

# INFECTIVE KERATITIS

*This didactic lecture was presented by Dr. Shabbir Hussain on 26-08-2001 in IMA hall.*

As the name suggests, it is the inflammation of the cornea, resulting from the menace of micro-organisms.

The keratitis may be :

1. Bacterial
2. Fungal
3. Viral.

Keratitis can be categorized clinically into:-

1. Superficial
  - a. Purulent - Bacterial & Fungal
  - b. Nonpurulent - Viral & Allergic
2. Deep

## Bacterial Keratitis

### Signs and Symptoms

The patient will present with

1. Pain
2. Lacrimation
3. Redness
4. Photophobia & Blepharospasm.
5. Visual acuity is reduced
6. Mucopurulent discharge may be present, likely to be thick.

Biomicroscopically, the presentation will be

1. Conjunctival and circumcorneal vessels are engorged and inflamed.
2. Oedematous cornea
3. Localised epithelial excavation with the sequestrum partly disintegrated and cast off.
4. Ulcer is saucer shaped, walls project above the normal corneal surface.
5. Surrounding area show greyish discoloration (cloudiness) suggestive of the progressive stage of the ulcer-microscopic tissue examination reveals leucocytic infiltration
6. In severe cases there is pronounced anterior chamber reaction, often with hypopyon.
7. Intraocular pressure is mostly elevated. .

### PATHOPHYSIOLOGY

The most common infective organisms and their gram staining characteristics are

**Staphylococcus aureus** Gram positive cocci singly or pairs or clusters.

**Pneumococci** Gram positive diplococci

**Streptococci** Gram positive cocci in chains

**Pseudomonas aeruginosa** Gram negative rods

**N. gonorrhoeae** Gram negative diplococci

**Moraxella** Gram negative diplobacilli

**N.gonorrhoeae, N.meningitides and Coryne bacterium diphtheriae** are the only organisms which can penetrate the intact cornea.

Once the corneal defenses are breached, specifically the epithelial, the cornea is prone to infection.

Possible causes include :

1. Direct corneal trauma
2. Chronic eyelid disease and structural malposition of the lids
3. Tear film abnormalities affecting the ocular surface
4. Hypoxic trauma from contact lens wear.
5. Deficient nutrition as in keratomalacia
6. Neuroparalytic keratitis - Bell's palsy
7. General malnutrition

Pathogenic bacteria colonize the corneal stroma and immediately become antigenic, both directly and indirectly, by releasing enzymes and toxins, this sets up an antigen-antibody immune reaction which leads to an inflammatory reaction

These toxins diffuse through the cornea into the anterior chamber and exert an irritative effect on the vessels of the iris and ciliary body resulting in leucocytosis and thus polymorphonuclear cells are poured out into the aqueous which settle down in the anterior chamber as hypopyon.

The PMN's also aggregate at the area of infection creating an infiltration.

The PMNs phagocytize and digest the bacteria. The collagen stroma is poorly tolerant of the bacterial and leukocytic enzymes and undergoes degradation, necrosis and thinning.

While these events are taking their course

1. **Vascularisation** develops from the limbus supplying the nutrition to restore the loss and also supply antibodies which play an important role in combating bacterial infection.
2. **Cicatrisation** is by formation of new fibrous tissue which is not arranged regularly as in the normal lamellae, thus resulting in scar formation ending up with opacity. (**Bowman's membrane does not regenerate and hence some degree of permanent opacity remains after the ulcer has healed**).

### Complications :-

- 1 . Ectatic cicatrix
2. Desmetocele

3. Perforation (opposite iris) if small, iris seals the perforation forming anterior synechae and if large prolapse of iris results.
4. Perforation (opposite pupillary area) resulting in anterior capsular cataract or corneal fistula.
5. Total cornea sloughs off leaving a thin peripheral rim of cornea resulting in total prolapse of iris exudation covers this iris to form pseudocornea
6. Secondary glaucoma
7. Purulent iridocyclitis
8. Pan ophthalmitis

## MANAGEMENT AND TREATMENT

This is based on :

### 1. Control of infection.

Culturing the infection is the ideal way to determine the infecting organism but is often difficult or impractical. The morphologic characteristics of the bacteria seen on gram stain can then be used as a guideline for an initiation of an antibiotic regimen in the treatment of bacterial ulcers. This approach is universally accepted, however this may not be practical in our conditions. So first and foremost, we must control infection and not delay treatment while waiting for the culture results.

