Chapter

1

Conjunctiva, Cornea and Sclera

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Clinical Cases

- Limbal Dermoid
- Ocular Surface Squamous Neoplasia (OSSN)
- Corneal Ulcer
- Peripheral Ulcerative Keratitis (PUK)
- Keratoconus
- Corneal Dystrophy
- Fuch's Endothelial Dystrophy
- Peters' Anomaly
- Iridocorneal Endothelial Syndrome (ICE)
- Spheroidal Degeneration
- Band-shaped Keratopathy (BSK)
- Bullous Keratopathy
- Graft Failure
- Dry Eye
- Scleritis

Corneal Diagnostics

- Commonly Used Stains and Cultures in Relation to Infectious Keratitis
- Specular Microscopy

LIMBAL DERMOID

History

Age: Dermoids are present at birth but may not be detected until the first or second decade of life.

Gender: Both sexes are equally affected.

Chief complaints

- An enlarging ocular mass
- Cosmetic disfigurement
- Decreased vision

History of present illness

- A painless ocular mass appears to enlarge as the body matures at puberty.
- The mass gives rise to foreign body sensation while blinking.
- Growth of this lesion is generally very slow but in presence of inflammation, it rapidly grows.

- Occasionally, a history of inflammation might be present.
- In limbal dermoid, visual morbidity may result from the encroachment of the lesion into the visual axis, development of astigmatism, amblyopia or formation of a lipid infiltration on the cornea.

Family history: It is not inherited.

Examination

Systemic Examination

- Auricular–pre-auricular appendages, auricular fistulae (in combination with limbal dermoid constituting Goldenhar syndrome) (Fig. 1.1).
- Other abnormalities include hemifacial microsomia, microtia, and vertebral anomalies.

Ocular Examination

BCVA: Variable VA depending on the size and location of the dermoid.

Eyelids: Coloboma of the eyelid is usually present.

Ocular motility: Duane retraction syndrome (DRS) and other ocular motility disorders might be present.

Lacrimal passage: Anomalies may be present.

Eyeball: Microphthalmia and staphyloma may be present.

Cornea: Epibulbar mass, corneal staphyloma and dellen formation may occur. A detailed description of epibulbar mass is to be noted considering the following points:

- ***Location of the mass:*** Frequently, epibulbar dermoids are found at the inferior temporal limbus. Rarely, they may only affect the cornea or the bulbar conjunctiva.
- ***Laterality:*** Involvement is unilateral. More than one dermoid may be present.
- ***Size:*** Size varies from 1 mm to a few mm. It may involve the limbus, the entire cornea or the interior part of the eye.
- ***Shape of the mass:*** Epibulbar dermoids have a round or dome-shape and keratinized surface (Fig. 1.2).

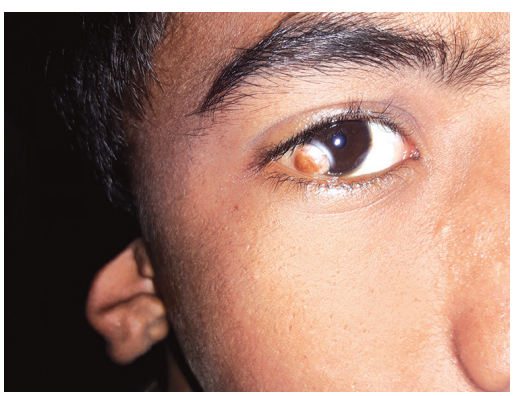

Fig. 1.1: Limbal dermoid in a case of Goldenhar syndrome

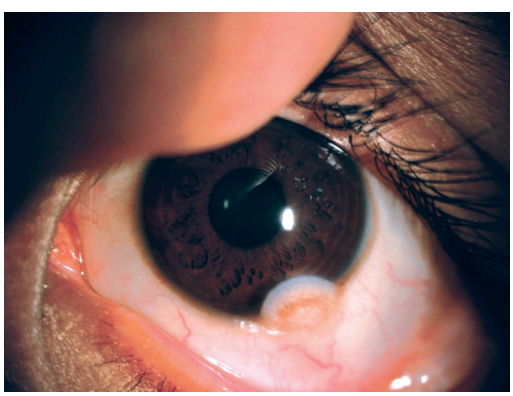

Fig. 1.2: Limbal dermoid

- ***Colour:*** Dermoid cyst is a soft, yellowish and solid lesion. Dermoids are whitish, and pale; Dermolipoma is a soft, movable, yellowish, small structure found mostly at the outer and upper part of the bulbar conjunctiva.
- ***Appendages:*** Look for epidermal appendages like skin with hair follicles, cilia, sweat gland, connective tissue, muscle, tooth, fat, lacrimal gland, cartilage and vascular or neurologic tissue.
- ***Nature of the mass:*** It appears fleshy and may have fine superficial vascularization. The lesion may be cystic or solid.

Iris: Iris coloboma, aniridia and lipodermoid may present.

Lens: Lipodermoid may involve lens also.

Fundus: Optic nerve hypoplasia and fundal coloboma may be there.

Provisional diagnosis: It is a case of isolated epibulbar dermoid or Goldenhar syndrome.

Frequently Asked Questions

Q1. What are the features of Goldenhar syndrome?

Ocular features	Systemic features
• Megalocornea • Limbal dermoid • Coloboma of iris and lids • Squint, Duane's syndrome (DRS) • Fundus: Optic nerve hypoplasia, coloboma • Refractive errors	• Wide mouth • Maxillary and mandibular hypoplasia • Preauricular tags and hearing loss • Vertebral defects

Q2. What is dermoid?

Dermoid are benign congenital tumors that contain choristomatous tissue or growth of tissue not normally present at that particular site.

Q3. What is the mechanism of dermoid formation?

There are two possible explanations for dermoid formation:

a. A developmental defect causing metaplastic transformation of the mesoblast between the rim of the optic nerve and surface ectoderm.
b. Sequestration of pluripotent cells during embryonic development of the surrounding ocular structures.

Q4. What are the types of dermoid?

Depending on the nature of the contents:

a. ***Solid dermoid (not cystic):*** A mass with surface epithelium resembling epidermis and dermis containing a few hairs overlying thick bundles of collagen, which make up the bulk of mass.
b. ***Complex choristoma:*** It contains a variety of abnormal tissues like cartilage, lacrimal tissue, smooth muscle, adipose tissue, and neural tissue.
c. ***Dermolipoma (lipodermoid):*** It is composed of abundant adipose tissue with minimum adnexae, usually in the supero-temporal fornix. The deep portion of the lipodermoid is attached to the muscles and fascia.

d. ***Osseous choristoma:*** It is mostly seen in females. This is composed of compact lamellar bone surrounded by dense and collagenous bone. It appears as a small, solid, circumscribed, red-white bony lesion behind the limbus, between the superior and lateral rectus muscles.
e. ***Smooth muscle hamartoma:*** A variant of dermoid which is mainly formed with spindled smooth muscle, fibrous stroma, lobules of adipose tissue. Clinically it has a greyish, cyst-like appearance.

Depending on the location:

a. The most common dermoid is the limbal dermoid. Limbal dermoids are usually superficial lesions but may involve deeper ocular structures.
b. The second type purely involves only the superficial cornea, sparing the limbus, the Descemet's membrane and the endothelium.
c. The third type of dermoid involves the entire anterior segment, replacing the cornea with a dermolipoma that may involve the iris, the ciliary body and the lens.

Q5. How would you do a workup for limbal dermoid?

The diagnosis of a dermoid requires a directed clinical examination. Specific laboratory studies are generally not necessary. Imaging studies may be required for orbital dermoids.

- **MRI of the orbit:** Some dermoids are deeply extended, especially lipodermoid, into orbital fat, muscle and fornices.
- **UBM and AS-OCT:** To know the posterior limit of the dermoid especially involving the cornea, anterior chamber angle, ciliary body, and lens.
- **X-ray spine:** For hemivertebra or scoliosis.
- **Audiometry:** For hearing assessment.

Q6. What is the treatment of epibulbar dermoid?

Treatment of limbal dermoid includes:

a. Removal of irritating cilia.
b. Lubricating eye drops.
c. Excision of the lesion if it causes significant cosmetic disfigurement or interference with vision. Recurrence may happen following excision.

Q7. How do we do surgical excision of limbal dermoid?

Always, the approach for excision should be from the corneal side. A cleavage plane should be created first between the cornea and dermoid. Excision of superficial part of the cornea and sclera along with dermoid tissue (sclero-keratectomy) is performed. An attempt for complete removal is not necessary. A large scleral defect should be covered either with a conjunctival flap, amniotic membrane or donor's sclera. For a deep corneal excision, a lamellar keratoplasty or patch graft is necessary to reinforce the excision site. The excised tissue should be sent for histopathological examination.

OCULAR SURFACE SQUAMOUS NEOPLASIA (OSSN)

History

Age: Older age. The average age of occurrence has been noted to be 60 years, ranging from 20 to 88 years.

Gender: Men are more commonly affected.

Chief complaints:

- Ocular mass lesion with cosmetic disfigurement
- Foreign body sensation, redness or irritation
- Patients may be asymptomatic
- Chronic redness and irritation
- Diminution of vision

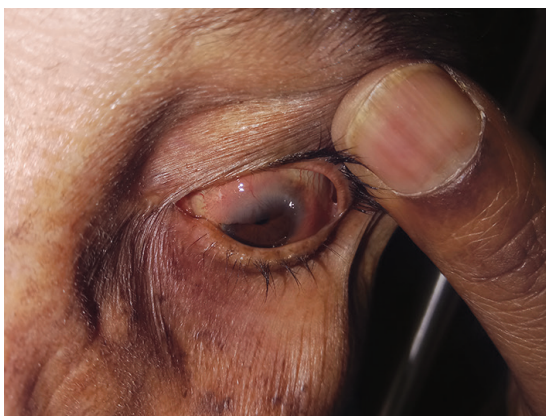

Fig. 1.3: OSSN with extensive corneal involvement

History of present illness: It usually starts in interpalpebral conjunctiva, then grows and straddles the limbus. It may or may not involve the cornea. OSSN may grow within months to years without any symptoms. Diffuse type of OSSN can masquerade as chronic conjunctivitis, whereas nodular variety has a propensity for rapid growth. Sometimes, it may present as chronic redness and irritation. VA is not affected unless extensive corneal involvement happens (Fig. 1.3). Diplopia may occur if extraocular muscle is infiltrated in cases of invasive OSSN. OSSN lesion may develop over pre-existing pterygium and pinguecula. Invasive OSSNs are aggressive in HIV-infected persons.

Family history: Not present.

Personal history: Take a history of exposure to UV rays and HIV. HPV genotypes 6 and 11 have been demonstrated in many papillomas as well as dysplastic and malignant lesions of the cornea and conjunctiva. Take a history of ocular surface injury and smoking.

Drug history: Chemicals like trifluridine, arsenicals and immunosuppressive drugs.

Examination

Systemic Examination

a. **Dermatological:** Xeroderma pigmentosa, pemphigoid, eczematous conditions and basal cell carcinoma.
b. **Systemic metastases:** They are uncommon but may be seen with invasive OSSN. Visceral malignancies like lung, colon, prostate, liver, and NHL are associated with OSSN. Common sites of metastasis are the preauricular node, submandibular node, cervical nodes, parotid, lungs and bones.

Ocular Examination

- Sessile fleshy elevated lesions in the interpalpebral region.
- It may grow over a pre-existing pinguecula.
- The clinical appearance of OSSN is characterised by epithelial thickening and the lesion may extend onto the peripheral cornea.
- Approximately 95% of conjunctival intraepithelial neoplasia (CIN) lesions occur at the limbus or adjacent to the limbus, where the most mitotically active cells reside.

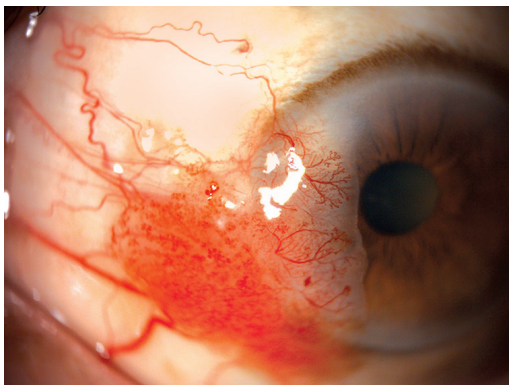

Fig. 1.4: OSSN (strawberry)

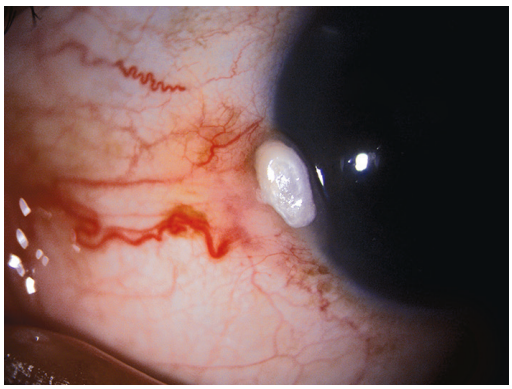

Fig. 1.5: OSSN (leukoplakia)

- Typically, patients present with a gelatinous or plaque-like interpalpebral conjunctival grey or white lesion with or without well-defined borders.
- The lesion may be flat or elevated and may be associated with feeder vessels.
- Broadly, OSSN is classified into three categories: Gelatinous (most common), papilliform or leukoplakic (10%).
- Gelatinous OSSN has a hairpin configuration of the associated conjunctival vessels. This configuration contrasts with the "red-dot" or "strawberry" pattern seen in squamous papillomas (Fig. 1.4). A gelatinous mass may be of three types—nodular, circumscribed (most common) and diffuse variety.
- Papillomatous lesions have cork screw—like surface blood vessels.
- Leukoplakia refers to the whitening and thickening of the tumor's surface as a result of surface hyperkeratinisation (Fig. 1.5).
- Larger lesion fixed to the underlying structures is likely to be malignant.
- There may be pigmentary changes mimicking malignant melanoma.
- The corneal part of OSSN often has a translucent, greyish, frosted appearance and often has a characteristic fimbriated or pseudopodia-like configuration. There may be an adjacent neoplastic pannus.
- Clinically, invasive lesions resemble those of CIN but are more elevated.
- Invasive OSSN involves a greater portion of the limbus and is larger in size than non-invasive lesions.
- Mucoepidermoid OSSN may arise anywhere on the conjunctival surface and may be locally invasive (ocular, orbital and regional lymph node).
- They are immobile, firmly fixed with the underlying structures and have a feeder's vessel.
- Diplopia may be present due to extraocular muscle involvement.

Provisional diagnosis: A ---- year M/F suffering from OSSN in left/right eye.

Frequently Asked Questions

Q1. What is the definition of OSSN?

The term ocular surface squamous neoplasia (OSSN) presently refers to the entire spectrum of dysplastic, pre-invasive and malignant squamous lesions of the conjunctiva and cornea.

Q2. Classify OSSN.

The term ocular surface squamous neoplasia was coined by Lee and Hirst. It has three grades:

a. **Benign dysplasia:** Papilloma, pseudoepitheliomatous hyperplasia, benign hereditary intraepithelial dyskeratosis.
b. **Pre-invasive OSSN:** Conjunctival/corneal carcinoma *in situ*.
c. **Invasive OSSN:** Adenoid squamous carcinoma, mucoepidermoid carcinoma, spindle cell carcinoma.

Q3. What is the incidence of OSSN?

The incidence varies from 0.13 to 1.9/100000. It is predominantly seen in dark-skinned Caucasians, the age of onset being significantly higher in areas closer to the equator.

Q4. What are the predisposing factors for OSSN?

a. UV radiation
b. HPV and HIV infection
c. Chronic exposure keratopathy
d. Ocular surface injury
e. Chemicals like trifluridine and arsenicals
f. Pemphigoid, eczematous conditions
g. Smoking
h. Older age
i. Xeroderma pigmentosa
j. Immunosuppression
k. Gender: Men are more commonly affected

Q5. Name some eye diseases which are related to UV ray irradiation.

a. Cataract
b. Pterygium
c. Pinguecula
d. Corneal degeneration
e. OSSN
f. Climatic droplet keratopathy

Q6. What are the differential diagnoses of OSSN?

a. Pterygium
b. Pinguecula
c. Pyogenic granuloma
d. Papilloma
e. Malignant melanoma
f. Benign nevus

Q7. What are the histological findings of OSSN?

The epithelium is hyperplastic with loss of goblet cells, loss of normal cell polarity, hyperchromatic nucleus, polymorphism and mitotic figures. A chronic inflammatory response is often present in the substantia propria.

Q8. Mention the roles of different imaging modalities in diagnosis of OSSN.

- **Optical coherence tomography (OCT):** The distinctive features of OSSN are hyperreflectivity, thickened epithelium and abrupt transition from normal to abnormal tissue.
- **Impression cytology:** It is a non-invasive method to diagnose and clinically monitor patients with OSSN. However, it is unable to detect the depth of involvement.
- **Confocal microscopy:** This has also been reported to be helpful in guiding treatment since it is able to reveal cellular details. The main disadvantages include the difficulty of use and limited field of view.
- **High-frequency UBM:** It may be helpful in determining the extent of invasion into the eye.

Q9. How will you treat a case of OSSN?

A. **Surgical therapy**

a. Both epithelial dysmaturation and corneal epithelial dysplasia are considered benign lesions and are treated with corneal scraping and wide conjunctival-limbal margin excision.
b. The "no touch" technique is used during excision of OSSN lesions.
c. OSSN lesions involving the limbus should be excised with at least a 3–4 mm uninvolved conjunctival margin because seemingly uninvolved tissue clinically may still contain dysplastic cells. The underlying tenon should be removed simultaneously. Precaution should be taken to avoid damage to the underlying extraocular muscle.
d. Involved corneal epithelium and pannus are then scraped off with a Beaver blade or surgical sponge after instillation of absolute alcohol (called "alcohol epitheliectomy") to the cornea to loosen the cells. Bowman's layer should not be damaged during this process.
e. Cryotherapy is applied to the conjunctival edges after lifting the bulbar conjunctival edge using a double rapid freeze-thaw technique to destroy any remaining dysplastic cells.
f. If the margins test positive or there are any concerns for residual disease, topical chemotherapy may be used after excision.
g. In cases of SCC or immobile OSSN; partial sclerectomy and keratectomy is done followed by a thin lamellar scleral flap placement or lamellar keratoplasty after the removal of the lesion.
h. The area of surgical resection may be left open or closed with an amniotic membrane graft.
i. Enucleation and exenteration may be done if there is an invasion inside eyeball and into the orbit.
j. Radiation may be considered as adjunctive therapy in certain cases that have been recalcitrant to other modalities of treatment.

B. **Medical therapy**

- The use of topical chemotherapeutic agent has the advantage of treating the entire ocular surface, thus avoiding surgical complications such as positive margins, scarring and limbal stem cell deficiency.

- **Indications for topical therapy:** Extensively invasive tumor, recurrent tumor and tumor with an extensive corneal component.
- **Interferon-α-2b (IFNα-2b):** It may be injected into subconjunctival space or may be used topically. The concentration for the topical application is typically 1 million IU/ml. The efficacy rate after topical IFNα-2b ranges from 80% to 100%.
- **Topical mitomycin C (MMC 0.04%):** It may be used for a week, four times a day followed by one week off to be repeated for 2 to 3 more cycles. A temporary punctal plug (both upper and lower) is placed before start of therapy which is removed after completion of topical therapy.
- **5-fluorouracil (5-FU):** This is given in 4 times a day dose (1% 5-FU) for one week followed by four weeks off. Subsequently the same is to be repeated for four cycles more.
- **Anti-VEGFs:** These are efficacious in treating OSSN.

Q10. What is the rationale for cryotherapy in OSSN excision?

- Cryotherapy is a supplemental modality which destroys subclinical and microscopic tumor cells.
- By devitalizing malignant and potentially malignant cells by cryotherapy, the need for potentially radical surgeries like orbital exenteration is avoided or delayed especially in invasive tumors.
- Cryotherapy is a recommended modality in recurrent lesions.

Special notes on cryotherapy

- Cryotherapy is applied on the under the surface of bulbar conjunctiva after lifting it from the scleral bed covering the conjunctival side of the lesion.
- Direct application of cryotherapy probe over the scleral bed is to be avoided.
- The tumor bed is sanitized with cautery application and absolute alcohol.
- Corneal side is best avoided while doing cryotherapy.
- Parameters: Size of ice ball 4–5 mm, double freeze and thaw.
- Complications of cryotherapy: Painful eye, chemosis, cataract, uveitis, localised corneal or scleral thinning and accidental scleral application may cause phthisis bulbi.

Q11. What is the recurrence rate for OSSN after surgical excision?

The recurrence rate is substantially higher in the setting of positive surgical margins. Even if the surgical margins are negative, up to one-third of eyes may experience a recurrence within ten years. A recurrent OSSN may be more invasive and thus needs to be treated with aggressive medical, surgical or combination therapy.

Q12. What are the causes of chronic cicatrizing conjunctivitis?

The causes are

- Trachoma, adenovirus, OSSN, trauma to the conjunctiva, multiple surgeries, and radiation exposure to the conjunctiva.
- TEN, SJS, OCP
- SLE, DLE, Rosacea
- Sarcoidosis, graft versus host disease (GVHD), Sjögren's syndrome
- Inflammatory bowel disease.

CORNEAL ULCER

History

Age: No age is immune.

Gender: No predilection is found.

Chief complaints:
- Ocular pain
- Decreased vision
- Redness, discharge, foreign body sensation and photophobia

History of present illness: A careful history can lead to a proper diagnosis.
- ***Onset:*** Rapidity of progression indicates the virulence of the infecting agent. Generally, rapid onset and progression of ulcer are noted in *Pseudomonas aeruginosa* and *Staphylococcus aureus*. The slow onset and indolent course are associated with fungi, parasites and other bacteria like coagulase-negative Staphylococcus, Nocardia, Moraxella and atypical Mycobacteria.
- ***Pain and photophobia:*** Superficial ulcer causes more pain and photophobia as compared to deep stromal ulcer due to highly innervated superficial corneal layer involvement. Acanthamoeba keratitis causes excruciating pain due to radial neurokeratitis. Sudden relief of pain is an indication of perforation of a corneal ulcer. The general rule is that in bacterial infections, the symptoms are more than the signs and vice versa in fungal infections.
- ***Discharge and redness:*** Watery discharge is noted in viral infection or small ulcer caused by bacteria. Mucopurulent or purulent discharge is associated with bacterial keratitis. Greenish-yellow discharge is noted in Pseudomonas infection. Perilimbal congestion with or without conjunctival congestion is noted depending on the ulcer area and virulence of the organism. Pseudomonas lesions have a rapid melting of the corneal stroma with copious, tenacious, sticky, greenish-yellow discharge.
- ***Diminution of vision:*** Visual acuity depends on the location of ulcer, presence of hypopyon, haemorrhage and uveitis. The involvement of the central cornea obviously will cause profound loss of vision.
- ***A history of injury and the injuring agent:*** The occurrence of fungal infection is noted in injuries with vegetable matter or insect sting cases (Farmers are more prone to fungal infection); Bacillus infection is seen in patients with broomstick injuries; gram-positive infection is common with metal foreign body and so on.
- ***A history of past such similar episodes:*** Typically, this suggests the possibility of viral infections.
- ***History of contact lens use:*** More prone to develop a sterile infiltrate and microbial keratitides like Acanthamoeba and Pseudomonas.
- ***Prior treatment history:*** Obtain a detailed history of the antibiotic used, the frequency of use and the compliance of the patient with therapy. Failure to respond to adequate dose and duration of appropriate antibiotics suggests the possibility of a fungal or parasitic infection.
- ***Use of topical steroids and homemade ayurvedic or similar indigenous preparations:*** Use of these preparations may precipitate the keratitis.

Past ocular surgery: Bullous keratopathy following cataract surgery, kerato-refractive surgery, pterygium excision and any intraocular surgery may predispose to keratitis. Indolent lesions, history of prior corneal surgery, typical morphology, failure to respond to usual antibacterial therapy and slow progress suggest atypical bacterial infection.

History of systemic illness: Moraxella keratitis is usually associated with alcoholics, diabetic individuals and debilitated patients. In AIDS and advanced malignancy cases, keratitis caused by Candida is very common. Other predisposing factors are connective tissue disorders with or without dry eye, debilitating diseases, malnutrition, lagophthalmos, severe anemia, and leprosy. In children, microbial keratitis may occur in conditions like measles, diarrhoea, malnutrition and chronic allergic conjunctivitis.

Examination

Ocular Examination

BCVA: Note vision

Eyeball: Exophthalmos, proptosis is known predisposing factors for keratitis.

Eyelid: One should look for lagophthalmos, lid retraction, trichiasis, lid coloboma, entropion and blepharitis. All are associated with an increased chance of microbial keratitis.

The extent of ocular adnexal inflammation and discharge: Presence of lid swelling, inability to open the eyes, a severe intolerance to light, and nature and type of discharge are to be noted. Compress over the lacrimal sac area and note for discharge coming out via punctum or do a syringing to look for the patency of the nasolacrimal duct. Pneumococcal infection is more common in dacryocystitis.

Conjunctiva: The presence of conjunctival redness and chemosis are indicators of the severity of the infection. Pale chemosis is typical of allergic conjunctivitis. VKC can be associated with a superior corneal epithelial defect, shield ulcer or infective keratitis and phlyctenular keratitis.

Sclera: Sclerokeratitis usually occurs in cases of immunologic disorders and Acanthamoeba keratitis.

Cornea: Ulcer should be described by mentioning the following points:

- ***Location:*** Central ulcers are caused by Staphylococcus, Pseudomonas and Fusarium. In contrast, peripheral ulcers are caused by coagulase-negative Staphylococcus and *Mycobacterium tuberculosis*. The superior quadrant is involved in VKC and an inferior ulcer is noted in exposure keratopathy and Staphylococcal blepharitis.
- ***Size of the ulcer:*** The dimension of the ulcer should be measured in the longest axis and the meridian 90 degrees opposite. The size of the infiltration should be measured separately.
- ***The shape of the ulcer:*** Ring-shaped ulcer is noted in Acanthamoeba and Staphylococcus infection (Fig. 1.6). The oval and punched out ulcer is seen in neurotrophic ulcer. Pneumococcal ulcers are serpiginous with one healing edge trailing the active edge. Dendritic, amoeboid, and geographic shape suggests viral aetiology (H simplex and H zoster infection) (Fig. 1.7). In H simplex keratitis, dendrites are more likely to be single, central and long with thin branches having terminal bulbs. More additional features in herpes zoster keratitis are dual staining with both sodium fluorescein and rose Bengal, associated typical skin

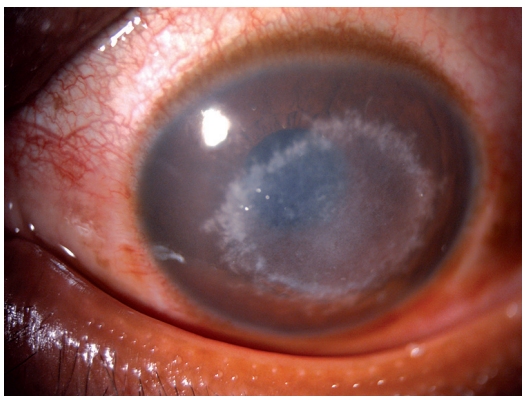

Fig. 1.6: Ring ulcer in acanthamoeba keratitis

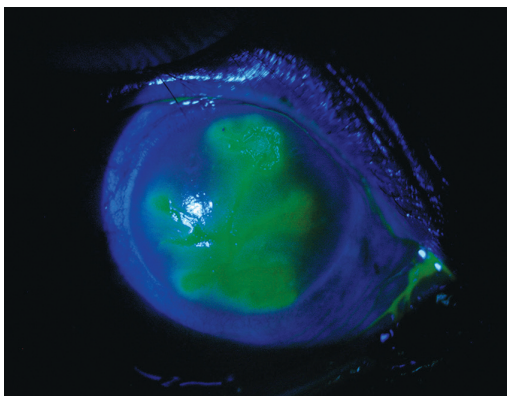

Fig. 1.7: Geographic or dendritic ulcer

lesions and neurological signs. However, some early fungal hyphate lesions can mimic dendrites, as can early Acanthamoeba keratitis. A "cracked windshield" appearance indicates a possible Mycobacterial infection.

- ***Edges of the ulcer:*** Actively progressing ulcers have an indistinct margin with "fimbriated" edges, whereas "rounded well-defined" edge is an indicator of a healing or sterile ulcer. Fungal lesions can have satellite or feathery lesions surrounding the main infiltrate. Acanthamoeba keratitis can show infiltrates along the nerves and this is called radial neurokeratitis. Overhanging margins are seen in Mooren's ulcer.
- ***Infiltrate size, depth, thinning:*** In active bacterial keratitis, the epithelial defect is often larger in size than the area with infiltration. However, in fungal keratitis, the size of the defect can be smaller than the area with infiltration. The depth of the infiltration must be noted in terms of superficial, mid, deep, or total corneal stromal thickness involvement. Severe infiltration with ground glass appearance around the ulcer is seen in Pseudomonas infection. The term "string of pearls" (multiple pinhead -sized infiltrates adjoining the edge of the defect) is classically described in Nocardia infection. A dry-looking infiltrate is more likely to be fungal, although with virulent filamentous fungi, a rapidly progressing "wet" ulcer is also possible.
- ***The base of the ulcer:*** Usually, the base is filled up with exudates and necrotic materials; however, dry base may be seen in fungal infection. The colour of the debris is very important.
- ***The presence of pigment:*** It is a sign of fungal keratitis. Ghost scar around the main ulcer is an indicator of viral aetiology.
- ***Corneal thinning and perforation:*** The presence of corneal thinning or descemetocele formation must be carefully looked for. A Seidel test must be performed to look for aqueous leakage.
- ***Surrounding area of the ulcer:*** Grossly oedematous and hazy in Pseudomonas infection.
- ***Neovascularisation:*** Fine, superficial neovascularisation is mostly seen in contact lens wearers, blepharitis, superior limbic keratoconjunctivitis and vernal conjunctivitis. The corneal pannus is subepithelial fibrovascular tissue in-growth from the limbus onto the cornea. Deep stromal neovascularisation can be seen in eyes with extended use of contact lens, chronic blepharo-conjunctivitis, interstitial keratitis (IK), trachoma, toxic chemical injuries, graft rejection and phlyctenulosis.

Anterior chamber: The presence and extent of AC reaction indicate the severity of the keratitis. The height of the hypopyon is similarly a clue to the activity of the disease. An active or fresh hypopyon in bacterial ulcer is characterized by whitish colour, with a concave upper border and relatively mobile fluid (Fig. 1.8). Haemorrhagic hypopyon is seen in pneumococcal keratitis and herpes zoster viral keratitis. Immobile or fixed hypopyon with a convex upper border is seen in fungal keratitis (Fig. 1.9). There may be an inverse relationship between the size of the ulcer and amount of hypopyon in mycotic keratitis.

Iris and pupil: Examine pupillary border carefully for rubeosis, it indicates chronicity of the disease. Synechiae formation and uveal tissue prolapse may happen if the ulcer perforates.

Corneal sensation: Corneal sensation is decreased in herpetic keratitis (Fig. 1.10) and neuroparalytic keratitis.

Lymph nodes: Preauricular, submandibular and postauricular lymph nodes can also be involved.

IOP: The IOP can be elevated in chronic infection due to anterior uveitis, possible peripheral anterior synechiae and a pupillary block. Noncontact tonometry or digital tonometry should be performed.

