VIRAL AND PROTOZOAL KERATITIS

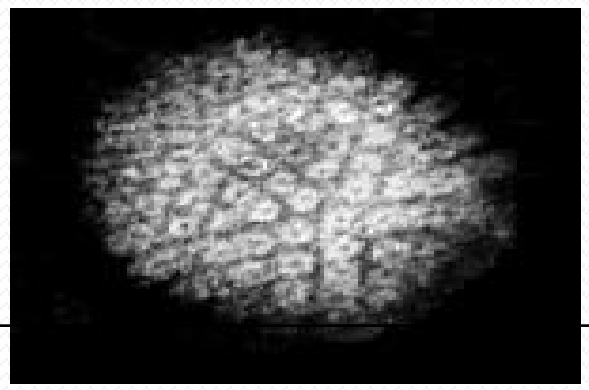
Ophthalmology

HERPES VIRUS

- Are ubiquitous human pathogen capable of causing both asymptomatic infection and active disease
- Humans are natural reservoir of HSV
- 2 types – HSV 1- oropharynx
  HSV 2 – genital area
- Ocular disease typically caused by type 1
- Causes primary infection in children and neonates

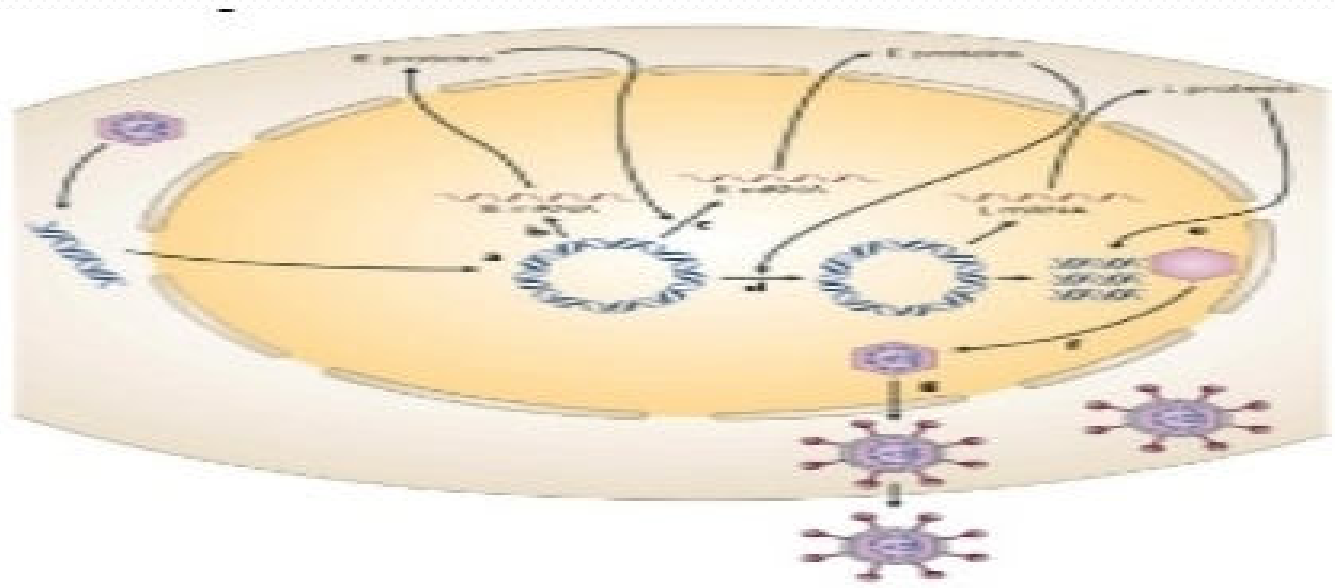
MODE OF INFECTION:

