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**

- 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
     - 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

**Disclosures**

- Aerie Pharmaceuticals
- Alcon
- Biotissue
- Diopsys
- MacuLogix
- Nidek
- Nova Oculus
- Optovue
- Quantel
- Reichert
- RevolutionEHR
- Shire
**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) 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
    - Famciclovir 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
- 70% effective in 60-69 year olds
- > 70 year olds
  - 97.6% in year 1
  - 90.9% 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

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
- Dx:
  - 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
  - Petchial sub-conj hemes
  - SEF's (sub-epithelial infiltrates)
  - Pseudomembranes/membranes
  - Often seen in EKC

EKC

- Timecourse

Shingles in immunocompetent adults aged > 50 years:
- With high efficacy among aged > 50 years, and modest waning of protection over 5 years following vaccination, REZ has the potential to prevent substantial herpes zoster disease burden. Vaccinating adults over age 50 will prevent disease incidence in middle, and the vaccine will likely continue to provide substantial protection beyond 5 years as expected.

REZ use in immunocompetent adults who previously received ZVL: In separate clinical trials, REZ estimates of efficacy against herpes zoster were higher than ZVL estimates in all age categories. The difference in efficacy between the two vaccines was most pronounced among recipients aged > 70 years. Studies have shown that ZVL effectiveness was substantially over time, leaving recipients with reduced protection against herpes zoster. REZ elicited similar safety, immunogenicity, and immunogenicity profiles regardless of prior ZVL status; therefore, ZVL recipients will likely benefit from vaccination with REZ.

Current herpes zoster infection. REZ is not a treatment for herpes zoster or postherpetic neuralgia and should not be administered during an acute episode of herpes zoster.

Post-herpetic neuralgia: There is no evidence to establish whether REZ is safe in pregnant or nursing women. There is currently no ACIP recommendation for REZ use in this population. Consider delaying vaccination with REZ in such circumstances.

Zostavax use in immunocompetent adults aged > 50 years:
- With high efficacy among aged > 50 years, and modest waning of protection over 5 years following vaccination, ZVL has the potential to prevent substantial herpes zoster disease burden. Vaccinating adults over age 50 will prevent disease incidence in middle, and the vaccine will likely continue to provide substantial protection beyond 5 years as expected.

Zostavax use in immunocompetent adults who previously received ZVL: In separate clinical trials, ZVL estimates of efficacy against herpes zoster were higher than ZVL estimates in all age categories. The difference in efficacy between the two vaccines was most pronounced among recipients aged > 70 years. Studies have shown that ZVL effectiveness was substantially over time, leaving recipients with reduced protection against herpes zoster. ZVL elicited similar safety, immunogenicity, and immunogenicity profiles regardless of prior ZVL status; therefore, ZVL recipients will likely benefit from vaccination with ZVL.

Post-herpetic neuralgia: There is no evidence to establish whether ZVL is safe in pregnant or nursing women. There is currently no ACIP recommendation for ZVL use in this population. Consider delaying vaccination with ZVL in such circumstances.

**Timing of REZ for persons previously vaccinated with ZVL:** Age and time since usage of ZVL may be considered to determine when to vaccinate with REZ. Ideally maintain the safety and immunogenicity of REZ vaccination administered 5 years after ZVL. Demonstrated time intervals have not been studied. However, there are no data or theoretical concerns to indicate that REZ would be less safe or less effective when administered at an interval of < 5 years. Clinical trials indicated lower efficacy of ZVL in adults aged > 70 years; therefore, a shorter interval may be considered based on the recipient’s age when ZVL was administered. Based on expert opinion, REZ should not be given < 2 months after receipt of ZVL.

**Persons with a history of herpes zoster:** Herpes zoster can recur. Adults with a history of herpes zoster should receive REZ. It is important to emphasize the incidence of herpes zoster, vaccination should be delayed until the acute stage of the illness is over and symptoms abate. Studies of safety and immunogenicity of REZ in this population are ongoing.

**Persons with chronic medical conditions:** Adults with chronic medical conditions (e.g., chronic renal failure, diabetes mellitus, advanced malignancy, and chronic pulmonary disease) should receive REZ.

**Signs:**
- Red eye (conj hyperemia)
- Watery discharge
- Follicles in the inferior fornix & conj
- (+) PA node
- Red/swollen eyelids
- Petchial sub-conj hemes
- SEF's (sub-epithelial infiltrates)
- Pseudomembranes/membranes

**EKC (Eye Keratitis Conjunctivitis):**

- **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 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

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
**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***

**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

**Debridement of the dendritic ulcer???
**Oral antivirals???
**IOP control
- Avoid prostaglandins???
- Steroids???

**Follow-up**
- Day 1, 4, 7

**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

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

- **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**

- **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
**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**

**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

**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**

- **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
  - Artifical 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

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: VIRA L 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