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).

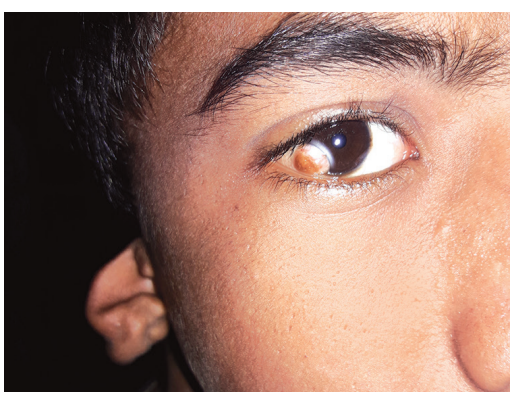

Fig. 1.1: Limbal dermoid in a case of Goldenhar syndrome

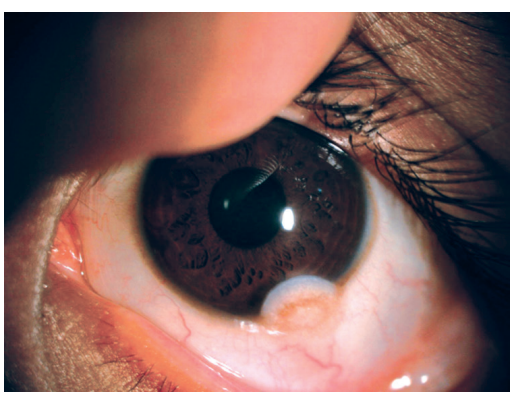

Fig. 1.2: Limbal dermoid

- ***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

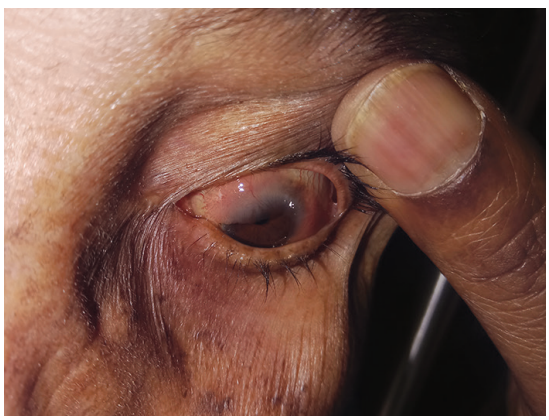

Fig. 1.3: OSSN with extensive corneal involvement

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.

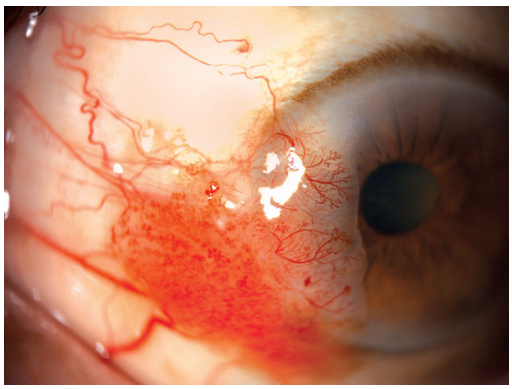

Fig. 1.4: OSSN (strawberry)

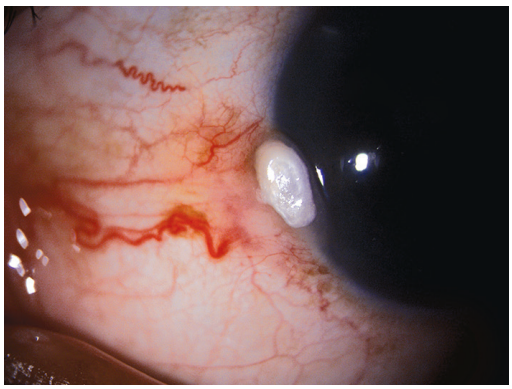

Fig. 1.5: OSSN (leukoplakia)

