HERPES SIMPLEX
KERATITIS

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Herpes simplex virus

- DNA virus
- Two types: HSV-1 and HSV-2
- Morphologically similar
- Similar morphologically to other herpesviruses including varicella-zoster, Epstein-Barr, and cytomegalovirus
- Different in viral antigen
HSV-1 usually involves the oropharynx

HSV-2 usually involves the genital area

Ocular disease is caused by type HSV-1

Neonates - 75% is caused by HSV-2
Humans are the only natural reservoir of HSV.

Major portals of entry are the mucous membranes and external skin.

Primary infection manifests clinically in only 1–6% of people infected with the virus.

Male:female ratio (1.67:1).
EPIDIMIOLOGY

§ After peripheral entry into the host and primary infection HSV travels in a retrograde fashion to trigeminal ganglion.

§ Here it resides during the lifespan of the host

§ Cornea itself can be a reservoir of virus.
EPIDIMIOLOGY

Reactivation Factors:-

§ Sunlight, trauma (including surgery), heat, abnormal body temperature, menstruation, other infectious diseases, emotional stress, Prostaglandin analog.

§ After reactivation virus spreads down the nerves to the eye to cause recurrent disease
CLASSIFICATION

- Congenital and neonatal ocular herpes
- Primary ocular herpes
- Recurrent ocular herpes
Congenital and neonatal ocular herpes

§ acquired through genital herpes in the mother and during parturition

§ 80% of cases - HSV-2

§ periocular skin lesions, conjunctivitis, epithelial keratitis, stromal keratitis, and cataracts.

§ progress to disseminated disease and/or central nervous system involvement
Primary ocular herpes

§ By the age of 5 years - 60% of the population infected with HSV

§ Only 6% - develop clinical manifestations
Primary ocular herpes

- typically affect the perioral region
- follicular conjunctivitis
- keratoconjunctivitis
- preauricular adenopathy
- and periocular and eyelid skin vesicles
Recurrent ocular herpes

- Blepharitis
- Conjunctivitis
- Keratitis
Recurrent ocular herpes

Blepharitis-

§ Vesicular lesion

§ Ulceration

§ Heals without scar
Recurrent ocular herpes

Conjunctivitis -

- Recurrent Follicular
- Dendritic ulcer
Recurrent ocular herpes

Keratitis-

- typically unilateral
- Bilateral - 3% of patients (40% history of atopy)
Classification of HSV keratitis

- Infectious epithelial keratitis
- Stromal keratitis
- Endothelitis
- Neurotrophic keratopathy
Infectious epithelial keratitis

- Cornea vesicles
- Dendritic ulcer
- Geographic ulcer
- Marginal ulcer
Infectious epithelial keratitis

Corneal vesicles

§ small vesicles in the epithelium
Infectious epithelial keratitis

§ Within 24 hours, the vesicles coalesce to form the typical **dendritic ulcer**:

§ most common presentation of HSV keratitis

§ branching, linear lesion

§ terminal bulbs

§ swollen epithelial borders that contain live virus.

§ Rose Bengal stain taken up by the swollen epithelial cells at the ulcer's border
Infectious epithelial keratitis

Geographical ulcer

§ An enlarged dendritic ulcer

§ previous use of topical corticosteroids

§ Scalloped margin

§ differentiate from healing abrasions and neurotrophic keratopathy - smooth margin
Infectious epithelial keratitis

Marginal Ulcer

- proximity to the limbus
- accompanying blood vessels
- infiltrated with white blood cells
- anterior stromal infiltrate
- more symptomatic than central dendritic ulcers
# Infectious epithelial keratitis

<table>
<thead>
<tr>
<th></th>
<th>HSV marginal ulcer</th>
<th>Staphylococcal marginal infiltrate</th>
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</thead>
<tbody>
<tr>
<td>Etiology</td>
<td>Active HSV</td>
<td>Immunologic response to staphylococcal antigen</td>
</tr>
<tr>
<td>Epithelial defect</td>
<td>Always</td>
<td>Absent (if present, late)</td>
</tr>
<tr>
<td>Neovascularization</td>
<td>Often</td>
<td>Rare</td>
</tr>
<tr>
<td>Progression</td>
<td>Centrally</td>
<td>Circumferentially</td>
</tr>
<tr>
<td>Blepharitis</td>
<td>Unrelated</td>
<td>Usually</td>
</tr>
<tr>
<td>Location</td>
<td>Any meridian</td>
<td>Typically 2, 4, 8, 10 o’clock meridians</td>
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</table>
Infectious epithelial keratitis

Sequelae of infectious epithelial keratitis-

- complete resolution of the infectious lesion
- dendritic epitheliopathy
- stromal scarring
- 25% of patients develop subsequent stromal inflammation
Neurotrophic keratopathy

§ impaired corneal sensation

§ decreased tear secretion

§ chronic use of topical medications

especially antivirals.
Neurotrophic keratopathy

- Irregularity of the corneal surface and lack of the normal corneal luster
- Punctate epithelial erosions
- Persistent epithelial defect
- Stromal ulceration
- Oval in shape with smooth borders. The neurotrophic ulcer has a thickened border formed by heaped-up epithelium
Neurotrophic keratopathy

Complications

§ stromal scarring

§ neovascularization

§ necrosis, perforation

§ secondary bacterial infection.
Stromal keratitis

- Necrotizing stromal keratitis
- Immune stromal (interstitial) keratitis
Necrotizing stromal keratitis

- Direct viral invasion of the corneal stroma
- The combination of replicating virus and severe host inflammatory response
- Necrosis, ulceration, and dense infiltration of the stroma with an overlying epithelial defect
- Treatment with high-dose anti-inflammatory and antiviral medications
- Thinning and perforation within a short period of time
Immune stromal (interstitial) keratitis

- Incidences - 21% within 2 years and 26% to 48% within 7 years of infectious epithelial keratitis.

