

3.2 Cornea: keratitis (Infective & non-infective)

Plan

Anatomy

General terms

Keratopathy

Inflammatory (Keratitis)

Infective (Bacterial, fungal, viral & amoeba ulcers)

non infective (Immune & hypersensitivity)

Corneal ulcer complications & their management

Ectasias: Keratoconus (keratoplasty)

Dystrophies

Degenerations

Common etiology like metabolic, exposure, neurotrophic

Ungrouped keratopathies

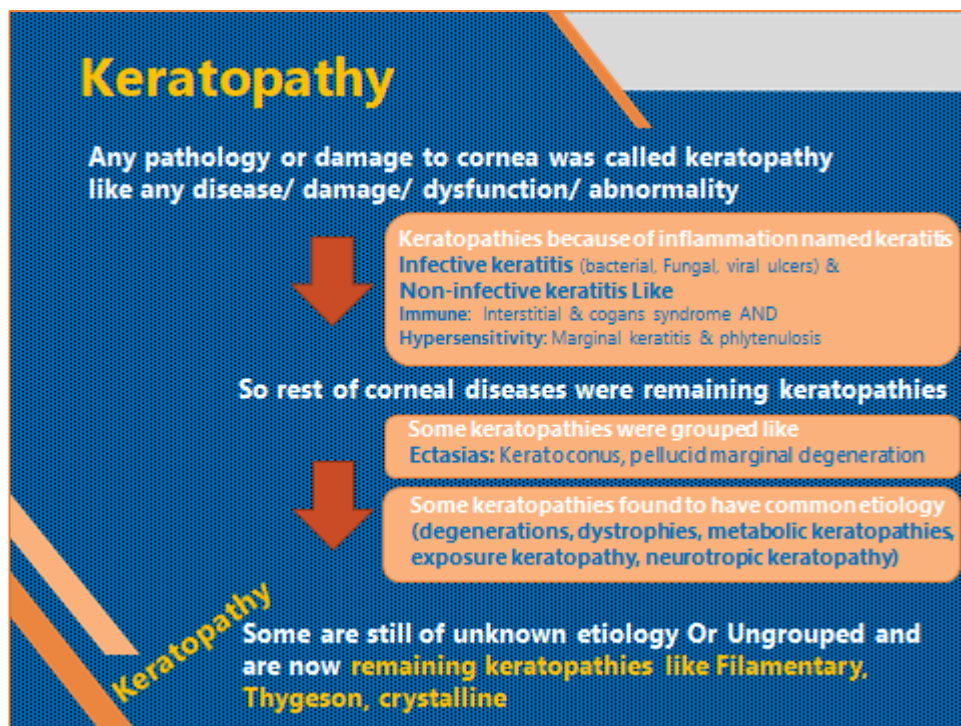
Contact lenses

Refractive surgery

Topography??? – small presentation

Red in module Red eye

Black in module decrease vision

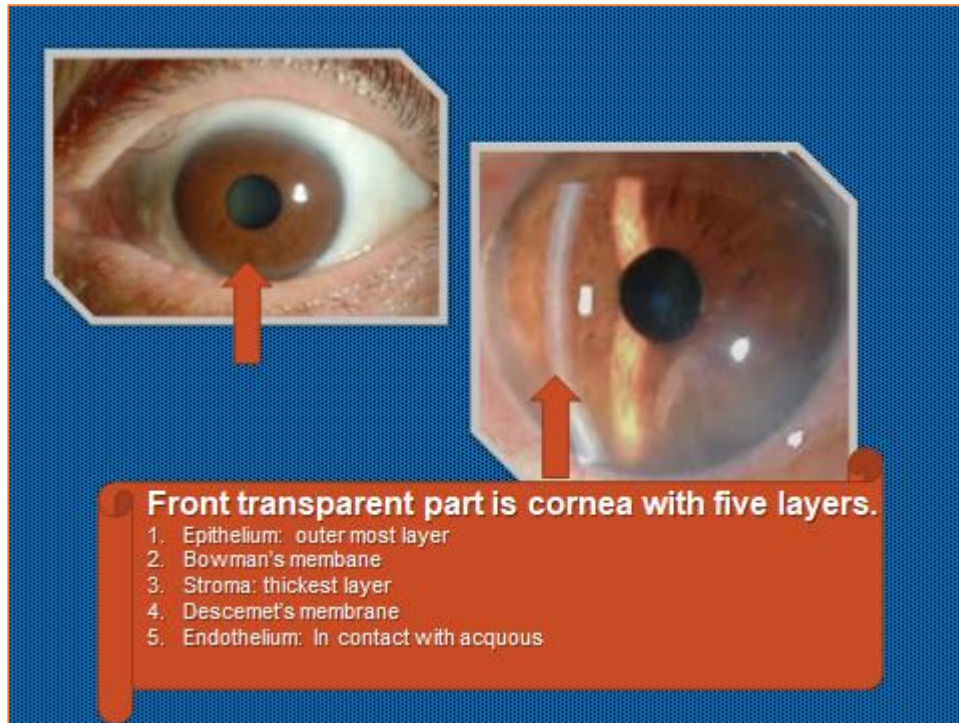


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Anatomy



General terms

Keratopathy: Any disease, damage or pathology of cornea was initially called keratopathy.