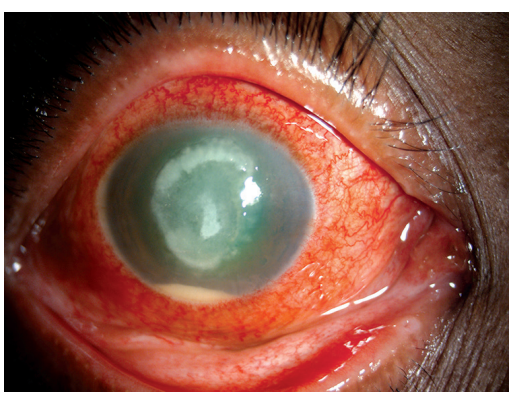

Fig. 1.8: Bacterial keratitis

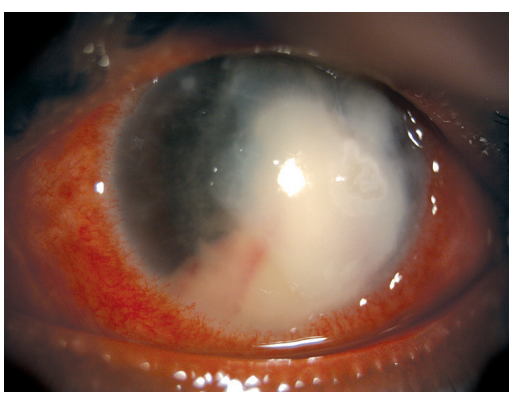

Fig. 1.9: Fungal corneal ulcer

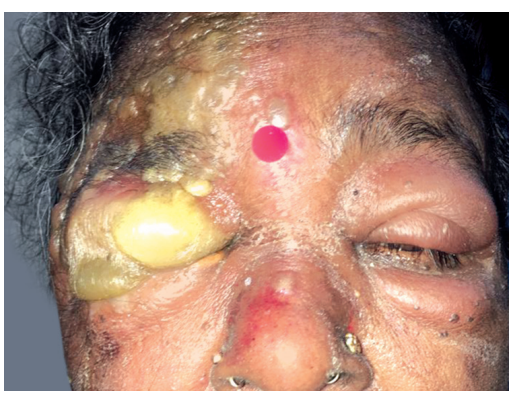

Fig. 1.10: Herpes zoster ophthalmicus

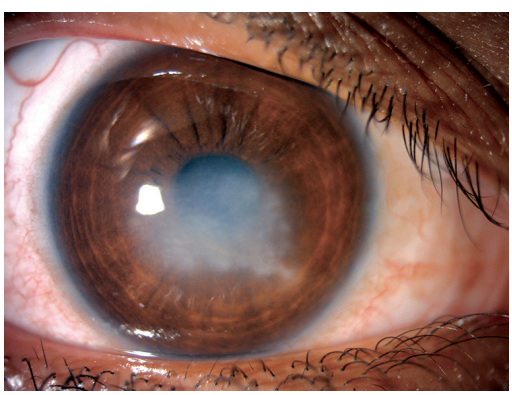

Fig. 1.11: Viral endothelitis or disciform keratitis

Lens: Anterior polar cataract may develop if the ulcer perforates.

Provisional diagnosis: Corneal ulcer involving RE/LE probably of bacterial/viral/fungal/Acanthamoeba/atypical bacterial in origin.

Frequently Asked Questions

Q1. What are the differential diagnoses of a corneal ulcer?

a. **Bacterial corneal ulcer** (*see* Fig. 1.8)
- History of contact lens use.
- Pain, lacrimation, photophobia, blepharospasm, FB sensation (symptoms are more than signs).
- Varying degree of diminution of vision.
- Ciliary congestion.
- Purulent discharge.
- Unifocal lesion.
- Ulcerated area is wet-looking with a sharp margin.
- Surrounding area of the ulcer is cloudy.
- Aggressive course.
- Rapid progression.
- Response to antibacterial drugs.

b. **Fungal** (*see* Fig. 1.9)
- Very often, history of trauma with vegetable matter.
- Foreign body sensation, photophobia, lacrimation, blurring of vision (signs are more than symptoms).
- Satellite lesions and ring infiltrate (satellite lesions mean two discrete lesions separated by uninvolved cornea).
- Pigmented ulcers.
- Ulcer is elevated, dry-looking with greyish-yellow stromal infiltration.
- Relatively, immobile, or fixed hypopyon with convex border. There may be a disproportionate relationship between the size of the ulcer and the amount of hypopyon.
- Immune ring due to deposition of the immune complex around the ulcer.
- Endothelial plaque (may be pigmented).
- Relatively indolent course.

c. **Viral**
- Past history of a similar attack.
- Old scars of herpes zoster.
- Palpable lymph node.
- Lacrimation, foreign body sensation, photophobia, blurring of vision, eyelid oedema.
- Serous discharge.
- Initially, punctate epithelial lesions or subepithelial lesions.
- Superficial ulcer is centrally located with fewer infiltrations around the ulcer.

- Dendrites.
- Corneal sensation is diminished or absent.
- Ciliary congestion and keratouveitis (accompanied by a sharp rise of IOP).
- In typical form, dendritic ulcer develops, visible with Rose Bengal and sodium fluorescein staining.
- Disciform keratitis (*see* Fig. 1.11).
- Slow progression of the ulcer.

d. **Acanthamoeba keratitis** (*see* Fig. 1.6)
- History of contact lens wear and pond bathing.
- Severe pain, watering, photophobia and decreased vision (patient is very much symptomatic).
- Waxing and waning course.
- Indolent nature.
- Epithelial surface is irregular and greyish pseudo-dendrites are seen.
- Peri-neural infiltrations or radial keratoneuritis (swollen and inflamed corneal nerves).
- Ring abscess formation with an indolent course.
- Complication: Scleritis, secondary bacterial keratitis.

e. **Atypical bacterial keratitis**
- Indolent lesion.
- History of prior corneal surgery.
- Failure to respond to usual antibacterial therapy and slow progress.
- Some unusual sites may be involved like around the side port entry and around main port after clear corneal phacoemulsification.

f. **Microsporidiosis**
- ***In immuno-compromised individuals:*** It causes opportunistic disseminated infection, usually presents with an epithelial disease like keratoconjunctivitis. The epithelial disease is characterized by coarse, multifocal, granular, punctate epithelial keratitis with mild follicular or papillary conjunctivitis.
- ***In immuno-competent individuals:*** Usually presents with deep stromal keratitis. There is a history of a recent outbreak of kerato-conjunctivitis. This is believed to be acquired from eye contact with soil and mud-related activities or contact lens use. Stromal keratitis is marked by mid to deep stromal infiltrates mimicking herpetic disciform keratitis with no epithelial or endothelial lesions.

Q2. Define corneal ulcer.

It is the break-in continuity of corneal epithelium with an accumulation of inflammatory cell infiltrates into the adjacent stroma.

Q3. Define keratitis.

Inflammation of the cornea is marked by cellular infiltration, and oedema and is often accompanied by conjunctival reactions like congestion and chemosis. It may be an ulcerative type or non-ulcerative type.

Q4. What do you mean by interstitial keratitis (IK)?

IK is inflammation of corneal stroma without involving the epithelium and endothelium, e.g. syphilis, tuberculosis and leprosy.

Q5. How would you document corneal ulcers and why?

Documentation is very important and should be done daily for all in-house ulcer cases. This helps to assess whether the ulcer is improving or deteriorating on therapy. It is documented as follows:

- **Fluorescein stained area:** Green
- **Infiltrates:** Yellow
- **Surrounding oedema:** Blue
- **Ghost vessels:** Dotted red lines (straight)
- **Superficial vessels over cornea:** Wavy, branching lines in red
- **Deep vessels over cornea:** Straight lines in red

Heavy infiltrates with the fuzzy border associated with dense oedema signifies the progressive stage of ulcer. Reducing infiltrates arranged regularly with a clear outline and reducing oedema indicates a regressive ulcer. The vertical height of hypopyon measured at slit lamp and should be documented along with anterior chamber reactions. Reducing the vertical height of hypopyon along with clearing of AC reaction signifies healing ulcer.

Q6. What is the severity grading of microbial keratitis?

The severity may be classified into two:

a. ***Non-severe:*** Suppuration area less than 6 mm diameter, superficial two-thirds of stroma involved, slow rate of progression and less chance of perforation.
b. ***Severe:*** Suppuration area more than 6 mm diameter, deeper 1/3rd of stroma involved, rapid rate of progression and a high chance of perforation.

Q7. What are the risk factors or predisposing factors for corneal ulcer?

- Trauma
- Chronic dacryocystitis
- Trichiasis
- Blepharitis
- Dry eye
- Exposure keratitis
- Neurotrophic keratopathy
- Contact lens wear
- Use of topical steroid and immuno-suppressive drug intake
- Diabetes mellitus and immuno-deficiency state
- Bullous keratopathy
- Keratomalacia and nutritional deficiency.

Q8. Enumerate the causative organisms of corneal ulcers.

- **Bacterial:** Pseudomonas, *Staphylococcus aureus* and *albus*, *Streptococcus pyogenes*, Pneumococcus, *E. coli*, *B. proteus*, *Neisseria gonorrhoeae*, Moraxella, Haemophilus and *C. diphtheriae*.
- **Fungal:** Aspergillus, Fusarium, *Candida albicans*

- **Viral:** H simplex, herpes zoster, adenovirus
- **Protozoan:** Acanthamoeba keratitis
- **Helminthic:** Onchocercal keratitis
- **Immunologically mediated diseases:** Phlyctenular keratitis, marginal ulcer, Mooren's ulcer, rosacea keratitis.
- **Non-infective:** Neurotrophic keratitis, atheromatous corneal ulcer, exposure keratopathy.

Please note that microbial keratitis may develop in cases mentioned under immunologically mediated disorders and non-infectious causes.

Q9. How will you manage a case of bacterial keratitis?

a. Proper history taking.
b. Slit lamp examination of ulcer with Rose Bengal and sodium fluorescein staining.
c. Identification of microorganism: Scraping of ulcer base and margins.
d. Scrapped materials are used for smear preparation with staining and culture.

Staining

- ***Gram staining:*** Bacteria
- ***KOH preparation and Giemsa staining:*** Fungi
- ***Calcofluor white staining:*** Acanthamoeba

Culture media

- ***Blood agar and glucose broth:*** Aerobic bacteria, facultatively anaerobic bacteria.
- ***Chocolate agar:*** Aerobic bacteria, facultative anaerobic bacteria, Gram-negative bacteria.
- ***Sabouraud's dextrose agar media:*** Fungi, Nocardia.
- ***Thioglycollate broth:*** Aerobic bacteria and anaerobic bacteria.
- ***Non-nutrient agar seeded with E. coli:*** Acanthamoeba.
- ***Brain heart infusion broth plate with antibiotic:*** Fungi, Nocardia.
- ***Cooked meat broth:*** Anaerobic bacteria.
- ***Lowenstein-Jensen media:*** Mycobacterium species.

Specific treatment for bacterial keratitis: Anyone or combination of the following regimen can be used for the treatment of bacterial corneal ulcer.

a. ***Topical broad-spectrum antibiotic:*** Fluoroquinolones (moxifloxacin, gatifloxacin, ciprofloxacin) is started every ½ hourly immediately and switch over to suitable antibiotic according to culture-sensitivity reports.
b. ***Fortified or concentrated antibiotics for better penetration and efficacy:***
   - Cefazoline 5% + tobramycin 1.3%: Initially, eye drops are instilled ½ to 1 hourly. The frequency of antibiotic drops is decreased to 2–3 hourly once healing is ensured.
   - Fortified ceftazidime 5% and fortified vancomycin 5% eye drops are very effective; frequency and dosing as above.
   - Fortified Linezolid 2 mg/ml (0.2%) is currently used for methicillin resistant *Staphylococcus aureus*.

c. Subconjunctival injection of antibiotics, e.g. cefazoline, vancomycin, gentamicin, amikacin, ceftriaxone, ceftazidime as an adjunct to topical therapy for initial 1–2 days.
d. Oral antibiotic in case of a perforated ulcer, scleral involvement, bilateral ulcer, and marginal keratitis.

General measures

a. Oral analgesics and wear dark glasses.
b. Oral (acetazolamide) and topical IOP reducing agents (timolol maleate 0.5 %) to control IOP.
c. Atropine sulphate eye drop to reduce ciliary spasm.
d. Artificial tears promote epithelial healing.

If the above therapy fails, the following measures are taken

- Debridement of necrotic tissue.
- Therapeutic keratoplasty in case of a large-sized corneal perforation.
- Bandage contact lens in case of a small perforation.

(*Special note:* Topical steroid and eye pad are strongly contraindicated in microbial keratitis).

Q10. How do you take a scraping in a case of infectious keratitis?

a. Scraping is done under topical anaesthesia in slit lamp (preferable) or under an operating microscope.
b. Instruments for scraping: Blunt end of number 15 Bard-Parker blade or Kimura platinum spatula.
c. Take scraping both from the ulcer base and from the advancing edge of the ulcer crater.
d. While taking scraping, avoid touching the eyelashes or lid margin with the blade. Conjunctival and lid swabs have limited values.
e. The scrapped material is transferred to glass slides for 10% KOH, Gram stain and special stains like Giemsa, ZN stain (AFBs)
f. Other part of the scrapped material is inoculated into culture media. Commonly used media are blood agar (mostly used), chocolate agar (Moraxella, Neisseria, and Haemophilus), thioglycolate broth (anaerobes), SDA, PDA and non-nutrient agar with *E. coli* overlay (Acanthamoeba), etc.
g. Plates are to be cultured for at least 7 days before declaring as "no growths". Typical fungal colonies develop in 2 weeks.
h. While interpreting the culture report, knowledge about normal flora of the eye and common laboratory contaminants is essential.
i. Isolates are more likely to be significant if the same organism is obtained in repeated samples, the same organism is obtained in more than one culture media and smear results are consistent with the culture report.

Q11. What is IVCM?

IVCM (*In-Vivo* Confocal Microscopy)

- Provides optical section with good resolution and contrast (sensitivity is 90%, specificity is 78%).

- Used for early diagnosis of keratomycosis (Aspergillus-branching at 45 degrees; Fusarium-branching at 90 degrees; Candida-round and budding structure).
- Gives depth of invasion, hence, prognostic value (normally, the diameter of the stromal nerve is 25–30 µm).
- Limitations: The procedure requires a skilled operator, it is costly and findings are user-dependent.

Q12. What are the indications of monotherapy in bacterial keratitis?

Monotherapy is indicated in

- ***Ulcer size:*** Less than 3 mm diameter.
- ***Ulcer depth:*** Less than 50% of stroma involved.
- ***Ulcer location:*** Mid peripheral or peripheral ulcer.

Hence, combination/fortified therapy is indicated in

- Central ulcer involving more than half of corneal stroma.
- Ulcer size more than 3 mm.
- Worsening disease on monotherapy.

Q13. What are the indications of subconjunctival injection of antibiotics in bacterial keratitis?

The indications are

- When frequent topical applications are not possible.
- When fortified preparations are not available.
- To initiate treatment when topical administration is delayed.

Cefazoline (100 mg), ceftazidime (100 mg), vancomycin (25 mg), tobramycin (20 mg), amikacin (20 mg), ceftriaxone (100 mg).

If two drugs are to be injected in subconjunctival space; they should be injected at separate sites with two separate syringes.

Q14. Describe the management of fungal keratitis.

a. Proper history taking.
b. Slit lamp examination of ulcer with sodium fluorescein staining.
c. Take corneal scraping and the materials are used for staining and culture sensitivity.
   Staining: Commonly used stains are 10% potassium hydroxide (KOH), Indian ink, Gram stain, Giemsa, periodic acid-schiff, and methenamine silver.
   Culture media: Sabouraud's dextrose agar, potato dextrose agar.
d. Polymerase chain reaction (PCR) to look for fungal proteins especially in cases where microbiology is inconclusive.
e. Specific treatment
   - **Polyenes:** It forms a complex with ergosterol that destabilizes the fungal wall. Epithelial debridement may improve penetration (highly lipophilic).
     Amphotericin B (0.15%): It is indicated for yeasts. It is quite unstable, rapid degradation happens to light. It causes renal and haematological toxicity.
     Natamycin (5%): It is a broad-spectrum antifungal drug and the drug of choice for filamentous agents.

- **Imidazoles:** It is effective in cases where therapy fails with other agents. It acts by interfering with CYP450-mediated pathways in ergosterol synthesis. Miconazole, fluconazole (0.3%) and ketoconazole (1%) are the prototypes. *Voriconazole (1%):* It is indicated in cases responding poorly to topical natamycin, deep keratomycosis and in pre-perforation stage. It has good oral bioavailability (96%) and ocular penetration.
- **Flucytosine:** It is converted to 5-fluorouracil.

f. Oral antifungal agents
- Non-responsive to topical therapy even after 7–10 days.
- Ulcer size greater than 5 mm
- More than 50% of stroma involved
- Associated with scleritis
- Associated with endophthalmitis
- Perforated ulcer
- Paediatric cases
- Bilateral cases and in post-therapeutic PK cases

g. Surgical treatment
- Tissue adhesive: Used in less than 2 mm perforation.
- Therapeutic patch graft (ulcer size up to 5 mm). The choice of deep anterior lamellar keratoplasty (DALK) in keratomycosis is not a good option due to the increased chance of recurrence.
- Intrastromal injection of voriconazole: Dose is 50 µg in 0.1 ml. This is also called "targeted drug delivery". This may be repeated after 72 hours and should not be performed in presence of extreme keratolysis and Descemet's membrane perforation.
- General measures (oral analgesics, antiglaucoma medications, cycloplegic and lubricants)

Special notes about therapeutic PK in keratomycosis should be remembered:
- Host trephination should be at least 1 mm away from infiltrates.
- Excised button should be sent for culture and drug sensitivity.
- Start oral antifungals in the post-operative regimen.
- If C/S shows no fungus, then stop the antifungals after 2 weeks.
- If C/S shows fungus, then continue the antifungals for 6–8 weeks.
- AC washes with intracameral antifungal should be undertaken.
- Peripheral iridotomy is a must.
- It is a good practice not to touch the lens in phakic patients.
- Role of topical steroid post-therapeutic PK is controversial and should not be started within the first 2 weeks after surgery.

Q15. Mention some common sites of recurrence following therapeutic PK.

The common sites are the vitreous cavity, anterior chamber and graft-host junction.

Q16. Describe the management of Acanthamoeba keratitis (AK).

a. Proper history taking.
b. Slit lamp examination of ulcer with Rose Bengal and sodium fluorescein staining.

c. Scraping of ulcer base and margins: Materials are used for smear preparation and culture. Calcofluor white staining is used to identify Acanthamoeba and non-nutrient agar seeded with *E. coli* is used as culture media.

d. Specific treatment:

Aminoglycosides: Neomycin 1.0% (but not gentamicin)

Biguanides: Drug of choice (disrupts DNA): Polyhexamethylene biguanide (PHMB) 0.02–0.2%

Chlorhexidine: Topical chlorhexidine 0.02–0.06%.

Diamidines (disrupts cell membrane): Propamidine isothionate (brolene) 0.1%, Hexamidine 0.1%

Imidazoles: Ketoconazole, clotrimazole, voriconazole 1%

e. Surgical treatment: Therapeutic penetrating keratoplasty and therapeutic DALK are indicated in limbal involvement, keratitis threatening the DM and frank perforation.

f. The role of steroid is controversial. The steroid helps to convert cysts into trophozoites.

Current indications:

- Increase in deep vascularisation
- Recurrence
- Inflammatory complications of AK (like heavy AC reaction and associated scleritis) and severe pain.

Special notes:

- Acanthamoeba keratitis contributes to 2% of all culture-positive corneal ulcers in India, 80–90% of all contact lens associated keratitis in the USA and UK but only less than 5% of contact lens associated keratitis in India.
- Steroids should not be started until 2 weeks after the start of biguanides.
- Biguanides should be continued for 4 weeks after the stoppage of the steroid.
- A combination of diamidine and biguanides or diamidine and amino glycosides are used 1 hourly initially. Once healing is ensured, tapering is done over several weeks to months and continued for a year.

Q17. What are the complications of Acanthamoeba keratitis?

- Scleritis (consider steroid treatment)
- Iris atrophy
- Persistent dilated pupil
- Intraocular spread
- Cataract

Q18. What is Pythium keratitis?

Ocular pythiosis: Keratitis caused by *Pythium insidiosum* (fungus like organism, sporangia containing biflagellate zoospores multiply by asexual reproduction). Mainly, reported from tropical, temperate areas with the humid environments and recently from parts of southern India.

Risk factors: Contact with aquatic, agricultural trauma, horsetail injury, soil, dust, etc.

Clinical features: It mimics mycotic keratitis. Greyish necrotic ulcer bed with a feathery edge, DM folds, endothelial plaque and hypopyon may be present. In severe cases, it may perforate or may involve adjacent sclera. Periorbital cellulitis is another presentation of ocular pythiosis.

Diagnosis

- Corneal scraping for KOH and Gram stain, mimics hyphae organism in light microscopy (hence, misleading), broader hyphae with branching at a right angle (differentiates pythium from fungus)
- Other stains: Acridine orange and lactophenol blue.
- Culture: SDA, blood agar, chocolate agar. Typically shows flat, feathery, yellow-brown colonies with filiform margins.
- IVCM: Refractile filaments branching at right angles oriented in alphabetical shapes.
- PCR and newer modality MALDI-TOF (Matrix Assisted Laser Desorption Ionization – Time of Flight mass Spectrometry).

Management

Medical: A combination of oral azithromycin and topical linezolid (0.2%), azithromycin and voriconazole had been used.

Surgical: Therapeutic PK is indicated in non-responding and advanced cases.

Q19. What are the types of fungi affecting the eye (aetiology of keratomycosis)?

A. Filamentous
   a. **Septate, non-pigmented:** Fusarium, Aspergillus and Penicillium.
   b. **Septate, pigmented (dematiaceous):** Curvularia and Cladosporium
   c. **Non-septate:** Rhizopus (Mucormycosis)

B. Non-filamentous (yeast, *Candida albicans*)

Q20. What are the stages of corneal ulcer?

a. Stage of infiltration
b. Stage of progression
c. Stage of healing
d. Stage of cicatrisation

Q21. Enumerate the complications of corneal ulcer.

- Anterior synechiae
- Posterior synechiae
- Corneal perforation with or without iris prolapse
- Corneal fistula formation
- Hypotonous eyeball with shallow AC
- Descemetocele or keratocele formation
- Sloughing corneal ulcer with spontaneous expulsion of the crystalline lens and vitreous
- Purulent iridocyclitis
- Expulsive haemorrhage

- Anterior capsular or anterior polar cataract
- Secondary glaucoma
- Vascularisation of cornea
- Scleritis
- Adherent leucoma
- Anterior staphyloma formation
- Endophthalmitis and panophthalmitis
- Phthisis bulbi

Q22. Define hypopyon.

Accumulation of "pus" in the anterior chamber is called hypopyon. It consists of polymorphonuclear leucocytes and fibrin. Hypopyon is sterile until the cornea is perforated in most cases of bacterial keratitis. Hypopyon of fungal keratitis is non-sterile as fungal hyphae can penetrate an intact cornea. Hypopyon occurs from iritis induced by toxins of microorganisms.

Q23. What is hypopyon corneal ulcer or ulcer serpens?

It is a specific form of corneal ulcer caused by Pneumococcus. This ulcer progresses in a serpiginous fashion. Chronic dacryocystitis may be a co-existing feature.

Q24. Name some microbial agents which can penetrate the intact cornea.

a. *C. diphtheriae*
b. *N. gonorrhoeae*
c. *N. meningitides*
d. *H. influenzae*

Q25. What are the indications of topical steroids in keratitis?

Generally, topical steroid is contraindicated in microbial keratitis. In certain conditions, topical steroids can be used.

a. Phlyctenular kerato-conjunctivitis
b. Acne rosacea keratitis
c. Mooren's ulcer
d. Disciform keratitis

Q26. Which organisms cause dendritic keratitis?

Herpes simplex type I (HSV1) and rarely by type 2 (HSV2) and varicella-zoster (chickenpox) (Fig. 1.7).

Q27. How is it transmitted?

Transmission of infection occurs by direct contact from the infective patient or asymptomatic healthy carrier. A person once infected becomes a permanent carrier of the virus and tends to break out periodically on nose, lips and cornea. Sunlight, cold, fever and menstruation are the triggering factors.

Q28. Describe the clinical features of HSV1 keratitis.

A. **Primary lesions:** Occurs in children as blepharoconjunctivitis. Stromal keratitis is very rare.

B. **Recurrent form of keratitis:**
- Initial feature is superficial punctate keratopathy presenting with numerous minute whitish lesions. Later, they desquamate to form erosion.
- The lesions coalesce and infiltrate in all directions in a branching pattern with knobs at the ends (dendritic form).
- Geographical keratitis (map-shaped epithelial ulcer with secondary stromal involvement).
- Marginal ulcer (near limbus).
- Viral necrotising keratopathy: Localized or diffuse stromal ulcer with infiltration.
- Stromal interstitial keratitis.
- Endothelitis: This is an antigen–antibody complex mediated inflammation of endothelium. Important features are deep stromal edema along with keratic precipitates on the endothelium. Depending upon the nature of corneal involvement, it may be disciform, linear or diffuse.
- High intraocular pressure and iridocyclitis with hypopyon.

Q29. How do you treat herpetic eye disease?

Epithelial disease	Stromal keratitis	Endothelial keratitis with uveitis
• Never use topical steroid • Eye ointment: Acyclovir 5 times/day for 10–14 days (Extended use can cause ocular toxicity).	• Topical steroid • Acyclovir 400 mg 2 times/day per orally while on steroid treatment for prophylaxis • No role of topical acyclovir.	• Topical steroid • Acyclovir 400 mg 5 times/day for 7–10 days, then reduced to prophylactic dose. • Cycloplegic and antiglaucoma medications to control elevated IOP.

Indications for prophylaxis

a. Recurrences of HSV keratitis (any type).
b. Recurrent inflammation with scar/vascularisation involving visual axis.
c. After keratoplasty procedures in patients with HSV-related corneal scarring. (HEDS recommendation: Oral acyclovir 800 mg TDS followed by 400 mg BD for a year at least).
d. Post-operatively for patients with a history of HSV ocular infection, now undergoing ocular surgery or laser.
e. History of ocular HSV during immunosuppressive state/treatment.

Q30. What are the external stressors which contribute to the recurrence of herpetic eye disease?

These stressors are:
- Extreme weather, dry dusty environment
- Menstruation, fever
- Sunlight
- Mood changes
- Trauma, intraocular surgery
- Immunological stressors including HIV

Q31. Describe the clinical features of herpes zoster viral keratitis (HZVK).

Prodromal phase (precedes the appearance of rash)	**Skin lesions** (occurs after 3–5 days)	**Eye lesions** (develops in 50% of patients within 2 days of onset of rash)
• Tiredness, fever, malaise, headache. • Superficial itching, tingling sensation, burning sensation. • Deep boring pain over an area supplied by ophthalmic division of the trigeminal nerve.	• Initially, painful erythema, and vesicle formation over a period of 2–4 days. After this, the vesicle turns into pustular form. • Other signs and symptoms: • Involvement of naso-ciliary nerve (Hutchinson sign) • Cranial nerve palsy (3rd, 4th and 6th) • Postherpetic neuralgia	• Small punctate corneal epithelial lesions, later dendritic lesions like herpes simplex but without terminal bulbs. • Stains with Rose Bengal and sodium fluorescein. • Nummular keratitis (Fine granular subepithelial deposit). • Stromal keratitis / disciform keratitis. • Conjunctivitis / episcleritis/ scleritis

Please note that clinical manifestations of herpetic eye disease in children are different from those in adults. In children, there is more chance of bilateral involvement and recurrence in the first year after initial episode.

Q32. What are the differences between the ocular manifestations of herpes simplex vs. herpes zoster infection?

The different manifestations can be as follows:

Epidemiological difference:

- Primary herpes simplex affects children less than 5 years of age and recurrent forms of infection are seen in middle-aged patients. Herpes zoster involves elderly and immunosuppressed individuals.

The Differences in clinical manifestation:

- In herpes zoster infection complete dermatomal distribution, bilaterality, pain, post-infection scarring and post-herpetic neuralgia are usual features. These features are less commonly seen in herpes simplex infection.
- Dendrites of herpes simplex are central, well-defined, large and have terminal bulbs. Herpes zoster presents with smaller, peripheral, elevated plaque-like dendrites having no terminal bulbs.
- Herpes simplex infection includes follicular blepharo conjunctivitis, typical dendritic epithelial lesions, immune mediated stromal keratitis (rare in children), metaherpetic ulcer, endothelitis, trabeculitis, episcleritis, scleritis and acute retinal necrosis (ARN). Herpes zoster infection has combined features of ocular, dermatological and neurological involvement in varying degrees. Common eye manifestations include episcleritis, scleritis, conjunctivitis, keratitis, anterior uveitis, ARN, and PORN.

Q33. Is Lasik surgery advisable in a patient with a history of herpetic eye disease?

Lasik is inadvisable in a case with the previous history of stromal keratitis but it is advised with extreme caution in a case with a previous history of epithelial keratitis.

Q34. When will you consider using steroids in microbial keratitis?

The use of steroids is controversial, extreme caution is needed. Use steroids only after adequate antimicrobial coverage.

Disadvantages of steroid therapy

- Risk of worsening an active infection.
- Decreases fibroblastic activity and decreases wound healing.
- Promotes recurrence of pseudomonal infection.

Advantages of steroid therapy

- Steroid is believed to decrease scarring and uveitis by reducing inflammation.

Indications

- Culture positive cases
- Sensitive to antibiotics
- Responding clinically
- Ulcer has been sterilized
- If patient follows-up and compliance is good

Contraindications

- Suspected or proven fungal keratitis and viral epithelial keratitis.

Q35. What were the conclusions of the steroids for corneal ulcer trial (SCUT)?

The conclusions were as follows: Steroids had no significant effect on overall acuity outcome, there was no apparent increased risk of corneal perforation and no major safety concerns were identified.

Q36. What do you do when the ulcer is not responding to treatment?

- Stop antibiotics for 24 hours.
- Repeat scraping and send for microbial examination (staining and culture)
- Plan corneal biopsy
- Suitable corneal button must be kept on standby (for tectonic replacement, if required).
- Dermatological trephine is used encompassing the base and the active edge of the ulcer.
- Specimen divided and sent for microbiological analyses and histological staining.
- Restart intensive antibiotics; consider other diagnoses (e.g. sterile ulcers, Acanthamoeba keratitis, and Pythiosis).
- If the above measures fail, consider therapeutic penetrating keratoplasty.

Q37. What are the causes of sterile ulcers?

a. **Post-infection (treated, resolved):** Herpes (meta herpetic ulcer).
b. **Ocular surface inflammation:** Lids and lashes (entropion, ectropion, trichiasis, lid defects), skin (Stevens-Johnson syndrome, ocular pemphigoid, ocular rosacea), lacrimal gland (keratoconjunctivitis sicca).
c. **Neurotrophic keratitis:** DM, 5th CN palsy.
d. **Exposure keratitis:** VII CN palsy, lagophthalmos, proptosis.
e. Nutritional keratitis (vitamin A deficiency).

f. Neoplasia (acute leukaemia).
g. Immune-mediated connective tissue diseases like rheumatoid arthritis, Wegener's granulomatosis, systemic lupus erythematosus, polyarteritis nodosa, Mooren's ulcer, TMD, marginal keratitis, allergic conjunctivitis.
h. Iatrogenic trauma, postsurgical, chemical, thermal, radiation injury.

Q38. How do you diagnose and manage a case of microsporidial keratitis?

It is an obligate intracellular spore-forming parasite/fungi.

Stain: Modified trichrome

Treatment:

Medical: Topical fumagillin, topical 4th generation fluoroquinolone (levofloxacin, moxifloxacin), oral albendazole (especially if the patient is immunocompromised).

Surgical: Therapeutic epithelial debridement and therapeutic PK for non-resolving stromal disease.

Q39. How to confirm a case of viral keratitis?

The diagnosis of viral keratitis is mainly clinical.

However, the following laboratory methods are used:

a. Tzanck smear: Giemsa or PAP smear to stain intra-nuclear eosinophilic inclusion body (called Cowdry type A)
b. ELISA (high sensitivity but low specificity)
c. PCR
d. Cell culture

Q40. Who are at risk for the development of herpetic eye disease?

At-risk persons are

Atopic people (an important cause of bilateral, herpetic eye disease).

- Diabetes, organ transplant recipient, measles, HIV, VKC.
- Drugs: Antiglaucoma medications mainly PG analogues and anti-VEGF.