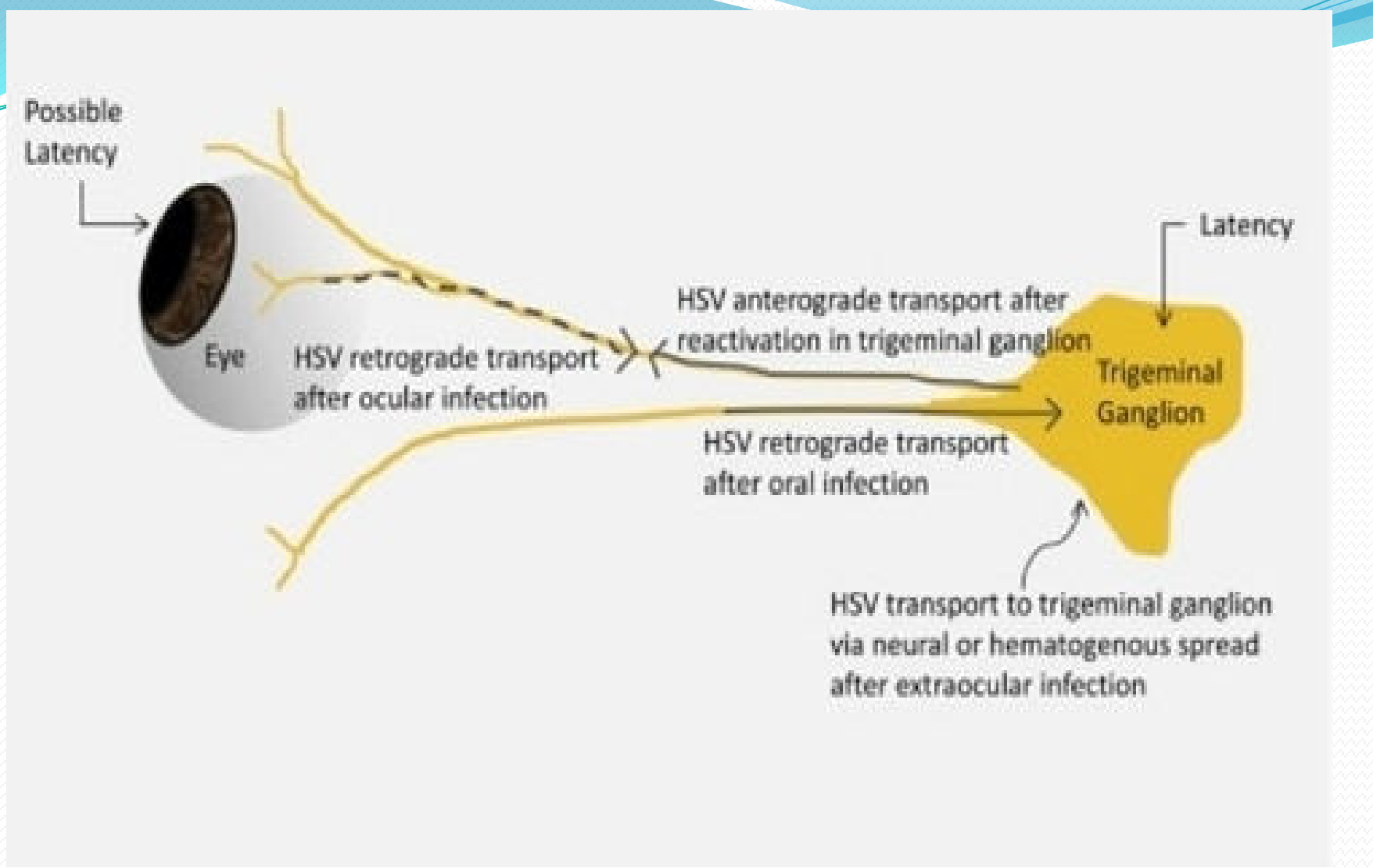
- IP – 3- 9 days
- HSV 1 – close contact
- HSV 2 – venereal – birth canal



MECHANISM OF ACTION

- HSV (epitheliotropic & cytolytic) binds to one or more cellular receptor – heparin sulphate
- Virus fuses with cell membrane
- Enters the cell and nucleus where the transcription of viral DNA occurs – protein





- TG is the most common source of recurrent HSV infection.
- Primary infection may subsequently reactivate by travelling via ophthalmic division of 5th CN to the eye.

PATHOGENESIS

Factors for reactivation –

- UV rays
- Trauma
- Heat, abnormal body temperature
- Other infectious disease
- Emotional disease
- Menstrual stress
- Steroids, immunosuppresant, PGs

CLINICAL FEATURES

Suspicion of viral keratitis arises if there is

- Associated skin lesions, recurrences of these lesions
- Stress-induced recurrence
- Immuno compromised status
- History of contact
- Symptomatic eye (Pain ,Photophobia ,Blurred vision, Tearing ,Redness) with minimal conjunctival and corneal signs
- Superficial dendrites with loss of corneal sensation

