The Herpes Group
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I. Defining the Herpes Group: Epidemiology
II. Herpes Simplex: Natural History, Risks, Diagnosis, Morbidity and Management
III. Herpes Zoster: Natural History, Risks, Diagnosis, Morbidity and Management
IV. Antiviral Treatment and Pain Management
IV. The Vaccines: Indications, Prevention and Controversies
V. Pertinent Questions

Disclosures
- Allergan Pharmaceutical Advisory Panel
- AMO Global Medical Advisory Panel
- Acanthamoeba Outbreak Panel (ad hoc)
- Bausch & Lomb Scientific Advisory Panel
- Global Steering Committee
- Panel On Fusarium Keratitis (ad hoc)
- Ciba Vision Post-Market Surveillance Study Group
- Johns Hopkins Adjudication Committee (ad hoc)
- Center for Disease Control & Prevention: Contact Lens Advisory Panel
- Johnson & Johnson Global Professional Advisory Panel
- Shire, Ophthalmic Advisory Panel
- Speaker’s Bureau: Vistakon, Ciba Vision, CooperVision, Bausch & Lomb, AMO, Alcon, Genzyme, Shire

1. Question Related to the Herpes Group

- A patient presents with a two day onset of herpes zoster ophthalmicus and asks: “Can my grandchildren or spouse get this?” How might you best respond?

- A. “Your grandchildren have likely had the vaccine for chickenpox and cannot get the chickenpox virus from you.”
- B. “You should avoid contact with your grandchildren regardless since they might get the chickenpox virus and your spouse can get this if she has never had chickenpox.”
- C. “You cannot give this to anyone since you have the shingles and not chickenpox.”
- D. “You should avoid contact with anyone even if they have had the chickenpox virus.”
2. Question Related to the Herpes Group

Which of the following statements best describes the current advisory panel’s recommendation regarding the zoster vaccine for health care providers?

- A. It should not be administered to any health care provider for fear that they are possibly going to give the virus to their patient.
- B. Any health care provider over 60 is free to receive the vaccine with a 48 hr. break from patient contact.
- C. There is essentially no risk of a health care provider giving the virus to their patient.
- D. Patients over 50 who have had a recent bout of shingles should immediately receive the zoster vaccine.

3. Question Related to the Herpes Group

Bilateral herpes simplex keratitis is not a common clinical entity, but which of the following should be considered when it occurs?

- A. occult cancer
- B. atopy in the young
- C. aspirin overdose
- D. A and B are correct

4. Question Related to the Herpes Group

A 60 yo patient is taking Valtrex 500mg daily for HSV prophylaxis and is considering getting the zoster vaccine. What recommendations should you offer?

- A. No special instructions should be applied.
- B. The patient should discontinue the oral anti-viral for 48 hrs. prior and 2 weeks after the vaccine is administered.
- C. The patient needs to discontinue an oral anti-viral for at least one year prior to vaccine administration.
- D. The patient should discontinue the oral anti-viral 2 weeks prior and 48 hrs. after the vaccine administration.

5. Question Related to the Herpes Group

A recent ARVO abstract suggested treating acute adenoviral infections with which of the following agents?

- A. ganciclovir .15% (Zirgan)
- B. hypochlorous acid 0.01% (Neutrox/Avenova)
- C. doxycycline monohydrate 100mg
- D. valacyclovir (Valtrex) 500mg

6. Question Related to the Herpes Group

Which of the following antiviral medications is most prone to producing TTP/HUS with prolonged use especially in HIV and transplant recipients (bone marrow and renal)?

- A. Famciclovir
- B. Acyclovir
- C. Valacyclovir
- D. Valganciclovir

7. Question Related to the Herpes Group

Patients with a previous Zoster inflammatory keratitis or keratouveitis have the potential for which of the following responses when receiving the Zoster vaccine?

