggested to be compression of the trabecular meshwork secondary to a high iris insertion.
  - DD: ICE syndrome
    - share many clinical features, including iridocorneal adhesions, glassy membranes over the angle and anterior surface of the iris, iris atrophy, corectopia, increased intraocular pressure, and corneal edema.
  - Mx:
    - Risk factors for severe disease included the presence of iridocorneal adhesions and increased intraocular pressure. Only 27% of patients had iridocorneal adhesions, yet 57% of patients with iridocorneal adhesions required corneal transplantation. Similarly, only 14% of patients in this

series had increased intraocular pressure, yet 62% of patients with increased intraocular pressure required corneal transplantation.

- HP:
  - epithelium and stroma: chronic edema, subepithelial fibrosis, and band keratopathy
  - Descemet's membrane and the endothelium: thickening of Descemet membrane with rare foci of bilayered large endothelial cells, to 3–4 layered broad patches of flattened endothelial cells and irregular thickness of Descemet's membrane with focal absences
  - ABZ: Normal, thinner in early onset
  - PNBZ: Absent or minimal, Changes to a thick PCL-like layer with scant BM*
-

- **Fuchs' Endothelial Corneal Dystrophy**
  - slowly progressive disease with initial onset in the **fifth** through seventh decades in life.
  - **50% autosomal dominant, variable penetrance**
  - **Females** are predisposed to Fuchs' dystrophy and develop corneal guttae **2.5 times** more frequently than males, progressing to corneal edema 5.7 times more often than males.
  - CF:
    - The **first stage** is **asymptomatic**. Slit-lamp examination discloses central corneal guttae, but vision and corneal thickness are normal. **Guttae**, irregularly scattered excrescences in the posterior cornea, are often associated with fine pigment dusting
    - In this **second stage**, patients have **painless decreased vision**, especially upon awakening. Vision may improve as the day progresses as evaporation promotes corneal deturgescence. Glare and haloes may be noted. **Stromal edema** occurs in the setting of corneal guttae, most typically in the fifth decade of life
    - **Epithelial edema** characterizes the **third stage**. Initially, fine epithelial **microcysts** are noted. The epithelial surface is roughened, with an irregular surface texture. **Vision invariably deteriorates** during this stage and marked fluctuations in vision are common. Occasionally, erosive symptoms are the presenting complaint. Large intraepithelial and subepithelial bullae may rupture, resulting in **severe eye pain** and rendering the patient susceptible to infection.

- In the **fourth stage**, growth of avascular subepithelial connective tissue occurs, causing reduced vision from scarring. The cornea is opaque and compact. Pain is decreased, but vision is severely reduced to the hand motions level. Corneal sensation is decreased or absent. With time, peripheral corneal vascularization may occur.

- **Differential diagnosis**
  - gutta formation without corneal edema has been observed in **interstitial keratitis**
  - gutta: **macular dystrophy and posterior polymorphous dystrophy**.
  - **Corneal pseudoguttae**: transient, representing edema of the endothelial cells, and disappear with resolution of the underlying condition →can be seen after trauma, intraocular inflammation, infection, toxins, and thermokeratoplasty
  - **Central herpetic disciform keratitis**: keratic precipitates (KP)
  - **Chandler's syndrome**: unilateral
- **medical management:**
  - topical hypertonic saline solutions
  - dehydration of the cornea by a blow dryer in the morning or throughout the day
  - lowering the intraocular pressure may reduce the hydrostatic pressure, which acts to push fluid into the cornea and thereby decrease corneal edema.
  - Bandage lenses may be helpful in the treatment of recurrent erosion caused by epithelial bullae. a loosely fit, high-water-content soft contact lens, e.g., Kontur lens, may be used to reduce the irritation and pain
- **Surgical Mx:**
  - **cell count of less than 1000** should raise concern about the possibility of corneal decompensation with intraocular surgery.
  - corneal **thickness of over 640 microns** (μm) increases the risk of corneal decompensation with cataract surgery
  - **central corneal thickness exceeds the mid-peripheral thickness**, this may be a indication of clinically significant corneal thickening.
  - endothelial transplantation
  - optical PK/ Triple Sx

- **CCT < 600 microns, ECD > 1000 → cataract surgery f/by DSAEK-OPK**

- **HP**:
  - LM: increase in cellular size and irregularity of shape, **DM thickens 2-3 times**
  - EM: normal ABZ of type 7 collagen, PNBZ is of type 4 collagen. Besides a thin or **absent PNBZ, the most typical finding in FECD is an abnormal posterior collagenous layer (PCL) which is responsible for most of the thickness.**
  - Thinning of the endothelium over the enlarging guttate bodies may result in complete baring of these bodies as the disease progresses: like those in peripheral Hassal-Henle warts

- **Genetics**:
  - many patients have no known inheritance pattern
  - one family traced for → single locus at **13p**

- **Congenital Hereditary Endothelial Dystrophy**
  - rare corneal dystrophy except in Saudi Arabia and south India
  - bilateral, symmetric, noninflammatory corneal clouding without other anterior segment abnormalities that is usually evident at birth or within the early postnatal period
  - **Differential diagnosis**
    - **Mucopolysaccharidoses**: clouding is not present at birth, typically developing within the first few years, urinalysis or corneal biopsy will usually identify the abnormal metabolic
    - **congenital glaucoma**: ncreased IOP, often an increase in corneal diameter, Haab's striae, and, in severe disease, buphthalmos.
    - **Transient corneal edema** can occur in congenital rubella, but, in contrast to CHED, there is episcleral injection, typically a nuclear cataract, increased intraocular pressure, posterior synechiae, miosis, and chorioretinopathy.
    - **Syphilitic interstitial keratitis** also produces an inflamed eye with corneal clouding, deep stromal vascularization, and iris atrophy, but it rarely occurs within the first year of life
    - **Dystrophies at birth-natal age groups**: CHED, PPCD and CHSD.

- CHED 1 (AD)
    - Photophobia and tearing
    - corneal clouding is not present at birth, developing late in the first year
    - chromosome 20p11
- CHED 2 (AR)
    - gray-blue, ground-glass haziness of the corneal stroma noted within the first week to 6 months
    - fine nystagmus
    - chromosome 20p13-12
    - **Harboyan syndrome** (CHED 2 and perceptive deafness (CDPD)) is an autosomal recessive disease mapped at overlapping loci 20p13. Novel **SLC4A11 mutations** have been found in seven families.
    - prognosis for graft clarity and visual rehabilitation is dependent upon the age of onset
    - HP:
        - corneal showed alterations secondary to chronic corneal edema, appearing thin or atrophic with hydropic changes of the basal epithelium
        - stroma was generally thickened to two to three times
        - Descemet's membrane was usually observed to be thickened.
        - The endothelial cells were absent, markedly reduced in number, or showed evidence of significant degeneration
    - EM:
        - normal 110 nm ABZ of approximately 3 μm thickness, but **an abnormal, poorly demarcated PNBZ merging into, or mixed with, a PCL.**

- **X-Linked Endothelial Corneal Dystrophy (XECD)**

PUK

- From DOS article

Corneal Infections

Herpes Simplex Keratitis

- HSV-1 usually involves the oropharynx and HSV-2 usually involves the genital area
- ocular disease is caused by type 1 rather than type 2, with the exception of herpetic keratitis in neonates in which 75% is caused by HSV-2
- icosahedral-shaped capsid surrounds the core, which contains the double-stranded deoxyribonucleic acid (DNA) and associated phosphoproteins of the viral chromatin.
- HSV binds to one or more cellular receptors, heparin sulfate probably being one of them
- **Epidemiology**
    - Humans are the only natural reservoir
    - primary infection manifests clinically in only 1–6% of people infected with the virus
    - high male:female ratio (1.67:1) in patients more than 40 years of age. In younger patients, no difference was observed.
- **Pathogenesis**
    - After peripheral entry into the host and primary infection with viral replication within an end organ, HSV travels in a retrograde fashion to various ganglia including the trigeminal, cervical, and sympathetic gangliae, and possibly the brain stem.
    - Latently infected neurons have not been found to produce infectious virus. However, a region of the viral genome that is retained within the host cell nucleus during latency is responsible for RNA transcripts termed latency-associated transcripts (LATS).
    - the trigeminal ganglion is the most common source of recurrent HSV infection.
    - Systemic antibodies have no known role in the development of recurrent disease despite their role in the host response to active primary and recurrent infection
    - activation of recurrent HSV ocular disease:
        - Sunlight, trauma (including surgery), heat, abnormal body temperature, menstruation, other infectious diseases, and emotional stress, Prostaglandin F2 alpha analog and prostamide glaucoma medications

latanoprost and bimatoprost have also been implicated in ocular or even periocular HSV

- CD8+ T-cell inhibition of HSV-1 reactivation show viral inactivation via the use of lytic granules degrading precursors to viral gene expression. These CD8+ T cells maintain latency without causing neuronal apoptosis

- Immune defense mechanisms

- **Congenital and neonatal ocular herpes**
  - HSV-2 accounts for 80%
  - periocular skin lesions, conjunctivitis, epithelial keratitis, stromal keratitis, and cataracts.
  - maternal IgG to HSV may cross the placenta, it does not appear to be sufficient to prevent ocular disease completely.
  - The use of antibody titers for diagnosis is not useful because of pre-existing maternal antibody and the delayed production of IgM.

- **Primary ocular herpes**
  - By the age of 5 years, nearly 60% of the population has been infected with HSV. Latent infection → viral carrier state.
  - Only 6% of infected actually develop clinical manifestations, which typically affect the perioral region rather than the eye.
  - Can present as acute follicular conjunctivitis, keratoconjunctivitis, preauricular adenopathy, and periocular and eyelid skin vesicles

- **Recurrent ocular herpes**
  - Liesegang's review: 36% at 5 years and 63% at 20 years
  - ***HEDS study: 18%***

- **Blepharitis**
  - vesicular lesion involving a focal area of the eyelid with surrounding erythema
  - ulceration and crusting and heals without a scar unless secondarily infected.

- Conjunctivitis
  - follicular conjunctivitis, self-limiting

- may develop follicular conjunctivitis. In many patients, this conjunctivitis is self-limiting
- may constitute up to 23% of cases of acute conjunctivitis

- Keratitis
  - Recurrent HSV keratitis is typically a unilateral disease. Bilateral herpetic keratitis occurs in approximately 3% of patients with ocular HSV.
  - Infectious epithelial keratitis (Cornea vesicles, Dendritic ulcer, Geographic ulcer, Marginal ulcer)
    - photophobia, pain, and a thin, watery discharge; DOV if central
    - branching, linear lesion with terminal bulbs and swollen epithelial borders that contain live virus
    - true ulcer in that it extends through the basement membrane.
    - Fluorescein staining with negative stain of terminal bulbs, rose Bengal is toxic to HSV and will decrease the yield of the culture.
    - HSV dendritic epitheliopathy: not ulcerated and simply represents healing epithelium after the infection.
    - An enlarged dendritic ulcer that is no longer linear is referred to as a geographic ulcer. (22% of all epithelial)
    - marginal ulcer: proximity the limbus, quickly infiltrated with white blood cells, more symptomatic because of the intense inflammation
    - four recognized sequelae

    1. complete resolution
    2. infectious epithelial keratitis
    3. stromal scarring: ‘ghost scarring’ or ‘footprints’ of HSV keratitis.
    4. stromal disease (25%) → Necrotizing keratitis represents true viral infection of the stroma, whereas immune stromal keratitis is mediated by antibody-complement reactions to viral antigen.

  - Neurotrophic keratopathy
    - arises from impaired corneal innervation in combination with decreased tear secretion.
    - irregularity of the corneal surface and lack of the normal corneal luster.
    - oval in shape with smooth borders, in direct contrast to the geographic ulcer, which is irregular in shape with scalloped borders

- Stromal disease
  - 2% of initial episodes, 20–48% of recurrent ocular HSV
  - 2 cases where stroma is involved primarily. Necrotizing stromal keratitis occurs from direct viral invasion of the stroma, whereas immune stromal keratitis is the result of an immune reaction within the stroma.
- Necrotizing stromal keratitis
  - necrosis, ulceration, and dense infiltration of the stroma with an overlying epithelial defect.
  - Risk factor: use of topical corticosteroids without antiviral coverage
- Immune stromal (interstitial) keratitis
  - 20% of patients with ocular HSV
  - due to retained viral antigen within the stroma. This antigen triggers an antigen-antibody-complement (AAC) cascade that results in intrastromal inflammation.
  - stromal inflammation with overlying epithelium almost always intact
  - often accompanied by anterior chamber inflammation, ciliary flush, and significant discomfort.
  - immune ring: AAC precipitate similar to a Wessely ring
  - stromal neovascularization: sectoral, with a single frond of vessels, to complete, involving all quadrants of the cornea. Ghost vessels, in and of themselves, do not cause decreased vision or increased risk of penetrating keratoplasty rejection.
- Endotheliitis
  - corneal stromal edema without stromal infiltrate
  - keratic precipitates (KP), overlying stromal and epithelial edema, and iritis.
  - three forms of HSV endotheliitis are disciform, diffuse, and linear
  - Disciform endotheliitis: MC, ocular discomfort, Limbal injection, disc-shaped area of stromal edema,
  - Diffuse endotheliitis: rare,
  - Linear endotheliitis:
- Iridocyclitis
  - most commonly accompanies immune stromal keratitis or endotheliitis, but, as previously stated, it may occur as the only inflammatory finding.

- Diagnosis:
    - ophthalmic examination
    - viral culture: within several days of the onset and may require up to 1 week of incubation
    - Cytologic examination of specimens stained with Giemsa or Wright stains
    - Immunologic tests
    - Polymerase chain reaction (PCR)

- Management:
    - 4 valuable insights of HEDS
        1. Oral antiviral prophylaxis reduces recurrences of epithelial and of stromal keratitis.
        2. Use of topical corticosteroids is of benefit in stromal keratitis.
        3. Use of oral acyclovir may be of help in iridocyclitis.
        4. Prophylactic oral acyclovir helps prevent recurrences of herpetic keratitis, particularly stromal with a history of recurrence.

Acanthamoeba Keratitis

- free-living protozoan that is ubiquitous in nature
- found commonly in water, soil, air, cooling towers, heating, ventilating, and air conditioning (HVAC) systems, and sewage systems.
- Unlike disseminated Acanthamoeba infection, corneal disease is not associated with immunosuppression.
- three morphologic groups: group 1,2,3
    - major human pathogens belong to Group II
    - Twelve lineages referred to as T1-T12

- **MC: A Polyphaga, A Castellani**
- Stages: trophozoite & cyst
- Trophozoite – Mobile
- Cyst - stable & highly resistant form

- **Pathogenesis**
  - Exposure to contact lens - 70-85%
  - Corneal trauma.
  - Natural immunity exists.
  - Host response by acute inflammatory cells especially around cyst & necrotic organisms. Contaminated contact lens solution + Microtrauma to Epithelium by contact lens
  - acanthamoeba infection by trophozoite
- **Clinical features**
- Presentation: Blurred vision with acute pain disproportionate to signs.
- Signs:
- Early
  - Epithelial irregularity & infiltration pseudodendrite or raised epithelial ridges
  - Radial keratoneuritis
  - Stromal infiltration, satellite lesion, disciform lesion, ring infiltrate
  - Conjunctival follicles.
  - Preauricular nodes.
- Late
  - Stromal opacification
  - Scleritis
  - Descematocele formation
- **Diagnosis**
  - Gram & Giemsa stain
  - Calcofluor white stain - stains wall of cyst.
  - acridine orange.
  - Immunofluorescent antibody stain.
  - PAS & methenamine silver.
  - Confocal microscope - confirmatory pear shaped cyst & irregular trophozoite
  - Phase contrast Microscope
  - **PCR and Corneal Biopsy**
  - *Transported in:* **Page saline** with sample of contact lens saline & case.-Ideal.
  - Alternative media is buffered **charcoal yeast extract agar**-Lower efficacy (72%)

  - **E-coli on non nutrient agar** (1.5%) at 25 and 37 degree C, May require up to 14 days to grow - Create track by eating E Coli.
- **Differential diagnosis**
  - Diagnosis By Exclusion
  - Herpetic keratitis - no systemic association
  - Fungal
- **Treatment**
- Biguanides-Cationic Antiseptics - inhibits membrane function
  - Chlorhexidine, Solution, 0.02%
  - Polyhexamethylene, Solution, 0.02% (PHMB)-BAQUACIL
- Aromatic Diamidines - inhibits DNA synthesis
  - Propamidine isethionate, Solution, 0.1% (BROLENE)
  - Pentamidine isehionate, Solution 0.1% (PENTAM)
- Aminoglycoside - inhibits protein synthesis
  - Neomycin Solution, 1.75 mg/ml Ointment 3.5 mg/g
- Azoles - destroys cell wall
  - Clotrimazole, suspension, 1%
  - Fluconazole, solution, 0.2%
  - Ketoconazole, oil solution, 5%
  - Miconazole, solution, 1%
  - Initially - hrly x 48 hrs.
- Corticosteroid - reduces inflammation. Very Cautious use (While continuining anti-amoebic agents): Prevents encystment of Trophozoite in vitro and may therefore enhance effectiveness of Topical treatment. Topical steroids have shown to prolong effective treatment and used in specific conditions like Limbitis,Scleritis and uveitis
- **Course & outcome**
- Majority eradicated by medical therapy.
- **Treatment of Complications**
  - Scleritis:-consider immunosuppressant with steroids/ cyclosporine.
  - Corneal Scaring:- Two Types Therapeutic or Penetrating Keratoplasty

Bacterial Keratitis (lecture notes)

Fungal Keratitis (lecture notes)

- 6-20% worldwide
- 49% india
- 65% in 21-50 years
- M:F= 1.5:1
- Season: monsoon, early winter
- Risk factors:
    - Ocular
        - Trauma: vegetative matter
        - Chronic inflammation
        - CL wear
        - Topical antibiotics and steroids
        - Prior ocular surgery (LASIK, PK, Cataract)
    - Systemic
        - NIDDM, HIV, Leprosy
- Classification of fungi
    - Filamentous septate
        - Non-pigmented
            - Fusarium solani
            - Aspergillus fumigatous, flaus, niger

        - Acremonium
        - Paecilomyces
    - Pigmented
        - Curvelaria
        - Alternaria
        - Cladosporium
        - Helminthosporum (diechslera)
  - Filamentous non-septate: rhizopus
  - Yeasts: candida albicans, tropicalis
- Symptoms
  - Indolent, FB sensations
  - Increasing pain
  - Diminution of vision
- Signs
  - Dry rough texture
  - Feathery margins
  - Abscesses
  - Satellite lesion
  - Endothelial plaques
  - Fixed hypopyon
- Specific signs
  - Demataceous fungi: brown pigmentation
  - Fusarium: severe sourse, deep extension, perforation
  - Aspergillus: indolent course
  - Yeast: collar button configuration

- Laboratory diagnosis
    - Smears: DEEP SCRAPING
        - 10% KOH sensitivity 91-99%
        - Gram stain sensitivity 45-73%
        - Lactophenol cotton blue sensitivity 45-73%
        - Grocott's methenamine silver sensitivity 80-90%
    - Culture
        - Sabouraud dextrose agar (**without cycloheximide**)
        - Positive culture 52-68%
        - Initial growth occurs within 72 hours
        - Wait at least 7 days before culture negative report
    - Newer diagnostic modalities
        - PCR: 74% within 4 hours
        - Confocal microscopy
            - Fungal keratitis sensitivity 94% and specificity 84%
            - Acanthamoeba keratitis sensitivity 100% and specificity 84%
- Antifungal drugs
    - Polyenes: natamycin, nystatin, amphotericin B
    - Azoles: fluconazole, itraconazole, voriconazole, posaconazole, ravuconazole
    - Fluorinated pyrimidines: flucytosine
    - Echinocandins: caspofungin, micafungin
- Topical antifungals
    - 5% natamycin hourly – daytime, 2 hourly bedtime → 2 hourly daytime, taper in 4-7 days
    - If worsening → add 0.15% amphotericin or 2% fluconazole for candida
    - Therapy for 3-4 weeks

    - Limitations
        - Commertially available preparations less
        - Poor ocular penetrations
        - Poor bioavailability
        - Toxicity
    - Topical voriconazole 1%: powder for parenteral use, alternaria and scedosporium keratitis, inhibits CYP450 dependent 14-sterol demethylase, FUNGISTATIC
- Systemic antifungals
    - Indications
        - Large ulcers
        - Severe deep keratitis
        - Scleritis
        - Post-PK
        - endophthalmitis
    - drugs
        - ketoconazole 200 BD
        - fluconazole 200 BD
        - itraconazole 100 BD
        - voriconazole 200 BD
        - LFT should be done every 2 weekly
- Targeted drug delivery
    - Injections
        - Intracameral
            - Non responsive to medical therapy
            - Thick hypopyon
            - Endothelial exudates

        - Deep anterior chamber exudates
        - Amphotericin 5-7.5 ug/0.1ml/5%D
        - Voriconazole 50-100 ug/0.1ml
    - Intracorneal/ intrastromal
        - Deep mycotic keratitis
        - Non perforated corneal ulcer
        - Non responsive to conventional topical+ systemic anti-fungal therapy for 4 weeks
- Remember flow chart of management. (read it)

