

# MANAGING HERPES SIMPLEX KERATITIS

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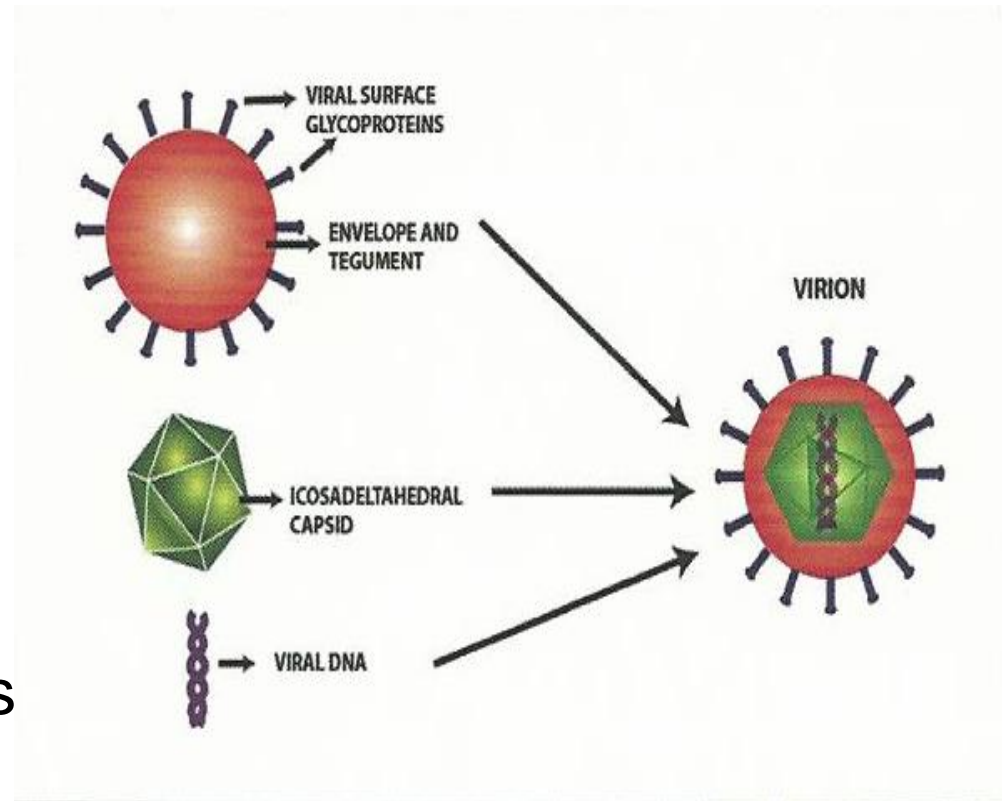
# Learning Objectives

- Describe clinical presentations of herpes simplex keratitis
- Explain available therapies



# Structure of Herpes Simplex Virus

- Herpes simplex virus types 1 and 2 (HSV-1, HSV-2)
  - Double-stranded DNA
  - Viral-derived capsid
  - Host-cell derived envelope
  - Glycoprotein projections



# Epidemiology of Ocular HSV

- Initial exposure: childhood “viral” illness
- Ocular manifestation: reactivation of latent virus
  - Blepharitis, follicular conjunctivitis, keratitis, keratouveitis, acute retinal necrosis
- 50,000 new and recurring cases annually
  - Recurrence rate: 27% at one year