- A. It will likely stimulate the immune response and invigorate the inflammatory response.
- B. The inflammation present won’t be affected since the inflammation is due to residual cytokines in the stroma and not dependent on humoral or cell mediated immunity.
- C. The inflammation is more often active viral replication than we once thought and the immunization will have no negative effect (or could even help).
- D. All of the above are possible responses to vaccination and the pros and cons have to weighed heavily.
The Herpesviridae Family

- 8 distinct DNA viruses; all can establish latency in the sensory ganglia
- HSV and HZV are the most common; Epstein Barr is also found to cause corneal insult.
- HSV-1 is the most common ocular pathogen; HSV-2 is more responsible for genital infections with an increasing number from HSV-1.
- Neonates often infected with HSV-2.
- Health care costs for the herpes group are over $1 billion each year.

HSV-1

- Oro-labial or cutaneous (oral-facial-ocular)
- Acquired during childhood
- Latent in trigeminal ganglia
- Genital recurrence infrequent (if any genital involvement)
- Common triggers: Reactivation of virus from triggers such as fatigue, emotional stress, hormonal changes, fever and other stressors to immune system such as Excimer laser treatment and prostaglandin eye drops
- Common location: vermillion border of lip (“cold sore” or “fever blister”)

HSV-2

- Genital
- Acquired sexually
- Latent in sacral sensory ganglia
- Genital recurrence common
- Common triggers: Intercourse, hormonal changes, stressors to immune system
- Common locations: Shaft of penis, labia, buttocks
- Transmission is four time more likely from male to female than female to male

Herpes Simplex Prevalence

- 25% are seropositive by age 4, nearly 100% are affected by age 60.
- Most are asymptomatic on primary infection.
- Skin eruptions are not common after primary infection.
- Recurrent HSV is commonly found along the oral or nasal mucosa with a mean age of onset 37.4 years (Liesegang et al 1989).
- 36% after 5 years
- 63% after 20 years
- After a second episode, 70-80% had another recurrence within 10 yrs.

Herpes Simplex Features

- Initial ocular presentation occur on lid and conjunctiva 50% of the time. (anterior cornea 60% and stroma 6%).
- Unilateral follicular conjunctivitis is always suspicious for HSV infection. Steroids will trigger infectious keratitis.
- Conjunctival dendrites may be present without corneal findings. An iritis with high IOP is concern for HSV.
- In children, primary infection manifests with fever and cutaneous outbreak around the lids. Outbreak is prolonged and less responsive to therapy.
- Bilateral involvement or prolonged HSV suggests comorbid disease (i.e. atopy, immuno deficiency or immuno suppression). Two or more atopic conditions manages risk of HSV had by over 20 fold for HZO.

Cimetidine (H2 blocker and immune-modulator) may be an effective oral agent.


Trigeminal Nerve
Corneal Presentations

- **Four clinical presentations:** epithelial, stromal, endotheliitis, and neurotrophic keratopathy

- **Epithelial (Infectious):** corneal vesicles, dendritic ulcer, geographic ulcer, marginal ulcer (10% progress to stromal disease within one year)

- **Stromal (Immune):** infiltration, vascularization, haze and scarring/necrotizing

- **Endotheliitis:** an infectious and inflammatory reaction (HSV or CMV), found as a disciform, diffuse or linear pattern with stromal involvement. Use oral anti-virals and topical steroids. Trabeculitis with increased IOP is common.

- **Neurotrophic:** results from altered corneal innervation and decreased tear production
Case 14 - Painless Herpes Simplex (not a classic dendrite)

**Viral Detection**

- Cell Cultures
- ELVIS (enzyme-linked virus inducible system)**
- PCR (polymerase chain reaction/DNA detection) - Intelligent MDx

HSV can be recovered by swabbing an untreated dendrite with a soft tipped applicator inoculating it into viral transport media or a viral culturette.

