Section 3

CORNEAL AND EXTERNAL EYE DISEASES
THE CORNEA

Opening Question: What is the Anatomy of the Cornea?

“The cornea is a transparent structure in the anterior segment of eye....”

Anatomy of the Cornea

1. Gross anatomy
   - General dimensions:
     - 11.5 mm horizontal diameter
     - 10.5 mm vertical diameter
     - 1 mm thick periphery
     - 0.5 mm thick centrally
     - Anterior surface radius 7.7 mm
     - Posterior surface radius 6.8 mm
   - Deep layers appear to merge into stroma
   - Stroma (substantial propia):
     - 90% of cornea thickness, 400 µm centrally
     - 80% water
     - Glycosaminoglycans in extracellular matrix
       - Three major fractions:
         - Keratan sulphate (50%)
         - Chondroitin phosphate (25%)
         - Chondroitin sulphate (25%)
   - Descemet's membrane:
     - Basement membrane of the endothelium (keyword)
     - 10 µm thick
     - Secreted and regenerated by endothelial cells
     - Type IV collagen fibrils
     - Hassall-Henle bodies
     - Terminates abruptly at limbus (Schwalbes line)
   - Endothelium:
     - Single layer, polygonal, cuboidal cells
     - Tight junctions (control of corneal hydration)
     - Microvilli
     - Incapable of regeneration: Repair occurs by cellular hypertrophy and sliding
     - Line passages of trabecular meshwork

2. Microscopic anatomy
   - Five layers:
     - Epithelium:
       - Stratified squamous, nonkeratinized, nonsecretory epithelium (keyword)
         - 5–6 layers deep
         - Superficial cells have microvilli (needs tears to keep cornea smooth)
         - Basement membrane — strongly attached to Bowman's layer
       - Bowman's layer:
         - 8–12 µm
         - Acellular
         - Consists of interwoven type IV collagen fibrils which are anterior condensation of substantia propia
         - Incapable of regeneration, replaced by fibrous tissue if damaged (i.e. scars)
         - Ends abruptly at limbus

Exam tips:
- One of the most common basic science questions in life viva and MCQ examinations.

Overall yield: ⭐⭐⭐⭐ Clinical exam: Viva: ⭐⭐⭐⭐ Essay: ⭐⭐ MCQ: ⭐⭐⭐⭐
Physiology of Cornea

1. Three main functions:
   - Light transmission (400–700 nm light)
   - Light refraction:
     - Total refractive power of cornea 43 D (70% of eye’s refractive power)
     - Refractive index of cornea 1.376
   - Protection

2. Corneal metabolism:
   - Energy needed for maintenance of transparency and dehydration

   Glucose:
   - Cornea obtains glucose mainly from aqueous
   - Tears and limbal capillaries appear to provide minimal contribution
   - Glucose can be stored in epithelium as glycogen
   - ATP obtained through glycolysis and Kreb’s cycle

   Oxygen:
   - Endothelium acquires oxygen from aqueous
   - Epithelium acquires oxygen from either capillaries at the limbus or precorneal film

Why is the Cornea Transparent?

“Corneal transparency is due to a combination of factors including....”

Cornea Transparency

- Relative dehydration of cornea due to:
  - Anatomic integrity of endothelium and epithelium
  - Endothelial pump removes fluids from stroma
  - Evaporation of water from tear increases osmolarity of tear, which draws water from cornea

- Normal intraocular pressure (if too high, relative hydration occurs)
- Relative acellularity, lack of blood vessels and pigments
- Regular matrix structure of corneal fibrils:
  - Destructive interference of light occurs
  - Consistent refractive index of all layers

Exam tips:
- Variations to questions include “What are the factors which keep the cornea dehydrated?”

What is the Nerve Supply of the Cornea?

“The cornea is innervated by the V CN.”

Nerve Supply

- V CN
- Ophthalmic division
- Long posterior ciliary nerves gives off:
  - Annular plexus at limbus

- Subepithelial plexus just below Bowman’s membrane
- Intraepithelial plexus
**Opening Question:** What are the Congenital Abnormalities of the Cornea?

**Megalocornea**

1. **Corneal diameter > 13 mm (or 12 mm at birth):**
   - Buphthalmos must first be excluded (no axial myopia, no cornea opacity, normal IOP)
   - Distinction between simple megalocornea (large cornea without structural abnormalities and associated ocular malformations) and anterior megalophthalmos (large cornea with structural abnormalities/ocular malformations)

2. **Inheritance:** AD (simple megalocornea) or SLR (anterior megalophthalmos)

3. **Clinical features (anterior megalophthalmos):**
   - Congenital
   - Males (90%)
   - Bilateral (80%), symmetrical, nonprogressive
   - Normal cornea
   - Normal thickness and endothelial cell density
   - No Descemet's rupture (i.e. no Haab's straie)
   - Normal posterior segment
   - Normal visual development

4. **Ocular associations (anterior megalophthalmos):**
   - Astigmatism
   - Atrophy of iris stroma
   - Ectopic lentis and cataract
   - Glaucoma (but not congenital glaucoma!)

5. **Systemic associations (anterior megalophthalmos):**
   - Dwarfism
   - Achondroplasia
   - Myotonic dystrophy
   - Fetal alcohol syndrome

**Microcornea**

1. **Corneal diameter < 10 mm**

2. **May occur as:**
   - Isolated cornea abnormality
   - Nanophthalmos (small but normal eye)
   - Microphthalmos (small and abnormal eye)

3. **Inheritance:** AD, AR, sporadic

4. **Ocular associations:**
   - Shallow AC
   - Glaucoma
   - Hyperopia
   - Persistent hyperplastic primary vitreous
   - Congenital cataract
   - Anterior segment dysgenesis
   - Optic nerve hypoplasia

5. **Systemic associations:**
   - Dwarfism
   - Achondroplasia
   - Myotonic dystrophy
   - Fetal alcohol syndrome

**Cornea Plana**

1. **Flat cornea:**
   - Radius of curvature < 43D (may be 20–30D)
   - Pathognomonic when corneal curvature is the same as adjacent sclera!

2. **Inheritance:** AD, AR, sporadic
3. Bilateral, peripheral opacification of cornea
4. Ocular associations:
   • Sclerocornea
   • Microcornea
   • Congenital cataract
   • Glaucoma

**Sclerocornea**
1. Diffuse scarring and vascularization of cornea
2. Epithelium thickened, Bowman's membrane absent
3. May be AD/sporadic
4. Classification:
   • Isolated sclerocornea: No other abnormalities
   • Sclerocornea plana: With flat cornea (mean K < 38D)
   • Peripheral sclerocornea with anterior chamber cleavage abnormalities: Peter's, Rieger's anomalies
   • Total sclerocornea

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Q **Tell me about Goldenhar's Syndrome.**

**Clinical Features**

1. Ocular features:
   • Megalocornea
   • Coloboma of iris and lids
   • Squint, Duane's syndrome
   • Fundus — optic nerve hypoplasia, coloboma
   • Refractive errors

2. Systemic features:
   • Wide mouth
   • Maxillary and mandibular hypoplasia
   • Preauricular tags and hearing loss
   • Vertebral defects
Complications of Chemical Injury

1. Acute problems:
   - Corneal abrasion and perforation
   - Infection
   - Glaucoma

2. Long-term problems:
   - Ocular surface:
     - Trichiasis, distichiasis, entropion
     - Cicatricial conjunctivitis, dry eyes, symblepharon, ankyloblepharon
   - Cornea:
     - Persistent epithelial defect
     - Limbal stem cell failure and persistent ocular surface disease
     - Stromal scar
   - Intraocular complications:
     - Glaucoma
     - Diffuse trabecular damage iritis
     - Cataract

“Chemical injuries are ocular emergency.”
“They can be mild or potentially blinding.”

Classification of Chemical Injury (Hugh’s Classification)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Signs</th>
<th>Prognosis</th>
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<tbody>
<tr>
<td>1</td>
<td>Corneal epithelial damage No limbal ischemia</td>
<td>Excellent</td>
</tr>
<tr>
<td>2</td>
<td>Corneal hazy but iris details seen Ischemia &lt; 1/3 of limbus</td>
<td>Good</td>
</tr>
<tr>
<td>3</td>
<td>Corneal hazy but iris details hazy Ischemia &lt; 1/2 of limbus</td>
<td>Fair</td>
</tr>
<tr>
<td>4</td>
<td>Opaque cornea Ischemia &gt; 1/2 of limbus</td>
<td>Poor</td>
</tr>
</tbody>
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Updated classification (ref Dua H et al, Br J Ophthalmol 85(11):1379)
- Updated grading scheme with prognostic value
- 6 grades
- Main criteria for classification:
  - Extent of limbal staining (vs ischemia):
    Staining of greater value in predicting epithelial recovery
  - Area of bulbar and fornical conjunctival staining: Conjunctiva important in ocular surface stabilization when limbus severely compromised
Exam tips:
• One of the few true ocular emergencies.
• Need to know difference between “acidic” and “alkaline” injuries.

Notes:
• “What are the possible mechanisms of glaucoma?”
  • Acute shrinkage of collagen
  • Uveitis, trabeculitis
  • Lens-induced inflammation
  • Peripheral anterior synchiae
  • Steroid response

Q How do You Manage a Patient with Severe Chemical Injury?

“Chemical injury is an ocular emergency….”

Management of Chemical Injury

1. Acute management
  • Irrigate eyes immediately copious amounts of sterile fluid (normal saline preferred):
  • Remove particulate matter
  • Debride devitalize tissues
  • Start antimicrobial treatment
  • Start steroids immediately (to decrease mediators of inflammation and stabilize lysosome in white blood cells)
  • Minimize steroids after 10 days (because steroids decrease fibroblast and collagen synthesis)
  • Alternatively, medroxyprogesterone can be used (no anti-anabolic effects)

2. Manage epithelial defect
  • Conservative:
    • Tear substitutes and lubricants
    • Vitamin C (antioxidant, cofactor in collagen synthesis)
    • Ascorbate or citrate (antioxidant, cofactor in collagen synthesis)
    • N acetylcysteine (collagenase inhibitor, contributes to cross-linkages and maturation of collagen)
    • Sodium EDTA (collagenase inhibitor — calcium chelator, calcium required for collagenase activity)
    • Bandage contact lens
    • Punctal occlusion in severe dry eyes
    • Lid closure (taping, pressure pad, tarsorrhaphy)
  • Lysis of conjunctival adhesions (glass rods)
  • Surgical:
    • Tissue glue
    • Conjunctival flap

3. Long-term management
  • Ocular surface reconstruction:
    • Lid surgery (cicatricial entropion, trichiasis and distichiasis)
    • Conjunctival replacement (AMT or cultivated conjunctiva)
  • Ocular surface surgery
    • Principles:
      • Removal of dysplastic epithelium
      • Wide excision of fibroplastic undergrowth
      • Judicious diathermy
      • Epithelial replacement (autografts/allografts/cultivated transplants)
  • Cornea:
    • Keratoplasty (limbal, lamellar, penetrating)
  • Intraocular:
    • Antiglaucoma treatment
    • Cataract surgery
  • Controversial:
    • Retinoic acid (promote surface keratinization)
    • Fibronectin (growth factor)
    • Epidemal growth factor
    • Subconjuctival heparin (to facilitate limbal reperfusion)
Cicatricial Conjunctivitis

1. Infectious:
   - Adenovirus
   - Herpes simplex
   - Trachoma
   - *Corynebacterium diphtheriae*
   - Beta hemolytic streptococcus

2. Noninfectious:
   - Autoimmune:
     - Ocular cicatricial pemphigoid
     - Steven-Johnson syndrome
   - Vernal/atopic keratoconjunctivitis
   - Dermatological:
     - Ocular rosacea
     - Scleroderma
   - Neoplasia:
     - Squamous cell carcinoma, Bowen’s disease
   - Trauma:
     - Mechanical, chemical injury
   - Others:
     - Long-term timolol use
**TOPIC 4**

CORNEAL OPACITY, SCARRING AND EDEMA

*Overall yield: ***  Clinical exam: ***  Viva:  Essay:  MCQ: ****

**Q Opening Question:** What are the Causes of Corneal Scarring?

“Corneal scarring can be divided into the location of the scarring...”