Selection of antibiotics for initial treatment :

- . Non specific --using broad spectrum antibiotics . Specific - using antibiotic based on gram staining

Modification of antibiotic depending on :

- . Response to initial treatment
- . Resistance to antibiotics based on culture report

Routes of administrations :

- . Topical
- . Subconjunctival
- . Systemic

Some common antibiotics with their indication and dosage

NAME	SPECIAL INDICATION	DOSE		
		SYSTEMIC	SUB-CONJUNCTIVAL	TOPICAL
<b>Gentamycin</b>	Gm -ve org. and most Staph. Sp.	3-5 mg/kg/day I/V or I/M in divided doses - 8 hourly	20 mg	0.3% drops and ointment
<b>Tobramycin</b>	Same as Gentamycin	Same as Gentamycin	5-20 mg	0.3% drops
<b>Ampicillin</b>	Gm +ve org. (except penicillinase producing Staph.) and some Gm -ve org.	500 mg orally 6 hourly, 3-6 g/day I/V or I/M divided doses 6 hourly	50-100 mg	
<b>Cloxacillin</b>	Penicillinase producing Staph	250-500 mg orally, 6 hourly		
<b>Cephalexin</b>	Gm +ve cocci and Gm -ve rods	500 mg orally 6 hourly		
<b>Cefazolin</b>	Gm +ve cocci and Gm -ve rods	25-50 mg/kg/day I/V or I/M in divided doses 8 hourly	100 mg	5% concentration used as topical drops (vol. 5ml - 5ml of Normal saline in 250 mg vial) (vol 10ml - 10 ml of Normal saline in 500 mg vial)
<b>Ceftazidime</b>	Gm -ve organisms, specially Pseudomonas	1-2 gm I/V 8-12 hourly	100 mg	
<b>Ciprofloxacin</b>	Broad spectrum including most aerobic Gm-ve org., S aureus and S epidermidis	500 mg orally 12 hourly, 200 mg I/V 12 hourly		0.3% drops and ointment
<b>Ofloxacin</b>	Broad spectrum	200-800 mg/day orally 200 mg I/V 12 hourly		0.3% drops

<b>Norfloxacin</b>	Gm +ve and Gm -ve org. including Pseudomonas. Not effective against anaerobes	400 mg orally 12 hourly		0.3% drops
<b>Lomefloxacin</b>	Good coverage of Gm -ve org. Less potent against Gm +ve	400 mg orally or I/V 12 hourly		Initially 5 drops in 20 min or 1 drop every hour for 6/10 hours. Then 1 drop 2-3 times a day.
<b>Sparfloxacin</b>	Broad spectrum. Gm +ve and Gm -ve org. including anaerobes	400 mg orally on day 1, followed by 200 mg once a day		0.3% drops

Immediately begin therapy with a broad spectrum antibiotic. Recommended therapy is the fluoroquinolone, depending on the severity of the infection, ciprofloxacin 0.3% two drops every 15 minutes for six hours, followed by two drops every 30 minutes for 18 hours, and then tapered depending on patient response. Another fluoroquinolone, ofloxacin 0.3% is also an effective treatment for bacterial keratitis. Both fluoroquinolones are as effective at managing bacterial keratitis as fortified antibiotics, but with significantly fewer side effects.

Now sparfloxacin 0.3% drops are available, which may be used considering its spectrum, lowest MIC, better concentration and penetration in aqueous.

## 2. Rest

Local rest is attained by cycloplegics by preventing ciliary spasm. (atropine 1 % is mandatory) and also prevents formation of synechiae.

## 3. Protection from external factors

Pad and bandage is given ,unless there is much conjunctival discharge ,in this event the pad should be replaced by shield or dark glasses.

## 4. Scraping and cauterisation

If the ulcer progresses inspite of the above measures the removal of the necrotic material may be hastened by scraping or ulcer may be cauterized. Cauterisation - 100% carbolic acid or trichloroacetic acid 10 to 20 %. Carbolic acid has the advantage of penetrating deeper than it is actually applied, thus is commonly used .It acts as caustic and an antiseptic.

## Other forms of therapy:

Preventing corneal perforation by lowering the intraocular pressure by acetazolamide and if there is perforation then pressure pad bandage along with antibiotics, atropine should be continued.

## Role of surgery

Limited role in the treatment of active stage of bacterial keratitis. Therapeutic keratoplasty is indicated in active bacterial keratitis ,if there is large corneal perforation. Once the ulcer has healed and if the scar is superficial then lamellar keratoplasty is indicated and in cases of deep scars total full thickness keratoplasty is indicated.

## Hypopyon ulcer

Develops depending on

- . The virulence of the organism - pyogenic organism, staph, strept., pseudomonas, pneumococcus
- . Resistance of the tissues - old age, debilitated and alcoholic.

