

## HSV, HZO, & EKC: VIRAL EYE DISEASE ALPHABET SOUP

Nathan Lighthizer, O.D., F.A.A.O.  
Assistant Dean, Clinical Care Services  
Director of Continuing Education  
Chief of Specialty Care Clinics  
Chief of Electrodiagnostics Clinic  
Oklahoma College of Optometry  
lighthiz@nsuok.edu

## Herpes Zoster

- ▣ Nearly 1 million Americans develop shingles each year
- ▣ Ocular involvement accounts for up to 25% of presenting cases
- ▣ Over 50% incur long term ocular damage

## Herpes Zoster

\*\*\*Varicella-Zoster Virus\*\*\*

- ▣ Herpes DNA virus that causes 2 distinct syndromes
  1. Primary infection – Chicken pox (Varicella)
    - ▣ Usually in children
    - ▣ Highly contagious\*\*\*
    - ▣ Very itchy maculopapular rash with vesicles that crust over after ≈ 5 days
    - ▣ 96% of people develop by 20 years of age
    - ▣ Vaccine now available



## Herpes Zoster

\*\*\*Varicella-Zoster Virus\*\*\*

- ▣ Herpes DNA virus that causes 2 distinct syndromes
  1. Primary infection – Chicken pox (Varicella)
    - ▣ Usually in children
    - ▣ Highly contagious\*\*\*
    - ▣ Very itchy maculopapular rash with vesicles that crust over after ≈ 5 days
    - ▣ 96% of people develop by 20 years of age
    - ▣ Vaccine now available



## Herpes Zoster

- ▣ Herpes DNA virus that causes 2 distinct syndromes
  2. Reactivation – Shingles (Herpes Zoster)
    - ▣ More often in the elderly and immunosuppressed (AIDS)
      - Systemic work-up if Zoster in someone < 40
    - ▣ Can get shingles anywhere on the body
    - ▣ Herpes Zoster Ophthalmicus (HZO)
      - Shingles involving the dermatome supplied by the ophthalmic division of the CNV (trigeminal)
      - 15% of zoster cases



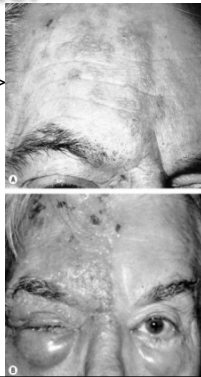
## Herpes Zoster

- ▣ Symptoms:
  - Generalized malaise, tiredness, fever
  - Headache, tenderness, paresthesias (tingling), and pain on one side of the scalp\*\*\*
    - ▣ Will often precede rash
  - Rash on one side of the forehead
  - Red eye
  - Eye pain & light sensitivity

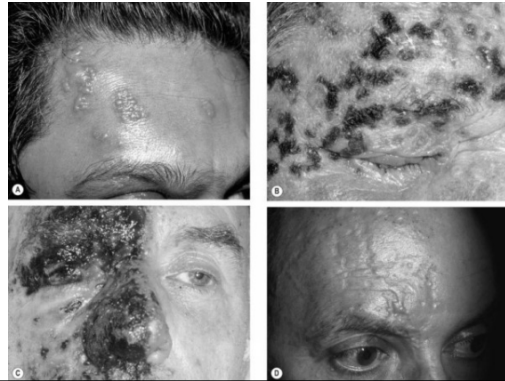
## Herpes Zoster

### □ Signs:

- Maculopapular rash -> vesicles -> pustules -> crusting on the forehead
- Respects the midline\*\*\*
- Hutchinson sign
  - rash on the tip or side of the nose\*\*\*
- Classically does not involve the lower lid



## Herpes Zoster



## Herpes Zoster

### □ Other Eye Disease (Acute):

- Acute epithelial keratitis (pseudodendrites)
- Conjunctivitis
- Stromal (interstitial) interstitial keratitis
- Endotheliitis (disciform keratitis)
- Neurotrophic keratitis