**Corneal Scarring**

1. **Superior cornea:**
   - Superior limbic keratoconjunctivitis
   - Trachoma
   - Vernal keratoconjunctivitis

2. **Central cornea:**
   - Disciform keratitis
   - Keratoconus (hydrops)
   - Fuch’s endothelial cell dystrophy
   - Bullous keratopathy
   - Lipid keratopathy
   - Band keratopathy

3. **Inferior cornea:**
   - Neurotrophic keratopathy
   - Exposure keratopathy
   - Marginal keratitis

4. **Diffuse scarring:**
   - Interstitial keratitis
   - Trauma
   - Ocular surface diseases (Stevens-Johnson syndrome, ocular cicatricial pemphigoid)
   - Trachoma

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**Clinical approach to a superior corneal scar**

“This patient has stromal scarring seen at the superior half of the cornea....”

**Look for**

- **Trachoma:**
  - Trichiasis, entropion of upper lid
  - Herbert’s pits
  - Evert upper lid (Arlt’s line)

- **Vernal keratoconjunctivitis:**
  - Punctate epitheliopathy, macroerosions, shield ulcers, plaque, subepithelial scar
  - Trantas dots
  - Pseudogerontoxon (cupid’s bow)
  - Evert upper lid (giant papillae)

- **Superior limbic keratoconjunctivitis:**
  - Superior conjunctival injection
  - Punctate epitheliopathy, corneal filaments
Clinical approach to central corneal scar or edema

“This patient has a central corneal stromal scar/edema.”
“The visual axis is involved.”

Look for

- Disciform keratitis:
  - Lid scarring (usually very subtle)
  - Epithelial edema
- Descemet’s folds
- Wessley ring
- Keratic precipitates
- AC activity
- Keratoconus:
  - Parastromal thinning
  - Vogt’s straie
  - Fleischer’s ring
  - Prominent corneal nerves
- Fuch’s endothelial cell dystrophy:
  - Epithelial edema
  - Subepithelial scarring
  - Stromal thickening
- Corneal guttata
- Pseudophakic bullous keratopathy:
  - Epithelial bullae
  - IOL

I’d like to

- Check corneal sensation (disciform keratitis)
- Check IOP (Fuch’s endothelial dystrophy, disciform keratitis)

How do You Manage a Patient with Bullous Keratopathy?

“Management of bullous keratopathy depends on the etiology, severity and visual potential and whether patient has symptoms of pain.”
“In mild cases, conservative treatment is usually adequate....”
“In severe cases, if the visual potential is good...”
“On the other hand, if the visual potential is poor and the eye is painful....”

Bullous Keratopathy

1. Etiology:
   - Pseudophakic bullous keratopathy
   - Fuch’s endothelial cell dystrophy
   - End-stage glaucoma
   - Long-standing inflammation
   - Chemical burns

2. Conservative treatment:
   - Lubricants
   - Hypertonic saline
   - Lower intraocular pressure
   - Avoid steroids

3. Surgical treatment:
   - If good visual potential, consider optical keratoplasty
   - If poor visual potential and eye is painful, consider palliative procedures for pain relief:
     - Tarsorrhaphy, botox to lids
     - Conjunctival flap (see page 169)
     - Retrobulbar alcohol
     - Enucleation (very last resort)

- Therapeutic contact lens
- Hair-dryer
Exam tips:
- Very similar approach to management of neovascular glaucoma! (see page 81).
- See also management of Fuch's endothelial dystrophy (page 138) and glaucoma and cataract (page 29).
Q Opening Question No. 1: How do You Manage a Patient with a Corneal Ulcer?

“Corneal ulcer is a potentially blinding condition which needs immediate ophthalmic management.”

Management of Corneal Ulcer

1. Admit patient if necessary
2. Identify predisposing factors:
   • Contact lens wear
   • Ocular trauma
   • Ocular surface disease
   • Systemic immunosuppression
3. Perform a corneal scrape for microbiological analyses
4. Intensive topical antibiotic treatment:
   • Gutt. gentamicin 15 mg/ml hourly (or gutt tobramycin)
   • Gutt. cephazolin 50 mg/ml hourly (or gutt cefuroxime)
5. Systemic antibiotic treatment if:
   • Ulcer near limbus (scleral extension)
   • Perforated ulcer (endophthalmitis)

Exam tips:
- “Prepare specific antibiotic regimes with exact dosage and frequency of treatment” gentamicin frequently does not sound as impressive as “I would prescribe topical gentamicin 15 mg/ml hourly for the next 24 hours.”

Q When will You Consider Using Monotherapy with Antibiotics?

- Cautious in using monotherapy
- Broad spectrum antibiotic (e.g. gutt. ciprofl oxacin, levofl oxacin, moxifl oxacin)
- Indications:
  - Small, peripheral ulcer
- Culture positive
- Organism is NOT Pseudomonas or Streptococcus
- Organism sensitive to antibiotics
- Patient follow-up and compliance good

Q When will You Consider Using Steroids?

- Use of steroids is controversial, extreme caution needed
- Use only after adequate antimicrobial treatment
- Indications:
  - Culture positive
- Sensitive to antibiotics
- Responding clinically
- Ulcer has been sterilized
- Patient follow-up and compliance good
**Q** What do You do When the Ulcer is not Responding to Treatment?

- Stop antibiotics for 24 hours
- Rescrape and/or corneal biopsy
- Steps in corneal biopsy:
  - LA or GA
  - Corneal tissue on standby (for tectonic replacement)
  - Dermatological trephine with biopsy area encompassing base and active edge of ulcer
- Specimen divided and sent for microbiological analyses and histological staining
- Re-start intensive antibiotics
- Consider other diagnosis (e.g. sterile ulcers?)
- Consider penetrating keratoplasty

**Q** What are the Causes of Sterile Ulcers?

**Sterile Ulcers**

1. Post infection (treated, resolved)
   - Herpes (metaherpetic ulcer)
   - Bacterial
   - Fungal
2. Nearby (contiguous) ocular surface inflammation
   - Lids and lashes (entropion, ectropion, trichiasis, lid defects)
   - Skin (Stevens-Johnson syndrome, ocular pemphigoid, ocular rosacea)
   - Lacrimal gland (keratoconjunctivitis sicca)
3. Neurotrophic keratitis
   - DM
   - V CN palsy
   - Herpes zoster
4. Exposure keratitis
   - VII CN palsy
   - Lagophthalmos
   - Proptosis
5. Nutritional keratitis (Vitamin A deficiency)
6. Neoplasia (acute leukemia)
7. Immune-mediated
   - Connective tissue diseases:
     - Rheumatoid arthritis
     - Wegener’s granulomatosis
     - Systemic lupus erythematosus
     - Polyarteritis nodosa
     - Mooren’s, Terrien’s
     - Marginal keratitis
     - Allergic conjunctivitis
8. Iatrogenic/trauma
   - Postsurgical, topical eyedrops
   - Chemical, thermal, radiation injury

Exam tips:
- Remember “N”on “I”nfected ulcers.

**Q** Opening Question No. 2: Tell me about Fungal Keratitis.

“Fungal keratitis is a potentially blinding condition which needs immediate ophthalmic management.”

**Fungal Keratitis**

1. Types of fungi:
   - **Filamentous** fungi (multicellular, hyphae present):
   - **Septate** (most common cause of fungal keratitis)
     - Monilial (*Fusarium, Aspergillus, Penicillium*)
     - Dermatiaceous (*Curvularia*)
   - **Nonseptate** (cause orbital infections)
     - *Mucor, Rhizopus*
   - **Yeasts** (unicellular, no hyphae)
     - *Candida, Cryptococcus*
   - **Dimorphic** (filamentous at 25°C and yeasts at 37°C):
     - *Blastomyces, Coccidioides* (orbital infections, rarely affect cornea)
2. Predisposing factors:
   - Ocular trauma (filamentous), particularly with organic matter (e.g. vegetation, soil)
   - Ocular surface disease and systemic immunosuppression (yeasts)
3. **Clinical features:**
   - Grayish white ulcer
   - Elevated
   - Indistinct borders, feathery edges
   - Satellite lesions
   - Ring infiltrate
   - Endothelial plaque (may be pigmented)

4. **Stains:**
   - Indian ink
   - Gram stain
   - Giemsa
   - Periodic acid shift
   - Methanamine silver

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**Exam tips:**
- Another common variation is, “Tell me about fungal keratitis.”

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**Q How do You Treat Fungal Keratitis?**

“Fungal keratitis is a potentially blinding condition which needs immediate ophthalmic treatment.”

“**Treatment**

1. All medication work by interfering with ergosterol metabolism (keyword)
2. Polyenes
   - Amphotericin B:
     - Forms complex with ergosterol that destabilizes the fungal wall
     - Good for yeasts
     - Epithelial debridement may improve penetration (highly lipophilic)
     - Unstable, rapid degradation to light
     - Systemic toxicity: Renal, anemia, fever
   - Natamycin:
     - Mechanism of action similar to amphotericin B
     - Good for filamentous fungi
3. Imidazoles
   - Act by interfering with CYP450 mediated pathways in ergosterol synthesis
   - Miconazole, fluconazole, ketoconazole
   - Voriconazole:
     - Relatively new agent with good oral bioavailability (96%) and ocular penetration
     - Effective in cases that have failed therapy with other agents
     - Toxicity: Transient visual disturbances, liver, renal
4. Flucytosine
   - Converted to 5 Fluorouracil
   - Adjunct treatment

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**Q Opening Question No. 3: What are the Characteristics of Acanthamoeba Keratitis?**

“Acanthamoeba keratitis is a potentially blinding condition which needs immediate treatment.”

**Acanthamoeba Keratitis**

1. **Microbiology**
   - Protozoan:
     - Active trophozoite form
     - Dormant cystic form
     - Highly resistant to hostile environment (e.g. chlorinated water)
2. **Predisposing factors:**
   - Contact lens wear
   - Ocular trauma
3. **Clinical features:**
   - In early cases, mimics herpetic epithelial keratitis

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4. **Stains:**
   - Calcofluor white
   - Acridine orange

5. **Culture (nonnutrient agar with E. coli lawns)**
Q How do You Treat Acanthamoeba Keratitis?

“Acanthamoeba keratitis is a potentially blinding condition which needs immediate treatment.”
“It is difficult to treat, needs multiple drugs, long duration of treatment and may involve surgery.”

Treatment:
1. Aminoglycosides:
   - Neomycin (but not gentamicin)
2. Biguanides (disrupts DNA):
   - Polyhexamethylene biguanide (PHMB)
   - Chlorhexidine
3. Diamidines (disrupts cell membrane):
   - Propamidine isethionate (brolene)
   - Hexamidine
4. Imidazoles:
   - Econazole

Exam tips:
- Notice the answer to this question is identical to the answer to the question on fungal keratitis treatment.
- The drugs are difficult to remember. A simple mnemonic is “ABCDE.”
TOPIC 6

HERPETIC EYE DISEASES

Overall yield: ★★★ Clinical exam: ★★★★ Viva: ★★ Essay: ★★ MCQ: ★★★

Opening Question: What is the Difference between the Ocular Manifestations of Herpes Simplex vs Herpes Zoster?