Q41. Name some surgical factors facilitating herpetic reactivation.

Reactivation occurs in the following cases:

- Cataract surgery
- PK and lamellar keratoplasty
- YAG PI and capsulotomy
- PRK, ALT and following CL fitting

Q42. What is interstitial keratitis?

Interstitial keratitis is a nonsuppurative, chronic inflammation of the stroma without involvement of the epithelium or endothelium.

Q43. What are the causes of interstitial keratitis?

The causes of interstitial keratitis are:

Infective: Congenital (or acquired) syphilis, tuberculosis, leprosy, herpes, onchocerciasis, and Lyme disease.

Noninfective: Cogan's disease (combination of hearing loss, vertigo, interstitial keratitis with PAN) and sarcoidosis.

Q44. What are the causes of corneal hypoesthesia?

Corneal hypoesthesia can be physiological or pathological.

Physiological	Pathological
• Increasing age • Peripheral cornea • In the early morning • Eyes with brown iris	• **Congenital:** Riley-Day syndrome, congenital corneal hypoesthesia, corneal dystrophies (Reis-Bucklers dystrophy, lattice dystrophy) • **Acquired:** Diabetes mellitus, leprosy, herpes simplex • **Iatrogenic:** Topical eye drops (timolol, anaesthetic abuse) • **Surgery** (limbal section ECCE, penetrating keratoplasty, epikeratophakia) • **Contact lens wear**

Q45. What are the causes of a persistent epithelial defect?

a. Neurotrophic keratitis
b. **Exposure keratitis:** Lagophthalmos, proptosis
c. **Lid abnormalities:** Ectropion, entropion, distichiasis, trichiasis
d. **Limbal stem cell deficiency:** Chemical injury, ocular cicatricial pemphigoid (OCP), Stevens-Johnson's syndrome (SJS)
e. **Inflammatory:** Marginal keratitis, connective tissue diseases
f. Neoplasia
g. **Iatrogenic:** Post-surgery, radiation, anti-glaucoma drops, topical antiviral medications, anaesthetic abuse

Q46. When do you perform a corneal biopsy?

This is performed in clinically suspected infectious keratitis cases where two consecutive smears and cultures are negative. The patient also shows no clinical improvement on initial broad-spectrum antimicrobial therapy.

Indications:

a. Infective keratitis (culture-negative, not responding to treatment).
b. Acanthamoeba keratitis (organism is deep in the stroma).
c. OSSN.

Procedure:

- Stop antibiotic for 24–48 hours
- Local anaesthesia
- Choose between the lesion and healthy cornea avoiding visual axis
- Debride slough
- Use a dermatological trephine with 2 mm, 3 mm or 4 mm diameter to mark tissue
- Lamellar dissection of tissue with blade
- Divide tissue for histology and culture

Q47. What are the indications of AC paracentesis?

- In clinically suspected keratomycosis with negative scraping and negative biopsy.
- In progressive keratitis with increasing hypopyon.

Q48. When and how do you perform corneal glueing?

- **Composition:** Corneal glue is made of isobutyl cyanoacrylate (Histoacryl)
- **Indications:** Small perforation <2 mm in size
- **Procedure:**
  - Apply topical anaesthesia.
  - Debride slough and necrotic tissue.
  - Dry the affected cornea.
  - Apply glue onto cellophane plastic disc.
  - Apply glue and cellophane disc on perforation and allow to dry
  - Apply bandage contact lens

Q49. How does the tissue adhesive (TA) act?

Besides giving tectonic support, TA acts by the exclusion of PMN cells in tear film as well as PMNs of the stromal layer. It is also bacteriostatic.

Q50. What is the fate of tissue adhesive?

The adhesive is left *in situ* until it loosens spontaneously and the bed is vascularised.

Q51. What are the complications of tissue adhesive?

The complications of tissue adhesive are superior tarsal conjunctivitis and anterior synechiae formation.

Q52. Mention indications and disadvantages of performing a conjunctival flap.

Indications	Disadvantages
• Poor visual potential • Chronic epithelial/stromal ulcer after resolution of active infective disease • Neurotrophic ulcer • Chemical injury • Bullous keratopathy • Descemetocele	• Temporary treatment • No view of the cornea (so, post-procedure follow-ups of the ulcer will be difficult) • Low drug penetration • Postoperative complications (buttonhole, epithelial cyst, retraction of a flap, bleeding, ptosis)

Q53. How do you perform a Gunderson (conjunctival) flap?

a. Scrape epithelium
b. 360° conjunctival peritomy
c. Dissect and mobilise superior conjunctiva 2 mm in excess of corneal diameter
d. Bring down flap
e. Stitch the superior edge of the flap to the tenon and the inferior edge of the flap to the inferior limbal conjunctiva with 8–0 vicryl/silk suture.

Q54. Name some landmark trials related to infectious keratitis.

A. **Steroid for culture positive bacterial ulcer trial (SCUT)**

Aims: 1% prednisolone vs. placebo drop was given in culture-positive bacterial ulcer cases.

Results: No overall difference in BCVA at 3 months. No significant difference in epithelisation time, perforation rate and infiltrates size.

B. **Mycotic ulcer treatment trial (MUTT)**
Aims: To compare 1% voriconazole with 5% natamycin in culture positive filamentous keratomycosis. Both the drugs were given hourly till the epithelium healed, then 4 times a day.
Results: Significantly better clinical and microbiological outcomes in natamycin group. Voriconazole should not be used as monotherapy.

C. **Herpetic eye disease study (HEDS)**
HEDS 1: The main study objectives were:
a. To see the effects of topical steroids in stromal keratitis patients on topical trifluridine.
b. To see the effects of oral acyclovir in stromal keratitis with topical steroid plus topical trifluridine.
c. To see the effects of oral acyclovir in herpetic kerato-uveitis and endothelitis with topical steroid plus topical trifluridine.

HEDS 2: Main objectives were:
a. Whether the early treatment with oral acyclovir in epithelial keratitis cases will help to reduce secondary stromal involvement.
Conclusion: No benefit.
b. To see the efficacy of low-dose oral acyclovir in reducing recurrence of HSV infection.
Conclusion: 41% reduction in recurrence.
c. To determine the role of external stressors in recurrence. (Study Conclusion: Neither age, ethnicity, gender or a history of non-ocular HSV disease increased the risk of recurrence of HSV infection of the eye).

Q55. What are the alternatives to acyclovir drugs?

The recent emergence of acyclovir resistant strains warrants use of alternative antivirals. Resistance to acyclovir is due to mutation in the thymidine kinase (TK) gene. Alternative drugs are ganciclovir and valacyclovir.

PERIPHERAL ULCERATIVE KERATITIS (PUK)

History

Age

- Unilateral Mooren's ulcer is typically seen in older people (above 60 years) and bilateral Mooren's ulcer affects young patients.
- Terrien's marginal degeneration (TMD) is seen in patients above 40 years of age (40–50 years).
- PUK in RA and SLE are seen in young patients.
- VKC is common among children below 14 years of age.

Gender:

- SLE is common among females.
- TMD/Mooren's ulcer: Male predominance.

Chief complaints

- Pain
- Redness

- Difficulty to tolerating bright light
- Watering and foreign body sensation

History of present illness:

- ***Presentation:*** Mooren's ulcer presents with moderate pain, redness, and photophobia. TMD and PMD are typically less symptomatic. VKC is associated with ocular redness and itching.
- ***Vision loss:*** Vision loss may happen due to induced irregular astigmatism in all types of PUK but a sudden drop of vision may occur in PMD due to hydrops.
- ***Unilateral/bilateral:*** Most of the cases of the TMD and connective tissue disorder-related PUKs are bilateral though the presentation may be asymmetric. Typically, Mooren's ulcer is unilateral but bilateral involvement is noted in aggressive or 'malignant type' of Mooren's ulcer.

Past history: History of ocular surgery (in recent past), history of trauma, chemical burn or herpetic infection is significant.

Examination

Systemic Examination

- Morning stiffness lasting more than one hour, systemic polyarthritis involving large and small joints with rheumatoid factor positive indicates rheumatoid arthritis (RA).
- Typical young female patient presenting with photosensitive malar rash in a butterfly orientation, discoid rashes over face and scalp, renal and CNS involvement along with features of polyserositis (ascites, pleural and pericardial effusion) and anti-dsDNA and antinuclear antibody positive makes the diagnosis of systemic lupus erythematosus (SLE).
- Involvement of both the upper and lower respiratory tract along with renal involvement (glomerulonephritis and nephrotic syndrome) with cANCA positive points towards Wegener's granulomatosis (WG).
- Sparing of the upper respiratory tract along with pANCA positive makes the diagnosis of polyarteritis nodosa (PAN).
- Asthma, eczema, and skin allergy are seen in VKC patients.

Ocular Examination

BCVA: Vision is impaired due to induced astigmatism and profound loss of vision is seen in acute hydrops.

- Typical ropy discharge, cobblestone papillae, greyish discoloration of conjunctiva is noted in VKC.
- Conjunctiva adjacent to the region of Mooren's ulcer is congested, gelatinous and chemosed.

Limbus: Horner-Trantas dots and Herbert's pits are present in VKC patients.

Sclera

- Typically, the sclera is not involved in Mooren's ulcer and Terrien's marginal degeneration.
- Anterior non-necrotising scleritis is associated with RA, WG, PAN and SLE.

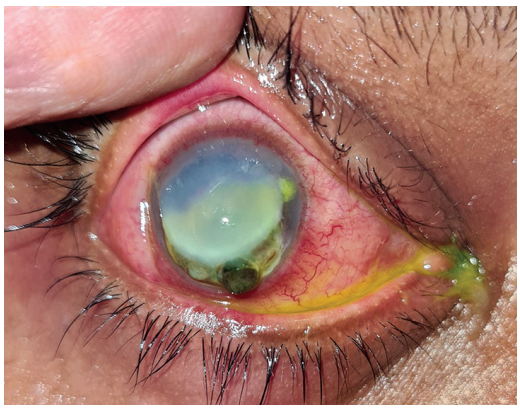

Fig. 1.12: Mooren's ulcer

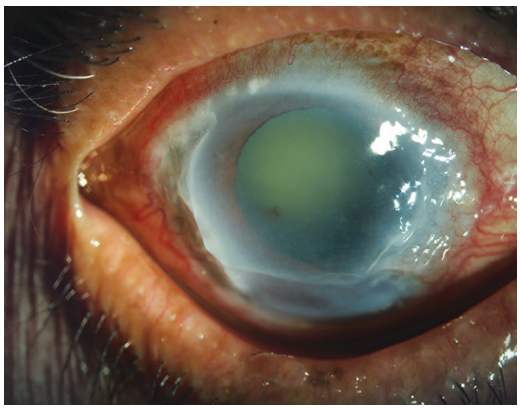

Fig. 1.13: Mooren's ulcer

- Anterior necrotizing scleritis without inflammation is classically seen in longstanding seropositive RA, characterized by a yellowish necrotic patch followed by extreme scleral thinning and perforation (scleromalacia perforans).
- About 30% of cases of collagen vascular disease is associated with posterior scleritis (lid oedema, proptosis, vitritis, disc oedema, exudative RD, choroidal folds, and "T" sign in orbital USG).

Cornea:

- ***VKC:*** Punctuate superior limbic keratopathy, plaque formation, shield ulcer, pseudo gerontoxon and superior micropannus are found in VKC.
- ***Mooren's ulcer:*** A typical gutter with overhanging edge accompanied by oedema, stromal infiltrates and ulceration in the interpalpebral region is classically found in Mooren's ulcer (Figs 1.12 and 1.13).
- ***RA:*** Gradual peripheral corneal thinning sparing the central part (called "contact lens cornea"), sometimes sclerosing keratitis (gradual peripheral corneal thickening and opacification adjacent to an area of scleritis) and acute stromal melting especially in the peripheral cornea adjacent to an area of intense inflammation is present in RA.
- ***SLE:*** Marginal corneal infiltrates with thinning and punctate epithelial keratopathy is present in SLE.
- ***WG, PAN:*** They present with typical Mooren's ulcer-like circumferential lesion with involvement of adjacent sclera. Sclera is not involved in Mooren's ulcer.
- ***TMD:*** Superior subepithelial infiltrates, vascularisation and gutter formation (between the limbus and unaffected part of the cornea) is found in TMD (Fig. 1.14).
- ***PMD:*** PMD is typically characterized by bilateral inferior corneal thinning (area of thinning is below the area of maximal protrusion) with a normal band of tissue between the limbus and degenerated cornea (Fig. 1.15).

Anterior chamber: Anterior chamber reaction may be seen in CVDs and progressive Mooren's ulcer.

Lens: Steroid-induced cataract is seen in chronic cases.

Posterior segment: Vitritis, disc oedema, choroidal folds, exudative RD, subretinal mass, ring detachment of choroid and typical "T" sign in orbital USG (due to fluid in subtenon space) are present in collagen vascular diseases.

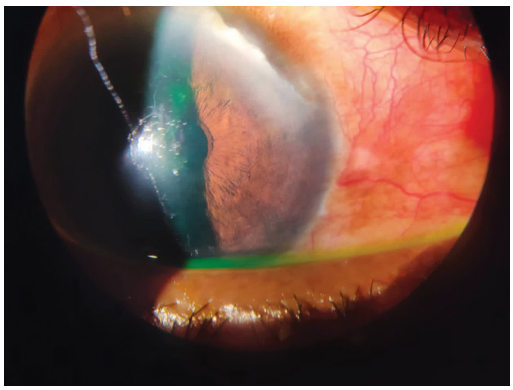

Fig. 1.14: Terrien's marginal degeneration (TMD)

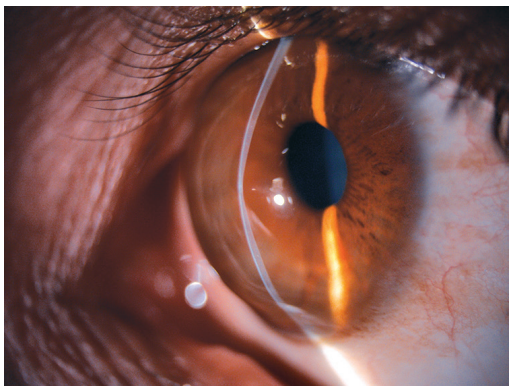

Fig. 1.15: Pellucid marginal degeneration (PMD)

Provisional diagnosis:

a. ***Mooren's ulcer:*** Painful gutter formation with an overhanging edge in the interpalpebral area with a tendency for circumferential spread.
b. ***Terrien's marginal degeneration:*** Male dominant, early-onset, bilateral, superior thinning with vascularisation and gutter formation in a relatively quiet eye.
c. ***Pellucid marginal degeneration:*** Bilateral inferior corneal thinning but area of protrusion is above the area of maximal thinning giving rise to high irregular astigmatism (typical "crab claw" in topography).

Frequently Asked Questions

Q1. What is a PUK?

PUK includes the entities causing inflammatory peripheral corneal ulcers and their sequelae.

Q2. What are the differential diagnoses of PUK?

Common differential diagnoses are

- Mooren's ulcer
- Terrien's marginal degeneration
- Pellucid marginal degeneration
- Collagen vascular diseases like RA, WG, PAN and SLE.

Q3. What are the causes of peripheral ulcerative keratitis?

PUK is a limbal-based disease with inflammatory changes in the limbus; therefore, it is more immune-related than infective. Causes of peripheral ulcerative keratitis:

Systemic causes	Ocular causes
• **Connective tissue diseases:** Rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Wegener's granulomatosis (WG), polyarteritis nodosa (PAN), relapsing polychondritis. • Sarcoidosis • Leukaemia	• **Infective:** Bacterial, viral, Acanthamoeba, and fungi • **Non-infective:** Mooren's ulcer, Terrien's marginal degeneration, Marginal keratitis, pellucid marginal degeneration, acne rosacea, exposure keratopathy, neurotrophic keratopathy, trauma

Please note that, though TMD and PMD are not aetiologies of PUK, they come in differential diagnoses of PUKs.

Q4. How do you differentiate Terrien's marginal degeneration from Mooren's ulcer?

	Mooren's	Terrien's
Age	Type 1: Above 60 years Type 2: Young age	After the 4th decade
Sex	Male dominance	Male dominance (75%)
Unilateral/bilateral	Type 1: Unilateral, Type 2: Bilateral	Bilateral
Presentation	Moderately painful, red-eye, photophobia and loss of vision.	Very little pain and redness Loss of vision
Triggering factors	The previous history of corneal insult (surgery, infection, trauma etc.)	No such factors
Ulcer characteristics	• Peripheral ulceration of inter-palpebral area involving the superficial one-third of the stroma associated with variable epithelial defect. • Ulcer having a overhanging edge, no lucid interval between the limbus and the ulcer • Progressive circumferential and stromal thinning with an under-mined and infiltrated leading edge. • Vascularization involving the bed of the ulcer up to its leading edge but not beyond. • The healing stage is characterized by thinning, vascularisation and scarring.	• Classically involves superior part of cornea with a clear interval from the limbus, epithelium intact with sloping inner edge having lipid line, bridging vessels. • Fine, yellow, punctate stromal opacities associated with mild superficial vascularisation. Circumferential thinning results in a peripheral gutter, while central part rises sharply. • Pseudopterygium develops in long standing cases other than 3 and 9 o'clock position.
Corneal perforation	Very common	Rare

Q5. How can you classify Mooren's ulcer?

Mooren's ulcer are classified in accordance with Watson's criteria (based on clinical features, anterior segment fluorescein angiography findings and treatment response).

- **Type 1:** (unilateral Mooren's ulcer): Very much painful, seen among patients more than 60 years, venular occlusion of local deep episcleral and conjunctival vessels along with disruption of limbal arcades in angiography.
- **Type 2:** Less severe pain, bilateral, young patient, initial circumferential spread, then progresses towards central cornea and vascular leakage with new vessel formation at the base of ulcer in angiography.
- **Type 3:** Bilateral indolent ulcer in an elderly patient with a little inflammation and normal vascular architecture in angiography.

Q6. What is the fate of Mooren's ulcer?

The ulcer spreads circumferentially along the limbus. This may be accompanied by iris prolapse due to perforation of the extremely thinned-out cornea (*see* Figs 1.12 and 1.13).

Q7. Can a Mooren's ulcer be seen superiorly?

It can be seen superiorly when it starts from the surgical wound in the superior quadrant although Mooren's ulcer is typically seen in the interpalpebral zone.

Q8. What are the histopathological findings of the cornea in a case of Mooren's ulcer?

The findings of Mooren's ulcer are:

- Stromal necrosis and chronic inflammatory cell infiltrates.
- Destruction of basement membrane and stroma of varying amounts.
- Preservation of Descemet's membrane and endothelial layer.

Q9. How can you manage a case of Mooren's ulcer?

Management is in accordance with Chow and Foster's step care approach.

The modalities are:

- Steroid (topical and systemic)
- Conjunctival resection
- Systemic immunosuppression
- Superficial lamellar keratectomy, BCL placement and keratoplasty (chance of recurrence in the graft)

Q10. How to differentiate between circumferential ring lesions of Mooren's ulcer from other collagen vascular diseases (CVDs like WG, PAN)?

In CVDs, the adjacent sclera is typically involved. Scleral involvement is not seen in Mooren's ulcer.

Q11. How to differentiate between keratoconus (KCN) and PMD?

Though, both KCN and PMD present with inferior corneal thinning and high irregular astigmatism, certain differences are there:

Features	Keratoconus	PMD
Maximum thinning and protrusion.	At the apex of the cone	Maximum protrusion occurs above the area of maximum thinning
Iron deposition, cone formation, and corneal scarring.	Present	No such
Topography	Asymmetric bow tie appearance	Crab claw appearance
Pachymetry	Inferior paracentral thinning in KCN	Inferior band

Q12. How can you manage a case of PMD?

a. **Non-surgical:** Spectacle; RGP CL; special CLs (Boston CL or Rose K lens) in early cases.

b. **Surgical:** CXL and DALK (severe cases).

Q13. How would you manage a patient with PUK?

Ocular investigations: Scraping for culture and sensitivity if there is a suspicion of infective cause.

Systemic investigations: CBC, ESR, VDRL, FTA, ANA, dsDNA, cANCA, RF, CXR, Mantoux test

Ocular treatment:

- ***Infection:*** Antibiotics/antivirals/antifungals (as per microbiological report).
- ***Autoimmune:*** Topical steroid/topical cyclosporine.
- ***Exposure/neurotrophic:*** Tarsorrhaphy, botulinum toxin injection, lubricants and BCL. Rosacea/marginal keratitis—oral doxycycline systemic treatment: Systemic steroids and immunosuppressants.

Q14. What is the rationale for conjunctival resection?

The conjunctiva adjacent to the Mooren's ulcer liberates inflammatory cells producing cytokines and auto-antibodies against the cornea. Hence, the role of conjunctival resection still works in presence of frank perforation leading to iris prolapse. Cryo application to the adjacent conjunctiva is an alternative to conjunctival resection.

Q15. What is the extent of conjunctival resection?

Conjunctiva is resected 2 clock hours extra on either extreme of Mooren's ulcer and 4 mm behind the limbus.

Q16. Can you explain why the peripheral part of the cornea is mostly affected?

The peripheral part of the cornea has access to circulating immune complexes by the way of diffusion from the perilimbal plexus of blood vessels in cases with systemic vasculitis.

Q17. How can you classify the causes of PUKs?

The causes of PUKs can be of two types:

Systemic causes: RA (most common), WG, PAN, SLE, sarcoidosis etc.

Local causes: It has two subtypes:

a. *Micro ulcerative:* MGD, rosacea, Staphylococcus blepharitis, infections, etc.
b. *Macro ulcerative:* MU (most common), exposure keratopathy, infections, etc.

Please note: Infections can present both as micro as well as macro ulcerative forms. Common infectious causes are gram-positive Staphylococcus, Herpetic eye disease, fungi and Acanthamoeba.

Q18. How the collagen vascular disease (CVD) associated PUKs are managed?

It should be multi-disciplinary approach with the rheumatologists and immunologists.

a. Goal of therapy is to control the systemic vasculitis (by immunosuppressive therapy) along with control of ocular lesions.
b. Systemic steroid is the cheapest and most commonly used first line immunosuppressive drug.
c. If the disease is unresponsive or unacceptable side effects of systemic steroid develop, consider second line drugs like cyclosporine or methotrexate or cyclophospamide or azathioprine. Even mycophenolate mofetil can be used.

Q19. Is there any role of biologicals in the management of PUK?

The following biologicals had been used in refractory cases of PUK: Infliximab (3–5 mg/kg IV), adalimumab (40 mg SC weekly), and etanercept (50 mg SC weekly). They are all TNF-alpha antagonists. In addition, B cell inhibitor (rituximab) can also be used.

Cost is the main limiting factor for use of biologicals. Recently with the advent of bio similar molecules, the cost of therapy has come down considerably.

Q20. How do the biologicals act?

The hyperemic peripheral conjunctiva as well as circulating immune complexes diffusing through perilimbal plexus of vessels liberate pro-inflammatory cytokines (like tumor necrosis factor-alpha) which in turn triggers the production of matrix metalloproteinases (MMPs). Biologicals block this pathway.

Q21. What are the side effects of biologicals?

Side effects are: Reactivation of latent infection (TB), congestive cardiac failure, deep vein thrombosis, pulmonary thrombosis, etc.

Q22. What are the indications of topical steroid therapy in PUK?

Topical steroid is indicated in mild cases with less than 2 o'clock hour involvement and less than 50% of stromal necrosis.

Q23. What topical agent is advised in moderate cases of PUK?

In moderate cases (2–4 o'clock hours involvement with more than 50% stromal necrosis), topical 2% cyclosporine is advised along with systemic immuno-suppressive drugs.

Q24. What are the dangers of topical steroids in PUK?

Steroids will inhibit the fibroblasts which are responsible for collagen production. Topical steroids can be given with simple epithelial defect, can be used with extreme caution in cases where stromal necrosis has just started (associated infectious aetiology should be excluded at the start of therapy by diagnostic scraping and microbiological evaluation) and it should be avoided after 50% of stromal melting occurs.

Q25. How can you differentiate between inflammatory infiltrate from an infectious infiltrate?

This is very important as the management differs in either case. A detailed history and a meticulous slit lamp examination are required. In general, an inflammatory infiltrate is smaller in size; area of epithelial defect is absent or very small and unassociated with discharge, lid signs or anterior chamber reactions.

KERATOCONUS

History

Age: Keratoconus is usually detected around 15 years (mid-teen age). Earlier the presentation, more is the chance of progression to a more severe disease.

Gender: This is a male-dominant disease. Females constitute one-third of all cases.

Occupation: More common among the urban populations with higher socio-economic status.

Chief complaints

- Gradual decrease in vision with frequent change of glass.
- Appreciation of two images in one eye. Troublesome glares are reported especially at night.
- Inability to tolerate contact lenses.

History of present illness: Initially vision might not be affected but the patient gives a history of frequent changes of glasses. A background allergic conjunctivitis is obtained. The power of the glass (or contact lens) will continue to increase until a situation is attained when BCVA fails to achieve the 6/6 standard or a contact lens failure occurs. Associated symptoms like decreased night vision, generalized itching for eczema, breathlessness for asthma and cardiac ailments must be enquired for.

Past history: Past history of allergy, trauma, contact lens use, repeated need for refractions for a quick change of power of glass, and refractive procedures (in post-LASIK ectasia cases) are to be taken.

Family history: A history of the same disease in siblings with Down syndrome may be obtained. Enquire about the same disease in the family.

Examination

Systemic Examination

Very often keratoconus may be associated with the following syndromes:

- ***Marfan's syndrome:*** Limbs longer as compared to trunk, high arched palate with cardiac abnormalities (aortic dilation, aortic valve prolapse, aortic regurgitation and dissecting aneurysm of ascending aorta).
- ***Rieger syndrome:*** Dental abnormalities (hypodontia and microdontia), maxillary hypoplasia, redundant paraumbilical skin and broad nasal bridge.
- ***Crouzon syndrome:*** Short antero-posterior head distance, midfacial hypoplasia, curved nose ("parrot beak"), inverted 'V'-shaped palate, mandibular prognathism and "frog-like face".
- ***Down syndrome:*** Typical facies (round face, small chin, short neck with macroglossia) with mental retardation.
- ***Ehlers-Danlos syndrome:*** Thin, hyperelastic skin with hypermobile joints, recurrent dislocations, dissecting aneurysm and mitral valve prolapse.

Ocular Examination

Vision: This may be normal in early cases. Usually, asymmetry in refractive data between two eyes with higher cylindrical power is noted. A sudden drop of vision accompanied by pain, watering and photophobia signify acute hydrops.

Orbit and adnexa

- Hypertelorism, shallow orbit with pseudo-proptosis in Crouzon syndrome.
- Epicanthic folds are seen in Ehlers-Danlos syndrome.
- Epicanthal folds and upward slant of palpebral fissure in Down syndrome.

Conjunctiva: Giant papillae (size more than 1mm) may be seen in chronic contact lens wearers and VKC patients.
Sclera: Blue sclera is seen in Ehlers-Danlos, osteogenesis imperfecta and Marfan syndrome.

Limbus

- Pannus may be present due to long standing contact lens use.
- Limbal papillae are seen in allergic conjunctivitis. Long standing VKC might present with limbal stem cell deficiency.
- Tranta's dots are seen in allergic conjunctivitis (AKC), VKC and contact lens users.
- External examination (gross ocular examination by torchlight)
- Bulging of the lower eyelid is noted if the patient is asked to look down. This is Munson's sign which is present in advanced keratoconus. Munson's sign is the 'V'-shape protrusion of the lower lid in downgaze. The steep cornea can be appreciated in moderate to severe cases.
- If you throw torchlight from the temporal side of the limbus with the patient looking straight, you will notice that the light is focused as an arrow on the nasal side of the limbus (Rizutti's sign). In a normal person, if you perform this test, you will see the light is not focused at a particular point on the nasal limbus and is perceived as an arc around the nasal limbus.

Cornea (Slit lamp evaluation)

- Typical inferior corneal ectasia and thinning with vertical stress lines involving deep stroma (Vogt's striae) (Fig. 1.16). This stria disappears on putting pressure on the globe to reappear again after releasing the pressure. Vogt's striae are vertical stress marks in the DM at the apex of the cone.
- Thinning of the cornea is usually at the apex of the cone in keratoconus (Fig. 1.17) and below the apex in PMD.
- Brownish ring (Fleischer's ring) due to deposition of iron pigment at the epithelial layer around the base of the cone. This is the earliest slit lamp sign. A subtle ring is sometimes missed in the white light of slit lamp, is better appreciated in blue or green light. This ring helps to locate the cone and also gives us an idea about the size of cone.

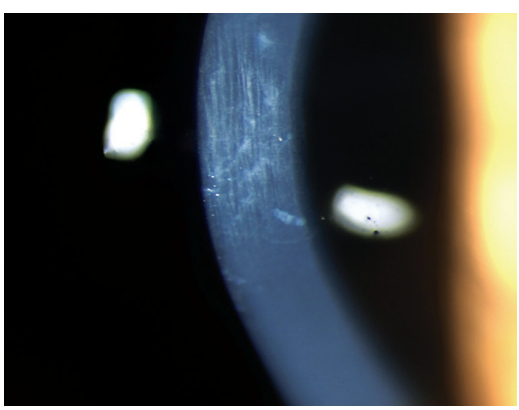

Fig. 1.16: Vogt's striae

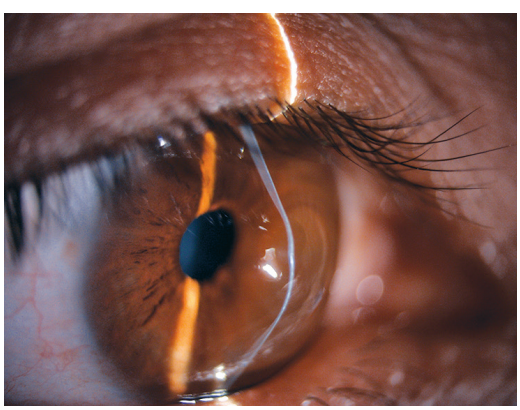

Fig. 1.17: Keratoconus

- Acute corneal hydrops: It is a condition characterized by stromal edema due to leakage of aqueous through a tear in the Descemet membrane. The patient presents with a sudden painful decrease in vision and photophobia (Fig. 1.18).
- Visible corneal nerves.
- Please note that Haab's striae in congenital glaucoma are horizontal.
- Corneal scarring: Apical scarring is seen at the apex of the cone where there is in-growth of epithelium through ruptured Bowman's membrane in advanced keratoconus. Descemet's membrane scarring is seen in post-hydrops.

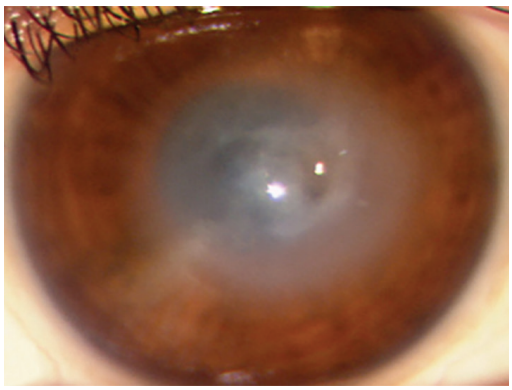

Fig. 1.18: Acute corneal hydrops

Iris

- Hypoplasia of dilator pupillae muscle is seen in Marfan syndrome.
- Stromal hypoplasia with corectopia and ectropion uveae is seen in Rieger syndrome.
- Aniridia is seen in Crouzon syndrome.
- Brush field spots are obtained in Down syndrome.

Lens

- Bilaterally, symmetrical upward subluxation of the lens in Marfan syndrome.
- Cataracts may be seen in Crouzon syndrome and Down syndrome.
- Lenticular subluxation is seen in Ehlers-Danlos syndrome.

Anterior chamber including angles

- Normally anterior chamber is deep.
- Dense iris processes with thickened trabecular sheets are noted in Marfan syndrome.
- Posterior embryotoxon due to prominent Schwalbe's line, iris processes are seen in Rieger anomaly.