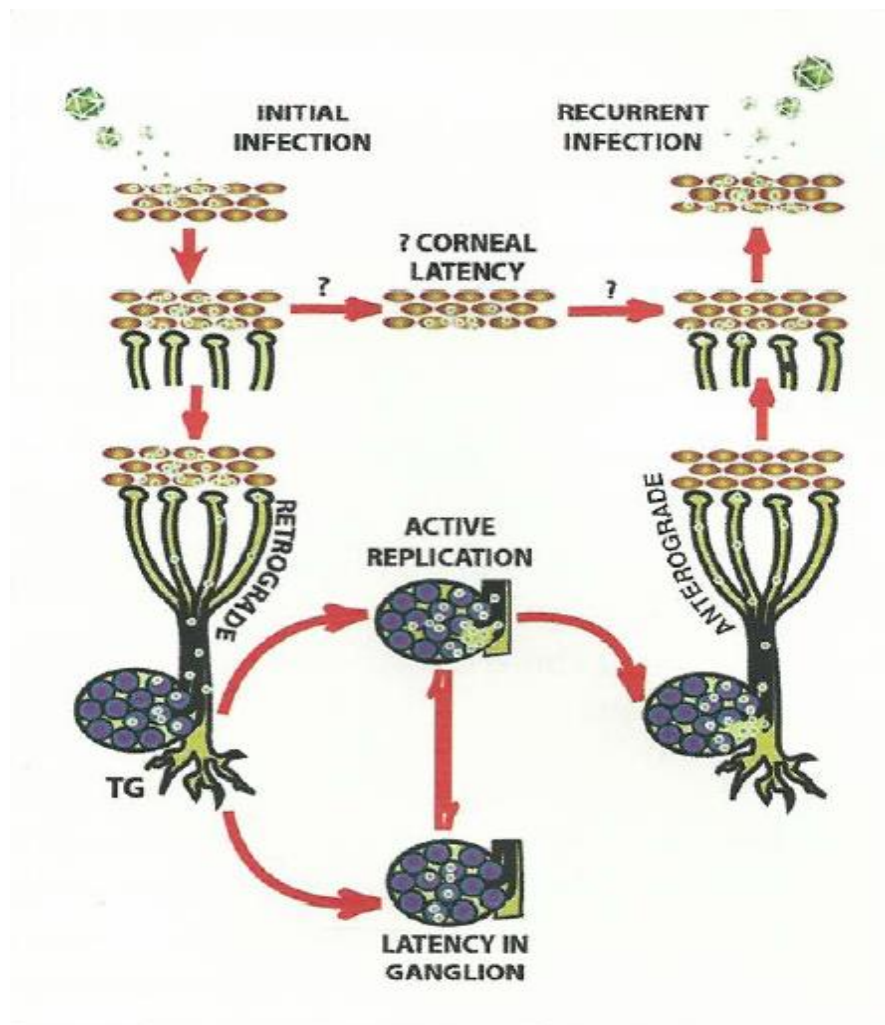
# Primary HSV Ocular Infection

- Less common presentation
- Pediatric age
- Fever, malaise
- Skin rash
- Unilateral follicular conjunctivitis – suspect HSV





# Life Cycle of Herpes Simplex Virus



# Recurrent HSV Infection

- Orofacial: Cold sores on lip, cheek or tongue
- Ocular: Most frequently involves cornea
  - Epithelial keratitis – active virus
  - Stromal keratitis – immunologic





# HSV Keratitis Classification

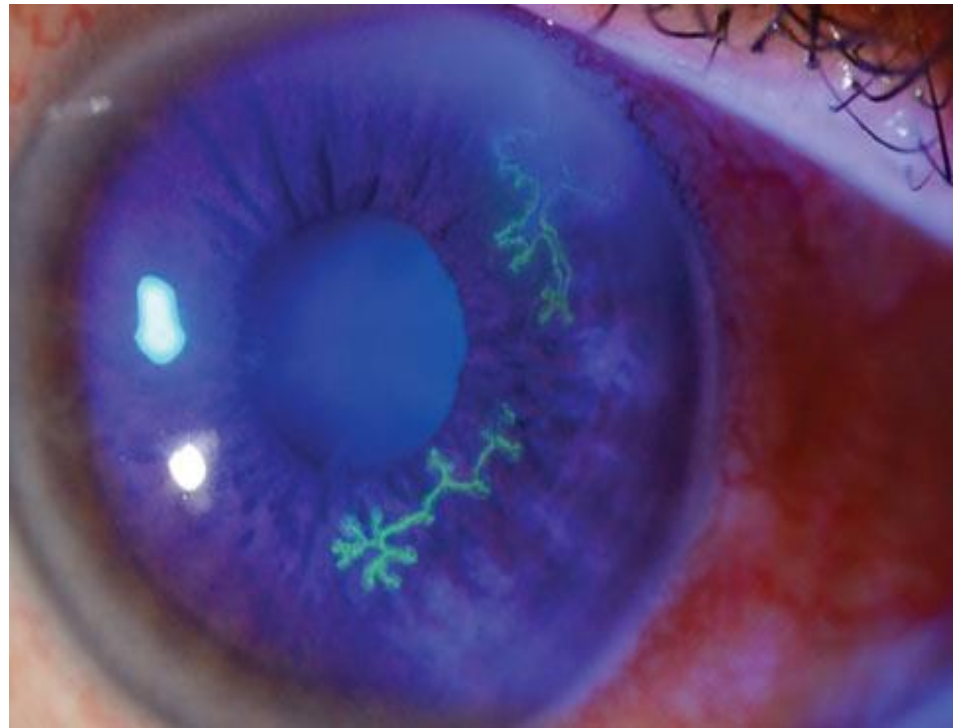
HSV CATEGORY	COMMON NOMENCLATURE	TREATMENT
Epithelial Keratitis	<ul style="list-style-type: none"><li>▪ Dendritic Keratitis</li><li>▪ Geographic Keratitis</li></ul>	Antiviral (topical or oral) or debridement
Stromal Keratitis without ulceration	<ul style="list-style-type: none"><li>▪ Interstitial Keratitis</li><li>▪ Immune Stromal Keratitis</li></ul>	Topical steroid + oral antiviral prophylaxis
Stromal Keratitis with ulceration	<ul style="list-style-type: none"><li>▪ Necrotizing Keratitis</li></ul>	Oral antiviral in therapeutic doses + topical steroid
Endothelial Keratitis	<ul style="list-style-type: none"><li>▪ Disciform Keratitis</li></ul>	Oral antiviral in therapeutic doses + topical steroid