“Herpes simplex is caused by the virus herpes simplex virus type 1.”
“Herpes zoster is caused by the virus zoster varicella virus.”
“The different manifestations can be divided into....”

<table>
<thead>
<tr>
<th></th>
<th>Herpes simplex</th>
<th>Herpes zoster</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age pattern</strong></td>
<td>Primary — &lt; 5 years</td>
<td>Elderly</td>
</tr>
<tr>
<td></td>
<td>Recurrent — Middle ages</td>
<td>Immunosuppressed</td>
</tr>
<tr>
<td><strong>Skin manifestations:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Dermatome</td>
<td>Incomplete</td>
<td>Complete</td>
</tr>
<tr>
<td>2. Bilaterality</td>
<td>Rare</td>
<td>Never</td>
</tr>
<tr>
<td>3. Pain</td>
<td>Less</td>
<td>More</td>
</tr>
<tr>
<td>4. Postherpetic neuralgia</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>5. Skin scarring</td>
<td>Rare</td>
<td>Common</td>
</tr>
</tbody>
</table>

| **Ocular manifestations** |                     |                                |
| 1. Dendritic keratitis | • Central              | • Peripheral                   |
|                       | • Large                | • Small                        |
|                       | • Well-defined dendrite| • Broad, stellate-shaped       |
|                       | • Central ulceration (stains with Fluorescein) | • Raised, plaque-like (stains with Rose Bengal) |
|                       | • Terminal bulbs       | • No terminal bulbs            |
| 2. Spectrum          | 1. Blepharoconjunctivitis: • Follicular  | Each stage has skin, ocular and neural complications |
|                     | • Cicatricial          | A) Acute herpes zoster         |
|                     | 2. Epithelial disease: • Dendritic ulcer | 1. Episcleritis/scleritis     |
|                       | • Geographic ulcer     | 2. Conjunctivitis              |
|                       | • Marginal ulcer       | 3. Keratitis:                  |
|                       | • Neurotrophic/metaherpetic ulcer | • Punctate epithelial keratitis |
|                       |                      | • Microdendrite                |
|                       |                      | • Nummular keratitis          |

(Continued)
The Ophthalmology Examinations Review

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<table>
<thead>
<tr>
<th>Herpes simplex</th>
<th>Herpes zoster</th>
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<tbody>
<tr>
<td>• Necrotizing keratitis</td>
<td>4. Anterior uveitis</td>
</tr>
<tr>
<td>• Interstitial (immune) keratitis</td>
<td>5. Acute retinal necrosis</td>
</tr>
<tr>
<td>4. Endothelitis:</td>
<td>B) Chronic herpes zoster</td>
</tr>
<tr>
<td>• Disciform</td>
<td>1. Mucous secreting conjunctivitis</td>
</tr>
<tr>
<td>• Diffuse</td>
<td>2. Keratitis:</td>
</tr>
<tr>
<td>• Linear</td>
<td>• Nummular keratitis</td>
</tr>
<tr>
<td>5. Corneal complications:</td>
<td>• Disciform neurotrophic</td>
</tr>
<tr>
<td>• Pannus, stromal vascularization and scarring</td>
<td>• Neutrophic and exposure keratitis</td>
</tr>
<tr>
<td>• Trophic keratitis</td>
<td>• Mucous plaque</td>
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<td>• Lipid keratopathy</td>
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<tr>
<td>6. Acute uveitis</td>
<td></td>
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<tr>
<td>7. Episcleritis/Scleritis</td>
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<tr>
<td>8. Acute retinal necrosis</td>
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**Q** What are the Results of the Herpetic Eye Disease Study?

1. **Three components:** To assess effectiveness of:
   - Topical steroids in stromal keratitis in patients on topical antivirals — **safe and effective** in stromal keratitis (*Ophthalmol* 1994; 101: 1871)
   - Oral Acyclovir (400 mg 5x/day) in stromal keratitis in patients on topical steroids and topical antivirals — **no benefit** in stromal keratitis (*Ophthalmol* 1994; 101: 1871)
   - Oral Acyclovir (400 mg 5x/day) in uveitis in patients on topical steroids and topical antivirals — **effective** in uveitis (*Ophthalmol* 1996; 114: 1065)

2. **Additional trial:**
   - Oral Acyclovir (400 mg bd for 1 year after resolution of ocular HSV) in preventing recurrence of HSV — **decreased** rate of recurrence of ocular HSV (all disease types), especially important after resolution of stromal keratitis (*New Engl J Med* 1998; 339: 306)

**Q** What are the Causes of Iris Atrophy?

“The causes of iris atrophy include….”

**Causes of Iris Atrophy**

1. Iatrogenic (postoperative)
2. Injury to iris
3. Inflammation:
   - Herpes simplex (sectoral atrophy), herpes zoster
   - Fuchs' uveitis, Posner Schlossmann syndrome
4. Increased IOP (glaucoma):
   - Post angle closure glaucoma (spiral atrophy)
   - Iridocorneal endothelial syndromes (scattered atrophy with corectopia, pseudopolyopia)
   - Pigment dispersion syndrome (atrophy at periphery of iris)
   - Pseudoexfoliation syndrome (atrophy at pupil border)
5. Ischemia:
   - Anterior segment ischemia
**Exam tips:**
- Be careful, this clinical sign can be easily missed.
- The causes can be remembered by “I”ris atrophy.

**Q What are the Causes of Corneal Hypoesthesia?**

“Corneal hypoesthesia can be physiological or pathological.”

**Corneal Hypoesthesia**

1. **Physiological:**
   - Increasing age
   - Peripheral cornea
   - In the morning
   - Brown eyes

2. **Pathological**
   - Congenital:
     - Riley Day syndrome
     - Congenital corneal hypoesthesia
     - Corneal dystrophies (Reis-Buckler dystrophy, lattice dystrophy)
   - Acquired:
     - Diabetes mellitus
     - Leprosy
     - Herpes simplex
   - Iatrogenic:
     - Topical eyedrops (timolol, atropine, sulphur drugs)
     - Surgery (limbal section ECCE, penetrating keratoplasty, epikeratophakia)
   - Contact lens wear
TOPIC 7
PERIPHERAL ULCERATIVE KERATITIS

Overall yield: ★★★  Clinical exam: ★★★  Viva: ★★  Essay: ★  MCQ: ★★★

Q Opening Question: What are the Causes of Peripheral Ulcerative Keratitis?

Causes of Peripheral Ulcerative Keratitis

1. Systemic
   • Connective tissue diseases:
     • Rheumatoid arthritis (RA)
     • Systemic lupus erythematosus
     • Wegener’s granulomatosis
     • Polyarteritis nodosa (PAN)
     • Relapsing polychondritis
   • Sarcoidosis
   • Leukemia

2. Ocular
   • Infective:
     • Bacterial, viral, acanthamoeba, fungi
   • Noninfective:
     • Mooren’s ulcer
     • Terrien’s marginal degeneration
     • Marginal keratitis
     • Pellucid marginal degeneration
     • Acne rosacea
     • Exposure keratopathy
     • Neurotrophic keratopathy
     • Trauma

Exam tips:
• Peripheral ulcerative keratitis (or PUK) differential diagnoses can be classified either as systemic and ocular or infective and noninfective.
• PUK is a limbal-based disease with inflammatory changes in the limbus; therefore, it is more “immune”-related than “infective.”
• See also “Connective tissue diseases and the eye” (page 413).

Clinical approach to peripheral ulcerative keratitis
“The most obvious lesion in this patient is peripheral corneal thinning seen at the interpalpebral region.”

Look for
• Mooren’s ulcer:
  • Overhanging central edge of ulcer
  • Stromal white infiltrate central edge of ulcer
• Epithelial defect
• Cataract

Section 3: Corneal and External Eye Diseases 129
• Terrien’s marginal degeneration:
  • **Gradual** outer slope and central steep slope (*but not* overhanging)
  • Intact epithelium
  • Gray white demarcation line central edge of thinning

• Other eye:
  • Unilateral (Mooren’s ulcer)
  • Bilateral (Terrien’s, connective tissue diseases)

**Scleral involvement (important sign):**
  • Scleritis (connective tissue diseases)
  • No scleral involvement (Mooren’s ulcer, Terrien’s marginal degeneration)

• Exclude:
  • Blepharitis (marginal keratitis)
  • Skin hyperemia, telangiectasia, papule, nodules, rhinophyma (rosacea)
  • Systemic features:
    • Hands (RA)
    • Malar rash (systemic lupus erythematosus)

**I’ll like to**
  • Examine fundus for evidence of vasculitis, optic neuropathy (connective tissue diseases)
  • Examine patient for systemic signs (connective tissue diseases)

---

**Q How would You Manage a Patient with PUK?**

“I would like to investigate the specific etiology of the PUK and manage accordingly.”

**Management of PUK**

1. **Investigation**
   - **Ocular:**
     • Scrapings for culture and sensitivity
   - **Systemic:**
     • CBC, ESR
     • VDRL, FTA
     • ANA, dsDNA

2. **Treatment**
   - **Systemic steroids**
   - **Immunosuppressives**

**Q How do you Differentiate Terrien’s Marginal Degeneration from Mooren’s Ulcer?**

**Terrien’s Marginal Degeneration vs Mooren’s Ulcer**

<table>
<thead>
<tr>
<th>Terrien’s marginal degeneration</th>
<th>Mooren’s ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Early onset:</strong></td>
<td><strong>1. Two forms:</strong></td>
</tr>
<tr>
<td>• Males (75%)</td>
<td>• Early onset: Progressive, bilateral</td>
</tr>
<tr>
<td>• Bilateral</td>
<td>• Later onset: Limited, unilateral</td>
</tr>
<tr>
<td><strong>2. Symptoms:</strong></td>
<td><strong>2. Symptoms:</strong></td>
</tr>
<tr>
<td>• Little pain and redness</td>
<td>• Severe pain and redness</td>
</tr>
<tr>
<td><strong>3. Clinical features:</strong></td>
<td><strong>3. Clinical features:</strong></td>
</tr>
<tr>
<td>• Starts at <strong>superior</strong> and</td>
<td>• Starts at <strong>interpalpebral</strong></td>
</tr>
<tr>
<td><strong>inferior</strong> quadrant</td>
<td><strong>cornea</strong></td>
</tr>
<tr>
<td>• Epithelium intact</td>
<td>• <strong>Epithelial</strong> defect</td>
</tr>
</tbody>
</table>

(Continued)
Stepwise Treatment Approach for Mooren’s Ulcer

- **Step 1:** Topical steroids
- **Step 2:** Oral steroids and immunosuppressives

**Terrien’s marginal degeneration**
- Sloping inner edge of “ulcer” with lipid line and bridging vessels
- No clear interval
- Low risk of perforation
- Eye not inflamed
- Otherwise eye is normal

**Mooren’s ulcer**
- Overhanging inner edge of ulcer
- Clear interval between limbus and ulcer
- Risk of perforation
- Eye is inflamed
- Cataract, glaucoma may be present

**Q How do You Manage a Patient with Mooren’s Ulcer?**

“The management of Mooren’s ulcer depends on the severity of disease.”
“And involves both medical and surgical treatment.”

**Stepwise Treatment Approach for Mooren’s Ulcer**

- **Step 3:** Conjunctival excision/recession
- **Step 4:** Tectonic Lamellar keratoplasty/penetrating keratoplasty

**Tell me about Acne Rosacea.**

“Acne rosacea is a skin disease of idiopathic origin.”
“It commonly occurs in middle-age women.”
“It has both skin and ocular manifestations.”

