


**On behalf of Vision Expo, we sincerely thank you for being with us this year.**

**Vision Expo Has Gone Green!**

We have eliminated all paper session evaluation forms. Please be sure to complete your electronic session evaluations online when you login to request your CE Letter for each course you attended! Your feedback is important to us as our Education Planning Committee considers content and speakers for future meetings to provide you with the best education possible.



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**HERPETIC EYE DISEASE: FROM ACYCLOVIR TO ZOSTER**

JESSICA STEEN OD, FAAO, DIPL ABO



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**FINANCIAL DISCLOSURES**

- Speaker-Carl Zeiss Meditec, Bausch and Lomb, Oyster Point Pharma, Thea Pharma, Alcon, Allergan
- Advisory Board-Bausch and Lomb, Carl Zeiss Meditec, Santen, Peripherex, Ocuphire, Ocuterra, Oyster Point Pharma, Allergan, Iveric Bio
- Shareholder-Clearside Biomedical (<0.01% ownership)
- All relevant relationships have been mitigated

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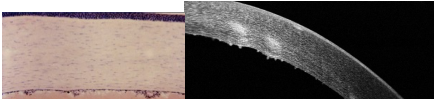
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**55 YEAR OLD BLACK MALE**

- 2 week history of blurred vision OS
- No photophobia, ocular discomfort
- 20/25 OS; Stromal edema, Descemet's folds, KPs
- 2+ cells in the anterior chamber, I+ flare



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**JUST ANOTHER ANTERIOR UVEITIS?**

- Intraocular pressure: 12mmHg OS, 42mmHg OS

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**Now What?**

- Why is the pressure 42mmHg?*
- Causes of hypertensive uveitis?*
- Lower the eye pressure in office?*
- How do we manage the inflammation?*
- How do we manage the most likely underlying cause?*

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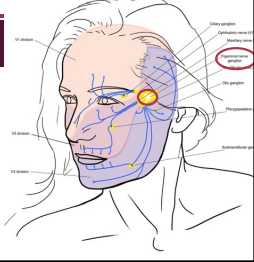
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**HERPES SIMPLEX**

- Primary HSV-1 infection following direct contact
  - At least 90% of the population carry latent HSV-1 by age 60
- Reactivation following a period of latency
  - Enters sensory neurons and moves into the sensory ganglia
    - Trigeminal ganglion
      - Ophthalmic division
        - Frontal nerve, nasociliary nerve, lacrimal nerve



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**PRODUCT SELECTION**

- 1) Clinical presentation guides diagnosis
- 2) Selective toxicity and resistance
- 3) ADRs
- 4) Route/mode of administration
  - Solutions/suspensions = conjunctiva, cornea
  - Ointments = may be better for external lid/lid margin
  - Oral = must be considered for internal infections
  - Oral antiviral agents for anterior segment disease

8

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**FOR EFFECTIVE TREATMENT ...**

- Accurate diagnosis
- Appropriate drug selection
  - Typically empirical
- Appropriate treatment strategy
  - Dosage, route of administration, patient characteristics, natural history of disease, ADRs, cost
- Informed follow-up

9

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**FAILURE OF THERAPY**

- May be due to:
  - Inaccurate diagnosis
  - Organism resistance
  - Inadequate dosing regimen
  - Toxicity/allergy
  - Non-adherence

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**Herpes Simplex Keratitis**

*Distinct mechanism of pathogenesis based on corneal layer*

The diagram illustrates the layers of the cornea. From top to bottom, they are: epithelium (a thin, multi-layered outermost layer), Bowman's membrane (a thin, acellular layer), stroma (the thick, middle layer), Descemet's membrane (a thin, acellular layer), endothelium (a single layer of cells), and the cornea (the entire structure). A small inset image shows a human eye with a corneal lesion.

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**HSV KERATITIS ORAL ANTIVIRAL DOSING**

	HSV	Active HSV: Therapeutic dose (epithelial keratitis)	HSV prophylaxis (stromal keratitis without epithelial ulceration)
famciclovir	500mg TID 7-10 days	250mg BID-TID x 7-10 days	250mg BID
acyclovir	800mg 5x/day 7-10 days	400mg 3-5x/day x 7 days-10 days	400mg BID
valacyclovir	1g TID 7-10 days	500mg BID-TID x 7-10 days	500mg QD

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12

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**Which agent is best?**

**Acyclovir**  
**Valacyclovir**  
**Famciclovir**

**Most common adverse effects:**

Headache  
 Nausea  
 GI upset

13

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**SPECIAL POPULATIONS**

- Pediatric patients
  - Acyclovir or valacyclovir
- Patients greater than the age of 65
  - Famciclovir may be preferred
- Pregnant patients
  - All agents are "FDA Pregnancy Category B"
    - May prefer acyclovir or valacyclovir
  - **Caution and relative contraindication**
    - Kidney dysfunction

