ORAL PRESCRIBING FOR THE PRIMARY CARE OPTOMETRIST

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Financial Disclosure

- Allergan
- Bausch & Lomb
- Carl Zeiss Meditec
- Ivantis
- Kala
- Santen

Objectives

- General Prescribing Precautions
- Prescribing Resources
- Commonly prescribed drug categories:
  - Antiviral agents
  - Antibacterial agents
  - Glaucoma medications
  - Anti-inflammatory/corticosteroids
  - ~~Pain Management~~

General Prescribing Precautions

- Case History:
  - Allergies
  - Renal Impairment
  - Hepatic disease
  - Current medications
- Special Populations
  - Pregnancy/lactation
  - Pediatric population
  - Geriatric population

Pregnancy/Lactation

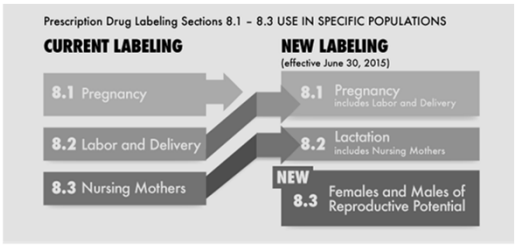
- Mother is intended target of therapy, but fetus is inadvertent recipient of drug
- Highest risk of fetal abnormality is when drug is given within 1st 6 weeks post-conception
- Want to minimize drug use during pregnancy but care for mother
- Must weigh risk:benefit
- Utilize nasolacrimal occlusion to minimize systemic absorption (topical)
- Consider consulting with patient's obstetrician

FDA Pregnancy Categories

- Category A: Adequate well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy
- Category B: *Animal* reproductive studies have failed to demonstrate a risk to the fetus, and there are no adequate human studies
- Category C: *Animal* reproductive studies have shown an adverse effect on the fetus and there are no adequate human studies; potential benefits may warrant use of the drug in pregnant women despite potential risks

FDA Pregnancy Categories

- Category D: There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies; potential benefits may warrant use of the drug in pregnant women despite potential risks
- Category X: Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk; risks involved in the use of the drug in pregnant women clearly outweigh potential benefits.



OTHER RESOURCES:
- **Drugs in Pregnancy and Lactation** (Briggs, et al)
- Mothertobaby.org

Geriatric Patient Considerations

- Systemic Disease + multi-drug therapy may lead elderly patients to experience more adverse effects
- 75-90% of elderly eye care patients use one or more drug
  - Be cautious of drug-drug interactions/contraindications
  - Be cautious of redundant prescription (many doctors)
  - Be cautious of combined topical/systemic use of same medication class

Geriatric Patient Prescribing

- *Topical* therapy dosing is not usually adjusted
- RENAL FUNCTION is most important factor in determining appropriate systemic medication dosing (always adjusting DOWN from the standard adult dose) – use Creatinine Clearance or CrCl
- Normal Creatinine Clearance:
  - Men 100-125 ml/min Women 90-120 ml/min
  - Normal serum Cr is 0.5-1.2 mg/dl
- Calculation (Cockcroft-Gault Equation):

$$\frac{(140\text{-age}) \times \text{Weight (kg)}}{72 \times \text{serum Cr (mg/dl)}} \quad (\times\ 0.85 \text{ for women})$$

Pediatric Patients

- Calculations for pediatric dosing for TOPICAL medications are not typically adjusted
- Can adjust SYSTEMIC dosing based on age, weight, or body surface area (BSA)
  - Dosing calculation is always done to calculate a LOWER dose than standard adult dose

Pediatric Dosing: Young's Rule

- Based on age

$$\frac{\text{Age (years)}}{\text{Age} + 12} \times \text{Adult Dose} = \text{Pediatric Dose}$$

Example: 6 year old gets acetaminophen every 4 hours. Adult dosage is 650mg every 4 hours