## Herpes Zoster

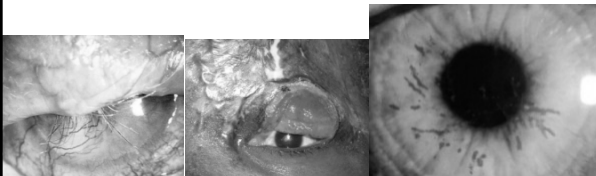
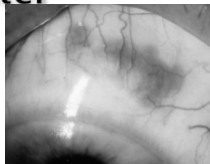
### □ Other Eye Disease (Acute):

- Episcleritis
  - Scleritis
  - Anterior uveitis
  - IOP elevation
  - Retinitis
  - Choroiditis
  - Neurological complications (nerve palsies)
  - Vascular occlusion
- Treat the complications just like as if they were primary conditions

## Herpes Zoster

### □ Other Eye Disease (Chronic):

- Neurotrophic keratitis – 50%
- Scleritis
- Mucous plaque keratitis – 5%
- Eyelid scarring



What is your medication of choice when treating herpes zoster ophthalmicus?

- A. Acyclovir 400 mg 5x/day
- B. Acyclovir 800 mg 5x/day
- C. Valtrex 500 mg 3x/day
- D. Valtrex 1000 mg 3x/day
- E. Famvir 250 mg 3x/day
- F. Famvir 500 mg 3x/day
- G. Zirgan 5x/day

## Herpes Zoster

### □ Treatment:

- Treat the complications just like as if they were primary conditions
- Oral antivirals – must be started within 72 hours of symptoms\*\*
  - Acyclovir 800mg 5x/day x 7-10 days
  - Valtrex 1000mg 3x/day X 7-10 days
  - Famciclovir 500mg 3x/day X 7-10 days
- Topical ointment to skin lesions to help prevent scarring
  - Bacitracin, erythromycin

## Herpes Zoster

### □ Prevention:

- Zostivax vaccine
  - Live attenuated herpes virus
  - Only given to people who know they had chicken pox as a child\*\*\*
  - Only studied in patients > 60 yo
    - 51% reduction in incidence of HZ
    - 60% reduction in symptom severity in those who got HZ
    - 66.5% reduction in post-herpetic neuralgia



## Herpes Zoster

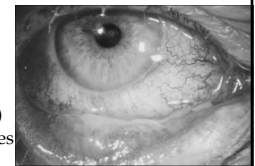
### □ Post-herpetic Neuralgia

- Constant or intermittent pain that persists for more than one month after the rash has healed
- Older patients with early severe pain and larger area are at greater risk
- Can be so severe that it leads to depression & suicide
- Improves with time
  - Only 2% of pts affected 5 years out
- Tx:
  - Cool compresses
  - Topical capsaicin ointment or lidocaine cream
  - Analgesics (Tylenol 3, Vicoden)
  - Amitriptyline 25mg PO TID
  - Neurotin (Gabapentin)

## Viral conjunctivitis

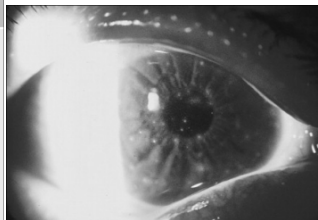
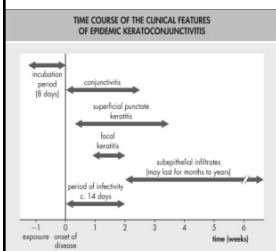
### □ Signs:

- Red eye (conj hyperemia)
- Watery discharge
- Follicles in the inferior fornix & conj
- (+) PA node\*\*\*
- Red/swollen eyelids
- Petechial sub-conj hemes
- SPK
- SEI's (sub-epithelial infiltrates)
- Pseudomembranes/membranes often seen in EKC



## EKC

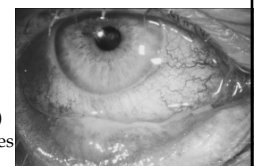
### □ Timecourse



## Viral conjunctivitis

### □ Signs:

- Red eye (conj hyperemia)
- Watery discharge
- Follicles in the inferior fornix & conj
- (+) PA node\*\*\*
- Red/swollen eyelids
- Petechial sub-conj hemes
- SPK
- SEI's (sub-epithelial infiltrates)
- Pseudomembranes/membranes often seen in EKC