**Acne Rosacea**

1. **Skin involvement:**
   - Persistent erythema
   - Telangiectasia
   - Papules, pustules
   - Hypertrophy of sebaceous glands
   - Rhinophyma

2. **Ocular involvement:**
   - Blepharitis almost always develops at some time
   - Severe lesions occur in region of 3%
     - 20% eyes involved first
     - 50% skin involved first
     - 25% simultaneous skin and eye involvement
   - Eyelids:
     - Recurrent blepharitis
     - Meibomitis
     - Styes, Chalazoins
   - Conjunctiva:
     - Papillary conjunctivitis
   - Cornea:
     - Punctate epithelial keratitis
     - Stromal keratitis, peripheral thinning, vascularization
     - Subepithelial opacification
     - Ulceration, scarring and melting

**Treatment**

- Oral tetracycline:
  - Effective for both skin and ocular lesions
  - Basis of therapeutic response unknown, not related to antibacterial effect on *Staph aureus*
- Ampicillin and Erythromycin also found to be effective
- Possible to taper and stop therapy but recurrence is high (50%)
- Also given topically
TOPIC 8

INTERSTITIAL KERATITIS

Overall yield: ⭐ ⭐ Clinical exam: ⭐ ⭐ ⭐ Viva: ⭐ Essay: MCQ: ⭐

Opening Question: What is Interstitial Keratitis?

“Interstitial keratitis is a nonsuppurative, chronic inflammation of the stroma.”
“Without primary involvement of the epithelium or endothelium.”
“The common causes include….”

Causes of Interstitial Keratitis

1. Infective
   - Congenital (or acquired) syphilis
   - TB
   - Leprosy
   - Herpes
   - Onchocerciasis
   - Lyme disease

2. Noninfective
   - Cogan’s disease (associated with polyarteritis nodosa)
   - Sarcoidosis

Clinical approach to interstitial keratitis

“On examination of the anterior segment…."
“There is midstromal corneal opacity.”
“Involving the visual axis.”
“There are ghost vessels seen within the lesion.”

Look for
- Mutton fat keratic precipitates (TB, syphilis, leprosy, sarcoid)
- AC activity
- Lens opacity
- Fellow eye — bilateral (congenital syphilis)

I’ll like to
- Check corneal sensation (herpes, leprosy)
- Check fundus for: Optic atrophy, salt and pepper retinopathy (syphilis)
- Ask for history of deafness, tinnitus, vertigo (Cogan’s dystrophy)
- Systemic examination for rheumatic conditions
- Investigate for cause:
  - CBC, ESR
  - CXR
  - Mantoux test
  - VDRL, FTA
  - Connective tissue screen (polyarteritis nodosa)
TOPIC 9

CORNEAL DYSTROPHY

Opening Question: What are Corneal Dystrophies? How are They Different from Corneal Degenerations?

“Corneal dystrophies are a group of **inherited, noninflammatory** corneal conditions characterized by….”
“Corneal degenerations are a group of **sporadic, age-related** corneal conditions characterized by….”

<table>
<thead>
<tr>
<th>Dystrophy</th>
<th>Degeneration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inherited, noninflammatory condition of cornea</td>
<td>Sporadic, age-related condition of cornea</td>
</tr>
<tr>
<td>1. Inherited, AD (1)</td>
<td>1. Sporadic</td>
</tr>
<tr>
<td>2. Early onset</td>
<td>2. Late onset</td>
</tr>
<tr>
<td>• Bilateral</td>
<td>• Unilateral or bilateral</td>
</tr>
<tr>
<td>• Symmetrical</td>
<td>• Asymmetrical if bilateral</td>
</tr>
<tr>
<td>• Axial, do not extend to periphery (2)</td>
<td>• Peripheral</td>
</tr>
<tr>
<td>• One layer of cornea</td>
<td>• Different corneal layers</td>
</tr>
<tr>
<td>• Otherwise eye is normal</td>
<td>• Other age-related changes present</td>
</tr>
</tbody>
</table>

(1) Except for Macular (AR)
(2) Except for Macular and Meesmann’s Dystrophy (Extends to periphery)

What are the Pathological Features of Epithelial Corneal Dystrophies?

“Epithelial dystrophies affect the epithelium, basement membrane (BM) and Bowman’s membrane of the cornea.”

<table>
<thead>
<tr>
<th>Microcystic (map-dot-fingerprint)</th>
<th>Reis-Buckler</th>
<th>Meesmann’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inheritance</td>
<td>• AD (Incomplete penetrance) if bilateral can be sporadic</td>
<td></td>
</tr>
<tr>
<td>Pathology</td>
<td>• Abnormal epithelial cells with microcysts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Thickened BM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Duplication of BM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Fibrillar material deposited between BM and Bowman’s membrane</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Granular deposits in BM that stain with Masson’s trichrome</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Periodic acid shift positive substance deposited in BM</td>
<td></td>
</tr>
</tbody>
</table>

(Continued)
**Microcystic (map-dot-fingerprint)**  
- Recurrent corneal erosion (RCE) in 10%; most asymptomatic  
- Lesions look like dots, cysts, lines, fingerprint, maps

**Reis-Buckler**  
- RCE  
- Honeycomb appearance  
- Corneal hypoesthesia

**Meesmann’s**  
- Photophobia  
- Tiny epithelial cysts extend to periphery

### Clinical features
- Recurrent corneal erosion (RCE) in 10%; most asymptomatic  
- Lesions look like dots, cysts, lines, fingerprint, maps

### Treatment
- Conservative  
- Treat RCE  
- One of earliest to require PKP  
- Highest risk of recurrence after PKP

### Notes
- Type 2:  
  - Patients older  
  - VA better  
  - Systemic amyloidosis associated  
  - Less numerous lines  
  - Lines more peripheral  
  - PKP rarely needed

### Q What are the Pathological Features of Stromal Corneal Dystrophies?

“Stromal corneal dystrophies affect the stroma of the cornea.”
“There are three classical types…”

<table>
<thead>
<tr>
<th>Lattice</th>
<th>Granular</th>
<th>Macular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inheritance Pathology</td>
<td>AD</td>
<td>AD</td>
</tr>
<tr>
<td>Pathology</td>
<td>Amyloid material</td>
<td>Hyaline material</td>
</tr>
<tr>
<td>Stains:</td>
<td>Congo red</td>
<td>Masson trichrome</td>
</tr>
<tr>
<td></td>
<td>PAS positive</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Birefringent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dichroism</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Crystal violet</td>
<td></td>
</tr>
<tr>
<td></td>
<td>metachromasia</td>
<td></td>
</tr>
<tr>
<td>Clinical features</td>
<td>RCE</td>
<td>RCE</td>
</tr>
<tr>
<td></td>
<td>Linear, branch-like pattern</td>
<td>Bread-like crumbs</td>
</tr>
<tr>
<td></td>
<td>Intervening stroma clear</td>
<td>Intervening stroma clear</td>
</tr>
<tr>
<td></td>
<td>Peripheral stroma clear</td>
<td>Peripheral stroma clear</td>
</tr>
<tr>
<td>Notes</td>
<td>Type 2:</td>
<td>Type 2:</td>
</tr>
<tr>
<td></td>
<td>Patients older</td>
<td>Patients older</td>
</tr>
<tr>
<td></td>
<td>VA better</td>
<td>VA better</td>
</tr>
<tr>
<td></td>
<td>Systemic amyloidosis associated</td>
<td>Larger ring-shaped lesions</td>
</tr>
<tr>
<td></td>
<td>Less numerous lines</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lines more peripheral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PKP rarely needed</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>Treat RCE</td>
<td>PKP needed early</td>
</tr>
<tr>
<td></td>
<td>PKP by 40 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**Exam tips:**
- Common clinical and viva examination.  
- Remember the mnemonic, “Marilyn Monroe Always Gets Her Man in L A City” = “Macular Mucopolysaccharides Alcian Granular Hyaline Masson Lattice Amyloid Congo.”
What are the Features of Amyloidosis?

“Amyloid is an eosinophilic hyaline substance with some characteristic staining characteristics.”
“The manifestations can be classified as....”

**Amyloidosis**

1. **Staining characteristics**
   - Congo red positive
   - Birefringent and dichroism
   - Crystal violet metachromasia
   - Fluorescence in ultraviolet light with thioflavin T stain
   - Typical filamentous structure on electron microscopy

2. **Classification**
   - Primary localized amyloidosis:
     - Most common form of ocular amyloidosis
     - Conjunctival involvement
     - Lattice dystrophy
     - Primary systemic amyloidosis
     - Secondary localized amyloidosis:
       - Long standing ocular inflammation
         - e.g. trachoma, interstitial keratitis
     - Secondary systemic amyloidosis:
       - Long standing chronic systemic diseases
         - e.g. RA, leprosy

What is Crystalline Dystrophy of Schnyder?

“Crystalline dystrophy of Schnyder is a stromal dystrophy associated with abnormal cholesterol metabolism.”
“The clinical features include....”

**Crystalline Dystrophy of Schnyder**

- AD
- Localized abnormality in cholesterol metabolism
- Minute crystals in stroma
- Stromal haze
- Associated with corneal arcus and Vogt’s limbal girdle
- Associated with hypercholesterolemia in 50%
- Stain: Oil Red O

What are the Pathological Features of Endothelial Dystrophies?

“Endothelial dystrophies affect the Descemet’s membrane and endothelium of the cornea.”
“There are three classical types....”

<table>
<thead>
<tr>
<th></th>
<th>Fuch’s endothelial dystrophy</th>
<th>Posterior Polymorphous dystrophy (PPMD)</th>
<th>Congenital Hereditary Endothelial dystrophy (CHED)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inheritance</td>
<td>AD</td>
<td>AD or AR</td>
<td>AR</td>
</tr>
<tr>
<td>Pathology</td>
<td>Abnormal deposition of collagen material in Descemet’s membrane</td>
<td>Focal thickening of Descemet’s membrane</td>
<td>Endothelium not visible</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Middle aged women</td>
<td>At birth or young</td>
<td>Stroma diffusely thickened and opacified</td>
</tr>
<tr>
<td>4 signs:</td>
<td>Corneal guttata</td>
<td>“Polymorphous” picture</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stromal edema</td>
<td>Vesicles, geographical or hand-like opacities on Descemet’s membrane (“tram-tracks”)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bowman’s membrane scarring</td>
<td>May be associated with glaucoma (progressive synechial angle closure) and Alport’s syndrome</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Epithelial edema/bullous keratopathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>See below</td>
<td>PKP in about 10%</td>
<td>PKP needed <strong>very early</strong></td>
</tr>
</tbody>
</table>

Section 3: Corneal and External Eye Diseases
Q How do You Manage a Patient with Fuch’s Endothelial Dystrophy and Cataract?

“The management of Fuch’s endothelial dystrophy with cataract can be a difficult decision.”
“There are two clinical problems which must be managed simultaneously, depending on the severity of each condition.”
“Factors to consider include patient and ocular factors....”