Keratitis: Keratopathy because of inflammation is called keratitis. Keratitis may be infective (bacterial, fungal, viral or amoeba) or non-infective (Immunogenic or hypersensitivity).

Corneal ulcer: Usual clinical name for infective keratitis like bacterial ulcer, fungal ulcer and viral ulcer.

Hypopyon: Inflammation of iris and ciliary body causes release of leucocytes and fibrin. These get collect in anterior chamber and settle inferiorly which is called hypopyon. Hypopyon may because of infective keratitis or inflammation (uveitis).

Hypopyon ulcer: If an ulcer is causing hypopyon then it can be called hypopyon ulcer. Hypopyon ulcer may be bacterial or fungal.

Purulent keratitis: Most ulcers produce pus and sometimes called purulent keratitis

Suppurative keratitis: When a corneal ulcer produces pus

Ulcer serpens: Ulcer because of pseudomonas

Mycotic ulcer: Another name for fungal ulcers

Pathogenesis or Stages of ulcer: It is described in four stages.

Infiltration stage: There is infiltration of leucocytes with intact epithelium.

Active stage: Necrosis of epithelium with ulcer development with surrounding edema.

Regressive stage: Ulcer regresses with treatment or host response.

Cauterization stage: Healing of ulcer with epithelization with scarring.

Keratitis

Initially all the corneal diseases were called keratopathy.
Then corneal diseases because of inflammation were named keratitis.
Keratitis is broadly classified as infective keratitis and non-infective keratitis.



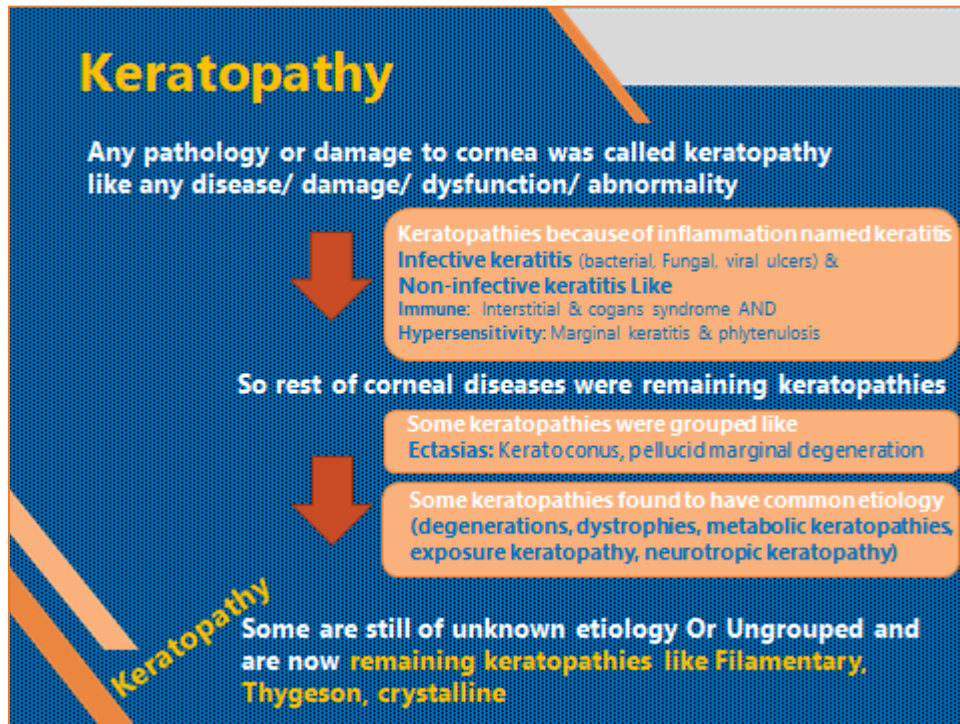
Infective keratitis

- Bacterial keratitis or bacterial corneal ulcer (page 00)
- Fungal keratitis or fungal corneal ulcer (page 00)
- Viral keratitis or viral corneal ulcer (page 00)
- Amoebic keratitis or amoebic ulcer (page 00)



Non-infective keratitis

- Immune keratitis: Interstitial keratitis, Cogan's syndrome (page 00)
- Hypersensitivity keratitis: Marginal keratitis, Phlyctenulosis (page 00)



Bacterial keratitis/ulcer

Bacteria causing keratitis

Bacteria are **classified** into 5 groups according to their basic shapes:
They can exist as single cells, in pairs, chains or clusters

- spherical (cocci):

Gram +ve: *Staph Aureus*, *Staph epidermidis*, *Staph pneumoniae*

Gram -ve

- rod (bacilli):