## EKC



## EKC conjunctivitis

- ▣ **Diagnosis**
  - Based on clinical symptoms
- ▣ **Treatment:**
  - Cool compresses
  - Artificial tears
  - “get the red out drops”
    - Vasoconstrictors such as Visine
  - Hygiene\*\*\*
  - Quarantine/Isolation
  
  - Betadine 5% solution???
  - Zirgan???
  - Lotemax/Pred Forte QID??? – not until late

## EKC conjunctivitis

- ▣ **Diagnosis**
  - Based on clinical symptoms
- ▣ **Treatment:**
  - Cool compresses
  - Artificial tears
  - “get the red out drops”
    - Vasoconstrictors such as Visine
  - Hygiene\*\*\*
  - Quarantine/Isolation
  
  - Betadine 5% solution???
  - Zirgan???
  - Lotemax/Pred Forte QID??? – not until late

## Herpes Simplex

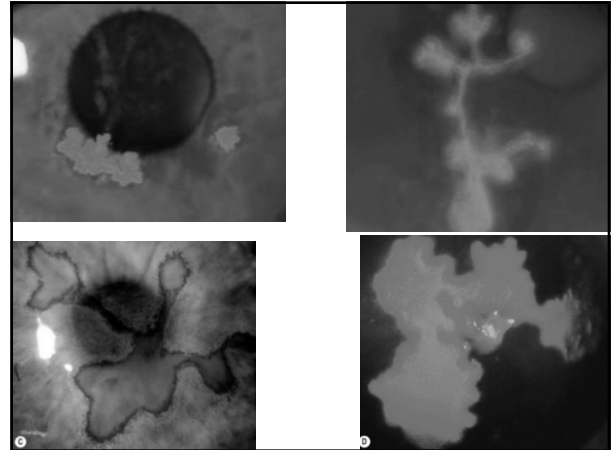
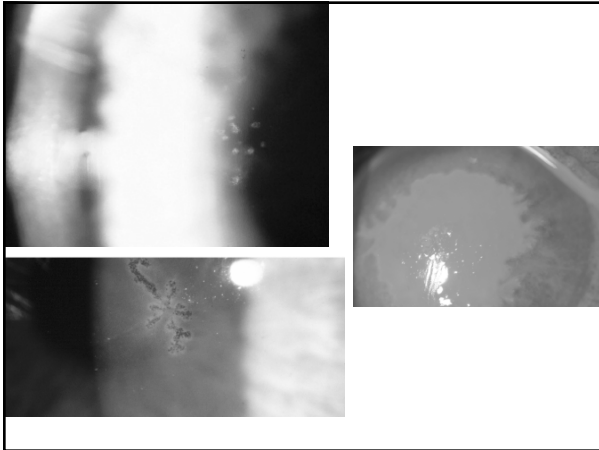
- ▣ **Most common virus found in humans**
  - 60-99% are infected by 20 years old
- ▣ **Double stranded DNA virus**
  - HSV type 1 (HSV-1)
  - HSV type 2 (HSV-2)
- ▣ **Primary infection**
  - Occurs in childhood via droplet exposure
  - Subclinical infection in most
- ▣ **Secondary infection (recurrence)**

## Herpes Simplex

- ▣ **Recurrent infection:**
  - After primary infection the virus is carried to the sensory ganglion for that dermatome (trigeminal ganglion) where a latent infection is established.
  - Latent virus is incorporated in host DNA and cannot be eradicated
  - Stressors (trauma, UV light, fever, hormonal changes, finals week, etc) cause reactivation of the virus and it is transported in the sensory axons to the periphery -> clinical signs/symptoms
- Ocular recurrence -> 10% at one year, 50% at ten years

## Herpes Simplex Keratitis

- ▣ **Epithelial Keratitis:**
  - **Symptoms:**
    - Ocular irritation, redness, photophobia, watering, blurred vision
  - **Signs:**
    - Swollen opaque epithelial cells arranged in a coarse punctate or stellate pattern
    - Central desquamation results in a dendrite\*\*\*
      1. Central ulceration
      2. Terminal end bulbs
    - \*\*\*Corneal sensation is reduced\*\*\*