Viral Keratitis (Lecture notes)

- Herpetic Eye Disease: HSV, HZV
- Non herpetic eye disease: adenoviral

- Primary ocular herpes
    - Confined to epithelium
    - Blepharoconjunctivitis
    - Preauricular LAP
- Recurrent ocular herpes
    - Infections:
        - Epithelial: dendritic, geographical
        - Stromal: necrotizing, immune → most devastating, heavy infiltration, deep vascularization, corneal thinning, perforation
        - Endothelial: disciform, linear, diffuse
    - Neurotrophic keratopathy
    - Herpetic marginal ulceration: peripheral corneal ulceration, underlying anterior stromal infiltrate, adjacent limbal congestion

Herpes Zoster Eye Disease

- Acute phase:
    - punctate epithelial keratitis
    - micrdendritic ulcers
    - nummular keratitis
    - disciform keratitis
- chronic phase
    - mucus plaque keratitis
    - neurotrophic keratitis
    - nummular keratitis
    - disciform keratitis

- Laboratory Diagnosis
    - Giemsa staining sensitivity 57% and specificity 85%
    - PCR specificity 70%
    - Viral culture 70%
    - Immunological tests
- Topical antivirals
    - Acyclovir 3% ointment
    - Vidarabine 3% ointment
    - Trifluothymidine 1% solution
    - Idoxuridine 1%
- Topical steroids: for stromal component
- Systemic acyclovir
    - Recurrent stromal-epithelial keratitis
    - Immunocompromised patients
    - HSV keratitis in a corneal graft
    - 400 mg 5 times a day for HSV, 800 mg 5 times a day for VZV

- **Metaherpetic keratitis**
    - Medical
        - Withdraw epitheliotoxic drugs
        - Intensive lubricants
        - Cycloplegics
        - Steroids
    - Surgical
        - Conjunctical flap
        - AMG
        - Glue for small perforation
        - Patch graft
        - Tectonic graft

- Adenoviral keratitis
    - EKC
    - 8,19,37
    - 10% transmission ot household contacts
    - Severe follicular kerato conjunctivitis
    - Hemorrhagic conjunctivitis
    - Acute stage
        - Cold compresses
        - Lubricants
        - Prophylactic antibiotics
    - Nummular opacity
        - Topical steroids: 6 weeks
        - Topical cyclosporine
        - Lubricants

Akanthamoeba Keratitis (lecture notes)

- 1% of all infectious keratitis
- Risk factors
    - 85% CL users
    - Home made saline
    - Contaminants/ swimming pool
    - Trauma
    - Vegerable matter
    - Orthokeratology
- CF
    - Unilateral
    - Severe pain due to keratoneuritis
    - Immunocompetent patients
    - Fails to respond to antibacterial, antiviral or antifungal treatment
- Signs
    - Epithelial irregularities: punctate, linear, pseudodendritiform, haze 25-50%
    - Patchy stromal infiltrate 5-50%
    - Radial pretineural infiltrate (pathognomonic)
    - Ring infiltrates 19-90%
    - Satellite lesion, stromal thinning, lysis, perforation
    - Absence of corneal neovascularization
    - Slow progression, period of remission
    - Days to months
    - Scleritis 11-40% (immunological response)

- Diagnosis
    - Microbiology
        - Corneal scrapings, CL, case, solution
        - Confocal
        - Corneal biopsy
    - Cysts: polygonal and double walled appearance on calcoflour white 0.1%
    - Culture: non nutrient agar with e.coli/aeromonas/klebsiella, blood agar, chocolate agar
- Treatment
    - Biguanide: PHMB 0.02%, chlorhexidine 0.02%
    - Diamidine: propamidine 0.1%, hexamidine 0.1%
        - Taper till 6 months
    - Miconazole and clotirmazole 1-2%

Stages of Corneal Ulcer

- **Stage of infiltration**
    - Infiltration of PMNL/Lymphocytes into the epithelium and stroma
- **Stage of progression**
    - Necrosis and sloughing of the necrotic material
    - Surrounding area is packed with leucocytes. Wall of the ulcer projects due to edema and infiltration of cells
    - Zone of infiltration extends beyond and underneath the ulcer margin
    - Ciliary congestion
    - Involvement of iris and ciliary body (due to absorption of toxin)–causing iritis/cyclitis
    - Hypopyon formation
- **Stage of regression**

- Induced by immunodefence mechanism and treatment
- Line of demarcation develops around the ulcer area
- Necrotic material is sloughed off and the ulcer bed enlarges.
- As the surrounding infiltration and swelling disappears, the floor and edges become smooth and transparent.
- Superficial vessels grow in from the limbus near ulcer, to restore the loss of substance and supply antibody.

- **Stage of cicatrization**
  - Vascularisation of ulcer
  - Regeneration of collagen and formation of fibrous tissue (causes corneal opacity)

Pterygium

- An Elastotic Degenerative condition of conjunctiva with a wing like encroachment of conjunctiva on to the Cornea.
- Pathogenesis –
  - Environmental causes- UV exposure, dust heat , wind exposure
  - peri-equatorial '**pterygium belt' latitudes 37°** north and south of the equator.
  - Heredity:
    - Loss of heterozygosity (17q,9p) and microsatellite instability-- *Spandidoras (1997), Detorakis et al(1998)*
    - p53 mutation--*Tan et al (1997)*-- pterygium is not a degeneration but a growth abnormality.
  - **Coroneo Effect** -Nasal segment of cornea gets highest UV exposure effect
  - Limbal Stem cell defect with Fibroblast Activation: conjuctivalisation, inflammation and vascularisation
  - HSV & HPV --*Spandidoras et al (1994)*--HSV in 45% of pterygia, *Dushku et al(1999)* ruled out HPV. *Gallagher et al(2001)* –HPV may play a role in recurrence
- Classification
  - Primary Pterygium
  - Recurrent Pterygium
  - Atrophic Pterygium: Older pts, thin translucent body with thin vessels

- Pogressive Pterygium: Thick fleshy growth seen in Younger pts

- Grading
  - Size
    - 1: just touching cornea
    - 2: midway between 1 & 3
    - 3: upto pupil margin
  - **Tan Grading:**
    - T1 (atrophic) denotes a pterygium in which episcleral vessels underlying the body of the pterygium are unobscured and clearly distinguished
    - Pterygia in which the episcleral vessel details are indistinctly seen or partially obscured are categorized as grade T2 (intermediate)
    - Grade T3 (fleshy) denotes a thick pterygium in which episcleral vessels underlying the body of the pterygium are totally obscured by fibrovascular tissue

- **Clinical features**
  - Males:female-2:1,
  - young -20-40yrs and elderly,
  - incidence proportional to proximity to equator.
  - diminution of vision-astigmatism, usually with the rule, can be against / oblique/ irregular, late stages dv due to encroachment into pupillary area
  - intermittent episodes of inflammation
  - cosmesis
  - diplopia-- symblepheron formation (more common in recurrent cases)

- Medical Management
  - Symptomatic Grade 1 and 2 pterygium
  - protection from sunlight
  - Eye drops – Tear substitutes, Decongestants

- Local injections – anti VEGFs, Steroid

- Surgical Management

  Indications-

  - Symptomatic patients: recurrent irritation, redness and watering
  - Visual need: covering visual axis or threatening visual axis, causing irregular astigmatism, Grade 2 and 3 Pterygium
  - Cosmetic
  - Therapeutic: suspected associated neoplastic degeneration, motility restriction

four main groups

1.Bare sclera excision

- 1948, D'Ombrain
- high recurrence rates ranging from 24% to 89%

2.Excision with conjunctival closure/transposition

- high recurrence rates of 37% /29%

3.Excision with antimitotic adjunctive therapies

- Beta irradiation: Strontium-90, recurrence rate – 10%
- Mitomycin C: the postoperative use of topical mitomycin C as eyedrops, and the intraoperative application of surgical sponges soaked in MMC, recurrence rate – 0 to 38%

4.Ocular surface transplantation techniques.

- Conjunctival autograft transplantation
- Variations of conventional conjunctival autografting
- Conjunctival rotational autograft
- Annular conjunctival autograft
- Cultivated conjunctival transplantation

- Conjunctival limbal autograft transplantation
- Amniotic membrane transplantation.

- **Adjuvants – to reduce recurrence**

  Mitomycin C- For recurrent pterygia

  Intra op or post op

  Uncommonly used

  Late Scleral necrosis & melt

  Thiotepa – used post op

  Beta radiation with Strontium 90

  Excimer Laser in PTK mode – for corneal smoothening

- Complications.
  - Graft contration
  - Graft edema
  - Graft necrosis
  - Granuloma formation
  - Excessive cautery- scleral necrosis
  - Infection
  - Recurrence
  - Corneal scaring
  - Ocular motility restriction
  - Surgical induced Necrotising Scleritis (SINS)

- **Pterygium Recurrence Rate**---*Alp et al 2002*

  MMC: Intra OP: 3.33-42.7 /Post OP:0-54.5
  Beta radiation: 0.5-33

Excimer PTK: 4.5-91
AMG: 3.8-37.5
CAG: 2.6-39
LCAT: 0-14.6
Simple Excision: 29.2 -89

- Recurrent pterygium
    - surgical trauma-excess cautery, excess tenonectomy, post op inflammation and infection, incomplete removal .
    - Mean recurrence time – Hirst et al (1994)

      1st recurrence - 123 days, 2nd - 97 days, 3rd - 67 days.

      Avisar et al (2001) – 91% recurrence in 1 year

- A true pterygium must be differentiated from a pseudopterygium, which may occur after trauma. Pseudopterygium has been reported secondary to inflammatory corneal disease. ***A probe may be passed at the limbus under a pseudopterygium.*** Further distinction can be made, since pseudopterygia may be found anywhere on the cornea and are usually found obliquely, whereas true pterygia are horizontal in the 3 or 9 o'clock positions.
-

Corneal Complications of Intraocular Surgery

1. Epithelial: Abrasion, Edema, Filaments, Toxic keratopathy
2. Thermal burns: Cautery, Phacoemulsification probe
3. Infection: Bacterial, Fungal, Herpes simplex keratitis
4. Descemet's membrane: Tear, Detachment
5. Endothelial injury: Aphakic bullous keratopathy, Pseudophakic bullous keratopathy, Brown-McLean syndrome, Phakic bullous keratopathy, TASS

Descemet's membrane Detachment

- Risk factors for Descemet's membrane detachment include blunt knife entry, oblique insertion of instruments, entry of instruments or viscoelastics into a false plane above

Descemet's membrane, or history of ocular conditions disrupting Descemet's membrane such as congenital glaucoma, birth forceps injury, keratoconus, and Terrien's marginal degeneration.

- can spontaneously reattach with medical treatment alone, with a ***mean resolution time of 10 weeks***.
- With large detachments or slow resolution, ***descemetopexy*** with air, sulfur hexafluoride (SF6), perfluoropropane 14% (C3F8) gas injections, sodium hyaluronate or through-and-through corneal mattress sutures may help
- Bullous keratopathy or corneal scarring may occur, requiring endothelial or penetrating ***keratoplasty in 7-8% of cases***

Aphakic/Psudophakic bullous keratopathy

Imbibition pressure = IOP - Swelling pressure

- Incidence:
    - ICCE with IOL: 0-0.8%
    - Complicated Cataract Surgery: 0-11.3%
    - Iris clip lens: 9%
    - ECCE with ACIOL: 15%
    - ECCE/Phaco with PCIOL: 0.1% to 0.47%

PBK with different IOL

PCIOL: 0.06%

ACIOL: 1.2%

Iris-clip lens: 1.5%

- Histopathology:
    - attenuation and loss of corneal endothelial cells
    - epithelial bullae and stromal edema
    - thickening of the posterior collagenous layer of Descemet's membrane

- decrease in stromal keratocytes
- Subepithelial and retrocorneal fibrous proliferation
- *epithelial basement membrane has decreased amounts of **fibronectin, laminin, and collagen type IV**, which function as adhesive proteins leading to epithelial bullae*
- *accumulation of antiadhesive proteins, such as **tenascin-C and thrombospondin-1***

- **Pathogenesis:**
  - 12% reduction of the central corneal endothelial cell density in eyes having intracapsular cataract extraction
  - **9% central endothelial cell loss at 1 year** after phacoemulsification and posterior chamber lens insertion, with **11.5% loss at 3** years, followed by only 0.3% per year greater loss than in control eyes.
  - **Bates model** predicts decompensation of the cornea at **542cells/mm2** and a time to decompensation of almost **40 years** for uncomplicated cases.

- **Causes of ABK and PBK**

1. Pre-existing endothelial disease

a) Fuchs' dystrophy, cornea guttata
b) Pseudoexfoliation
c) Trauma
d) Angle-closure glaucoma

2. Intraoperative factors

a) IOL-to-cornea touch
b) Irrigating solutions
c) Instrumentation
d) Sterilization technique: **AbTox Plazlyte**, a sterilization technique that can degrade brass to copper and zinc on cannulated surgical instruments, resulted in irreversible endothelial cell destruction
e) Ultrasound damage
f) Vitreous loss, nuclear loss
g) Drug toxicity
h) Intracameral anesthesia
i) Descemet's membrane detachment

3. Postoperative factors

a) Long-term cell loss

b) Vitreous-to-endothelial touch
c) IOL dislocation – touch
d) Flat anterior chamber
e) Peripheral anterior synechiae
f) Pseudophakodonesis
g) Inflammation
h) Toxic materials

- **Treatment:**
    - Anterior stromal puncture may help reduce tearing and pain, and improve vision through regression of epithelial bullae and epithelial edema in patients with early corneal edema
    - Annular keratotomy has also been reported with good success for patients with pain
    - Endokeratoplasty has become the treatment of choice over conventional penetrating keratoplasty for patients with diseased endothelium.
    - Conjunctival flap: In 1958, Gundersen introduced the technique of using conjunctiva alone without use of tenon's capsule to cover the cornea.
    - AMG with basement membrane surface up in all cases. *The side of BM could be distinguished from stromal side by touch with sponge. The former was not sticky, while the later was & could be caught by the sponge.*
    - Cautenisation of Bowman's membrane
    - Diamond burr polishing of basement membrane
    - Phototherapeutic keratectomy for bullous keratopathy
        - ***Superficial PTK showed improvement in 62% cases***
        - ***Intermediate PTK showed improvement in 40% cases***
        - ***Deep PTK: Mean ablation performed was of 206 um, 66% showed improvement***
        - preterminal neural plexus of cornea is located just deep to Bowman's membrane. Hence moderately deep ablation would have superior effect on decreasing the pain; by ablation of neural plexus.
    -

Brown-McLean syndrome

- unusual form of peripheral corneal edema occurring long after cataract surgery
- edema extends 2–3 mm centrally from the limbus and up to 360 degrees, although the superior limbus may remain clear
- central corneal endothelium may have decreased cell density but rarely becomes edematous

TASS

- sterile postoperative inflammatory reaction most likely caused by a noninfectious agent that gains entry into the anterior segment at the time of surgery and results in toxic damage to intraocular lenses.
- 12 to 48 hours after anterior segment surgery
- hallmark of this inflammation, which distinguishes it from infectious endophthalmitis is Gram stain and culture negativity
- blurred vision (60%), anterior segment inflammation (49%), classically with limbus-to-limbus diffuse corneal edema and cell deposition.

Mechanical Injury

- perform a complete examination and not to become distracted by the injury itself
- errors are rarely made by commission; rather, errors of omission are the rule.
- **Abrading Injuries:**
    - ***Epithelial abrasions:***
        - If Bowman's membrane has not been disturbed, the surface will heal without scarring. If Bowman's membrane is removed, or the corneal stroma is involved, corneal scarring of some degree will result.
        - quite symptomatic, often out of proportion to the degree of visible injury. The exception to this rule is found in patients with ultraviolet keratitis (welder's ‘burn’) or contact lens overwear.

        - pain, photophobia, foreign body sensation, and tearing
        - cycloplegic agent, topical antibiotics, and application of a tight patch/ BCL.
        - NSAIDs for pain control, did not result in a delay in healing.
        - Most corneal abrasions heal spontaneously without difficulty in 24 to 48 hours
    - ***Stromal abrasions***
        - occur in the setting of a tangential blow with an abrasive or sharp object.
        - abrasion without a flap, the therapeutic options depend on the amount of tissue remaining.
        - If a corneal flap is present, the therapeutic goal becomes stabilization of the remaining tissue in its proper anatomic location.
        - major complications seen in these patients is keratorefractive alteration, which can be difficult to correct.

- **Blunt Trauma**
    - ***Contusion injuries:*** result from direct impact and may involve tissue bruising and fractures.
    - ***Concussion injuries***, on the other hand, arise from the rapid acceleration, deceleration, or oscillation of tissues as a result of the impact and energy transfer to the surrounding tissues
    - ***Diffuse endotheliopathy:*** eyes with angle recession <180 degrees had a 12% decrease in endothelial cell density compared to the fellow uninjured eye. Eyes with greater than 180 degrees of recession had a 21.2% decrease compared to their fellow eyes.
    - ***Endothelial rings***
    - ***Stromal injuries and fractures***
    - ***Obstetric injuries***

- **Injuries Caused by Radiant Energy**
    - ***UV Radiation***
    - ***Infrared Radiation***

- **Thermal Burns**
- **Foreign Body Injuries:**
    - Second to corneal abrasions, corneal foreign bodies are the most common form of ophthalmic trauma.
    - Sclerotic scatter may highlight transparent intrastromal foreign material, whereas retroillumination from the iris or fundus will help delineate discontinuities in the stroma.
    - In most cases of superficial foreign bodies, a tuberculin syringe with an attached 27- or 30-gauge needle is an effective instrument for removal.
    - Rusting begins almost immediately after the object is embedded, and a ring may begin to form as early as 3 hours after injury

- **Stings**
    - ***Bee and wasp stings***
    - ***Jellyfish stings***

Chemical Injuries of the Eye

- A strong acid or base can be thought of as being more or almost completely dissociated into cations (+) and anions (−) in solution. And they have ph towards extremes of limits.
- In biologic systems, **alkaline agents saponify the lipids of cell membranes**, causing both rapid and deep penetration. **Acids, on the other hand, precipitate and denature proteins** somewhat limiting further penetration. Alkalis penetrate lipid layers more readily and rapidly; however, acids bind proteins, limiting penetration but potentially increasing the local duration of exposure to the anion. Acid anions with higher binding potentials can cause damage at higher pH than anions with lower binding potentials.
- An **amphoteric substance** is loosely related to buffers in that it is capable of acting like either an acid or a base, and as such, it can neutralize both acids and bases. Two products have been introduced taking advantage of this phenomenon: ***Diphoterine, and Hexafluorine***, both developed by Prevor Laboratories in France. Diphoterine is an amphoteric, hypertonic, polyvalent compound for use in ocular and skin decontaminations of about 600 chemicals, including acids, alkalis, reducers, oxidizers, alkylating agents, and radionucleotides. Additionally, the binding reaction is not exothermic. Hexafluorine is

its counterpart for ocular and dermal exposures to hydrofluoric acid as well as fluorides in acidic environments.

Acid Injury

- acids are components in ***rust removal products, pool cleaners, and car batteries***
- **Most serious is hydrofluoric acid & MC is sulfuric acid. (Survey)**
- Traditionally, acid injuries have been considered ***less destructive*** to the eye than alkali injuries.
- **Collagen shrinkage** immediately raises the intraocular pressure, and the effect persists for at least 3 hours through the elaboration of prostaglandins, possibly from the presence of H+ ions in the aqueous. Additionally, the **stroma liberates ascorbic acid** (vitamin C). In severe acid injuries, ascorbate levels in the aqueous plummet after 24 hours, probably due to either breakdown of the blood–aqueous barrier or damage to the active transport mechanism of the ciliary body. Ascorbate is an essential element in the elaboration of collagen, and its loss can lead to stromal ulceration.
- **mucopolysaccharides**, which are initially unharmed by acid, are either liberated from damaged tissue or destroyed, contributing to decreased tear breakup time, punctate staining (PEE), or slow-healing epithelial defects.
- **Epithelial breakdown** can result in stromal edema, especially in the first 24–36 hours; however, as long as the endothelium is undamaged, stromal hydration largely normalizes upon reepithelialization.
- ***Hughes Classification and prognosis in acid injuries of the eye (ESCLator) (for Chronic Injury)***

Grade	Epithelial opacity, defect	Stromal edema, opacity	Conjunctival involvement	Limbal ischemia	Recovery	1 Vision impairment, 2 scarring, 3 vessels
(I) Mild	Opacified white	None to minimal, none	Erythema, opacification, chemosis	None	Rapid	1, 2, 3 none to little
(II) Moderate	Opacified white,common at 24–36 hours	Mild to moderate, none	Opacification, chemosis, petechia or subconjunctival hemorrhage	None to minimal	Epithelial healing likely within 10 days	1 mild, 2 faint anterior scar possible, 3 little tendency
(III) Severe	Entire epithelium opacified white	Moderate to severe, mild opacity obscures	Opacification, hemorrhages, necrosis	≤1/3	Epithelial healing possible in weeks to months, ulcers/ perforation possible	1 moderate to severe, 2 moderate anterior scar, 3

Grade	Epithelial opacity, defect	Stromal edema, opacity	Conjunctival involvement	Limbal ischemia	Recovery	1 Vision impairment, 2 scarring, 3 vessels
		iris details				peripheral usual
(IV) Very severe	Opacified white (if present) and sloughs rapidly	Marked, severe	Necrosis may be extensive	>1/3	Protracted (months-years), sloughing of stroma possible with ulceration/perforation	1, 2, 3 extensive, like severe alkali injuries

- **Treatment**
- **copious and continuous irrigation** of clean water or other nontoxic irrigant: low osmotic washes such as tap water or high buffer capacity agents such as ***diphoterine or Cederroth Eye Wash Solution*** should be considered for use as initial rinsing agents.
- never use a base to neutralize an acid because it can magnify the injury.
- irrigating lens should be inserted into the fornices while the solution is flowing.
- checking the fornices for particulate matter by double inversion of the lids and sweeping them with moist, sterile cotton swabs
- end point, a ***pH check of the tears 5 to 10 minutes following irrigation*** might be useful, and if the pH is less than 7, irrigation should continue.
- Following irrigation, a more thorough ophthalmologic examination should ensue, including vision, external and slit lamp examinations, epithelial and limbal involvement, stromal edema, and intraocular pressure.
- **broad-spectrum topical antibiotic** to guard against infection in the face of an epithelial defect
- Moderately long-acting **cycloplegic** agents
- topical or oral **anti-glaucoma** agents
- Topical ***NSAIDs drugs should be used cautiously*** due to the possibility of corneal melting in conjunction with epithelial defects
- significant inflammation and/or secondary iritis may benefit from cautious use of ***topical steroids in the first 7 to 10 days***; however, the use of steroids beyond this time may increase corneal ulcerations or perforations.
- **Systemic ascorbic acid (vitamin C)** has been shown in an animal study to reduce the rate of corneal ulceration in acid injuries.