1. In adults the commonest causative organism is pneumococcus and the ulcer formed is called *ulcus serpens*.
2. Typical *ulcus serpens* is greyish white or yellow disc near the center of the cornea. the edges are grey with clear center, well marked in one particular direction.
3. A cloudy grey area made up of fine lines surrounds the disc but is also marked in one direction.
4. The ulcer increases in size and depth ,on the side of the densest infiltration which looks like a yellow crescent, tissues breakdown and the ulcer spreads, on the other side it undergoes cicatrization and the edges may be covered by fresh epithelium, in this manner it travels forwards.

## FUNGAL KERATITIS

**Causative** organism - Common ones :

- . *Aspergillus Fumigatus*
- . *Penicillium*
- . *Fusarium Solari*
- . *Scopulariopsis*
- . *Candida Albicans*

What **potentiates** a fungus :

- . Impaired host defenses
- . Impaired cellular immunity --- diseases like leukemia ,diabetes
- . Treatment with antibiotic and steroids
- . Surgical manipulation
- . Pre existing corneal disease
- . Injury

How host becomes **favourable**

Drugs:

1. Antibiotics---

- . Alters normal conj flora
- . Alters cell permeability
- . Removes competitor organism and permits potential pathogens to multiply unrestrictedly

2. Steroids

- . Diminish host resistance
- . Impair killing of organism within phagocytes
- . Depress inflammatory response and suppress antibody formations . Decrease phagocytosis ,decrease vascular permeability

Pre-existing corneal disease breaking down mechanical barrier and impairing host defense

- . H. Zoster and simplex
- . Bullous Keratopathy
- . Facial palsy with lagophthalmos
- . Dry eye syndrome
- . Leprosy
- . Old scars
- . Old ulcer

How the fungus **reaches** the cornea:

- . Outer environment
- . Infection in the neighbourhood structures . Penetrating wounds and corneal surgery .

Vegetative injury

- . Contact lenses

## Clinical Course

History

Site

- . Central and inferior temporal (vegetative injury in farmers)

## Clinical Picture

- . Pain
- . Redness
- . Lacrimation
- . Blepharospasm
- . Severe ocular reaction
- Ciliary congestion
- Thick flare in AC

## Biomicroscopic presentation

Hyphate ulcer

- . Distinct branching lines radiating from ulcer margin
- . Satellite lesion -- micro abscess if seen histologically
- . Branching lines from the ulcer margin distinguishes fungal ulcer from bacterial one.

Elevated lesion

- . Ulcer itself appears lifted above the surrounding cornea. . The lifted area is not soft but solid in appearance

Corneal ring

- . Definite white ring in the mid periphery of the cornea with healthy cornea between the ring and ulcer margin - immune ring
- . Diagnostic of fungal infection

Hypopyon

- . Is almost the rule.
- . Higher the hypopyon more ominous the sign and chances of perforation.
- . Fungi are known to negotiate the intact descemets membrane.

Endothelial plaque

- . Not sole characteristic of fungal ulcer but important sign
- . Its presence endanger the sustenance of the eye
- . May appear with tiny and trivial ulcer but severe uveitis present which may prompt steroid therapy.

Vascularisation

- . Is absent inspite of severe ocular reaction

Glaucoma

- . Raised IOP is common in fungal keratitis

Microbiological

- . Scrapping from the ulcer taken from edge and floor
- . 10 to 20 % KOH -- slide - 20 minutes
- . Branching hyphae

Other tests

- . "B" Scan - when posterior segment involvement is suspected (fungal endophthalmitis)
- . Immunofluorescence staining
- . Electron microscopy

## TREATMENT

**Medical:**

- . Antifungal agents are classified into the following groups:
- . Polyenes include the antifungals natamycin, nystatin, and amphotericin B.
- . Polyenes are effective against both filamentous and yeast forms.
- . Amphotericin B is the first choice agent against fungal keratitis caused by yeasts.
- . Natamycin has a broad-spectrum of activity against filamentous organisms. The penetration of topically applied amphotericin B is found to be less than that of topically applied natamycin through the intact corneal epithelium.
- . Azoles (imidazoles and triazoles) include the antifungals ketoconazole, miconazole, fluconazole, and clotrimazole.
- . Oral fluconazole and ketoconazole are absorbed systemically with good levels in the anterior chamber and cornea; therefore, they should be considered in the management of deep fungal keratitis.
- . Fluorinated pyrimidines, such as flucytosine, are other antifungal agents. It usually is administered in combination with an azole or amphotericin B.
- . Treatment should be instituted promptly with topical antifungal drops, initially every hour during the day tapered to 4hrly interval for 3-4 days, then reduced to 4 times a day for atleast 14-21 days or till there is resolution of active stage.
- . Subconjunctival injections also may be used in cases of severe keratitis, or when poor compliance exists.
- . An oral antifungal (eg, ketoconazole, fluconazole) should be considered for cases of deep stromal infection.
- . Fluconazole has been shown to penetrate better into the cornea after systemic administration compared to other azoles and is associated with fewer adverse effects.
- . Cycloplegics are mandatory, other drugs may be added to the treatment depending on the intraocular pressure etc.