CLASSIFICATION OF OCULAR DISEASE

- *1.Congenital & Neonatal*
- *2. Primary infection*
- *3. Recurrent infection*

CONGENITAL AND NEONATAL OCULAR HERPES

May be acquired by one of the three periods :

- Intrauterine (5%)
- Peripartum(10%)
- Postpartum (85%)

- **Intrauterine infection** occurs in 1/300,000 births, with features of microophthalmia, retinal dysplasia, optic atrophy and chorioretinitis.
- HSV infections in latter two periods are further classified as skin, eyes, or mouth (SEM) with or without the other involvement seen in intrauterine infections.
- Ocular herpes include one or all: conjunctivitis, epithelial keratitis, stromal immune reaction, cataract, necrotizing chrioretinitis.

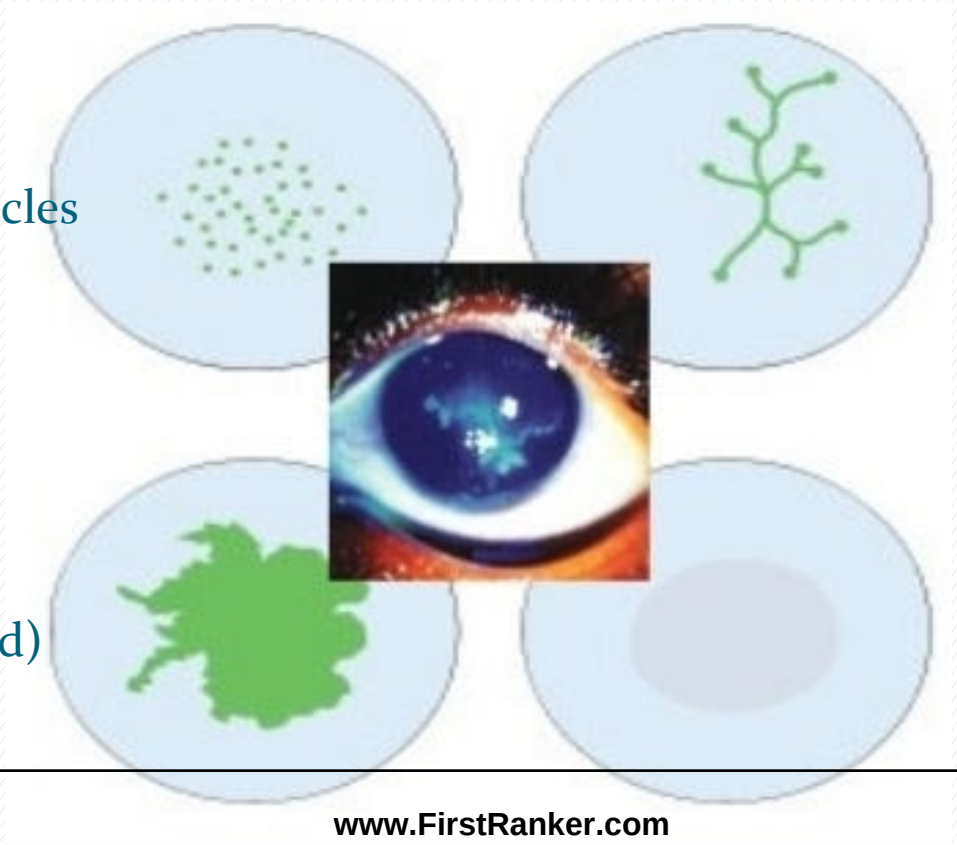
PRIMARY INFECTION

- After 6 months – maternal anti-HSV IgG
- ***Cutaneous involvement–***vesicular periocular skin eruptions , vesicular ulcerative blepharitis
- ***Acute follicular conjunctivitis***
- ***Keratoconjuctivitis*** with non-suppurative lymphadenopathy
- ***Diffuse punctate keratitis*** – that evolves into multiple scattered micro dendrite figures.
- ***As a rule confined to epithelium clinically – d/t lack of previous immunologic stimulus***

Treatment-Topical antivirals supported by antibiotics & cycloplegics

RECURRENT INFECTION

- Patients with recurrent herpes have both cellular and humoral immunity against the virus.