- **AMT** is being utilized in both acute and chronic chemical
- **LSCD** occurs most frequently in high-grade chemical injuries with extensive perilimbal ischemia.
- limbal stem cell transplants range from conjunctival limbal autografts (CLAU), living related and cadaveric donors, to ex vivo culture expanded limbal epithelium.
- (DALK) with limbal stem cell transplantation with or without AMT
- limbus-to-limbus penetrating grafts.

Alkali Injuries of the Eye

- Nonperforating ocular injuries of this type result in destruction of cellular components, denaturation and degradation of collagenous tissues, and release of inflammatory mediators by alkaline ***hydrolysis of a broad range of intracellular and extracellular proteins***, invading cells, and basal epithelial cells.
- The hydroxyl ion (OH) saponifies the fatty acid components of cell membranes, resulting in cell disrupttion and death, while the cation is responsible for the penetration of the specific alkali. Cations react with carboxyl COOH group of stromal collagen and GAGs.
- with the carboxyl groups (COOH) of stromal collaThe type of alkali causing eye injury can be **ammonia, lye, potassium hydroxide, magnesium hydroxide, or lime. Most serious is ammonia/ lye & MC is Lime. (Survey)**
- The pain, lacrimation, and blepharospasm following an ocular alkali injury result from direct injury of free nerve endings located in the epithelium of the cornea, conjunctiva, and eyelids.
- a **wave of hydroxyl ions** rapidly penetrates the eye, causing saponification of cellular membranes with massive cell death and partial hydrolysis of corneal glycosaminoglycans and collagen.
- ***spiking rise in the intraocular pressure***, lasting about 10 minutes, caused primarily by shrinkage of the collagenous envelope of the eye. A more prolonged rise in pressure quickly follows, secondary to prostaglandin release.
- ***Repair***:
    - loss of epithelial adhesion might result from accelerated degradation of fibrinogen by plasminogen activator, a substance probably secreted in excessive amounts by the basal epithelial cells in the alkali-injured eye.

- Healing of the corneal stroma: (1) degradation and removal of necrotic debris, and (2) replacement of portions of the fixed cells, collagenous matrix, and glycosaminoglycans.
- Moderate injuries probably cause some endothelial cell death but mostly interfere with the pump mechanism, leading to a variable degree of reversible corneal edema. Severe injuries will destroy endothelium, which leads to severe corneal thickening.

- ***Classification of Alkali Injuries***:

  Roper Hall classification (for Chronic)

  Grade I: There is no corneal opacity or limbal ischemia and the prognosis is excellent.

  Grade II: The cornea is hazy with visible iris details, there is ischemia of less than one-third of the limbus and the prognosis is good.

  Grade III: There is sufficient stromal haze to obscure iris details, ischemia of one third to one half of the limbus and the prognosis is guarded.

  Grade IV: The cornea is opaque with no view of iris or pupil, there is ischemia of more than one-half of limbus and the prognosis is poor. A new classification has been proposed by Dua et al that take into account the extent of limbal involvement in clock hours and the percentage of conjunctival involvement. Dua et al stressed the inadequacy of the currently followed RoperHall classification that is reflected in the inconsistencies of success rates reported in literature. This is particularly true for grade IV burns (50-100% limbal ischemia) which are equated with poor prognosis.

Dua's classification

Grade Prognosis Limbal Conj. Analogue Involvement Involvement Scale
I Very good 0 clock hours 0% 0/0%

II Good =3 clock hours = 30% .1-3/1-29.9%

III Good >3-6 clock hours >30-50% 3.1-6/31-50%

IV Good -guarded >6-9 clock hours >50-75% 6.1-9/51-75%

V Guarded-poor >9-<12 clock hours >75-100% 9.1-11.9/75-99.9%

VI Very poor Total limbus Total conj.inv. 12/100%

- **Treatment:**

McCulley's 4 stages:

Immediate, Acute 0-7 days, early repair 7-21 days, late repair after 21 days.

- **Immediate**
  - **Thorough washing of eye with saline or water for at least 30 min**
  - **Assessment of injury with history and examination**
- **Acute**
  - Topical steroids 2 hourly inhibits PMN proliferation and function
  - Topical sodium citrate 10% 2 hourly inhibits PMN degranulation by Ca chelation
  - Tetracycline 1% ointment QID inhibits collagenase enzyme by chelating with Zn.
  - Oral sodium ascorbate 500mg QID promotes collagen synthesis
  - Topical sodium ascorbate 20% 2 hourly promotes collagen synthesis
  - Tear substitutes 2 hourly promotes epithelial healing
  - Cycloplegics TDS or BD relieves pain
  - Topical/oral antiglaucoma therapy, if needed
  - Conjunctival/tenons advancement for grade-IV. Improves vascularization
- **Intermediate stage**
  - Review of patient
  - Rapidly taper steroids after 10 days
  - Continue topical and oral medication
  - Look for stromal ulceration
  - Prevent symblepharon formation
  - Look for re-epithelialisation
- **Sequelae**
  - Symblepharon formation
  - Limbal stem cell deficiency

- ***immediate irrigation*** at the scene of the accident with clear water and subsequently the emergency room for 1 to 2 hours with isotonic buffered saline.
- ***Reformation of the aqueous humor*** with buffered phosphate solution lowered the pH by an additional 1.5 pH units. It is premature to suggest that all severe alkali injuries should undergo paracentesis.
- **Diphoterine (Prevor)** is a proprietary amphoteric compound which has been much heralded as a universal emergency irrigant for eyes injured with acidic or alkaline compounds.
- sticky paste of lime: ***EDTA 0.01 M***
- intraocular pressure rise after alkali injury can usually be treated by topical alpha- or beta-blockers and topical and/or systemically administered carbonic anhydrase inhibitors
-

- **Limbal stem cell ischemia is looked for and graded by the newer classification.**

Grade-I Involves little or no loss of limbal stem cells and presents with little or no evidence of ischemia

Grad-II Involves subtotal loss of limbal stem cells and presents with ischemia of less than one half of the limbus.

Grade-III Involves total loss of limbal stem cells with preservation of proximal conjunctival epithelium and presents with ischemia of one half the entire limbus.

Grade-IV Involves total limbal stem cell loss as well as loss of proximal conjunctival epithelium and extensive damage to entire anterior segment.

- **The severity of injury will show the following healing patterns.**

Grade-I Healed cornea with normal epithelium

Grade-II Epithelial defect, smaller in size

Grade-III No epithelization, inflammation

Grade-IV Sterile corneal ulcer + conjunctival defect, inflammations

Autologous Serum Eyedrops

Serum is the fluid component of full blood that remains after clotting.
plasma is obtained when clotting is prevented by mixing a full blood donation with an anticoagulant and removing all corpuscular elements by centrifugation

persistent epithelial defects or severe dry eyes, OSR, RES, SLK
first evaluated in 1984 by Fox

Rationale:

1. vitamin A, epitheliotrophic and neurotrophic growth factors, immunoglobulins and fibronectin
2. lacks antigenicity
3. without preservatives and hence toxicity due to additives is not an issue.

Production Process (CCDS)

1. Clotting phase: 2 h at room temperature
2. Centrifugation: 15-min centrifugation at 3,000 *g* results in good separation of serum and blood clot, without inducing haemolysis
3. Dilution: 20%, 33%, 50% or 100%, BSS rather than saline should be used
4. Storage: drops can be refrigerated or stored frozen. 3months if stored at –20 °C and for 1month if stored at 4 °C.

Umbilical Chord Serum: prepared like autologous serum (5 min centrifugation at 1,500 rpm), diluted to a 20% concentration in 0.9% saline and used as an alternative treatment for promoting corneal epithelial wound healing.

Keratoplasty

Sir Benjamin Rycroft in his Doyne lecture divided keratoplasty evolution into ***four*** periods:

ITCAR

1. Inspiration (1789–1824)
2. Trials and Frustration (1825–1872)
3. Conviction (1873–1905)
4. Achievement (1906–1965)
5. Refinement and Innovation (1966-present) (added by others later)

- **Von Hippel** favored lamellar transplantation, performing the first successful human corneal transplant in 1886, in which a full-thickness rabbit cornea was placed into a human recipient corneal lamellar bed.
- first documented successful corneal **penetrating** transplant performed by **Eduard Konrad Zirm** in 1906
- **Franz Reisinger**, who first described the term ***'keratoplasty'***
- work of Ramon Castroviejo that had the most profound influence on modern-day keratoplasty.
- first **eye bank** by R. **Townley Paton** in **1945**
- Max Fine led to the recognition that keratoplasty could be successfully performed for the treatment of aphakic bullous keratopathy
- immunologic discoveries of A. **Edward Maumenee** and the simultaneous introduction of topical ***corticosteroids***
- **PLK**
    - 1998, **Melles** el al. described the technique of PLK→ just like DLEK
    - **Terry and Ousley** developed new instrumentation and performed a similar procedure in the United States, calling it DLEK.
    - 2004, **Melles**→ DSEK
    - **Gorovoy** advocated the use of a microkeratome→ DSAEK
    - **Melles** et al. described a technique, currently known as DMEK
- **ALK**
    - 1985, **Archila**→ deep lamellar dissection by injecting 1 cc of air
    - 1994, **Sugita and Kondo**→ removed the anterior stromal tissue by standard lamellar dissection, followed by hydrodelineation with saline through a 27-gauge cannula
    - 1998, **Morris** et al. modified the technique Sugita utilized by adding a viscoelastic after hydrodelineation
    - **Anwar and Teichmann's** description of the 'Big Bubble Technique for DALK' in 2002
    - **Vajpayee**→ Double Bubble Technique for DALK

Decision-Making in Keratoplasty

- EBAA statistics from 2009 revealed that **45%** of all keratoplasty procedures performed in the United States were **partial-thickness** corneal grafts.
- **Ocular surface reconstruction procedures**

  1. Dry eye states
  2. Neurotrophic states
  3. Limbal stem cell deficiency states

  They include, but are not limited to punctal occlusion, tarsorrhaphy, superficial keratectomy, amniotic membrane transplantation, and limbal stem cell transplantation.

- **ALK:**
  - anterior 85–95% of the cornea, definitely sparing Descemet's membrane and endothelium
    1. Corneal ectasias (keratoconus, keratoglobus, pellucid marginal degeneration)
    2. Stromal dystrophies (granular, lattice, macular, and others)
    3. Scars from previous infections (bacterial, fungal, viral, parasitic, atypical)
  - Lamellar keratectomy (LK)
    1. Manual peeling technique
    2. Microkeratome-assisted keratectomy
    3. Excimer laser phototherapeutic keratectomy
    4. Femtosecond laser-assisted keratectomy
  - Tectonic, reconstructive, and excisional anterior lamellar Keratoplasty
  - Automated lamellar therapeutic Keratoplasty (ALTK)
    - conditions affecting the anterior one-half to two-thirds of the cornea and usually sparing the surface.
  - Deep anterior lamellar Keratoplasty (DALK)
    - takes advantage of the potential space between Descemet's membrane and the stroma to cleave the entire host stroma off Descemet's membrane
  - Femtosecond laser-assisted lamellar Keratoplasty (FALK)

- **PLK**

1. Posterior corneal dystrophies (Fuchs', nonguttate endothelial dystrophy, posterior polymorphous)
2. Aphakic and pseudophakic corneal edema and bullous keratopathy
3. Iridocorneal endothelial syndrome (ICE)
4. Other causes of endothelial dysfunction (trauma, foreign body, age, etc.)

- **Advantages**
  1. Rapid visual rehabilitation
  2. No suture-related complications
  3. Decreased incidence of allograft rejection
  4. Intact globe, resistant to traumatic wound dehiscence
  5. Predictable corneal toricity, minimal topographic change
  6. Predictable, small hyperopic refractive shift (1.0–1.5 diopters)
- transplanted tissue usually measures **100–200 µm** in thickness and includes the donor endothelium, Descemet's membrane, and a lamella of posterior stroma. Thinner donor tissue is associated with a lower incidence of **graft dislocation (<1%)** and rapid clearing of vision.
- ***most endothelial cell loss from the donor appears to take place during the insertion*** of the graft into the recipient's anterior chamber, various injectors, cartridges, and inserters have been developed to ameliorate this problem. One example is the ***Neusidl Corneal Inserter (NCI)***

- **PK**

1. Combined endothelial and stromal disease (Fuchs' dystrophy with corneal ectasia or macular stromal dystrophy)
2. Severe corneal opacification and inability to ascertain the status of the endothelium by history or examination
3. Keratoconus after hydrops with tears in Descemet's membrane; successful deep anterior lamellar keratoplasty is unlikely
4. Other causes of corneal opacification and lack of familiarity with selective keratoplasty techniques

- Conventional PK
- Femtosecond Assisted PK

- **Permanent keratoprosthesis surgery**
  1. Eyes with multiple graft failures
  2. Stem cell deficiency states (aniridia, etc.)
  3. Corneas with four-quadrant deep stromal vascularization

Penetrating Keratoplasty

- **Patient Selection:**
  - Age: advantages of advancing age is that the immune system is less likely to mount a graft-destroying rejection
  - Mild to moderate mentally challenged individuals sometimes greatly benefit
  - Ocular surface disease is a leading cause of corneal transplant failure. Dry eye, neurotrophic, or exposure keratitis patients often benefit from topical ciclosporin, punctal occlusion, and tarsorrhaphy.
  - **Preoperative glaucoma** is a risk factor for graft failure, with a ***relative risk factor of 2.5***.

- **Preoperative Preparations**
  - Infection control
  - Intraocular pressure control
  - Lens management
  - Donor corneal tissue management
    - allow approximately **60 minutes of warming time**
    - **donor rim fungal** culture is associated with endophthalmitis in the recipient in **3%**
    - **donor rim bacterial** culture is associated with recipient endophthalmitis in **1%**
  - Anticipate **suprachoroidal hemorrhage**

- **0.45% to 1.08%** of cases
- 0.56% with general anesthetic and 4.3% with local anesthetic.
- ***risk factors*** include older age, glaucoma, previous vitrectomy, tachycardia, systemic hypertension, arteriosclerosis, anticoagulant therapy, and prior suprachoroidal hemorrhage

- **Phakic Penetrating Keratoplasty**

  Goals

  1. obtain good wound alignment with minimal astigmatism

  2. avoid endothelial cell damage.

- lid speculum
- scleral fixation ring: potential scaffold to maintain scleral support, exerting its influence once the eye is opened if scleral rigidity is insufficient. Another option is to proceed without a fixation ring or sutures, to avoid associated globe distortion and astigmatism.
- Marking of host cornea: donor graft is usually centered on the host cornea or over the pupillary axis
- ***donor tissue trephine is routinely sized 0.25 mm larger*** than the host trephine because, using current techniques, donor corneal tissue cut with a trephine from the endothelial surface measures approximately 0.25 mm less in diameter than host corneal tissue cut with the same diameter trephine from the epithelial surface. ***Keratoconus patients also may benefit from using same-diameter trephines*** for both donor and host tissue, which in effect undersizes the donor button and helps reduce postoperative myopia.
- Trephination of donor cornea: endothelial side facing up using a sharp disposable blade in a guillotine punch block apparatus
- Trephination of host cornea:
- Placement of viscoelastic material in the anterior chamber
- Placement of the donor corneal tissue in the host bed
- Placement of four interrupted radial 10/0 nylon **cardinal sutures**:
  - Suture depth is approximately 90% to prevent wound gape

  - The second suture, placed 180° away at 6 o'clock, is the **most critical** in terms of tissue alignment and subsequent astigmatism.

- Complete suturing
  - the ***most prevalent suturing error*** in corneal transplantation surgery is tying ***too tightly***.

- Readjustment of sutures to minimize astigmatism: An **inexpensive plastic ring (Karickhoff keratoscope, DORC keratoscope**, or the like) or even the **round end of a safety pin** can be used effectively for this purpose.

- Administering medications: **Subconjunctival** dexamethasone, 4 mg; subconjunctival gentamicin, 20 mg; and subconjunctival cefazolin, 25 mg, or another suitable antibiotic are injected.

Femtosecond Laser-assisted Penetrating Keratoplasty

- creation of a more structurally stable and predictable wound configuration with the objectives of faster recovery of vision and higher optical quality compared to conventional blade trephination.

- The first femtosecond laser platform to accomplish the full-thickness corneal cuts for PKP was the **Intralase**™ (IntraLase Femtosecond Laser, AMO, Irvine, CA)

- A second femtosecond laser platform, **FEMTEC** (20/10 Perfect Vision, Heidelberg, Germany) has also subsequently created stable full-thickness PKP wounds and demonstrates short-term visual results analogous to other femtosecond laser-assisted PKP studies.

- Intralase enabled keratoplasty (**IEK**)

- The two most popular patterns remain the ***'top-hat' and 'zig-zag' incisions***.

- 'zig-zag' incision may prove to be the most biomechanically sound incision pattern.

Keratoplasty Suturing Techniques

- **Castroviejo's original suturing technique** utilized a continuous silk suture coursing back and forth in multiple passes across the external surface of a **square graft**, using the suture to support the graft in place against the intraocular pressure.
- After four cardinal sutures, a **diamond-shaped pattern of corneal striae** will appear in the donor cornea. At this point, the wound approximation should be symmetric in all four quadrants.

1. Interrupted sutures (IS)

- standard means of keratoplasty wound closure.
- 10-0 nylon using a 160-degree single-curve 6-mm needle
- A **2-1-1 closure** facilitates burial of the knot, but adequate suture tension is more difficult to establish than with a **3-1-1 knot**. **Slipknots (1-1-1-1)** allow for intraoperative adjustment.
- **Eight** sutures, in general, is the minimal number required to keep the wound **watertight**, and **16** sutures is the average number for a **complete** interrupted suture wound closure
- A total of 24 or 32 interrupted sutures may be necessary in pediatric grafts, keratoconus patients, same-size donor–host grafts, or large-diameter grafts.
- **Knots can be buried in the host tissue** so that when the suture is removed there is less tension on the graft–host junction, ***reducing the chance of dehiscence*** should the sutures be removed during the early stages of wound healing. Alternatively, the knots **can be buried in the donor** tissue to help ***reduce inflammation and vascularization*** since the knot is farther from the limbal vessels.

2. Combined continuous and interrupted sutures (CCIS)

- With a continuous suture in place the interrupted suture may be removed for astigmatism control earlier than if interrupted sutures were used alone.
- 2 interrupted 10-0 nylon sutures and a continuous 12-bite 10-0 or 11-0 nylon running suture
- should not be used if there is vascularization or infectious keratitis or any other need for total suture removal in some portions of the wound before others

3. Single continuous suture (SCS)

- technically more unforgiving than interrupted sutures, because one irregular bite can impair the integrity of the closure and once passed cannot be removed without removing the entire suture
- **ease of placement**, the ease with which the suture can be removed at a later date, and the potential for suture adjustment intra- and postoperatively to reduce astigmatism.
- Antitorque suturing is not necessary for continuous sutures with 12 or more bites.

Antitorque suture: radial overlying sutures and antitorque intrastromal suture bites. The overlying radial sutures produce minimal suture torque and induce astigmatism.

Torque suture: radial intrastromal sutures and overlying torquing suture bites. These torquing suture bites rotate the graft and induce astigmatism.

4. Double continuous suture (DCS)

- **benefits of a single continuous suture with the added safety** of a second suture should one suture break or need to be removed early.
- requires **more expertise** than a single continous suture, because both continuous sutures must have regular and symmetric bites to close the wound without disturbing the wound.