**Surgical:**

- . Frequent corneal debridement with a spatula is helpful; it debulks fungal organisms and epithelium, and enhances penetration of the topical antifungal agent.
- . Those cases which fail to respond to medical treatment and may result in corneal perforation, the treatment of choice is therapeutic penetrating keratoplasty, a small number of patients have been treated successfully with conjunctival flap.
- . Topical antifungal therapy in addition to systemic fluconazole or ketoconazole should be continued following penetrating keratoplasty.
- . The main goals of surgery are to control the infection and to maintain the integrity of the globe.

## NON PURULENT KERATITIS

**Viral**

- H. Zoster, Simplex
- Measles, vaccinia, mumps
- Virus responsible for Bechets and Reiter's syndrome
- Lid infection due to the viruses of molluscum contagiosum and warts

**CONSTITUTIONAL**

- . Phlyctenular
- . Acne Rosacea

**Punctate epithelial erosions --- Viral**

- . Minute defects in the epithelium which stain with fluorescein
- . Acute onset with conjunctivitis
- . Recurrence is common, fever is there

**Punctate epithelial keratitis - Viral**

- . Bilateral - runs a course for months or a year
- . Epithelial opacities are superficial slightly raised, grey dots scattered over the central cornea, do not stain with fluorescein but turns red with rose Bengal.
- . When the lesion extends to Bowman's membrane it is called punctate sub epithelial keratitis.

**TREATMENT**

- . Symptomatic . Antiviral
- . Steroid
- . Cycloplegic

**H.Zoster --- Vorticella zoster virus**

- . Along the ophthalmic division of the fifth nerve --- Skin lesions are there.
- . Ocular complications arise during the subsidence of eruptions
- . Associated with involvement of naso-ciliary branch of trigeminal

Biomicroscopically - multiple white dots in the epithelium, this may extend deep into the stroma - subepithelial punctate keratitis.

**TREATMENT**

- . Symptomatic . Antiviral
- . Steroid
- . Cycloplegic

**Phlyctenular Keratitis**

- . Associated with phlyctenular conjunctivitis

- . Allergic reaction to endogenous allergen -n tuberculo-protein . At the limbus or within the corneal margin
- . Localised infiltration of epithelium and subepithelium layers

### **Acne Rosacea Keratitis**

- . Seen in--elderly women
- . Associated with mucopurulent conjunctivitis
- . Yellowish white infiltrates and small ulcer appear in the cornea which always becomes heavily vascularised

## **DEEP KERATITIS**

- . Congenital syphilis . Tuberculosis
- . Viral infection

### **Interstitial Keratitis**

- . Stroma
- . Infective or allergic origin

**Cogan's Syndrome** - interstitial keratitis and deafness. Young adults, keratitis associated with vertigo, tinnitus and deafness

### **Interstitial keratitis due to inherited syphilis**

- . Children, age' of 5 and 15
- . Following injury or an operation -prone to congenial syphilis
- . Irritation with ciliary congestion.
- . Hazy patches appear in deep layers of cornea near the margin or toward the centre
- . May start from the margin to migrate to the center or if at the center fuse together so that cornea appears lusterless and dull
- . 2-4 weeks corneais hazy resembling ground glass in which dense spots are seen
- . Vascularisation occurs ---deep radial bundles covered by hazy cornea, thus the brightness of the vascularity is toned down to a dull redish pink - salmon patches
- . Opacity extends beyond the vascularisation which seems to push the opacity in front of the vessels . Superficial vascularisation with heated up conjunctiva at the limbus
- . Intense pain ,lacrimation ,photophobia and blepharospasm
- . Vision reduces to hand movements
- . 2 to 4 months
- . Cornea clears from margin to center
- . Cloudness disappears - vessels obliterate appears as fine opaque lines.
- . Rarely ulcerates as the deeper layers are involved
- . Uveitis

Diagnostic --- Evidence of congenial syphilis

## **TREATMENT**

Systemic - antisyphilitic

Local - guarding against the effects of uveitis -- atropine is routine steroids

## **KERATITIS DISCIFORMIS**

- . Adults, unilateral
- . Viral - tissue response due to antigens liberated from the virus in the epithelium and antibodies produced in stroma
- . Central grey disc in stroma with dense central opacity
- . Biomicroscopically --- Thickening of cornea, Folds in Descemet's membrane, Immune ring
- . Persists for weeks or months, leaving permanent opacity
- . Vision is considerably impaired

## **TREATMENT**

Local -- steroids