CLASSIFICATION OF HSV KERATITIS

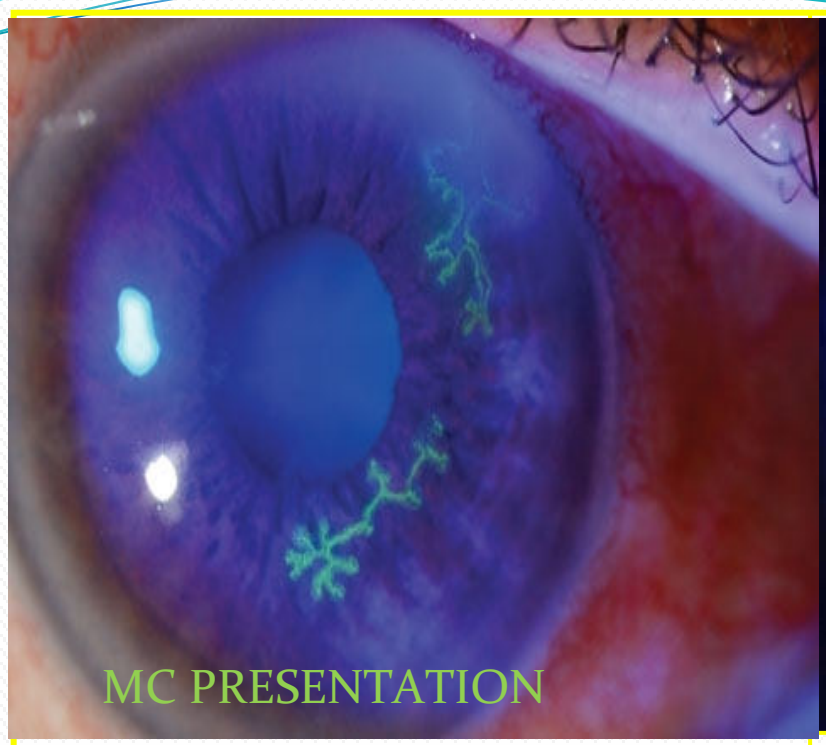
- The disease may present as any one or a combination of the following:

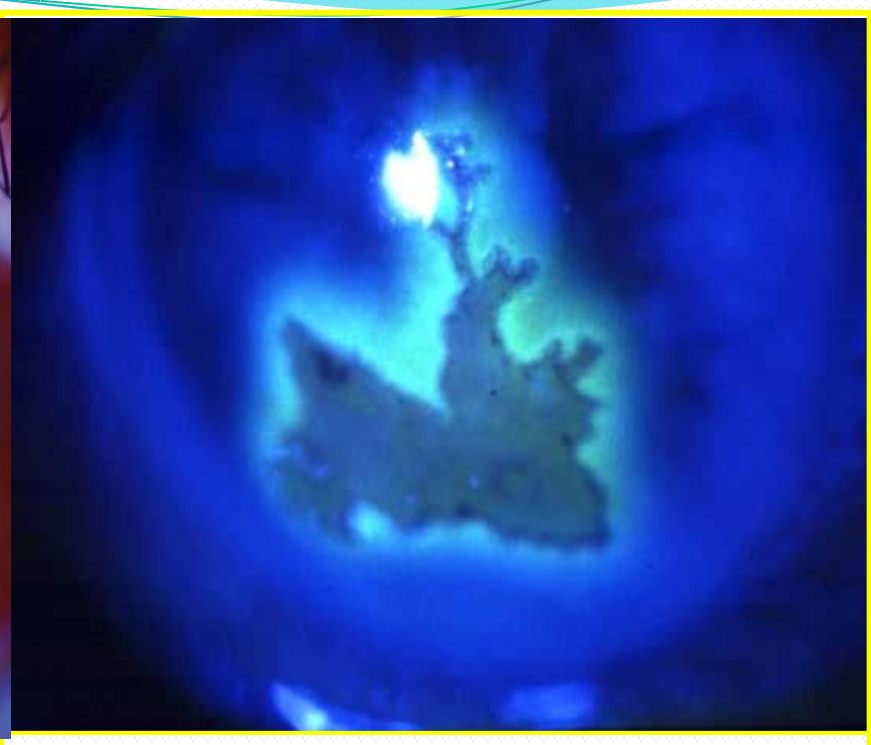
1. ***Blepharoconjuctivitis***
2. ***Episcleritis, scleritis***
3. ***Infectious epithelial keratitis –(IEK)***
4. ***Neurotrophic keratopathy***

5. ***Stromal keratitis***
   - Necrotizing stromal keratitis
   - Immune (interstitial) keratitis
   - Immune rings
   - Limbal vasculitis
   - Disciform keratitis

6. ***Endothelitis***
   - Disciform
   - Diffuse
   - Linear
7. ***Iridocyclitis***
8. ***Trabeculitis***

Herpes simplex epithelial keratitis





- Dendritic ulcer with terminal bulbs
- Stains with fluorescein
- May enlarge to become geographic

In herpes, corneal sensation is reduced in approx 70 % of the patient.