** High degree of sensitivity and specificity within 24 hrs.
Pediatric Herpes Simplex

- Frequently misdiagnosed as simply blepharitis or conjunctivitis.
- Recurrence rates are higher than adults (50%).
- Generally show severe inflammation and stromal disease; adults most commonly have dendritic keratitis.
- Managed best with adjusted oral doses of acyclovir.


Eczema Herpeticum

- Manifests as a rash, fever with typical viral lab results; buccal mucosal swabs will likely show active virus.
- Bilateral eye involvement (simultaneous) includes disciform corneal findings and atopic dermatitis or other pre-existing skin disorders.
- Diagnosis: culture for HSV; secondary bacterial infections are common
- Treatment: compresses, antiviral therapy (topical and systemic); anti-pruritics; patients are in great need of desensitization therapy.
Measles

- Highly contagious viral infection, recent outbreak in Anaheim, CA
- Can be fatal
- Excellent, safe vaccine available
- Concept of herd immunity (community immunity) is crucial to minimize spread

Herpes Simplex Masquerades

- Various conditions present with branching lesions (dendritiform): Acanthamoeba, healing abrasions, stromal dystrophy, Fabry, tyrosinemia, HZV, and Darrier.
- Corneal drug toxicity
- **Key Reminder**: HSV is the only ulcerative lesion; the rest are NOT excavated!
Acanthamoeba Keratitis can be an outbreak disease: History in the USA

<table>
<thead>
<tr>
<th>Time period</th>
<th>Total cases</th>
<th>Cases average Per year</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974-1983</td>
<td>31</td>
<td>3</td>
<td>(new infection hard to diagnose)</td>
</tr>
<tr>
<td>1984-1985 Outbreak</td>
<td>110 estimate</td>
<td>115 (6 x normal rate)</td>
<td>95% soft contact lens wearers, nearly all used non-Sterile solutions to soak lenses due to FDA approved salt tablets</td>
</tr>
<tr>
<td>1984-2003 (June '03)</td>
<td>100 estimate</td>
<td>19</td>
<td>Excludes 137 cases in the Iowa flooding outbreak '93-'96; this is the normal disease rate</td>
</tr>
<tr>
<td>June 2004-June 2007</td>
<td>485 cases from CDC</td>
<td>121 (2008 continues at 85 cases/yr or 4.5x the normal rate)</td>
<td>Outbreak cause? EPA: decrease of water disinfection level and a constant small number of patients using water in their lens care regimen?</td>
</tr>
</tbody>
</table>

Clinical Features of Acanthamoeba Keratitis

- **EPITHELIAL**: patchy epithelial involvement (stellate, irregular or pleomorphic epitheliopathy), “bull’s eye” lesion, white spots, persistent epithelial defect, elevated corneal lines
- **STROMAL**: lack of vascularization, granulomatous or non-suppurative inflammation, radial nerve infiltrates (“lightning flash”), ring infiltrate
- **OTHERS**: pseudoguttata, hyphema, hypopyon, pseudomembrane, scleritis, episcleritis, adenopathy, decreased corneal sensation (initial)

**poor response to therapy may suggest co-infection**
Confocal Images of Trophs and Cysts

Post-Surgical TISSUE Analysis

Therapy for Acanthamoeba Keratitis

- **ANTIBIOTICS** / Aminoglycosides**
- **ANTI FUNGALS** (anti-trophozoite agents)
- **ANTIPARASITICS** / Aromatic Diamidines
- **BIOCIDES / CATIONIC ANTISEPTICS**

Note: No one case acts in the same manner

**Aminoglycosides have now shown increased neomycin resistant strains with an increased predisposition for trophozoite transformation; concentration of BAK in antibiotic can be therapeutic.
Clinical Outcome In Treating Acanthamoeba Keratitis

- Propamidine and neomycin: 9/19 (47%) Meisler
- Propamidine and PHMB: 8/10 (80%) McCulley
- Propamidine and chlorhexidine: 40/42 (96%) Wilhelmus
- **Role of corticosteroid treatment is controversial!**
- Intensive monotherapy with either PHMB or chlorhexidine may be equally as effective (Wills Series), but oral Voriconazole may be beneficial with deep corneal disease. (Tu et al.)