- **Suture Adjustment**
  - Topographical analysis using **keratometry, photokeratoscopy, or videokeratography**, individually or in combination, is helpful in planning suture adjustment
- **Suture removal**
  - if corneal astigmatism is satisfactory with sutures in place, ***sutures should remain until there is some indication for removal, such as graft rejection, scarring, vascularization, patient discomfort, suture breakage, infection, or decreased vision (residual astigmatism)***. Leaving sutures in place as long as possible maintains topography, if acceptable, and decreases the risk of dehiscence.
  - All the dehiscences occurred within 2 weeks of suture removal, which was perfomed between 14 and 42 months postoperatively.

- **Single interrupted sutures**
  - A tight suture, or any suture felt to be distorting the corneal topography, can be removed as early as 6–8 weeks postoperatively in a well-constructed keratoplasty with 16 interrupted sutures. However, adjacent sutures should generally not be removed for 6 months postoperatively.
- **Combined continuous and interrupted sutures**
  - One to three weeks later, the patient's corneal topography is remeasured to assess changes induced by suture removal and to determine whether removal of additional sutures is indicated.
  - ***The average astigmatism is 4 diopters after all sutures are removed, using most suturing techniques***.
- **Single continuous suture**
  - ***adjustment*** of the single continuous suture can change corneal topography and still support the wound suture
  - McNeill first described adjustment of a single continuous suture to reduce postkeratoplasty astigmatism in 1988
  - The ***suture is advanced from the flat meridian toward the tight meridian*** to equally distribute suture tension around the wound.
- **Double continuous suture**
  - adjusted the deeper, tighter 10-0 nylon suture to alter corneal topography and reduce astigmatism, and left the shallower suture in place as a safety net

Intraoperative Complications of Penetrating Keratoplasty

- **Scleral perforation** with fixation sutures: Flieringa rings, the McNeill-Goldman blepharostat
- Improper trephination
  - power of the lens must be adjusted to account ***for 2 to 3 diopters of induced hypertropia***

  - eccentric placement of the trephine can result in large amounts of postoperative astigmatism.

- Damaged donor button
- **Retained Descemet's membrane**: The iris architecture should be inspected carefully, and the iris should be gently picked up and identified with forcep
- Iris–lens damage
- Torn posterior capsule
- Vitreous loss with pseudophakic bullous keratopathy and posterior chamber intraocular lenses
- Anterior chamber hemorrhage
- **Expulsive choroidal hemorrhage: 0.47% to 3.3%**

Postoperative Management

Immediate postoperative care (first 24 hours)

- Antibiotics should be given preoperatively, intraoperatively, and postoperatively
- ***Oral fluoroquinolone*** administration may also be considered in high-risk cases (ciprofloxacin has highest ocular penetration among all fluoroquinolones)
- Prophylactic Antiglaucoma
- A pressure patch and Fox shield
- **Systemic steroids** are commonly administered in high-risk keratoplasty in the early postoperative period, usually at a dose of 1 mg/kg per day over the first 5 to 7 days. **Acyclovir** in a prophylactic dose of 400 mg twice daily or **valacyclovir** 500 mg daily is given perioperatively in cases with previous known herpetic involvement, especially previous stromal keratitis.
- **Azathioprine at a dose of 1–2 mg/kg/day** and **ciclosporin A** orally have been used as an adjuncts to oral and topical steroids in high-risk cases but the side-effects profile has limited their widespread use. **Tacrolimus at a dose of 0.16 mg/kg per day** has been shown to be effective in prevention of rejection with less systemic impact.

Early postoperative care (1 to 7 days)

- should be examined in the first 36 hours following surgery
- presence of concomitant **external eye and eyelid disease** including blepharitis, lagophthalmos, spastic entropion, and trichiasis.
- without topical fluorescein to assess the surgical wound, level of corneal edema, anterior chamber reaction, and overall status of the anterior segment
- fluorescein allows for a better evaluation of the status of the corneal epithelium, wetting of the ocular surface, and tension on the suture material
- The **intraocular pressure** may be measured in more regular corneas by applanation.
- Treatment of early intraocular pressure elevations involves the use of **topical beta-blockers** followed by carbonic anhydrase inhibitors and brimonidine.

Postoperative care (1 to 12 weeks)

- period of **greatest change** and highest risk for the corneal graft.
- **Topical antibiotics should generally be discontinued once the epithelium is intact.** Continuing long-term topical antibiotic therapy selects out more resistant organisms, but does not act significantly to prevent infection in the absence of other problems such as persistent epithelial defects, suture removal, exposure, trauma, or wound leaks.
- **Persistent elevated anterior chamber flare may be associated with higher incidence of rejection.**
- **Epithelial rejection lines** begin at the graft periphery and migrate towards the center of the graft with time. They are seen as hazy elevations in the epithelium and may stain with either fluorescein or rose Bengal. These lines are usually seen in a relatively quiet or mildly inflamed eye. They are seen at a median of approximately 3 months following surgery and may occur in up to 14% of corneal transplants.
- **Signs of stromal rejection** are seen as a haze or infiltrate spreading from the graft periphery towards the center of the donor cornea. These are associated with findings of **endothelial rejection**, and are frequently accompanied by stromal vascularization. The classic finding of endothelial rejection is a rather sharply demarcated line (**Khodadoust line**) that is seen as contiguous keratic precipitates.

- **Epithelial downgrowth**, occurring 1 to 12 weeks after penetrating keratoplasty or suture manipulation, may also appear as an advancing line with signs of inflammation.
- In the absence of complications, topical **steroids should be tapered during the first 6 months** following penetrating keratoplasty.
- An assessment of **intraocular pressure should be done on each postoperative visit**.
- **Macular edema** is often suspected when the visual function does not match the surgeon's estimation of the anterior segment in the postoperative period.

Postoperative care (after 3 months)

- average postoperative astigmatism was in the **4 to 6 diopter range**
- **Contact lens correction** is generally indicated for convenience when the other eye requires contact lenses, in cases of high toricity and anisometropia, and in aphakia.
- **Higher oxygen permeability** (Dk value) lenses with base curves flatter than the flattest K-reading are generally used.
- **Corneal sensitivity may take years** to return to normal in the corneal graft, and this may be a significant factor in the development and late recognition of microbial keratitis from contact lens wear or suture erosion.
- Significant iatrogenic complications may be induced by the chronic long-term administration of topical steroids in the postkeratoplasty patient.

Postoperative care in infants and children

- **intense inflammatory reaction** in the anterior segment following Keratoplasty
- Epithelial and stromal **healing is very rapid** in children, resulting in early suture loosening, exposure, secondary vascularization, and subsequent rejection. Infants and young children may need to be examined every 2 days until the sutures are removed, usually in a few weeks following surgery.

Early Postoperative Complications

- **Wound Leaks and Wound Displacement**: Pupillary block or choroidal detachment can also cause a shallow or flat anterior chamber, but a coexistent wound leak must be ruled out. **Seidel's test** is useful for detecting an area of leakage and may be positive even in the presence of a flat anterior chamber. If nonsurgical attempts fail to seal the leak after 24 to 48 hours, surgical repair is recommended.

- **Persistent Epithelial Defects**: reepithelialization and the maintenance of an intact epithelium is critical for postoperative wound healing, improved visual acuity, graft transparency, graft survival, and protection of the stroma against infection and melting.

  The postoperative prevention and treatment of epithelial defects may include the use of a ***permanent or temporary tarsorrhaphy, pressure patching, a bandage soft contact lens, a collagen shield, or an amniotic membrane transplant***. Using nonpreserved artificial tears and limiting medication toxicity to the epithelium are essential. Once an epithelial defect is present, it must be treated aggressively. If the defect persists for more than 1 week, it will heal more slowly. The risks of stromal scarring and ulceration increase significantly with defects present longer than 3 weeks.

  The possibility of ***active herpes virus infection*** must always be considered when an epithelial defect does not respond to treatment. Surgical incision of the trigeminal nerve has been shown to reactivate latent herpes simplex virus in humans.

- **Filamentary Keratitis**: abnormal collections of mucus and epithelial cells on the corneal surface. Patients with minimal symptoms should be treated with **hypotonic artificial tears** because more mucoid solutions may contribute to the formation of filaments. In patients with severe symptoms, the filaments should be carefully removed with a forceps followed by treatment with hypotonic tears and/or topical **acetylcysteine**, which has a mucolytic action. **Punctal occlusion** can also be beneficial, and in severe cases a soft bandage contact lens may be indicated.

- **Suture-related Complications**:
  - Suture exposure:
  - Suture-related infection:
  - Suture-related immune infiltrates:

    Suture-related immune infiltrate: *Multiple, Usually occurs on the host side of the graft-host interface, No overlying epithelial defect*

    Infectious suture abscess: *Solitary, May occur on the graft or host side of the graft-host interface, Associated with an overlying epithelial defect*

  - **Kaye dots**: discrete white dots in the donor corneal epithelium in a 1–2-mm region central to the graft sutures. found primarily in the depressed zone central to the

swollen donor cornea edge. Their formation may be a ***non-specific response of the epithelium*** to an area of tissue angulation. Disappears within 30 days.

- **Elevated Intraocular Pressure**:
    - pneumotonometer or an electronic tonometer
    - Tight suturing, long suture bites, larger trephine sizes, a smaller recipient total corneal diameter, same-size donor–host trephination, and increased recipient peripheral corneal thickness were shown to result in greater iridocorneal angle compression and elevated intraocular pressure.
    - retained viscoelastic, intraocular inflammation, anterior synechia causing angle closure, and pupillary block.
    - topical beta-blocker, topical alpha-2 receptor agonists, and/or an oral carbonic anhydrase inhibitor may be considered at the conclusion of surgery. ***Prostaglandin analogs and miotic agents should be avoided since they may worsen anterior segment inflammation***.
- **Postoperative Inflammation**: uncontrolled inflammation may lead to the formation of intraocular fibrin due to ***breakdown of the blood-aqueous barrier***. Fibrin can serve as a scaffold for the formation of strands or membranes, leading to the development of pupillary block and glaucoma or direct damage to the endothelial cells.
    - intense hourly topical corticosteroids & Mydriatics.
    - **Intraocular TPA -25 micrograms**.
- **Anterior Synechia** Formation:
- **Pupillary Block**:
- **Choroidal Detachment and Choroidal Hemorrhage**:
- **Hyphema**:
- **Fixed Dilated Pupil**: The development of a fixed, dilated pupil following penetrating keratoplasty for keratoconus has been observed as part of a syndrome associated with iris atrophy, scattered pigment on the lens capsule and corneal endothelium, and secondary glaucoma with posterior synechia: ***Urrets Zavalia Syndrome***
- **Postoperative Infection**:
    - The incidence of **endophthalmitis after penetrating keratoplasty ranges from 0.2% to 0.77%.**

- **Primary Donor Failure**: irreversible edema of the corneal graft in the immediate postoperative period. It is due to inadequate endothelial cell function of an unhealthy donor endothelium, inadequate tissue preservation, or surgical trauma.

Postkeratoplasty Astigmatism

1. **Host factors**: Peripheral corneal thinning or Ectasia, Scleral Ectasia, Scarring, Aphakia, Wound healing, Wound edge profile, Epithelial healing, Shape, Postoperative melting
2. **Donor factors**: Diameter, Intrinsic astigmatism, Edge profile, Shape
3. **Surgical factors**: Suture tension, Suture length, Suture depth, Suture radiality, Intraocular pressure, Suture technique, Intraocular lens implantation, Timing of suture removal, Surgeon experience, Trephine tilt, Scleral ring placement

- Large-diameter penetrating keratoplasties (**LDPKs**), defined as grafts that are **8.75 mm** or larger

4. **Donor-host interaction**: Override/underride, Wound healing, Postoperative trauma

- Relaxing incisions
    - can be placed in the graft-host junction or in the graft itself.
    - A relaxing incision placed in the graft is termed '**astigmatic keratotomy (AK)**'.
    - The term '**arcuate keratotomy**' describes the creation of one or more arc-shaped relaxing incisions in the corneal stroma or graft-host interface.
    - Relaxing incisions in the graft-host junction are of the arcuate variety and astigmatic keratotomy incisions can be of the arcuate or straight (transverse) variety. Relaxing incisions and astigmatic keratotomy incisions are associated with a coupling effect. **Coupling** is defined as the simultaneous flattening of the steep meridian in which the incision is placed and the steepening of the flat meridian 90 degrees away from the incision. When the ***coupling ratio*** (the amount of flattening in the meridian of the incision divided by the induced steepening in the opposite meridian) is 1.0, the spherical equivalent remains unchanged. When there is a positive coupling ratio (>1.0), a hyperopic shift occurs. When there is a negative coupling ratio (<1.0), a myopic shift occurs

- If the relaxing incisions themselves cannot correct the astigmatism, **compression sutures** may be placed across the graft–host interface 90 degrees away from the relaxing incisions
- **Wedge resections** involve the excision of a wedge of corneal tissue in order to reduce post-PKP astigmatism.
- **LASIK** has been introduced as another attempt to surgically correct post-PKP astigmatism.
- **Photorefractive keratectomy**

Corneal Allograft Rejection

- allograft rejection is a form of delayed hypersensitivity.
- Studies Streilein and associates, have raised the possibility that **anterior chamber associated immune deviation (ACAID) phenomena** contribute to graft survival and that allograft rejection represents a breakdown in the protection afforded the graft by ACAID.
- Risk Factors
    - young recipient age (less than 40 years) (CCTS)
    - large-diameter corneal grafts (nearby limbal vasculature, Langerhans cells in periphery)
    - prior graft failure, particularly due to rejection (8% in one, 40% in two)
    - pre-existing inflammation
- Clinical Features
    - circumcorneal (ciliary) flush
    - Anterior chamber flare indicates elevated levels of protein in the aqueous humor
    - cellular infiltration of the cornea as discrete subepithelial infiltrates: an early sign of rejection
    - Epithelial rejection 10%, earlier in the postoperative period (1 to 13 months)
    - Isolated stromal rejection: uncommon but can be seen as stromal infiltrates and neovascularization. In very aggressive episodes of graft rejection the stroma can become necrotic during severe or prolonged bouts of rejection.

- Endothelial rejection is the most common of the three types, with reported rates of from 8% to 37% of cases undergoing rejection. Endothelial keratic precipitates occur as scattered lesions or as a linearly oriented wave of leukocytes migrating from the peripheral cornea toward the center. Referred to as the **Khodadoust line**: hallmark of corneal allograft rejection, but it is not a sine qua non for rejection. In patients who have received posterior lamellar donor tissue (DSAEK) cellular keratic precipitates occur only on the transplanted endothelial layer. Often, there is associated edema of the stroma overlying the area that has been traversed by the advancing keratic precipitates.
- Edema of the graft
- Corneal thickness usually stabilizes by the third postoperative month, and if the corneal ***thickness is greater than 0.59 mm at the sixth postoperative month there is a greater risk of ultimate graft failure***.
- elevated intraocular pressure can be a sign of rejection

- DD
  - **Recurrence of herpes simplex keratouveitis** is the most difficult condition to differentiate from corneal allograft rejection: typical dendriform epithelial lesion, endothelial keratic precipitates in herpetic inflammation are not confined to the graft but involve as well the peripheral host endothelium.
  - **epithelial downgrowth**: inflammation is not a prominent part, not respond to steroid therapy.
  - **low-grade corneal infection**: candida

- Mx:
  - Corticosteroid therapy by topical, periocular, or systemic administration is the treatment of choice for acute corneal allograft rejection reaction.
    - CCTS: higher-frequency postoperative topical steroids, close follow-up of the patient, and the aggressive treatment of suspected or diagnosed rejection reaction (including the use of hourly topical prednisolone acetate for mild reactions plus intravenous methylprednisolone pulse therapy [3-5 mg/kg IV push] followed by 5 days of oral prednisone [1 mg/kg/day] for severe reactions)
  - immunosuppressive agents such as ciclosporin, tacrolimus, and mycophenolate mofetil
  - biologic methods: intracameral administration of anti-T-lymphocyte monoclonal antibodies.

Infections after Penetrating Keratoplasty

- **Microbial Keratitis**
  - **1.76% to 12.1%,** most within first year
  - three general categories
    1. contaminated donor button
    2. intraoperative contamination
    3. recurrence of host infection.
  - ***Streptococcus pneumoniae (27%) and Staphylococcus aureus (20%)*** followed by Gram-negative organisms (20%) and fungal organisms (13%)
  - Topical corticosteroids should be stopped in the presence of an acute graft infection. Only when the organism has been identified and the infection brought under control should the clinician consider restarting corticosteroid therapy.
  - Preferably, the epithelium should be intact before corticosteroids are reintroduced.
  - Graft decompensation was documented in 13–57% of eyes.
- **Suture Abscess**
  - infiltrate in either the donor or recipient cornea which is in direct contact with, or adjacent to, suture material
  - **2-3.3%** of penetrating keratoplasties after an average of 21.5–30.8 months
  - S. epidermidis, S. pneumoniae, and S. aureus, although cases of Gram-negative infection
  - DD: A ***sterile suture infiltrate*** occurs with an exaggerated inflammatory response usually within the first few weeks after surgery. In this situation there are usually multiple lesions typically on the host cornea, and the overlying epithelium is intact.
  - careful removal of the offending suture followed by corneal scrapings for smears, cultures, and sensitivities
- **Infectious Crystalline Keratopathy**

- 1983, as a noninflammatory, intrastromal bacterial colonization of a corneal graft
- ***crystalline branching opacities in the anterior or midstroma*** due to intralamellar aggregates of Gram-positive cocci occurring several months following penetrating keratoplasty and after the long-term use of topical corticosteroids.
- most commonly reported causative organism in ICK is **Streptococcus viridans**.
- Bacteria are thought to gain access to the corneal stroma via epithelial ingrowth into a suture track or by direct access through an epithelial defect.
- Scrapings or corneal biopsy
- **fortified topical antibiotic** drops given in an intensive dosing regimen. Antibiotic coverage for S. viridans includes topical penicillin G 333 000 units/mL, cefazolin 33–50 mg/mL, or vancomycin 33–50 mg/mL.
- use of **Nd:YAG laser** to disrupt the protective glycocalyx matrix surrounding the organisms causing ICK

- **Endophthalmitis**
  - Incidence: **0.08% to 0.77%.**
  - **immediate postoperative period (within 72 hours)**
    - Contaminated donor tissue or corneal storage media
    - Prolonged storage of corneal tissue for more than 5 days
    - Preoperative warming of corneal tissue to room temperature for 1 hour prior to transplantation
    - ***50% had positive donor rim cultures out of which, in 97% cases organism maching cultures***
    - Additional risk factors for postoperative endophthalmitis include intraoperative communication with the vitreous, placement of an intraocular lens with polypropylene haptics, and a history of drug allergy.
  - **late postoperative period (months to years)**
    - secondary to an acquired infection. Ulcerative keratitis within the graft or at the graft-host interface may progress to perforation and subsequent endophthalmitis. Concurrent endophthalmitis and ICK from the same organism has been reported 3 months after penetrating keratoplasty.

- overall rate of **donor rim culture positivity was 14%,** with the predominant organism being **S. epidermidis (39%)**
- 75% bacterial in origin, whereas fungi are implicated in another 20%
- CF:
  - pain
  - marked inflammation with or without hypopyon
  - diminished or poor red reflex.
  - wound dehiscence may also be present
- aspiration of aqueous humor as well as vitreous sampling
- Diagnostic vitrectomy or vitreous aspiration
- Mx:
  - Intraocular injection of **vancomycin** 1 mg in 0.1 mL and **ceftazidime** 2.25 mg in 0.1 mL should be carried out after a diagnostic or therapeutic Vitrectomy
  - for fungal endophthalmitis is very high, intravitreal injection of **amphotericin B** 0.005 mg in 0.1 mL should be performed.
  - **intravitreal dexamethasone** may help in the early reduction of inflammation in exogenous bacterial Endophthalmitis
  - broad-spectrum fortified topical antibiotics should be administered with an intensive dosing regimen of at least every hour around the clock.
- only 3% of all eyes with endophthalmitis after penetrating keratoplasty had a visual acuity of 20/40 or better. Acuity of 20/50 to 20/200 was achieved in 17% of cases. An additional 17% of eyes had acuity ranging from 20/300 to hand motions.

- **Herpetic Keratitis after Keratoplasty**
  - HSV keratitis: relatively infrequent indication for penetrating Keratoplasty → **4.2%.**
  - recurrent herpetic dendritic keratitis in 10–25% of patients during the first year of follow-up and in 9–21.6% during 2 to 5 years of follow-up
  - in case of recurrence or without prophylaxis: **15–28%** of patients having recurrences in the ***first*** year and **18–45%** during the ***second through fifth*** years.