## Herpes Simplex Keratitis

### □ Epithelial Keratitis:

- Symptoms:
  - Ocular irritation, redness, photophobia, watering, blurred vision
- Signs:
  - Swollen opaque epithelial cells arranged in a coarse punctate or stellate pattern
  - Central desquamation results in a dendrite\*\*\*
    1. Central ulceration
    2. Terminal end bulbs
  - \*\*\*Corneal sensation is reduced\*\*\*

## Herpes Simplex Keratitis

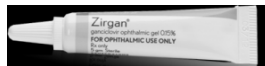
### □ Epithelial Keratitis:

- Signs (con't):
  - Mild associated subepithelial haze
  - Elevated IOP\*\*\*
  - Persistent SPK and irregular epithelium as the ulcer is healing
- Differential diagnosis:
  - Herpes zoster
  - Healing corneal abrasion
  - Acanthamoeba keratitis
  - Medicamentosa

## Herpes Simplex Keratitis

### □ Epithelial Keratitis:

- Treatment:
  - Zirgan (ganciclovir gel 0.15%)
    - 5x/day until the dendrite disappears
    - 3x/day for another week
  - Viroptic (trifluridine solution 1%)
    - 9x/day until the dendrite disappears
    - 5x/day for another week
  - Oral antivirals (if topical not well tolerated):
    - Acyclovir 400 mg 5x/day X 7-10 days
    - Valtrex 500 mg 3x/day X 7-10 days
    - Famvir 250 mg 3x/day X 7-10 days



## Herpes Simplex Keratitis

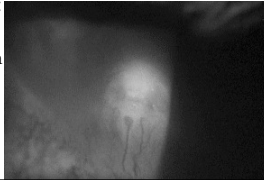
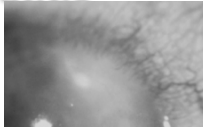
### □ Epithelial Keratitis:

- Treatment (con't):
  - Debridement of the dendritic ulcer???
  - Oral antivirals???
  - IOP control
    - Avoid prostaglandins???
  - Steroids???
- Follow-up
  - Day 1, 4, 7

## Herpes Simplex Keratitis

### ▣ Marginal keratitis:

- Very rare
- Looks like a marginal infiltrate....but
- In HSV marginal keratitis:
  1. Much more pain
  2. Deep neovascularization
  3. No clear zone between infiltrate and limbus



## Herpes Simplex Keratitis

### ▣ Immune Stromal Keratitis (ISK):

- 2% of initial ocular HSV presentations
- 20-61% of recurrent disease
- 88% non-necrotizing
- 7% necrotizing
- \*\*\*Can be visually devastating\*\*\*

## Herpes Simplex Keratitis

### ▣ Immune Stromal Keratitis:

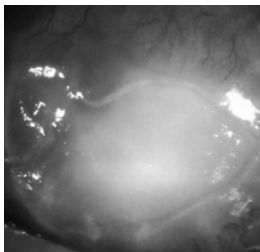
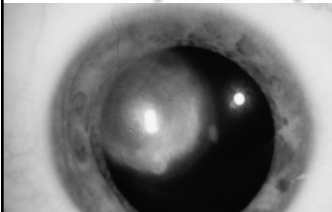
- Symptoms:
  - Gradual blurred vision
  - Halos
  - Discomfort/Pain
  - Redness

## Herpes Simplex Keratitis

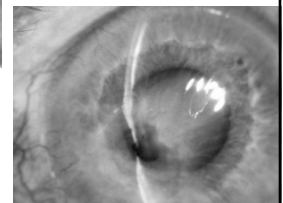
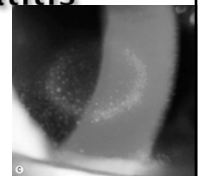
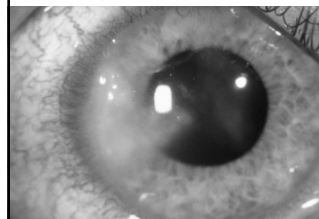
### ▣ Immune Stromal Keratitis:

- Signs (non-necrotizing):
  - Stromal haze (inflammation & edema)
  - Neovascularization (deep)
  - Immune ring
  - Scarring and/or thinning
  - Intact epithelium\*\*\*
- Signs (necrotizing):
  - All of the above
  - More dense infiltration
  - Often w/ overlying epithelial defect
  - Necrosis and/or ulceration
  - \*\*\*high perforation risk\*\*\*

## Herpes Simplex Keratitis



## Herpes Simplex Keratitis



The treatment of choice for immune stromal keratitis is

- A. Oral antivirals
- B. Topical antivirals
- C. Topical steroids with prophylactic antiviral cover
- D. Debridement

## Herpes Simplex Keratitis

### ▣ Immune Stromal Keratitis:

- Treatment:
  - Topical steroids
    - Pred Forte QID-q2H
    - Durezol BID-QID
    - Lotemax QID
  - Topical anti-viral cover
    - Viroptic (trifluridine 1%) QID
    - Zirgan (ganciclovir 0.15%) QID
  - Topical cyclosporin (Restasis), AT's, ung's to facilitate epithelial healing if ulceration is present

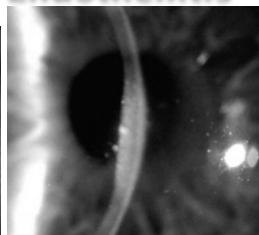
## Herpes Simplex Keratitis

- ▣ Endotheliitis: AKA Disciform Keratitis
  - Not considered a primary form of stromal keratitis
    - Stromal edema is present secondary to endothelial inflammation
  - Symptoms:
    - Blurred vision
    - Halos
    - Discomfort/Pain
    - Redness

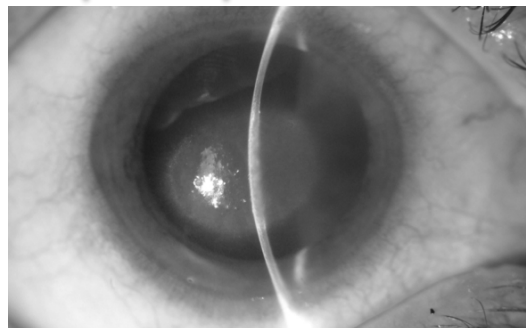
## Herpes Simplex Keratitis

- ▣ Endotheliitis: AKA Disciform Keratitis
  - Signs:
    - Central zone of stromal edema often with overlying epithelial edema
    - KP's underlying the edema
    - AC reaction
    - IOP may be elevated
    - Reduced corneal sensation
    - Healed lesions often have a faint ring of stromal or subepithelial opacification and thinning

## Herpes Simplex Endotheliitis



## Herpes Simplex Endotheliitis

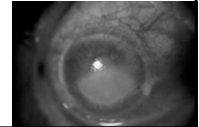


## Herpes Simplex Keratitis

- ▣ **Endotheliitis:** AKA Disciform Keratitis
  - Treatment:
    - Topical steroids
      - Pred Forte QID-q2H
      - Durezol BID-QID
      - Lotemax QID
    - Topical anti-viral cover
      - Viroptic (trifluridine 1%) QID
      - Zirgan (ganciclovir 0.15%) TID
    - Topical cyclosporin (Restasis), AT's, ung's to facilitate epithelial healing if ulceration is present

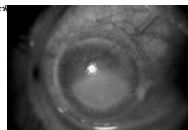
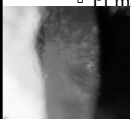
## Herpes Simplex Keratitis

- ▣ **Neurotrophic Keratitis:**
  - Keratopathy occurs from loss of trigeminal innervation to the cornea resulting in complete or partial anaesthesia
  - The cornea is numb so the pt doesn't blink
  - Sx's:
    - Irritation/burning/FB sensation
    - Redness
    - Tearing
    - Decreased vision