Calculation: $\frac{6}{6+12} \times 650\text{ mg} = 216\text{ mg every 4 hours}$

Pediatric Dosing: Webster's Rule (Modified Young's)

- Based on age and the fact that children are heavier (fatter) now

$$\frac{\text{Age + 1 (years)}}{\text{Age + 7}} \text{ X Adult Dose = Pediatric Dose}$$

Example: $\frac{6+1}{6+7}$ X 650 mg = 350 mg

Pediatric Dosing: Clark's Rule ****

- Based on weight (more accurate)

$$\frac{\text{Weight in lbs}}{150} \text{ X Adult Dose = Pediatric Dose}$$

Example: 6 year old weighs 50 lb, 60 lb, 70 lb

$\frac{50/60/70}{150}$ X 650 mg = 216/260/303 mg

Pediatric Dosing

- Body surface area is a complicated but precise formula
- Can use FDA labeling ***
- Need to be able to calculate body weight lbs to kg (2.2 lbs per kg)
- Oral solutions and suspensions over tablets/pills

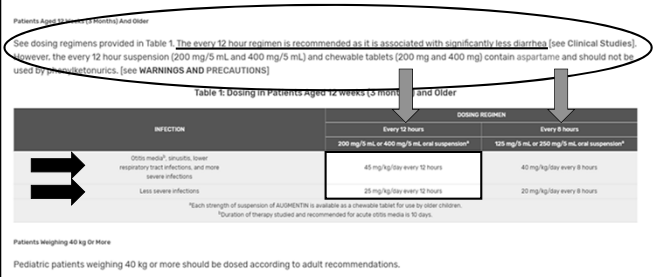
Simple Weight/Dose Calculations

- PDR/package insert lists dose by weight (rxlist.com)
- Weight given is almost always in Kg
- Dose provided is FULL 24 HOUR dose
- Must know (look up) the frequency of dosing/day
- Must know (look up) concentration of liquid dose forms
- Must know (look up) strength of all solid dosage forms

Ex: Pediatric Augmentin

- A 6 year old patient presents with a moderate-severe preseptal cellulitis (infection of soft tissue of eyelid). You want to prescribe the oral antibiotic Augmentin (amoxicillin/clavulanic acid).
  - Patient is otherwise healthy and up to date on immunizations
  - Patient is not taking any medication
  - Patient has no medication allergies
  - Patient weighs 45 pounds

EX: Pediatric Augmentin



Patients Aged 12 Weeks (3 Months) And Older

See dosing regimens provided in Table 1. The every 12 hour regimen is recommended as it is associated with significantly less diarrhea [see Clinical Studies]. However, the every 12 hour suspension (200 mg/5 mL and 400 mg/5 mL) and chewable tablets (200 mg and 400 mg) contain aspartame and should not be used by phenylketonurics. [see WARNINGS AND PRECAUTIONS]

Table 1: Dosing in Patients Aged 12 Weeks (3 Months) and Older

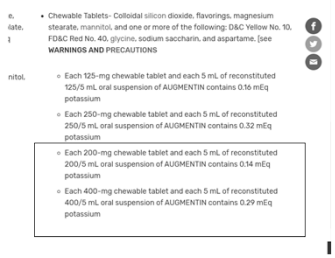
INFECTION	DOSING REGIMEN	
	Every 12 hours	Every 8 hours
	200 mg/5 mL or 400 mg/5 mL oral suspension[a]	125 mg/5 mL or 250 mg/5 mL oral suspension[a]
Otitis media[b], sinusitis, lower respiratory tract infections, and more severe infections	45 mg/kg/day every 12 hours	40 mg/kg/day every 8 hours
Less severe infections	25 mg/kg/day every 12 hours	20 mg/kg/day every 8 hours

[a]Each strength of suspension of AUGMENTIN is available as a chewable tablet for use by older children.
[b]Duration of therapy studied and recommended for acute otitis media is 10 days.

Patients Weighing 40 kg Or More

Pediatric patients weighing 40 kg or more should be dosed according to adult recommendations.

