Diseases of the Cornea

CONEAL INFECTIONS/ INFECTIVE KERATITIS / ULCER

- Epithelial defect with infiltration caused by various microbial agents
- BACTERIAL
- FUNGAL
- VIRAL
- ACANTHAOMEBA

Infective keratitis

- Infective keratitis rarely occurs in the normal eye because of the human cornea's natural resistance to infection.
- Natural Defence Mechanisms
  - Lids : Mechanical barrier / Blinking
  - Intact Corneal Epithelium
  - Tears : IgA, Lysozyme, Mucin
  - Normal Ocular flora prevents overgrowth of path. organisms

Predisposing factors

- Extrinsic Factors
- Ocular Surface Disease
- Corneal Epithelial Abnormalities
- Systemic Conditions

Extrinsic Factors

- **Trauma**, including chemical and thermal injuries, foreign bodies, and local irradiation

- **Use of contact lenses** : Overnight wear, Misuse (overwear) , Inadequate disinfection of contact lenses, Contamination of the contact lens storage case , contaminated contact lens solution

Extrinsic Factors

- **Previous ocular and eyelid surgery**, especially corneal surgery, including refractive surgery and penetrating keratoplasty
- **Loose sutures**
- **Medication-related factors** (e.g., contaminated ocular medications,topical nonsteroidal anti-inflammatory drugs, anesthetics, corticosteroids,)
- **Immunosuppression (**topical and systemic)

Ocular Surface Disease

- Tear-film deficiencies
- Abnormalities of the eyelid anatomy (Entropion, ectropion) and function (Incomplete closure - exposure keratitis)
- Misdirection of eyelashes : Trichiasis
- Adjacent infection (conjunctivitis, blepharitis, canaliculitis, dacryocystitis)

Corneal Epithelial Abnormalities

- Corneal abrasion or epithelial defect
- Disorders predisposing to recurrent erosion of the cornea
- Viral keratitis (herpes simplex virus or varicella zoster virus keratitis)
- Neurotrophic keratopathy (e.g., trigeminal neuropathy, herpes keratitis)
- Corneal epithelial edema, especially bullous keratopathy

Systemic Conditions

- Diabetes mellitus
- Debilitating illness, especially malnourishment and/or respiratory dependence
- Dermatological/mucous membrane disorders (e.g., Stevens-Johnson syndrome, ocular mucous membrane pemphigoid)
- Atopic dermatitis/blepharoconjunctivitis

Systemic Conditions

- Collagen vascular disease
- Substance abuse
- Immunocompromised status
- Gonococcal infection with conjunctivitis
- Vitamin A deficiency
- Acoustic neuroma or neurological surgery causing damage to the Vth or VIIth cranial nerves

Pathogenesis

- The development of corneal ulcer is in 4 stages

I. Stage of progressive infiltration
II. Stage of active ulceration
III. Stage of regression
IV. Stage of cicatrization

Pathogenesis

I. Stage of progressive infiltration ; Adherence and entry of organisms, release and diffusion of tissue toxins and enzymes, and resultant tissue destruction

II. Stage of active ulceration : The epithelium sheds off and infiltration extends well beyond the edges of epithelial defect

Pathogenesis

III. Stage of regression : Microbial destruction is halted, Microbial growth is controlled, epithelium starts regrowth, necrotic areas of ulcer sheds off, giving impression that ulcer has increased in size but inflammation & pain decreases and pt is symptomatically better

IV. Stage of cicatrization: The epithelium heals and necrotic stromal area is replaced by scar and pts sign and symptoms improve

BACTERIAL KERATITIS

- **Common causative agents : (affecting corneal epithelial integrity)**
  - Staph. epidermidis
  - Staph. Aureus
  - Strept. Pneumonia / viridans
  - H.infleunza
  - P.aeruginosa
  - N.gonorrhea
  - Enterobactereriaceae : Proteus, serratia, enterobacter etc

Clinical features

- Depends on virulence of organism, its toxins and enzymes and the response of host tissue
- Symptoms : Pain, Foreign body sensation, Watering, Photophobia, Redness of eyes, Purulent discharge, decrease vision