Gram +ve: *Corynebacterium Diphtheria*, *Corynebacterium xerosis*

Gram -ve: *Pseudomonas aeruginosa*, *Enterobacterae*---*Klebsiella*

- spiral (spirilla)

--*Serratia*

--*Proteus*

- comma (vibrios)

--*E coli*

- corkscrew (spirochaetes)

Common causes

- Staph Aureus: G+c
- Staph Epidermidis: G+c
- Strep Pneumoniae: G+c
- Strep others: G+c
- P Aeruginosa: G-b
- Enterobacteriaceae: G-b
(*Klebsiella*, *Serratia*, *Proteus*, *Escherichia coli*)
- n

Most common
Gram positive Cocci

Clinical features

Bacterial keratitis is most common keratitis. The most common bacteria involved are **gram positive cocci** like staph aureus and staph epidermidis, strep pneumonia & **gram negative bacilli** like pseudomonas aeruginosa and Enterobacteriaceae (klebsiella, E coli, proteus, Serratia). Management is usually as outpatient and only atypical and non-responding cases are admitted.

Symptoms:

Bacterial corneal ulcer presents as acute painful red eye. Pain is moderate to severe because of loss of epithelium, ciliary spasm and IOP

Redness is because of vascular dilation secondary to inflammation.

Other symptoms are reduced vision, photophobia, lacrimation, and foreign body sensation.

Signs:

Conjunctival congestion will be seen with inflammation of lids in severe cases.

Usually, a whitish lesion will be seen which will stain with fluorescein. Mucopurulent discharge can be seen some cases. In severe infections inflammatory cells may collect in anterior chamber to form hypopyon.

Investigations

In most cases investigation is not needed. Investigations are only done in cases of

- Atypical features (suspicion of fungal or amebic ulcer)
- Non responding ulcers
- Large ulcers
- Melting of cornea

Investigations involve

- Microscopy
- Gram staining & giemsa staining
- Culture & sensitivity

Treatment

Ulcer Management Options

01. Commercial eye drops
02. Fortified eye drops
03. Debridement of ulcer
04. Subconjunctival injection
05. Intra-Stromal Anti-microbials / Intra-Cameral/ AC wash
06. Amniotic membrane
07. Povidone-iodine eye drops
08. Pack CXL
09. Keratoplasty (PK / DALK)
10. Conjunctival Flap
11. Tarsorrhaphy / Botox
12. We Fail
13. Systemic antibiotics & Topical cycloplegics / ?Steroids

Most ulcers successfully treated with commercially available eye drops

Most ulcers are bacterial

1. Broad spectrum antibiotics:

Gram positive cocci are most common organisms so cefazolin, vancomycin and fluconazoles are usually used antibiotics. Other broad-spectrum antibiotics used are tobramycin &

Most of bacterial ulcers are treated with commercially available antibiotic eye drops.

If ulcer is not healing then other options are used.

2. Fortified eye drops mean higher than usual concentration of drug in eye drops and they are used in bigger or non-responding ulcers.

3. Debridement means debulking of ulcer or removing surface part of ulcer mechanically with surgical blade.

4. Subconjunctival injection is depot injection under conjunctive for sustained delivery of drug.

5. Intrastromal injection means injection drug directly in to stroma so high concentration if drug is directly delivered while intra-cameral injection injecting drug in anterior chamber for ulcers which have entered endothelium and anterior chamber.

6. Povidone-iodine is directly applied to ulcer to directly kill microbes.

7. Pack-CXL is a new way of treatment, in which microbes are killed with ultra violet light.

8. Keratoplasty is replacing ulcerated cornea with donor cornea. It is only done in cases which are not responding to other modes of treatment.

9. Conjunctival flap is surgically bringing conjunctiva to cover corneal ulcer. This acts as bandage and also brings inflammatory cells including leukotrienes from blood for healing.

10. Tarsorrhaphy is temporary closure of lids to help healing.

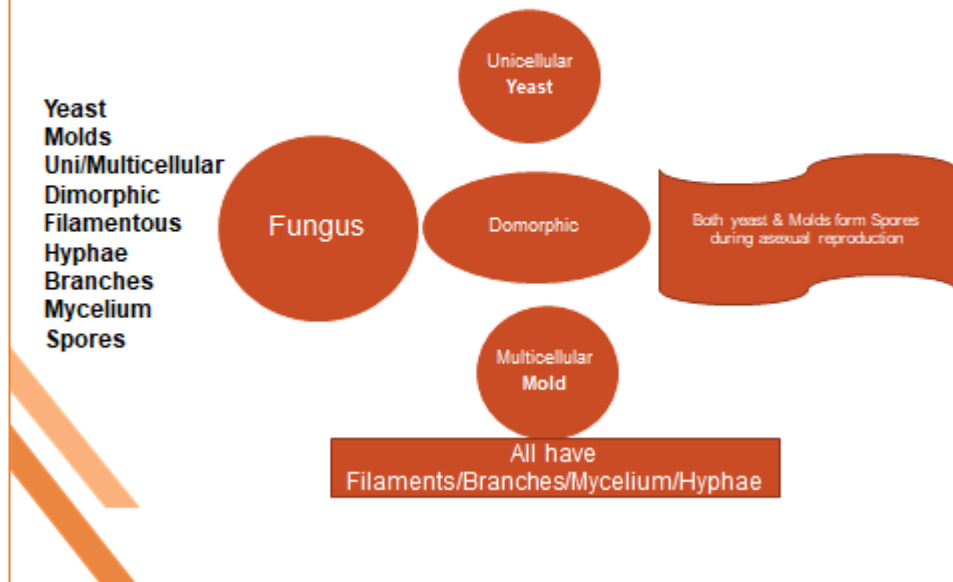
11. We don't always succeed in treatment and eye can be lost at times.