Fundus evaluation

- Myopic fundus with peripheral retinal degeneration is found in high myopia and Marfan syndrome
- Arteriolar attenuation, para venous bony spicules and waxy pallor of the optic disc is noted in retinitis pigmentosa
- Patches of peripheral chorioretinal atrophy and granularity (salt and pepper fundus), disc oedema and subsequent disc pallor, bull's eye maculopathy and absent light reflex is found in Leber congenital amaurosis.

Retinoscopy

- "Oil droplet" reflex in ophthalmoscopy (early cases) and scissors reflex (in retinoscopy) is obtained due to irregular myopic astigmatism. This is the earliest sign of keratoconus. The reflex in retinoscopy will show a split in the image called scissoring reflex because the light reflected back passes through different portions of the cornea having different refractive power.

Intraocular pressure and pachymetry

- Thinning in the inferior quadrant is diagnostic.
- Elevated IOP is seen in Rieger syndrome and Marfan syndrome and Crouzon syndrome.

Provisional diagnosis: A case of bilateral corneal ectasia with thinning most probably due to keratoconus.

Frequently Asked Questions

Q1. Define keratoconus.

Keratoconus is a progressive, noninflammatory and non-infectious ectatic corneal condition characterized by central or paracentral stromal thinning, apical protrusion, and irregular astigmatism (classical triad).

Q2. What are the causes of keratoconus?

Causes of keratoconus are:

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

Secondary:

a. Systemic: Chromosomal disorders (e.g. Down syndrome)
b. Connective tissue disorders (e.g. Marfan syndrome, osteogenesis imperfecta)
c. Cutaneous disorders (e.g. atopic dermatitis)
d. Ocular: Congenital ocular anomalies (e.g. aniridia, Leber congenital amaurosis, RP), contact lens wear

Q3. What are the histological characteristics of keratoconus?

Triad of thinned stroma, epithelial iron deposit, breaks in Bowman's membrane layer. DM and endothelium are normal unless hydrops has developed.

Q4. What are the early and late clinical features of keratoconus?

Early signs	Late signs
• Keratoscopy/Placido's disc (irregular rings) • Retinoscopy (scissor reflex) • Direct fundoscopy (oil drop sign/ Charleux drop sign) • Vogt's striae • Prominent corneal nerves	• Paracentral stromal thinning • Corneal scarring • *Munson's sign* (bulging of lower lids when patient looks down) • *Rizutti's sign* (conical reflection of nasal cornea with slit lamp light from the temporal side) • Corneal edema in cases of acute hydrops

Q5. What are the other causes of corneal ectasia (D/D)?

Conditions producing ectatic cornea are:

a. Keratoconus (KCN).
b. Terrien's marginal degeneration (TMD): Ectasia of the upper part of the cornea.
c. Pellucid marginal degeneration (PMD): Ectasia involves the lower part of cornea with lobster claw or butterfly pattern in topography, high against the rule astigmatism and area of thinning is below the area of ectasia.
d. Post-LASIK ectasia.

Q6. What are the epidemiological significances of keratoconus?

- A male dominant disease.
- Usually diagnosed in mid-teen age around 15 years. Earlier presentation signifies rapid progression and poor prognosis. KCN study showed more eye rubbing among teens.
- Usually bilateral disease but may be asymmetric. A high index of suspicion clinches the diagnosis, especially in a background of inequality of refractive data, higher cylindrical values, and asymmetry in the topography of the upper and lower half of the cornea with reduced pachymetry.
- More common amongst the urban populations with higher socioeconomic status.
- With improvements in topographic diagnostics during the last decade, the prevalence is increasing.

Q7. What is the practical significance of different signs of keratoconus?

- Scissors reflex is the earliest sign.
- Amongst all the slit lamp findings, Fleischer's ring is the earliest. This ring not only helps to locate the cone but also helps to assess the size of the cone as well.
- Visible corneal nerves are also seen in Hansen's disease, neurofibromatosis, primary amyloidosis, Refsum's disease, multiple endocrine neoplasias (MEN), and ichthyosis.

Q8. What is subclinical keratoconus?

This is a subtype of keratoconus, also, known as forme fruste keratoconus which is not detected by slit lamp examination. It is diagnosed by topography only.

Q9. What is the relationship between ocular allergy and keratoconus?

- Frequent eye rubbing is a proven risk factor for the development of keratoconus.
- It is a good practice to evert the eyelid in keratoconus patients to look for signs of active allergic conjunctivitis.
- Limbal type rather than the palpebral type of allergic conjunctivitis will incite more eye rubbing which causes epithelial micro-trauma and releases Fas ligand which enhances keratocyte apoptosis.
- A longstanding allergic conjunctivitis in a keratoconus patient may present with limbal stem cell deficiency.

Q10. What are the indications of corneal topography?

- Young patient.
- Asymmetrical refractive data between two eyes.
- Higher cylindrical values.
- BCVA not improving to 6/6.
- Presence of active ocular allergy.
- Family history of keratoconus.

Q11. What are the typical findings of keratoconus in topography?

- Increase in central corneal curvature (as evident by lots of hot colours with increased K value greater than 47D).

- Asymmetry in superior and inferior halves of the cornea (I-S asymmetry greater than 1.4 D) as evident by asymmetrical bow tie appearance.
- Decreased pachymetry signifying corneal thinning.

Q12. What is posterior keratoconus?

Posterior keratoconus	Posterior manifestation of keratoconus
It is a congenital, noninflammatory condition that is characterized by an abnormal posterior corneal curvature. This is accompanied by overlying stromal opacification and other ocular and systemic abnormalities. It has no relation with keratoconus. Example: Peter's anomaly.	Keratoconus is presumed to start at the back of the cornea until it progresses anteriorly. This is a posterior manifestation of keratoconus. This entity is effectively diagnosed by newer generation topography machine like pentacam.

Q13. How can you manage a case of keratoconus?

A. **Conservative treatment (usually good enough in 90% of patients):**
- Spectacles
- Special contact lens (RGP or Rose K lenses/scleral lenses) in non-progressing cases.
- Treat vernal keratoconjunctivitis aggressively.

B. **Collagen cross-linking (CXL):** Till date, collagen-cross linking (CXL) is the only proven modality (besides abstinence from eye rubbing) that can prevent progression of keratoconus. It cross-links the corneal collagen after denuding the epithelium by photosensitive riboflavin and UV-A, thus increasing the biomechanical strength of the cornea. This should be performed as soon as progression of keratoconus is documented. A photo-sensitizing agent (riboflavin 0.1%) is applied to cornea and collagen cross-links are induced with UV-A irradiation (370 nm).

C. **Intracorneal ring segments (ICRS):** ICRS (Intracorneal ring segments made of PMMA) are performed along with/after CXL, placed in the mid-stroma of the cornea at 70–80% depth. Single/paired 180 degrees rings flatten the cornea by their hammock effect. These PMMA-made semi-circular segments are placed into the corneal stroma around the cone. By peripheral stretching, they can reduce central corneal bulging. They can correct up to 2–3 D of myopia or myopic astigmatism. They are indicated in KCN cases of contact lens failure patients and in KCN cases having clear central cornea with no apical scars. The minimum corneal thickness required at the site of placement is 450 µm and keratometry value between 46 and 60 D.

D. **Corneal transplants:** Keratoplasty procedures are indicated if the patient is unable to achieve good vision with a contact lens or becomes intolerant to contact lens wear and develops scarring after acute hydrops. Most cases are treated with deep anterior lamellar keratoplasty (DALK), nowadays due to a lower risk of endothelial rejection, faster wound stabilization and less prolonged post-operative need for topical steroids. Penetrating keratoplasty (PK) is indicated in advanced keratoconus with post-hydrops scar, and progressive disease despite CXL and ICRS treatment. There is a high chance of long-term graft survival. Some patients develop fixed dilated pupil post-surgery (called Urrets-Zavalia syndrome).

Q14 What are the methods to bare Descemet's (DM) membrane in DALK?

The idea in DALK is to remove the stromal layers to reach or bare the DM. The following methods are used:

- ***Big bubble technique (Anwar's technique):*** Classic technique where air is injected at 60–80% stromal depth to create a DM detachment.
- ***Visco-assisted DALK:*** Viscoelastic materials are injected between DM and posterior stromal lamellae to create a separation plane.
- Manual layer-by-layer dissection is used to bare DM when we fail to achieve a big bubble.
- ***Hydro delamination:*** Instead of air, BSS is injected to separate DM from the posterior stroma.
- ***FEMTO-assisted DALK:*** Incisions are made at predictable depth by Femtosecond laser and then air is injected to achieve a big bubble. This is the latest method with provisions for customized donor-recipient configuration but cost is the limiting factor.

Q15. What is the treatment algorithm in non-progressing keratoconus?

- If vision is maintained, prescribe glass or contact lens.
- If the patient is unwilling to wear contact lens; phakic IOL (ICL) may correct refractive errors to some extent.

Q16. What is the treatment algorithm for progressive keratoconus?

- As soon as progression is documented, do CXL to prevent progression.
- Post-CXL stabilization, glass or contact lens is prescribed and the patient is followed up at regular intervals with vision check and tomography.

Q17. What are the pre-requisites and complications of ICRS treatment?

The pre-requisites are:

a. Clear central cornea without apical scars.
b. Keratometry value between 46 and 60 D.
c. The minimum pachymetry at the site of placement is 450 µm.
d. CL failure cases.

The complications of ICRS

- ***Intraoperative:*** Asymmetric implantation, faulty depth of the tunnel, decentred segments, false passage and corneal perforation. With greater use of Femtosecond laser rather than the manual procedure in tunnel making, the incidence of these complications is reduced.
- ***Post-operative:*** Tunnel infection, tunnel melting, extrusion of segments, neovascularisation along the tunnel.

Q18. What is hydrops?

- Break in DM with an entry of aqueous humour into the corneal stroma.
- Presents with a sudden drop in vision with whitening of the cornea.
- AS-OCT is done to confirm the diagnosis. It not only locates the DM break but also gives an appearance of a typical spongiform stroma with pockets of aqueous ("fluid clefts ") within the stroma.

- The condition is medically managed by cycloplegic, topical steroids and hyperosmolar drops and ointments.
- Surgical correction is by injection of air in the anterior chamber (called air descemetopexy).
- Some surgeons advocate primary DALK at the first presentation of acute hydrops. Most people will wait for 2–3 months for scar remodelling and DM break stabilization before undertaking DALK.

Q19. What investigations can you perform to evaluate for keratoconus?

Keratometry: To confirm the clinical diagnosis and identify any progression of the condition.

Pachymetry: An added value of pachymetry has emerged due to the new procedure called corneal collagen cross-linking for stopping the progression of corneal ectasia. This procedure can be done when the ectasia has been documented to be progressing but the corneal thickness is above 400 µm.

Corneal topography: Commonly used topography apparatus are Tomey (Placido's disc-based imaging), orbscan II (slit-scan and placido's disc-based imaging) and Pentacam (based on Scheimpflug imaging). The pentacm is useful in identifying posterior corneal changes which may be missed prior to refractive surgery. The characteristic topographic features of keratoconus are:

- Area of increased corneal power surrounded by concentric areas of decreasing power.
- Inferior–superior power asymmetry.
- Asymmetrical bow tie with skewed radial axes (Fig. 1.19).
- Thinning of the cornea at the apex.
- Inferior paracentral thinning (Fig. 1.20).

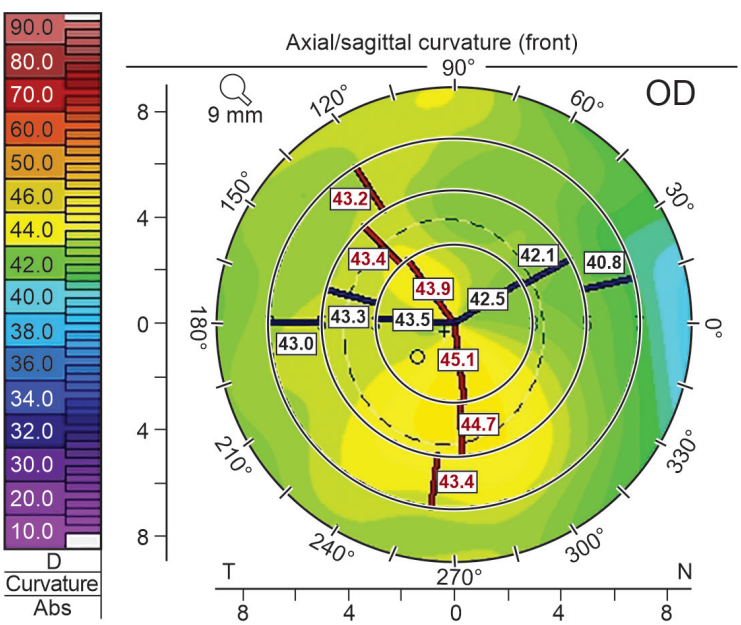

Fig. 1.19: Asymmetrical bow tie with skewed radial axes

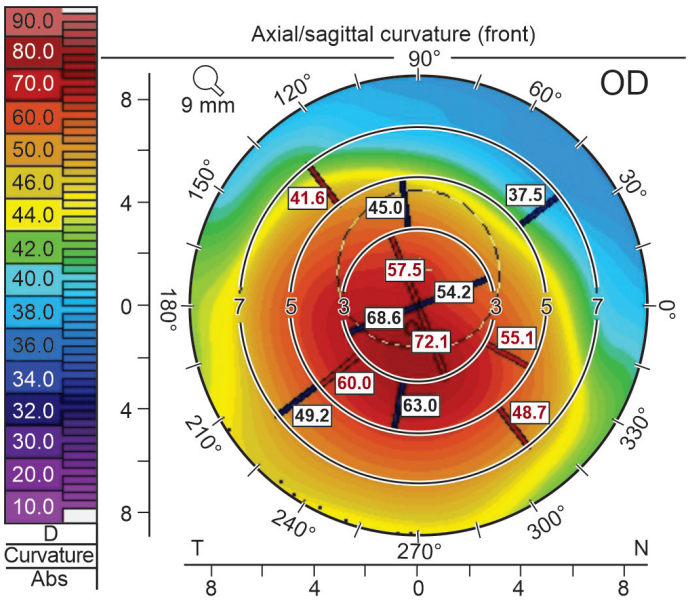

Fig. 1.20: Inferior paracentral thinning

Corneal topography indices for keratoconus are:

- Keratometry (K) value more than 47 D.
- Interior superior diopteric asymmetry (I-S) value > 1.4 D (Rabinowitz and McDonnell).
- KISA % is more than 100. KISA% is an algorithm that topographically quantifies the phenotypes of keratoconus.
- Asymmetric bow-tie with skewed radial axes pattern (AB/SRAX).

Q20. What are the other causes of prominent corneal nerves?

Ocular causes: Keratoconus, keratoconjunctivitis sicca, Fuchs' endothelial dystrophy, trauma, congenital glaucoma.

Systemic diseases: Leprosy, neuroflbromatosis, multiple endocrine neoplasia type IIb (medullary CA of the thyroid gland, parathyroid CA, pheochromocytoma), Refsum's disease, ichthyosis, a normal variant with increasing age.

Q21. What are types of contact lenses used in the management of keratoconus?

The following types of contact lenses are used:

- RGP lenses are the number one choice. Three fitting techniques are used.
  a. ***Apical clearance:*** The contact lens sits on the periphery and does not touch the central part of the cornea. This type of fitting decreases the chance of central scarring but may obstruct pre-corneal tear exchange due to tight peripheral fit.
  b. ***Apical touch:*** Here the contact lens touches the central cornea, so there is an increased chance of scarring on long-term use.
  c. ***Three points touch method:*** Most preferred method producing good vision and comfort where the contact lens rests on three points (central plus two mid-peripheral corneal zones).

- ***Scleral contact lens:*** They are indicated in presence of advanced ectasia as a substitute for keratoplasty. They provide good visual outcomes with stable centration and comfort to the patients on long-term use. The prototype is a ROSE P contact lens which sits on the sclera without touching the limbus or the cornea. Boston Ocular Surface Prosthesis (BOSP) is another prototype which is fluid-filled scleral contact lens. As these contact lenses do not touch the cornea, so there is less chance of corneal frictional damage.
- ***ROSE K contact lens:*** These lenses have a small central optical zone. They provide good visual outcomes with stable centration.
- ***Piggyback lens:*** This is basically a RGP lens fitted on a soft contact lens. This gives better comfort to the patient (due to the soft contact lens component) and the RGP component will provide stable vision.

CORNEAL DYSTROPHY

History

Age

Pediatric age group: Meesmann's juvenile hereditary epithelial dystrophy, Reis-Bucklers, lattice dystrophy, congenital hereditary endothelial dystrophy (CHED) and posterior polymorphous endothelial dystrophy (PPED) are common in this age group.

Puberty: Granular dystrophy

Adult age group: Macular dystrophy (third decade), epithelial BM dystrophy

Elderly populations: Fuchs' dystrophy.

Gender: Fuchs' dystrophy is common among females.

Chief complaints:

- Painless, progressive loss of vision in both the eyes.
- At an advanced stage, profound loss of vision.
- Sometimes accompanied by pain, redness, watering and difficulty to tolerate bright light.

History of present illness: The entity is mostly bilateral but it may be asymmetric. Initially the patient may not be symptomatic. With increasing age, the disease becomes more symptomatic with typical lesions appearing on the cornea. In most cases of endothelial dystrophy, initially, there may be early morning visual disturbances (signifying early endothelial failure with early deep stromal edema).

Past history: History of recurrent attacks of pain, redness, watering and photophobia (recurrent epithelial erosion syndrome) may be present. The following entities might present with recurrent erosions: EBMD (Cogan's), Meesmann's juvenile hereditary epithelial dystrophy, Reis-Bucklers' dystrophy, and lattice dystrophy.

Examination

General Examination

Cranial and peripheral neuropathy especially facial nerve palsy, skin laxity, renal and heart failure are seen in type II lattice dystrophy (familial amyloidosis—Meretoja syndrome).

Ocular Examination

Vision: Most of the entries are initially asymptomatic. Vision may be reduced during the episode of recurrent epithelial erosion but is regained once the epithelial erosion heals. Profound vision loss occurs in advanced cases of stromal dystrophy and endothelial dystrophy.

Ocular adnexa and conjunctiva: They remain normal.

Limbus: Ciliary congestion may be present in cases presenting with recurrent epithelial erosion syndrome.

IOP: Note IOP. PPED may be associated with angle closure glaucoma.

Cornea: Each dystrophy has a characteristic features:

- ***Reis-Bucklers' dystrophy:*** Presents with a superficial ring or polygonal opacities.
- ***Meesmann's juvenile hereditary epithelial dystrophy:*** Small round central epithelial cysts in the interpalpebral area are classic features.
- ***Epithelial basement membrane dystrophy (Cogan):*** Fingerprint, map-like, dots and micro-cystic lesions are found in the subepithelial region (Fig. 1.21).
- ***Lattice dystrophy:*** Typical multiple, fine wavy, spidery or arborizing lines at the stromal layer involving both central and peripheral part of cornea are initial features. With passage of time, they progress deeper into the central cornea with intervening stromal haze (Fig. 1.22).
- ***Granular dystrophy:*** Multiple breadcrumbs-like opacities at the stromal level with normal intervening cornea are classical features. With time, the number of opacities increases but they never reach up to the limbus and they coalesce together to form a confluent lesion (Figs 1.23 and 1.24).
- ***Macular dystrophy:*** Grayish white opacities appear in the central part of the deep stroma which joins together later to produce diffuse clouding up to the limbus by the third decade (Fig. 1.25).
- ***Fuchs' dystrophy:*** Central guttae and stromal edema are early features. Epithelial bullae (some of them may be ruptured) with stromal scarring and degenerative pannus at the basement membrane are noted in an advanced case.

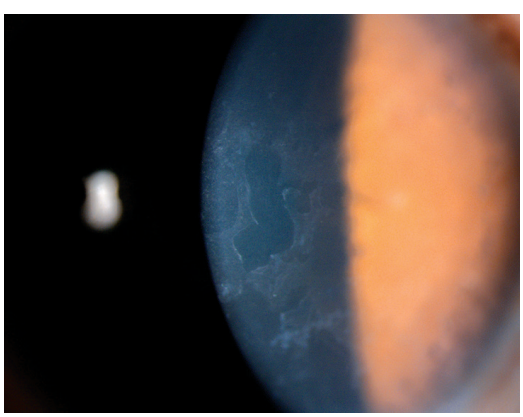

Fig. 1.21: Epithelium basement membrane corneal dystrophy

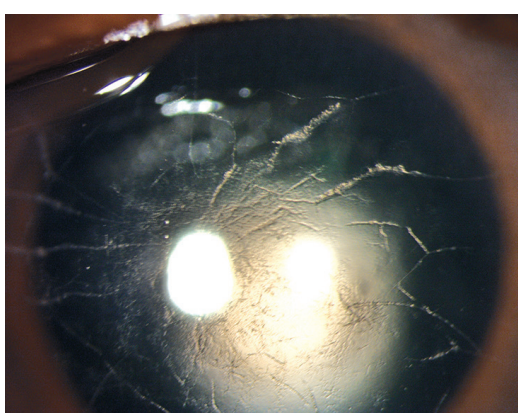

Fig. 1.22: Lattice corneal dystrophy

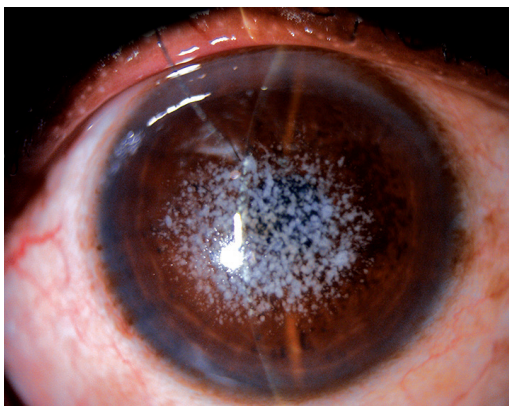

Fig. 1.23: Granular corneal dystrophy

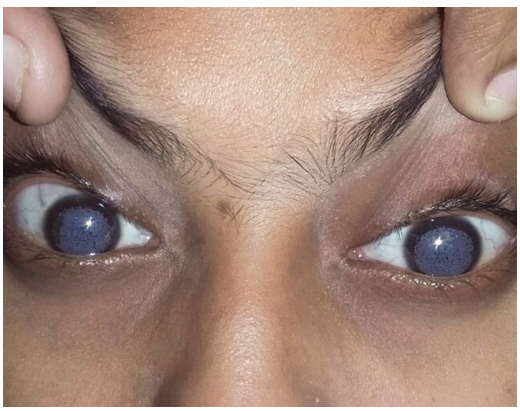

Fig. 1.24: Granular dystrophy

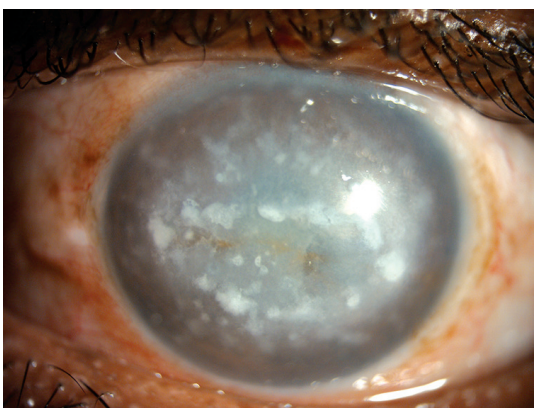

Fig. 1.25: Macular corneal dystrophy

- ***Posterior polymorphous endothelial dystrophy (PPED):*** Subtle vesicles or guttae-like structures at the posterior corneal surface are noted.

Fundus: Viewing of fundus is not possible in presence of significant corneal opacification.
Provisional diagnosis: A case of (------) corneal dystrophy.

Frequently Asked Questions

Q1. How can you differentiate corneal dystrophies from corneal degenerations?

- Corneal dystrophy is an inherited (AD), usually early onset, slowly progressive, a bilateral corneal disease involving the central part of the cornea.
- Corneal degeneration is a sporadic, age related, late onset, unilateral/bilateral disease involving the peripheral part of cornea.

Note: Macular dystrophy is inherited as autosomal dominant (AD) and peripheral cornea may be involved in macular and Meesmann dystrophies.

Q2. What are the pathological features of epithelial corneal dystrophies?

Epithelial dystrophies affect the epithelium, basement membrane (BM) and Bowman's membrane of the cornea. The main differentiating points are:

Cystic (map dot)	Reis-Bucklers	Meesmann
• **Presentation:** Mostly asymptomatic, recurrent corneal erosion, lesions look like maps, finger prints, dots and lines. • **Inheritance:** AD, may be sporadic as well. • **Histopathology:** Abnormal epithelial cells, fibrillar material, microcystic changes, thickened BM, duplication of BM. • **Management:** Treat recurrent erosions with tear substitutes and BCL.	• **Presentation:** Honeycomb appearance, recurrent erosions and reduced corneal sensation. • **Inheritance:** AD, C1 in IC3D • **Histopathology:** Granular deposits in BM that stain with Masson trichrome. • **Management:** Management of recurrent erosions, high chance of recurrence following penetrating keratoplasty.	• **Inheritance:** AD, C1 in IC3D. • **Histopathology:** PAS positive substance deposited in BM. • **Presentation:** Photophobia, small epithelial cysts. • **Management:** Conservative.

Q3. What are the pathological features of stromal corneal dystrophies?

Lattice dystrophy (C1 in IC3D)	Granular dystrophy (C1 in IC3D)	Macular dystrophy (C1 in IC3D)
• **Presentation:** Linear branching pattern sparing peripheral cornea and clear intervening areas. • **Inheritance:** AD • **Histopathology:** Amyloid material deposited which can be stained with Congo red and PAS. • **Types:** Type 1 is the classic type. Type 2 is called Meretoja syndrome: Elderly patient, a smaller number of lines at the central cornea, more lines at the periphery, associated systemic features like Hound facies, brow ptosis, bilateral 7th cranial nerve palsy, dermatochalasis, lagophthalmos and peripheral neuropathy. • **Management:** Optical PK	• **Presentation:** Multiple bread crumbs like stromal deposition with intervening clear stroma. • **Inheritance:** AD • **Histopathology:** Hyaline material, stained with Masson trichrome. • **Types:** Type 1 is the classic type and seen in elderly patients. • Type 2 is also called Avellino syndrome (combination of granular and lattice dystrophy. • **Management:** Early optical PK is indicated.	• **Presentation:** Younger patients than other two types of stromal dystrophy. Cornea: Diffusely cloudy stroma sparing the periphery. • **Histopathology:** Mucopolysaccharides, stained with Alcian blue. • **Inheritance:** AR • **Management:** Early optical PK. The highest chance of recurrence among all types of stromal dystrophies.

Q4. How can you manage a case of corneal dystrophy?

- **Epithelial BM dystrophy:** Lamellar or penetrating keratoplasty.
- **Meesmann's dystrophy:** Usually does not need any treatment.

- **Stromal dystrophy:** Penetrating keratoplasty in most cases by middle age.
- **Granular dystrophy:** PTK (excimer laser) to treat superficial recurrences.
- **Endothelial dystrophy without stromal scarring:** Endothelial transplantation (DSEK, DSAEK, UTDSAEK or DMEK).
- **Endothelial dystrophy with significant stromal scarring:** Penetrating keratoplasty.

(*DSEK:* Descemet stripping endothelial keratoplasty, *DSAEK:* Descemet stripping automated endothelial keratoplasty, *UTDSAEK:* Ultra-thin DSAEK, DMEK: Descemet membrane endothelial keratoplasty).

Q5. What are the advantages of DALK over PK?

Advantages of DALK are early visual stabilization with less postoperative astigmatism, better wound strength and lesser risk for rejection which allows earlier steroid taper.

Complications of DALK: Intraoperative DM rupture, double anterior chamber formation, interface haze, higher order aberration.

Q6. What are the features of amyloidosis?

Amyloid is an eosinophilic hyaline substance with some typical staining characteristics.

The manifestations can be classified as

Primary localized amyloidosis: The most common form of ocular amyloidosis with conjunctival involvement, e.g. lattice dystrophy.

- Secondary localized amyloidosis: Long-standing ocular inflammation, e.g. trachoma, interstitial keratitis.
- Primary systemic amyloidosis.
- Secondary systemic amyloidosis: Long-standing chronic systemic diseases, e.g. RA, leprosy.

Staining characteristics:

- Congo red: Positive birefringence and dichroism.
- Crystal violet: Metachromasia.
- Fluorescence in ultraviolet light with thioflavin T stain.

Electron microscopic features:

- Typical filamentous structure on electron microscopy

Q7. What is crystalline dystrophy of Schnyder?

Crystalline dystrophy of Schnyder is stromal dystrophy associated with abnormal cholesterol metabolism.

The clinical characteristics include:

- 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%

Q8. What are the pathological features of endothelial dystrophies?

Endothelial dystrophies affect the Descemet's membrane and endothelium of the the cornea.

There are three classical types:

Fuchs' dystrophy (C1, C2 or C3 in IC3D)	**Posterior polymorphous dystrophy** (PPED, C1 or C2 in IC3D)	**Congenital hereditary endothelial dystrophy** (CHED, C1 or C2 in IC3D)
• Middle aged females. • Inheritance: AD. • Corneal guttata. • Initially deep stromal oedema. • BM scarring. • Epithelial oedema and bullous keratopathy in advanced cases. • Abnormal deposition of collagen material in DM. • Early onset FD is a distinct entity with equal gender predominance, Presentation at the first decade and associated with thicker DM. • Treatment: Endothelial transplantation (EK).	• Presentation at birth or at a young age. • Inheritance: AD/AR. • Vesicles and "tram track" opacities on DM give rise to "polymorphous" picture. • Associated disease: Alport's syndrome and angle closure glaucoma. • Optical PK has a poor prognosis.	• Inheritance: AR. • Diffusely thickened and opacified stroma prevents proper visualization of endothelium. • Treatment: Optical PK.

Q9. How can you differentiate corneal guttae from pseudo-guttae?

- Pseudo-guttae are temporary guttae due to transient corneal oedema due to varied aetiologies (like intraocular inflammation, trauma, toxins liberated by invading organisms, etc.). They usually disappear with a resolution of individual causes.
- True guttae are usually associated with Fuchs' dystrophy, PPED, macular dystrophy and interstitial keratitis (IK).

Q10. How do you manage a patient with Fuchs' endothelial dystrophy and cataract?

These are two clinical problems which must be managed simultaneously, depending on the severity of each condition. Both patient and ocular factors are to be taken into consideration.

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 corneal decompensation:
   - History of blurring of vision in the morning

- Greater than 10% difference in corneal thickness readings taken in the day
- Severity of oedema on clinical examination
- Pachymetry >650 µm corneal thickness
- Endothelial cell count <1000 cells/mm^2

Special notes:

a. Do cataract surgery only if the cornea is reasonably clear and allow cataract surgery with thickness less than 600 µm and endothelial cell count greater than 1000/square mm.
b. Consider a combined EK with cataract surgery if CCT is more than 640 µm and the specular count is less than 800 cells/square mm.

Q11. What is IC3D classification of corneal dystrophy?

The International Committee for classification of corneal dystrophy includes various parameters (like clinical, genetic, histopathological, etc.) to classify corneal dystrophies. This is known as IC3D classification.

Categories:

- ***Category 1:*** Well-defined dystrophy where the gene has been identified and mapped with a known specific mutation.
- ***Category 2:*** A well-defined dystrophy which has been mapped to one or more chromosome loci but the gene is yet to be identified.
- ***Category 3:*** Well-defined dystrophy where the chromosome locus is not yet discovered.
- ***Category 4:*** Suspected new or already documented entities although the evidence for being a distinct entity is yet to be confirmed.

Q12. What are Hassall-Henle bodies?

They are normally present in elderly population resembling guttae of FD but unlike classical guttae, they are located in the corneal periphery and are not associated with progressive corneal oedema.

Q13. What are the causes of crystalline keratopathy?

Infectious diseases: It occurs when there is a suboptimal inflammatory response to organisms (e.g. *Streptococcus viridians*, *Staphylococcus epidermidis*).