Signs

- Edema of lids Marked blepharospasm
- Conjunctival congestion / chemosis
- Corneal Epithelial defect with infiltration in the form of Yellowish white area of ulcer, oval or irregular in shape
- Margins are swollen & over hanging
- Floor covered with necrotic material
- Stromal edema
- Muddy iris/ Small pupil due to asscociated iritis
- Increased IOP / Secondary glaucoma
- Hypopyon (Leucocytes / white blood cells collected in ant chamber)

Hypopyon Corneal ulcer

- Associated iridocylitis due to release of bacterial toxins
- Outpouring of leucocytes from uveal tissue into AC, gravitate to bottom to form hypopyon
- Sterile

Development of Hypopyon ulcer

- Two factors

I. Virulence of organisms : Staphylococci, streptococci,Gonococci, Moraxella but Pseudomonas and pneumococci are most dangerous

II. Resistance of tissues : Much more common in old, debilitated, alcoholics etc

Staphylococcal ulcers

- Compromised corneas
- Round or oval ulcer with grayish stromal white infiltration with distinct margins
- Surrounding epithelial corneal oedema
- Fibrin plaque and hyopyon may be there
- Staph aureus more severe infiltration than epidermidis

Pneumococcal Ulcers

- Usually post trauma
- Progress from site of injury towards centre
- Leading edge has thick infilteration
- Ulcus serpens : due to its tendency to creep over cornea in serpiginous fashion
- Ant chamber reaction usu severe with hypopyon

Gram Negative Organisns

- Mucopurulent discharge
- Dense suppuration with necrosis
- Diffuse epthilelial odema , away from site of ulcer due to inflammation (Surrounding cornea is also hazy)
- Loss of corneal transparency
- Ring ulcer
- Keratolysis/ sloughing/ melting / perforation

Moraxella

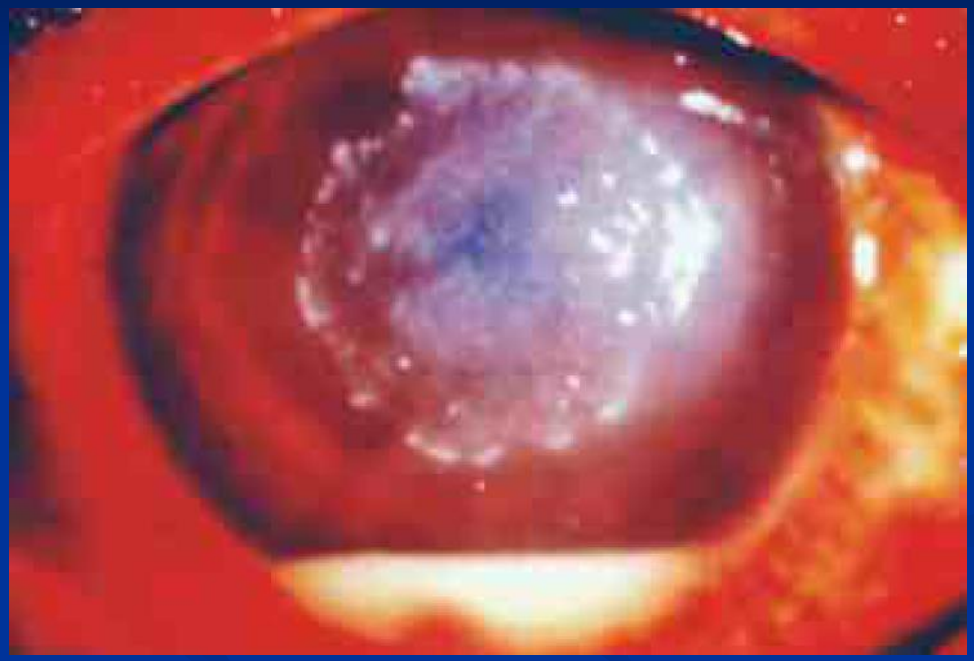
- Post trauma in debilited pts like alcoholics, diabetes, malnourished
- Oval ulcer in inferior cornea
- Tend to remain localised while it spread in depth

Mycobacteria

- Full thickness corneal infiltrate with surrounding corneal folds : cracked wind shield appearance
- Satellite lesions
- Infectious crystalline keratopathy
- Post LASIK infections