Management of Fuch’s Endothelial Dystrophy

1. Patient factors — consider surgery early if
   • Young age
   • High visual requirements
   • Poor vision in fellow eye

2. Ocular factors
   • Severity of cataract
   • Severity of cornea decompensation:
     • History of blurring of vision in morning
     • Greater than 10% difference in corneal thickness between early morning and measurements later in the day

<table>
<thead>
<tr>
<th>Severity of corneal decompensation</th>
<th>Severity of cataract</th>
<th>Possible options</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>0</td>
<td>• Conservative treatment (lubricants, hypertonic saline, lower IOP, soft bandage contact lens)</td>
</tr>
<tr>
<td>+++</td>
<td>+++</td>
<td>• Combined cataract extraction and corneal transplantation (DSAEK or PKP) (triple procedure)</td>
</tr>
</tbody>
</table>
| +++                                | 0                    | • PKP first
• Cataract extraction later, after development of cataract |
| +++                                | +                    | • Triple procedure indicated
• Alternatively corneal transplantation (DSAEK or PKP) first, cataract extraction later but discuss with patient about advantages of triple procedure* |
| +                                  | +++                  | • Cataract extraction first, corneal transplantation (DSAEK or PKP) later
• Alternatively, discuss with patient about advantages of triple procedure |
| 0                                  | +++                  | • Cataract extraction first
• Corneal decompensation likely to develop, corneal transplantation (DSAEK or PKP) later |

*Disadvantages of individual procedures (PKP and cataract extraction in separate sittings):
• Two operations, increased cost and increased rehabilitation time
• Corneal graft more likely to fail
• Visibility poor during the second procedure
• IOL power difficult to calculate
*Fuch’s endothelial dystrophy is one of the main indications for endothelial keratoplasty

Exam tips:
• Remember there are no RIGHT or WRONG answers.
• First, be as conservative as possible. Give extremes of each scenario, then go to the more controversial middle ground.
• Opening statement is similar in all situations: “There are two clinical problems which must be managed simultaneously. Factors to consider include....” Then give your own scenario.
• See also management of neovascular glaucoma (page 82), bullous keratopathy (page 118) and glaucoma and cataract (page 29).
Clinical Features of Keratoconus

1. Early signs:
   - Keratoscopy/Placido’s disc (irregular rings)
   - Retinoscopy (scissoring reflex)
   - Direct fundoscopy (oil drop sign)
   - Vogt’s striae
   - Prominent corneal nerves

2. Late signs:
   - Paracentral stromal thinning
   - Fleischer’s ring
   - Corneal scarring
   - Munson’s sign (bulging of lower lids when patient looks down)
   - Rizuti’s sign (conical reflection off nasal cornea with slit lamp light from temporal side)

Exam tips:
• Remember the causes of CONES are the 5 “C”s!

What are the Histological Characteristics of Keratoconus?

Triad of
• Thinned stroma
• Epithelial iron deposit
• Breaks in Bowman’s membrane layer
  (Descemet’s membrane and endothelium are normal unless hydrops has developed)

Opening Question: What are the Clinical Features of Keratoconus?

“Keratoconus is a noninflammatory ecstatic corneal condition.”
“Characterized by central or paracentral stromal thinning, apical protrusion and irregular astigmatism.” (classical triad)
“The clinical features can be early and subtle or late and gross.”

What are the Causes of Keratoconus?

Causes of Keratoconus

1. Primary
   • Idiopathic (prevalence: 400/100,000)
   • AD in 10%

2. Secondary
   • Systemic:
     • Chromosomal disorders (e.g. Down’s syndrome)
   • Ocular:
     • Congenital ocular anomalies (e.g. aniridia, Leber’s congenital amaurosis, retinitis pigmentosa)
     • Contact lens wear
Clinical approach to keratoconus

“On examination of this patient’s anterior segment, there is evidence of keratoconus.”

Look for

- Classical signs:
  - Paracentral stromal thinning
  - Vogt’s striae
  - Prominent corneal nerves
  - Fleischer’s ring
  - Corneal scarring
- Secondary causes:
  - Down’s syndrome, Turner’s syndrome
  - Marfan’s syndrome
  - Aniridia, ectopic lens

I’ll like to

- Evert lids to look for features of vernal keratoconjunctivitis
- Examine fundus to exclude RP

Exam tips:

- Be very careful when you are asked to examine a young patient with an otherwise NORMAL SLIT LAMP EXAM (page 149) because the ocular findings of keratoconus can be subtle.
- Clue: A Placido’s disc may be conveniently located next to the patient!

When would You Consider Corneal Grafting for Keratoconus?

1. Conservative treatment first (usually good enough in 90% of patients):
   - Spectacles
   - Special contact lens
   - Collagen cross-linking:
     - New technique in which photo-sensitizing agent (riboflavin) is applied to cornea and collagen cross-links are induced with UV-irradiation
     - Shown to retard keratoconus progression

2. Indications for corneal grafting:
   - Unable to achieve good vision with contact lens
   - Intolerant to contact lens wear
   - Scarring after acute hydrops

3. Special preoperative and intraoperative factors to consider:
   - Most cases are treated with lamellar keratoplasty these days
   - Lower risk of endothelial rejection
   - Young patients
   - Treat vernal keratoconjunctivitis aggressively
   - Large graft (but reduce graft over-sizing to reduce myopia)
   - Eccentric graft
   - Trephination:
     - Hard to fit trephine (may need hot probe to flatten cornea)
     - Shallow trephine (0.3 mm)
What are the Other Causes of Prominent Corneal Nerves?

Causes of Prominent Corneal Nerves

1. **Ocular diseases:**
   - Keratoconus
   - Keratoconjunctivitis sicca
   - Fuch's endothelial dystrophy
   - Trauma
   - Congenital glaucoma

2. **Systemic diseases:**
   - Leprosy
   - Neurofibromatosis
   - Multiple endocrine neoplasia type IIb (medullary CA thyroid, parathyroid CA, pheochromocytoma)
   - Refsum's disease
   - Ichthyosis
   - Normal variant with increasing age
**Crystalline Keratopathy and Miscellaneous Keratopathies**

**Opening Question:** What are the Causes of Crystalline Keratopathy?

1. **Infectious diseases**
   - Infectious crystalline keratopathy:
     - Occurs when there is **suboptimal** inflammatory response to organisms (e.g. post PKP)
     - Common organisms: *Streptococcus viridans*, *Staphylococcus epidermidis*

2. **Noninfectious diseases**
   - Lipid deposit
   - Crystalline dystrophy of Schnyders
   - Mineral deposit:
     - Argyrosis (silver)
     - Band keratopathy (calcium)
   - Chrysiasis (gold)
   - Protein deposit:
     - Cystinosis
     - Dysproteinemia (multiple myeloma)
   - Medication deposit:
     - Topical ciprofloxacin
     - Amiodarone
     - Tamoxifen
     - Phenothiazines
     - Indomethacin
     - Chloroquine
   - Idiopathic:
     - Crystalline dystrophy of Bietti

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**Clinical approach to vortex keratopathy**

“On slit lamp examination, there are…”
“Grayish/brownish corneal epithelial deposits.”
“Radiating from a point **below** the pupillary axis.”
“The lesions are seen in both eyes.”
“And are consistent with a diagnosis of vortex keratopathy.”

**Look for**
- Lens opacity (amiodarone, Fabry’s disease)
- Bull’s eye maculopathy (chloroquine), crystalline retinopathy (tamoxifen)
- Optic disc (tamoxifen)
I’ll like to
• Ask patient for a history of:
  • Arthritis (indomethacin)
  • Breast CA (tamoxifen)
  • Cardiac diseases (amiodarone)
  • Connective tissue diseases (chloroquine)
  • Dementia, psychiatric diseases (chlorpromazine)

Exam tips:
• One of few differential diagnoses for NORMAL SLIT LAMP EXAM (page 149).
• The causes can be remembered as “ABCD.”

Tell me about the Mucopolysaccharidosis.

“Mucopolysaccharidosis are a group of systemic storage diseases due to deficiency of lysosomal enzymes.”
“There are numerous specific types, each with its own systemic and ocular features.”
“The systemic features include mental retardation, coarse facies, skeletal abnormalities and cardiac diseases.”
“In general, the ocular features include corneal deposits, retinal degeneration and optic atrophy.”

<table>
<thead>
<tr>
<th>Type</th>
<th>Name</th>
<th>Cornea deposition</th>
<th>Retinal degeneration</th>
<th>Optic atrophy</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 H</td>
<td>Hurler</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>All are AR except Hunter’s (SLR)</td>
</tr>
<tr>
<td>1 S</td>
<td>Scheie</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>Hurler and Scheie have the most severe corneal lesions</td>
</tr>
<tr>
<td>2</td>
<td>Hunter</td>
<td>−</td>
<td>++</td>
<td>+++</td>
<td>“Hunter” are males and have clear corneas</td>
</tr>
<tr>
<td>3</td>
<td>Sanfilippo</td>
<td>−</td>
<td>+++</td>
<td>+</td>
<td>4 and 6 no retinal degeneration</td>
</tr>
<tr>
<td>4</td>
<td>Morqio</td>
<td>+</td>
<td>−</td>
<td>+</td>
<td>5 became “S”cheie</td>
</tr>
<tr>
<td>5</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Maroteaux–Lamy</td>
<td>+</td>
<td>−</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

Tell me about Wilson’s Disease.

“Wilson’s disease is a metabolic systemic disease.”
“Characterized by deficiency in alpha 2 globulin (ceruloplasmin).”
“Resulting in deposition of copper throughout the body.”

Wilson’s Disease
1. Systemic features
   • Liver (40%)
   • CNS (40%)
   • No mental retardation
   • Basal ganglia (flapping tremors)
• Spasticity, dysarthria, dysphagia
• Psychiatric problems
• Laboratory results:
  • Normal total serum copper
  • Low serum ceruloplasmin
  • High urine copper

2. Ocular features
   • Kayser Fleisher ring (KF ring):
     • 90% of all patients: Almost 100% if CNS involved
     • Deposition in Descemet’s membrane
     • Green “sunflower” cataract
     • Accommodation difficulty (deposition in ciliary muscles)

3. Treatment
   • Decrease copper intake
   • Penicillamine (KF ring will resolve with treatment)

Exam tips:
• KF rings in one of few differential diagnoses for NORMAL SLIT LAMP EXAM (page 149).
SCLERITIS

Q Opening Question: What is Scleritis?

“Scleritis is an inflammatory disease of the sclera.”
“It can be classified into....”

Scleritis
1. Classification
   • Anterior scleritis (Watson and Hayreh)
     • Non-necrotizing (40%):
       • Diffuse (benign disease)
       • Nodular (visual loss in 25%)
     • Necrotizing (40%):
       • With inflammation (visual loss in 75%: Mortality in 25%):
         • Veno-occlusive
         • Granulomatous
         • SINS
       • Without inflammation (scleromalacia perforans (benign))
     • Posterior scleritis (20%)
2. Systemic associations (50%)
   • Noninfective:
     • Rheumatoid arthritis (RA) (40%)
     • Systemic lupus erythematosus, Wegener’s granulomatous, polyarteritis nodosa, relapsing polychondritis
   • Infective:
     • Surgically induced necrotizing scleritis (SINS)
     • Infective:
       • Herpes zoster
       • TB, syphilis
3. Investigations
   • CBC, ESR
   • VDRL, FTA
   • Collagen disease markers
   • CXR
4. Treatment
   • Treat associated systemic diseases
   • Treat associated ocular complications (glaucoma, cataract)
   • Treatment of scleritis depends on type and severity:
     • Anterior scleritis, non-necrotizing (NSAIDs)
     • Posterior scleritis (oral systemic steroids)
     • Anterior scleritis, necrotizing with inflammation (IV steroids and immunosuppressive agents)

Q What are the Clinical Features of Posterior Scleritis?

“Posterior scleritis is an inflammatory disease of the sclera posterior to the equator.”
“It represents about 20% of all scleritis....”

Posterior Scleritis
1. 20% of all scleritis
2. 20% associated with systemic diseases
3. 80% associated with concomitant anterior scleritis
4. Visual prognosis is poor (80% develop visual loss)
5. Clinical presentation vary
   • 80% present as either disc swelling or exudative RD (important differential diagnosis of VKH)
   • Other presentations:
     • Subretinal mass (more common in females)
     • Ring choroidal detachment (more common in males)
     • Vitritis
     • Macular edema, subretinal exudation, choroidal folds

Section 3: Corneal and External Eye Diseases
Exam tips:
- 20:80 rule.