Treatment

- Aciclovir 3% ointment x 5 daily
- Ganciclovir ophthalmic gel 0.15% - 5 times daily } 2-3wks
- Supported by antibiotics and cycloplegics
- Debridement if non-compliant

D/D OF DENDRITIC KERATITIS

- Herpes zoster dendritic keratitis (pseudodendrites)
- Acanthamoeba keratitis
- Contact lens keratopathy
- Antiviral toxicity

Herpes simplex disciform keratitis

Signs	Associations
	
• Central epithelial and stromal oedema • Folds in Descemet membrane • Small keratic precipitates	• Occasionally surrounded by Wessely ring

Treatment – topical steroids (pred 1% or dexa 0.1%) + with antiviral cover

COTND….

- **Oral** (in immunodeficient or children)

:: Acyclovir 400 mg PO 5t/d * 14 days, or

::Famcyclovir 500 mg PO twice daily for 14 days, or

:: Valacyclovir 500 mg PO twice daily for 14 days, or

Neurotrophic keratopathy (Metaherpetic)

- Damage to gasserian ganglion
- Impaired corneal innervations
- Decreased tear secretion
- Excess use of antivirals

Signs –

- Irregular cornea with loss of corneal lustre
- Characterized by persistent epithelial defect
- Oval in shape with gray, thickened smooth borders

Rx-Stop all unnecessary medications
Gentle debridement of boggy epithelium
Artificial tears
Mild steroid :If active stromal keratitis +ve
Therapeutic soft CL
Doxycycline 100mg PO once daily to inhibit collagenase
Cycloplegics: if iritis is +ve
Tarsorrhaphy to treat chronic exposure
Cyanoacrylate glue – if perforation occurs

PRIMARILY A CLINICAL DIAGNOSIS

LABORATORY INVESTIGATIONS

Specific tests

- Viral culture (gold standard)
- Antigen detection – Immunofluorescence, Elisa
- PCR
- Serology

Non-specific tests –

- Cytology --Giemsa stain (multinucleated giant cells)
  --Papanicolaou stain - intranuclear eosinophilic inclusion bodies
- Electron microscopy

INDICATIONS FOR ORAL ACYCLOVIR

Oral Acyclovir

- Linear endothelitis
- Diffuse endothelitis
- Severe trabeculitis
- Immunocompromised patients
- Paediatric patients refractory to topical
- Prophylaxis for post-PKP with h/o HSV
- Prophylaxis against recurrent IEK

PROPHYLAXIS AGAINST RECURRENCE

::Frequent recurrent infection if b/l or involving an only eye

::Post –PK patients with history of HSV keratitis

- Tab acyclovir 400 mg BD * 12- 18 months
- Tab famcyclovir 250 mg OD * 12 -18 months
- Valacyclovir 500mg OD * 12 - 18 months
  (for immunocompromised pt)

VARICELLA ZOSTER VIRUS

- Incidence & epidemiology:

I. Spread by saliva droplets, or direct contact with infected rash.
II. The maculopapular rash appears in successive crops, lesions of various stages present simultaneously.
III. Contagious period approx 1 day before rash & continues approx 1 week after app of each crop of lesion or until the cutaneous sores crust over.
IV. IP: 12- 17 days after contact.

CLINICAL DISEASE

- **Congenital varicella syndrome**

- If mother contracts varicella during first or second trimester of pregnancy.
- Ocular findings ~ ***chorioretinits, optic nerve atrophy or hypoplasia, congenital cataract*** and Horner Syndrome.
- No specific treatment.
- Vaccinate all women with no history of previous varicella.