Nocardia

- Usu post trauma
- Multiple anterior stromal pin head size infiltrates arranged in a ring like pattern known as wreath pattern



- Lesion remain localized to superficial layers as no tissue damaging enzymes are produced

Complications:

- Corneal perforation – secondary endopthalmitis
- Corneal sloughing :Expulsion of contents: phthisis bulbi
- Vision loss
- Corneal opacity : nebular / macular : irregular astigmatism
- Corneal Opacity : leukoma (scar tissue formation with or without corneal vascularization)
- Adherent leukoma
- Anterior Staphyloma

General examination

- Built
- Nourishment
- Anaemia
- Immunological status
- Drug abuse

Ocular examination

- Diffused light examination
- Lid and Tear film status
- Regurgitation test and syringing
- Biomicroscopic Slit Lamp examination (staining with 2% fluorescein dye)

Laboratory investigation

- Laboratory investigation Hb, TLC, DLC, ESR
- Microbiological investigation (scrapping from the margins and base of the ulcer under LA) Gram and Giemsa stain (gram +ve) 10% KOH (fungal hyphae) Calcofluor white (CFW) (fungal filaments, Acanthamoeba cysts and trophozoits) Blood agar medium culture (aerobic) Sabourauds dextrose agar medium without chlorhexidine (fungi), Non nutrient agar laid with E. Coli for Acanthamoeba.

Laboratory investigation

- Blood agar medium (most bacteria except neisseria, hemophilus and moraxella (NHM)) .
- Chocolate agar medium (for NHM).
- Cooked meat broth (anerobic and fastidious)
- Brain heart infusion (for aerobic & fungi): When scanty sample

Corneal Biopsy

- Deep stromal infiltration
- Negative corneal scrapping
- Esp Fungal infections
- Not responding to t/t
- 6 or 7 - 0 silk suture / skin biopsy punch

Confocal Microscopy

- Non invasive method to visualize microbial agents in cornea
- Esp helpful in Acanthamoeba, Fungal infections, microsporidia and some bacteria

Treatment

- Specific treatment for the cause
- Non specific supportive therapy
- Physical and general measures

Specific treatment for the cause

- Initiate **topical broad-spectrum antibiotics**:
  - concenterated tobramycin 1.3 % (aminoglycoside gram -ve) alternating with fortified cefazolin 5 % (cephalosporin for Gram + ve) one hourly.

- If the corneal ulcer is small, peripheral and no impending perforation is present, intensive monotherapy with **fluoroquinolones (Moxifloxacin, Gatifloxacin, ofloxacin, ciprofloxacin)** is an alternative treatment.

- Modify antibiotics depending upon c/s report

Preparation of fortified antibiotics

- Preparation of fortified antibiotics Tobramycin 1.36 mg / ml (1.3 %) : Mix Tobramycin eye drops 0.3 % + 2ml of 40 mg/ml sol of Tobramycin injection. Refrigerate and use within 14 days
- Cefazolin 50 mg/ml (5%) : 500 mg parentral antibiotic diluted with 10 ml (2.5 ml sterile water added to 7.5 ml of artificial tears or 10 ml of artificial tears). Refrigerate and use within 7 days
- Frequency : 1 hourly round the clock for 2-3 days then 2 hourly during day and 4 hourly during night. Once healing is ensured 4- 6 hourly

Non specific supportive therapy

- Oral NSAIDS for pain
- Topical cycloplegics like atropine / homatropine
- Oral and topical antiglaucoma drugs
- Lubricating drops
- Multivitamin preparation

Physical and general measures

- Good diet
- General and ocular hygiene
- Dark goggles
- Rest

Non healing ulcer

- Removal of known cause Local (IOP, concretions , foreign body. Trichiatic lashes)
- Systemic causes (diabetes, anaemia, malnutrition, steroids)
- Mechanical debridgement
- Cauterisation of the ulcer
- Soft contact lens bandage
- Peritomy (severing of perilimbal conjunctival vessels)
- Review of c/s reports , repeat c/s, corneal biopsy if required
- Rule out drug toxicity

Treatment of impending perforation:

- No stain Pressure bandage
- Lowering of IOP
- Tissue adhesive glue (cynoacrylate)
- Soft contact lens Bandage
- Conjunctival flap
- Penetrating keratoplasty

Treatment of perforated corneal ulcer

- Less than 2.5mm : Cyanoacrylate glue + BCL
- More than 2.5 mm : Patch graft / Penetrating keratoplasty.
- Nothing Available : Conjunctival graft

Treatment of Healed ulcer / Corneal opacity

- Refraction
- Contact lenses esp RGP
- Optical Iridectomy
- Phototherapeutic keratectomy (PTK)
- Lamellar Keratoplasty if lesion is not full thickness
- Penetrating keratoplasty : Full thickness /deep lesions/ endotheilal dysfunction

Fungal / Mycotic Keratitis.

An opportunistic fungal infection of the eye that causes ulceration and inflammation, usually following trauma to the cornea by vegetative matter, soil or surgery. Prolonged treatment with corticosteroids may also be a predisposing factor.

Fungal Keratitis

- Fungal keratitis is challenging corneal disease and presentations is very different from bacterial keratitis.
- Difficulty arise in making correct clinical and laboratory diagnosis.
- The treatment of fungal keratitis is also difficult due to poor availability of antifungal drugs and delay in starting treatment.
- Treatment is required on long term basis, intensively and often cases require therapeutic keratoplasty.

Fungal Keratitis

- Fungi enter into corneal stroma through epithelial defect, which may be due to trauma, contact lens wear, bad ocular surface or previous corneal surgery.
- In stroma fungi multiply and causes tissue necrosis and inflammatory reaction.
- Organisms enter deep into the stroma and through an intact Descemets membrane into the anterior chamber and iris. They can also involve Sclera.

Fungal Keratitis

- The spread is due to the fact that the blood borne growth inhibiting factors may not reach the avascular tissue like cornea and sclera.

Risk Factors

1. Trauma outdoor/ or the one which involves plant matter (including contact lenses)
2. Topical medications: corticosteroids, anaesthetic drug abuse and topical broad spectrum antibiotics use for long time (resulting in non-competitive environment for growth)

Risk Factors

3. Systemic use of steroids
4. Corneal surgeries (Penetrating keratoplasty, refractive surgery)
5. Chronic keratitis (herpes simplex, herpes zoster, Vernal or allergic keratoconjunctivitis, and neurotrophic ulcer)
6. Diabetes , Chronically ill / hospitalised patients, AIDS and leprosy

Causative fungi

I. **Yeast:** Candida species (albicans), Cryptococcus

II. **Filamentous septated**

A. Non-pigmented hyphae: Fusarium species (solani), Aspergillus species (fumigatus, flavus, niger)

B. Pigmented hyphae (dematiaceous): Alternaria, Curvularia , Cladosporium species

Causative fungi

III. Filamentous non-septated : Mucor and Rhizopus species

IV. Diphasic forms: Histoplasma, Coccidiodes, Blastomyces

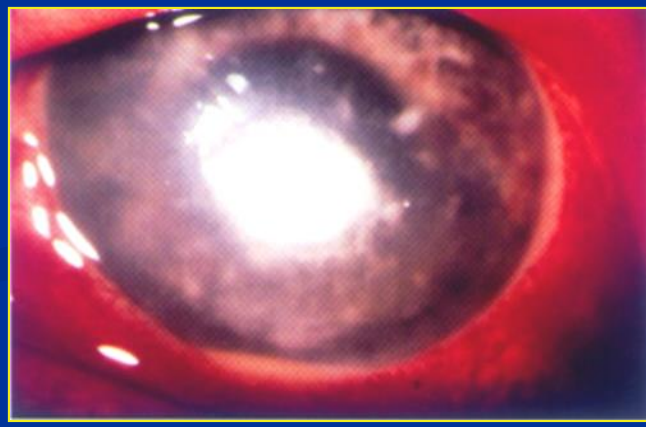
Clinical Features

Symptoms

- Onset is slow
- Symptoms are less compared to signs
- Diminution of vision, pain, foreign body sensation

Signs

- Diminution of vision, depending on location of ulcer
- Conjunctival and ciliary congestion
- Epithelial defect
- Stromal infiltrates
- Elevated areas, hyphate (branching) ulcers, irregular feathery margins
- Dry and rough texture