Parallels with Fusarium Keratitis 2006 Outbreak

- Concurrent outbreaks of keratitis among CLU
- Multi-purpose solution implicated
  - Fusarium: Bausch & Lomb ReNu with MoistureLoc
  - No contamination
  - Insufficient anti-microbial efficacy
- “Topping off” solution in case common risk factor
- Reduce anti-microbial efficacy
- Concern about safety of multi-purpose solutions

Epidemic Intelligence Conference CDC, April, 2012

- Multiple CL hygiene practices were associated with increased risk of AK. The observed persistence of AK might be due to enhanced disease awareness and clinical suspicion following the 2007 investigation.
- To prevent infection, CL wearers should observe recommended CL care practices.
- **RISK FACTORS:** topping off solutions: 4.54X, recently starting CL use: 3.22X, storing CL in water: 5.37X and handling CLs with wet hands: 2.17X

Acanthamoeba Keratitis Among RGP Lens Wearers

- 37 patients in 2 investigations (case control study)
- **Significant risk factors:** ortho-keratology (OR-undefined), sleeping while wearing lenses (OR-8.00), storing lenses in tap water (OR-16.0), and topping off care solution in case (OR-4.80)
- “Nearly one quarter of patients were ortho-keratology wearers. Using tap water and topping off care solutions were identified as modifiable risks. RGP wearers should avoid exposing their lenses to tap water.” Cope JR, Collier SA, Schein OD, et al: Acanthamoeba keratitis among RGP contact lens wearers in the United States, 2005 through 2011. Ophthalmol.; June, 2016.

Microsporidia Keratitis

- Presents as a superficial punctate, multifocal keratitis and a stromal keratitis is possible following trauma
- Nasopharyngeal or urinary colonization in HIV infected patients
- Improvement with voriconazole, albendazole and topical fumagillin bicyclohexyl ammonium salts
- Repeated debridement (perhaps even swabbing) seems to be therapeutic especially in immuno-competent patients.
- *may be best classified as a fungus*
Tyrosinemia (Type II)

- Richner-Hanhart syndrome: rare protein and amino acid metabolic disorder.
- Characterized by: corneal dendriform lesions, painful planar and plantar hyperkeratosis and retardation.
- Treatment: dietary restrictions of tyrosine and phenylalanine

Indolent Ulcerations of the Cornea

- Sterile ulcerations: vitamin A deficiency, vernal shield ulcers, HSV, other corneal irritants
- Must be differentiated from an infectious process (infiltrate present)
- Often difficult to manage without surgical intervention that includes flaps, tarsorrhaphy, autologous serum, or amniotic membrane transplant.

Crack Keratopathy

- Neurotrophic ulcer results from: hypesthesia and reduced tearing (inherent), chemical burn (alkal), direct toxic irritant to the cornea (smoke), and mechanical rubbing due to eye irritation.
- Ulceration is oval with smooth, rolled edge.
- Diagnosis by exclusion when suppuration is present and pain is not proportional.
- Persistent ulcers may continue even after cessation.
- Treatment: tarsorrhaphy, amniotic membrane transplant or Pro-Kera graft, support for chemical dependency.
Treatment and Management of HSV

- Topical and/or orals can be used for any infectious process.
- Steroids are the mainstay for stromal/immune disease.
- Avoid prolonged use of topical agents beyond 14-21 days.
- Limbal deficiency and conjunctival scarring are possible due to toxicity. At >10-14 days, a neurotrophic state is probably playing a role.
- Debridement is only indicated if there are new epithelial lesions with a history of stromal disease in the past.
- Oral prophylaxis is indicated with 2 or more episodes of infectious keratitis. Must monitor renal function.