**Remind patients to drink plenty of water while undergoing therapy!**



14

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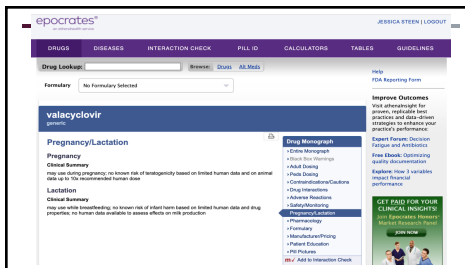
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The screenshot shows the Epocrates website interface. At the top, there are navigation tabs: DRUGS, DISEASES, INTERACTION CHECK, PILL ID, CALCULATORS, TABLES, and GUIDELINES. Below these is a search bar with 'Drug Lookup' and a dropdown menu showing 'No Formulary Selected'. The main content area is for 'valacyclovir'. It includes sections for 'Pregnancy/Lactation', 'Pregnancy', 'Clinical Summary', and 'Lactation'. On the right side, there are additional sections: 'Drug Monograph', 'Improve Outcomes', and 'GET FASD FOR YOUR CLINICAL INQUIRY'. The 'Improve Outcomes' section lists various clinical outcomes like 'Improve patient adherence' and 'Reduce patient costs'. The 'GET FASD' section is a promotional banner for a clinical inquiry tool.

15

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**HYPERTENSIVE UVEITIS**

- Herpes simplex virus should always be considered as an underlying cause
- Valacyclovir 500mg BID\*\*
- Durezol QID (pink cap) OS
- Homatropine in office
  - Atropine 1% QD OS
- Dorzolamide-timolol BID OS
- Follow up?

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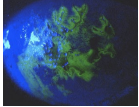
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**HSV EPITHELIAL KERATITIS**

- Direct infection of epithelial cells
  - Active herpes virus
  - Requires **therapeutic** dosage of agent
- Acyclovir: 400mg 3-5 times per day for 7-10 days
- Valacyclovir: 500mg 2-3 times per day for 7-10 days
- Famciclovir: 250mg 2-3 times per day for 7-10 days



- Topical ocular antiviral medications may be considered in place of an oral agent\*
- Corneal debridement

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**EMERGING RESISTANCE**

- Consider resistance of HSV-1 to acyclovir in immunocompromised individuals
  - Especially associated with prophylaxis and long-term treatment
- Most acyclovir-resistant HSV isolates are cross-resistant to penciclovir

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**TOPICAL OPTIONS**

- Zigan (ganciclovir 0.15% ophth. gel), 5g
  - Inhibits viral DNA-polymerase
  - 5x per day in HSV epithelial keratitis until dendrite heals, then TID for approximately 5 more days
  - Preserved with **BAK**
  - Preferred in pediatrics due to topical dosing
- Viroptic (trifluoridine 1%), 7.5mL
  - Toxic:** thimerosal & mechanism of action
    - Phosphorylation of thymidine kinase in viral and epithelial host cells
    - Prevents DNA synthesis
  - 9x/day until epithelium heals, then QID for one week
- Acyclovir ointment (acyclovir 3%)
  - Applied to herpetic skin pustules



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**Risk of Recurrence of HSV Keratitis**

- 9.6% at one year
- 22.9% at two years
- 40% at 5 years
- 67% at 10 years
- Liesegang TJ, Arch Ophthalmol 1989
- UV exposure, laser treatment, trauma, surgery increase risk of recurrence
- Immunosuppressive medications
  - Including steroids

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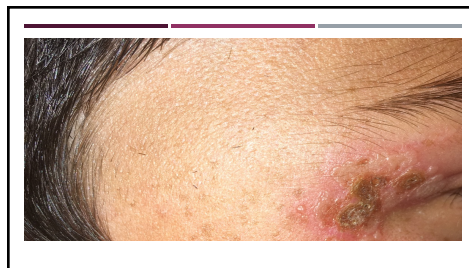
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### Herpes Simplex Blepharitis

*Any concerns based on the patient's age?*

*Anything other than oral treatment?*

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### HERPES ZOSTER OPHTHALMICUS

- Occurs due to reactivation of the varicella zoster virus
- Prodromal sensation preceding vesicle development
  - Burning or shooting sensation