Non-infectious diseases:

- Lipid deposit
- Crystalline dystrophy of Schnyder
- ***Mineral deposition:*** Argyrosis (silver), band keratopathy (calcium), chrysiasis (gold)
- ***Protein deposition:*** Cystinosis, dysproteinemia (multiple myeloma)
- ***Drug deposition:*** Topical ciprofloxacin, amiodarone, tamoxifen, phenothiazines, indomethacin, chloroquine
- ***Idiopathic:*** Crystalline dystrophy of Bietti

Q14. How do you clinically approach a patient of vortex keratopathy?

History of: Arthritis (indomethacin), breast CA (tamoxifen), cardiac diseases (amiodarone), connective tissue diseases (chloroquine) and use of chlorpromazine.

On slit lamp examination: Look for greyish/brownish corneal epithelial deposits in both eyes radiating from a point below the pupillary axis. Search for lens opacity (amiodarone, Fabry's disease), bull's eye maculopathy (chloroquine), crystalline retinopathy (tamoxifen) and optic disc changes (tamoxifen).

Q15. Define mucopolysaccharidosis.

A mucopolysaccharidosis are a group of systemic storage diseases due to deflciency of lysosomal enzymes. There are various 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.

Q16. What is Wilson's disease?

Wilson's disease is a metabolic systemic disease characterized by a deflciency in alpha-2 globulin (ceruloplasmin) resulting in the deposition of copper throughout the body.

- **Systemic features:** Flapping tremors, spasticity, dysarthria, dysphagia and psychiatric problem without mental retardation.
- Laboratory investigations reveal normal total serum copper with low serum ceruloplasmin and high urine copper. Hepatic involvement is seen in 40% of patients.
- **Ocular features:** Classical feature is the Kayser-Fleischer ring (KF ring) which is found in 90% of patients. This is present in almost 100% of cases if CNS is involved. Copper deposition occurs in Descemet's membrane, in the crystalline lens causing green "sunflower" cataracts and in ciliary muscle resulting in accommodation difficulty.
- **Treatment:** Decrease copper intake and penicillamine (KF ring will resolve with treatment).

FUCHS' ENDOTHELIAL DYSTROPHY

History

Gender: The entity is more common in females (F: M= 4:1).

Age: Fuchs' dystrophy is a disease presenting in the 6th decade of life.

Race: More common in Whites and Blacks but rare in Asians.

Family history: Often present.

Chief complaints: The patient presents with gradual dimness of vision without pain.

History of present illness: Initially, patients are asymptomatic. Patients present with mild reduction of vision without any pain and other eye symptoms. The loss of vision is maximum in the morning and the vision improves as the day progresses. Later in advanced cases, profound vision loss happens with pain, watering and difficulty in tolerating bright light.

History of past illness: Inquire about the past history of trauma, intraocular surgery and herpetic eye disease.

Ocular Examination

Vision: Variable vision (depends on the stage)
Eyelid: Normal or mild oedema maybe there

Cornea (slit lamp biomicroscope)

- Corneal guttata (excrescences of Descemet's membrane) on specular reflection—the earliest sign (Fig. 1.26).
- Descemet's membrane is roughened and irregular producing a beaten metal appearance on specular reflection.
- Fine KPs adherent to the endothelium.
- Corneal thickness is increased (initially not affected).
- Stromal oedema.
- Subepithelial oedema with microcystic bullae in advanced stages.
- Subepithelial fibrosis (basement membrane scarring) and pannus in advanced cases.
- Recurrent corneal erosion.
- Prominent corneal nerves may be present.

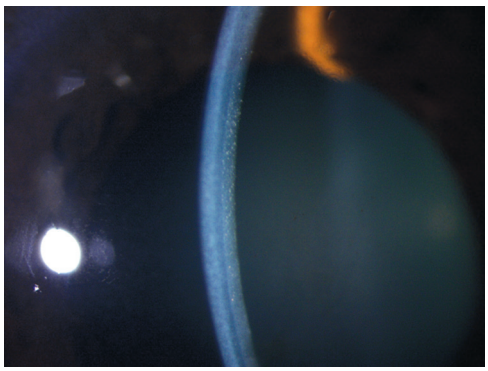

Fig. 1.26: Corneal guttata

Anterior chamber: Deep with some degree of cataract (in phakic cases) and PC-IOL may be there in post-operative cases.

Iris: May show patches of depigmentation.

Gonioscopy: Angles are open and unremarkable.

Posterior segment: Fundus findings are unremarkable. Disc changes are seen in cases of secondary glaucoma.

Provisional diagnosis: This is a case of Fuchs' dystrophy.

Frequently Asked Questions

Q1. What is Fuchs' dystrophy?

	Onset	Laterality	Iris features	Cornea	Gonioscopy	IOP	Specular microscopy
Rieger anomaly and syndrome	Early childhood/ adulthood	Bilateral	Iris stromal hypoplasia, ectropion uveae, corectopia, full-thickness iris defects	Posterior embryotoxon, corneal opacity	Broad leaves of iris stroma adhere to the cornea anterior to the Schwalbe line	50% of patients have raised IOP	Normal endothelial pattern
Posterior polymorphous corneal dystrophy (PPCD)	At birth or soon after birth to middle age	Bilateral	Mild iris abnormalities	Subtle vesicular (doughnut-like) endothelial lesions with diffuse corneal opacity at the posterior part of the cornea (polymorphous features)	PAS	Raised	Vesicles, bands, polymegathism with decreased endothelial cell count

(Contd.)

(Contd.)

	Onset	laterality	Iris features	Cornea	Gonioscopy	IOP	Specular microscopy
Fuchs' endothelial dystrophy	Old age, female preponderance	Bilateral	No iris abnormalities	Central stromal edema, cornea guttata (irregular warts or excrescences of Descemet's membrane)	No PAS	Elevated	Polymorphism, polymegathism with decreased cell count, beaten metal appearance
Congenital hereditary endothelial dystrophy (CHED)	Since birth	bilateral	No iris abnormalities	Diffuse corneal oedema, blue-grey, ground glass appearance to total opacification	–	IOP normal	–
ICE syndrome	Adult to middle age	Unilateral	Variable iris atrophy, corectopia, polycoria, ectropion uveae, nodules, holes, naevus	Diffuse corneal edema, typically shows a hammered silver appearance in the posterior surface of the cornea	Extensive PAS is the hallmark of ICE syndrome	Elevated in 50% cases	Specular microscopy shows polymegathism and pleomorphism

It is a bilateral non-inflammatory, progressive loss of endothelial cells characterised by guttae, stromal edema, Descemet's fold, and microcystic corneal edema.

Q2. What is the D/D of Fuchs' dystrophy (FD)?

- **ICE (iridocorneal endothelial syndrome):** ICE syndrome presents in young females with a classic hammered silver appearance of cornea and glaucoma. Classical iris signs are essential iris atrophy, corectopia and polycoria.
- **CHED:** CHED presents in the first decade (equal gender predominance) with severe corneal oedema. This causes specular microscopy impossible.
- **PPED:** This entity presents among the early teenage groups with no gender predilection. Classical features include polymorphous figures (vesicles, bands, etc.) at the posterior part of the cornea with glaucoma.

Q3. Which investigation would you suggest in this case?

a. **Specular microscopy:** It shows pleomorphism, polymegathism, and the presence of guttata appearing as dark bodies. Total cell count diminishes over time. It is the method of choice.

b. **Confocal microscopy:** It is a valuable tool in presence of corneal edema where specular microscopy fails. It confirms the presence of guttate appearing as hyporeflective images.

c. **Anterior segment OCT (AS-OCT):** It will show the extent of stromal swelling, any secondary stromal scarring and the presence of bullae. Intraoperative OCT (i-OCT) is an invaluable tool in patients undergoing endothelial keratoplasty (EK) to guide proper graft orientation and graft adherence in real-time. In post-EK cases, AS-OCT will determine the position, apposition of donor lenticule, edge of lenticule and any host-donor lenticule interface abnormalities.
d. **Pachymetry:** Central corneal thickness (CCT) will help formulate the management plan. Increasing CCT is an indirect indicator of endothelial stress with gradual endothelial failure. In post-endothelial keratoplasty cases, serial measurements of CCT (besides specular microscopy) will give a fair idea of endothelial reserve in the graft.

Q4. What are the pathological features of Fuchs' endothelial dystrophies?

Fuchs' endothelial dystrophy is associated with a mutation in the gene that codes for the alpha 2 chain of type VIII collagen. It affects Descemet's membrane first followed by the endothelial layer of the cornea. On electron microscopy, Descemet's membrane shows an abnormal posterior banded layer and a fibrillar layer making it thickened. The changes in Descemet's membrane serve as an indicator of the dysfunction of the endothelium. Endothelial cells are attenuated and lost over time. Cell loss is considered due to apoptosis.

Q5. What are the different stages of the Fuchs' endothelial dystrophy classified clinically?

Stages	Corneal features	Particular layers involvement	Vision
Stage 1	Corneal guttata with fine pigments dusting over the endothelium	Only central Descemet's membrane	Normal
Stage 2	Guttata enlarge and fuse with each other producing roughened Descemet's and a beaten metal appearance, localised or entire corneal edema, epithelial microcystic edema	Descemet's membrane, endothelium, posterior or entire stroma and epithelium	Vision is affected
Stage 3	Above features plus scarring in Bowman's layer, pannus formation, recurrent epithelial erosions	All layers are involved	Profound vision loss

Q6. How can you differentiate corneal guttae from pseudo-guttae?

Pseudo-guttae are temporary guttae due to transient corneal oedema due to varied aetiologies such as intraocular inflammation, trauma, and toxins liberated by invading organisms. They usually disappear with the resolution of individual causes.

True guttae are usually associated with Fuchs' dystrophy, PPED, macular dystrophy and interstitial keratitis (IK).

Q7. What are Hassall-Henle bodies?

They are normally present in elderly populations resembling guttae of FD but unlike classical guttae, they are located in the corneal periphery and are not associated with progressive corneal oedema.

Q8. How can you manage the case?

The definitive management is corneal transplantation. If the patient presents late with extensive stromal scarring and endothelial decompensation, penetrating

keratoplasty (PK) is advised. If the patient presents early, endothelial keratoplasty (EK) is the procedure of choice.

Q9. How do you manage Fuch's endothelial dystrophy and cataract patients?

These two clinical problems must be managed simultaneously, depending on the severity of each condition. Both patient and ocular factors are to be taken into consideration.

1. **Patient factors-consider surgery early in:**
   - Young age
   - High visual requirement
   - Poor vision in the fellow eye
2. **Ocular factors**
   - Severity of cataract
   - Severity of corneal decompensation
   - History of blurred vision in the morning
   - Greater than 10% difference in corneal thickness readings taken during the day
   - Severity of oedema on clinical examination
   - Pachymetry >650 µm corneal thickness
   - Endothelial cell count <1000 cells/mm^2

Special notes:

I. Do cataract surgery only if the cornea is reasonably clear and has a thickness of less than 600 µm and endothelial cell count greater than 1000/square mm.

II. Consider a combined EK with cataract surgery if CCT is more than 640 µm and the specular count is less than 800 cells/square mm.

Q10. What are the types of endothelial keratoplasty (EK)?

EK is of two types: Descemet stripping endothelial keratoplasty (DSEK) and Descemet membrane endothelial keratoplasty (DMEK).

- ***DSEK:*** Descemet's stripping endothelial keratoplasty (manual or automated). Host DM and endothelium are replaced by donor DM and endothelium along with minimal posterior stroma (around 50–80 µm) in the graft.
- ***DMEK:*** Descemet's membrane endothelial keratoplasty. Host DM and endothelium are replaced by donor DM and endothelium. No stromal tissue is incorporated into the graft.

Q11. What are the advantages and disadvantages of endothelial keratoplasty?

Advantages of endothelial keratoplasty

- Reduced astigmatism
- Smaller wound—lower risk of wound dehiscence
- Replaceable and repeatable
- Reduced risk of rejection (stromal)

Disadvantages of endothelial keratoplasty

- Interface scarring
- Technically more difficult

Q12. What are the complications of endothelial keratoplasty?

Early

- Graft detachment
- Glaucoma
- Delayed epithelial healing

Late

- Glaucoma: Due to PAS formation
- Endothelial rejection
- Endothelial failure

Q13. What are the newer experimental techniques in endothelial failure cases?

- Intracameral injection of Rho-kinase inhibitor. This is done in Fuchs' dystrophy cases presenting with large central guttae.
- A central descemetorrhexis is done followed by intracameral injection of Rho-kinase inhibitor.
- Intracameral cultured human endothelial cells injection.

PETERS' ANOMALY

History

Age of presentation: Usually presents since birth

Race and gender: No predilection

Presentation:

- Parents notice whiteness of the cornea in one eye or both eyes since birth.
- Patients are often seen initially by the paediatrician and found to have an abnormal red reflex with corneal opacity.
- Nystagmus or abnormal vision may be noted by the parents.

Systemic Examination

Systemic association: Include congenital cardiac defects, craniofacial dysplasia and skeletal, central nervous system, and urogenital anomalies. Systemic findings are seen in up to 60% of patients. Bilateral Peters is more strongly associated with systemic malformations (71.8%) as compared to unilateral Peters anomaly (36.8%).

Ocular Examination

Visual acuity: Subnormal vision with amblyopia is a usual feature.

Eyeball: Microphthalmos is very common.

Cornea: Presents with unilateral or bilateral central/paracentral corneal opacities of variable size and density (Fig. 1.27). Large cornea if secondary glaucoma exists. Cornea plana and sclerocornea may be there.

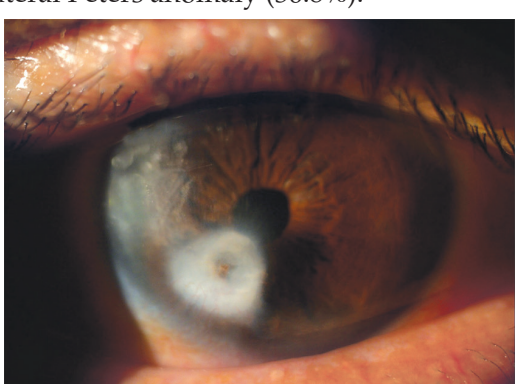

Fig. 1.27: Corneal opacity in Peters' anomaly

Iris: Iris hypoplasia, iris coloboma, correctopia, iris strands arising from collarette attached to the cornea and iridocorneal adhesions may be present.

	Peters' anomaly	Sclerocornea	Dermoid	CHED	PPCD
Cornea	Central corneal opacity with the normal periphery	Full–thickness opacity encroaches from the periphery	Yellow-white elevated nodules may contain mesodermal appendages	A blueish-grey ground-glass appearance but can be as severe as complete corneal opacification	Diffusely scattered, well-circumscribed areas of stromal haze localized to the posterior 1/3 of the stroma. It is less severe to CHED
Lens	Cataractous	Normal	Normal	Normal	Normal
Laterality	Mostly bilateral	Bilateral	Unilateral	Bilateral	Bilateral

Lens: Anterior polar cataract develops as a result of kerato-lenticular adhesion. This is an important sign of type 2 Peters' anomaly.

AC depth: May be shallow and irregular.

Gonioscopy: PAS and angle abnormalities are very common.

IOP: High IOP noted in 50–70% of patients.

Fundus: Look for fundal coloboma, PHPV, optic nerve hypoplasia

Provisional diagnosis: This is a case of Peters' anomaly.

Frequently Asked Questions

Q1. What is Peters' anomaly?

Peters' anomaly is a congenital disorder, characterized by a central corneal opacity (leucoma) due to defects in the posterior stroma, Descemet membrane, and endothelium.

Q2. What are the types of Peters' anomaly?

It can be classified into 2 types:

Type I (milder form): Involves the iris, corneal endothelium, and Descemet's membrane.

Type II (severe form): Involves the lens in addition to the above. It is mostly bilateral.

Q3. What is Peters' plus syndrome?

Peters' plus syndrome is an autosomal recessive congenital disorder affecting the beta-1, 3-galactosyltransferase-like glycosyltransferase gene (B3GALTL) on chromosome 13. It includes short stature, developmental delay, dysmorphic facial features, and cardiac, genitourinary, and central nervous system malformations.

Q4. What is the aetiology of Peters' anomaly?

Peters' anomaly falls within the spectrum of anterior segment dysgenesis in which abnormal cleavage of the anterior chamber occurs. A central part of the cornea does not develop properly causing absent DM and endothelium in the central part of the cornea (called 'internal ulcer of von Hippel'). It has been

postulated that failure of separation of the cornea from the iris causes this phenomenon. Multiple genetic loci have been identified as causes for Peters' anomaly including PAX6, PITX2, PITX3, FOXC1, FOXE3, CYP1B1, MAF and MYOC. Peters can occur sporadically, but autosomal dominant and recessive inheritance have been reported.

Q5. Enumerate the risk factors for the development of Peters' anomaly.

The following risk factors are said to be associated with Peters' anomaly:

- Premature infants
- Heparan sulfate deficiency
- Fetal alcohol syndrome
- Intrauterine infection and teratogenic exposures during pregnancy

Q6. What is the differential diagnosis of Peters' anomaly?

1. **Congenital corneal opacity (STUMPED)**
   S : Sclerocornea
   T : Tears in Descemet's membrane
   U : Ulcers
   M: Metabolic disorders
   P : Peters
   E : Endothelial dystrophy [congenital hereditary endothelial dystrophy (CHED), posterior polymorphous corneal dystrophy (PPCD)].
   D : Dermoid
2. **Anterior segment dysgenesis**
   - Axenfeld-Rieger anomaly and syndrome
   - Iridocorneal endothelial syndrome

Q7. Outline the management of Peters' anomaly.

- **Perform EUA.** Assess the corneal opacity, corneal diameter, size and shape of the pupil, iris, lens, IOP and fundal glow.
- **Ultrasound-biomicroscopy:** It is used to examine the anatomic relationship between the lens, iris and cornea. Ultrasound biomicroscopy is useful in detecting central corneal opacity, the thinning, or absence of Descemet's membrane, angle status and iridocorneal and keratolenticular adhesions.
- **Anterior segment OCT:** It shows a thinned-out opaque central cornea with kerato-lenticular and iridocorneal adhesions.
- Treatment of corneal opacity
- Pupil dilatation with phenylephrine for a very small central corneal opacity or patient waiting for optical iridectomy. Atropine and cyclopentolate are avoided for this purpose.
- **Peripheral optical iridectomy:** For a small central corneal opacity with a clear lens. This surgery can be performed even 1 week after birth.
- **Penetrating keratoplasty:** For a large disabling corneal opacity. The surgery should be performed at age 2–12 months. Peters anomaly type 1 has a significantly higher rate of graft clarity (80%) than type 2 (20%).
- **Penetrating keratoplasty with lensectomy/vitrectomy:** For a large corneal opacity and cataract. Pupilloplasty or iridoplasty is also performed.

- Treatment of glaucoma
- Topical antiglaucoma medication
- Trabeculotomy with trabeculectomy
- Glaucoma valve surgery or tube shunt
- Cryoablation for advanced cases

Q8. Describe histopathological features in Peters' anomaly.

Histologically, in Peters type I, the cornea at the area of opacity has an endothelium with underlying iridocorneal synechiae that extend from the iris collarette to the border of the corneal opacity. There are diverse histological changes in Descemet's membrane. Most commonly, Descemet's membrane of the cornea is absent.

IRIDOCORNEAL ENDOTHELIAL (ICE) SYNDROME

History

Age: Commonly seen in the age group between 20–50 years.

Race: No predilection.

Laterality: Typically, unilateral.

Gender: Mostly seen among women.

Clinical presentation: Many cases are asymptomatic, however, patients may come with decreased vision, pain, glare, monocular double vision, multiple images, and noticeable iris changes. Pain may be worse in the morning and improves later in the day. In advanced cases, vision drops significantly and pain persists throughout the day.

Hereditary predisposition: Not found.

Systemic associations: Not found.

Ocular Examination

BCVA: Initially vision is not affected asymptomatic but with progressive PAS and advanced corneal oedema; vision drops along with pain, watering and photophobia.

Cornea: Typically shows a hammered silver appearance in the posterior surface of the cornea similar to Fuchs' endothelial dystrophy in all types of ICE syndrome. Later corneal oedema sets in causing reduced visual acuity and pain.

Iris:

- Normal or mild iris atrophy with correctopia—suggesting Chandler syndrome (Fig. 1.28).
- Iris shows variable iris atrophy, stromal protrusion or pedunculated, pigmented iris nodules resembling iris nevi—suggesting Cogan-Reese syndrome.

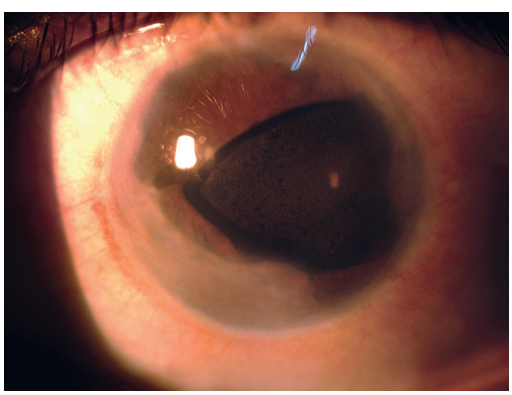

Fig. 1.28: Iridocorneal endothelial syndrome (ICE)

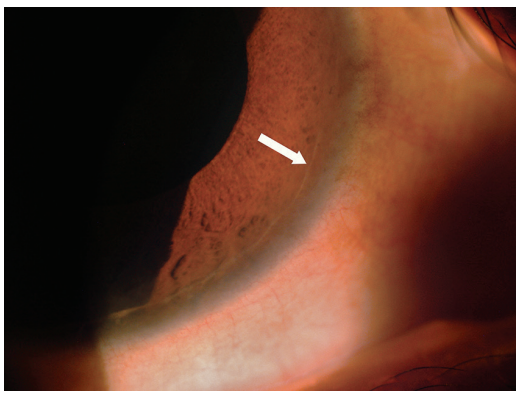

Fig. 1.29: Posterior embryotoxon

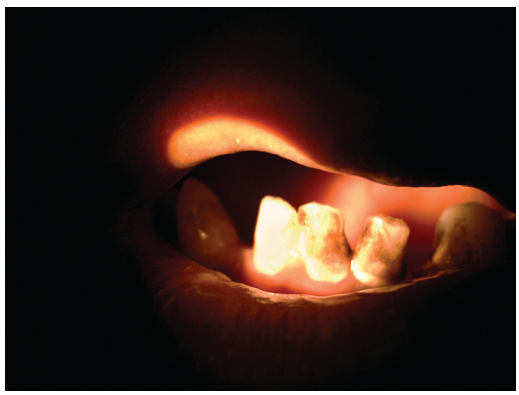

Fig. 1.30: Dental anomalies in Rieger's syndrome

- Extensive iris atrophy with correctopia, polycoria, ectropion uveae, stretch holes and melt holes—suggesting progressive or essential iris atrophy.

Table 1.1: Clinical features of the different ICE syndrome subtypes

Types of ICE syndrome	Iris	Pupil	Cornea	Anterior chamber angle
Chandler syndrome	Near normal or mild iris atrophy, no full-thickness holes	Correctopia, ectropion uveae rare	Early and marked oedema, endothelial dystrophy, and ICE-cells at confocal microscopy	PAS
Progressive iris atrophy	Marked iris atrophy with full-thickness hole(s)	Polycoria, ectropion uveae	Endothelial dystrophy, ICE-cells at confocal microscopy, and corneal oedema may occur	PAS
Cogan-Reese syndrome or iris-nevus syndrome	Normal or variable iris atrophy (50%), pigmented, pedunculated nodules (hallmark sign) and iris atrophy	Correctopia, ectropion uveae	Endothelial dystrophy, ICE-cells at confocal microscopy, and corneal oedema may occur	PAS

Gonioscopy: Extensive and progressive peripheral anterior synechiae are the hallmark of ICE syndrome. Abnormal corneal endothelial cells act like epithelial cells and may grow into the angle to block trabecular meshwork outflow.

IOP: It is associated with high IOP in more than 50% of patients.

Fundus: Except for optic disc changes rest of the fundus is normal.

Provisional diagnosis: This is a case of ICE syndrome.

Frequently Asked Questions

Q1. What is iridocorneal endothelial (ICE) syndromes?

ICE syndromes are a spectrum of diseases characterized by a "beaten metal appearance" of the corneal endothelium, corneal oedema, increased intraocular pressure, peripheral anterior synechiae, and iris changes.

Q2. What is the mechanism of ICE syndrome?

The exact mechanism is unknown, however, there appears to be a component of abnormal corneal endothelium that proliferates onto the iris forming a membrane that then obstructs the trabecular meshwork, leading to iris distortion. Clinical features of the different ICE syndrome subtypes have been described in Table 1.1.

Q3. What are the differences between various iris holes?

Stretch holes develop 180 away from the most prominent membrane covering the iris. Melt holes develop in areas of the iris that are not under stretch or traction.

Q4. What is the mechanism of elevated IOP in this case?

A cellular membrane is formed which passes over the iris and passes across trabecular meshwork. This causes progressive and extensive PAS with the rise of IOP.

Q5. What is the mechanism of correctopia in this case?

Contraction of the membrane coating the iris will pull the iris towards the most prominent membrane. This causes displaced/ectopic pupils (correctopia).

Q6. What are the roles of confocal microscopy in this case?

Confocal microscopy demonstrates epithelial-like endothelial cells with hyper-reflective nuclei (ICE cell).

Q7. Outline the management of this case.

Initially, glaucoma is managed by aqueous suppressants. For corneal decompensation, endothelial keratoplasty is advised if not associated with significant stromal scarring. In advanced corneal decompensation, penetrating keratoplasty is performed.

Q8. What are the challenges of endothelial keratoplasty in ICE syndrome?

PAS is to be lysed before graft introduction. Bleeding from the anterior chamber angle (with subsequent fibrinous reaction) and recurrence of PAS may cause graft dislocation in the postoperative period.

Q9. What are the causes of poor outcomes of trabeculectomy in this case?

Membranes can obstruct the sclerotomy as well as the inner lining of the filtering bleb. These may contribute to the failure of trabeculectomy in ICE syndrome. Even the valve orifices may be occluded by the membranes.

There are three classical types

Fuchs' dystrophy (C1, C2 or C3 in IC3D)

- Middle-aged females.
- Inheritance: AD.
- Corneal guttata.
- Initially deep stromal oedema.
- BM scarring.
- Epithelial oedema and bullous keratopathy in advanced cases.
- Abnormal deposition of collagen material in DM.
- Early onset FD is a distinct entity with equal gender predominance.
- Presentation at the first decade and associated with thicker DM.
- Treatment: Endothelial transplantation (EK).

- Presentation at birth or at a young age.
- Posterior polymorphous dystrophy (PPED, C1 or C2 in IC3D)
- Inheritance: AD/AR.
- Vesicles and "tram track" opacities on DM give rise to a "polymorphous" picture.
- Associated disease: Alport's syndrome and angle closure glaucoma.

Optical PK has a poor prognosis.

Congenital hereditary endothelial dystrophy (CHED, C1 or C2 in IC3D)

- Inheritance: AR.
- Diffusely thickened and opacified stroma prevents proper visualization of the endothelium.
- Treatment: Optical PK.

SPHEROIDAL DEGENERATION

History

Laterality: Unilateral/bilateral

Gender predominance: Male

Genetic disposition: Non-hereditary

Race: The highest prevalence of spheroidal keratopathy is seen in Labrador communities located in Eastern Canada between latitudes 55–56° north of the equator, where the ultraviolet light reflected from ice and snow serves as the greatest risk factor.

Chief complaints: Painless, progressive loss of vision. If a sterile ulcer develops, a patient may present with pain, watering and difficulty tolerating bright light.

History of present illness: Initially the patient may be asymptomatic. With the gradual progression of the disease, he/she may present with loss of vision. A sudden foreign body sensation. The sudden onset of pain, watering and photophobia heralds the onset of secondary ulceration.

Ocular Examination

- **Vision:** Vision is typically affected when the lesion involves the visual axis.
- **Lids:** Associated lid margin abnormalities, goblet cell dysfunction, distichiasis, and shallow fornices may be present.
- **Conjunctiva:** Pinguecula may be a precursor of spheroidal degeneration. The presence of yellow or golden spherules or "droplets" at or beneath the conjunctival epithelium.
- **Cornea (Slit lamp examination with low magnification):** Yellow or ambered-coloured, oily subepithelial droplet lesions in the interpalpebral region is typical (Fig. 1.31). Gradually, it progresses toward the centre of the cornea. The lesions are located in the

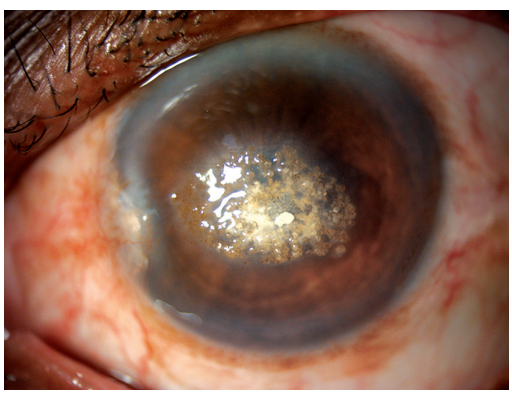

Fig. 1.31: Spheroidal degeneration

superficial corneal stroma, Bowman's membrane, subepithelium, and rarely in the epithelium in the advanced stage of the disease. Droplets are often confluent and form a big mass in the Bowman's membrane. The rest of the cornea is absolutely normal. In the secondary type, lesions start at sites of the previous pathologies. Lattice dystrophy may be present.

- **Lens:** Usually lens is cataractous as the entity is mostly seen among elderly populations.

Provisional diagnosis: This is a case of spheroid degeneration.

Frequently Asked Questions

Q1. What is spheroidal keratopathy?

It is a degenerative condition of the cornea and/or conjunctiva, which is characterized by the deposition of fine, homogeneous, translucent, golden-yellow, spherules of varying size in the interpalpebral region of the superficial corneal stroma, Bowman's membrane, subepithelium and at the epithelium.

Q2. Differential diagnosis of spheroidal degeneration.

- Corneal amyloid degeneration,
- Familial subepithelial amyloidosis
- Band keratopathy
- Climatic proteoglycan stromal keratopathy
- Primary lipoidal degeneration of the cornea
- Salzmann nodular degeneration
- Limbal girdle of Vogt, type II

Q3. What is the possible aetiology of spheroidal keratopathy?

The corneal deposition in spheroidal keratopathy is proteinaceous by nature. The possible source of this protein is the diffusion of serum proteins which comes from the adjoining limbal vessels. Over the period, this protein is altered by the ultraviolet rays in presence of other risk factors such as increasing age, dry eyes, malnutrition, corneal trauma, or microtrauma resulting from wind, sand or ice, low humidity, welding burns and extreme temperatures. The other pathological conditions of the corneal surface such as post-keratitis, lattice corneal dystrophy and glaucoma are considered associated risk factors.

Q4. What are the other names of spheroid degeneration?

Other names are climatic droplet keratopathy, keratinoid degeneration, Labrador keratopathy and chronic actinic keratopathy.

Q5. What are the possible complications of spheroidal degeneration?

Uncomplicated degeneration may progress to epithelial defects, recurrent corneal erosions, sterile ulceration and microbial keratitis.

Q6. Histopathology of spheroidal degeneration.

The amorphous droplets are located in the superficial corneal stroma, Bowman's membrane, subepithelium, and epithelium. Sometimes, droplets coalesce to form large masses in the Bowman's membrane.

Under light microscopy

- Lesions stain blue-green with toluidine blue
- Bright red with methyl green-pyronin
- Variable pink with Gomori's aldehyde fuchsin
- Eosinophilic with hematoxylin and eosin (H & E)

Under electronic microscopy: Finely granular structures are collected on bands of collagen.

Q7. How do you classify spheroid degeneration?