12. Topical cycloplegics are added in most cases to relieve pain because of ciliary spasm.

13. Topical steroids are added in selected cases with caution to reduce inflammation.

Fungal keratitis/ulcer

Confused Terminology



Classification Diagnostic groups

1. Filamentous Septate Non pigmented (Hyaline; Translucent)
Fusarium, Aspergillus
2. Filamentous Septate pigmented/Dematiaeous/Phaeoid
(Dematiaceous; having color usually olive, black, grey / phaeoid; dark)
Alternaria, Curvalaria
3. Filamentous Non Septate
Mucor
4. Yeast: Candida

Clinical features:

Fungal keratitis is seen usually after agriculture trauma. The most common bacteria involved are molds like *Fusarium* and *aspergillus*. Management is usually as outpatient and only atypical and non-responding cases are admitted.

Symptoms:

Fungal corneal ulcer presents as sub-acute painful red eye. Pain is moderate to severe because of loss of epithelium, ciliary spasm and IOP

Redness is because of vascular dilation secondary to inflammation.

Other symptoms are reduced vision, photophobia, lacrimation, and foreign body sensation.

Signs:

Conjunctival congestion will be seen with inflammation of lids in severe cases.

Fungal corneal ulcer usually has some typical features which are

1. Infiltrate: spreading of ulcer in stroma
2. Feathery or hyphate Margin: feather like extension of ulcer
3. Speculated; Spikes or points on surface
4. Dry raised ulcer with crenate (rounded or scalloped margins)
5. Elevated edges/ Rough texture/Gritty feel on scraping
6. Satellite lesions: Main ulcer with small ulcers around
7. Endothelial/posterior plaque: extension of ulcer towards anterior chamber
8. Immobile convex cheesy Hypopyon: thick upwards shaped hypopyon
9. Gray-Brown pigmentation (Dematiaceous fungi like *Calvaria*)
10. Wessely Immune Ring - Deposition of immune complexes in form of ring
11. Collar button appearance- small ulcer which expands like collar button

Investigations

Fungal keratitis is more difficult to treat. Investigations are only done in cases of