- **Transmission of Unusual Infections**
    - Rabies
        - Total 8 cases till now- death within 7 weeks
    - Creutzfeldt-Jakob disease
        - 1-2 cases
    - Hepatitis virus
        - 2 cases
    - Human immunodeficiency virus
        - No cases

Retrocorneal Membranes

- ***epithelial downgrowth**: epithelialization that extends into the anterior chamber*

  ***epithelial ingrowth**: epithelialization under the LASIK flap.*
- **Epithelial Downgrowth**
    - **0.6%** of all traumatic and surgical perforations
    - **0.27%** after PK
    - Cataract extraction remains the most frequent cause
    - Pathogenesis:
        - delayed closure or dehiscence of the surgical wound, often with a fistula or inadvertent bleb and incarceration of tissue in the surgical margin.
    - dull aching pain, photophobia, and blurred vision. Clinical examination reveals a hypotonous, normal, or elevated intraocular pressure, and the incision site may contain incarcerated tissue, a conjunctival bleb, or a fistula.
    - argon laser photocoagulation and specular microscopy are often sufficient for diagnosis when combined with the clinical picture
    - The argon laser settings ***of 0.1-0.2 s, 100-500 µm spot size, and 100-500 mW*** are used to outline the extent of epithelial invasion over the iris. The

involved areas turn white when the laser energy is applied as opposed to an inapparent burn to the normal iris. The specular microscope can also confirm the diagnosis if the leading edge of the epithelium can be visualized by focusing just posterior to the endothelium.

- Confocal microscopy has been shown to aid in the diagnosis of epithelial downgrowth.
- **glaucoma** is the most common presenting sign and a common pathway for eventual enucleation.
- Mx:
  - Radiation was the treatment of choice from 1930 to the 1960
  - Maumenee's eradication technique:
  - Naumann and Rummelt ‘s block excision:
  - endoscopic photocoagulation

- **Fibrous Ingrowth**
  - fibrous proliferation and invasion of the tissues surrounding the surgical site
  - ***distinct from epithelial downgrowth, less likely to result in enucleation***
  - **Penetrating keratoplasty** is the most recognized source
  - **50-60%** of failed Keratoplasty
  - Pathogenesis:
    - Subepithelial connective tissue and corneal stromal fibroblasts participate in normal traumatic and surgical wound healing, and an exuberant response leading to fibrous ingrowth can be easily imagined.
  - translucent membrane on the posterior surface of the cornea near the wound. The edges may be frayed or irregular, and, ***unlike epithelial downgrowth, the stroma of the membrane may be vascular***
  - no ancillary diagnostic tests have been useful to confirm
  - medical management of inflammation, glaucoma, or corneal edema is sufficient, and the fibrous proliferation matures into a quiescent scar and can even fade considerably

- DD:
    - Beveled corneal incisions
    - Peripheral corneal edema
    - pigmented membrane can appear on the posterior surface of the cornea as a result of proliferation of iris stromal melanocytdes from trauma or surgery.

Glaucoma after Penetrating Keratoplasty

- most devastating complication after penetrating Keratoplasty
- practical definition of PKP glaucoma is an IOP > 21 mmHg after penetrating keratoplasty, with or without associated visual field loss or optic nerve changes, necessitating the addition of medications to reduce the intraocular pressure.
- PKP glaucoma treatment escalation definition: Treatment escalation was either surgical or medical; in the case of medical escalation, only sustained increases in medication burden compared to baseline were included; treatment to deal with brief IOP spikes in the early postoperative period was excluded from analysis.
- Incidence: IOP > 25 mmHg occurred in 37% of phakic eyes, 88% of aphakic eyes, and 100% of eyes undergoing combined cataract extraction with penetrating Keratoplasty
- Risk factors:
    - Preexisting glaucoma
    - Aphakia
    - Anterior segment inflammation
    - Corneal diagnosis
    - Intraocular lens removal
    - Vitrectomy
    - Postkeratoplasty/extracapsular cataract extraction/intraocular lens
- The Pre-Keratoplasty Evaluation
    - Tonometry and a careful pupillary examination

  - ASOCT
  - UBM
  - afferent pupillary defect is an ominous clinical sign
  - Visual fields are frequently unreliable in the patient with cloudy media
  - flash VEP was the single best predictor of postoperative vision
- Clinical Presentation
  - most important is its detection
  - astigmatism and alterations in corneal thickness can influence the accuracy of applanation measurement techniques, with thinner corneas under-reading ‘true’ IOP
  - pneumotonometer, Tono-Pen and the dynamic contour tonometer all provide reasonable results in PKP eyes.
- glaucoma is a risk factor for corneal graft failure, whether it is preexisting or develops after penetrating keratoplasty.
  - graft survival probabilities using Kaplan–Meier analysis were 82% at 1 year and 66% at 2 years, versus 93% at 1 year and 87% at 2 years
  - high IOP causes damage to endothelial cells.
  - BAK found in most glaucoma medications

- Causes of glaucoma after penetrating Keratoplasty
  - Preexisting glaucoma: Primary, Secondary
  - Secondary angle-closure glaucoma
  - Trabecular meshwork collapse (aphakia): Six factors were found to be related to iridocorneal angle compression: (1) diameter of the host cornea, (2) size of the recipient bed, (3) length of the suture bites, (4) tightness of the sutures, (5) thickness of the recipient cornea, and (6) size of the donor button relative to the size of the recipient bed.
  - Postoperative glaucoma: Pupillary block, Iritis, Hemorrhage, Lens induced, Steroid response, Malignant, Viscoelastic induced

- Medical management
    - use of aqueous suppressants preoperatively and close monitoring
    - Miotics are generally ineffective and contraindicated in the early postoperative period.
    - Topical CAIs: reports of corneal decompensation
    - prostaglandin analogue: CME
- Surgical management when medical therapy fails
    - Laser iridoplasty and trabeculoplasty
    - Filtering surgery
    - Glaucoma Drainage Devices
        - corneal graft failure in eyes with GDD: immune, mechanical
    - Cyclodestructive Procedures

Pediatric Penetrating Keratoplasty

- Special problems:
    - **Preoperative problems**

1. Complete preoperative evaluation of the corneal pathology is usually not possible.
2. Need for specialized investigations such as ultrabiomicroscopic examination.
3. IOP evaluation usually not accurate in opaque corneas.
4. Patient should be evaluated for systemic associations in cases of congenital corneal opacities.

    - **Intraoperative problems**

1. Small size of the palpebral fissure reduces the working space available for manipulations.
2. Excessive lowering of the intraocular pressure is to be avoided as severe hypotony prevents optimal trephination of the recipient cornea.
3. Caution is to be exercised while performing the scleral fixation due to the higher risk of perforation as the sclera is thinner in pediatric eyes.
4. Use of Flieringa rings with unequal placement of fixation sutures may also result in increased distortion resulting in difficulty while suturing.
5. Need for performing associated procedures such as lensectomy, anterior vitrectomy, glaucoma procedures, and so on, is high.
6. Increased positive pressure of vitreous with forward shift of lens–iris diaphragm due to the low scleral rigidity and increased elasticity of pediatric eyes.
7. Increased difficulty in suturing and cheese wiring due to the thin peripheral corneal tissue in certain cases.

- **Postoperative Problems:**
  1. need for frequent examinations under anesthesia for postoperative follow-up evaluations
  2. frequent loosening of sutures necessitating replacement/early removal
  3. increased risk of rejection and infections
  4. Difficulties with repeated refractive error assessments, and reversal of amblyopia.
  5. Even with increased anatomic success of pediatric corneal grafts, visual rehabilitation remains a concern.

- prevalence of congenital corneal opacities is approximately 3/100,000. With congenital glaucoma included this rises to 6/100,000
- most common primary cause of congenital corneal abnormalities in the developed nations is Peter's anomaly (40.3%), followed by sclerocornea (18.1%), dermoid (15.3%), congenital glaucoma (6.9%), microphthalmia (4.2%), birth trauma, and metabolic disease (2.8%).

- Indications:

1. Congenital:
    a. CHED
    b. Non CHED with Glaucoma: Congenital glaucoma, peter's, anterior segment dysgenesis
    c. Non CHED without Glaucoma: Sclerocornea, dermoid, birth trauma, metabolic dz, keloid, aniridia
2. Acquired, nontraumatic: Herpes simplex keratitis, Bacterial keratitis, Stevens–Johnson syndrome, Keratoconus, Neurotrophic keratitis, Interstitial keratitis, Fungal keratitis, Exposure keratopathy
3. Acquired, traumatic: Corneal or corneoscleral laceration, Blood stain, Nonpenetrating injury with scar

- clear grafts in 80% of pediatric patients at 1 year and 67% at 2 years. excellent prognosis for graft survival in eyes with CHED and a fair prognosis for graft survival in eyes with non-CHED congenital opacities and acquired opacities.
- Reasons for graft failure:
    - Allograft rejection
    - Primary graft failure
    - Graft decompensation
    - Infection
    - Corneal ulcer
    - Glaucoma
    - Trauma
    - Phthisis bulbi

- Complications of pediatric Keratoplasty:
    - Allograft rejection: 22 to 44%, lower reversal rate, CsA 2% QID → OD in 3 months
    - Graft infection: 10 – 50%

- Persistent epithelial defects (PED): poor graft host junction apposition and faulty suturing, early suture loosening, drug toxicity, tear, and surface abnormalities
- Corneal ulcer
- Cataract: 2%
- Glaucoma: 5 – 9%
- Retinal detachment: 3-5%
- Endophthalmitis: 2%
- Wound leak or dehiscence: 2 – 10%
- Expulsive choroidal hemorrhage: 2-3%
- Inadvertent lens loss
- Phthisis bulbi: 4-13%

Outcomes

1. Congenital:
    a. CHED **(25% to 90%)**
    b. Non CHED with Glaucoma: Congenital glaucoma **(50% or less)**, peter's **(62%)**, anterior segment dysgenesis
    c. Non CHED without Glaucoma: Sclerocornea **(70% in eyes with sclerocornea and 83% for partial sclerocornea)**, dermoid, birth trauma, metabolic dz, keloid, aniridia
2. Acquired, nontraumatic: Herpes simplex keratitis, Bacterial keratitis, Stevens–Johnson syndrome, Keratoconus, Neurotrophic keratitis, Interstitial keratitis, Fungal keratitis, Exposure keratopathy
3. Acquired, traumatic: **(55-100%)**Corneal or corneoscleral laceration, Blood stain, Nonpenetrating injury with scar

Large-Diameter Corneal Grafts

- 1951 Castroviejo: large-diameter penetrating keratoplasty, or sclerokeratoplasty,
- Two types
    - Total penetrating Keratoplasty: sclerokeratoplasty
    - Large-diameter lamellar grafts: **Malbran procedure** → advanced keratoconus

- Indications
    - uncontrolled Pseudomonas corneal ulcers, keratomycoses, and other severe necrotizing corneal
    - chronic progressive peripheral corneal ulceration, corneal melting (as in some cases of Mooren's ulcer), rheumatoid keratolysis, or descemetocele formation
    - large-diameter lamellar graft: pellucid marginal degeneration, advanced or eccentric keratoconus, and keratoglobus
- topical and systemic antirejection medications must be administered postoperatively.

PK in Herpes Simplex Disease

- Stromal keratitis is the leading cause of permanent corneal transparency loss
- penetrating corneal graft survival for herpetic eye disease/scar is ***86% at 1 year, dropping to 75% at 5 years, and to 59% at 10 years postoperatively***
- A recurrence-free or **inflammation-free interval** for transplantation of such cases has not been determined yet, but it is considered as a period of at least **6 months**.
- **Preoperative Measures**
    - Control of inflammation
    - Vascularization

- Corneal sensation: Reduced corneal sensation may cause reduced epithelial growth and differentiation with consequent development of epithelial defects
- Antiviral prophylaxis: **Oral antiviral agents** inhibit viral replication at the trigeminal ganglion, avoiding recurrence of ocular disease. Topical antivirals do not have the capability of arresting viral replication in the central nervous system but, if the recurrence appears, they may locally inhibit viral replication.
- Uveitis, glaucoma, and recurrent graft rejection episodes – all of which damage the corneal endothelium – are common after PKP for herpetic keratitis.

- **Operative Technique**
  - Graft size
  - Perforated eyes
  - Suture: interrupted
  - 'Triple procedure'
  - Anterior lamellar Keratoplasty
  - Femtosecond laser
  - Boston keratoprosthesis
- **Postoperative Management**
  - Use of corticosteroids
  - Suture removal
  - **Persistent epithelial defects**: **33% and 44%**, ***Herpetic keratitis must be in the differential*** diagnosis of early- and late-onset postkeratoplasty epithelial defects with or without a history of previous infections.
  - **Recurrence of HSV keratitis**: **6% and 44%**. 23% of corneal grafts performed for herpes simplex keratitis that develop a recurrence may undergo an episode of rejection.
  - **The allograft rejection**: **29% and 46%**
  - Herpes simplex virus in corneas for transplantation
  - Secondary graft failure
  - Glaucoma

- Wound dehiscence
- Secondary infections

High-Risk Penetrating Keratoplasty

- 'transplantation antigens,' fall into two categories: major and minor
  - The genes that encode the **major transplantation antigens** in humans are located within the major histocompatibility complex (MHC) and individually are called human leukocyte antigen (HLA).
    - **Class I** antigens are transmembrane glycoproteins designated HLA-A, HLA-B, and HLA-C. They are expressed on most nucleated cells.
    - **Class II** antigens are encoded by HLA-D genes and include HLA-DP, DQ, and DR antigens. Class II antigens are found on specific immunocompetent antigen-presenting cells (APCs) of the lymphoreticular system.
  - **Minor transplantation antigens** are encoded by genes outside the MHC at numerous loci spread throughout the genome. They are only available for detection if processed and presented on the surface by class I or II MHC molecules of the host. ABO blood group antigens, which differ from most classic minor antigens because they are highly glycosylated. In the cornea, ABO antigens are expressed by epithelial cells, and are upregulated during graft rejection.

- **CCTS Risk factors**
  1. Corneal stromal vascularization >= 2 quadrants, deep, 7% per quadrant
  2. Prior graft loss, especially from allograft rejection: Rejection rates in patients with comparably vascularized recipient beds are approximately 40% after the first graft, 68% after the second graft, and 80% after the third graft.
  3. Increased graft diameter and eccentric grafts: but in recent study → smaller ?? independent ??

4. Anterior synechiae: three or four quadrants of iris synechiae
5. Previous intraocular surgery
6. Herpes simplex keratitis
7. History of anterior segment inflammatory disease
8. Ocular surface disease
9. Young age, especially infants and children

- **Management:**
    - Controlling ocular inflammation
    - Rehabilitating the ocular surface
    - Tissue matching: HLA is conflicting, ABO has some definitive role
    - Surgical technique
    - Postoperative considerations: Teaching each patient the symptoms of rejection facilitates its early recognition. A useful acronym is **RSVP**, which stands for ***redness, sensitivity to light, visual loss, and pain.***
    - Immunosuppression
        - **Corticosteroids**: large systemic doses prednisone (1 mg/kg) around the time of surgery, which can then tapered on an individualized schedule within 2 months. A typical regimen involves prednisolone acetate 1% every 2 hours for the first few weeks with a gradual decrease over the next several months.
        - **Calcineurin inhibitors**
            - Ciclosporin A: It inhibits the transcription of many factors necessary for T-cell activation, most prominently IL-2. Topical & Systemic
            - Tacrolimus
        - **Antimetabolites**
            - Azathioprine
            - Mycophenolate mofetil

- Rapamycin

- **Monoclonal antibodies**
  - **Daclizumab** (Zenapax) and basiliximab (Simulect)
  - **Campath-1H** is a 'humanized' monoclonal antibody

Anterior Lamellar Keratoplasty

- **Indications**
  - Tectonic: to restore normal corneal thickness by using tailor-made lamellar corneal patches to match the defect on the patient (lesion-fit keratoplasty)
    1. Descemetocele
    2. Pellucid marginal degeneration
    3. Advanced Terrien's marginal degeneration
    4. Sterile Mooren's ulcer and other forms of peripheral corneal melts related to autoimmune disorders (as in rheumatoid arthritis and Wegener's granulomatosis).
  - Optical: to enhance vision:
    1. Ectatic disorders: keratoconus, keratoglobus, keratotorus (Schlappi's pellucid marginal degeneration)
    2. Scars:
    3. Dystrophies: epithelial, Bowman's membrane, stromal dystrophies
    4. Degenerations:
    5. Post refractive surgery complications:
    6. Advanced recurrent pterygium involving central cornea
    7. Special circumstances:
  - Therapeutic: Resistant corneal infections, Dermoids and some tumors, Inflammatory mass, Perforations

- Cosmetic: Corneal opacity

- Contraindications
    - endothelium is unhealthy
    - big-bubble technique is contraindicated if there is a pre-existing break in the Descemet's membrane (post hydrops) or there are deep scars (however small) involving the Descemet's membrane

- benefits of anterior lamellar Keratoplasty

1. Extra ocular surgery:
2. No risk of endothelial graft rejection:
3. No need for long term steroid prophylaxis:
4. Rapid functional recovery of vision:
5. No interface haze: in DALK
6. Very good BSCVA.
7. No significant endothelial cell loss:
8. Lesser postoperative glaucoma:
9. Less astigmatism then penetrating keratoplasty:
10. Penetrating Keratoplasty can be done if recurrences.
11. Better long-term graft survival
12. No late failures
13. Easier follow-up
14. A lower-quality donor cornea can be used
15. Allows larger grafts when needed without risking rejection

- Techniques can be grouped into: (4)

1. Stroma to Stroma (manual, microkeratome, and laser-assisted)
2. DM to DM
3. DM to Stroma (2 & 3 can develop subgraft clefts, pseudochambers, or folds in donor Descemet's membrane; hence this type of interface is not recommended)
4. Stroma to DM (only manually)

Two main categories

1. pre-Descemet's membrane procedures

2. Descemet's membrane procedures,

- Techniques
    - Layer-by-layer dissection
    - Stromal delamination
    - Automated therapeutic lamellar Keratoplasty
    - Intrastromal dissection
    - Cleavage separation
    - Donor preparation

- Additional Equipment for DALK
    - Pachymeter
    - Slit lamp microscope
    - Blunt-tipped scissors and spatula

- Intraoperative Complications
    - Perforations and ruptures of Descemet's membrane: Most common complication

- Postoperative Complications
    - Pseudoanterior chambers, or double anterior chambers
    - Pupillary block and fixed dilated pupil (Urrets-Zavalia syndrome)
    - Sclerocorneal inflammation: Postkeratoplasty atopic sclerokeratitis (PKAS) is a rare form of acute inflammation of the ocular surface associated with suture loosening and melting of the graft.
    - Suture-related complications
    - Interface infection

- Outcomes of ALK:

- Visual Outcomes: no statistically significant difference in best corrected visual acuity (BCVA) from 6 months postoperatively through to 5 years postoperatively in DALK vs PK in KC.
- Graft Survival: endothelial cell count 12 months to 2 years postoperatively was significantly greater following DALK than PK
- Suture Management: in PK early removal of sutures can result in unpredictable refractive changes, graft movement, and instability.
- Resistance to Trauma: DALK must theoretically be stronger than a cornea which has undergone PK.
- Surgical Planning: no risk of endothelial rejection and there may be a reduced risk of suture-related events and full-thickness wound dehiscence.
-

Endothelial Keratoplasty

Indications

1. Endothelial dystrophy: Fuchs', posterior polymorphous,
2. Bullous keratopathy: pseudophakic, aphakic
3. Endothelial failure: from trauma, previous surgery, angle closure, tubes
4. Iridocorneal endothelial (ICE) syndrome
5. Failed penetrating Keratoplasty (if acceptable refractive result was achieved)

Contraindications

1. Stromal opacity or scarring that limits visual potential
2. Keratoconus, ectasia
3. Hypotony/pre-phthisical eye

Assessment of anterior chamber space and specialized techniques advised in eyes with:

1. Anterior synechiae
2. Glaucoma tubes
3. Iris abnormalities
4. Anterior chamber intraocular lens

- **Benefits**
    1. maintenance of the **structural integrity of the eye**
    2. more **rapid visual** recovery
    3. **minimal change in refractive spherical** equivalent.

- **Patient Selection**
    - Age: There is certainly no upper age limit for the procedure. 2-90 years
    - Duration of corneal edema:
        - some eyes can achieve 20/20 vision within a week of EK.
        - longstanding corneal edema: remodeling by keratocytes appears to progress from the periphery inward, with the central area over the pupil clearing last.
    - Lens Considerations
        - generally preferable to **perform cataract surgery before the transplant**, either as a staged or combined procedure
        - Removal of the crystalline lens first also creates more room in the anterior chamber
        - opportunity to preserve accomodation by leaving an eye phakic after EK must be weighed against the additional risk and cost of subsequent cataract surgery.