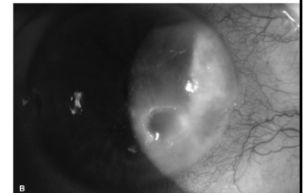
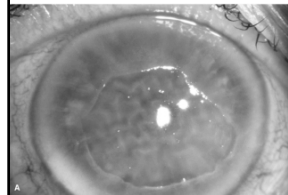
## Neurotrophic Keratopathy

- ▣ Signs:
  - Decreased corneal sensation\*\*\*
  - Interpalpebral SPK
  - **Persistent epithelial defects** in which the epithelium at the edge of the lesion appears rolled and thickened, and is poorly attached
  - Advanced cases may have sterile ulceration, keratitis, and/or corneal melt
    - Pt may be surprisingly asymptomatic\*\*



## Neurotrophic Keratopathy

- ▣ Signs:



## Neurotrophic Keratopathy

- ▣ Tx:
  - Find out the cause
  - D/C any meds that may be responsible
  - Lubricate, lubricate, lubricate\*\*\*
    - Preservative free AT's, gels, and ung's q1h-QID
  - Topical Ab drops and/or ung (Polytrim QID, etc)
  - Taping the eyelids at night to ensure adequate closure
  - In severe cases:
    - Patching, tarsorrhaphy, Botox to induce ptosis

## Neurotrophic Keratopathy

- ▣ Tx:
  - Healing an ulcer that won't heal
    1. Autologous serum
    2. Prokera
      - Amniotic membrane in a CL skirt
  - 1. Also could use a scleral lens



## Autologous Serum

1. Draw 40cc of blood through venipuncture
2. Centrifuge for 5 minutes @ 1500 rpm
3. Centrifuging will divide the blood into its separate components
4. Place 1cc of serum in each bottle
5. Add 4cc of saline to make a concentration of 20% serum eye drops
6. 20% serum eye drop concentration



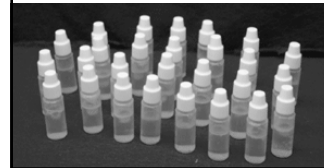
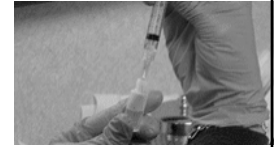
Table 1. Comparison of the biochemical properties of normal human tears and serum<sup>1,2</sup>

	Tears	Serum
pH	7.4	7.4
Osmolality	296	296
EGF (ng/ml)	0.2-3.0	0.5
TGF-β (ng/ml)	2-10	6-33
Vitamin A (ng/ml)	0.02	46
Lysine (ng/ml)	1.4	6
IgA (μg/ml)	1190	2
Fibrinogen (μg/ml)	21	295

EGF=epithelial growth factor; TGF=transforming growth factor

## Autologous Serum

- Severe dry eye patients
- Graft vs. Host Disease
- Filamentary Keratitis
- Neurotrophic keratitis
- Chronic Stainers



## Herpes Simplex Epithelial Keratitis

- ▣ My Regimen:
  - Zirgan 5x/day until the ulcer heals, then 3x/day for one week
  - Oral Valtrex 500 mg 3x/day for 7-10 days
  - Artificial tears
  - L-Lysine 2 grams daily?
  - Debride the ulcer?
- ▣ RTC 1 day, 4 days, 7 days

## Herpes Simplex Keratitis

- ▣ Prophylactic Treatment:
  - Reduces the rate of recurrence of epithelial and stromal keratitis by ≈ 50%
    - Acyclovir 400 mg BID
    - Valtrex 500 mg QD
    - Famvir 250 mg QD
  - L-lysine 1 gram/day
  - Frequent debilitating recurrences, bilateral involvement, or HSV infection in an only eye

## Herpes Simplex

- ▣ Visual Prognosis:
  - 90% 20/40 or better after 12 years
  - 3% 20/100 or worse after 12 years

## HSV, HZO, & EKC: VIRAL EYE DISEASE ALPHABET SOUP

Nathan Lighthizer, O.D., F.A.A.O.  
 Assistant Dean, Clinical Care Services  
 Director of Continuing Education  
 Chief of Specialty Care Clinics  
 Chief of Electrodiagnostics Clinic  
 Oklahoma College of Optometry  
 lighthiz@nsuok.edu