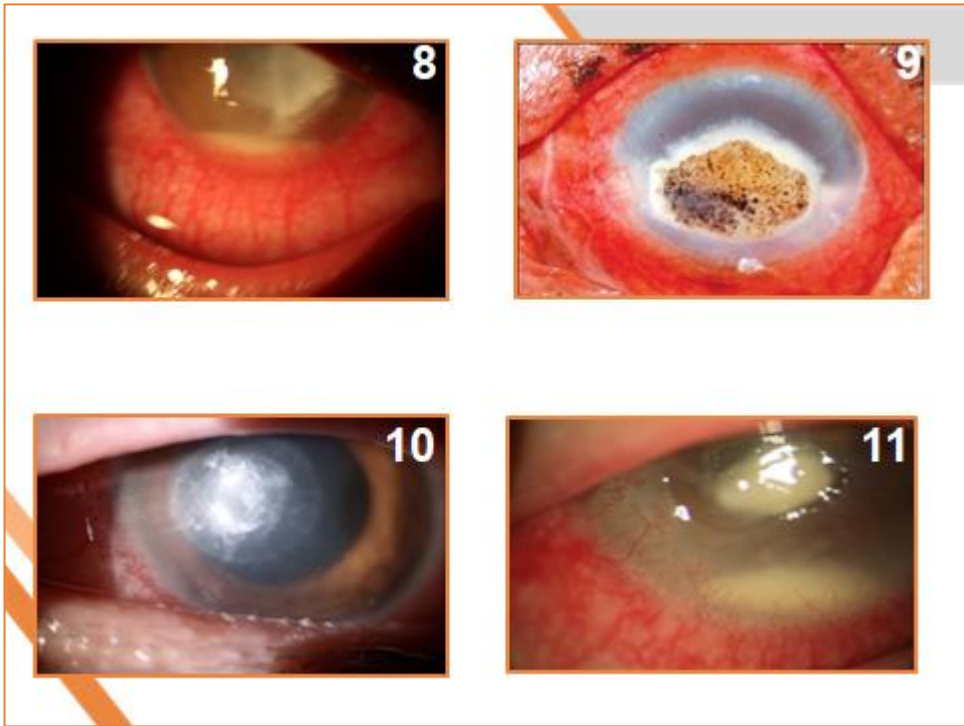
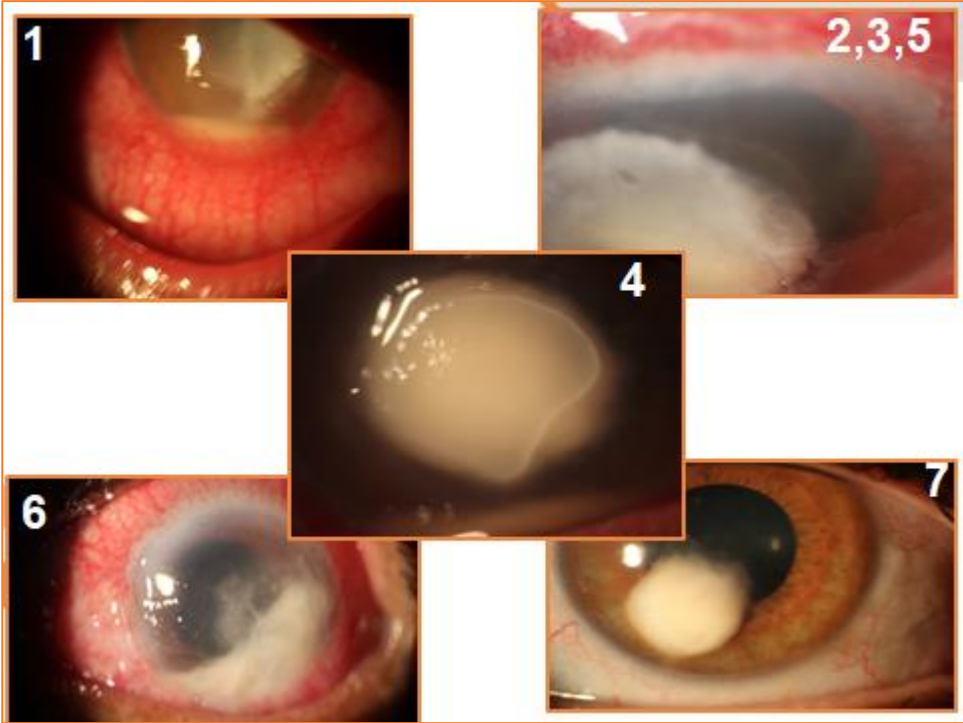
- Atypical features
- Non responding ulcers
- Large ulcers
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Investigations involve

- Microscopy
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- Culture & sensitivity

Infective keratitis
Fungal

Infective keratitis



Treatment:

Ulcer Management Options

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Most ulcers successfully treated with commercially available eye drops

Most ulcers are bacterial

1. It is difficult to treat fungal ulcer as compared to bacteria ulcer because only natamycin is available as eye drops but even that does not penetrate much. So, we have to make eye drops from injectable voriconazole and fluconazole. Available drugs are
Polyenes: (Natamycin – only topical antifungal, does not penetrate much & amphotericin B)
Azoles: Ketoconazole, Miconazole, Voriconazole (best against molds & yeast), Fluconazole
 If ulcer is not healing then other options are used.
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3. Debridement means debulking of ulcer or removing surface part of ulcer mechanically with surgical blade.
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11. We don't always succeed in treatment and eye can be lost at times.
12. **Topical cycloplegics are added in most cases to relieve pain because of ciliary spasm.**
13. **Topical steroids are added in selected cases with caution to reduce inflammation.**

Viral keratitis/ulcer

Viruses that cause corneal disease are

1. Herpes Simplex
2. Varicella Zoster
3. Epstein Barr
4. Adenovirus
5. Cytomegalovirus (usually in immunocompromised patients)

Herpes Simplex keratitis

Herpes simplex keratitis is leading cause of corneal blindness in developing world.

Estimated prevalence is 150 per 100,000 population.

Herpes simplex keratitis is mostly unilateral.

Atopy appears to be risk factor for bilateral disease.

Herpes simplex is associated with gastric ulcer, malaria and pulmonary tuberculosis.

Key slide

Herpes Simplex

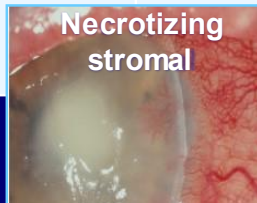
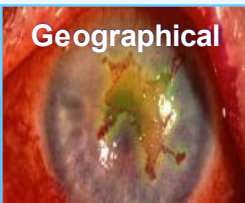
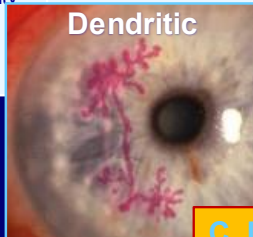
Primary/Recurrent
Periocular, ocular & corneal signs
Epithelial/Stromal/Endothelial

Varicella Zoster

Primary: Varicella
Recurrent: Herpes Zoster (Shingles)
Systemic & Topical antiviral