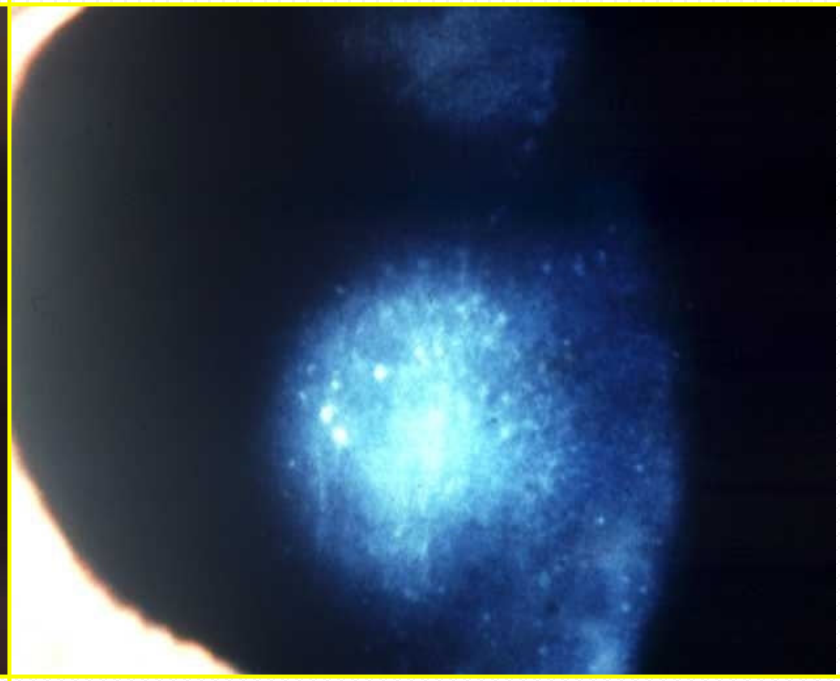
HZO

- First described by Hutchinson in 1865
- MC involves ophthalmic division of 5th nerve
- Frontal branch is MC involved
- Nasociliary involvement – 76% ocular involvement

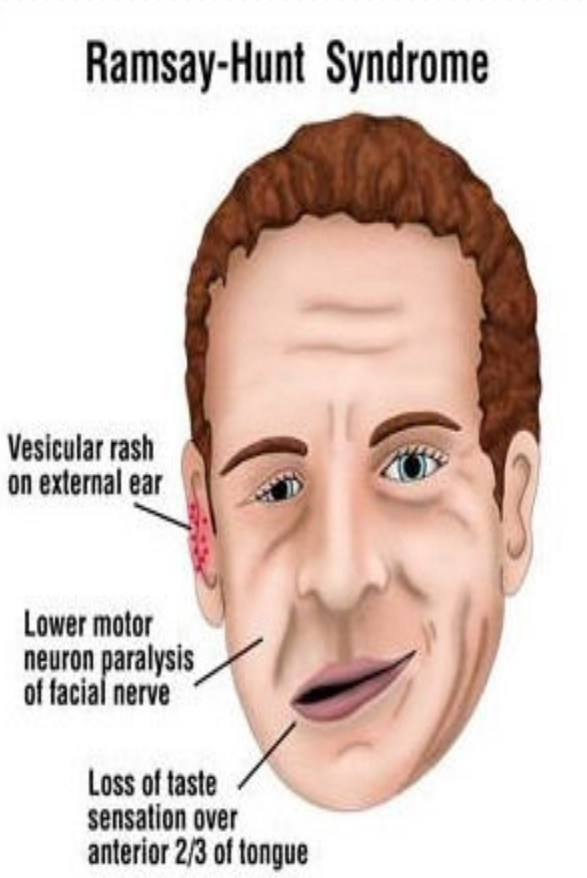
- **Hutchinson's sign – vesicles at the side & tip of nose precedes HZO**

- HZO lies dormant in TG

Herpes zoster keratitis

Acute epithelial keratitis	Nummular keratitis
	
• Develops in about 50% within 2 days of rash • Small, fine, dendritic or stellate epithelial lesions • Tapered ends without bulbs • Resolves within a few days	• Develops in about 30% within 10 days of rash • Multiple, fine, granular deposits just beneath Bowman membrane • Halo of stromal haze • May become chronic

OPHTHALMIC COMPLICATIONS



- Ramsay Hunt syndrome – 7th nerve palsy + loss of taste over ant 2/3rd tongue + earpain + vesicles in external auditory canal or pinna

DIAGNOSIS

- Diagnosis based on acute or recent history of systemic ds with ocular or periocular involvement with vesicles.

+

INVESTIGATIONS- vesicular fluid for PCR, immunomicroscopy

TREATMENT

- ACTIVE DISEASE

1. Antivirals(treat for 7 days , starting within 72 hrs) Famcyciclovir 500mg PO TDS
   Valacyclovir 1 g PO TDS
   Acyclovir 800mg PO 5t/d

2. Lesions of lid, conjunctiva or cornea (dendritic or rarely geographical keratitis) – topical AV (trifluridine applied 9t/d * 7-10 days) plus an topical AB.