Treating Principles

- Treat the epithelial disease first (virtually ignoring the immune/stromal response) and then treat stromal disease. Orals may be sufficient!
- When using steroids, use a prophylactic dose of orals to hopefully prevent epithelial recurrence.
- Taper steroids using a “full” dose of orals and/or topicals until the dendrite has cleared watching for medicamentosa effects. Steroids can be increased with a prophylactic oral dosing (Valtrex 500mg daily, ACV 400mg BID, Famvir 500mg daily).
- When stromal disease is controlled taper steroid gradually. You might never be able to D/C completely to control stromal disease. Prophylactic orals may be required indefinitely.

HEDS Studies

- Oral Acyclovir 400mg BID for one year significantly reduced the risk for recurrence of ocular HSV, stromal keratitis (only in those who had a history of stromal disease) and oro-facial HSV. Is there a role in HZV?
- No benefit of oral prophylaxis to prevent progression from surface (epithelial) involvement to stromal disease.
- Oral antivirals are considered for epithelial disease to reduce the viral load in the ciliary ganglion and associated nerves. Its value in acute disease is still being debated.

HSV Resistance

- If viral resistance is suspected, send a viral culture for PCR and sensitivities.
- “Super” strains (TK mutants) do encode for key enzyme and prolonged prophylactic use of orals may play a role. Consider Viva A under these circumstances.
- Non-compliance can certainly mimic resistance.
- GI absorption of polar medications, even with a pro-drug may limit serum concentrations of antiviral medications (especially with lactose intolerance). In this case, IV ACV may be helpful.
- Viral resistance in an immune-competent patient is rare, but if suspected HSV-DNA polymerase inhibitors can be injected intraocularly (i.e. Foscarnet) Any resistance raises the concern for immuno-suppression or compromised state.
Herpes Zoster: Shingles

- VZV is the etiologic agent of both varicella (chickenpox) and emergence from latency/reactivation (shingles)
- Approximately one million cases annually in the United States.
- Unlike HSV, HZV typically happens once in life (30% of adults). Half of adults who live to age 85 will get zoster. The rate rises sharply after 50.
- HZV established latency in the sensory root ganglia (maintained by a T-cell immune response that wanes with advancing age)
- Can erupt anywhere on the body; 15% involves the ophthalmic division (HZO) of the CN 5. Eye care professionals often see the most devastating cases. Thoracic dermatome is the most common.

HZV Clinical Manifestation Phases

1. Pre-eruptive Phase (Pre-herpetic neuralgia)
   - sensory phenomena along one or more skin dermatomes lasting 1-10 days (48hr. avg.); pain or less commonly itching or paresthesias with malaise, myalgia, photophobia, fever

2. Acute Eruptive Phase

3. Chronic Phase (PHN)

Herpes Zoster: Shingles

- Exposure to cases of chickenpox may serve as a “booster vaccine”.
- Recurrent disease: concern for reduced cell mediated immunity...HRV, thymoma, occult CA (especially lymphoid malignancies), etc.
- Most common diseases associated with HZV infection are pulmonary, diabetes mellitus and cardiovascular. IBd increases risk and certain medications are independent risks such as corticosteroids, thiopurines and anti-TNF.
- **Overall, increased risk for CA (lymphatic tumor) among HZV patients. Risk for multiple myeloma is increased in older women; risk for bone and soft tissue cancers in men following HZV infection.**

Zoster Sine Herpete

- Atypical episode of HZV: chronic radicular pain/sensitivity without rash and wanes from sub-acute to chronic.
- Reactivation may result in meningitis, cerebellitis, isolated cranial nerve palsy (ophthalmoplegia or Ramsay Hunt), vasculopathy, myelopathy and various inflammatory disorders of the eye.
- VZV DNA in cerebrospinal fluid or blood mononuclear cells or the presence of IgG antibody in CSF or IgM antibody in CSF or serum.
- Continuing challenge is establishing a diagnosis at a time when treatment will still provide a benefit.