	Periocular signs A	Ocular signs: B	Corneal signs: Epithelial C	Corneal signs: Stromal D	Corneal signs: Endothelial E
1 Primary General: 5 th nerve Patterns: children Symptoms: Irritation Photophobia	Vesicular dermatitis Non suppurative lymphadenopathy	Blephroconjunctivitis Follicular conjunctivitis	Dendritic/ Geographical Topical antiviral	Necrotizing stromal keratitis Topical steroids Topical antiviral	Disciform (Endothelitis) Topical steroids Topical antiviral
2 Recurrent General: migration & reactivation Activated by low immunity etc Symptoms:			Dendritic/ Geographical Topical antiviral	Necrotizing stromal keratitis Topical steroids Topical antiviral	Disciform (Endothelitis) Topical steroids Topical antiviral



C, D & E usually in Recurrent herpes simplex

Herpes Simplex keratitis

Primary Herpes Simplex	Recurrent Herpes Simplex
<p>General: Primary infection of any of the 3 branches (ophthalmic, maxillary, mandibular) of cranial nerve V leads to latent infection of nerve cells in trigeminal ganglion. Intraneuronal spread of HSV within ganglion allows patients to develop ocular disease without ever having had primary ocular HSV infection</p>	<p>General:</p> <ul style="list-style-type: none"> ■ Has been thought of as reactivation of virus in the sensory ganglion. ■ Virus migrates down nerve axon to produce lytic infection in ocular disease. ■ Recent evidence suggests, virus may subsist latently within corneal tissue, serving as a potential source of recurrent disease
<p>Symptoms:</p> <ul style="list-style-type: none"> ■ Irritation ■ Photophobia ■ Tearing ■ Reduction in vision (when central cornea is affected) ■ Corneal anesthesia usually occurs early in the course of infection and thus symptoms may be minimal 	<p>Symptoms:</p> <ul style="list-style-type: none"> ■ Irritation ■ Photophobia ■ Tearing ■ Reduction in vision (when central cornea is affected) ■ Corneal anesthesia usually occurs early in the course of infection and thus symptoms may be minimal
<p>Signs:</p> <ul style="list-style-type: none"> ■ Blepharoconjunctivitis ■ Follicular conjunctivitis ■ Punctate keratitis ■ Dendritic ulcer (Epithelial lesions) ■ Geographical (Epithelial lesions) ■ Stromal keratitis (Stromal lesions) ■ Disciform / Endothelitis (Endothelial) ■ Trophic/meta herpetic ulcer ■ Trabeculitis ■ Iritis 	<p>Signs:</p> <ul style="list-style-type: none"> ■ Dendritic ulcer (Epithelial lesions) ■ Geographical (Epithelial lesions) ■ Stromal keratitis (Stromal lesions) ■ Disciform / Endothelitis (Endothelial)

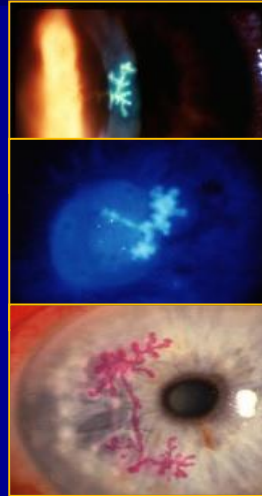
Epithelial lesions of recurrent and occasionally primary herpes simplex

2C

- Primary/Recurrent
- Epithelial/Stromal/Endothelial

Clinical findings: Dendritic

- Most characteristic lesion, occurs in corneal epithelium
- Typical branching, linear pattern with feathery edges and terminal bulbs at ends.
- Visualized by fluorescein staining. Fluorescein staining reveals dendritic ulcer typical of herpes
- Can be stained with Rose Bengal
- Treated with topical 3% acyclovir



Epithelial lesions of recurrent and occasionally primary herpes simplex

2C

- Primary/Recurrent
- Epithelial/Stromal/Endothelial

Clinical findings: Geographical

- Form of chronic dendritic disease.
- Delicate dendritic lesions take a broader form.
- Corneal sensation is diminished



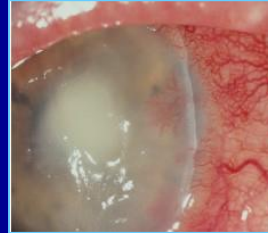
Stromal lesions of recurrent and occasionally primary herpes simplex

2D

- Primary/Recurrent
- Epithelial/Stromal/Endothelial

Clinical findings: Necrotizing stromal keratitis

- Rare condition
- Active viral replication in stroma
- Signs
 - Stromal necrosis & melting
 - Anterior uveitis & epithelial defect
 - May lead to scarring & vascularization
- Treatment
 - Topical steroids
 - Topical anti virals



Endothelial lesions of recurrent and occasionally primary herpes simplex

2E


- Primary/Recurrent
- Epithelial/Stromal/Endothelial

Clinical findings: Disciform

- Most common form of stromal disease in HSV infection
- Edema is most prominent sign
- Edematous stroma without significant infiltration and usually without vascularization.
- Keratic precipitates may lie directly under disciform lesion but may also involve the endothelial lesion
- Iris atrophy is seen