- 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

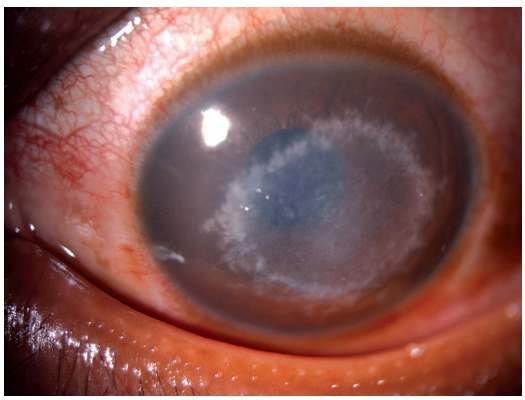

Fig. 1.6: Ring ulcer in acanthamoeba keratitis

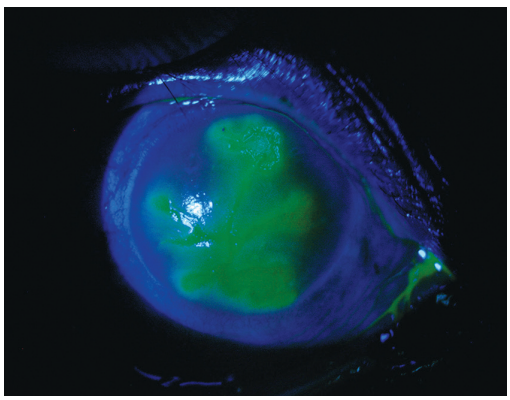

Fig. 1.7: Geographic or dendritic ulcer

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.

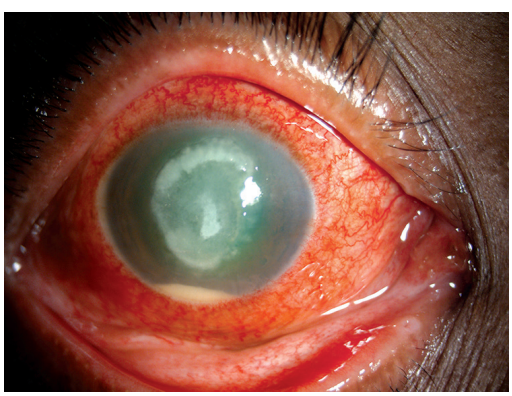

Fig. 1.8: Bacterial keratitis

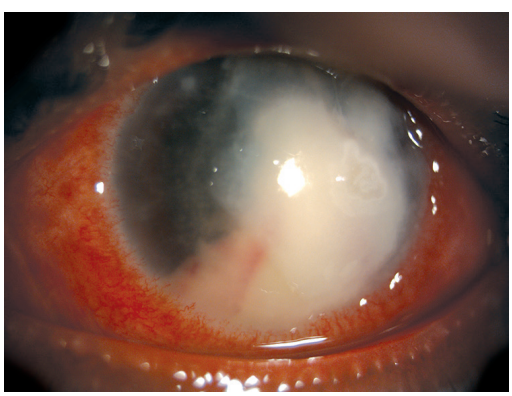

Fig. 1.9: Fungal corneal ulcer

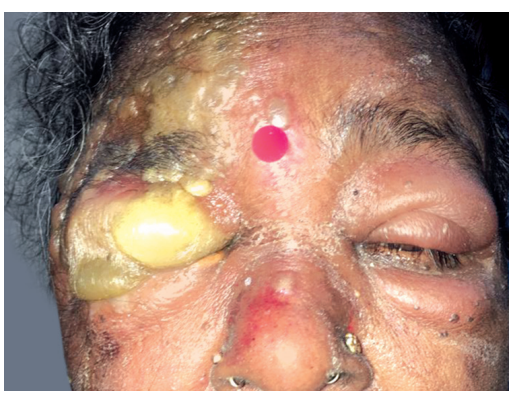

Fig. 1.10: Herpes zoster ophthalmicus

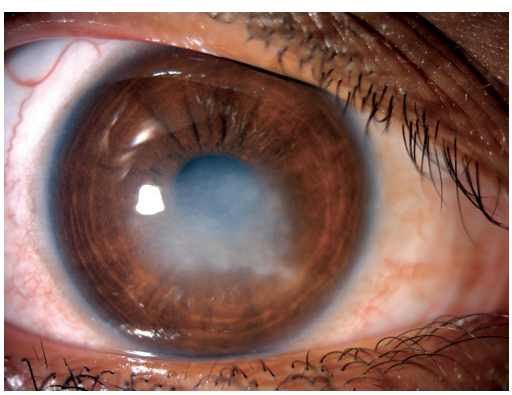

Fig. 1.11: Viral endothelitis or disciform keratitis

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.