Herpes Zoster Ophthalmicus

- Involves the ophthalmic division of the fifth cranial nerve (V1). Presents with or without eye involvement. V2 ocular involvement is much less common. Most prevalent between 50-59 with over 30% of all cases younger than 60.

- Without oral antivirals, 50-70% of HZO patients will experience ocular involvement. 30% will be chronic. 5% may be recurrent. Recent data shows recurrent/chronic disease to exceed 50%. No differences found in recurrence/chronicity based on age.

- Long list of ocular complications including: persistent keratitis, conjunctivitis, scleritis, uveitis, oculomotor palsy, corneal nerve palsy, and optic neuropathy.

- Longterm complications include: cataracts, glaucoma, corneal scarring and PHN.

- ASSOCIATED COMPLICATIONS: HZO increases the risk of stroke by 4.5X within one year of infection. Varicella zoster vasculopathy causes stroke secondary to chronic viral infection of large and small cerebral arteries. VZV has been associated with temporal arteritis (possible trigger?).

- Risk factors: uveitis, ocular hypertension, immunosuppression and lack of vaccination.

- Plausibility exists that recurrent and chronic disease can be caused by viral replication and infection, by inflammatory response, or both. May be an active period of sub-clinical viral transcription & translation held in check by CMI rather than latency.

- Recurrent and chronic disease recurrence is observed.

- Incidence and prevalence of HZO is increasing likely due to: older population with inherent immune senescence, pharmacologic immunosuppression, immunocompromise, and universal varicella vaccination of the young (fewer booster exposures to maintain CMI).

Recurrent Herpes Zoster

- Recurrent episodes (different locations) are somewhat atypical and practitioners must consider a sinister etiology. (1:200 up to 5 years/Kaiser Permanente)
- Patients should be worked up for occult malignancy or other reduced cell mediated immunity concerns (body scans, T4 and T8 subsets may be needed).
- HIV/CMV titers are suggested.
- Thymus gland imaging may reveal a thymoma.

Pseudodendrites in Herpes Zoster

- Part of the list of corneal complications of acute/chronic infectious and immune keratitis (4-13%).
- Can be found in the acute stages or months to years later (Herpes zoster pseudodendrites, dendritic plaques, or late Varicella zoster dendritiform keratitis).
- The lesions harbor viral DNA and warrant antiviral treatment to prevent further corneal damage.
- CASE SERIES (Pavan-Langstan et al.): topical 0.15% ganciclovir gel (and maybe a repeat of orals) is an effective treatment for persistent pseudodendrites.

Zoster Kerato-uveitis

- Complications are similar to HSV keratitis and include: punctate or pseudo-dendritic keratitis (mucous plaque), stromal infiltrates, endotheliitis and neurotrophic keratopathy.
- Uveitis is not uncommon in severe cases.
- Risk of chronicity & recurrence is relatively high when there is associated ocular hypertension and uveitis.
**Acute Retinal Necrosis**

- A rare presentation of herpetic or other viral disease: varicella-zoster is most common cause, but possible in HSV, EBV, CMV infections.
- Characterized by large areas of retinal whitening and necrosis that spreads centripetally with a high rate of accompanying detachment and vascular occlusion.
- Can be seen in patients with some level of immune dysfunction.
- PCR analysis of the vitreous is confirmatory, but diagnosis is generally made by clinical assessment.
- Treatment includes IV acyclovir 10-15mg/kg TID for 5-10 days followed by oral regimen for 6-12 weeks. Intra-vitreal injection of foscarnet or ganciclovir can be considered.