3. Late onset immune stromal ds treated similar to stromal herpes infection.

4. Pain prevention-
   TCA's(eg nortryptyline, desipramine) 25-75 mg PO * 3months
   Nonnarcotic or short term narcotic analgesic .

5. Immunocompromised patients with any zoster –
   I.V Acyclovir 15 – 20 mg/kg/day

ADENOVIRUS KERATOCONJUCTIVITIS

- Medium-sized (90–100 nm),
- nonenveloped (without an outer lipid bilayer) icosahedral viruses composed of a nucleocapsid and a double-stranded linear DNA genome.

- OCULAR MANIFESTATIONS

1. Epidemic keratoconjunctivits
2. Pharyngoconjunctival fever
3. Nonspecific follicular conjunctivitis
4. Chronic adenoviral keratoconjunctivitis

EPIDEMIC KERATOCONJUCTIVIS

- Serotype AD 8, 19, & 37.
- Most serious adenoviral ocular illness
- In young adults during the fall and winter months
- U/L in 2/3rd pt
- IP 8 days
- Sign and symptoms:

  Acute tearing, FBS, photophobia, followed by lid and conjuctival edema and hyperemia, follicular and papillary conjuctival response with or without hge or membrane formation, & tender LN's

PHARYNGOCONJUCTIVAL FEVER

- Serotype Ad 3 and 7
- Similar to EKC except that the keratitis is usaully mild and b/l, and subepithelial infiltrates are less frequent and more transient.

CHRONIC ADENOVIRAL KERATOCONJUCTIVITIS

- Serotype Ad 2,3,4 and 19.
- Uncommon, often recognized cause of ant segment inflammatory and scarring ds.

DIAGNOSIS & TREATMENT

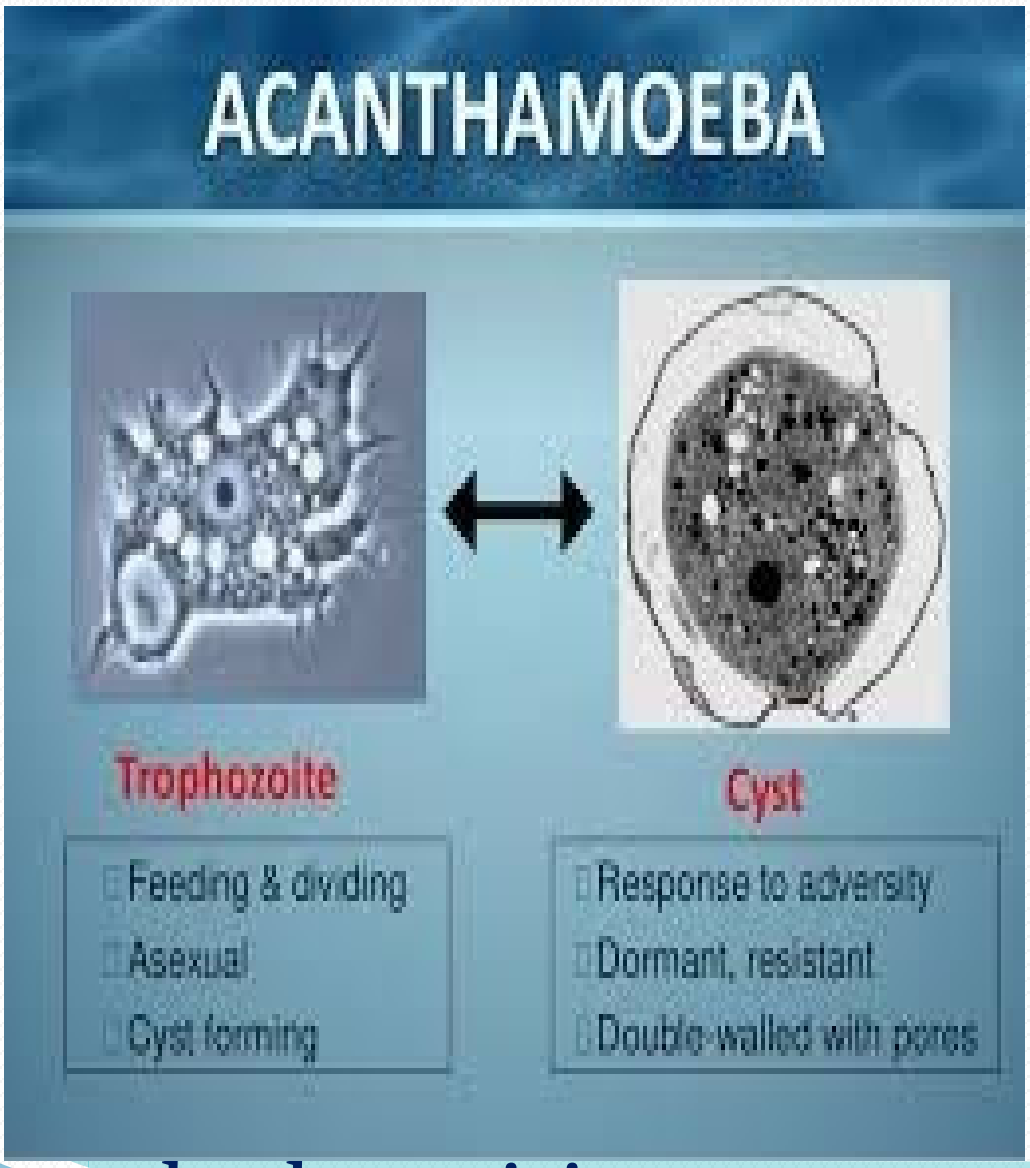
- Cytologic scrappings - mixed lymphocytic and neutrophil infiltrate and degenerated epithelial cells.
- Giemsa staining may reveal early eosinophillic intranuclear bodies.