- **Challenging Eyes**
    - Failed penetrating grafts: **EK graft that is 1 mm larger in diameter than the failed PK**, avoid stripping Descemet's membrane and endothelium from the failed PK

- Glaucoma tubes:
- Shallow anterior chambers: Performing a peripheral iridectomy, use of microforceps
- ACIOLs: to be replaced by SFIOLs
- Iris abnormalities, aniridia and aphakia: generally avoid stripping the recipient Descemet's membrane, pull-through technique helps ensure that the graft is secured at all times

- **Donor Preparation**
- **Issues to Consider**
  - General: Preparation immediately before surgery or 'pre-cut tissue.'
  - Uniform thickness: donor of approximately **180 µm** → much easier handling and unfolding of the tissue
  - Diameter: **3 mm less than the smallest diameter of the recipient cornea**, larger EK are more difficult to unfold
  - Shape: **meniscus shape** is produced by most microkeratomes and femtosecond laser → thinner in the center than at the edges →**1.5 diopter (D) hyperopic shift**
  - Stromal bed consistency: smooth stromal bed surface is desired for improved Snellen vision.
  - Scleral rim size: 16–18 mm total diameter
  - Endothelial cell count: 2000–3000 cells/mm2
  - Donor age: 2-75 years
  - Preservation to cutting to surgery time: death due to implantation time longer than 165 hours as well as a cut to implantation time of less than 94 hours is acceptable

- **Methods-4**
  - **Manual dissection**: PLK & DLEK

- Securing donor rim onto the artificial anterior chamber. Trephination of the donor rim with a 9.0-mm Hessberg-Barron vacuum trephine. Manual dissection of the anterior stroma with 0.12 forceps and a crescent knife is started at the keratectomy edge. After removal of the anterior cap, the residual stromal bed is smooth and ready for final resection.

- **Automated microkeratome dissection**: smoother but bed profile is often of a meniscus shape, which has been associated with postoperative hyperopic shift.

  - Donor disc secured into position with the anterior ring lock. Microkeratome track is placed on top of the anterior ring lock. The applanation lens is used to verify adequate vacuum. (<< refers to the circular gauge within the applanation cone; < refers to actual corneal applanation reflex; when within the circular gauge, the vacuum is considered to be adequate.) The cornea is moistened with BSS and the microkeratome pass is made. Microkeratome has produced a free anterior cap and a smooth residual bed. The donor is placed endothelial-side up onto a Barron vacuum trephine, while the trephine diameter is confirmed with calipers. After trephination with a 9.0-mm trephine blade, the donor is ready for insertion.

- **Femtosecond laser dissection:**

  - The donor rim is placed onto an artificial anterior chamber and centered with the femtosecond laser applanation cone. A spiral ablation pattern is started centrally. The ablation extends to the 9.0-mm zone, while the side cut is visible. A 15-degree hinge is located at the 6 o'clock position. The anterior flap is lifted with a flap elevator. The residual bed is evaluated and has surface irregularity that corresponds to the spiral ablation pattern, an inherent weakness of the IntraLase.

  - many promising applications such as customized EK lenticules with a smooth central zone (i.e. to improve Snellen vision) and a roughened peripheral zone (i.e. to facilitate adhesion), it is very expensive compared to other methods.

- **Submerged cornea using backgrounds away (SCUBA) technique:** addresses the challenges of handling and visualizing a thin EK donor which consists of just Descemet's membrane and the endothelium (i.e. 20 μm thickness) →DMEK

- After securing the donor rim to a Barron vacuum trephine and stabilization with 0.12 forceps, a closed tying forceps are used to scroll the peripheral Descemet's membrane. The donor endothelium is stained with trypan blue. Under submersion with either BSS or Optisol GS, the Descemet's/endothelial layer is gently peeled with tying forceps to begin the process. At this point, the process is two-thirds complete, with an intact Descemet's endothelial layer. After removal, the tissue usually scrolls with the endothelium facing outward. It is placed into trypan blue to allow visualization after insertion.

- **Surgical Techniques**
  - **Barraquer** first proposed selective replacement of the corneal endothelium for treatment of corneal edema in 1950
  - **Donor Tissue Preparation:**
    - avoid an eccentric cut of the posterior corneal tissue
    - potential **priming effect on donor endothelium from glutathione and/or glucose in BSS Plus,** thereby maximizing the endothelial pump function of the donor endothelium, allowing for better adherence when presoaking prepared donor tissue.
  - **Intraoperative Techniques:**
    - The horizontal and vertical diameters of the eye
    - centration point is determined on the recipient cornea followed by marking the epithelium
    - **Wound creation**
      - one to three paracentesis incisions, Marking the noncutting edge blade prior to paracentesis, as peripheral as possible to minimize graft touch or graft dislocation with cannula
      - anterior chamber maintainer
      - incision into the anterior chamber is typically created using a diamond or metal keratome, 3 mm and later enlarged to 5 m, scleral, limbal, or clear cornea
    - **Recipient preparation**

- **reverse Sinskey hook** or similar device is typically used to **underline or score** the endothelium/DM 1–2 mm inside the previously made epithelial trephine mark
- Once the circular zone of recipient tissue has been removed, it can be unfolded on the corneal epithelium for careful inspection to detect any potential retained fragments left inside the eye.

- **Techniques to Improve Donor Adherence**
  - **'vent incisions'** as described by Price and Price
  - **Vent incisions + surface massage** with a specially designed roller or a long cannula
- **Donor Insertion Techniques**
  - **endothelium should be coated with viscoelastic** to minimize future endothelial trauma with avoidance of any gentian violet touch to the corneal tissue directly, as it is endothelial toxic.
  - compression forceps such as Kelman-McPherson forceps.
  - noncompression forceps (Irrigation must be in the 'off' position)
  - A trifold technique or 'burrito' fold has also been described for tissue insertion with forceps through a 3-mm incision.
  - A shovel may also be used as an insertion device
  - suture pull-through insertion technique
  - Injectors like The Busin glide
- **Donor Apposition Techniques**
  - Two to four sutures are typically required to close a 5-mm wound
  - Once sutures are placed, the tissue is unfolded unless a pull-through or inserter technique was used, in which case the tissue is already in proper orientation with endothelium down and stroma side up.
  - BSS or air may be irrigated through the paracentesis or wound between the fold of the tissue to complete the unfolding process
  - The pressure must be high after air insertion to ensure tissue apposition, as the inability to achieve a high pressure at this point of the surgery is the single most important risk factor for dislocation.

- pressure is maintained for at least 10 minutes, an air–fluid exchange can be performed to reduce the risk of pupillary block from an anterior chamber full of air.
- Phenylephrine should be avoided as it may increase graft dislocation in a similar manner as it increases flap slippage with LASIK.

- **Early Postoperative Management**
  - shield is typically placed after topical cycloplegic, antibiotic, and antiinflammatory drops
  - supine position 6-24 hours

- **DMEK**
  - idea of DMEK was first introduced by Melles in 1998, the first successful report of DMEK did not occur until 2006
  - advantage:
    - avoidance of expensive mechanical microkeratomes, femtosecond lasers, and an artificial anterior chamber.
    - avoidance of a recipient stroma–donor stroma interface as in DSEK, quicker visual acuity recovery and better final visual acuities
  - A **SCUBA technique** (submerged cornea using backgrounds away) has been described for donor tissue preparation by Geibel
  - It is important to not leave extra endothelium/DM within the 9-mm trephine mark, unlike with DSEK, as recipient–donor overlap is a risk factor for dislocation with DMEK.

- **EK & Glaucoma**
  - risk factors for increased corneal endothelial damage,

        - whether from carbonic anhydrase inhibitor toxicity to the endothelium
        - intraocular pressure (IOP)-induced endothelial damage
        - shallow angles with increased risk of peripheral iris synechiae and resulting iris–cornea touch
        - endothelial trauma from trabeculectomy or a glaucoma drainage device (GDD)
    - main difficulty: ability to maintain an air bubble after air insertion, as both types of fistula immediately shunt air from the anterior chamber

- **EK & Phacoemulsification**
    - cataract surgery is performed prior to the EK procedure to avoid exposing the donor to unnecessary ultrasound energy and other potentially traumatic insults related to the cataract removal
    - paracentesis in the triple procedure should be more vertical than the standard
    - While EK has minimal effects on postoperative keratometry, it does affect the postoperative corneal power. hyperopic shifts between 0.75 and 1.5 diopters.
    - **Intraoperative Issues**
        - Small vertical paracenteses
        - mark all paracentesis blades with gentian violet
        - use a cohesive viscoelastic for all aspects of the surgery
        - adequate incision size is important to minimize endothelial trauma: 4-5 mm
        - To minimize the tendency for this anterior displacement, it is helpful to make sure that the capsulorhexis is smaller than the IOL optic.
    - Postoperative Results
        - refractive spherical equivalent was within 1 diopter of emmetropia in 73% of eyes
        - postoperative refractive results had a mean shift of +1.46 diopters from the targeted outcome

- **Intraoperative Complications**
    - Damaged donor tissue: small scleral rim, during insertion
    - Eccentric trephination: increase the risk of graft detachment,
    - Thin donor tissue: tend to fold over on itself, prismatic optical effect that an uneven graft
    - Retained Descemet's membrane: prevent proper attachment of the DSAEK graft, with subsequent graft detachment
    - Air management: keep the patient in a strict supine position or the use of higher buoyancy gases
    - Others complications: Expulsive choroidal hemorrhage, Anterior chamber hemorrhage, Lens damage

- **Postoperative Complications**
    - **Donor dislocation**: most common complication → reported upto 23-35% ,with newer techniques its <1%
    - **Primary graft failure**: any graft that fails to clear within the first 2 weeks after the DSEK surgery. donor cornea should have at least 2000 cells/mm2. 2% to 45% in the literature.
    - **Secondary graft failure** is the term used when the donor endothelial tissue is detached from the recipient stromal cornea, therefore preventing the cornea from clearing.
    - **Graft rejection**: presence of anterior chamber cells with or without keratic precipitates and concomitant corneal edema. 2.2% to 14%.
    - **Pupillary block glaucoma**: may lead to formation of PAS. high intraocular pressure, peripheral anterior synechiae, iridocorneal adhesions, and a shallow AC.
    - **Endothelial cell loss**: 31% to 50% at the 6-month postoperative examination.
    - **Refractive change**: hyperopic refractive shift
    - **Interface deposits and epithelial ingrowth**:
    - **Retinal complications**: Suprachoroidal hemorrhage, RD, CME

- The speed of visual recovery after DSAEK is generally superior to that of traditional PK, with many patients recovering excellent uncorrected and corrected vision in a matter of weeks rather than months or years.

Management of Corneal Perforations

Etiology

- Infectious (bacterial, fungal, viral [herpes simplex, herpes zoster])
- Inflammatory (collagen vascular disease, acne rosacea, atopic disease, Wegener's granulomatosis, Mooren's [idiopathic] ulcer)
- Trauma (chemical, thermal, ultraviolet [UV], penetrating)
- Xerosis (idiopathic, Sjögren's syndrome, Stevens-Johnson syndrome, ocular cicatricial pemphigoid, vitamin A deficiency)
- Exposure (seventh nerve palsy, thyroid-related ophthalmopathy, ectropion, floppy eyelid syndrome)
- Neurotrophic (postviral, tumor, trauma, postsurgical [cataract extraction, penetrating keratoplasty])
- Degeneration/ectasia (Terrien's marginal degeneration, keratoconus, keratoglobus, pellucid marginal degeneration)
- Surgical (cataract extraction, LASIK, PRK, epithelial sparing PRK, pterygium excision with mitomycin-C, glaucoma filtering/shunt surgery)
- Toxic/keratolytic (topical NSAIDs, topical antibiotics [gatifloxacin], topical corticosteroids, silicone oil)

- **Know difference between terms**

1. Corneal Ulcer

2. Descemetocele

3. Perforation

- **Symptoms**
  - Pain
  - Decreased visual acuity
  - Increased ‘tearing’
- **Signs**
  - Shallow or flat anterior chamber (perforation)
  - Positive Seidel test (perforation)
  - Uveal tissue to the posterior cornea or frank prolapse (perforation)
  - Hypotony (perforation)
  - Central clear zone (often bulging) within area of infiltrate or thinning (descemetocele)
  - Radiating folds in Descemet's membrane emanating from the base of the ulceration (descemetocele)

- **Treatment**
  - **Tissue adhesives**
    - Cyanoacrylate glue: 1960, Webster, small, relatively central perforations 1–2 mm or less,
    - 2-octyl-cyanoacrylate: DERMABOND
    - Iso-Dent: DENTAL GLUE
    - Human Fibrin Glue
    - Commercial superglue ??: methyl-2-cyanoacrylate
  - Penetrating keratoplasty
    - Larger perforations not amenable to repair using tissue adhesive or tissue adhesive failures
  - Patch graft

        - lesions that are too large to use tissue adhesive but small enough to obviate the need for a full-sized penetrating

    - Amniotic membrane transplantation
        - multilayed procedure
    - Medical management

- **Prevention of Corneal Perforation**
    - Bandage soft contact lens
    - Conjunctival flap
    - Tarsorrhaphy
    - Amniotic membrane transplantation
    - Miscellaneous: simple pressure patching, aggressive lubrication, punctal occlusion, and the use of topical ciclosporin

Therapeutic Lamellar Keratoplasty

- Optical Indications
    - Reis-Bücklers' dystrophy, spheroidal degeneration (Labrador keratopathy), and superficial leukomas
- Tectonic Indications
    - Peripheral noninflammatory corneal thinning disorders: PMD, TMD
    - Peripheral inflammatory corneal disease
    - Central thinning and Ectasia

Therapeutic Keratoplasty

- primary purpose is either to restore the structural integrity of the eye (tectonic keratoplasty) or to resolve an infectious or inflammatory keratitis that is refractory to conventional medical therapy.
- Indications
    - Infections
    - persistent epithelial defects and sterile melts
- Postoperative Management
    - Eradicate all remnants of infection, and prevent reinfection.
    - Promote reepithelialization of the cornea and wound healing.
    - Control inflammation with corticosteroids.
    - patient's intraocular pressure should be followed carefully. Glaucoma is seen in approximately 50% of optical penetrating keratoplasties.
- Prognosis
    - clear therapeutic grafts in 73% of bacterial corneal ulcers, 60% of fungal corneal ulcers, 50% of Acanthamoeba corneal ulcers, and 36% of herpes ulcerations with inflammation.
    -

Surgical Management of Superficial Corneal and Conjunctival Disease

Molluscum Contagiosum

- completely excised with a blade or cautery
- can be treated with cryotherapy
- simply curetting the central umbilication and making the lesion bleed

Superior Limbic Keratoconjunctivitis

- patients should undergo thyroid testing
- Medical treatments: artificial tears, antihistamine and mast cell stabilizer drops, ciclosporin drops, nonsteroidal antiinflammatory drops, steroid drops, autologous serum, and steroid injection.
- Surgical treatments: punctal occlusion to silver nitrate solution cautery, cryotherapy, thermal cautery, suture stabilization, and conjunctival recession or resection, with or without amniotic membrane grafting.

Conjunctivochalasis

- An ellipse of excess conjunctiva is marked and removed with Westcott forceps.

Recurrent Corneal Erosions

- Two most common underlying conditions:
    1. previous corneal trauma
    2. corneal dystrophy (typically anterior basement membrane dystrophy [ABMD]).
- ointment lubrication
- BSCL
- ASP
- Epithelial debridement alone, or combined with a diamond burr (DB) polishing procedure or with excimer laser phototherapeutic keratectomy (PTK)

Band Keratopathy

- simple observation in asymptomatic cases to lubricating drops, gels, and ointments for irregular corneal surfaces to removal of the calcium in more advances cases.
- chelation with disodium ethylenediamine tetraacetic acid (EDTA), **not calcium EDTA**.
- 2-3% solution.

Partial Limbal Stem Cell Deficiency

-

Phototherapeutic Keratectomy

- FDA approval:
  - PRK: 1995
  - **PTK: 1995**
  - LASIK: 1998
- Advantage
  - Precision: 0.25 µm of tissue, or about 1/2000 of the corneal thickness.
  - shape of the laser spots can be adjusted
  - allows the surgeon to remove superficial corneal abnormalities
- disadvantage
  - does not discriminate between abnormal and normal tissue

- **FDA-approved indications for PTK**

(1) superficial corneal dystrophies (including granular, lattice, and Reis-Bücklers dystrophies),

(2) epithelial basement membrane dystrophy and irregular corneal surfaces (e.g. secondary to Salzmann's nodular degeneration, keratoconus nodules or other irregular surfaces), and

(3) corneal scars and opacities (e.g. due to trauma, surgery, infection, and degeneration)

- **Contraindications**
  - immunocompromised host, uncontrolled ocular disease such as uveitis, blepharitis or dry eyes, and any condition thought to adversely affect corneal healing.

- laser should not remove greater than one-third of the corneal thickness and should leave at least 250 μm of tissue after the procedure.
- **Side Effects and Complications**
    - Pain
    - Poor epithelial healing
    - Haze/scar
    - Infection
    - Induced hyperopia (common)
    - Induced myopia
    - Induced regular and irregular astigmatism
    - Decreased uncorrected and best-corrected vision
    - Recurrence of herpes simplex virus infection
    - Recurrence of the condition (especially stromal dystrophies, Salzmann's nodular degeneration, keratoconus nodules)
    - Graft rejection/failure

Conjunctival Flaps

- 1958, Gundersen
- Indications
    - Persistent corneal epithelial defect
    - Unresponsive ulcerative microbial keratitis
    - Corneal thinning and perforation
    - Corneal limbal disease
    - Scleral necrosis

    - Glaucoma surgery complications
    - Surface preparation for a cosmetic scleral shell
- Disadvantages
    - vision may be significantly decreased in cases where the flap covers the visual axis
    - prevents monitoring of disease progression by making direct visualization
    - limited assessment of the intraocular pressure
    - compromises the donor site should the patient need a trabeculectomy in the future
- Types
    - Total conjunctival flap
        - thin, bipedicle, bridge flap described by Gundersen
    - Bipedicle bridge flap
    - Single pedicle flap
    - Advancement flap
- Complications
- Intraoperative complications
    - Buttonhole formation
    - Dissection of an inadequate flap
    - Excessive hemorrhage
- Postoperative complications
    - Retraction of the flap
    - Ptosis
    - Cystic flap
    - Opacification and vascularization
-

Iris Reconstruction Surgery

- Iris Suture Techniques: **McCannel's** technique and its modification
    - The sliding knot intracameral suture: **Siepser**
    - Pupil cerclage procedure
    - Iridodialysis Repair
- Iris Relaxing Incisions
- Scissors Sculpting
- Vitrector Sculpting
- Iris Prostheses
    - Large-incision, rigid diaphragm devices: Morcher GMBH, PMMA
    - Rigid small-incision devices: multipiece 'IPS' prosthesis, Morcher 50 Series in the bag prosthesis
    - Flexible small-incision iris prostheses: Custom Flex,

Keratoprosthesis

- ***Guillaume Pellier de Quengsy*** in 1789, who first proposed that an artificial cornea could be implanted in place of a natural cornea opacified by disease or infection: ***Father of Keratoprosthesis***
- ***Nussbaum***– First human KPro (1855)
- Candidates for keratoprosthesis implantation can be classified into ***three main prognostic groups***. In increasing order of success, these groups are:

  Bilateral blindness in severe cases of

  1. **autoimmune-related** corneal opacity and ulceration (SJS & OCP)

2. **chemical injury**
3. corneal **allograft failure** (nonautoimmune).

- **Contraindications**
    - Children (less than 17 years)
    - No PL/ Phthisis/ Advanced glaucoma/ RD
    - Failure to grasp gravity of surgical program/ mentally unstable
    - Refusal to commit to long term follow up
    - The “happily blind”
    - Unreasonable expectations of outcome
    - Cosmesis

- Types of keratoprosthesis

  PERMANENT

    - Intralamellar
    - Penetrating
        - Anterior
        - Posterior : Choyce
    - Perforating
        - Anterior fixation: Cordona, Ceramic, Dohlman
        - Posterior fixation: Nut and Bolt type
        - Intralamellar fixation: Osteo Odonto Keratoprosthesis, chondrokeratoprosthesis, onychokeratoprosthesis

  TEMPORARY

    - Disposable: Eckardt, Aachen keratoprosthesis

- Multiple use: Landers Foulk type2, Landers widefield, Venu

- **Designs and Materials**

  Optical cylinder

  Polymethyl methacrylate (PMMA) – most commonly used material

  Glass, Ceramic, Quartz, Silicon

  Supporting flange

  Biological Skirts

  - Tooth root & alveolar bone (OOKP– Strampelli)
  - Bone (Temprano)
  - Cartilage (Casey)

  Synthetic Skirts

  - PMMA (Choyce, Boston KPro)
  - Dacron (Pintucci KPro)
  - Polycarbonate (Champagne cork KPro)
  - Hydroxy-apatite (Leon-Barraquer KPro)
  - Hydrogel (AlphaCor KPro)
  - Polyurethane (Seoul KPro)
  - Expanded PTFE (Legeais KPro)

- three devices are most widely used.

  1. **OOKP:**
     - first used in Italy by ***Strampelli*** in the 1960s and later modified by ***Falcinelli***.
     - **PMMA optical cylinder** into an excised **monoradicular tooth root**, and is implanted in two stages in conjunction with a mucous membrane graft.
     - **retention rate of 66–85%** at 10–18 years from implantation.

- **most invasive** and technically difficult of the keratoprosthesis techniques and the one associated with the **worst cosmesis**, and would not be considered for any patient with functional vision in the other eye.