# Epithelial Keratitis

- Dendritic ulcer
- Geographic ulcer
- Others:
  - Marginal ulcer
  - Metaherpetic (trophic) ulcer

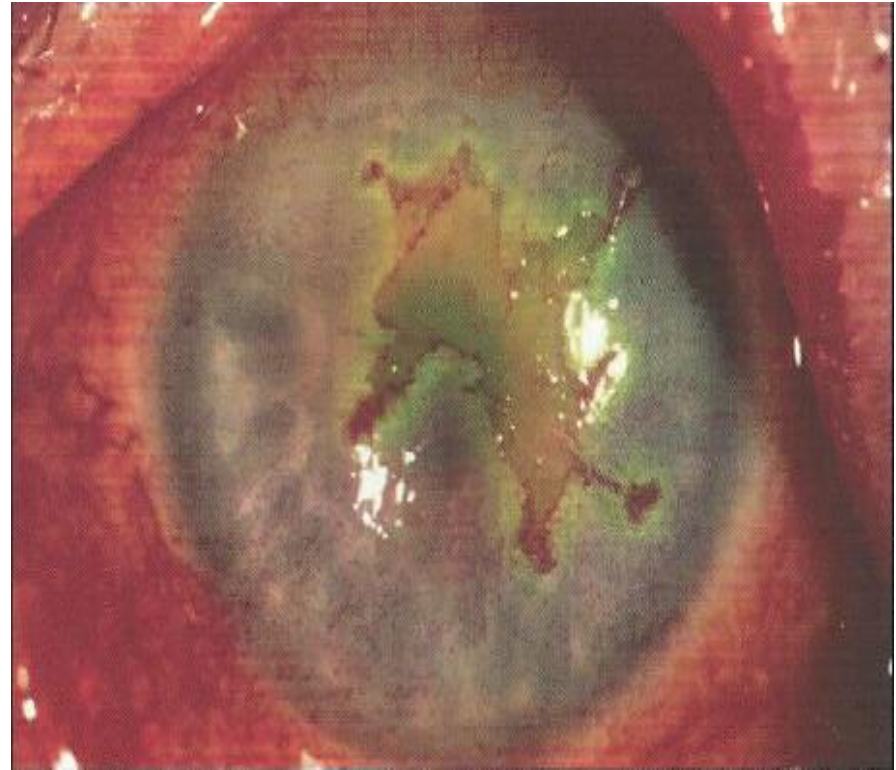
# Epithelial Keratitis: Dendritic Ulcer

- Classic corneal lesion
- Branching with terminal bulbs
- Raised borders
- Consist of HSV-infected cells
- Dendritic scar (ghost dendrite) may remain