- Antivirals are ineffective , except cidofovir.
- Topicals NSIAD'S : relief of inflammation. No effect onviral replication or appearance of corneal infiltrates.
- Cycloplegics as needed for iritis.
- Topical antibiotic ointment to lubricate and protect the cornea in presence of membranes.
- Ice packs, antipyretics and dark glasses as needed.

ACANTHAMOEBA

- Genus Acanthamoeba:- a family of free-living, ubiquitous cyst-forming protozoans.

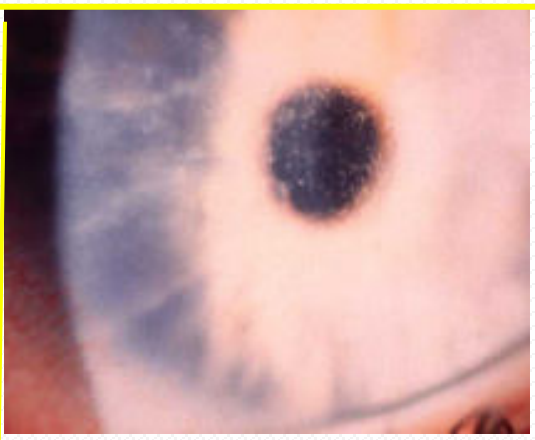
- Life cycle:- 2 forms
- Generally rare infection characterized by periodic outbreaks



Acanthamoeba keratitis

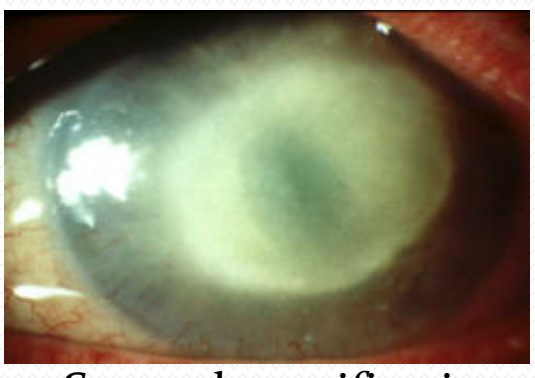
- Contact lens wearers at particular risk
- Symptoms worse than signs
- Pain disproportionate to clinical signs in early presentation

Small, patchy anterior stromal infiltrates



Perineural infiltrates (radial keratoneuritis)

Ulceration, ring abscess & small, satellite lesions



Stromal opacification

CORNEAL SCRAPINGS

Epithelial scrapings for LM

- H & E stain
- Giemsa
- PAS stain
- CFW stain
- Acridine orange stain

CULTURE

Non-nutrient agar with e.coli

Treatment -Medical therapy given for 135 days

-Biguanides(chlorhexidine or polyhexamethylenebiguanide (0.02%) effective against both forms