EX: Pediatric Augmentin



- Chewable Tablets- Colloidal silicon dioxide, flavorings, magnesium stearate, mannitol, and one or more of the following: D&C Yellow No. 10, FD&C Red No. 40, glycine, sodium saccharin, and aspartame. [see WARNINGS AND PRECAUTIONS]
  - Each 125-mg chewable tablet and each 5 mL of reconstituted 125/5 mL oral suspension of AUGMENTIN contains 0.16 mEq potassium
  - Each 250-mg chewable tablet and each 5 mL of reconstituted 250/5 mL oral suspension of AUGMENTIN contains 0.32 mEq potassium
  - Each 200-mg chewable tablet and each 5 mL of reconstituted 200/5 mL oral suspension of AUGMENTIN contains 0.14 mEq potassium
  - Each 400-mg chewable tablet and each 5 mL of reconstituted 400/5 mL oral suspension of AUGMENTIN contains 0.29 mEq potassium

Pediatric Dosing Calculation

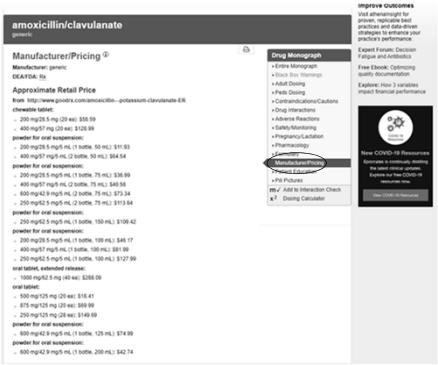
- Convert pounds to kg 45 lb/2.2 = 20.45 kg
- Daily Dose = 45mg/kg/day 45mg X 20.45 kg = 920.25 mg/DAY
- Given twice daily 920.25/2 = 460 mg/DOSE

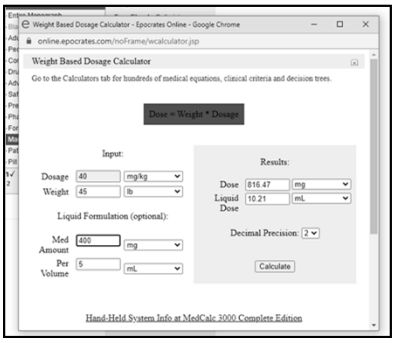
Chewable tablets 200mg and 400 mg
Oral Suspension 200mg/5ml and 400mg/5ml

- 400mg/5ml = 460/X ml = 2300/400
- X = 5.75 ml/dose (max dose; easiest to say 5ml)

Prescribing Resources:

- www.rxlist.com
- Epocrates
- Local physician/pharmacist





Antiviral Therapy – Review of Herpetic Eye Disease

HERPES SIMPLEX

- **Herpes Simplex**
  - Leading cause of corneal blindness and infection-related vision loss in USA
  - 50,000 new and recurring cases of herpes simplex keratitis each year
  - Can affect any layer of the eye
  - Primary infection: subclinical, flu-like symptoms, may have vesicles around eyes, lips, nose; virus travels to trigeminal ganglion, where it becomes latent
  - Recurrence: the cause of most of the damage from HSK
    - Recurrence rate after 1st episode: 27% at year 1; 63% at year 20.
    - Triggers: sun, fever/illness, injury, surgery, ?psychological stress
    - **CLASSIFICATION OF RECURRENCE IS CRITICAL FOR APPROPRIATE MANAGEMENT**