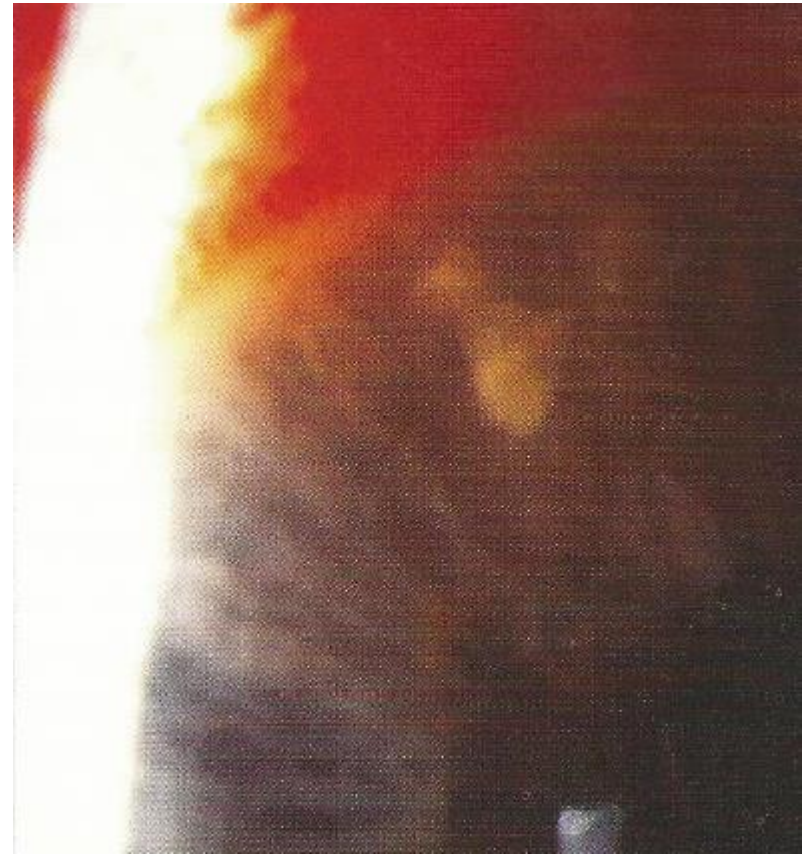
# Epithelial Keratitis: Geographic Ulcer

- Caused by replicating virus
- Larger epithelial defect
- Branching and terminal bulbs at periphery
- Immunocompromised, on topical steroids, untreated dendrite



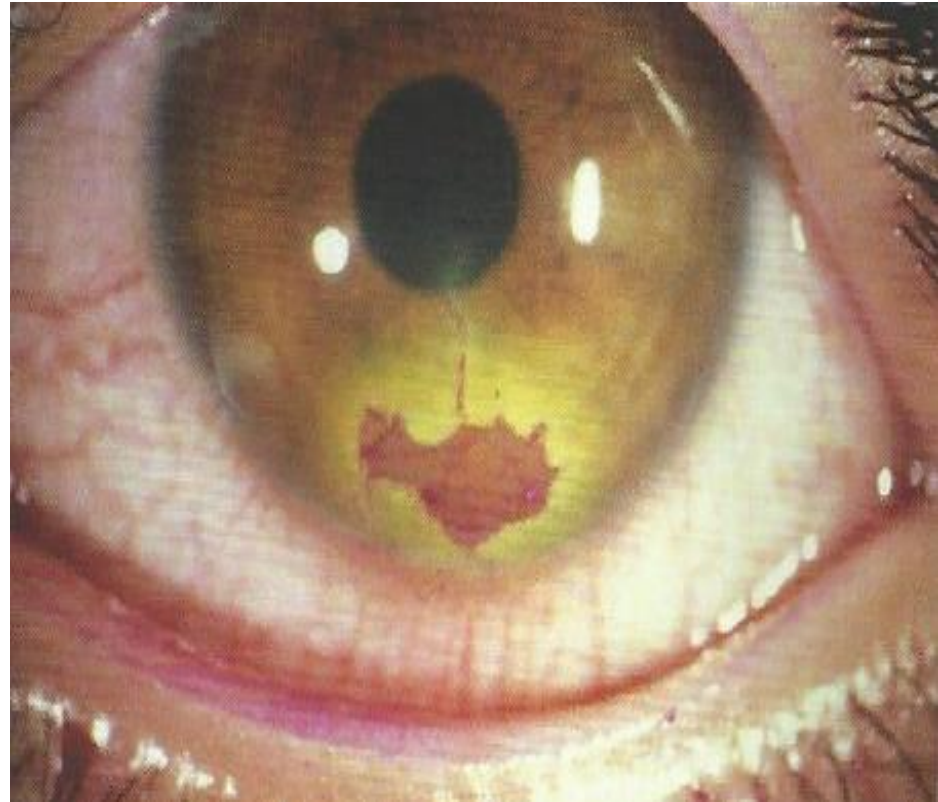
# Epithelial Keratitis: Marginal Ulcer

- Lesion near limbus
- Resembles Staph ulcer
- More stromal inflammation
- More resistant to treatment