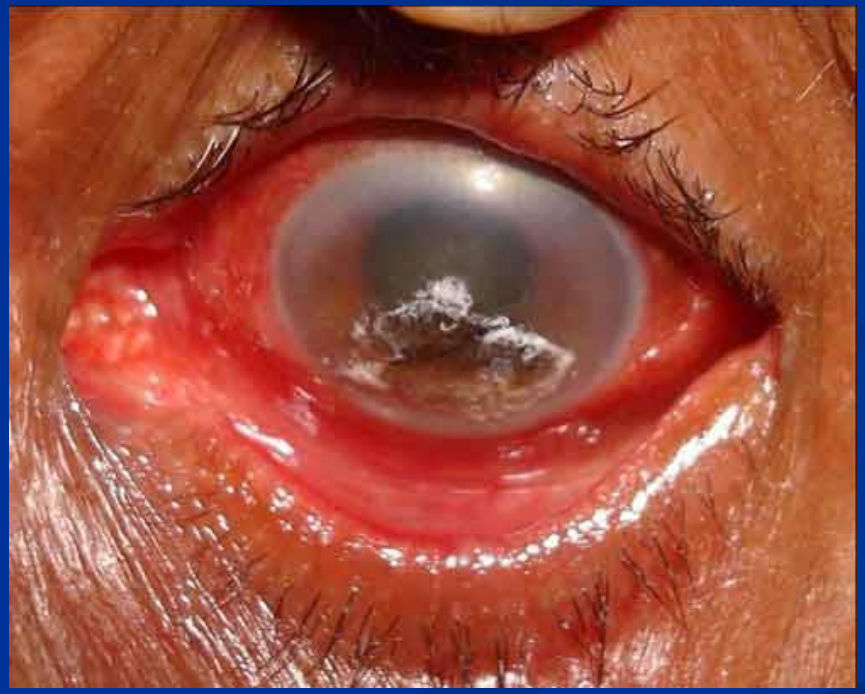
Advanced fungal Keratitis with surrounding infiltrateds .

Signs

- Satellite lesions
- Wesseley's immune ring : due to deposition of immune complexes and inflammatory cells around the ulcer
- Brown pigmentation due to dematiaceous fungus (Curvularia lunata)
- Intact epithelium with stromal infiltrates
- Endothelial plaque
- Anterior chamber reaction : hypopyon: Fixed and immobile

Fungal Keratitis with Hypopyon

Fungal Keratitis



Fungal Keratitis – Pigmented Lesion

Laboratory Diagnosis

- The Gram and Giemsa stains are used as initial stains
- Potassium Hydroxide (KOH) 10-20 wet mounts
- Culture Media: Sabouraud dextrose agar without chlohexidine
- Anterior chamber tap under aseptic conditions to aspirate hypopyon and or endothelial plaque

Treatment

- Natamycin 5% suspension: frequency will depend on severity of condition
- Candida species respond better to Amphotericin B 0.15%
- Fluconazole 2%
- Miconazole 1%
- Scrapping every 24 to 48 hours
- Treatment is required for 4 – 6 weeks

Treatment

- Sub-conjunctival injection of Miconazole 5 – 10 mgm of 10 mgm/ml suspension (indicated in severe form of keratitis, scleritis and endophthalmitis)
- Intracameral injection of Amphotercin B
- Systemic:

  Fluconazole or Ketoconazole is indicated in severe form of keratitis, scleritis and endophthalmitis

Surgical Treatment

1. Daily debridement with spatula/ blade every 24 – 48 hours
2. Surgical treatment is required in approximately 1/3rd cases of fungal keratitis due to failure of medical treatment or perforation
3. Surgical treatment in the form of :

   therapeutic keratoplasty, conjunctival flap or lamellar keratoplasty

Surgical Treatment

- Surgery is usually indicated within 4 weeks due to failure of medical treatment or recurrence of infection
- Unfavorable outcome is due to scleritis, endophthalmitis and recurrence
- Cryotherapy with topical antifungal treatment or corneoscleral graft in cases of fungal scleritis and keratoscleritis

Thanks