Classification of recurrent HSK

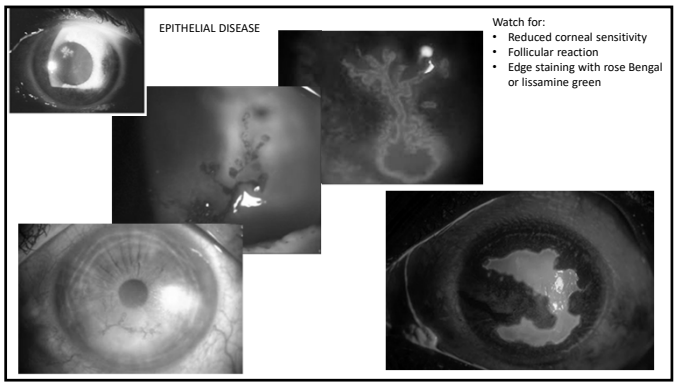
- Epithelial disease = ACTIVE VIRUS REPLICATION/INFECTION
  - Dendritic keratitis
  - Geographic keratitis
- Stromal disease = IMMUNE RESPONSE
  - MANY different labels or names
  - Can have intact or ulcerated epithelium
- Endothelial = IMMUNE RESPONSE

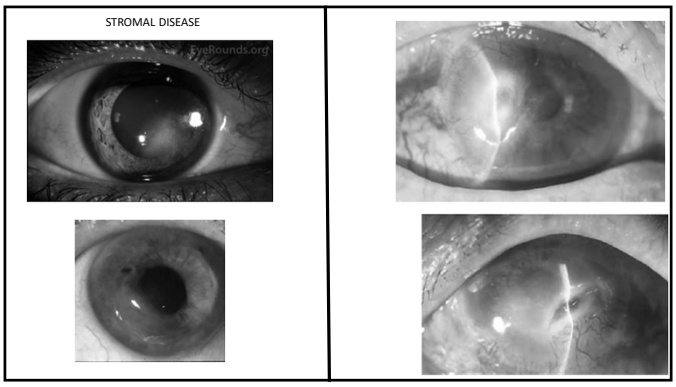
- VERY DIFFERENT MANAGEMENT OF THESE

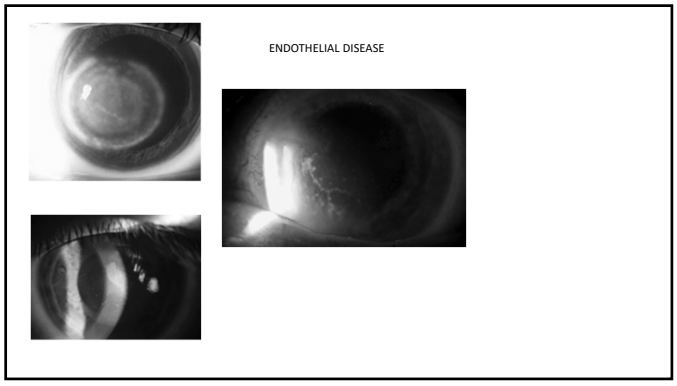
Table 1: **HSV KERATITIS CLASSIFICATION**

HSV CATEGORY	COMMON NOMENCLATURE	BASIC TREATMENT APPROACH
Epithelial keratitis	• Dendritic keratitis • Geographic keratitis	Antiviral (topical or oral) or debridement
Stromal keratitis without ulceration	• Interstitial keratitis • Immune stromal keratitis	Topical steroid + oral antiviral prophylaxis
Stromal keratitis with ulceration	• Necrotizing keratitis	Oral antiviral in therapeutic doses + topical steroid
Endothelial keratitis	• Disciform keratitis	Oral antiviral in therapeutic doses + topical steroid

Weiner G. "Demystifying the Ocular Herpes Simplex Virus", EyeNet January 2013

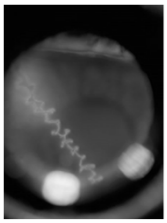






Treatment of HSK – EPITHELIAL DISEASE

- THERAPEUTIC ANTIVIRAL (Topical -OR- Oral)
  - TOPICAL
    - Trifluridine (Viroptic) q2h while awake (not to exceed 9x/day) until re-epithelialized, then 4x/day for another 5-7 days
    - Gangiclovir (Zirgan) 5x/day until re-epithelialized, then 3x/day for additional 7 days
      - Better dosing and less toxic than trifluridine
      - More expensive than trifluridine
  - ORAL
    - Acyclovir 400mg 5x/day for 7-21 days
    - Valacyclovir 500mg 3x/day for 7-21 days
    - Famciclovir 250mg 3x/day for 7-21 days
    - ****DOUBLE DOSE FOR LARGE GEOGRAPHIC ULCER
  - Should resolve in approximately 1 week – 10 days
- NO STEROIDS