# Epithelial Keratitis: Metaherpetic (Trophic) Ulcer

- Epithelial ulceration
- No live virus
- “Trophic”: de novo
- “Metaherpetic”: follows dendritic or geographic ulcer
- Inability of epithelium to heal
- Smooth borders
- “Reverse staining”





# Treatment: Metaherpetic Ulcer

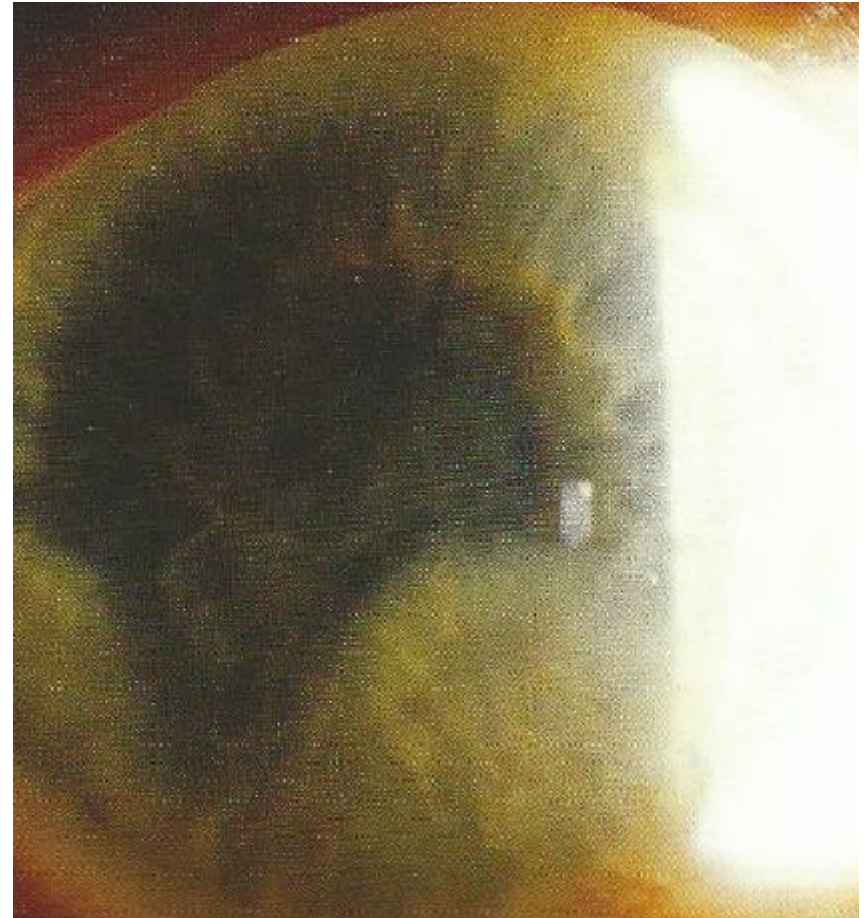
- Form of epithelial ulceration that does not have live virus
- Goal: rapidly heal epithelial defect
  - Stop use of toxic meds
  - Punctal occlusion
  - Tear film supplements
  - Bandage contact lens
  - Tarsorrhaphy
  - Cautious use of topical steroids

# Stromal Keratitis

- Immune-mediated response to nonreplicating viral particles in stroma
- Immune stromal keratitis
  - Interstitial keratitis
- Necrotizing keratitis
- Disciform keratitis (Endothelial keratitis)
- Keratouveitis