Clinical approach to scleritis

“There is a yellowish necrotic nodule seen in the superior sclera.”
“There is associated inflammation of the surrounding sclera and injection of scleral vessels.”

Or

“There is marked thinning of the superior sclera with little inflammation seen.”

Look for
- Corneal peripheral thinning (important sign for RA, systemic lupus, Wegener’s granulomatosis, Polyarteritis nodosa)
- AC activity and keratic precipitates
- Previous cataract or pterygium surgery (SINS)
- Bilateral disease (RA, systemic lupus, Wegener’s granulomatosis, Polyarteritis nodosa)
- Lid scarring (herpes zoster)
- Systemic features (RA, systemic lupus, Wegener’s granulomatosis, Polyarteritis nodosa)

I’ll like to
- Check IOP (glaucoma in scleritis)
- Check fundus for optic disc swelling, choroidal folds, RD
- Examine patient systemically (RA, systemic lupus, Wegener’s granulomatosis, Polyarteritis nodosa)

Exam tips:
- Be very careful when you see NORMAL SLIT LAMP EXAM (see page 149). Look at the sclera!
- Clue: Patients may have systemic features such as rheumatoid arthritis (RA) or appear Cushingoid from prolonged steroid therapy!
Notes

Differential diagnoses for a NORMAL SLIT LAMP EXAM

1. Cornea:
   - Keratoconus
   - Vortex keratopathy
   - Microcystic epithelial corneal dystrophy
   - Kayser–Fleischer ring
   - Fuch's endothelial dystrophy

2. Iris:
   - Rubeosis
   - Atrophy
   - Peripheral anterior synechiae

3. Lens:
   - Phacodonesis
   - Glankomflecken

4. Sclera:
   - Scleritis
**Topic 13**

**Corneal Grafts**

**Opening Question No. 1:** Tell me about Corneal Grafts.

“Corneal graft is a surgical procedure in which diseased host cornea is replaced by healthy donor cornea.”

“Broadly, corneal grafts can be either partial thickness/lamellar or full thickness/penetrating.”

“The indications for full thickness corneal graft are....”

“Prior to the operation, the patient must be evaluated for....”

**Exam tips:**
- This is a gift question! You should be able to talk for at least a few minutes without any interruption.

**Opening Question No. 2:** What are the Indications for Penetrating Keratoplasty (PKP)?

“The indications for corneal grafts can be....”

**Indications for PKP**

1. **Optical**
   - Bullous keratopathy (pseudophakic and aphakic)
   - Keratoconus
   - Corneal dystrophy
   - Corneal inflammatory diseases — interstitial keratitis, HSV
   - Corneal traumatic scars
   - Failed grafts

2. **Tectonic**
   - Corneal perforation
   - Peripheral corneal thinning

3. **Therapeutic**
   - Infective keratitis

**What are the Preoperative Factors and how to You Manage Poor Prognostic Factors Prior to PKP?**

1. Evaluate patient’s ocular condition and manage poor prognostic factors prior to PKP
   - Factors (Big 4 poor prognostic factors)
     - Ocular inflammation
     - Glaucoma
     - Corneal vascularization
     - Ocular surface abnormalities:
       - Associated lid abnormality (entropion, ectropion)
       - Tear film dysfunction and dry eyes
   - Other factors to consider:
     - Corneal hypesthesia
     - Cornea irregularity
   - Pre-existing cataract (consider triple procedures)
   - Structural changes of AC (peripheral anterior synchiae, rubeosis)

**Topical antibiotics/steroids/cyclosporin A if necessary**

2. **Assess visual potential**
   - Retinal and macular conditions (e.g. cystoid macular edema)
   - Amblyopia
   - Optic atrophy
Exam tips:
- Remember the BIG 4 poor prognostic factors well.

Q Opening Question No. 3: How do You Perform a PKP?

Steps in PKP

1. Preoperative preparation
   - GA
   - Maumenee speculum
   - Superior and inferior rectus bridle suture with 4/0 silk:
     - Flieringa ring if necessary (indications: Post vitrectomy, aphakia, trauma, children)
     - Overlay suture if necessary (7/0 silk at limbus)
   - Check recipient bed size with Weck trephine (usually 7.5 mm)

2. Donor button
   - Check corneoscleral disc
   - Harvest donor cornea button with Weck trephine on Troutman punch:
     - Approach from posterior endothelial side
     - Use trephine size 0.25–0.5 mm larger than recipient bed
   - Keep button moist with viscoelastic

3. Recipient bed
   - 3-point fixation (two from bridle suture, one with forceps)
   - Weck trephine imprint to check size and centration
   - Other types of trephine:
     - Baron Hessberg trephine and Hannah trephine (suction mechanism)

4. Fixation of graft
   - Set trephine to 0.4 mm depth
   - Enter into AC with blade
   - Complete incision with corneal scissors

   - Fill AC with viscoelastic
   - Place donor button on recipient bed
   - Four cardinal sutures with 10/0 nylon (at 12 o’clock first, followed by 6, 3 and then 9)
   - 16 interrupted sutures
     - Advantages of interrupted sutures:
       - Faster
       - Better for inflamed eyes and eyes with vascularization

   - Other suture techniques
     - Continuous suture:
       - Faster
       - Better astigmatism control
     - Not for cases where selective suture removal may be needed (e.g. infections)
   - Combined continuous and interrupted sutures

5. End of operation
   - Check watertightness and astigmatism with keratometer
   - Subconjunctival steroids/antibiotics

Notes
- “How do you check the corneoscleral disc?”
  - Container (name, date of harvest, etc.)
  - Media (clarity and color)
  - Corneal button (clarity, thickness, irregularity, surface damage)
- “Why is the donor button made larger than the recipient bed?”
  - Because donor button is punched from posterior endothelial surface
  - Tighter wound seal for graft
  - Increases convexity of button (less peripheral anterior synechiae postop)
  - More endothelial cells with larger button
How is the Donor Corneal Button Stored?

“Storage media can be divided into....”

**Storage Media**

1. **Short term (days)**
   - Moist chamber:
     - Humidity 100%
     - Temp 4°C
     - Storage duration: 48 hours
   - McCarey-Kaufman medium:
     - Standard tissue culture medium (TC199, 5% dextran, antibiotics)
     - Temp 4°C
     - Storage duration: 2–4 days

2. **Intermediate term (weeks)**
   - Dexsol/Opisol/Ksol/Procell:
     - Standard tissue culture medium (TC 199) plus chondroitin sulphate, HCO3 buffer, amino acid, gentamicin
     - Temp 4°C
     - Storage duration: 1–2 weeks
   - Organ culture:
     - Advantages: Decreased rejection rate? (Culture kills antigen-presenting cells)
     - Disadvantages: Increased infection rate?
     - Temp 37°C
     - Storage duration: 4 weeks

3. **Long term (months)**
   - Cryopreservation:
     - Liquid nitrogen
     - Temp: —196°C
     - Storage duration: 1 year
     - Disadvantages: Expensive and unpredictable results; usually not suitable for optical grafts

What are the Contraindications for Donation of Corneas?

“The contraindications included patients with....”

**Contraindications for Cornea Donation**

1. **Systemic diseases**
   - Death from unknown cause
   - CNS diseases of unknown cause
   - Creutzfeld-Jakob disease, CMV encephalitis, slow virus diseases
   - Infections:
     - Congenital rubella, rabies, hepatitis, AIDS, Syphilis
     - Septicemia
     - Malignancies
     - Leukemias, lymphomas, disseminated cancer

2. **Ocular diseases**
   - Intraocular surgery
   - History of glaucoma and iritis
   - Intraocular tumors

3. **Age**
   - < 1 year old
     - Corneas are difficult to handle
     - Small diameter; friable
   - Very steep cornea (average K = 50D)
   - > 65 years
     - Low endothelial cell count

4. **Duration of death > 6 hours**

5. **Severe hemodilution**: Affects accuracy of serological testing

What are the Complications of Corneal Grafts?

“The complications can be divided into complications specific to corneal grafts and general complications of intraocular surgery.”

“They can occur in the early or late postoperative period....”

**Complication of Corneal Grafts**

1. **Early postoperative:**
   - Glaucoma or hypotony
   - Persistent epithelial defect
   - Endophthalmitis
   - Wound leak
   - Recurrence of primary disease

2. **Late postoperative:**
   - Rejection
   - Infective keratitis
   - Recurrence of disease
   - Astigmatism
   - Persistent iritis
   - Late endothelial failure
3. Other complications of intraocular surgery:
   - Cataract
   - RD
   - Expulsive hemorrhage
   - Retrocorneal membrane
   - CME

**Q** What are the Causes of Graft Failure?

“Graft failure can be divided into early failure and late failure.”

**Graft Failure**

1. Early failure (< 72 hours):
   - Primary donor cornea failure
   - Unrecognized ocular disease
   - Low endothelial cell count
   - Storage problems
   - Surgical and postoperative trauma:
     - Handing
     - Trephination
     - Intraoperative damage
   - Recurrence of disease process (e.g. infective keratitis)

   - Others:
     - Glaucoma
     - Infective keratitis

2. Late failure (> 72 hours):
   - Rejection (30% of late graft failures)
   - Glaucoma
   - Persistent epithelial defect
   - Infective keratitis
   - Recurrence of disease process
   - Late endothelial failure

**Exam tips:**
- Do not confuse graft failure with graft rejection (which is one of the causes of graft failure and may or may not lead to failure).

**Q** What are the Factors Which Affect Graft Survival?

“The factors which affect graft survival can be divided into….”

**Graft Survival**

1. Factors associated with higher risk of graft rejection:
   - Young age
   - Blood group incompatibility (Collaborative Corneal Transplant Study)
   - Repeat grafts
   - Size of graft (large graft)

   - Position of graft (eccentric graft)
   - Presence of peripheral anterior synechiae
   - Exposed sutures
   - Deep stromal vascularization

2. Other factors associated with graft failure:
   - Preexisting glaucoma and high IOP
   - Ocular surface (lids, tears)
   - Intraocular inflammation (iritis)

**Exam tips:**
- Remember the BIG 4 poor prognostic factors!
Q: How do You Grade Corneal Graft Prognosis According to Disease Categories?

Brightbill's Classification

GRADE I (Excellent)
- Keratoconus
- Lattice and granular dystrophy
- Traumatic leukoma
- Superficial stromal scars

GRADE II (Good)
- Bullous keratopathy
- Fuch's dystrophy
- Macular dystrophy
- Small vascularized scars
- Interstitial keratitis
- Failed Grade I PKP
- Combined PKP and cataract op

GRADE III (Fair)
- Active bacterial keratitis
- Vascularized cornea
- Active HSV keratitis
- Congenital hereditary endothelial dystrophy
- Failed Grade II PKP

GRADE IV (Guarded)
- Active fungal keratitis
- Congenital glaucoma
- Pediatric grafts
- Mild keratoconjunctivitis sicca
- Mild chemical burns
- Corneal blood staining
- Corneal staphylomas
- Failed Grade III PKP

GRADE V (Poor)
- Severe keratoconjunctivitis sicca (Stevens Johnson ocular cicatrical pemphigoid, chemical and thermal burns)

Exam tips:
- Just remember the ones in BOLD!

Q: Tell me about Graft Rejection.

“Graft rejection is a type 4 immune reaction.”
“It can be divided into epithelial, subepithelial, stromal and endothelial rejection.”