Johnson and Ghosh classification:

Trace: A small number of lesions either in one eye or both eyes or only one end of interpalpebral strips

***Grade 1*:** Lesions involving the interpalpebral cornea horizontally but not involving the central cornea

Grade 2: Central corneal involvement without affecting visual acuity

Grade 3: Central corneal involvement with a decline in visual acuity

Grade 4: Grade 3 features + elevation of the lesion

Other classification

- ***Primary corneal type:*** The lesions are located at the horizontal limbus within the palpebral fissure and gradually progress toward the central cornea. The rest of the cornea is clear.
- ***Secondary corneal:*** The lesions are usually located at sites of the previous pathologies.
- ***Conjunctival:*** The lesions are located at 3 and 9 o'clock positions interpalpebrally.

Q8. How do you manage this case?

The majority of patients do not require treatment.

a. If the patient is aphakic/pseudophakic/phakic with the clear crystalline lens: Excimer laser phototherapeutictic keratectomy (PTK) is the definitive management.
b. If the patient has significant lenticular opacity; cataract extraction with penetrating keratoplasty (PK) may be attempted. PTK followed by cataract extraction is another option in such cases. Alternatively, cataract surgery first followed by PTK after a gap of three months is a viable alternative approach.

Q9. What are the risks involved in PK plus cataract surgery in this case?

The chance of graft failure is very high as most patients have abnormal lid-globe relation, dry eye and poor goblet cell function.

BAND-SHAPED KERATOPATHY (BSK) OR DEGENERATION OF THE CORNEA

History

Age: May affect any age group.

Laterality: Usually unilateral.

Gender predominance: Not found.

Genetic disposition: No.

Chief complaints: The patient may have any of the following
- Foreign body sensation and ocular irritation
- Decreased vision
- Redness
- Photophobia
- Visible cosmetic changes to the eye

History of present illness: Initially, the patient may be asymptomatic but later presents with redness, foreign body sensation and loss of vision if the central cornea is involved. A few patients may seek medical attention for cosmetic reasons.

Ocular risk factors for BSK: So, ask for the following:
- Chronic uveitis.
- Any trauma to the cornea or eyeball.
- Previous surgery of the cornea or intraocular surgery like retinal detachment with silicone oil injection.
- Corneal pathological conditions such as keratoconjunctivitis sicca, phthisis bulbi, corneal dystrophies, lagophthalmos, interstitial keratitis, and climatic droplet keratopathy.
- Prolonged history of eye drops instillation such as phosphates or phosphate buffers such as steroids; mercury-based preservative drops such as pilocarpine initiates changes in the corneal collagen.
- Chemical exposure to mercury fumes, calcium bichromate and thiazides.

Systemic Evaluation

- Systemic hypercalcemia resulting from hyperparathyroidism, vitamin D toxicity, sarcoidosis, milk-alkali syndrome, cystinosis, hypophosphatemia, Paget's disease, multiple myeloma, and metastatic cancer to bone.
- Hereditary disorders: Norrie's disease
- Other systemic diseases: Juvenile rheumatoid arthritis, discoid lupus, gout, tuberous sclerosis, ichthyosis

Ocular Examination

Vision: Vision loss may happen once the lesion encroaches upon the central part of the cornea.

Eyeball: May be normal or phthisis bulbi.

Tonometry: Look for long-standing or end-stage glaucoma.

Cornea (Slit lamp examination)
- An anterior horizontal band across the cornea from 9 o'clock to 3 o'clock position separated from the limbus by a lucid interval (Fig. 1.32). This is pathognomonic for the diagnosis of BSK.

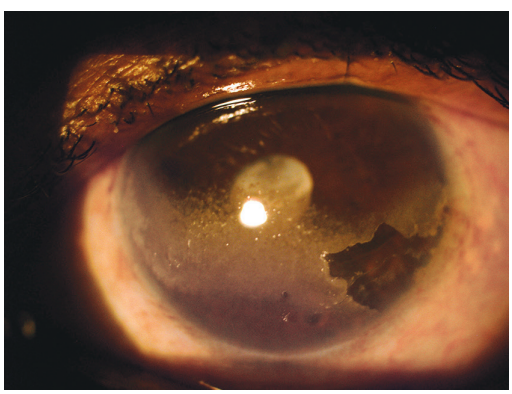

Fig. 1.32: Band-shaped keratopathy (BSK)

- A grey-white plaque with fine, dusty deposits in the sub-epithelium, Bowman's layer and the anterior stroma.
- Lucent holes in plaque (representing corneal nerves through Bowman's membrane).
- Flaky, peripheral plaque.

Anterior chamber: Look for signs of recurrent uveitis.

Posterior segment: Findings depend on systemic diseases such as vasculitis, soft exudate, exudative RD, vitreous haemorrhage, and vitritis, etc.

Provisional diagnosis: A case of band-shaped keratopathy of RE/LE

Frequently Asked Questions

Q1. What is band-shaped keratopathy?

It is a type of corneal degeneration which is characterised by band-shaped horizontal keratopathy formed by the fine dust-like calcium deposits in the sub-epithelium, Bowman's layer and the anterior stroma of the cornea. It can happen as a result of intraocular surgery or chronic intraocular uveitis, or idiopathic.

Q2. Describe the pathophysiology of band keratopathy.

Band keratopathy occurs from sub-epithelial calcium hydroxyapatite deposition over the course of months to years. Calcium deposits occur at sites of corneal injury or if there is a higher concentration of calcium on the ocular surface either from systemic hypercalcaemic conditions or external sources in the form of eye drops. The calcium hydroxyapatite deposits are the most stable form of calcium and are found in human bones and teeth. This calcium hydroxyapatite is insoluble in tears film and it gradually deposits into the epithelial basement membrane first followed by the anterior surface of Bowman's layer and anterior stroma if it is applied for a prolonged period. Initially, it is grey but later on, develops to a chalky-white colour in a band-like distribution. The band keratopathy typically starts at the inter palpebral region involving 3 o'clock and 9 o'clock positions of the cornea, eventually meeting centrally. The inter palpebral area is exposed to evaporate and helps in the deposition of insoluble calcium. There are characteristic lucent holes in the band which are formed due to the lack of Bowman's layer in the periphery of the cornea or by the increased buffering capacity of the limbal vessels that prevent the deposition of calcium. These lucent holes represent the corneal nerves penetrating through Bowman's layer. Patients become symptomatic if epithelial disruption happens.

Q3. Outline the baseline work-up of the patients with BSK if systemic disorders are suspected.

Baseline work-up is recommended in patients with band keratopathy who do not have an obvious intra-ocular trauma or surgical history such as silicone oil injection and history of multiple surgeries.

These investigation includes:

- Urinalysis (deposits, pH)
- High serum calcium
- Serum phosphorus (low phosphorus precipitates calcium deposition)
- Uric acid

- Creatinine
- Parathyroid hormone levels
- ACE and lysozyme levels (if sarcoidosis is suspected)
- Chest X-ray (if sarcoidosis is suspected)

Q4. What are the differential diagnoses of the BSK?

- Primary and secondary calcareous degeneration of the cornea
- Limbal stem cell deficiency
- Familial band keratopathy
- Spheroidal degeneration
- Salzman nodular degeneration and basement membrane dystrophy

Q5. How will you manage this case?

A. **Medical management:** For asymptomatic or is mildly symptomatic patients
   - Treat the underlying cause.
   - Avoid excessive intake of vitamin D and appropriate dietary changes.
   - Lubricating eye drops/gels or ophthalmic ointments may be helpful to treat patients with irritation, tearing, foreign body sensation and photophobia.
   - Prosthetic opaque contact lenses for patients concerned with the cosmesis of the eye.

B. **Surgical management:** Surgical management of band keratopathy is strongly considered after underlying systemic or ocular causes are treated or eliminated.
   - ***EDTA-chelation:*** 15% disodium ethylenediaminetetraacetic acid is performed by mixing 2 ml of this solution with 8 ml of 0.9% normal saline. Initially, the overlying epithelium is debrided under topical anaesthesia and then the EDTA solution is applied until the whole of the calcium plaques are cleared. Irregular surface post-debridement needs to be smoothed using a diamond-burr or an excimer laser phototherapeutic keratectomy. After the procedure, a bandage contact lens is applied over the cornea and the eye is patched for 24 hours. Topical non-steroidal drops and antibiotic drops are used after the procedure. Usage of phosphate containing topical agents such as steroid drops are avoided as they can precipitate calcium and cause a recurrence of the band keratopathy. The patient is advised for regular follow-ups as the disease may recur in future.
   - ***Dipotassium:*** EDTA (K2-EDTA) is a cost-effective alternate chelating agent for calcium band keratopathy.
   - Advanced cases, especially if calcium deposits into the bowman layer, may require a lamellar keratectomy.

Q6. What are the complications of post-treatment of band keratopathy include?

- Decreased vision or vision loss
- Recurrence of the calcium band
- Corneal scarring
- Corneal edema
- Secondary infection
- Irregular astigmatism
- Limbal stem cell deficiency

BULLOUS KERATOPATHY

History

Age: PPED becomes symptomatic in the paediatric age group though very rarely it may present with corneal edema since birth. Fuchs' dystrophy presents in the 6th decade and ICE syndrome is seen in the age group of 30–50 years.

Gender:
Male dominating: Congenital glaucoma
Female dominating: Fuchs' dystrophy and ICE syndrome.

Chief complaints:
- Loss of vision is gradual.
- Accompanied by pain, watering and difficult to tolerate bright light.

History of present illness: Initially the patient may be asymptomatic in PPED and early Fuchs' dystrophy. Later on, patient experiences mild loss of vision in the early morning but feels better as the day progresses. It signifies early endothelial stress with subtle corneal edema. There may be diurnal fluctuation of vision in early endothelial failure. With gradual endothelial failure, more severe edema spreads anteriorly causing persistent loss of vision. Visual loss becomes permanent as the patient develops stromal scarring in the background of longstanding corneal edema. It may be accompanied by pain, watering and difficult to tolerate bright light. This signifies epithelial edema with rupture of bullae.

Past history: History of cataract or any intraocular surgery is usually obtained. Sometimes past history of herpetic eye disease is present.

Examination

Systemic Examination

The presence of diabetes mellitus should be enquired for. They are prone to develop intra-operative DMDs.

Ocular Examination

Vision: Visual acuity depends on the severity of corneal oedema.

Conjunctiva and ocular surface: Bleb may be present following trabeculectomy. The pipe of the shunt device may be displaced to touch the endothelium. Hypotony may result from over filtration and as a side effect of MMC or 5FU application.

Limbus: Soft contact lens or a RGP or a BCL might be present. Soft contact lens on chronic use is more likely to cause corneal edema than RGP contact lens because of greater areas of corneal coverage, more stepper fit, less circulation of pre-corneal tear film (PCTF) and poor oxygen permeability. A BCL may be placed to give some symptomatic relief to the BK patient.

Cornea: Limbus to limbus edema presenting in the first day after surgery in presence of minimal symptoms is due to TASS. Use of instruments soaked in chemical disinfectants like cidex (glutaraldehyde) is an important causal factor.

Post-cataract surgery related striate keratopathy (diffuse or localized deep stromal edema with DM folds) clears up on the first week after surgery. In an established bullous

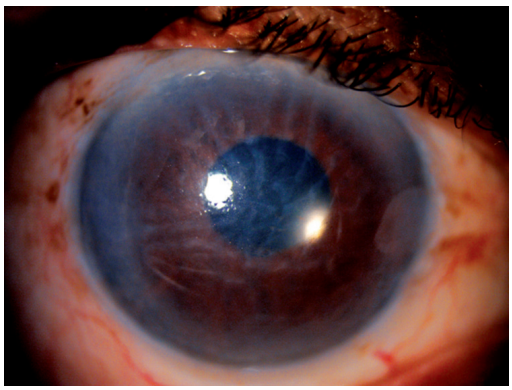

Fig. 1.33: Bullous keratopathy

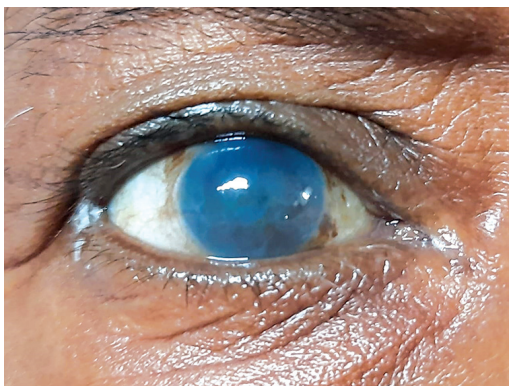

Fig. 1.34: Bullous keratopathy

keratopathy case, you will find diffuse pan corneal edema, thickened cornea, fixed DM folds and single or multiple epithelial bullae (Figs 1.33 and 1.34). Some of these bullae may rupture which makes the patient symptomatic. Delayed superior edema post-cataract surgery may be due to wound burn sequelae, localized DMD around main wound, vitreous strand touching the endothelium and lastly due to ingrowths (epithelial or fibrous).

Anterior chamber including angles: ACD may be less in hyperopic PBKs. Look for ACIOL haptic, sulcus placed PCIOL haptic or vitreous strand touching the endothelium.

Lens: Look for the type of IOL placed. In case of ACIOL, note the presence of PI and its patency. Haptic of a sulcus placed PCIOL may be touching the endothelium in the peripheral part.

Iris: Polycoria, naevus, essential iris atrophy and ectropion uveae are present in ICE syndrome. Patchy sphincter atrophy is seen following previous attacks of ACG and after HZO infection.

Posterior segment: Fundus is usually not visible in presence of significant corneal oedema. Disc evaluation is necessary (if possible) in cases of sub-acute angle closure glaucoma and in herpetic trabeculitis.

Provisional diagnosis: A case of right/left aphakic/pseudophakic bullous keratopathy.

Frequently Asked Questions

Q1. What are the causes of corneal edema following cataract surgery?

- **Preoperative:** Reduced endothelial count, endothelial dystrophies like Fuchs', CHED and PPED.
- **Intraoperative:** Hard cataract, lengthy surgery, complicated procedure, use of excessive phaco power, a hyperopic eye with shallow AC depth, etc.
- **Postoperative:** DMD, TASS, TEDS, vitreous or IOL touching the endothelium, Recurrence of herpetic kerato-uveitis, etc.

Q2. How do you manage a patient with bullous keratopathy?

Management of bullous keratopathy depends on the aetiology, severity, visual potential and whether patient has symptoms of pain.

Conservative treatment	Surgical treatment
• Lubricants • Hypertonic saline • Lower intraocular pressure • Avoid extended use of steroids • Therapeutic contact lens	• 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 (to create ptosis), conjunctival flap, retrobulbar alcohol, enucleation (very last resort).

Q3. Why BCL is used both as a palliative as well as therapeutic intent in corneal edema?

BCLs will give tectonic support to unruptured bullae (palliative intent). A loose-fit BCL will help epithelium regrowth under it in areas of the denuded cornea due to ruptured bullae (therapeutic intent).

Q4. How can you approach managing the case surgically?

If the eye has visual potential:

- Endothelial transplantation by DSEK/DSEAK/UTDSEAK and DMEK.
  In UTDSEAK an ultra-thin lenticule (less than 130 µm) is used. DMEK is the latest technique where only DM plus endothelium is transplanted.
- Optical PK (In advanced bullous keratopathy with significant stromal scarring).

If the eye has no visual potential:

- Rupture of bullae
- Bullectomy with amniotic membrane grafting (AMG).
- Phototherapeutic keratectomy (PTK)

Q5. What are the causes of corneal edema?

Post-surgery	Without surgical history
• Early postoperative edema (wound burn, DMD, use of excess phaco power to tackle hard cataract, hyperopic eye, surgery in a case of Fuchs' dystrophy, TASS and recurrence of herpetic keratouveitis) • Established corneal edema (ABK/PBK).	• CL use (tight fit soft CL), IOP is normal. • Endothelial dysfunction (due to Fuchs', CHED and PPED). IOP is normal. • With elevated IOP (recurrence of herpetic eye disease, iritis, NVG and ACG)

Q6. Why we should look for the other eye in a case of diffuse corneal edema?

- Diffuse edema precludes detailed evaluation in that eye. So, examination of the other eye might give us many clues.
- In advanced cases of BK, the other eye may show typical guttae (Fuchs'), typical vesicles at DM level with thickening of DM (PPED) and beaten metal appearance of the cornea in ICE syndrome.

Q7. What is toxic endothelial cell destruction syndrome (TEDS)?

a. Manifests as severe corneal edema within 24 hours of intraocular surgery.
b. Features: Diffuse corneal edema, star pattern folds at DM level, increased corneal thickness with vision reducing to HMCF.
c. The etiology is post-intraocular surgery breakdown of endothelial barrier function.
d. Treated with steroids, the prognosis is however guarded.

Q8. What is TASS?

Presentation: Toxic anterior segment syndrome manifests within 24 hours of cataract surgery with limbus-to-limbus corneal edema, DM folds, anterior chamber reaction with or without pain and hypopyon in presence of uninvolved vitreous.

Causes: Multifactorial; Use of improperly sterilized instruments, improper washes after using chemical disinfectants like cidex.

Management: Medically managed with hypertonic saline, cycloplegic, anti-glaucoma medications and most importantly steroids. If corneal edema persists, endothelial keratoplasty (EK) is required.

Q9. What is Descemet's membrane detachment (DMD)?

Descemet's membrane detachment (DMD) is an important cause of post-intraocular surgery localized corneal edema. Most of the DMDs are fortunately nonsignificant and self-resolving. Persistent extensive DMDs are unlikely to reattach spontaneously and will cause diffuse corneal edema, endothelial failure, scarring and vascularization. Important causes are the use of blunt instruments, excessive and repeated manipulations at the wound and in the anterior chamber, direct touch with the instrument and during wound hydration. A high degree of suspicion for DMD is required for all cases of persistent corneal edema following intraocular surgery. DMD is diagnosed by a meticulous slit lamp evaluation which shows a membranous structure at the back of cornea. If cornea is severely edematous, AS-OCT will be helpful to diagnose DMD.

Q10. What are the roles of AS-OCT in DMD?

The roles of AS-OCT in DMD are:

a. To diagnose DMD in presence of significant corneal edema.
b. To locate the position of DMD.
c. To find out the extent of DMD (Fig. 1.35).

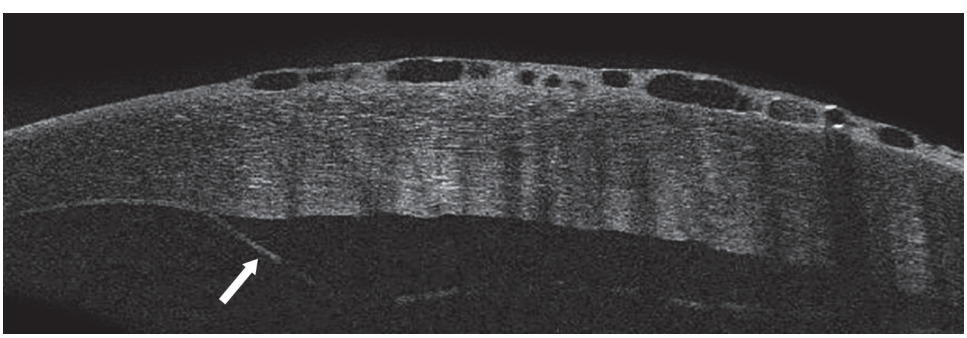

Fig. 1.35: Descemet's membrane detachment

d. To locate areas of the cornea with attached DM in presence of significant corneal edema (because these are the areas chosen for AC entry for desmetopexy).
e. To classify the DMDs.

Q11. What is air desmetopexy?

Injection of air (through the healthy cornea) to unroll and reattach a detached DM is called air desmetopexy. But for old cases of DMD where prolonged tamponade is needed and for inferiorly located DMDs, C3F8 gas tamponade is preferred.

Q12. What are the causes of localized corneal edema post-surgery?

- **Around wound:** Tight wound leading to wound burn.
- **Around wound and side ports:** Localized DMD.
- **Localised oedema in any part of cornea:** May be due to DMD. AS-OCT is an invaluable tool in this case.
- **Recurrence of herpetic endothelitis:** Localized haze and thickened cornea with KP.

GRAFT FAILURE

History

Age: The patient may be a child or an adult. Infectious keratitis, congenital glaucoma, congenital hypertrophic endothelial dystrophy, mucopolysaccharidosis and angle dysgenesis are indications for paediatric keratoplasty. In adults, common indications of keratoplasty are trauma, post-infections keratitis and endothelial dysfunction (Fuchs' dystrophy or post-intraocular surgery).

Gender: No predilection.

Chief complaints:

- Decreased vision
- Pain
- Redness
- Photophobia

History of present illness: State about:

- **Previous diagnosis or reason for keratoplasty:** Because some stromal dystrophies (lattice, granular and macular dystrophy) tend to recur in the transplanted cornea.
- **Visual recovery after surgery:** If the patient did not get good vision immediately after transplantation, this is due to primary graft failure. If the patient was enjoying good vision after transplantation but developed a gradual onset drop in vision months/years after the procedure, this is due to delayed graft failure. If a post-transplant patient suddenly develops loss of vision accompanied by pain, ciliary congestion and watering, they signify a graft rejection episode.
- **History of previous surgery:** The chance of graft survival decreases with the number of successive transplantation procedures.

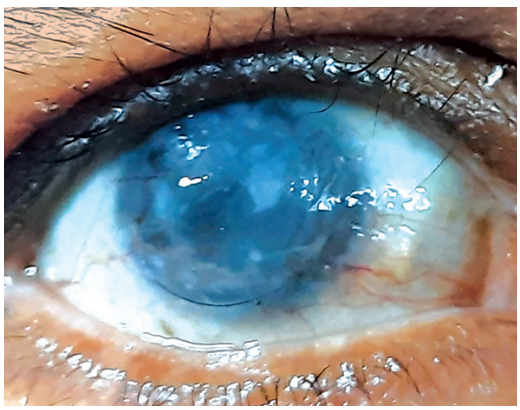

Fig. 1.36: Failed graft

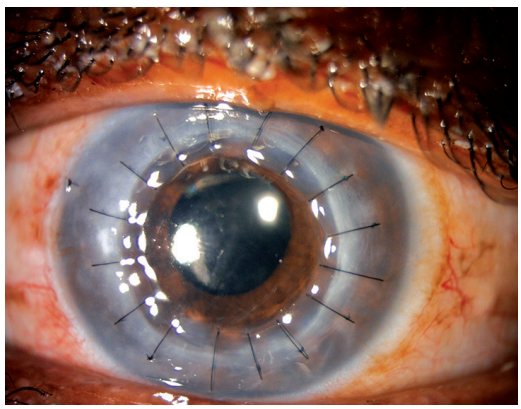

Fig. 1.37: Penetrating keratoplasty

- **Current medications/recent change of dosage of medications:** This is very important because the rejection episode may be triggered by premature withdrawal or reduction of the dose of steroids.

Past history:

- Medications prescribed after transplantation.
- Any recent change in medications or recent stoppage of any ocular medications.
- Whether it was the first surgery or it was a repeat procedure (the chance of graft survival decreases with repeat procedures) (Figs 1.36 and 1.37).

Examination

Ocular Examination

Vision: The patient may have a variable vision.

Ocular surface and adnexa

- Any obvious lid abnormalities, ingrown eyelashes (they may cause a PED due to recurrent rubbing on graft surface).
- Any obvious symblepharon or ankyloblepharon (they point towards past chemical burn, OCP and SJS).
- Evaluation for the presence of dry eye.

Conjunctiva: It is congested and chemosed in graft infection.

Cornea (slit lamp examination)

- Look for underlying diseases like corneal dystrophy, corneal opacity in vitamin-A deficiency and keratoconus in the fellow eye.
- Type of graft and clarity of graft: PK/anterior lamellar graft (interface usually visible, may have fine debris)/posterior lamellar graft (look for the graft lenticule). Graft clarity should be graded.
- Edge of graft: Interface scarring, sutures (in DALK and PK), any overriding edge in PK.
- Any persistent epithelial defect is present or not (sodium fluorescein dye test).

- Elevated rejection line staining with sodium fluorescein accompanied by subepithelial infiltrates point towards epithelial rejection episode.
- New keratic precipitates on donor endothelium or KPs oriented linearly (Khodadoust line) indicates endothelial rejection.
- Graft haze may be localized/diffuse. Ground glass-like diffuse graft haze may be due to stromal rejection.
- Sutures: If present, they should be documented in terms of number, nature (continuous or interrupted or combined), loose or broken, knots properly buried or exposed, accompanied by any blood vessel, sutures covered by epithelial/mucus plaque and overlying epithelial breakdown.
- Presence of vascularisation: Deep vascularisation denotes chronicity and extensive vascularisation indicates poor prognosis following keratoplasty.
- Any synechiae at the graft-host junction.
- Assess with Placido disc for post-operative astigmatism.

Anterior chamber

- If an assessment is possible, look for peripheral AC depth, any PAS and status of the lens (cataractous or not).
- Reaction in anterior chamber may be due to recurrence of infection (post-therapeutic PK), endothelial rejection or recurrence of herpetic kerato-uveitis.
- In the pseudophakic eye, if ACIOL is placed, then look for AC reaction, hyphaema, presence of PI and its patency.
- If a PCIOL is present, then look for its placement (in a bag or in sulcus), whether any part of haptic is touching the peripheral part of graft in sulcus placed IOL.

IOP: IOP (measured by NCT) is elevated in post-transplant glaucoma cases.

Posterior segment: It is obscured due to significant graft oedema or graft fibrosis. Evaluation of disc is necessary in cases of post-transplant glaucoma.

Provisional diagnosis: A case of primary/delayed graft failure in left/right eye due to .....cause. (please mention if you can identify the causal factor).

Frequently Asked Questions

Q1. What are the factors which affect graft survival?

The factors which affect graft survival can be categorised as follows.

Factors associated with a higher risk of graft rejection:

- Young age
- Blood group incompatibility (collaborative corneal transplant study)
- Repeat procedure
- Size of graft (large graft)
- Position of graft (eccentric graft)
- Presence of peripheral anterior synechiae
- Exposed sutures
- Deep stromal vascularisation

Other factors associated with graft failure:

- Pre-existing glaucoma and high IOP
- Ocular surface abnormalities (lids, tears)
- Intraocular inflammation (iritis)

Q2. How can you grade the graft clarity?

Graft clarity is graded as follows:

- ***Grade 4:*** Optically clear graft with excellent visualization of iris details.
- ***Grade 3:*** Faint graft haze with iris details visible.
- ***Grade 2:*** Marked graft haze resulting in a faint view of iris details.
- ***Grade 1:*** Opaque graft with no view of anterior chamber structures.

Q3. What is graft failure?

The donor cornea fails to serve the purpose for which it was transplanted. The causes may be varied, of which graft rejection, graft infection, post-graft glaucoma and recurrence of original disease in the graft are common causes.

Q4. What are the types of graft failure?

It can be two types:

- ***Primary graft failure:*** It occurs in the immediate postoperative phase—poor quality graft, traumatic handling of donor tissue, acute graft infection and endophthalmitis are common causes.
- ***Delayed graft failure:*** It occurs months or years after the original transplantation procedure. Common causes are suture-related, graft rejection, gradual attrition in endothelial reserve in grafted tissue and glaucoma.

Q5. What are the causes of graft failure?

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

Early failure (<72 hours)	Late failure (> 72 hours)
• Primary donor cornea failure • Unrecognized ocular disease • Low endothelial cell count • Tissue storage problems • Traumatic intraoperative handling of the graft • Faulty trephination and subsequent donor–host mismatch • Intraoperative damage • Post-operative infective keratitis • Trauma • Endophthalmitis	• Glaucoma • Persistent epithelial defect • Infective keratitis • Recurrence of the disease process (in certain corneal dystrophy) • Late endothelial failure • Rejection (30% of late graft failures)

Q6. What is graft rejection?

This is an acute immunological phenomenon (type-4) leading to a sudden drop of vision with pain, redness, photophobia and watering accompanied by varying degrees of graft oedema that might lead to graft failure. A diagnosis of graft rejection is done only when the graft was clear for at least two weeks after surgery.

Q7. What are the types of graft rejection?

There are three types:

Epithelial rejection: It is common but often reversible, an elevated epithelial rejection line is seen which stains with sodium fluorescein. Patient may not be very much symptomatic. Graft thickness does not increase.

Stromal rejection: Characterized by a sudden drop in vision with pan corneal oedema in a previously clear graft. Usually, stromal rejection is associated with other types of rejections.

Endothelial rejection: This type of rejection is fortunately rare, but if not treated aggressively, it will give rise to irreversible graft oedema leading to graft failure. It can be diffuse (scattered KPs around endothelium along with increased graft thickness) or localised (starts from the vascularised area of the peripheral cornea near graft–host junction characterized by Khodadoust line).

Q8. How do you manage a case of graft rejection?

- In-house admission is advised.
- For epithelial or subepithelial rejection: A topical steroid (1% prednisolone acetate) 3 hourly. The dose is tapered to half every 3 days.
- Endothelial rejection: Prednisolone acetate drops at 1 hourly interval along with steroid ointment (dexamethasone) at bedtime and topical cycloplegic.
- In presence of worsening graft oedema, give dexamethasone subconjunctival injection and intra-venous methyl prednisolone 125–500 mg single dose (CCTS recommendations).
- Post-rejection graft failure is diagnosed if the rejection episode is not cleared within two months resulting in irreversible graft oedema.

Q9. What is the basic difference between a graft rejection and a graft failure?

In graft failure, the donor tissue fails to serve the purpose for which grafting was performed. The causes are many, out of which graft rejection is an important cause. Graft rejection is an immunological phenomenon that may (or may not) lead to graft failure.

Q10. What are the risk factors for graft rejection?

- Younger recipients are susceptible to rejection due to an active immune system.
- Regrafts: Repeat procedures are prone to rejection due to host sensitization to alloantigen.
- Large and eccentric graft: Due to close proximity to limbal vessels, chance of rejection is increased.
- Corneal vascularisation: Deep vessels and more extensive vessels are important risk factors for rejection.
- Suture: A broken or loose suture might be associated with subepithelial dots (Kaye's dots). These sutures invite peripheral corneal vascularisation. Hence, the chance of rejection increases.
- Areas of anterior synechiae are potential sites for initiation of endothelial rejection.
- Persistent epithelial defects in donor tissue may trigger epithelial rejection.

Clinical features

Epithelial rejection	Subepithelial rejection	Stromal rejection	Endothelial rejection
Pathology: Epithelial rejection line (Krachmer's line in the graft starting from graft-host Junction): Advancing lymphocytes, replaced by epithelial cells from recipient. Signs and symptoms: Usually low grade, asymptomatic, eye is quiet	Pathology: Nummular white sub-epithelial infiltrates near the suture lines (Kaye's dots). Symptoms and signs: Mild anterior chamber activity	Pathology: Immunological Symptoms: Decreased VA, redness, pain, Signs: Limbal injection, AC activity, keratic precipitates, stromal oedema	Endothelial rejection line (Khodadoust line is typical but not essential to diagnose endothelial rejection)

Q11. What is the evidence that rejection is an immune phenomenon?

- Rejection of 2nd graft from the 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.

Q12. What are the causes of post-keratoplasty glaucoma?

Causes are:

a. Postoperative angle closure due to anatomy distortion and extensive PAS.
b. Retained viscoelastic material
c. Pupillary block (by air, vitreous or viscoelastic)
d. Pre-existing glaucoma
e. Steroid-induced
f. Persistent large hyphaema in immediate post-operative period

Q13. What are the importance of sutures in this case?

- If no sutures are visible, then it must be a case of delayed graft failure.
- Normally all interrupted sutures are removed by one year in vascularised cornea and by 18 months in other cases.
- In paediatric cases, by 6 months all sutures are removed as healing is faster.

Q14. What are the indications for earlier suture removal?

- Loose suture
- Broken suture
- Suture inviting blood vessel
- Any suture related abscess
- Suture covered with epithelial/mucous plaque

Q15. What are the donor–recipient graft size differences in various indications of penetrating keratoplasty?

- Normal adult cases: The donor button is 0.25–0.5 mm larger.

- In therapeutic PK, aphakic and paediatric cases, donor is oversized by 0.75–1.00 mm.
- In keratoconus: Same sized donor tissue.

