**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
  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
  - Numerous other ocular signs

- **Other Eye Disease (Acute):**
  - Acute epithelial keratitis (pseudodendrites)
  - Conjunctivitis
  - Stromal (interstitial) interstitial keratitis
  - Endotheliitis (disciform keratitis)
  - Neurotrophic keratitis

- **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
    - Famiclovir 500mg 3x/day X 7-10 days
  - Topical ointment to skin lesions to help prevent scarring
    - Bacitracin, erythromycin

- **Prevention:**
  - Zostavax 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

**Shingrix Vaccine**

- Shingrix is a non-live vaccine given intramuscularly in two doses.
- 38,000 patients in a phase III clinical trial
  - >90% efficacy sustained over 4 years
Shingrix vs. Zostavax

**Shingrix:**
- Efficacy in preventing shingles:
  - 96.6% effective in 50-59 year olds
  - 97.4% effective in 60-69 year olds
  - > 70 year olds
    - 97.6% in year 1
    - 84.7% in years 2-4
- Efficacy in preventing PHN:
  - 91.2% in > 50 year olds
  - 88.8% in > 70 year olds
- More cost effective
- Lasts longer

**Zostavax:**
- Efficacy in preventing shingles:
  - 70% effective in 50-59 year olds
  - 64% effective in 60-69 year olds
  - > 70 year olds
    - 38%
- Efficacy in preventing PHN:
  - 65.7% in 60-69 year olds
  - 66.8% in > 70 year olds

Efficacy in preventing PHN:
- 91.2% in > 50 year olds
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Signs:
- Red eye (conj hyperemia)
- Watery discharge
- Follicles in the inferior fornix & conj
- (+) PA node
- Red/swollen eyelids
- Petechial sub-conj hemes
- SPK
- SEFs (sub-epithelial infiltrates)
- Pseudomembranes/membranes

Viral conjunctivitis

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
    - Neurontin (Gabapentin)

EKC

- Timecourse
  - Humidity
  - Virology
  - Immunosuppression
  - Timecourse
**Viral conjunctivitis**

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  - Red/swollen eyelids
  - Petechial sub-conj hemes
  - SPK
  - SEI's (sub-epithelial infiltrates)
  - Pseudomembranes/membranes often seen in EKC

**EKC conjunctivitis**

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

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**Off-Label Adenoviral Treatments**

- Povidone Iodine (0.4%) – Dexamethasone (0.1%)
  - 9 eyes of 6 patients with confirmed Adenovirus enrolled
  - 8/9 enrolled showed clinical resolution by day 4
  - 6/6 patients with significant reduced DNA copies by day 5
  - 5/6 cultures positives with no infectivity by day 5

**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 course punctate or stellate pattern
  - Central desquamation results in a dendrite***
  1. Central ulceration
  2. Terminal end bulbs
  - ***Corneal sensation is reduced***

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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

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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

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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

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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***
**Immune Stromal Keratitis:**
- **Symptoms:**
  - Gradual blurred vision
  - Halos
  - Discomfort/Pain
  - Redness

- **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***

**Endotheliitis:** AKA Disciform Keratitis
- **Not considered a primary form of stromal 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
Neurotrophic Keratopathy

- **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.
  - **5x’s:**
    - Irritation/burning/FB sensation
    - Redness
    - Tearing
    - Decreased vision

- **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**

- **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.

Herpes Simplex 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.**

**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.

**Herpes Simplex Epithelial Keratitis**

<p>| Table 1: Comparison of the experimental outcomes of normal and experimental conditions. |
|------------------------------------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
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</thead>
<tbody>
<tr>
<td>Control treatment</td>
<td>100 ± 2.0</td>
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<td>100 ± 2.0</td>
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<tr>
<td>100 units of serum eye drops</td>
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<td>Total number of patients in each group</td>
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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

Pediatric HSV Keratitis

- Pediatric herpes simplex keratitis has an 80% risk of recurrence, a 75% risk of stromal disease, and a 30% rate of misdiagnosis
- 80% of children with herpes simplex keratitis develop scarring, mostly in the central cornea
- Results in the development of astigmatism
- 25% of children have more than 2 D of astigmatism, most of which is irregular
- Consider pediatric HSV when a patient has unilateral recurrent disease in the anterior segment

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

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