APPENDIX V: Selecting an Oral or Topical Antiviral Agent

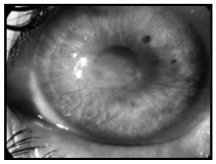
In select cases, the choice between an oral or topical antiviral agent may be guided by the following:

Preferred Treatment: Oral Antiviral
Patient physically unable to use gel or drops (i.e., patients with intention tremor or arthritis).
Contact lens wearers.
Pediatric patients' refractory to topical antiviral.
Patients that require lengthy treatment antiviral agents (greater than 21 days).
Patients with preexisting ocular surface disease who may be more susceptible to ocular surface toxicity.
Prophylactic treatment after ocular surgery.

Preferred Treatment: Topical Antiviral
Patients with renal impairment (all oral antiviral agents are nephrotoxic).
Elderly patients (≥ 65 years old) with renal impairment or when renal function is unknown at the time of drug administration.
Pregnant patients (all oral antivirals are Category B).
Nursing mothers — acyclovir was demonstrated in breast milk of nursing mothers taking valacyclovir as well as acyclovir. (No studies on famciclovir.)

Treatment of HSK – STROMAL DISEASE

- PRIMARY TREATMENT IS TOPICAL STEROID
  - May wait for antiviral to be on board for a 1-2 days first
    - Rarely needed more than 4x/day
    - SLOW, SLOW, SLOW TAPER (minimum dose to keep eye quiet)
    - Maintain as long as necessary (may not ever get off steroid)
- MUST USE PROPHYLACTIC ANTIVIRAL*
  - Purpose: prevent recurrence/reactivation at trigeminal ganglion
  - Can use topical but not for long – ORAL is best
  - Prophylactic dosing:
    - Acyclovir 400mg 2x/day
    - Valacyclovir 500mg once daily
    - Famciclovir 250mg once daily – or – 125mg 2x/day
  - *If with epithelial ulceration, use therapeutic dose



Treatment of HSK – EPITHELIAL DISEASE

- Epithelial disease = ACTIVE VIRUS in AC

- THERAPEUTIC ORAL ANTIVIRAL
  - Acyclovir 400mg 5x/d
  - Valacyclovir 500mg 3x/d
  - Famciclovir 250mg 3x/d
- TOPICAL STEROID (after 1-2 days)
  - Require taper, but often can taper more quickly than stromal disease

Table 2: ANTIVIRAL AGENTS FOR HSV EPITHELIAL KERATITIS

ORAL ANTIVIRALS		
Agent	**Treatment Dose**	**Prophylactic Dose**
Acyclovir	Adults: 400 mg three to five times per day Children: 12 to 15 mg/kg/day in divided doses	400 mg twice daily
Valacyclovir	500 mg three times per day	500 mg once daily
Famciclovir	250 mg three times per day	250 mg once daily or 125 mg twice daily
TOPICAL ANTIVIRALS		
Agent	**Treatment Dose** (for Short-Term Use Only)	
Trifluridine 1 percent	One drop every two hours, reduced to five times per day after three to seven days	
Ganciclovir gel 0.15 percent	Five times per day (better dosing and surface toxicity profile vs. trifluridine, but more expensive)	

Weiner G. "Demystifying the Ocular Herpes Simplex Virus", EyeNet January 2013

Which Oral Antiviral Agent to Choose?