Herpes Zoster keratitis

Primary Herpes Zoster (Varicella)	Secondary Herpes Zoster
<p>General:</p> <ul style="list-style-type: none"> ■ Ocular manifestations uncommon 	<p>General:</p> <ul style="list-style-type: none"> ■ Ocular manifestations common ■ Skin lesions first and more prominent ■ Children with zoster usually have benign disease, aged have severe
<p>Periocular signs:</p> <ul style="list-style-type: none"> ■ Usual eye lesions are pocks on lids and lid margins. 	<p>Periocular signs:</p> <ul style="list-style-type: none"> ■ Vesicular eruption along branches of ophthalmic division of 5th cranial nerve ■ Fever & malaise at onset ■ Skin red & edematous ■ Vesicles at tip of nose is Hutchinson sign (nasociliary) ■ Severe neuralgic pain due to neuritis 
<p>Ocular signs:</p> <ul style="list-style-type: none"> ■ Keratitis occurs rarely 	<p>Ocular signs:</p> <ul style="list-style-type: none"> ■ Superficial punctate keratitis is common ■ Unlike herpes simplex micro dendrites are small, peripheral, satellite & tapered ends (no bulbs) ■ Disciform may be seen rarely ■ Uveitis occurs that varies in severity according to immune status of the patient ■ Corneal anesthesia persists for long time
<p>Treatment:</p> <ul style="list-style-type: none"> ■ Topical antivirals 	<p>Treatment:</p> <ul style="list-style-type: none"> ■ Oral acyclovir particularly in immunocompromised ■ Therapy needs to be started within 72 hours after appearance of the rash ■ Oral dosage is 800 mg five times daily for 10-14 days. ■ Topical steroids, antivirals & cycloplegics as needed ■ Analgesics & anti-depressants

Acanthamoeba keratitis/ulcer

Acanthamoeba is free living protozoa which lives in soil and water.

Cysts are inactive form and resistant killing.

Cyst turn in to trophozoites and cause destruction.

Risk factors:

It more common in contact lens users and transfers from water used in cleaning contact lens storage boxes.

Symptoms:

Pain may be very severe in some and out of proportion to lesion

Lacrimation and photophobia are also present.

Signs:

Epithelial lesions may appear as punctate lesions.

Stromal lesion may be in the form of ring ulcer.

Diagnosis:

Cysts may be visible on microscopy.

Gram staining and Giemsa staining may show cysts.

Confocal microscopy can diagnose.

Treatment:

Treatment is difficult.

Polyhexamethyl Bigunide (PHMB) eye drops can kill cysts and trophozoites.

Chlorhexidine 0.02% eye drops

Propamidine (Brolene) eye drops

Voriconazole eye drops or other azole antifungal may help.

Complications of Infective keratitis

Complications of ulcer

Persistent Epithelial Defect (PED)

Gutter

Thinning/Melting

Descemetocoele

Perforation (AMT, Sclera, Tenon, Conjunctiva, Cornea)

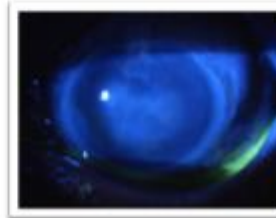
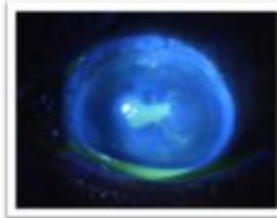
New Vessels

Scarring – Superficial & Deep

AC seeding/Extension

Endophthalmitis/Panophthalmitis

Options:
Lubrication; drops
Preservative free drops
Bandage contact lens
Tarsorrhaphy
Serum drops



Complications of ulcer

Persistent Epithelial Defect (PED)

Gutter

Thinning/Melting

Descemetocoele

Perforation (AMT, Sclera, Tenon, Conjunctiva, Cornea)

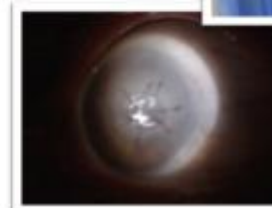
New Vessels

Scarring – Superficial & Deep

AC seeding/Extension

Endophthalmitis/Panophthalmitis

Options:
Conservative
Amniotic membrane
Keratoplasty



Complications of ulcer

Persistent Epithelial Defect (PED)

Gutter

Thinning/Melting

Descemetocoele

Perforation (AMT, Sclera, Tenon, Conjunctiva, Cornea)

New Vessels

Scarring – Superficial & Deep

AC seeding/Extension

Endophthalmitis/Panophthalmitis

Options:
Conservative
Amniotic membrane
Keratoplasty



Complications of ulcer

Persistent Epithelial Defect (PED)

Gutter

Thinning/Melting

Descemetocoele

Perforation (AMT, Sclera, Tenon, Conjunctiva, Cornea)