Graft Rejection

1. Pathophysiological basis of rejection:
   - Type 4 immunological reaction
   - Divided into: Epithelial, subepithelial, stromal and endothelial rejection
   - Immunological phenomenon

2. Risk factors:
   - Age (young age)
   - Repeat grafts
   - Size of graft (large grafts)
   - Position of graft (eccentric graft)
   - Peripheral anterior synechiae
   - Exposed sutures
   - Deep stromal vascularization

3. Clinical features:
   - Two weeks onwards (if less than two weeks, consider other diagnosis)
   - Epithelial rejection:
     - Epithelial rejection line (advancing lymphocytes, replaced by epithelial cells from recipient)
   - Usually low grade, asymptomatic, eye is quiet
   - Subepithelial rejection:
     - Nummular white infiltrates (Krachmer’s spots)
     - Mild AC activity
   - Stromal rejection:
     - Most important of the 4 types
     - Symptoms:
       - Decreased VA
       - Redness
       - Pain
     - Signs:
       - Limbal injection
       - AC activity
       - Keratic precipitates
       - Endothelial rejection line (Khodadoust line)
       - Stromal edema
   - Endothelial rejection:
     - Combination of stromal and endothelial rejection
Clinical approach to corneal grafts

“This patient has a corneal graft…."
“The graft has interrupted sutures…."

Look for
- Type of graft (important in modern context)
  - Anterior lamellar graft
    - Interface usually visible (may have fine debris)
  - Endothelial graft:
    - Posterior lamella (look for the edge)
    - Venting incisions (aid egress of fluid from graft-host interface)
    - Temporal scleral tunnel incision
    - PIs (prevent pupil block during air tamponade)
- Age of graft: Interface scarring, sutures
- Pseudophakic/aphakic (pseudophakic or aphakic bullous keratopathy)
- Rejection:
  - Hazy graft/local edema
  - Keratic precipitates, AC cells, Khodadoust line
  - Peripheral anterior synechiae
  - Stromal vascularization
- Other eye for corneal dystrophies, Keratoconus, (underlying disease)
- Peripheral anterior synechiae

I’ll like to
- Check IOP
- Assess with Placido disc

Notes
- “What is the evidence that rejection is an immune phenomenon?”
- Rejection of 2nd graft from same donor begins after shorter interval and progresses more rapidly
- Brief period of latency (2 weeks) before rejection
- Rejection correlates with amount of antigen introduced in graft
- Neonatally thymectomized animals reject grafts with difficulty
- “What are the problems of large grafts?”
  - Increased risk of rejection (nearer vessels)
  - Increase IOP (more peripheral anterior synechiae)
  - Large epithelial defect (limbal stem cell failure)
### Q What is the Role of Cyclosporin A in Corneal Grafts?

1. **Indications (high risk of graft rejection):**
   - Young patient
   - Repeat grafts
   - Large grafts/sclerokeratoplasty
   - Deep stromal vascularization
   - Limbal allografts (chemical injury, SJS)
   - Post-graft rejection

2. **Investigations prior to treatment**
   - Blood tests:
     - CBC
     - Renal function tests and uric acid levels
     - Fasting blood glucose and HB A1C
     - Liver function tests
     - Hepatitis B screen and serology for hepatitis C, herpes zoster, CMV and HIV

3. **Treatment regime:**
   - Cyclosporin A (neoral) 5 mg/kg/day in two divided doses
   - Treatment continued for at least one year
   - Dosage gradually tapered after three months

4. **Monitoring during treatment:**
   - BP, height and weight
   - CBC, renal function, liver function
   - CXR, ECG
   - Serum cyclosporin level
   - Co-management with renal transplant physician

### Q Tell me about Lamellar Keratoplasty.

“Lamellar keratoplasty is a partial thickness corneal graft.”

**Lamellar Keratoplasty**

1. **Indications**
   - Partial thickness corneal diseases:
     - Superficial corneal dystrophies (Reis-Buckler)
     - Superficial corneal scars
     - Recurrent pterygium
     - Corneal thinning (Terrien’s marginal degeneration)
     - Corneal perforation
     - Congenital lesions (limbal dermoid)
     - Superficial tumors
     - Endothelial dystrophies/endothelial failure

2. **Advantages**
   - Anterior lamellar keratoplasty:
     - Minimal donor tissue requirements
     - No intraocular entry
     - Faster wound healing and rehabilitation
     - Lower risk of rejection and less use of topical steroids
   - Endothelial keratoplasty (DSAEK — Descemet's Stripping Automated Endothelial Keratoplasty):
     - Reduced astigmatism
     - Smaller wound — lower risk of wound rupture
     - Replaceable and repeatable
     - Reduced risk of rejection (controversial)

3. **Disadvantages**
   - Interface scarring
   - Technically more difficult
   - Not suitable when residual lamella (Descemet's/endothelium in anterior lamellar keratoplasty, anterior stroma in endothelial keratoplasty) is not clear/intact

4. **Complications**
   - Anterior lamellar keratoplasty:
     - Intraoperative perforation
     - Astigmatism
     - Double anterior chamber
     - Interface haze/scarring
   - Endothelial keratoplasty:
     - Donor dislocation
     - Primary endothelial failure
     - Glaucoma
TOPIC 14

BASICS IN CONTACT LENS

Opening Question: What are the Indications for Contact Lens in Ophthalmology?

“The indications can be divided into…”

Indications for Contact Lens
1. Refractive (most common)
2. Therapeutic (see below)
3. Cosmetic:
   • Corneal scar
4. Diagnostic and surgical (goniolens, fundus contact lens)

What are the Therapeutic Indications for Contact Lens?

Therapeutic Indications for Contact Lens
1. Optical
   • Unicocular aphakia
   • Irregular astigmatism — keratoconus
2. Pain relief
   • Bullous keratopathy
   • Corneal abrasions
   • Post-photorefractive keratectomy
3. Promote corneal healing
   • Recurrent corneal erosion
   • Persistent epithelial defect
4. Protect cornea
   • Exposure keratopathy
   • Entropion, trichiasis
   • Post-ptosis operation or “Post-op ptosis”
5. Descemetocoele
6. Pharmaceutical delivery device

Exam tips:
• One “O” and five “P”s!

What are the Materials Used for Contact Lens?

“The ideal material for contact lens should be…”
“Currently, (the) materials include…”

Ideal Material
1. Optically clear
2. High oxygen transmission
   • Water soluble

...
3. Comfortable
   • Soft
   • Surface wettability
4. Low complication rate
5. Durable
   • High tensile strength
   • Resistant to deformation, tear
6. Ease of sterilization

Current Contact Lens Material
1. Hard — PMMA (polymethylmethacrylate)
2. Soft — hydrogel (HEMA)
   • High water content — extended wear soft contact lens (EWSCL)
   • Low water content — daily wear soft contact lens (DWSCL)
   • Silicone hydrogels — high gas permeability, for extended wear
3. Semi-flexible/rigid gas permeable (RGP)
   • CAB (cellulose acetate butyrate)
   • Silicone
   • Polycon (90% PMMA and 10% silicone)

**Tell me about Contact Lens. What are the Advantages and Disadvantages?**

“Soft contact lens can be broadly divided into extended wear (EWSCL) or daily wear (DWSCL).”
“They are made of hydrogel, with varying water contents....”

**Soft Contact Lens**
1. Advantages of soft CL:
   • Comfortable
   • Greater stability
   • Ease of fitting
   • Ease of adaptation
   • Rarely get overwear syndrome
   • Lack of spectacle blur
2. Disadvantages:
   • Poorer VA in eyes with astigmatism
   • Higher risk of complications
   • Durability low

3. Indications for DWSCL:
   • First time wearer
   • Part time wearer
   • Failed extended wear
4. Indications for EWSCL:
   • Infants, children and elderly
   • Lack of manual dexterity
   • Therapeutic indications

**What are the Pathophysiological Changes to the Eye with Contact Lens Wear?**

“The pathophysiological changes included....”

**Pathophysiological Changes to the Eye**
1. Desiccation
2. Microtrauma
3. Hypoxia
4. Hypersensitivity/toxicity
5. Endothelial blebbing (transient)

**What are the Complications of Contact Lens?**

“Contact lens complication can be divided into blinding and nonblinding complication.”

**Complications of Contact Lens Wear**

1. Blinding
   • Infective keratitis
   • Corneal scarring
   • Corneal warping (rarely)
   • Related to microtrauma:
     • Punctate epithelial erosions
     • Corneal abrasion
     • Superior limbic keratoconjunctivitis
2. Nonblinding (Note: Related to the four pathophysiological changes!)
   • Related to desiccation
   • Dry eye syndrome
   • Related to hypoxia:
     • Corneal edema
     • Epithelial microcysts, acute overwear syndrome (rupture of cysts)
     • Corneal vascularization

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• Related to hypersensitivity/toxicity:
  • Giant papillary conjunctivitis
  • Allergic conjunctivitis (disinfectant, preservative — thiomersal)
  • Sterile infiltrates

3. Contact lens changes
• Distortion, breakage
• Deposits:
  • Minerals — iron, calcium
  • Organic — mucin, lipid, protein
  • Microorganisms — bacteria, fungi

Q Tell me about Giant Papillary Conjunctivitis.

“GPC is one of the common contact lens complication….”
“Secondary to hypersensitivity.”
“GPC presents in different stages….”

GPC
1. Stages
• Stage 1: Preclinical GPC (symptoms only)
• Stage 2: Macropapillae (0.3 mm–1 mm)
• Stage 3: Giant papillae (> 1 mm)
• Stage 4: Subconjunctival scarring

2. Zones
• Zone I: Forniceal
• Zone II: Tarsal
• Zone II: Lid margin

3. Etiology
• Contact lens wear:
  • 30% of patients with EWSCL
  • 15% of patients with DWSCL
  • 1–5% of patients with RGP
• Hypersensitivity (asthma, hay fever)
• Trauma (foreign body and prosthesis)

4. Management
• Stage 1 and 2:
  • Lens hygiene
  • Decrease wearing time
  • Reevaluate fit and material/change to RGP if needed
  • Topical antihistamines and mast cell stabilizers
  • Topic steroids if necessary
• Stage 3 and 4:
  • Consider discontinuation of contact lens wear

Q How do You Fit Contact Lens?

Contact Lens Fitting
1. History
• Visual requirements, ocular diseases

2. Fitting procedure for soft contact lens
• Base curve — inversely proportional to the keratometry (K) reading:
  • Take mean K + 1 (aim for flatter contact lens)
  • Choose from three standard curves available (8.1, 8.4, 8.7 mm)
• Refraction
• Corneal diameter (13, 13.5, 14 mm)
• Ocular examination:
  • Palpebral aperture and tightness
  • SLE
  • Fundus exam
• Select trial lens (base curve/refraction/corneal diameter e.g. 8.4/-4.0D/13.5)
• Assess fit (with fluorescein staining):
  • Tightness (too flat or too steep)
  • Centering
  • Mobility
  • Aim for three-point touch
• Over-refract with contact lens on (e.g. If –1.5D gives VA of 20/20)
  • Prescribe final fit (e.g. 8.4/-5.5D/13.5)

3. Fitting procedure for hard contact lens
• Base curve:
  • Take mean K (do not need to add 1)
  • Choose from different individual curves (7.2 to 8.5)
• Refraction (choose from different powers for each base curve)
• Corneal diameter (8.8, 9.2, 9.6 mm)
Refractive surgery is a procedure to alter the refractive status of the eye. This usually involves procedure on the cornea or the lens. They can be broadly divided into incisional procedures, laser procedures or intraocular surgical procedures.