**Post Herpetic Neuralgia**

- A neuropathic pain syndrome that persists beyond 90 days or develops after shingles' rash has resolved (10-18%).
- Most frequent and debilitating complication of HZV regardless of the dermatomal distribution. PHN (post herpetic itch/pruritis) is a sub-category of PHN and poses a risk of self-injury.
- Main PHN risks: advancing age (>60), severity of acute zoster pain and rash, a painful prodrome, chronic illness, and ocular or upper body involvement.
- Treatment: rapid administration of oral anti-virals, cool compresses, topical capsaicin, analgesics, tricosaine patch, cimetidine, amitriptyline, gabapentin, pregabalin, nerve block, and acupuncture. *oral steroids and/or antivirals do not prevent the incidence of PHN*

**Antivirals**

- **Oral Agents**
  - Acyclovir
  - Valacyclovir*
  - Famciclovir*
  - Penciclovir*
- **Topical Agents**
  - Trifluridine (Viroptic/non-selective)
  - Ganciclovir (Zirgan/selective)
  - *Better bioavailability and longer intracellular half-life than Acyclovir

Pregnancy: orals B, topicals C

IV Acyclovir may be required when there is worsening neurologic/ophthalmic findings, immunocompromised state or disseminated disease.

*Does a longer course of treatment (beyond 7-14 days) for prophylaxis in HZO reduce the risk for recurrence/chronicity?*
Prevention Through Vaccination

- Prevention Through Vaccination
- Controversies...
- Should healthcare providers be vaccinated?
- When is vaccination appropriate after having the shingles?
- When should one stop antivirals before/after vaccination?
- Should patients with active kerato-uveitis or corneal dendritiform be vaccinated?
- Should we wait for the new vaccine (sub-unit)?

Varivax for Chickenpox

- Varicella vaccination
- Widespread use for the past 27 years and is universally accepted to reduce the risk for chickenpox.
- Environmental “boosters” have dropped rapidly which yields earlier incidence of shingles within the community.

Zostavax (Merck & Co.) Vaccine

- Vaccination does not confer lifelong immunity (most studies suggest 5-8 years, but exact duration is unknown). Protection likely wanes significantly after 5 years. Burden of pain decreases at 10 years.
- About a 38-70% reduction in HZV occurrence after vaccination (age dependent). Only a 40-70% reduction of the risk of experiencing post-herpetic neuralgia.
- Should probably be avoided in individuals who are experiencing any significant post-HZV corneal/intraocular inflammation.
- FDA recommendation over 50 yrs. of age and CDC is 60.(age for neuralgia is >60 and concern for duration without a booster).
- Patients with a history of HZO may have recurrent ophthalmic, dermatologic, or even disseminated disease after vaccination.

New Vaccine for Shingles (Glaxo, Smith, Kline- HZ/su)

- Phase 3 trial of sub-unit herpes zoster vaccine consisting of a single protein heat inactivated virus
- Unlike the live attenuated vaccine the HZ/su vaccine has an efficacy of 97.2% with age independent efficacy.
- HZ/su is adjuvanted DNA with AS01B that activates antigen-specific CD4+ T cells and antibody.
- Single protein that doesn’t replicate and may be suitable for immunosuppressed and compromised patients.
- Requires a 2 dose schedule with a phase 2 11% adverse event rate (severe headache, pain and fatigue).

Fuch’s Heterochromia Iridocyclitis

- Case Description: 73 yo male presents for a routine evaluation with a history of retinal detachment repair, early cataract extraction and a difference in eye color since childhood. He is currently bothered by floaters and notes that he periodically is treated for iritis. Cells are noted in the anterior vitreous. He has Fuch’s Heterochromia Iridocyclitis and his vitreous tap confirms rubella.

Fuch’s Heterochromia Iridocyclitis

- Fuch’s Uveitic syndrome is a multifactorial disease process. 5-10% of cases are bilateral.
- Features include heterochromia, iritis, stellate KPs, cataracts (PSCs most common), Russell’s blisters (iris crystals) and difficult to control glaucoma.
- Iris heterochromia may be a direct result of a sympathetic dysfunction.
- Associated sometimes with toxoplasmosis, herpes simplex, CMV and rubella.
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Rubella is a single strand RNA virus usually seen in the congenital form with the triad of heart defects, hearing loss and eye findings. Vaccine (1969) reduced incidence significantly.