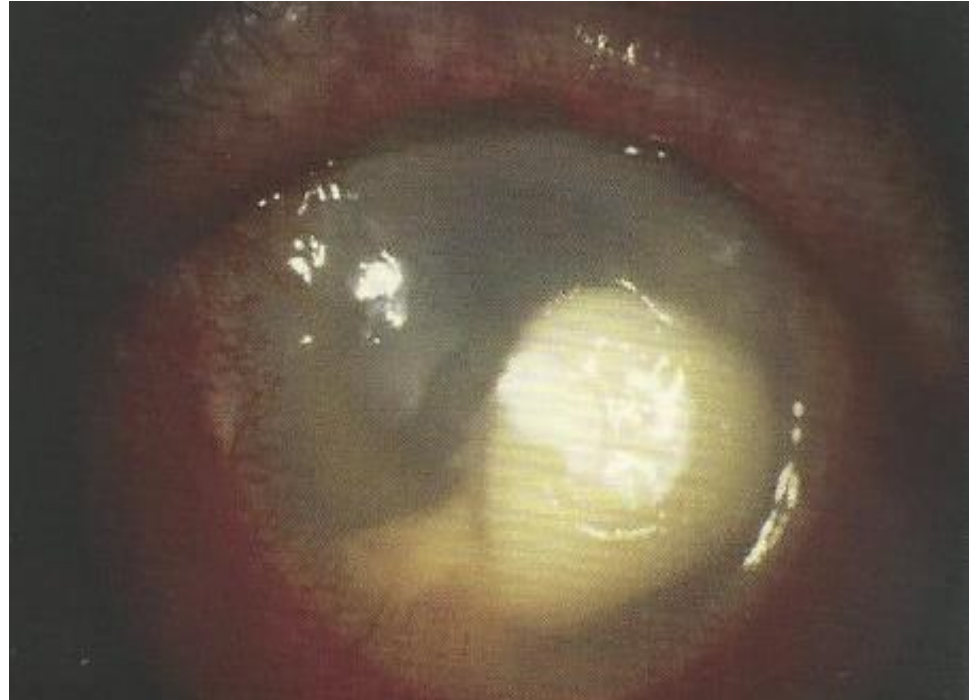
# Stromal: Immune Stromal Keratitis

- Inflammatory response to viral antigen in stroma
- Focal, multifocal, diffuse stromal opacities
- Interstitial keratitis – vascularization
  - Ghost-like
  - HSV most common cause



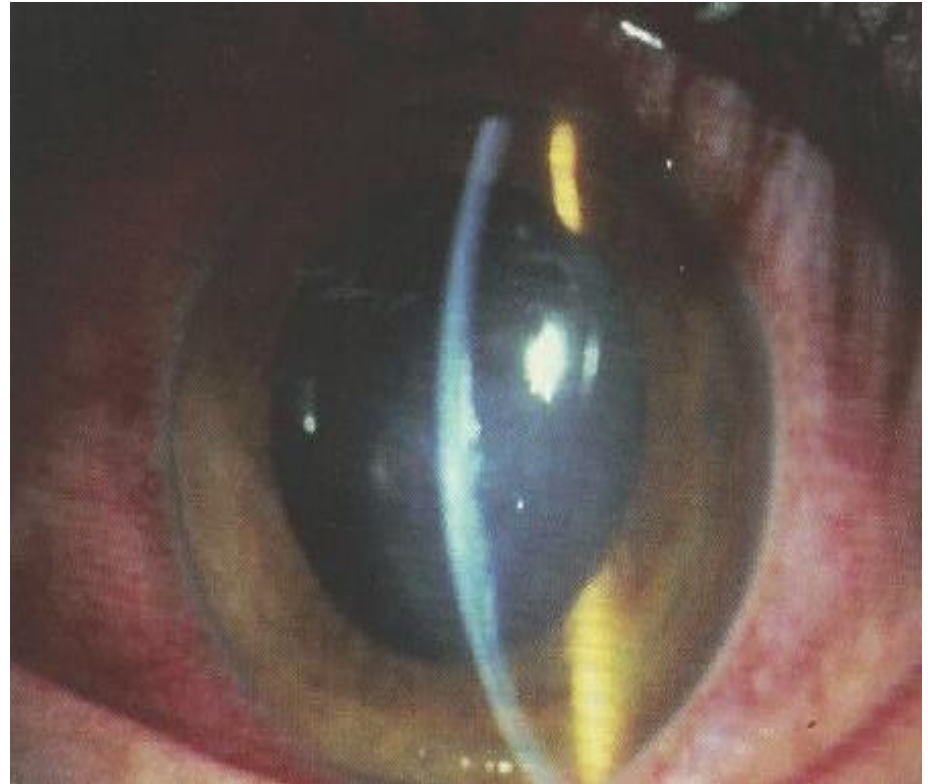
# Stromal: Necrotizing Keratitis

- Reaction to live viral particles in stroma
- History multiple recurrences
- Corneal melting, perforation
- Significant associated uveitis