Q16. Name a landmark trial for corneal transplantation.

The Collaborative Corneal Transplantation Study (CCTS)

- Evaluated the role of immunotyping in high-risk cases.
- High-risk cases were defined as cases with the previous history of rejection or deep corneal vascularisation of more than 2 quadrants.
- HLA matching (A, B or DR) did not substantially reduce the chances of graft rejection.
- ABO matching might be effective in reducing rejection.

Q17. What are the newer drugs used in rejection episodes?

a. **Cyclosporine A (2% topical and 8–15 mg/kg/day oral dose):** Specifically suppresses T cells.
b. **Tacrolimus (0.16 mg/kg/day):** A macrolide has similar action as cyclosporine A but it is more potent than cyclosporine A. It is a nephrotoxic drug.
c. Rapamycin.
d. IL-2 receptor monoclonal antibody.
e. **Azathioprine (1–2 mg/kg/day PO):** It decreases the need for high dose systemic steroids. Toxicity is noted in the liver, bone marrow and kidney.
f. **MMF (mycophenolate mofetil):** Recommended dose is 750 mg BD. It suppresses T and B lymphocytes. It has got toxicities on kidney, bone marrow and liver.

Q18. What are the incidences of rejection after various keratoplasty procedures?

- **DMEK:** 1–3%
- **DSAEK:** 8–14%
- **DALK:** 2–10%
- **Low-risk PK:** 5–17 %
- **High-risk PK:** As high as 68%

Q19. What are the newer experimental techniques in endothelial failure cases?

- Intracameral injection of Rho-kinase inhibitor. This is done in Fuchs' dystrophy cases presenting with large central guttae. A central descemetorhexis is done followed by intracameral injection of Rho-kinase inhibitor.
- Intracameral cultured human endothelial cells injection.

Q20. How do you clinically approach a patient of a corneal scar?

If patient has stromal scarring seen at the superior half of the cornea, look for:

a. ***Trachoma:*** Trichiasis, entropion of the upper lid, Herbert's pits, upper lid (Arlt's line).
b. ***Vernal keratoconjunctivitis:*** Punctate epitheliopathy, macro erosions, shield ulcer, Tranta's dots, pseudo-gerontoxon (cupid's bow) and giant papillae.
c. ***Superior limbic keratoconjunctivitis:*** Superior conjunctival injection, punctate epitheliopathy, corneal filaments.
d. Post-surgical scar.
e. TMD

If a the patient has a central corneal stromal scar/ edema and the visual axis is involved, look for:

a. ***Disciform keratitis:*** Lid scarring (usually very subtle), epithelial edema, Descemet's folds, Wessely ring, keratic precipitates, AC activity, reduced corneal sensation.
b. ***Keratoconus:*** Parastromal thinning, Vogt's straie, Fleischer's ring, prominent corneal nerves, typical topography.
c. ***Fuchs'endothelial cell dystrophy:*** Epithelial oedema, subepithelial scarring, stromal thickening, corneal guttae.
d. ***Pseudophakic bullous keratopathy:*** Epithelial bullae, type of IOL (especially ACIOL)

Causes of inferior corneal scarring are: Blepharoconjunctivitis, trauma, PMD, exposure keratopathy, etc.

Q21. What is keratoplasty?

Keratoplasty or corneal grafting is a surgical procedure in which a diseased host cornea is replaced by healthy donor cornea. Broadly, corneal grafts can be partial thickness/lamellar or full-thickness/penetrating.

Q22. What are the indications for penetrating keratoplasty (PKP)?

Indications for PKP are:

Optical	Tectonic	Therapeutic	Cosmetic
• Advanced bullous keratopathy • Advanced keratoconus with DM scarring • Corneal dystrophy • Corneal inflammatory diseases • Interstitial keratitis • HSV • Traumatic corneal scars • Failed grafts	• Corneal perforation • Peripheral corneal thinning	• Non-resolving infectious keratitis	• Large old scars (no visual prognosis)

Q23. What are the poor prognostic factors prior to PKP?

Evaluate: The patient's ocular condition and manage poor prognostic factors prior to PKP. Major poor prognostic factors are:

- Ocular inflammation
- Glaucoma
- Corneal vascularisation
- Ocular surface abnormalities: Tear film dysfunction, corneal irregularity, dry eye disorder and hypoesthesia.
- Triple procedure
- Retinal and macular conditions (e.g. cystoid macular oedema)
- Amblyopia
- Optic atrophy

Q24. How do you perform a PKP?

Preoperative preparation

a. GA/LA (depending upon the age and mental status).
b. Liebermann screw speculum.
c. Superior and inferior rectus bridle suture with 4/O silk (optional).
d. Flieringa ring, if necessary for post-vitrectomy, aphakia, trauma, and children.
e. Overlay suture, if necessary (7/0 silk at limbus).
f. Check recipient bed size with a disposable corneal trephine (usually 7.5 mm).

Donor button

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

Recipient bed

- 3-point fixation (two from bridle suture, one with forceps).
- Trephine imprint to check size and centration.
- Other types of trephines may be used: Barron-Hessburg trephine and Hanna trephine (a suction mechanism).
- Set trephine to 0.4 mm depth.
- Enter into AC with blade.
- Complete incision with corneal scissors.

Fixation of graft

- 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.

Q25. What are the advantages of different types of sutures performed in keratoplasty?

a. **Advantages of interrupted sutures:** Easier for beginners, better for inflamed eyes and eyes with vascularisation.
b. **Advantages of continuous suture:** Faster, better astigmatism control, not used where selective suture removal may be needed (e.g. infections).
c. **Advantages of combined continuous and interrupted sutures:** Better wound integrity.

Q26. Why the donor button is made larger than the recipient bed?

a. Because the donor button is punched from the posterior endothelial surface.
b. Tighter wound seal for graft.
c. Increases convexity of button (less peripheral anterior synechiae after surgery).
d. More endothelial cells with larger the button.

Q27. What are the different storage media for preservation of donor corneal button?

Storage media can be divided into

A. ***Short term (days)***
   a. *Moist chamber:* Humidity 100%, Temp 4°C, maximum storage duration 6–8 hours.
   b. *McCarey-Kaufman medium:* Standard tissue culture medium (TC199, 5% dextran, antibiotics), temperature 4°C, storage duration: 2–4 days.

B. ***Intermediate term (weeks)***
   a. *K-SOL:* Minimum essential medium (MEM), TC 199, Earles media, HEPES, chondroitin sulphate 2.5% and gentamicin.
   b. *DEXOL:* MEM, sodium pyruvate, non-essential amino acids, 1% dextran 40 and 1.35% chondroitin sulphate.
   c. *OPTISOL GS.:* MEM, 1.35% chondroitin sulphate, non-essential amino acids, sodium pyruvate, 1% dextran 40, antioxidants, gentamicin and streptomycin.
   d. *Organ culture:* Advantage: Decreased rejection rate (culture kills antigen-presenting cells). Disadvantage: Increased infection rate, temp 37°C. Storage duration: 4 weeks.

C. ***Long term (months to years)***
   a. *Cryo preservation:* Liquid nitrogen, temperature 196°C, storage duration: 1 year. Disadvantages: Expensive, unpredictable results, not suitable for optical grafts.
   b. Glycerol preservation
   c. Lyophilized/freeze-dried
   d. GISC (gamma irradiated sterile cornea)

Q28. What are the contraindications for a donation of the cornea?

Contraindications for cornea donation are:

Systemic diseases	Ocular diseases	Others
• Death from unknown cause • CNS diseases of unknown cause • Creutzfeldt-Jakob disease, CMV encephalitis, slow virus diseases • Congenital rubella, rabies, hepatitis, AIDS, syphilis • Septicaemia • Malignancies • Leukaemia, lymphomas, disseminated cancer	• Major corneal/retinal surgery • History of glaucoma and iritis • Malignant intraocular tumors • Death to enucleation time > 6 hours.	• Age less than 1 year old because of the steep cornea, friable tissue and small diameter. • Age more than 80 years because of the low endothelial count. • Severe haemodilution: Affects accuracy of serological testing.

Q29. How do you check the corneo-scleral disc?

- Container (name, date of harvest, etc.).
- Media (clarity and colour).
- Corneal button (clarity, thickness, irregularity, surface damage, endothelial cell count).

Q30. What are the complications of corneal grafts?

Complication of corneal grafts are:

Early postoperative	Late postoperative
• Raised intra-ocular pressure or hypotony • Persistent epithelial defect • Endophthalmitis • Wound leak • Recurrence of primary disease specially in therapeutic PK • Expulsive haemorrhage	• Rejection • Infective keratitis • Recurrence of disease (certain corneal dystrophies) • Astigmatism • Persistent iritis • Cataract • RD • Retrocorneal membrane • CME • Late endothelial failure

Q31. How do you grade corneal graft prognosis according to disease categories?

Brightbill's classification

Grade I (Excellent)	Grade II (Good)	Grade III (Fair)	Grade IV (Guarded)	Grade V (Poor)
• Keratoconus • Lattice dystrophy and granular dystropy • Traumatic leucoma • Superficial stromal scars	• Bullous keratopathy • Fuchs' dystrophy • Macular dystrophy • Small vascularised scars • Interstitial keratitis • Failed grade I PKP	• Vascularised cornea • Active HSV keratitis • Congenital hereditary endothelial dystrophy • Failed Grade II PKP • Combined PKP and cataract surgery • Active bacterial keratitis	• Active fungal keratitis • Congenital glaucoma • Paediatric grafts • Mild keratocon-junctivitis sicca • Mild chemical burns • Corneal blood staining • Corneal staphyloma • Failed Grade III PK • Severe keratocon-junctivitis sicca (Stevens-Johnson syndrome, ocular cicatricial pemphigoid)	Chemical and thermal burns

Q32. What are the problems of large grafts?

- Increased risk of rejection (nearer vessels).
- Increased IOP (delayed formation of the anterior chamber with decreased peripheral AC depth and more chance of peripheral anterior synechiae).
- Large epithelial defect (limbal stem cell failure).

Q33. What is the role of oral cyclosporine A in keratoplasty?

Indications (high risk of graft rejection):

- Young patient
- Repeat grafts
- Large grafts/sclerokeratoplasty
- Deep stromal vascularisation
- Limbal allografts (chemical injury, SJS)
- Post-graft rejection
- Cyclosporine A: 15 mg/kg/day for 2 days followed by 7.5 mg/kg/day for another 2 days, then to be continued for at least 6 months after reversal of rejection episode in a dose so as to maintain 100–200 mg/L blood level.

Parameters to be monitored during treatment: BP, height and weight, CBC, renal function, liver function, CXR, ECG, and serum cyclosporine level.

Q34. What is lamellar keratoplasty?

Lamellar keratoplasty is a partial thickness corneal grafting procedure wherein only specific layer/layers of the diseased cornea are replaced with the donor tissue.

Types: It can be divided into two types:

A. **Anterior lamellar keratoplasty**
   i. ***Superficial anterior lamellar keratoplasty (SALK):*** Here up to 250 microns of the anterior stroma is replaced.
   ii. ***Deep anterior lamellar keratoplasty (DALK):*** Here total stroma is replaced leaving bare DM.

B. **Posterior lamellar keratoplasty**
   i. ***Descemet's stripping endothelial keratoplasty (DSEK):*** Host DM and endothelium is replaced by donor DM and endothelium along with minimal posterior stroma (around 50–80 µm) in the graft.
   ii. ***Descemet's membrane endothelial keratoplasty (DMEK):*** Host DM and endothelium is replaced by donor DM and endothelium. No stromal tissue is incorporated in the graft.

Q35. Describe the steps of DALK procedure.

Deep anterior lamellar keratoplasty is generally performed under peribulbar anaesthesia supplemented with a sub-tenon block. In paediatric cases, the procedure is performed under general anaesthesia.

Preparation of donor tissue

- The donor tissue of the desired size (generally 7.5–8.0 mm) is fashioned out by punching from the endothelial side.
- The DM-endothelial layer is scrapped off using a merocel sponge.

[This step is withheld until the DM (of the recipient bed) is completely exposed as in the case of macro perforation while the recipient DM is being exposed, the same donor tissue may be utilized for penetrating keratoplasty].

Preparation of recipient bed

- A particular thickness trephination (at 75–80% stromal thickness) is done using a disposable corneal trephine.
- Superficial keratectomy is performed next using a crescent blade.
- A bevel-down 30-gauge needle is inserted into the corneal stroma paracentrally and the air is injected into the stroma to create a big bubble (called Anwar's big bubble technique).
- Anterior chamber pressure is lowered by making a paracentesis and a small bubble of air is injected into the anterior chamber through the paracentesis.
- With a side port, the centre of the big bubble is carefully deflated and viscoelastic material is injected along the posterior stromal space. The remaining stromal layers are carefully dissected out in a quadrantic manner so as to bare the DM.

  (Apart from air, high-density viscoelastic agents and BSS may be used to create a lamellar separation between the posterior stroma and DM. Manual layer-by-layer removal of the stroma may be required to bare the DM especially when the classic big bubble cannot be achieved despite repeated air injections into the stroma)

Securing the graft: The recipient bed and the donor tissue (containing all layers of cornea except DM and endothelium) are sutured with 16 interrupted 10:0 monofilament nylon sutures.

Indications: Partial thickness corneal diseases like:

a. Superficial corneal dystrophies (Reis-Bucklers)
b. Superficial corneal scars (not involving the DM and endothelium)
c. Recurrent pterygium with corneal thinning and irregularity
d. Corneal thinning (Terrien's marginal degeneration)
e. Impending corneal perforation
f. Congenital lesions (limbal dermoid)
g. Superficial tumors (OSSN)
h. Endothelial dystrophies/endothelial failure

Advantages of anterior lamellar keratoplasty

- Minimal donor tissue requirements
- No intraocular entry
- Faster wound healing and rehabilitation
- Lower risk of rejection and lesser use of topical steroid

Complications of anterior lamellar keratoplasty

- Intraoperative perforation of DM
- Astigmatism
- Double anterior chamber
- Interface haze/scarring

Advantages and disadvantages of endothelial keratoplasty

Advantages of endothelial keratoplasty	Disadvantages of endothelial keratoplasty
a. Reduced astigmatism b. Smaller wound—lower risk of wound dehiscence c. Replaceable and repeatable d. Reduced risk of rejection (stromal)	a. Interface scarring b. Technically more difficult

Complications of endothelial keratoplasty

Early	Late
• Graft detachment • Glaucoma • Delayed epithelial healing	• Glaucoma: Due to PAS formation • Endothelial rejection • Endothelial failure

Q36. Describe the steps of Descemet membrane endothelial keratoplasty (DMEK).

DMEK is performed under peribulbar anaesthesia.

Preparation of the donor button:

- Donor button is placed over a Teflon block with the endothelial side facing upwards.
- Trypan blue dye is instilled over the endothelium to stain it.
- A 9 mm light trephination is performed.
- A Sinskey hook is used to score the peripheral edges along the trephination mark.
- The detached DM-endothelial complex is grasped with a McPherson forceps and is carefully separated from its peripheral attachments.
- A skin biopsy punch is used to punch out a full-thickness stromal disc from the endothelial side.
- The DM-endothelial complex is reposited back after drying the fluid with a merocel sponge.
- The donor button is everted (endothelium) facing downwards and an 'S' mark is placed over the superior side (stromal) of the graft after the punched-out stromal disc is removed.
- The disc is replaced back and the donor button is everted again (endothelium facing upwards).
- Over the Teflon block.
- A handheld disposable trephine of the desired size is used to punch out donor lenticule composed of DM and endothelium only.
- The curled-up DM-endothelial tissue (floating in the BSS) is aspirated into a donor delivery system (just like a cartridge-injector system for foldable IOL insertion).

Preparation of recipient bed: This is essentially the same as in DSEK.

Graft insertion and unfolding:

- Through a clear corneal 2.7–3.00 mm incision, the graft is inserted into the anterior chamber.
- The chamber is deliberately made shallow and the curled-up donor tissue is unfolded by repeated bi-manual tapping over the epithelium.

- Air is gently injected under the graft to achieve graft–host apposition.
- Centration of the graft is checked, proper orientation is ensured by noting the pre-placed S mark.
- Some air from AC is removed.
- BCL is placed over the cornea especially if it was de-epithelized before for enhanced visualization.
- Immediately after the graft is inserted into the AC, the main port is to closed with a 10:0 nylon.
- Suture.
- This will ensure a closed chamber and will reduce the chance of graft ejection.

Q37. Describe the steps of DSEK.

DSEK is mostly performed under peribulbar anaesthesia in adults and general anaesthesia in paediatric patients. The following steps are involved in DSEK

Preparation of donor button

- The sclera-corneal button is mounted on an artificial anterior chamber with the endothelial side facing downwards.
- The infusion port is opened and a semicircular incision is given just inside the limbus with a guarded corneal knife of the desired depth.
- Lamellar dissector (long and short) is used to create a limbus to limbus lamellar separation in 360 degrees.
- The donor button is then taken away from the artificial anterior chamber and is placed in a punch trephine adapter with the endothelial side facing upwards.
- A standard 7.5–8.00 mm trephination is done from the endothelial side and the donor lenticule is separated from the remaining stromal bed.
- The donor button is ready now for insertion.

Preparation of recipient bed

- A side port entry into the anterior chamber is performed and the endothelial layer is stained with trypan blue dye.
- The anterior chamber is reformed with viscoelastic materials (alternatively an anterior chamber maintainer may be used).
- From the epithelial side, a light circular mark is done with an 8.00–8.5 mm trephine.
- With a reverse Sinskey hook, scoring of the edges of the recipient bed is performed and the detached DM-endothelial complex is removed by a DM-stripper.
- Now residual viscoelastic material is aspirated out.

Introduction of donor lenticule

- A clear corneal 4.5–5.0 mm incision is done. Some prefer a sclero-corneal tunnel (like SICS) preparation for donor tissue insertion. After entry into the anterior chamber with a keratome, donor tissue is inserted into the anterior chamber in a folded manner (60:40 taco; called "folded technique").
- Other "non-folded" methods of donor insertion are the suture pull-through technique, instrument pull-through technique and a simple needle-guided insertion technique (copious amount of viscoelastic is injected near the main wound, graft is placed with the endothelial side down and it is gently guided into the AC with a needle or a Sinskey hook).

Donor lenticular apposition

- After the donor lenticule is inserted into the anterior chamber, the main wound is secured with 3 to 4 interrupted 10:0 monofilament nylon sutures.
- Through the side port, the air is injected under the donor lenticule for good graft–host apposition. Centration of the graft is to be checked. Full-thickness multiple venting incisions, to keep the graft–host interface dry and apposed, are optional.
- If epitheliectomy (in order to increase visualization) was performed before, a bandage contact lens is placed over the cornea. The patient is instructed to stay in a supine position (atleast 45 minutes in each hour) for 24 hours after the procedure.

Q38. What are advantages of DMEK over other methods of endothelial keratoplasty (EK)?

- DMEK is more physiological than DSEK.
- The hyperopic shift that is noted post-DSEK, is not seen following DMEK as the donor lenticule does not have any stromal component in DMEK.
- Visual stabilization is faster following DMEK than DSEK.

Initial endothelial loss is more following DMEK as the unfolding of donor lenticule requires repeated intraoperative manipulations.

Q39. How can you manage an episode of recurrent epithelial erosion syndrome?

- **Medically:** Managed by an eye patch, tear substitutes, hyperosmotic drop.
- **Surgically:** Bullectomy, epithelial debridement and BCL placement, anterior stromal puncture and PTK.

Q40. How anterior stromal puncture (ASP) works?

- ASP is indicated in recalcitrant recurrent epithelial erosion cases not involving the visual axis.
- Multiple punctures are done with a 25G or a 26G needle through the epithelium up to the depth of anterior stroma.
- It induces localized scarring, (hence, best avoided in the visual axis) and the epithelial plugs will reduce recurrence as it acts like anchoring fibrils.
- Alternatively, Nd-YAG laser may be used to micro-puncture but it causes more scarring (hence, not preferred).

Q41. How does PTK work in recurrent erosion?

- Ablation is done trans-epithelial or after mechanical epithelial removal.
- A limited ablation upon the depth of BM (less than 20 µm) is carried out which provides a smooth surface for epithelial cell re-growth.
- There is a chance of a hyperopic shift post-PTK.

DRY EYE

History

Age: Commonly above 50 years

Gender: Women have higher rates due to hormonal changes

Presenting symptoms

- Foreign-body/burning/gritty or itching sensation
- Ropy mucoid discharge
- Excessive watering from eyes
- Redness
- Ocular dryness
- Photophobia
- Transient blurry vision

History of present illness: Patients with dry eyes involve both eyes. The most common presenting symptoms are foreign-body/burning/gritty or itching sensations. Symptoms are often exacerbated in smoky or dry environments such as the use of an indoor heater, fans, and air conditioner. Excessive reading or lengthy screen exposure time also worsens the symptoms. Often, the symptoms worsen as the day advances. In patients with meibomian gland dysfunction (MGD), the symptoms are often worse upon awakening in the morning.

Past ocular illness

- Ask for Stevens-Johnson syndrome, trachoma, ocular cicatricial pemphigoid, and chemical burns.
- Did the patient undergo any lacrimal gland surgery/radiation therapy or eyelid surgery?
- Did the patient undergo any refractive surgery or a regular contact lens wearer?

Systemic illness

- Dry eyes are associated with certain autoimmune diseases such as Sjögren's syndrome, SLE, DLE, RA, Wegener granulomatosis, dermatomyositis, diabetes, thyroid diseases, sarcoidosis, and IBD.
- Ask for post-traumatic stress and depression, menopausal and postmenopausal women.
- Some neurological disorders such as familial dysautonomia (Riley-Day syndrome), facial nerve palsy and Parkinson's disease are associated with dry eyes.
- Therefore, ask for dry mouth, arthritis, myalgia, cutaneous changes, malaise, weight loss, and lymphadenopathy.
- Patients suffering from Sjögren syndrome may have dyspareunia, Raynaud phenomenon, dental caries, gastritis, features of malabsorption, pulmonary disease, renal disease, polyneuropathy and lymphoma.

Medications: Antihistamines, decongestants, OCP, antihypertensive medications and antidepressants are responsible for dry eyes.

Ocular Examination

Visual acuity: A transient blurry vision that may be corrected after blinking.

Eyeball: May be proptosed if there is a thyroid disorder, lacrimal gland tumor, pseudotumor of orbit, or sarcoidosis.

Eyelid:

- Eyelid scarring in trachoma, SJS, chemical burns, and posterior blepharitis in meibomian gland dysfunctions.

- Foam or froth on the lid margins.
- Lagophthalmos in facial nerve palsy may be there.

Conjunctiva: May show keratinization and redness.

Cornea (Slit lamp examination):
- Punctate epithelial erosion that stains with fluorescein. Interpalpabral region (both cornea and conjunctiva) staining with fluorescein is common in tear film deficiency.
- Multiple filaments or mucous strands adhered to the corneal surface.
- Mucous plaques (composed of mucous, epithelial cells, lipids and protein) of various sizes over the corneal surfaces along with filaments are very common. Both filaments and plaques take well staining to 1% rose Bengal dye and lissamine green. Rose Bengal dye may give an intense burning sensation. A linear pattern of inferior conjunctiva and corneal staining by rose Bengal or lissamine is characteristic of meibomian gland dysfunction (MGD).

Tear film abnormality:
- The marginal tear meniscus film height is less than 1 mm (normal 1 mm) and
- Lots of debris and particles move with each blink (lipid-contaminated mucin).
- Tear film break-up time: A fluorescein strip is moistened with non-preservative saline and applied to the lower fornix and the patient is asked to blink several times. The tear film is examined with a blue filter of the slit lamp for the appearance of the first dry spots on the cornea. Three consecutive measurements are taken, and the median value is recorded as TBUT. A TBUT of less than 10 seconds is considered abnormal and indicates aqueous tear deficiency.
- Schirmer I measures both basic and reflex tearing and is performed without the use of a topical anaesthetic agent. A thin strip of filter paper (No. 41 Whatman filter paper, 35 mm long x 5 mm wide) is used for the test. The filter paper is folded 5 mm from the beginning and inserted gently at the junction of the middle and outer third of the lower lid without touching the cornea and lashes. A soft tissue paper may be used to dry all tears from the inferior fornix by capillary attraction without direct wiping before the paper strip is inserted. The patient's eyes are then closed for 5 minutes and the amount of wetting of the paper strip is noted. In the Schirmer II, the same procedure is followed to measure basic secretion but the test is performed under topical anaesthesia. Less than 10 mm of wetting without anaesthesia and less than 6 mm after anaesthesia is considered abnormal, whereas 5 to 10 mm is equivocal.

Lens/iris: No significant changes.

IOP: Remains normal.

Fundus findings: May show signs of vasculitis, soft exudate, haemorrhage, macular edema, etc.

Frequently Asked Questions

Q1. What are the differential diagnoses of dry eye?
- Adult blepharitis
- Allergic conjunctivitis

- Bell's palsy
- Contact lens-related complications
- Neurotropic keratitis
- Toxic keratopathy
- Ocular rosacea
- Thyroid ophthalmopathy

Q2. What is the classification of dry eye?

Keratoconjunctivitis sicca (KCS)	Xerophthalmia	Xerosis	Sjögren syndrome
Any eye with some degree of dryness	Dry eye associated with vitamin A deficiency	Extreme dryness and keratinization of ocular surface associated with conjunctival cicatrisation	Dry eye occurs due to lacrimal gland destruction and inflammation by an autoimmune mechanism.

Q3. What happens to Goblet cells in dry eye disease?

In dry-eye patients, decreased levels of mucin are observed which indicates a decreased number of goblet cells.

Q4. What are the complications of dry eye?

- Peripheral superficial corneal neovascularisation
- Epithelial breakdown
- Corneal melting
- Bacterial keratitis

Q5. What special investigations do you suggest for the diagnosis of dry eye?

a. **Analysis of tear proteins or tear-film osmolarity:** Normal values range from 275 to 295 mOsm/kg (275 to 295 mmol/kg). A higher osmolarity of the tear film indicates dry eye.
b. **Measurement of tear lactoferrin:** Tear lactoferrin is decreased in Sjögren syndrome.
c. **Serology for circulating autoantibodies:** For the diagnosis of connective tissue disorders.
d. **Meniscometry** (measurement of tear meniscus radius, height, and cross-sectional area).
e. **Impression cytology:** It is a non-invasive tool for assessing various ocular surface disorders including dry eye disorders such as keratoconjunctivitis sicca (KCS), cicatricial ocular pemphigoid, and vitamin A deficiency. It is performed by the application of cellulose acetate filter paper to the ocular surface for the collection of superficial layers of lining followed by histological, immunohistological, or molecular analysis of the cells. In dry eye number of goblet cells can be estimated.

Q6. How will you treat a case of dry eye?

Dry eye disease is not amenable to treatment. The only aim of treatment is symptomatic relief. The choice of treatment depends on the severity of the disease.

Patient education: Change of working environment, avoidance of smoking, the importance of frequent blinking at the time of screen work, risk of contact lens wear and risk of refractive surgery.

Mild dry eye: Artificial tears (cellulose derivatives, e.g. hypromellose: 1 drop 4–5 times daily) are appropriate for mild cases.

Moderate dry eye (use any one or combinations of the following drugs)

a. Frequent use of artificial tears every 1 to 2 hours.
b. Lubricating ointment or gel 3–4 times daily.
c. Carbomer preparations adhere to the corneal surface, therefore, have a longer effect.
d. Polyvinyl alcohol preparation (1.4%) is useful in mucin deficiency. It increases the tear film stability.
e. Sodium hyaluronate 0.1% preparation 1 drop 4–6 times daily. It promotes conjunctival and corneal epithelial healing.
f. Low-dose topical steroids for temporary use in acute exacerbation.
g. Systemic tetracycline may be helpful in meibomian gland dysfunctions.
h. Eyelid hygiene
i. Omega-3 fatty acid
j. Vitamin A therapy

Severe dry eye

a. Lubricating ointment or gel
b. Autologous serum
c. Cyclosporine 0.05% 2–3 times for severe dry eye secondary to inflammatory conditions. Cyclosporine often causes a burning sensation after application for a few weeks and takes 1–3 months to obtain significant results.
d. Room humidifiers
e. Both punctual occlusions by a silicone plug and consider for thermal cautery if plugs fall out (laser cautery is less effective). Permanent occlusions are indicated for severe dry eyes (Schirmer test values less than 5 mm).
f. Acetylcysteine 5–10% drops for patients with excess mucous plaques and filaments.
g. Permanent lateral tarsorrhaphy if all measures fail.

Dry eye disease severity grading scheme

Dry eye severity level	1	2	3	4
Discomfort, severity and frequency	Mild and/or episodic; occurs under environmental stress	Moderate episodic or chronic, stress or no stress	Severe frequent or constant without stress	Severe and/or disabling and constant
Visual symptoms	None or episodic mild fatigue	Annoying and/or activity-limiting episodic	Annoying, chronic and/or constant, limiting activity	Constant and/or possibly disabling

(Contd.)

(Contd.)

Dry eye severity level	1	2	3	4
Conjunctival injection	None to mild	None to mild	+/–	+/++
Corneal staining (severity/location)	None to mild	Variable	Marked central	N/A
Corneal/tear signs	None to mild	Mild debris, ↓ meniscus	Filamentary keratitis, mucus clumping, tear debris	Filamentary keratitis, mucus clumping, tear debris, ulceration
Lid/meibomian glands	MGD variably present	MGD variably present	MGD frequent	Trichiasis, keratinization, symblepharon
Tear film break-up time (seconds)	Variable	≥10	≥5	Immediate
Schirmer score (measures tear secretion) (mm/5 minutes)	Variable	≥10	≥5	≥2

MGD, meibomian gland dysfunction; - not present; + mild; ++ moderate; N/A, not applicable

Q7. What is the anatomical dimension of the the cornea?

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

Q8. What are the layers of cornea?

1. **Epithelium:** The epithelium layer is 50 µm thick, stratified squamous, nonkeratinized, non-secretory epithelium. Superficial cells have microvilli (needs tears to keep cornea smooth). The basement membrane is strongly attached to Bowman's layer.
2. **Bowman's layer:** It is 8–12 µm thick, acellular and consists of interwoven type IV collagen fibrils which are anterior condensation of substantia propria, incapable of regeneration, replaced by fibrous tissue if damaged (i.e. scars). This ends abruptly at the limbus, deep layers appear to merge into the stroma.
3. **Stroma (substantial propria):** The stroma is 400 µm thick and contributes 90% of corneal thickness. It contains 80% water, collagen fibres (mostly

type 1), keratocytes and an extra-cellular matrix. Three major fractions of glycosaminoglycans in the extracellular matrix are keratan sulphate (50%), chondroitin phosphate (25%) and chondroitin sulphate (25%).

4. **Dua's pre-Descemetic layer:** It is a newly discovered sixth layer of the cornea which lies between the stroma and the Descemet's layer and is an important landmark in lamellar corneal surgeries like Deep Anterior Lamellar Keratoplasty (DALK).
5. **Descemet's membrane:** The basement membrane of the endothelium is made of type IV collagen fibrils, 10 µm thick, secreted and regenerated by endothelial cells. Peripherally Hassall-Henle bodies are present. It terminates abruptly at the limbus (Schwalbe's line).
6. **Endothelium:** This layer is composed of a single layer, polygonal, cuboidal cells, incapable of regeneration. The tight junctions control corneal hydration. Repair occurs by cellular hypertrophy (polymegathism) and sliding. It is continuous with the endothelial lining of the trabecular meshwork. The cellular density of 6000 cells/mm^2 at birth slowly reduces with age and adult density is around 2500–3000 cells/mm^2. Critical density below which there is the development of corneal oedema is <500 cells/mm^2.

Q9. How does the cornea get nutrition?

- **Glucose:** The cornea obtains glucose mainly from aqueous, tears and limbal capillaries. Glucose can be stored in the epithelium as glycogen. ATP is obtained through glycolysis and the Krebs cycle.
- **Oxygen:** Endothelium acquires oxygen from aqueous and epithelium acquires oxygen from both capillaries at limbus and the precorneal film.