2. AlphaCor artificial cornea:

- developed by **Chirila** and coworkers in **Australia**
- nonporous transparent **optic** of poly-2-hydroxyethyl methacrylate (**pHEMA**) and peripheral porous **skirt** of the same material to allow infiltration with tissue stromal cells and blood vessels.
- also requires **two surgeries**
- device is **hydrophilic**, a **healthy tear film** is essential to prevent tissue melting.
- The most common indication for the AlphaCor is corneal **allograft rejection**.
- reportedly contraindicated in herpes simplex keratitis and autoimmune disorders, and can become opaque with specific combinations of topical medications.

3. Boston keratoprosthesis:

- formerly known as the **Dohlman-Doane** keratoprosthesis, was developed at the Massachusetts Eye & Ear Infirmary and the Schepens Eye Research Institute
- The **type I device** consists of **two plates sandwiched around a donor corneal allograft** or the patient's own cornea. Implantation is performed in **one stage**, and is technically similar to standard corneal transplantation. A soft contact lens is used indefinitely to prevent corneal desiccation and thus minimize the risk of corneal melts.
- When conjunctival cicatrix is significant or the patient has severe keratinizing dry eye, it is preferable to implant the **type II device**, which has an ***anterior extension of the lens to allow implantation through the surgically closed eyelid***.
- most commonly used in the world
- Common indications include corneal allograft rejection, opacity when accompanied by extensive corneal neovascularization making allograft success unlikely, opacity with limbal stem cell deficiency syndromes including but not limited to aniridia, and chemical injury.

- Common complications specific to the Boston keratoprosthesis design include retroprosthetic membrane formation, sterile vitritis, and worsening of glaucoma.

- **Cardona device** remains a paradigm in keratoprosthesis design
- **Pintucci** and coworkers developed a biointegrated keratoprosthesis with a PMMA optical cylinder and a porous Dacron mesh haptic, similar to that of Girard
- the **Worst 'champagne cork' keratoprosthesis** has been implanted in a large number of cases, particularly in India.

- **Boston Keratoprosthesis Type 1**
  - Boston KPro comes packaged with the following components: **anterior front part** (optic), **posterior back plate** (small or large size by surgeon choice), **titanium locking ring**, 3.0-mm dermatologic punch, white plastic hollow pin, double-sided adhesive tape, and a contact lens.
  - The Keratoprosthesis Unit (KPro plus donor graft carrier) is typically assembled prior to addressing the patient's cornea.

- **AlphaCor**
  - totally different skill set as the device is placed **intrastromally** and often utilizes a full **conjunctival (Gunderson) flap**.
  - soft, flexible prosthesis with a peripheral opaque skirt and a clear central portion
  - have an advantage in not requiring a donor cornea.
    1. half-thickness limbus-to-limbus stromal dissection
    2. central 3.0-mm trephination is completed through the cornea stromal bed.
    3. Conjunctiva is used to cover the implanted AlphaCor.

- **OOKP (Osteo-odonto-keratoprosthesis)**
  - integrates biologically an inert plastic- PMMA optical cylinder in a lamina fashioned from the patient's own tooth and its surrounding alveolar bone. The device is covered by a tough buccal mucous membrane or rarely by other biological

membranes including lid skin. This allows it to withstand the hostile environment of a keratinized, dry eye with lower rates of extrusion compared with KPros supported by nonbiological material.

- Stage 1a surgery involves harvesting a full-thickness **buccal mucous membrane graft and suturing this in place on the recipient eye**.
- In stage 1b, the preselected **donor tooth is harvested from the mouth with its root** and surrounding alveolar bone. This is used to prepare the **osteo-odonto-lamina**. The bone surrounding the tooth is shaped with a diamond-dusted flywheel and a hole is drilled through dentine to receive the anterior part of the PMMA optical cylinder, which is cemented into place. The osteo-odonto-lamina is ***implanted deep to the orbicularis oculi muscle of the lower lid in the fellow eye***. This remains in place for 2–4 months during which time the bone is invested with soft tissues.
- Stage 2 surgery is carried out after an interval of 2–4 months. The lamina is retrieved from its submuscular location, inspected, and excess soft tissues trimmed ready for implantation onto the eye. The **dentine side** which faces the cornea requires ***thorough soft tissue removal*** to avoid ingrowth into the eye. A Flieringa ring suture is used to support the eye. The cornea is trephined. The iris is removed with forceps and lens extraction by ECCE or ICCE is carried out. Posterior capsulotomy and anterior vitrectomy are then performed. The lamina is sutured to the cornea with the posterior part of the optical cylinder traversing the corneal opening.

- **Auro KPro**
  - Auro K pro design is similar to Boston Keratoprosthesis
  - made of clinical grade PMMA
  - 3 parts: the front plate, the back plate & Lock ring
  - For the eye that is pseudophakic and therefore, approximately emmetropic, and where the IOL is left in place at surgery, a single standard power (45 D) is manufactured
  - For aphakic eyes of different axial lengths, however, devices with varying degrees of power are made to allow a match to the patient's need as closely as possible.
  -

Postoperative Management of Keratoprosthesis

- All Boston Type I keratoprosthesis surgery patients require postoperative antibiotics, steroids, and, if possible, a bandage contact lens.
    - Antibiotics
    - Corticosteroids
    - Glaucoma management
    - Soft contact lens: decreases the evaporative forces on the ocular surface, and creates a moist chamber around the neck of the keratoprosthesis, maintaining hydration and viability of the carrier donor tissue. **Kontur lens**, 16.0 mm in diameter and 9.8 mm base curve with no power.

- AlphaCor™ artificial cornea is very similar to that of the Boston Type I keratoprosthesis with two notable differences:
    - There is no role for a bandage contact lens over the AlphaCor™ device.
    - AlphaCor™ researchers have documented the usefulness of topical medroxyprogesterone 1% suspension postoperatively. Its anticollagenase properties may decrease the incidence of melt/extrusion.

- As for the osteo-odonto-keratoprosthesis, it is essentially an all-or-none proposition. If and when it is successfully performed, there is very little postoperative care required other than a short course of systemic antibiotics, systemic steroids for the management of chronic or recurrent inflammation, and oral carbonic anhydrase inhibitors, as needed, for intraocular pressure control.

- **Complications and Management**
- Retroprosthetic membrane:
    - most common complication

    - increasing the topical steroids or placing a peribulbar injection of triamcinolone (20–40 mg).
    - early membranectomy with the YAG laser is indicated to avoid thickening of the membrane

- Loss of the soft contact lens:
- Sterile vitritis
- Elevated intraocular pressure
- Endophthalmitis
- Retinal detachment
- Corneal melts and keratoprosthesis extrusion

Ocular Surface Transplantation

- Eyes do not have natural protective layer skin. But have multifactorial system which his system includes the eyelids and eyelashes, the tear film, and the ocular surface, which is made up of the conjunctiva and the corneal epithelium.

Limbal Stem Cell Deficiency

- **Limbal stem cells**
- ***Stem cells:***
  - Undifferentiated
  - Long lived
  - Slow cycling
  - Clonogenic
  - Asymmetric division
  - Potency: usually pluripotent or multipotent
  - Plasticity: transdifferentiation
  - Niche: SC microenvironment
- ***SC progeny:***

- 'Transient cells'
- Transient amplifying cells – basal epithelium
- Postmitotic cells – wing cells
- Terminally differentiated cells –superficial squamous cells

- ***epithelial cells of the limbus and central cornea***

Limbus: CK 5/14+ve, CK 3/12-ve, CK 19+ve, P63+ve, CX 43-ve, Vimentin+ve

Central Cornea: CK 5/14 -ve, CK 3/12+ve, CK 19-ve, P63-ve, CX 43+ve, Vimentin-ve

- ***The current evidence of the limbal location of corneal stem cells (Corneal Surgery BrightBill)***

lacks the corneal epithelial differentiation associated keratin pair keratin 3 (K3) and keratin 12 (K12)
higher proliferative potential. limbal basal epithelium contains slowcycling cells identifi ed as the 'label-retaining cells'.
Abnormal corneal wound healing with conjunctivalization, vascularization, and chronic infl ammation occurs when the limbal epithelium is partially or completely removed.
relative preponderance of limbal neoplasms and the scarcity of corneal epithelial tumors, assuming that neoplasms arise mainly from relatively 'undifferentiated cells'
corneal epithelium can be maintained by cellular proliferation originating from limbal stem cells without contribution of the adjacent conjunctiva.

- These are undifferentiated electron dense basal cells present at the limbus
  - ☐ Contains minimal cytoplasm and organelles
  - ☐ Surface markers are - K19,Integrin ß1, Enolase α (lacks K3)

- The hallmark of limbal stem cell deficiency is 'conjunctivalisation' of the cornea and the most significant clinical manifestation is a persistent corneal epithelial defect

Symptoms: decreased vision, photophobia, tearing, blepharospasm, and recurrent episodes of pain (epithelial breakdown), as well as a history of chronic inflammation with redness

Signs

- Mild → severe
- Loss of limbal anatomy
- Conjunctival epithelial ingress onto cornea – stippled fluorescein staining
- Columnar keratopathy
- Unstable tear film over affected area
- Frank conjunctivalisation
- Corneal vascularisation – superficial and deep
- Fibrovascular pannus covering corneal surface
- Persistent epithelial defect
- Stromal melting
- Perforation, scarring, calcification
- Keratinisation

Classification

- Congenital
    - Aniridia: most common cause of congenital limbal stem cell deficiency
        - 1 in 64K-96K
        - iris deformities foveal hypoplasia, optic nerve hypoplasia, nystagmus, glaucoma, and cataract.
        - Aniridic keratopathy occurs in 90% of patients with aniridia
    - Dominantly inherited keratitis
    - Ectodermal dysplasia
        - dyshidrotic ectodermal dysplasia
        - keratitis–ichthyosis–deafness (KID) syndrome → keratodermatous ectodermal dysplasia (KED)
    - Multiple endocrine deficiency

- Acquired
    - Chemical injury
    - Thermal burns
    - Ultraviolet /ionising radiation
    - Autoimmune Disorders:
        - Steven-Johnson syndrome
        - OCP
    - Contact lens induced keratopathy
    - Iatrogenic limbal stem cell deficiency
        - prior surgery involving the corneoscleral limbus
        - Chronic use of topical medications, including pilocarpine, beta-blockers, antibiotics, and corticosteroids

- **Holland staging system**
    - system based on the status of the limbal stem cells and conjunctiva

Limbal stem cells lost (%)	Normal conjunctiva (stage a)	Previously inflamed conjunctiva (stage b)	Inflamed conjunctiva (stage c)
<50 (stage I)	Iatrogenic, CIN, contact lens (stage Ia)	History of chemical or thermal injury (stage Ib)	Mild SJS, OCP, recent chemical injury (stage Ic)
>50 (stage II)	Aniridia, severe contact lens, and iatrogenic (stage IIa)	History of severe chemical or thermal injury (stage IIb)	Severe SJS, OCP, recent chemical or thermal injury (stage IIc)

- Diagnosis

- **Based on**
    - Clinical examination
    - Presence of conjunctivalization
    - Disappearance of palisades of Vogt
- **Confirmed by**
    - Impression cytology: Make a definite diagnosis by showing conjunctivalization by the **presence of conjunctival goblet cells**
    - Biopsy – multilayered epithelium, intraepithelial lymphocytes, vessels
    - Vimentin and CK 19 positive cells in central cornea (normally present in peripheral cornea and limbus)

Treatment algorithm

General principles:

– Manage underlying factors, e.g., chronic inflammation, contact lens wear, topical medications

– Topical lubrication

– All associated problems, e.g., raised pressure, conjunctival adhesions, lid malpositions, should be addressed before undertaking ocular surface reconstruction

– Limbal transplants do not perform well in dry eyes

In acute limbus injury:

– If partial, i.e. some limbus is surviving – allow corneal epithelialisation to occur from limbus derived cells – SSCE

– If total:

a) Allow conjunctival epithelium to grow onto cornea

b) Transplant sheet of ex vivo expanded limbal epithelial cells

c) Avoid use of autologous or living related donor tissue until acute inflammation is well under control

In established cases:

– Treat eye lid problems, glaucoma and conjunctival adhesions first

– Partial or total

– Partial:

a) Visual axis not involved: symptomatic, lubricants of SSCE

b) Visual axis involved: SSCE

c) Dense fibrovascular pannus: sector limbal transplant

Total:

a) Unilateral: auto-limbal transplant

b) Ex vivo expansion of autologous limbal cells

c) Bilateral: allo-limbal transplant

d) Ex vivo expansion of cells (living related, living non-related, cadaver)

e) Amniotic membrane and autologous serum drops as adjuncts

f) Allo-transplants require systemic immunosuppression

- **Surgical Mx: (OSD & LSCD)**
    - **Sequential Sector Conjunctival Epitheliectomy (SSCE)**
        - removal of the conjunctivalised epithelium In cases with partial, mild to moderate conjunctivalisation of the cornea,without significant fibrovascular pannus
        - advantage of not overstressing the small remaining sector of limbal ‘stem’ cells.
    - **Conjunctival Limbal Autograft (CLAU)**

- Unilateral limbal deficiency , partial stem cell loss,
- Concurrent conjunctival inflammation
- No risk of rejection

- **Living Related Conjunctival Limbal Allograft (lr-CLAL)**
  - Bilateral limbal stem cell loss: cicatricial pemphigoid (OCP), Stevens-Johnson syndrome (SJS), and atopic keratoconjunctivitis
  - Large risk of transplant rejection
- **Keratolimbal Allograft (KLAL)**
  - disease entities that primarily affect the limbus with no or minimal involvement of the conjunctiva: Aniridia
- **Combined Conjunctival Limbal and Keratolimbal Allograft (C-KLAL)**
  -
- **Cadaveric Stem Cell Allograft**
  - Fresh Tissue
  - Age: < 40 years
  - Good Quality Donor Material
  - Risk of transplant rejection
- **Annular Corneo-scleral Allograft**
  - Prompt re-epithelization
  - Minimal vascularization (mechanical barrier)
  - Less risk of graft rejection
- **Large diameter LK**
  - Advantages
    - Removes superficial stromal opacities
    - Tectonic function
    - Smooth surface

        - Less astigmatism
    - **Disadvantage**
        - More risk of allograft rejection

- **Ex Vivo Tissue Engineered Procedures**
    - Ex Vivo Cultivated Limbal Transplantation
    - Ex Vivo Stem Cell Allografts
    - Ex Vivo Cultivated Conjunctival Transplantation
    - Ex Vivo Cultivated Mucosal Transplantation
    - Limbal Stem Cell Culture
        - This technique expands limbal epithelial progenitor cells from a small biopsy using a 3T3 fibroblast feeder layer or amniotic membrane.
        - Immunostaining techniques : resultant phenotype of HLEC grown on amniotic membrane retains a limbal origin, is predominantly basal epithelial cells, and remains undifferentiated
        - **Taking the Biopsy**
            - Avoid or eliminate the conjunctiva
            - as small as 1–2mm2 and 100 *m*m in depth.
            - Superior limbus if possible so as to include immature cells
            - The obtained tissue is placed with **Ham's F12 medium** containing 50 *m*g/ml gentamicin and 1.25 *m*g/ml amphotericin B until it is processed
            - exposed for 5min to **Dispase II** (1.2 U/ml in Mg2+ and Ca2+ free **Hank's balanced salt solution, HBSS**)
            - cultured in DMEM medium, which is a 1:1 mixture of DMEM and Ham's F12 medium
            - plated onto the basement-membrane side of the amniotic membrane, placed in the center
            - maintained for 2–3 weeks, by which time the epithelial cells have grown and spread to form a cell layer that covers an area 2–3 cm in diameter

- Amniotic Membrane Transplantation (AMT)

- Failure of LSCT
    - **Early Failure**
        - Rejection: acute rejection occurs in about 10–20% of cases and is most common in the first 1 to 12 months
        - Adnexal abnormalities
        - Inflammation
        - Dry eye
    - **Late Failure**
        - Sectoral conjunctivalization
        - Stem cell exhaustion
        - Late rejection

Algorithm for an approach to treat patients with severe OSD

a. Management of glaucoma

b. Correction of eyelid and eyelash abnormalities

c. Suppression of inflammation

d. Ocular surface transplantation

   i. Conjunctival limbal autograft (CLAU) for unilateral disease

   ii. Keratolimbal allograft (KLAL) for bilateral limbal deficiency with minimal to moderate conjunctival disease

   iii. Living related conjunctival limbal allograft (lr-CLAL) for bilateral limbal deficiency with moderate to severe conjunctival disease

iv. Combined conjunctival-keratolimbal allograft (C-KLAL) for bilateral limbal deficiency with severe conjunctival disease

e. Keratoplasty

i. Lamellar (LK) for patients with stromal opacification with normal endothelium

ii. Penetrating (PK) for patients with stromal opacification with loss of endothelial function

iii. Keratoprosthesis (K-Pro) for patients with good fornices but are not good keratoplasty candidates.

Amniotic membrane Transplantation

first documented ophthalmologic application: 1940's, in the treatment of ocular burns

five layers from within outward:

1. A single layer of highly metabolically active, columnar to cuboidal epithelium
2. A thin basement membrane
3. A compact layer made of reticular fibres virtually devoid of cells
4. A loose network of reticulum containing fibroblasts, called the fibroblast layer
5. A spongy layer of wavy bundles of reticulum bathed in mucin,which forms the interface with the chorion

mechanisms of action

1. promotes epithelialization
2. inhibits scarring
3. inhibits vascularization
4. reduces inflammation
5. provides a substrate for cell growth (**The most uncontroversial mechanism of action)**
6. antimicrobial effects
7. as a biological bandage

Composition

Enzymes: prostaglandin synthesis → phospholipases, prostaglandin synthase and cyclo-oxygenase

prostaglandin-inactivating → Prostaglandin dehydrogenase
Cytokines: anti-inflammatory cytokines → IL-1Ra and IL-10
Pro-inflammatory → IL- 6 & 8
Growth Factors: EGF, TGF*a*, KGF, HGF, bFGF, TGF-*b*1, and -*b*2
MMP & TIMPs:

- **Processing and Preservation**
  - **Now not used →** lyophilisation, air drying, glutaraldehyde and polytetrafluoroethylene treatment and irradiation
  - Now used → freezing is the commonest mode
- Solutions
  - DMSO in phosphate buffered saline
  - Eagle's minimum essential medium (MEM) & glycerol

- ***Graft***: When the membrane was used with the intention of it becoming incorporated into the recipients tissue
- ***Patch***: when the intention was for it to come away or be removed at a certain point following surgery

- **primarily as a graft or a patch with four objectives:**
  1. establish epithelial cover in an area where none existed
  2. to prevent corneal perforation in eyes at risk due to stromal melting
  3. to limit scarring where the clinical likelihood was high or where scarring (symblepharon/adhesions) previously existed
  4. to limit inflammation and neovascularisation.

- ***success***: when the membrane served the purpose that was intended
- ***partial success***: when the membrane did not serve the purpose that was intended but the objective was achieved
- ***failure***: when the objective was not achieved even though the purpose may have been achieved

Must remember following chart:

AM layer	Constituents	Biological properties
Epithelium	Growth factors* Cytokines	Maintains undifferentiated epithelial phenotype when culturing limbal stem cells
Basal lamina	Collagen IV/VII	Improves epithelial cell migration

AM layer	Constituents	Biological properties
	Laminin 1/5 Fibronectin[†]	Strengthens adhesions on basal cells Induces epithelial differentiation (including goblet cells in conjunctiva) Prevents apoptosis
Stromal matrix	TGF-beta Anti-inflammatory and antiangiogenic proteins Protease-inhibition factors	Suppresses corneal myofibroblasts, limbal and normal and pathological conjunctival fibroblasts proliferation and differentiation – inhibits cicatrization Traps inflammatory cells from other tissues, inducing rapid apoptosis Inhibits inflammation and neovascularization

- Methods
    - Graft (epithelial-side up):
    - Patch (epithelial-side down):
    - Combined approach:
-

Prokera

- Prokera is a medical devise designed by Dr Tseng where AM has been clipped into a dual, concave, polycarbonate ring set, acting as a biologic bandage. It can be inserted much like a contact lens without needing any sutures or glue.
- Prokera is a conformer type device made of amniotic membrane with a rigid frame so that it can be inserted into the conjunctival sac. It affords both cover to the surface and also keeps the bulbar and palpebral conjunctival surfaces apart. I have not used Prokera directly (its cost is prohibitive) but was effectively using a home made similar device even before Prokera was introduced: I place a sheet of 2 x 2 inches amniotic membrane over the surface of the eye and tuck the membrane into the superior, inferior, medial and lateral fornices of the conjunctival sac, with a squint hook or similar blunt instrument. I then take a plastic conformer shell of the desired size and insert it in the conjunctival sac such that a layer of the membrane is beneath it and the folded surface, above it. In patients who are bed ridden for example patients in acute stage of Stevens Johnson syndrome in the intensive care unit, that is all that is required. The membrane can be changed every other day or so.