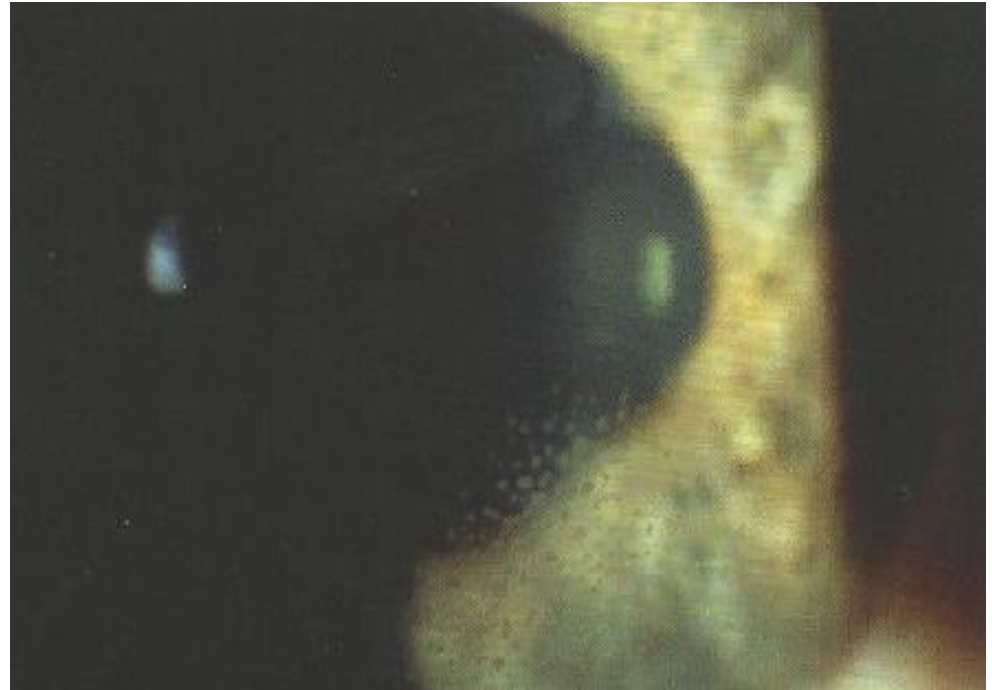
# Stromal: Disciform Keratitis (Endothelial Keratitis)

- Endothelial dysfunction from inflammatory response to viral antigen
- Disc-shaped area corneal edema
- Minimal inflammation in stroma
- Unilateral
- Confused with Fuchs
  - bilateral



# Stromal: Keratouveitis

- Uveitis predominates
- Mutton-fat KP
- Immune-mediated
- Unilateral uveitis with high IOP – suspect HSV





# Diagnosis: HSV Keratitis

- Clinical findings
- Lab tests seldom needed
  - Of no use in stromal keratitis
- Herpes Culture
  - HSV-1 or HSV-2 typing
- Serum Antibody Testing
  - Positive titers in adults indicates past infection
  - Nearly universal

# Diagnosis: Clinical Findings

- Patient is in far less pain than findings would suggest
- Photophobic or uveitis and high IOP
- Patient has history of ocular HSV

# Diagnosis: Reduced Corneal Sensation

- Hallmark of HSK
- Viral replication kills host neuron
  - Leads to hyposensitivity, poor tear production, persistent epithelial defects
- Test prior to topical anesthetic
  - Use dental floss or cotton wisp

# Long-Term Complications

- Recurrent disease
  - Increased inflammation, scarring, decreased corneal sensation
- Risk of stromal disease increases with recurrences of HSV epithelial keratitis
- Recurrent episode occurs adjacent to site of previous episode

# Treatment Fundamentals

- HSV epithelial keratitis (live virus)
  - Topical or oral antivirals
  - No steroids
- HSV stromal disease (little, if any, virus)
  - Topical steroids
  - Oral (never topical) antivirals as prophylaxis