Q10. Tell me the embryological origin of the cornea.

The formation of cornea is induced by the lens and the optic cup in the 7th week of intrauterine life.

- **Surface ectoderm:** Corneal epithelium
- **Mesenchyme:** Bowman's membrane
- **Mesenchyme and neural crest:** Stroma
- **Neural crest:** Endothelium (Descemet's membrane is secreted by the endothelium)

Q11. What is the XYZ hypothesis of corneal epithelial regeneration?

The XYZ hypothesis, proposed by Thoft el al in 1983, stated that both the limbal basal cells and the corneal epithelial basal cells are the source for the corneal epithelial cells and there is a balance among the division, migration and shedding of these cells. The hypothesis suggested that there is cell division and proliferation of the basal cells of the corneal epithelium (X) and the centripetal migration of the basal cells from the limbal stem cells (Y) which balances the sloughing of the superficial epithelial cells (Z), thus maintaining a constant equilibrium.

Here,

'X' denotes cell division and proliferation of the basal cells of the corneal epithelium.

'Y' denotes centripetal migration of the basal cells from the limbal stem cells.
'Z' denotes sloughing of the superficial epithelial cells, thus maintaining a constant equilibrium.
Hence, X + Y =Z

Q12. Why is the cornea transparent?

a. Relative dehydration of cornea due to anatomic integrity of endothelium and epithelium.
b. Endothelial Na-K ATPase pump removes fiuid from stroma.
c. Evaporation of water from tear increases osmolarity of tear, which draws water from cornea.
d. Normal intraocular pressure (if pressure is too high, relative hydration occurs).
e. Relative acellularity, lack of blood vessels and pigments.
f. Regular matrix structure of corneal fibrils leading to destructive interference of light.

Q13. What is the nerve supply of the cornea?

The cornea is innervated by the Vth cranial nerve (ophthalmic division: Long posterior ciliary nerves→annular plexus at limbus→subepithelial plexus just below Bowman's membrane→intraepithelial plexus)

Q14. What is the blood supply of the cornea?

The cornea is an avascular structure. Small loops derived from the anterior ciliary artery invade the periphery for about 1 mm which are located not in the cornea but in the subconjunctival tissue which overlaps the cornea.

Q15. What are the complications of chemical injuries?

Acute problems

- Corneal abrasion and perforation
- Infection
- Glaucoma
- Limbal ischemia (Fig. 1.38)

Fig. 1.38: Limbal ischaemia in chemical injury

Long-term problems

- Trichiasis, distichiasis,
- Cicatricial entropion/ectropion,
- 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

Q16. How do you classify chemical injuries to the eye?

Dua's classification (updated grading scheme with prognostic value): Classification is based on the extent of the limbal staining (vs. ischemia), epithelial, bulbar and forniceal conjunctival staining.

Updated classification by Dr Harmindar Dua et al in 2001: It has six grades.

Grade	Prognosis	Clinical findings	Conjunctival involvement
I	Very good	0 clock hours of limbal involvement	0%
II	Good	<3 o'clock hours of limbal involvement	<30%
III	Good	>3–6 o'clock hours of limbal involvement	>30–50%
IV	Good to guarded	>6–9 o'clock hours of limbal involvement	>50–75%
V	Guarded to poor	>9–<12 o'clock hours of limbal involvement	>75–<100%
VI	Very poor	Total limbal (12 o'clock hours involvement)	Total conjunctival involvement

Q17. What are the possible mechanisms of glaucoma in chemical injury?

- Acute shrinkage of collagen
- Uveitis, trabeculitis
- Lens-induced inflammation
- Peripheral anterior synechiae
- Steroid response

Q18. How do you manage a patient with severe chemical injury?

Acute management

- Irrigate eyes immediately with copious amounts of sterile fiuid (BSS/RL preferred) to remove the particulate matter, dilute the pH and debride the devitalised tissues. Do not forget to evert the upper lid to look for retained 'chuna' powder in superior subtarsal sulcus and remove accordingly. Start antimicrobial treatment.
- Start steroids immediately (to decrease mediators of infiammation and stabilize lysosomes in white blood cells). Minimize steroids after 10 days (because steroids decrease fibroblast and collagen synthesis).
- 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.
- Antiglaucoma medications.
- Oral analgesic and cycloplegic drops.

Surgical

- Primary AMG at initial presentation is showing promising results, punctal occlusion in severely dry eyes

- Lid closure (taping, pressure pad, tarsorrhaphy)
- Tissue glue in recent small perforation
- Conjunctival flap, tenoplasty.
- Lysis of conjunctival adhesions (glass rods)

Long-term management—managing complications

- Poor ocular surface/persistent epithelial defect → treat the underlying cause.
- Abnormal lids (cicatricial entropion, trichiasis, distichiasis) → Lid surgery.
- Mucous membrane grafting
- Remove abnormal dysplastic epithelium to promote re-epithelisation from cornea stem cells
- Amniotic membrane transplantation
- Limbal stem cell transplant-autologous conjunctivo-limbal grafts, autologous SLET or cultured limbal stem cell. Allogenic SLET or cadaveric stem cells transplantations are alternatives.
- Cornea scars → anterior lamellar/penetrating keratoplasty (consider keratoprosthesis if severe LSCD and following repeated failed grafts).

Q19. What are the other causes of cicatricial conjunctivitis?

Infectious: Adenovirus, herpes simplex, trachoma, *Corynebacterium diphtheriae*, β-haemolytic Streptococcus.

Non-infectious

- ***Autoimmune:*** Ocular cicatricial pemphigoid, Stevens-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

Q20. What are the indications for contact lenses in ophthalmology?

The indications can be divided into

- ***Refractive (most common):*** Aphakia correction, astigmatism correction.
- ***Therapeutic:*** *See* below
- ***Cosmetic:*** Corneal scar, leukocoria
- ***Diagnostic and surgical*** (gonio lens, fundus contact lens)

Q21. What are the therapeutic indications for contact lenses?

- Visual rehabilitation in uniocular aphakia, irregular astigmatism, and keratoconus.
- Pain relief: Bullous keratopathy, corneal abrasions, post-photorefractive keratectomy
- Promote corneal healing
- Recurrent corneal erosion
- Persistent epithelial defect
- Thygeson's keratitis

- Superior limbic keratoconjunctivitis
- Filamentary keratitis
- Exposure keratopathy
- Entropion, trichiasis
- Post-ptosis operation
- Impending perforation/perforated corneas (descemetocele)
- Pharmaceutical delivery device

Q22. What are the materials used for contact lenses?

Current Contact Lens Material

- ***Hard:*** PMMA (polymethylmethacrylate): Not in regular use nowadays due to low oxygen transmissibility.
- ***Soft-hydrogel (HEMA)***
  a. High water content (extended wear soft contact lens (EWSCL))
  b. Low water content (daily wear soft contact lens (DWSCL))
  c. Silicone hydrogels (high gas permeability for extended wear).
- ***Semi-flexible/rigid gas permeable (RGP):*** CAB (cellulose acetate butyrate), silicone, polycon (90% PMMA and 10% silicone).

Q23. What are the advantages and disadvantages of soft contact lenses?

A soft contact lenses can be broadly divided into extended wear (EWSCL) or daily wear (DWSCL). They are made of hydrogel, with varying water content.

Advantages of soft CL: Comfortable, greater stability, ease of fitting and lack of spectacle blur.

Disadvantages: Poorer VA in eyes with astigmatism, higher risk of complications and low durability.

Indications for DWSCL: First-time and part-time wearer failed extended wearer.

Q24. What are the pathophysiological changes to the eye with contact lens wear?

- Desiccation
- Microtrauma
- Hypoxia and hypercapnia
- Hypersensitivity/toxicity
- Endothelial changes (blebs and polymegathism).

These complications happen due to contact lens damage, breakage, and deposit of minerals iron, calcium, mucin, lipid and protein.

SCLERITIS

History

Age: Affects patients in middle age, commonly between 47 and 60 years.

Gender: Autoimmune-related scleritis is more common in women, with 60–74% predominance and men are more likely to have infectious scleritis than women.

Race: Blacks are more prone to scleritis and episcleritis.

Chief complaints

Patients of scleritis can present as follows:

- Appearance of a small painful red nodule in the white portion of the eye
- Redness and swelling of the white part of the eye
- Decreased vision
- Watering
- Extreme sensitivity to light

History of present illness

- The involvement may be unilateral (nodular scleritis is mostly unilateral) or bilateral (anterior necrotizing scleritis is mostly bilateral).
- Pain is an important feature of scleritis. The onset of pain is gradual but most patients develop severe boring or piercing pain over several days for which patients seek medical assistance. This pain is exacerbated by eye movements and may worsen at night. It improves later in the day. Sometimes, pain is not relieved even after taking analgesics. It may spread to involve the whole orbit, ear, scalp, face and jaw (necrotizing anterior scleritis is characterized by severe pain and extreme scleral tenderness. Patients with scleromalacia perforans experience mild pain or no pain).
- Redness is the primary sign of scleritis. It is associated with tearing and photophobia. The redness is not associated with mucopurulent discharge and is not cured by antibiotic eye drops. The treating ophthalmologist or general physician may mistake it for microbial conjunctivitis. Redness gradually increases over several days. It may be usually localized in the interpalpebral area or involve the whole sclera.
- Vision is less affected in patients with mild or moderate scleritis. But severe vision loss is noted in posterior scleritis and scleromalacia perforans.
- History of fever, weight loss, rash, and epistaxis to be enquired.
- There may be a similar type of attack either in one eye or both eyes most frequently in the same location.

Past ocular surgical history: Patients with a history of pterygium surgery with adjunctive mitomycin C administration or beta irradiation, excessive use of thermal cautery and two or more surgical procedures, squint surgery, and buckling surgery are at higher risk of scleritis due to overlying necrosis of the sclera.

History of systemic illness

A. **Connective-tissue or vasculitic disorders:** Scleritis is bilateral and necrotising in nature. Commonly associated autoimmune disorders include rheumatoid arthritis (RA), granulomatosis with polyangiitis (GPA), spondylo-arthropathies, and systemic lupus erythematosus (SLE). Other less commonly associated autoimmune conditions include inflammatory bowel disease, sarcoidosis, Vogt-Koyanagi-Harada disease, Cogan's syndrome and Takayasu disease.

   So, in scleritis patients make a routine enquiry about diseases related to the following:

   - Dermatological (skin, hair, nails)
   - Respiratory

- Cardiac
- Genitourinary
- Rheumatologic
- Gastrointestinal
- Neurologic
- Hematologic and lymphatic
- Pulmonary
- Ear, nose, sinus, and throat

B. **Infectious diseases:** Contagious spread from the cornea in microbial keratitis such as herpes simplex virus (varicella-zoster virus (VZV), syphilis, HIV, tuberculosis, other recurrent keratitis and endophthalmitis).
C. **Enquire about chemical injuries.**
D. **Take a history of blunt or penetrating trauma.**
E. **Chronic use of topical corticosteroids and systemic immunosuppression**
F. **Take a history of drugs taken for other systemic conditions:** Such as topiramate, bisphosphonates (pamidronate, alendronate, risedronate) and zoledronic acid.

Past medical history: Take the history of gastric ulceration, diabetes, liver disease, anemia, renal disease and hypertension. This is important for planning treatment modalities. Past and present therapies and responses to these interventions should be investigated.

Ocular Examination

An ocular examination should include a complete general eye examination with specific focus on the sclera.

BCVA: Decreased visual acuity may be caused by the extension of scleritis to the adjacent structures, leading to reactive myositis, keratitis, uveitis, glaucoma, cataract, and fundus abnormalities (a high incidence of visual loss is seen among patients with necrotizing scleritis and posterior scleritis).

Eyeball: Proptosis and periorbital oedema in posterior scleritis.

Ocular movement: Restricted in posterior scleritis and diffuse scleritis.

Eyelid: May be edematous and ptotic.

Conjunctiva: May be chemosed and congested.

Sclera (examination in daylight)

- There may be localized or sectoral involvement (nodular scleritis, surgically induced scleritis) or involvement of a large area (diffuse anterior necrotizing scleritis) (Fig. 1.39).
- The sclera may appear diffuse, deep bluish-red, or violaceous suggesting active scleritis (Fig. 1.40).
- In the case of nodular scleritis, nodules may be single or multiple in number (Fig. 1.41) or they may coalesce to form a giant nodule and appear in the interpalpebral region 3–4 mm away from the limbus. It has a deeper blush–red colour than episcleral nodules. It is immobile and often tender to palpation (Fig. 1.42).

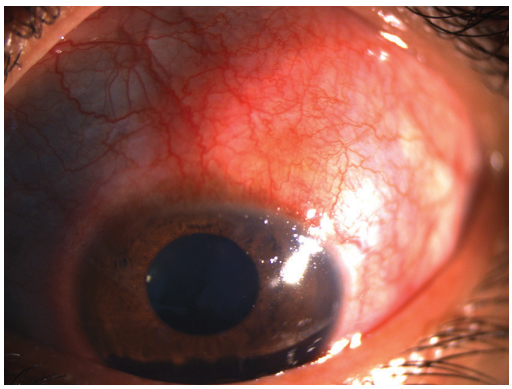

Fig. 1.39: Anterior diffuse scleritis

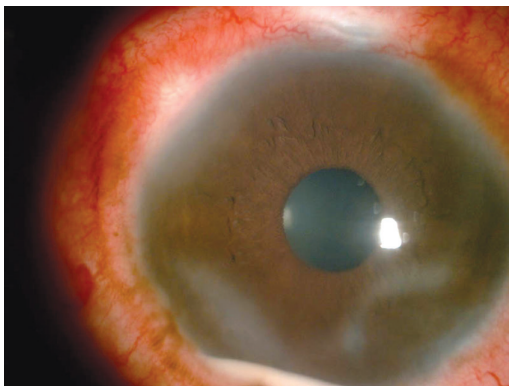

Fig. 1.40: Acute diffuse scleritis with hypopyon

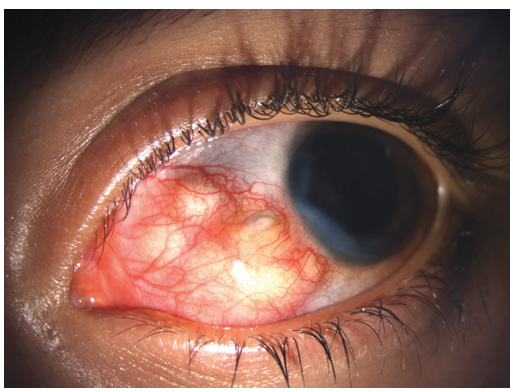

Fig. 1.41: Multiples confluent nodular scteritis

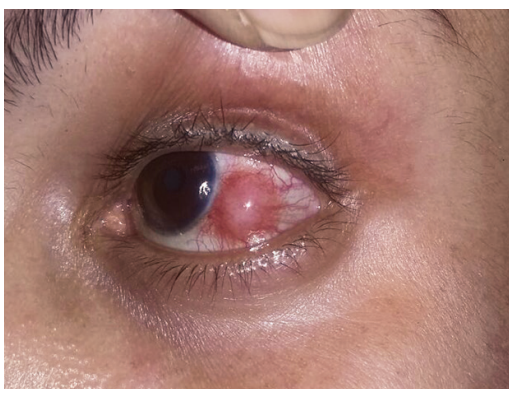

Fig. 1.42: Nodular scleritis

- Isolated avascular thickened scleral patch with no overlying conjunctival congestion indicating the vaso-occlusive type.
- In Wegener granulomatosis and polyarteritis nodosa, the disease starts adjacent to the limbus with overlying vascular congestion and then extends posteriorly.
- In scleromalacia perforans, the disease starts as a necrotic scleral plaque, adjacent to the limbus without vascular congestion. The scleral plaque is characterized by a black, grey, or brown area that is surrounded by active scleral inflammation. Sometimes, the area enlarges to form a central white sequestrum surrounded by a well-defined black or dark brown circle (Fig. 1.43). The slough may be replaced gradually by granulation tissue, leaving the underlying uvea bare or covered by a thin layer of tenon and conjunctiva.

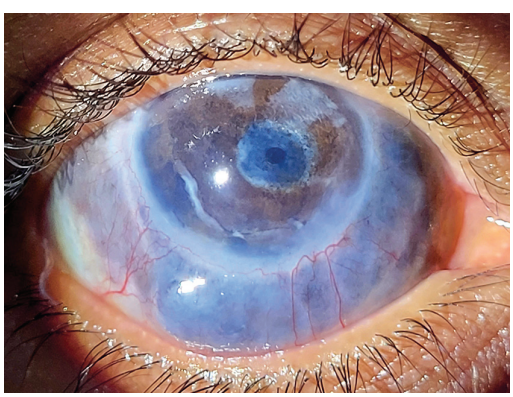

Fig. 1.43: Scleromalacia

- Areas of scleral thinning with translucency allow the uvea to be appreciated through the thin sclera and the formation of staphyloma suggests past several attacks of scleritis.

Sclera (Slit lamp examination)

In scleritis, the maximum congestion is in the deep episcleral network with some congestion in the superficial episcleral network.

- The posterior and anterior edges of the slit lamp beam are displaced forward because of underlying scleral and episcleral edema.
- Red-free light helps to identify maximum vascular congestion, areas with new vascular channels, and to differentiate between vascular and avascular areas.
- In scleritis, topical application of 2.5% or 10% phenylephrine only blanches the superficial episcleral network without significant effect on the deep episcleral network.

Cornea: May be irregularly raised and edematous (granulomatous necrotizing scleritis), acute infiltrative stromal keratitis, sclerosing keratitis and peripheral ulcerative keratitis.

Uvea: The presence of KPs, cells and flare denote aggressive scleritis.

Lens: Lens may be cataractous in long-standing scleritis.

IOP: May remain high during the active process of scleritis.

Fundus: Pathological changes are seen mostly with posterior scleritis. Common signs are as follows:

- Exudative retinal detachment (25% of cases)
- Uveal effusion syndrome (exudative RD and choroidal detachment)
- Choroidal folds (horizontal lines confined to the posterior pole)
- Subretinal inflammatory deposits or granuloma-characterized by a yellowish-brown subretinal deposit
- Vasculitis with or without soft exudates
- Retinal edema
- Disc oedema—inflammation of the nerve may happen in granulomatous posterior scleritis

Provisional diagnosis

Single/multiple nodular scleritis/acute anterior non-necrotising scleritis (diffuse or sectoral)

Acute anterior necrotizing scleritis (vaso-occlusive/granulomatous/surgery induced) scleromalacia perforans/posterior scleritis

Frequently Asked Questions

Q1. What do you mean by anterior scleritis?

Anterior scleritis is defined as scleral inflammation anterior to the extraocular recti muscle insertion.

Q2. Classify immune-mediated scleritis.

Anterior scleritis	Posterior scleritis
Non-necrotizing • Diffuse • Nodular	
Necrotizing • Vaso-occlusive • Granulomatous • Surgery induced	
Scleromalacia perforans	

Q3. Describe the clinical features of nodular scleritis.

- Mostly affects young females
- Less acute onset and more prolonged course than nodular episcleritis
- Presents as localised redness, tenderness of the globe and the appearance of scleral nodules either single or multiple in number
- Nodules are situated at the interpalpebral region and 3–4 mm away from the limbus
- Nodules have a deeper blue-red colour than episcleritis and immobile
- Multiple nodules may coalesce to form a big nodule
- Deep vascular plexus over the nodule is not affected when 2.5% phenylephrine is instilled
- Occasionally (10%) may turn into necrotizing scleritis
- On resolution, there may be an atrophic scar formation or thinning of the area

Q4. How will you differentiate a scleral nodule from an episcleral nodule?

An episcleral nodule is mobile, with no elevation of the scleral surface. Instillation of 2.5% phenylephrine drop blanches the conjunctival and episcleral vessels.

Q5. Enumerate the clinical features of the scleromalacia perforans.

- Typically affects elderly females suffering from rheumatoid arthritis.
- Presents with painless, non-specific irritation and keratoconjunctivitis sicca.
- Vision is unaffected
- On examination, a white necrotic scleral plaque near the limbus without any overlying vascular congestion. But vascular congestion is noted at the borders of the necrotic plaque. The scleral plaque is marked by a black, grey, or brown area that is surrounded by active scleral inflammation. Sometimes, the area enlarges to form a central white sequestrum surrounded by a well-defined black or dark brown circle.
- Progression is very slow
- The slough may be replaced gradually by granulation tissue, leaving the underlying uvea bare or covered by a thin layer of tenon and conjunctiva.

Q6. Mention the clinical features of the diffuse anterior non-necrotizing scleritis.

- Affects commonly middle-aged females with connective tissue disorders
- Presents with severe pain which spreads to the surrounding areas

- Redness may be localized or generalized
- The involved area is edematous and congested
- Later, it develps a slight grey–blue appearance
- History of recurrence is present

Q7. Describe the features of the anterior necrotizing scleritis.

- Mostly female patients (average age between 50 and 60 years)
- Bilateral involvement
- Persistent severe pain radiating to the surrounding areas, not cured by analgesics.
- Isolated avascular thickened scleral patch with no overlying conjunctival congestion indicating the vaso-occlusive type.
- In granulomatous scleritis, the disease starts adjacent to the limbus with overlying vascular congestion and then extends posteriorly. Adjacent parts of the cornea, sclera, and conjunctiva are edematous.
- In surgery-induced scleritis, the disease does not progress with time

Q8. What do you mean by posterior scleritis?

Posterior scleritis is defined as scleral inflammation posterior to the extraocular recti muscle insertion. It is characterized by the presence of proptosis, exudative RD, uveal effusion, choroidal folds, disc edema, and vasculitis.

Q9. What are the complications of scleritis?

Complications are frequent and include:

- Peripheral keratitis
- Uveitis
- Complicated cataract
- Glaucoma
- Central stromal keratitis
- Sclerokeratitis particularly with herpes zoster scleritis
- Sclerosing keratitis may present with crystalline deposits in the posterior corneal lamellae
- Vitritis (cells and debris in vitreous)

Q10. Why do is 'T' sign noted in posterior scleritis on USG?

In posterior scleritis, fluid is accumulated in subchoroidal space. This fluid appears as hypodense shadow on USG B scan. This hypodense shadow remains perpendicular to the optic nerve shadow giving rise to 'T' sign.

Q11. What are the features of infective scleritis?

Some of the pathognomonic features of infective scleritis are:

- Mostly unilateral
- Past history of ocular trauma, and herpetic infection
- Sometimes, a careful history taking reveals endogenous infection
- Males are commonly affected
- Scleral or subconjunctival abscess formation
- Conjunctival ulceration and sloughing
- Presence of scleritis lesion, associated with hypopyon or keratic precipitates

Q12. Mention the role of diagnostics and laboratory tests in the diagnosis of scleritis.

The diagnosis of scleritis is clinical. However, laboratory testing is often necessary to discover any associated connective tissue and autoimmune disease.

A. **Diagnostic procedures**

- B-scan ultrasonography-ultrasonographic changes include scleral and choroidal thickening, scleral nodules, distended optic nerve sheath, fluid in Tenons capsule, or retinal detachment.
- Orbital magnetic resonance imaging (MRI) may be used for the detection of posterior scleritis.

B. **Laboratory testing**

- Laboratory tests include complete blood count (CBC) with differential count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum autoantibody screen (including antinuclear antibodies), anti-DNA antibodies, rheumatoid factor, anti-neutrophil cytoplasmic antibodies, urinalysis, syphilis serology, serum uric acid and sarcoidosis screen.

Q13. How will you manage a patient with scleritis?

Medical therapy

- ***Oral NSAIDs:*** These are the first-line agent for mild-to-moderate scleritis. Non-selective COX inhibitors such as flurbiprofen, indomethacin and ibuprofen may be used. Indomethacin 50 mg three times a day or 600 mg of ibuprofen three times a day may be used.
- ***Corticosteroids (oral and topical):*** Topical corticosteroids may reduce ocular inflammation but treatment is generally systemic. Corticosteroids may be used in patients unresponsive to NSAIDS or those with posterior or necrotizing disease. This dose should be tapered to the best-tolerated dose. Pulsed intravenous methylprednisolone at 0.5–1g is reserved for severe scleritis.
- ***Immunomodulatory agents:*** Immunomodulatory agents should be considered for long-term therapy to avoid steroid-related complications. Commonly used agents are cyclophosphamide or mycophenolate. More recently, tumor necrosis factor (TNF)-alpha inhibitors such as infliximab have shown promise in the treatment of non-infectious scleritis refractory to other treatments.

Surgery

- A formal biopsy may be performed to exclude a neoplastic or infective cause but should be avoided in active disease. The surgeon should be prepared for scleral graft if necessary arises.
- Areas with imminent scleral perforation warrant surgical intervention, though the majority of patients often have scleral thinning or staphyloma formation that does not require scleral reinforcement.
- Small corneal perforations may be treated with a bandage contact lens or corneal glue.
- Cataract surgery should only be performed when the scleritis has been in remission for 2–3 months. Cataract surgery may bring back the scleral inflammation.

COMMONLY USED STAINS AND CULTURES IN RELATION TO INFECTIOUS KERATITIS

Stains

a. **Gram's stain:** Gram-positive cocci in pairs (*Streptococcus pneumoniae*), Gram-positive cocci in clusters (Staphylococcus).
b. **Giemsa's stain:** Acanthamoeba cysts (dark blue with pale blue cytoplasm), both mycotic filaments and bacteria appear purple blue.
c. **10% KOH:** It stains fungal filaments (due to chitin content) and Acanthamoeba cysts. The addition of 10% glycerol serves as a mordant and helps to keep the smear preserved for as long as six months.
d. **ZN stain:** For AFBs.
e. **Lactophenol cotton blue:** For keratomycosis.
f. **Kinyoun stain** (cold carbol fuchsin) for Nocardia.

Special Stains (Fluorescence Microscopy)

a. **Calcofluor white:** Used for Microsporidia, Acanthamoeba cysts and fungi. Please note that Acanthamoeba trophozoites are not stained. The stain may be coupled with 10% KOH for better detection.
b. **Auramine–rhodamine:** Used for Mycobacteria which gives bright orange or yellow under fluorescence microscope. Mycolic acid present in the cell wall binds with auramine–rhodamine.
c. **Acridine orange:** For bacteria, stains red if the organism is dead and green if it is alive.
d. **Fluorescent coupled Gram's stain:** Gives red in Gram-positive organism and green in Gram-negative organism.
e. **Tzanck smear:** Giemsa/PAP stains to show intranuclear eosinophilic inclusion body (Cowdry type A).

Culture Media

a. **Bacteria:** Blood agar, chocolate agar (heated blood agar) for Neisseria, Moraxella, and Haemophilus.
b. **Aerobic organisms:** Blood agar, brain heart infusion broth, thioglycollate broth, SDA, LJ media and non-nutrient agar.
c. **Anaerobic or micro-aerophilic organisms:** Thioglycollate broth.
d. **Fungal:** Sabouraud's dextrose agar, potato dextrose agar, blood agar.
e. **AFB:** Blood agar, chocolate agar, Lowenstein-Jensen media.
f. **Acanthamoeba:** Blood agar and non-nutrient agar with *E. coli* overlay. Initially, trophozoites appear on the surface within 48–72 hours which turn into cysts within 7–10 days.
g. **Viral culture:** Cell culture.

Special Tests

a. ELISA (high specificity but low sensitivity).
b. Polymerase chain reaction (PCR): Used mainly for organisms which are either difficult to detect in commonly used culture techniques or the organisms take a long time to grow (AFB). Cost and availability are the main limiting factors.
c. *In vivo* confocal microscopy (IVCM)

SPECULAR MICROSCOPY

Principle

Endothelial cells cannot regenerate and these are the cells which are arrested in the G1 phase of the cell cycle. Reflected light (where the angle of incidence is equal to the angle of reflection) coming from a tissue interface is captured for image formation. The instrument allows visualization between 25x and 60x. David Maurice and Laing were the pioneers to develop specular microscopy.

A Typical Specular Reflection Shows Four Zones

a. **Dark zone:** Aqueous humour.
b. **Endothelial zone:** Shows cellular morphology.
c. **Homogenous zone:** Stroma
d. **Bright zone:** Reflection from pre-corneal tear film.

Types

a. **Non-contact:** An increased angle of incidence eliminates reflection from the anterior corneal surface. Being non-contact, it can be used in presence of infection and trauma.
b. **Contact:** Here a coupling fluid having the same refractive index as that of the cornea is used to counter surface reflection. Being contact in with nature, though it gives an enlarged image, there is a chance of spread of infection if not sterilized properly. It might cause discomfort to some patients.
c. **Wide field:** An increased field is created by a scanning mirror.

Measurements

Specular image is captured by the following methods:

- **Manual:** Examiner can control the capture especially in presence of bad reflections.
- **Automated:** This gives a quick reading.
- **Semi-automated:** Best method in patients with poor fixation and irregular cornea.

Analysis

- **Qualitative:** Normal endothelial cell is a regular hexagon separated by dark boundaries.
- **Quantitative:**
  a. **Endothelial cell density (ECD):** Expressed as a number of cells/square mm.
  b. **Coefficient of variance (CV):** This is the SD of mean cell area divided by mean cell area and is expressed as percentage. The normal value is 40. Any value more than 40 is considered abnormal.
  c. **Pleomorphism:** Number (percentage) of cells having sides less than or more than 6. Normal cornea has 60–80% hexagonal cells. Pleomorphism suggests endothelial stress.
  d. **Polymegathism:** Increased size of endothelial cells found in old age. This is a typical method of corneal healing. When an endothelial cell is lost, the adjacent cells will increase their size (polymegathism) to seal the gap created by the loss of endothelial cells.

Eye bank specular microscope: This is a special type of specular microscope used to count endothelial cells in corneal buttons at eye bank. The tissue must be warmed to 25°C before taking an endothelial count. Minimum 2000 cells are a prerequisite for an optical grade tissue. Buttons meant for EK should have more endothelial cells (2500–3000) as there is a probability of intraoperative loss of endothelial cells during graft insertion and graft manipulations inside the anterior chamber.

Factors hindering the quality of specular imaging: Poor image quality is associated with dry eye disorders, epithelial oedema, significant stromal haze and DM pathologies.

Clinical indications of specular microscopy:

a. To diagnose endothelial dystrophies.
b. As a preoperative test for cataract surgery in a Fuchs' dystrophy
c. Postoperative assessment of endothelial cells after cataract surgery in Fuchs' dystrophy.
d. Post-keratoplasty (PK, DALK and EK) endothelial assessment.

Important Information About Corneal Endothelial Cells

Normal endothelial counts:

- ***At birth:*** 5000–6000 cells/square mm.
- ***At 5 years:*** 3500 cells/square mm.
- ***At 14–20 years:*** 3000 cells/square mm.
- ***Late adulthood:*** 2500 cells/square mm.

Normal endothelial cell loss: Average rate of loss is 0.6%/year.

Pseudo-guttae: These are similar drop-out images like to guttae. They are associated with endothelial infections (like herpes), intraocular inflammations (like TASS) and uveitis. Pseudo-guttae are reversible and they tend to disappear with the treatment of causal conditions.

DWEK: It means Descemetorhexis without endothelial keratoplasty. This is an alternative management modality in Fuchs' dystrophy in cases having peripheral endothelial cell count of more than 1000 cells/square mm.

Recommended endothelial count for using the tissue for optical purposes: It varies depending upon individual eye bank strategies. But most will recommend a count above 2000 cells/sq mm for optical PK and 2200 cells/sq mm for EK.

Systemic factors influencing endothelial health: Chronic kidney disease (CKD) patient on haemodialysis, diabetes mellitus, use of the anti-parkinsonian drug (amantadine), birth trauma by forceps application, etc.

Recent advances in the medical management of corneal oedema: Rho-kinase inhibitors (0.02% Netarsudil, 0.4% Ripasudil: as topical preparation) have been tried in corneal oedema associated with Fuchs' dystrophy and post-cataract surgery corneal oedema. The drug acts by increasing cell proliferation, slowing cellular apoptosis and enhancing cell adhesions.

Alternatively, they can be injected intracamerally along with cultured endothelial cells (tried in a mouse model) with variable success.