- Due to retained viral antigen within the stroma.

- This antigen triggers an antigen-antibody-complement (AAC) cascade that results in intrastromal inflammation.
Immune stromal (interstitial) keratitis

Clinical features

- ciliary congestion
- Stromal infiltration
- punctate stromal opacities-focal, multifocal, or diffuse.
- Stromal edema.
- Immune Wessely ring- AAC precipitate in ring form.
- anterior chamber inflammation
- significant discomfort
- Decreased vision
Immune stromal (interstitial) keratitis

Sequelea -

§ Deep neovascularization

§ Lipid deposition

§ Ghost vessels

§ Stromal scarring, thinning

§ Severe loss of vision.
Endotheliitis

- Localised keratic precipitates
- Overlying stromal and epithelial edema without stromal infiltrate
- Iritis
- Immunologic reaction to HSV-1 antigen in corneal endothelial cells
Endotheliitis

Types:

- Disciform
- Diffuse
- Linear
**Endotheliitis**

**Disciform endotheliitis -**

- most common presentation of endotheliitis
- Disc-shaped distribution of KP in central or paracentral cornea
- Disc-shaped area of edema corresponding to distribution of KP
- Photophobia, mild to moderate ocular discomfort, Limbal injection, visual acuity normal to severely reduced
Endotheliitis

Diffuse endotheliitis -

§ A rare presentation

§ Scattered KP spread over the entire endothelium

§ Stromal edema involving the entire cornea
Endotheliitis

**Linear endotheliitis** -

- Line of KP progressing from the limbus
- May be sectoral or circumferential
- Edema present peripheral to the line of KP, extending to the limbus
- Corneal decompensation common
Iridocyclitis

- Concomitant or subsequent
- Fine KP
- Segmental iris atrophy
- Iris masses, hemorrhages, hyphema.
- Elevation of intraocular pressure
  - Trabeculitis
  - Inflammatory cells blocking aqueous outflow
Diagnosis

- Clinical findings
- Cell culture
- Immunologic tests
- Polymerase chain reaction (PCR)
# Antivirals

<table>
<thead>
<tr>
<th>Route of administration</th>
<th>Therapeutic Doses</th>
<th>Prophylactic doses</th>
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| Oral, IV, Topical        | Topical 5 times x 7-10 days.  
                          | 400 mg PO  
                          | 5 times/day for 7-10 days | 400 mg PO bid |
| Valacyclovir             | Oral              | 500 tid x 7-10 days | 500 mg PO/day |
| Gancyclovir              | Topical, IV       | 5 times/day until cornea heals then 3 times/day for 7 days | - |
Management

**Infectious epithelial keratitis**-

- Physical debridement of the ulcer
- Topical antivirals
- Topical cycloplegics
- Broad-spectrum antibiotic- large geographic ulcers
- No steroids unless associated with stromal inflammation
Management

Neurotrophic keratopathy-

- discontinuation of all unnecessary topical medications, especially topical antivirals
- Frequent use of nonpreserved artificial tears
- broad-spectrum antibiotic
- gentle debridement of abnormal epithelium at the ulcer edge.
- persistent ulceration secondary to chronic low-grade inflammation-mild topical corticosteroid.
- therapeutic soft contact lens
- temporary tarsorrhaphy
Management

Immunologic disease

Stromal keratitis

- Topical corticosteroids
- Oral corticosteroid (severe)
- Topical antiviral (Acyclovir 3% ointment)
- Oral antiviral for prophylaxis (Acyclovir 400 mg BD)
Management

Immunologic disease

Endothelitis

§ Disciform-  Topical corticosteroid

§ Diffuse-   Topical corticosteroid and oral antiviral

§ Linear-    Topical and oral corticosteroid
             Oral antiviral
Management

Necrotising stromal keratitis-

§ high-dose anti-inflammatory (oral and Topical)

§ antiviral medications (oral and topical)
Management

Iridocyclitis/trabeculitis

§ Topical corticosteroids

In Severe cases-

§ oral acyclovir 400 mg five times a day
§ Oral corticosteroids
Topical corticosteroids

§ marginal keratitis

§ immune stromal keratitis

§ moderate disciform & diffuse endothelitis

§ Moderate iridocyclitis & trabeculitis
**Oral corticosteroids**

- severe stromal keratitis
- severe disciform & diffuse endothelitis
- all cases of linear endothelitis
- severe iridocyclitis & trabeculitis
Topical antivirals

- HSV blepharitis
- HSV conjunctivitis
- Infectious epithelial keratitis
- Prophylaxis for corticosteroids treatment of stromal keratitis
Management

Oral antivirals

- Primary HSV infection
- Severe diffuse endotheliitis
- Linear endotheliitis
- Severe iridocyclitis/trabeculitis
- Immunocompromised patients
- Pediatric patients refractory to topical medications
- Prophylaxis against recurrent infectious epithelial keratitis and stromal keratitis
- Prophylaxis for post-PK patients with history of HSV keratitis
Herpetic Eye Disease Study

A set of multicenter, randomized, placebo-controlled trials under the name Herpetic Eye Disease Study (HEDS) sponsored by the National Eye Institute was designed.

§ Oral antiviral prophylaxis reduces recurrences of epithelial and of stromal keratitis.

§ Use of topical corticosteroids is of benefit in stromal keratitis.

§ Use of oral acyclovir may be of help in iridocyclitis

§ Prophylactic oral acyclovir helps prevent recurrences of herpetic keratitis, particularly stromal with a history of recurrence
Thank you