# Managing HSV Epithelial Keratitis

- Debridement
  - Removes infected cells
  - Faster resolution, less scarring
- Topical antiviral
  - Viroptic (Trifluridine)
  - Zirgan (Ganciclovir gel)
- Oral antiviral
  - Zovirax (Acyclovir)
  - Valtrex (Valacyclovir)
  - Famvir (Famciclovir)



# Topical Antivirals for HSV Epithelial Keratitis

	<b>Viroptic</b>	<b>Zirgan</b>
	Trifluridine solution 1%	Ganciclovir gel 0.15%
Dosage	1 drop every 2 hours (daily dose: 9) until ulcer heals, then 5 times daily for 7 days	1 drop every 3 hours (daily dose: 5) until ulcer heals, then 3 times daily for 7 days
Refrigeration	Refrigerate	Room temp
Preservative	Thimerosal 0.001%	BAK

# Managing HSV Stromal Keratitis

- Topical steroids
- Simultaneous oral antiviral prophylaxis
  - Reduces risk of HSV reactivation at the trigeminal ganglion level
  - Zovirax
  - Valtrex
  - Famvir

# Oral Antiviral Agents for HSV Keratitis

Agent	Treatment Dose	Prophylactic Dose
Zovirax (Acyclovir)	400 mg five times daily	400 mg twice daily
Valtrex (Valacyclovir)	500 mg three times daily	500 mg once daily
Famvir (Famciclovir)	250 mg three times daily	250 mg once daily

# Using Steroids Correctly

- Not used in acute epithelial keratitis
- Essential for stromal keratitis
- Prednisolone acetate 1% QID
- S-l-o-w-l-y taper



# Using Antiviral Prophylaxis Correctly

- Oral antivirals
  - Primarily against reactivation at ganglion level
  - During topical steroid treatment for stromal disease
  - Patients with multiple recurrences (2 or more / year)
  - Keratitis close to visual axis
  - Immunocompromised patients
  - Long-term use for 1 year or more reduced risk of recurrent HSV

# Quiz Time

No Cheating!



# Case 1

- 42 year old female complains of red, irritated OD
- SLE: single dendrite
- Dx: first episode of HSV epithelial keratitis
- Options:
  - A. Viroptic drops 9x/day for 1 week, then taper
  - B. Zovirax 400 mg 5x/day for 1 or 2 weeks
  - C. Both regimens combined

# Case 1: Recommendation

- Each approach reasonable
- Consider full dose Viroptic drops
  - 9x/day until ulcer heals
  - then 5x/day for 1 week
  - then stop



# Case 2

- 51 year old male complains of irritated OS and mild photophobia, vision good
- History of three previous episodes HSV epithelial keratitis
- SLE: minimal scarring with adjacent new dendrite
- Dx: recurrent HSV epithelial keratitis
- Options:
  - A. Viroptic drops
  - B. Zovirax oral
  - C. Combination therapy

# Case 2: Recommendation

- Combination therapy
  - Viroptic 9x/day until ulcer heals, then 5x/day for 1 week
  - Full therapeutic dose Zovirax 400 mg 5x/day
  - Discontinue topical Viroptic within 2 weeks
  - Taper Zovirax to 400 mg BID for long-term prophylaxis (1 year)

# Case 3

- 46 year old female complains of blurry vision OS.
- History of treated herpetic dendrite 1½ years ago
- Vision: 20/40
- SLE: Mild stromal edema, no scarring
- Dx: First episode of HSV stromal keratitis
- Options:
  - A. Viroptic drops
  - B. Steroid drops
  - C. Zovirax oral
  - D. Combination therapy

# Case 3: Recommendation

- Combination therapy of topical steroids with oral antiviral coverage
  - Pred Forte QID and taper as necessary
  - Zovirax 400 mg BID until inflammation subsides

# Case 4

- 62 year old male complains of blurry vision OD
- History of two previous episodes of stromal keratitis
- Vision 20/50
- SLE: Mild to moderate edema and patchy scarring
- Dx: Recurrent HSV stromal keratitis
- Options:
  - A. Viroptic drops
  - B. Steroid drops
  - C. Zovirax oral
  - D. Combination therapy

# Case 4: Recommendation

- Combination therapy
  - Pred Forte 1% QID
  - Zovirax 400mg BID
  - Taper steroids s-l-o-w-l-y to avoid recurrence
  - Continue Zovirax long-term (1 year)

# Congratulations!



THANK YOU

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