New Vessels

Scarring – Superficial & Deep

AC seeding/Extension

Endophthalmitis/Panophthalmitis

Options:
Conservative
Keratoplasty



Complications of ulcer

Persistent Epithelial Defect (PED)

Gutter

Thinning/Melting

Descemetocoele

Perforation (AMT, Sclera, Tenon, Conjunctiva, Cornea)

New Vessels

Scarring – Superficial & Deep

AC seeding/Extension

Endophthalmitis/Panophthalmitis

Options:

Keratoplasty

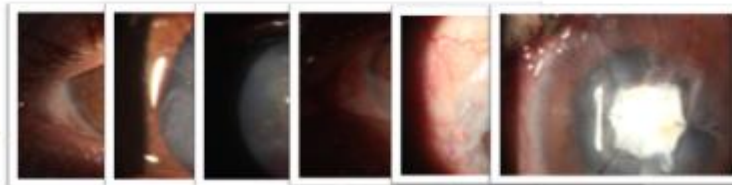
Sutures

Tissue Glue

Amniotic membrane

Conjunctival flap

Scleral patch



Treatment options

Persistent Epithelial Defect (PED)

Gutter

Thinning/Melting

Descemetocoele

Perforation (AMT, Sclera, Tenon, Conjunctiva, Cornea)

New Vessels

Scarring – Superficial & Deep

AC seeding/Extension

Endophthalmitis/Panophthalmitis

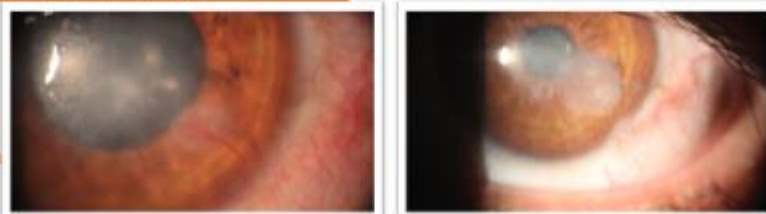
Options:

Conservative

Cautery

Anti VEGF

Keratoplasty



Complications of ulcer

- Persistent Epithelial Defect (PED)
- Gutter
- Thinning/Melting
- Descemetocoele
- Perforation (AMT, Sclera, Tenon, Conjunctiva, Cornea)
- New Vessels
- Scarring – Superficial & Deep
- AC seeding/Extension
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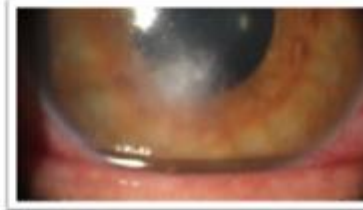
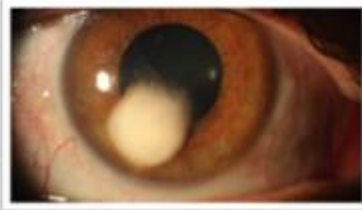
Options:
Conservative
Excimer Laser
DALK
Penetrating Keratoplasty



Complications of ulcer

- Persistent Epithelial Defect (PED)
- Gutter
- Thinning/Melting
- Descemetocoele
- Perforation (AMT, Sclera, Tenon, Conjunctiva, Cornea)
- New Vessels
- Scarring – Superficial & Deep
- AC seeding/Extension
- Endophthalmitis/Panophthalmitis

Options:
Treating ulcer
Intrastromal antimicrobials
Intracameral antimicrobials
Keratoplasty



Complications of ulcer

Persistent Epithelial Defect (PED)

Gutter

Thinning/Melting

Descemetocoele

Perforation (AMT, Sclera, Tenon, Conjunctiva, Cornea)

New Vessels

Scarring – Superficial & Deep

AC seeding/Extension

Endophthalmitis/Panophthalmitis

Options:

Treating ulcer

Intrastromal antimicrobials

Intracameral antimicrobials

Pars plana vitrectomy

Evisceration



Non-Infective keratitis: Immune related

Interstitial keratitis

It is immune related inflammation of corneal stroma with involvement of epithelium or endothelium.

Etiology is immune reaction.

Symptoms are gradual reduced visual acuity.

Signs are stromal opacity with ghost vessels in stroma

Treatment is nonspecific and symptomatic.

Cogan's syndrome

It is rare systemic autoimmune vasculitis.

There is also vestibuloauditory dysfunction.

Etiology is autoimmune.

Symptoms are redness, photophobia and pain

Signs are bilateral peripheral anterior stromal opacity with central progression.

Treatment is topical steroids.

Marginal keratitis

It is small ulcer very close to limbus.

Etiology is hypersensitivity reaction to staphylococcus exotoxins.

Symptoms are lacrimation, redness and pain.

Signs are small ulcer close to limbus with localized congestion.

Treatment is topical steroids.

Phlyctenulosis

It is rare self-limiting keratitis in children and young adults.

Etiology is hypersensitivity reaction to staphylococcus antigen.

Symptoms are severe pain, lacrimation and photophobia.

Signs are small peripheral corneal or limbal nodule with localized congestion.

Treatment is short course of topical steroids.