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23

### HERPES ZOSTER PREVENTION

- Prevention of primary varicella zoster: chickenpox vaccine or MMRV
- **Prevention of herpes zoster**
  - Inactivated vaccine (Shingrix)
    - 2 dose series
      - 97% efficacy in patients aged 50-69; 91% effective in preventing PHN
      - 90% efficacy in patients older than 70 years; 89% effective in preventing PHN
    - Shorter, less severe disease course
  - Greater efficacy than the live attenuated vaccine (51% efficacy)
    - Those who have had the LA-vaccine should also receive the inactivated vaccine
      - Vaccination is still recommended after herpes zoster infection (at least 1 year)

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**HERPES ZOSTER OPHTHALMICUS**

Herpes Zoster Ophthalmicus	
Acyclovir	800mg 5x/day for 7-10 days
Valacyclovir	1000mg TID for 7-10 days
Famciclovir	500mg TID 7-10 days

- Aim to treat within 72 hours of vesicle formation
- Hyperesthesia prior to vesicle formation
- Reduction in post-herpetic neuralgia
  - More common in older individuals, those with more severe symptoms, and females

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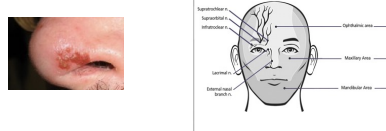
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**HUTCHINSON'S SIGN**

- If there is a lesion at the side of the nose and the eye looks uninvolved—go back and look again



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**LONG-TERM OUTCOMES**

- Prevention of recurrence
- Management of low grade, chronic inflammation
- ZEDS
  - Zoster Eye Disease Study
  - 12 month study: Valacyclovir 1000mg daily<sup>\*\*\*</sup> vs. masked placebo
    - Impact on the rate of new or worsening epithelial keratitis, stromal keratitis, endothelial keratitis or iritis vs. placebo
    - Does oral suppressive treatment reduce the severity and duration of post-herpetic neuralgia?
    - 652 patients; quadruple-masked; estimated completion date 7-31-2024

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**Beyond Keratouveitis**

Cranial nerve palsy  
 "Tolosa Hunt Syndrome"  
 Optic neuritis

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**Keratouveitis**

**Trabeculitis**

**Neurotrophic Keratitis**

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**CORTICOSTEROIDS**

- Difluprednate 0.05% (Durezol)
- Increased bioavailability & longer duration of action
  - Therefore possibility of greater IOP spike
- In general-dosed 1/2 as frequently as prednisolone acetate 1%
- Emulsion-shaking is **not** necessary
- Duratec vehicle
- Not preserved with BAK (sorbic acid)

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### DUREZOL

- What happens if you're treating an adult patient with acute anterior uveitis and after 6 days; IOP is 34mmHg!!
  - Stop the steroid!
  - Taper the steroid!
  - Manage the pressure!
    - Prostaglandin analog vs. something else

32

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### CORTICOSTEROIDS

- Prednisolone acetate 1%
  - Suspension; preserved with BAK
- Dosage based on severity of inflammation
  - Never** less than QID to begin
- Under-treatment is a significant concern
  - What's the difference between branded and generic prednisolone acetate?

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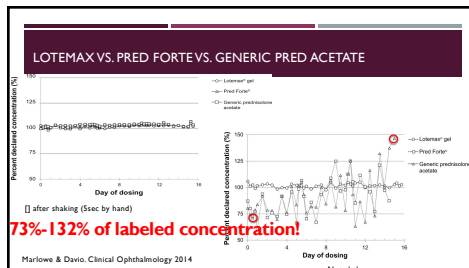
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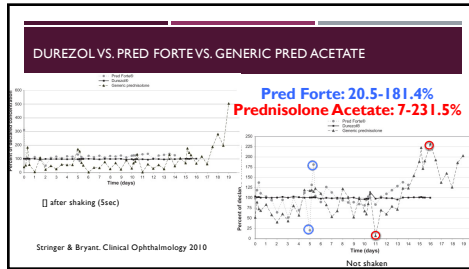
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- IMPACT OF LABELED CONCENTRATION VARIABILITY**
- Besides the obvious...
  - At first: drug levels not reaching clinical efficacy
  - Poor response to treatment—clinically appears as treatment failure
    - Change medication? Refer to uveitis specialist? Order serological evaluation?
  - Later: higher dose of steroid
    - Increased risk of adverse effect

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- BOTTOM LINE**
- Effective treatment begins with an accurate diagnosis
    - ...Which involves taking a very careful history
  - Carefully assess the risks and benefits of medication use prior to prescribing and monitor patients for effectiveness and side effects while undergoing treatment
  - Consider risk of recurrence and long-term complications in individuals with herpetic disease

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**Thank you!**

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**480.289.0613**

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