- In ambulatory patients, after inserting the membrane and conformer in the eye, I approximate the membrane covering the anterior surface of the plastic conformer shell and suture the edges together. I then trim off the excess membrane. It effectively becomes a conformer shell wrapped in membrane. It can stay in situ up to a week and even can be removed for examination of the eye and reinserted.
-

Refractive Surgery

- **Decision Making**
    - ***three major challenges***: to select the right patient, to select the right procedure, and to achieve the right outcome
    - Preoperative subjective questionnaires, such as the ***Dell Vision Questionnaire***, have two values: (1) to assess the **patient's attitudes and expectations** – documenting them in the clinical record, and (2) to **assess postoperative outcomes** by using the same or a related questionnaire.
    - Patient age: previously 18–21 years. Now **14** years

- Refractive error: 0.50 D to **10 D of myopia** and **4 D of hyperopia**, **Astigmatism up to 5** D
- Corneal thickness: adequate residual stromal bed thickness of **300 µm**. A residual thickness of 250 µm is a customary target. Abnormally thick corneas (greater than 620 µm) raise suspicion of endothelial dysfunction and warrant endothelial specular microscopy.
- Corneal topography: characteristics of early ***keratoconus or PMD, FF-KC*** should not receive LASIK, because they may be predisposed to further steepening (ectasia) after surgery.
- Keratometry: postoperative minimum value of 38 D and a maximum value of 50 D set the limits after surgery.
- Pupil size: very large pupils under mesopic conditions – 7.5 to 8 mm – seem at greater risk of optical aberrations.

- **Thin-flap LASIK:**
  - 100–110 µm flaps, also referred to as sub-Bowman's keratomileusis
  - more safely with regard to ectasia and corneal hypoesthesia
- **Surface Ablation**
  - photorefractive keratectomy (PRK): epithelium is removed manually or with an excimer laser (transepithelial PRK). PRK is especially effective in patients with recurrent corneal erosion and epithelial basement membrane degeneration
  - epi-LASIK: not used
  - laser assisted subepithelial keratomileusis (LASEK): no advantage in replacing the epithelium, since that delays recovery, does not reduce postoperative pain, and requires the healing epithelium to subsequently remove the epithelial flap.
- **Conductive Keratoplasty**
  - Lans in the 1880s.
  - can steepen the central cornea approximately 1 to 1.5 D
  - treating residual astigmatism after previous surgery and for creating monovision in presbyopes

- **Arcuate Transverse Keratotomy**
  - oldest corneal refractive surgery procedure
  - partial-thickness incisions are placed perpendicular to the steep corneal meridian to induce flattening and a coupled effect of steepening 90 degrees away. Also called astigmatic keratotomy, the most frequent indication for the technique is astigmatism correction at the time of cataract surgery with limbal relaxing incisions.
  - The closer the incision is to the center of the cornea, the greater the effect.
  - generally effective technique to treat 1–4 D of astigmatism.
- **Phakic Intraocular Lenses:**
  1. the Verisyse anterior chamber iris fixated phakic IOL (Ophtec, Boca Raton, FL, USA),
  2. the Visian posterior chamber plate ICL (STARR Surgical Company, Monrovia, CA),
  3. the Alcon (Alcon Laboratories, Fort Worth, TX) anterior chamber angle fixated ‘acrysof’ design.
  - treatment of myopia and astigmatism
  - cell counts of approximately 2400 cells/mm2
  - minimum anterior chamber depth of 3.2 mm
- **Intraocular Lens after Phacoemulsification**
  - IOL implantation is refractive surgery.
  - Toric IOLs may be used to treat up to 2.50D of astigmatism.
- **Retreatments and Sequential Procedures**
  - 10–20% will require a second treatment
  - Bioptics: the combination of an intraocular lens with the refractive outcome modified by excimer laser cornea sx
  - CK
  - Intacs intracorneal ring segments

- corneal cross-linking

- **Treatment of Presbyopia**
  - Simple monovision for presbyopia – myopia for near vision in the non dominant eye and full distance correction in the dominant eye
  - presbyLASIK

Patient Evaluation and Selection

- complete ocular history: patients with a history of ocular herpes simplex virus (HSV), strabismus, diplopia, previous refractive surgery, dry eye, or contact lens intolerance, Previous radial keratotomy (progressive hyperopic shift)
- Examination
  - Visual acuity
  - Refraction
  - Contrast sensitivity
  - Keratometery
  - Computed topography
  - Pupil examination: patients with pupils >6.5 mm will often have increased scores for total higher-order aberrations both pre- and postoperatively
  - Slit lamp examination
  - Fundus examination
  - Tonometry
  - Pachymetry
  - Endothelial cell evaluation
  - Anterior chamber depth
  - Dry eye testing
  - Monovision testing

- Ocular dominance determination
- Wavefront testing: unit of measure in wavefront testing is the root mean square (**RMS**) in microns (μm)
  - lower-order aberration → defocus (MC)
  - higher-order aberrations → spherical aberration and coma

wavefront-optimized versus a wavefront-guided treatment:

wavefront-optimized treatment, the laser treatment is designed to **minimize the increase in spherical aberration** which commonly occurs in myopic conventional ablation

wavefront-guided treatments virtually always provide **superior** visual results compared to conventional treatment on other platforms, such as the VISX laser.

- Informed Consent: geometrically greater need as it being elective procedure

Topographic Analysis

- True topography implies knowledge of the exact contour or shape.
- The term 'videokeratoscope' more accurately describes the technology of these instruments.
  - Orbscan combines optical sectioning with Placido reflection
  - Pentacam and Galilei utilize Scheimpflug imaging to measure the corneal surface.
- 'form fruste' keratoconus
- Displaced apex syndrome

Incisional Corneal Surgery

- Dutch ophthalmologist: Lans

Radial Keratotomy

- obsolete procedure
- -1.00 to -4.00 D of myopia
- does not involve removal of tissue
- **PERK study**: Prospective Evaluation of Radial Keratotomy
    - -2.00 to -8.75 D (mean: - 3.875 D)
    - 8 radial incisions were used for all patients
    - 53% of the 435 study patients had 20/20 or better uncorrected visual acuity (UeVA) and 85% were 20/40 or better.
    - most important finding in the 10-year PERK study was the continuing long-term instability of the procedure. A hyperopic shift of 1.00 D or greater was found in 43% of eyes between 6 months and 10 years postoperatively. There was an association between length of the incision and hyperopic shift, particularly if the incisions extended into the limbus.
- not only the curvature of the central cornea but also its overall topography, creating a multifocal cornea → flatter in the center and steeper in the periphery.
- 2 phenomena of postoperative refractive instability-
    - diurnal fluctuation of vision
    - progressive flattening effect of surgery

Incisional Correction of Astigmatism

Coupling:

When one meridian is flattened from an astigmatic incision, an amount of steepening occurs in the meridian 90' away. This phenomenon is known as coupling. When the coupling ratio (the amount of flattening in the meridian of the incision divided by the induced steepening in

the opposite meridia n) is 1.0, the spherical equivalent remains unchanged. When there is a positive coupling ratio (greater than 1.0), a hyperopic shift occurs.

Arcuate Keratotomy

- arcuate incisions of approximately **95% depth** are made in the steep meridians of the **midperipheral** cornea at the 7-mm optical zone

Limbal Relaxing Incisions

- LRIs are incisions set at approximately **600u depth**, or 50u less than the thinnest pachymetry at the **limbus**, and placed just anterior to the limbus

Onlays and Inlays

Keratophakia

- plus-powered lens is placed intrastromally to increase the curvature of the anterior cornea for the correction of hyperopia and presbyopia.
- The lenticule can be prepared either from donor cornea (homoplastic) or synthetic material (alloplastic).
    - Homoplastic Corneal Inlays
        - obsolete
        - aphakia and hyperopia of up to 20 D
    - Alloplastic Corneal Inlays
        - ability to be mass-produced in a wide range of sizes and powers that can be measured and verified
        - AcuFocus, ReVision Optics, and Presbia
        - The Kamra Inlay (AcuFocus Corneal Inlay): for the treatment of presbyopia.
            - **ultrathin (5 um**), biocompatible polymer that is microperforated to allow improved near vision and perhaps nutrient flow.

- The **3.8-mm** diameter inlay has a central aperture of 1.6 mm.
- In the nondominant eye, a corneal flap that is 200 flm thick is created, and the inlay is placed on the stromal bed, centered on the pupil. Although the inlay has no refractive power, the goal of the device is to have the central aperture function as a pinhole to increase depth of focus and improve near vision without changing distance vision.

Epikeratoplasty

- also called epikeratophakia
- obsolete
- suturing a preformed lenticule of human donor corneal tissue directly onto the Bowman layer of the host cornea

ICRS

- Intrastromal Corneal Ring Segments
- treat low amounts of myopia by displacing the lamellar bundles and shortening the corneal arc length
- placed in the midperipheral corneal stroma
- thicker the segment, the greater the flattening
- **Intacs**
    - 2 segments of 150' of arc
    - fixed outer diameter of 8.10 mm
    - 0.210, 0.250, 0.275,0.300,0.325,0.350,0.400 and 0.450 mm thickness
    - approximately 68%-70% stromal depth
- **Ferrara rings**
    - smaller optical zone
    - more of a flattening effect

  - *not FDA approved*
- Advantage: potentially REVERSIBLE
- Patient Selection
  - 21 years or older
  - with documented stability of refract ion, as demonstrated by a change of <0.50 D for at least 12 months prior to the preoperative examination
  - with 1.00 D of astigmatism or less
- Indication
  - low levels of myopia (- 1.00 to - 3.00 D spherical equivalent)
  - KC
  - KC+PMD?
  - Ectasia After LASIK
- contraindication
  - patients with collagen vascular, autoimmune, or immunodeficiency diseases
  - pregnant or nursing women
  - the presence of ocular conditions (such as recurrent corneal erosion syndrome, or corneal dystrophy) that may predispose the patient to future complications
- In cases of peripheral KC, single segment can be applied. When a Single segment is placed, it flattens the adjacent cornea but causes steepening of the cornea 180 away-the "**bean bag effect**" (when one sits on a bean bag, the bag flat tens in one area and pops up in another area).
- Complications
  - anterior chamber perforation
  - microbial keratitis
  - implant extrusion
  - shallow ring segment placement
  - corneal thinning over lntacs
  - reduced corneal sensitivity (5 .5%)

- induced astigmatism between 1 and 2 D (3.7%)
- deep neovascularization at the incision site (1.2%)
- persistent epithelial defect (0.2%)
- iritis/uveitis (0.2%)
- Visual symptom
  - difficulty with night vision (4.8%)
  - blurred vision (2.9%)
  - diplopia (1.6%)
  - glare (1.3%)
  - halos (1.3%)
  - fluctuating distance vision (1.0%)
  - fluctuating near vision (0.3%)
  - photophobia (0.3%)
-

Orthokeratology

- **corneal refractive therapy CRT**
- overnight use of rigid gaspermeable contact lenses to temporarily reduce myopia.
- The contact lens is fitted at a base curve flatter than the corneal curvature
- Paragon CRT: FDA approved rigid contact lens

Photoablation

Two broad groups:

1. **Surface Ablation:**

- Photorefractive keratectomy (**PRK**), laser subepithelial keratomileusis (**LASEK**), and epipolis LASIK (**epiLASIK**)
- Bowman layer is exposed either by debriding the epithelium through various methods or by loosening and moving, but ultimately preserving, the epithelium

2. **LASIK**

- Laser in situ keratomileusis
- excimer laser ablation is performed under a lamellar flap that is created with either a mechanical microkeratome or femtosecond laser

Wavefront-Optimized and Wavefront-Guided Ablations

- WGA
  - the treatment is aimed to correct the pre-operative HOAs
  - profiles that are customized for individual patients.
  - WGA are Good.
- WOA
  - the treatment attempts to reduce HOAs generated during surgery.
  - profile corrects expected HOAs for an average eye, and those that are anticipated as a result of the surgery. This means that an eye with higher than normal HOAs, will end up with near equally high HOAs after treatment in WOA.

Potential Contraindictions

- Connective tissue disease
- Dry-eye syndrome
- Stromal/ endothelial dystrophies
- Previous herpes infection
- Pregnant or nursing mother
- Ectatic corneas

- Patients with ***EBMD are better candidates for surface ablation than for LASIK*** because surface ablation may be therapeutic, reducing epithelial irregularity and improving postoperative quality of vision while enhancing epithelial adhesion
- **steeper** than 48.00 D are more likely to have **thin flaps or frank buttonholes** (central perforation of the flap) with mechanical microkeratomes. Corneas **flatter** than 40.00 D are more likely to have smaller-diameter flaps and are at increased risk for creation of a **free cap** due to transection of the hinge with mechanical microkeratomes.
- formula is used to calculate residual stromal bed thickness (RSBT): Central corneal thickness - thickness of flap - depth of ablation = RSBT
-

PRK-Photorefractive Keratectomy

- PRK was the first widely accepted surgical procedure to ablate corneal tissue
- 1980s, PRK using the 193 nm argon fluoride excimer laser
- up to −10 D of myopia and +4 D of hyperopia

- PRK Epithelial Removal
  - **Mechanical:**
    1. scraping using a Paton spatula, scalpel blade, Desmarres blade, or blunt no. 67 blade,
    2. motorized brush such as that described by Pallikaris or the Amoils Epithelial Scrubber
  - **Chemical**: 18–20% ethanol, 20 seconds
- Laser
  - Excimer laser: Broad-beam lasers & scanning laser
- Postoperative Management
  - broad-spectrum antibiotic

- topical NSAID
- topical steroids

- Complications
- Intraoperative
  - Eccentric ablations and decentrations
- Postoperative Complications
  - Epithelial problems
  - Dry eyes
  - Corneal infiltrates and infectious keratitis
  - Central islands
  - Irregular astigmatism
  - Undercorrection
  - Overcorrection
  - Haze, scarring
  - Regression

LASEK

- In the LASEK variant of surface ablation, the goal is to preserve the patient's epithelium.
- Instead of debriding and discarding the epithelium or ablating the epithelium with the excimer laser, the surgeon loosens the epithelium with 20% alcohol for 20 seconds and folds back an intact sheet of epithelium

Epi-LASIK

- largely supplanted LASEK because there is no alcohol damage to the epithelium.
- In epi-LASIK, an epithelial flap is fashioned with a microkeratome fitted with a modified dull blade and a thin applanation plate that mechanically separates the epithelium. In this

manner, epiLASIK preserves more viable epitheli al cells, may improve results compared with LASEK

LASIK

History

- Jose I. Barraquer, Bogota, Colombia → father of lamellar corneal refractive surgery
    - 1949: keratomileusis → keras ('horn,' here applied to the cornea) and mileusis (carving or chiseling).
    - myopic keratomileusis (MKM) → freeze myopic keratomileusis, or F-MKM.
    - Keratophakia
- **Kaufman and Werblin**: Epikeratophakia
- **Ruiz**: automated lamellar keratoplasty (ALK), and the keratome was named the automatic corneal shaper (ACS)
- Barraquer–Krumeich–Swinger (BKS) refractive system and its refined microkeratome (the BKS 1000)
- **Srinivasan**, an IBM researcher: ablative photodecomposition with argon fluoride 193
- **Trokel and L'Esperance**: photorefractive keratectomy (PRK)
- 1989, **Peyman**: erbium:YAG laser to ablate rabbit corneal stroma using infrared (thermal) rather than ultraviolet energy
- 1990, **Pallikaris**: laser in situ keratomileusis
- 1999, the **Summit Excimer Laser** (Summit Technologies, Waltham, MA) was the first laser to be approved by the FDA for use in LASIK.

Suction Ring

- The suction ring has 2 functions:

- to adhere to the globe, providing a stable platform for the microkeratome cutting head
- to raise the lOP to a high level, which stabilizes the cornea.

Microkeratomes

- Five major types of microkeratome exist:
    1. nondisposable horizontal motor
    2. nondisposable vertical moto
    3. disposable
    4. Waterjet
    5. picosecond or femtosecond laser microkeratomes

Femtosecond laser

- creates flaps by performing a lamellar dissection within the stroma.
- several extra steps
    - suction ring is centered over pupil and suction is applied
    - docking procedure
    - applanation lens is then centered over the suction ring
    - femtosecond laser treatment applied
- **Advantages of FEMTO**
    - Less increase in lOP required
    - More control over flap diameter
    - Size and thickness of flap less dependent on corneal contour
    - Centration easier to control

- Epithelial defects on flap are rare
- Less risk of free cap and buttonhole
- More reliable flap thickness
- Hemorrhage from limbal vessels less likely
- Ability to re-treat immediately if incomplete femtosecond laser ablation

- **Disadvantages**
  - Longer suction time
  - More flap manipulation
  - Opaque bubble layer may interfere with excimer ablation
  - Bubbles in the anterior chamber may interfere with tracking and registration
  - Increased overall treatment time
  - Difficulty lifting flap >6 months
  - Increased risk of diffuse lamellar keratitis
  - Increased cost
  - Need to acquire new skills
  - Delayed photosensitivity or good acuity plus photosensitivity (GAPP), which may require prolonged topical corticosteroid therapy
- Application of laser Treatment
  - Tracking
  - Centration
  - Ablation

- **Refractive Outcomes**
  - For Myopia: mild to moderate
    - 90% achieved 20/20
    - ~100% achieved 20/40

- For Hyperopia
  - 46%-59% of eyes had postoperative UCVA of20/20 or better, 92%-96% had UCVA of 20/40 or better, and 84%-91 % were within 1.00 D of emmetropia

Complications

Surface Ablation and LASIK

- Overcorrection
- Undercorrection
- Central Islands: steepening of at least 1.00 D with a diameter of 1 mm compared with the paracentral flattened area.
- Optical Aberrations:
  - glare, ghost linages, and halos
  - Night-vision complaints are often caused by spherical aberration
- Decentered Ablation: Centration is even more critical for hyperopic than myopic
- Corticosteroid-Induced Complications
- Endothelial Effects
- Dry Eye and Corneal Sensation
- Infectious Keratitis

Complications Unique to Surface Ablation

- Persistent Epithelial Defects
- Sterile Infiltrates
- Corneal Haze
  - Early: within 6 months
  - Late: after 6 months

Complications Unique to LASIK

- Microkeratome Complications
    - Buttonhole, free cap, decentration
    - Perforation
    - Epithelial Sloughing or Defects
    - Striae
        - Macrostria
        - Microstria
    - Flap subluxation has been reported to occur in up to 1.4%
    - Traumatic Flap Dislocation
    - **Diffuse Lamellar Keratitis**
        - "sands of the Sahara" (SOS),
        - can range from asymptomatic interface haze near the edge of the flap to marked diffuse haze under the center of the flap with diminished BCVA.
            1. Peripheral faint white blood cells; granular appearance
            2. Central scattered white blood cells; granular appearance
            3. Central dense white blood cells in visual axis
            4. Permanent scarring or stromal melting
    - **Pressure-Induced Stromal Keratitis PISK**
    - Epithelial Ingrowth
    - Interface Debris
    - Ectasia

Disturbances Related to Femtosecond Laser LASIK Flaps

- Good acuity, postoperative photophobia **GAPP**
- Rainbow glare

Collagen Shrinkage

- Lanz: dutch medical student
- Terrian: cautery to correct astigmatism
- Gasset and Kaufmann: thermokeratoplasty, 1975

Laser Thermokeratoplasty

- 1990s: holmium:yttrium-aluminum-garnet (Ho:YAG) laser → FDA approved
- noncontact Sunrise Hyperion system was approved by the FDA in 2000.

Conductive Keratoplasty

- 2002, the FDA approved the ViewPoint CK system
- Radiofrequency waves
- presbyopic patient with an endpoint of -1.00 to -2.00 D
- The number and location of spots determine the amount of refractive change, with an increasing number of spots and rings used for higher amounts of hyperopia.
-

C3R

(Read more details from KC topic.)

All FemtoSecond Sx

FLEX

- Femtosecond lenticule extraction or FLEx
- Femtosecond laser creates two cuts, a refractive and a nonrefractive as a single step. The first cut is made at the bottom of the refractive lenticle while the second one at its roof. Once the cuts are made, flap is lifted and refractive lenticule is removed. The flap is reposited in usual manner. It is important to make manipulation at correct plane between flap & lenticule and separate lenticule edge.

SMILE

- small incision lenticular extraction
- less invasive where by the entire lenticule can be extracted through a small incision without lifting up the flap.

INTRACOR

- done on TECHNOLAS Femtosecond work station.
- It applies energy inside the cornea without bringing it to the surface
- no incision of epithelium, endothelium or Bowman's or Descemet's membrane and thus ensure better healing with minimal risk of infection.
- The pulses are placed on concentric intrastromal circles centered about visual axis and extended at least up to 100 microns from the surface. The concentric patterns of cut fibers shift the centre of cornea slightly anteriorly and create a hyperprolate shape. At present myopia up -3D and astigmatism up to 2D have been tried. However the results are not very accurate. Also its role in presbyopia has been emphasized as it causes a biomechanical change in cornea that shifts centre slightly forward creating a pattern of hypersphericity thus allowing some near vision while retaining distance vision.
-

Intraocular Surgery

Phakic IOLs

(Read more from Lens.)

Bioptics

- term suggested by **Zaldivar** in the late 1990s
- PCPIOL implantation followed at a later time by LASIK to treat patients with extreme myopia and/or residual astigmatism
- Term adjustable refractive surgery (ARS), is also used
-

Refractive Lens Exchange

- considered only if alternative refractive procedures are not feasible
- may be preferable to a PIOL in the presence of a lens opacity that is presently visually insignificant but that may soon progress and cause visual loss
- Risk of intraocular surgery present