Correction of Myopia

1. Incisional procedures
   - RK (radial keratotomy)
     - Up to –5D
   - PERK (prospective evaluation of RK) study showed that 40% had hyperopic shift of 1D or more after 10 years
   - Obsolete procedure
   - Disadvantages of RK:
     - Weakened cornea
     - Diurnal variation in refraction
     - Hyperopic shift
   - Epikeratoplasty
     - Remove corneal epithelium and create peripheral annular keratotomy incision
     - Frozen donor corneal lenticule fixed to recipient cornea
     - Current indications (not many left with advances in PRK and LASIK):
       - Childhood aphakia
       - Keratoconus
       - Extremely high myopia
   - Keratomileusis
     - Cornea sliced off with microkeratome
     - Cornea cap then frozen, shaped and reapplied to corneal bed
   - ALK (automated lamellar keratoplasty)
     - Cornea cap sliced off with automated microkeratome
     - Second pass of microkeratome to cut a corneal disc from stromal bed
     - Cornea cap is then reapplied to corneal bed

2. Laser procedures
   - PRK (photorefractive keratectomy)
     - Up to –6D
   - LASIK (laser in-situ keratomileusis)
     - Modification of ALK, using laser for the second pass
     - Up to –15D
     - Variants:
       - Epi-LASIK: “Bladeless LASIK”: Epithelial sheet cleaved off surface (no flap)
       - LASEK: Surface epithelial sheet loosened with alcohol
       - Wavefront optimized ablations: Reduce spherical aberration — reduce night vision problems, glare and halos
       - Wavefront guided ablations: Customized ablation guided by individual wavefront map

3. Intraocular surgery
   - ICSR (intracorneal stromal ring)
     - PMMA half rings are threaded into peripheral mid stroma to effect a flattening of the cornea
     - Up to –6D
   - High myopia procedures (> –12D)
     - Clear lens extraction (with IOL)
     - AC phakic IOL implantation
       - Conventional four-point fixated AC IOL
       - Iris-fixated phakic IOL
       - Suffers from complications of ACIOLs:
         - Glaucoma
         - Iris chafing/uveitis
         - Hyphema
         - Corneal endothelial damage
     - PC phakic IOL implantation
       - Sulcus fixated phakic IOL
       - Silicon injectable IOL (implantable collamer lens)
The Ophthalmology Examinations Review

- Complications:
  - Glaucoma (angle closure, hence need for PI)
  - Iris chaîning/uveitis
  - Hyphema
  - Cataract

- Scleral sling:
  - Up to 18–22D
  - Use donor sclera/synthetic materials to sling around globe

Exam tips:
- Extremely common and important essay or viva topic. Keep up with the latest refractive surgery trends.

What are the Options in the Correction of Hyperopia?

Hyperopia
1. Hexagonal keratotomy
2. Epikeratoplasty
3. ALK
4. PRK and LASIK
5. Radial intrastromal thermokeratoplasty
   - Small coagulation burns applied to cornea stroma with retractable cautery probe

What are the Options in the Correction of Astigmatism?

Astigmatism
1. AK (Astigmatic keratotomy)
   - Preoperatively need to have keratometer readings, corneal topography and pachymetry
   - Procedure:
     - Guarded diamond knife
     - 95% corneal depth cut
     - 45 degrees at the steep axis

2. PARK (Photoastigmatic refractive keratectomy) and LASIK
3. Toric IOL
   - Plate haptic silicon design IOL after lens removal
   - Need precise axis orientation

Tell me about PRK.

“PRK is photorefractive keratectomy and is a form of refractive surgery.”

PRK
1. Procedure
   - 193 nm argon fluoride excimer laser used to ablate cornea
   - Every 10 micron = −1D of myopia
   - Three types of ablation:
     - Wide area ablation
     - Scanning slit
     - “Flying spot”

2. Indications and limitations
   - PRK works well for low and moderate myopia and astigmatism
   - For myopia < −6D
   - 80–90% see 20/40 or better
   - 70–80% predictability
   - 1% significant corneal haze
   - 1–5% loss of BCVA
   - High myopia > −6D
     - 50–75% see 20/40 or better
     - 30–70% predictability
     - 5–15% corneal haze
     - Up to 20% loss of BCVA
     - More regression
     - Higher retreatment rate

3. Advantages and disadvantages of PRK
   (see page 165)
What is LASIK?

“LASIK stands for Laser In-situ Keratomileusis and is a form of refractive surgery.”

LASIK

1. Procedure:
   - Microkeratome creates corneal flap that is hinged, either nasally or superiorly
   - Flap is reflected
   - Excimer laser ablates stroma of cornea for refractive correction
   - Flap is replaced without sutures
   - Femtosecond laser
     - Newer technique for creating flaps using multiple extremely short (femtosecond) pulses of IR light
     - Pattern of pulses programmable
     - Theoretical advantages:
       - Lower risk of flap complications
       - Fewer higher order aberrations induced
     - Possible disadvantages
       - Irregularity/haze at interface
       - Cost
       - Longer operating time

2. Indications and limitations:
   • Maximum refractive errors that can be treated are dependent on central corneal thickness
   • Contraindications:
     - Thin corneas and ectatic disorders (keratoconus) — absolute contraindication
     - Wound healing problems (e.g. connective tissue disease, diabetes)
     - Corneal infections (HSV)
     - Pregnancy (unstable refraction)
     - Glaucoma (relative contraindication — high pressure applied during procedure)
     - Dry eye and ocular surface problems
   • Current limits:
     - Myopia up to –15D
     - Hyperopia up to +5D
     - Astigmatism up to 4D
     - Compound myopic and hyperopic astigmatism

3. Advantages of LASIK (five distinct advantages):
   • Better predictability
   • More stability
   • Minimal pain
   • Rapid visual rehabilitation (< 24 hrs)
   • Low risk of corneal haze/scarring and therefore, less steroids needed

4. Disadvantages:
   • Expensive and complex microkeratome required, in addition to an excimer laser
   • More technical and surgical expertise required with steep learning curve
   • Risk of visually threatening complications
   • Risk of flap complications (see below) and reduced residual stromal thickness because of need for tissue for flap

5. Complications:
   • Flap complications:
     - Free flaps/incomplete flaps/button hole flaps
     - Flap striae/dislodged flaps
     - Flap melts
     - Flap striae
   • Interface complications:
     - Epithelial ingrowth
     - Interface debris
     - Interface haze
     - Diffuse lamellar keratitis (“Sands of Sahara”)
   • Induced irregular astigmatism
   • Decentration of ablation zone
   • Night vision problems (hence aspheric corrections)
   • Bacterial keratitis
   • Progressive ectasia of cornea

---

PRK

<table>
<thead>
<tr>
<th>Predictability/Accuracy</th>
<th>Up to –6D</th>
<th>Up to –15D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stability</td>
<td>Up to –6D</td>
<td>Up to –15D</td>
</tr>
<tr>
<td>Pain and rehabilitation</td>
<td>Pain from epithelial defect (1–2 days)</td>
<td>Minimal pain</td>
</tr>
<tr>
<td></td>
<td>Prolonged visual rehabilitation (up to 1 week)</td>
<td>Rapid visual rehabilitation (&lt; 24 hrs)</td>
</tr>
</tbody>
</table>

(Continued)
**PRK LASIK**

<table>
<thead>
<tr>
<th>Complication</th>
<th>PRK</th>
<th>LASIK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corneal haze</td>
<td>Up to 10% (destruction of Bowman's layer)</td>
<td>Minimal haze</td>
</tr>
<tr>
<td></td>
<td>• Poor contrast sensitivity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Halos</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Glare</td>
<td></td>
</tr>
<tr>
<td>Complications</td>
<td>Rare</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Irregular astigmatism</td>
<td>1%</td>
<td>3–10%</td>
</tr>
<tr>
<td>Training and equipment</td>
<td>Short training period</td>
<td>Steep learning curve</td>
</tr>
<tr>
<td></td>
<td>Less expensive equipment</td>
<td>More expensive equipment</td>
</tr>
<tr>
<td>Retreatment</td>
<td>Easier</td>
<td>More difficult</td>
</tr>
</tbody>
</table>

**Q What is Corneal Astigmatism?**

“An optical aberration resulting from variation in the refractive power of the cornea due to an asymmetry in its curvature.”

**Classification**

1. **Regular**
   - Steepest and flattest meridian are 90° from each other
   - Subdivided into “with the rule” and “against the rule”
   - Blurred retinal images can be improved with an appropriate cylindrical correction

2. **Oblique**
   - Steepest and flattest meridians at 90° to each other but are not within 30° of 90° or 180°

3. **Irregular**
   - Amount of astigmatism changes along a given meridian and varies from meridian to meridian
   - Secondary to irregular corneal surface

**Further Classification**

1. **Simple myopic astigmatism**
   - Emmetropic in one meridian and myopic in other

2. **Compound myopic astigmatism**
   - Both steepest and flattest meridians focused in front of retina

3. **Simple hyperopic astigmatism**

4. **Compound hyperopic astigmatism**

5. **Mixed astigmatism**
   - One meridian focused in front of retina, one behind

**Causes**

1. **Idiopathic**

2. **Secondary to ocular diseases**
   - Developmental — keratoconus
   - Degeneration — pellucid marginal degeneration, Terrien’s degeneration
   - Infection — scar formation
   - Inflammation — peripheral ulcerative keratitis (RA, Mooren’s ulcer)

3. **Iatrogenic**
   - Large incision cataract surgery
   - Penetrating keratoplasty

**Assessment of Astigmatism**

1. **Refraction**

2. **Keratometry**

3. **Corneal topography**
   - Placido disc
   - Computerized videokeratometry
   - Elevation based systems
   - Orbscan:
     - One of the commonest systems used
     - Combination of Placido and elevation based systems
     - Generates four maps:
       - Anterior float (anterior elevation)
       - Posterior float (posterior elevation)
       - Keratometry
       - Pachymetry
• Indications:
  - Assessment of regular and irregular astigmatism
  - Diagnosis of “forme fruste” keratoconus (important in pre-keratorefractive surgery assessment)

• Signs:
  - Inferior-superior asymmetry
  - Inferior steepening
  - Elevated anterior and posterior float
  - Inferior thinning
  - Inter-eye asymmetry

What are the Options in the Management of Corneal Astigmatism?

1. Glasses
2. Contact lens
3. Photorefractive keratectomy
4. Surgery — cuts in steep incision
   • Transverse and arcuate keratotomy

   - Semiradial incision
   - Trapezoidal keratotomy
### TOPIC 16

**MISCELLANEOUS CORNEAL PROCEDURES**

**Opening Question: When and How do You Perform a Corneal Biopsy?**

1. **Indications:**
   - Infective keratitis (culture negative, not responding to treatment)
   - Amoebic keratitis
   - Carcinoma intraepithelial neoplasia
   - Debride slough
   - Avoid visual axis
   - Choose between lesion and good cornea
   - Use a dermatological trephine with 2, 3 or 4 mm diameter to mark tissue
   - Lamellar dissection of tissue with blade
   - Divide tissue for histology and culture

2. **Procedure:**
   - Stop antibiotic for 24–48 hours
   - Topical anesthesia

**When and How do You Perform Corneal Gluing?**

1. **Composition:**
   - Corneal glue made of isobutyl cyanoacrylate (histoacryl)
   - Debride slough and necrotic tissue
   - Dry cornea

2. **Indications:**
   - Small perforation < 1 mm in size
   - Apply glue onto cellophane plastic disc
   - Apply glue and cellophane disc on perforation — leave to dry
   - Apply bandage contact lens

3. **Procedure:**
   - Topical anesthesia

**When do You Perform a Conjunctival Flap?**

1. **Indications:**
   - POOR visual potential
   - Chronic epithelial/stromal ulcer after resolution of active infective disease
   - Neurotrophic ulcer
   - Chemical injury
   - Bullous keratopathy
   - Descemetocoele

2. **Problems with conjunctival flap:**
   - Temporary treatment
   - No view of cornea
   - Low drug penetration
   - Postoperative complication (button hole, epithelial cyst, retraction of flap, bleeding, ptosis)