Referral is necessary to rule out associated disease(s). Vitrectomy with PCR testing can be revealing.

Glaucoma is often difficult to treat and a resultant sight threatening challenge. Shunts and filters (poorer prognosis) are often required.

Do not treat iritis aggressively (result of blood aqueous barrier breakdown). Cells/flare that linger are not that detrimental.

Questions Related to the Herpes Group

A patient presents with a two day onset of herpes zoster ophthalmicus and asks: “Can my grandchildren or spouse get this?” How might you best respond?

A. “Your grandchildren have likely had the vaccine for chickenpox and cannot get the chickenpox virus from you.”

B. “You should avoid contact with your grandchildren regardless since they might get the chickenpox virus and your spouse can get this if she has never had chickenpox.”

C. “You can’t give this to anyone since you have the shingles and not chickenpox.”

D. “You should avoid contact with anyone even if they have had the chickenpox virus.”
A patient presents with herpes zoster ophthalmicus and asks: “Can my grandchildren or spouse get this?” How might you best respond?

B. “You should avoid contact with your grandchildren regardless since they might get the chickenpox virus since you are contagious and your spouse can get it if they have never had chickenpox.”

Which of the following statements best describes the current advisory panel’s recommendation regarding the zoster vaccine for health care providers?

C. There is essentially no risk of a health care provider giving the virus to their patient.

Bilateral herpes simplex keratitis is not a common clinical entity, but which of the following should be considered when it occurs?

D. Aspirin overdose

A 60 yo patient is taking Valtrex 500mg daily for HSV prophylaxis and is considering getting the zoster vaccine. What recommendations should you offer?

D. The patient should discontinue the oral anti-viral 2 weeks prior and 48 hrs. after the vaccine administration.
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Which of the following antiviral medications is most prone to producing TTP/HUS with prolonged use especially in HIV and transplant recipients (bone marrow and renal)?

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- C. Valacyclovir
- D. Valganciclovir

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- The inflammation present won’t be affected since the inflammation is due to residual cytokines in the stroma and not dependent on humoral or cell mediated immunity. The inflammation is more often active viral replication than we once thought and the immunization will have no negative effect (or could even help).
- All of the above are possible responses to vaccination and the pros and cons have to weighed heavily.
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- Patients with a previous Zoster inflammatory keratitis or keratouveitis have the potential for which of the following responses when receiving the Zoster vaccine?
  - D. All of the above are possible responses to vaccination and the pros and cons have to weighed heavily.

What's Missing Here?

Key Points to Remember.......

- Bilateral HSV and recurrent HZV may signal a more sinister condition due to reduced cell mediated immunity. Think occult CA!

- Poor treatment responses may be due to resistant conditions (including prolonged prophylaxis), poor compliance and/or a neurotrophic state.

- Vaccine concerns include inoculating corneal graft patients, those already taking oral antivirals, and patients with persistent ocular disease following an initial HZV infection. This doesn't impart life-time immunity. Varivax for kids reduces immunity exposure for adults.

- Antiviral suppression therapy (prolonged) may have a role in chronic HZV as in HSV.

Key Points to Remember.......

- A “spider bite” is often MRSA or shingles, and not a bug bite.
  - Review of systems is paramount. Be concerned for systemic viral dissemination in those with debilitating diseases (i.e., diabetes, rheumatoid conditions, etc.), especially when oral steroids are used.
  - Acute retinal necrosis may not be as obvious as expected in an immuno-compromised or suppressed individual.
  - Avoid the use of Valtrix in HIV+ patients and transplant recipients/bone marrow & renal (concern for TTP/HUS 2.9%). However, not likely a problem with standard dosages. CMV-2g QID.
  - Iritis with high IOP is generally HSV until proven otherwise!