- Lactose intolerant
  - Valacyclovir preferred
- Pediatric Patient
  - Acyclovir (neonates and older) or valacyclovir (age 2)
- Pregnant Patients
  - All 3 are pregnancy category "B"
  - More evidence of safety with acyclovir and valacyclovir
- Elderly (greater than 65 years old)
  - Famciclovir (less risk of CNS reactions and renal failure than acyclovir and valacyclovir)
- CAUTION: Renal impairment

Herpetic Eye Disease Study (HEDS)

- Oral acyclovir trials
  - ADDING short term oral acyclovir to topical therapy in *epithelial* HSK does not reduce the incidence of stromal or uveitic disease
  - ADDING short term oral acyclovir to topical steroid therapy in *stromal* HSK doesn't provide benefit
  - **USE OF LONG TERM ORAL ACYCLOVIR PROPHYLAXIS DOES REDUCE RECURRENCE IN IMMUNOCOMPETENT PATIENTS**
    - **Therapy must be maintained to maintain the benefit**
    - **Should everyone with epithelial HSK be on prophylactic therapy?**
      - **Multiple recurrences/bilateral disease**
      - **Corneal transplant**
      - **Prior to intraocular surgery**

Great references for HSK review:

- "Demystifying the Ocular Herpes Simplex Virus" :

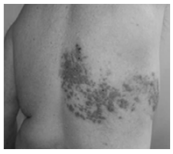
Demystifying the Ocular Herpes Simplex Virus - American Academy of Ophthalmology (aao.org)

- "Herpes Simplex Virus Keratitis: A Treatment Guideline 2014"

Herpes Simplex Virus Keratitis: A Treatment Guideline - 2014 - American Academy of Ophthalmology (aao.org)

Herpes Zoster Ophthalmicus

- Primary infection: Varicella Zoster
  - Much less common today due to immunization
- Reactivation of VZV = Herpes Zoster
  - Painful unilateral vesicular dermatomal rash
  - Pain precedes rash in 74% of cases
    - Moderate to severe stabbing
  - "Zoster sine herpete" = radicular dermatomal pain without rash (in eye: SEVERE uveitis)



What's New with Herpes Zoster?

- Increased incidence
- Younger age of onset
- Risk factors
- Zoster vaccine
- Zoster Eye Disease Study (ZEDS) – RCT to evaluate prolonged suppressive antiviral therapy to decrease complications (ongoing)

Herpes Zoster Misconceptions

- Herpes Zoster is rare
- Herpes Zoster is a disease of the elderly
- Herpes Zoster is a disease of the immunocompromised
- The increased incidence of Herpes Zoster is due to the vaccination against varicella/chickenpox
- Herpes Zoster is contagious

Herpes Zoster Misconceptions - Let's clear things up!

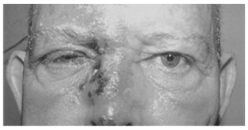
- 1.2 million new cases/year in US
  - 99% of Americans over the age of 40 had varicella
  - 1 in 3 Americans will have Zoster
  - 1 in 2 Americans age 85+ will have Zoster
- 90% are NOT immunocompromised
- Rate of HZ increases with age, but actual number of people with HZ is highest in 50s (median age of onset 56 years old)
- The increase in incidence began before the availability of vaccine
- HZ is not very contagious

Risk Factors

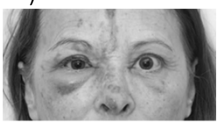
- Increasing age
- Female sex
- Immune compromise
- Family history
- Depression
- H/O previous episode
- Heart failure
- TBI
- Diabetes
- Asthma
- Acute kidney disease
- Statin use

Herpes Zoster Complications

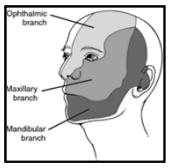
- Post-herpetic neuralgia (PHN)
  - Pain persisting beyond 3 months of onset
  - Occurs in 30% of HZO patients, mostly in those 65+ years old
  - Major risk factor for depression in elderly (#1 cause of suicide due to pain in patients over 70 years old)
  - Risk for PHN:
    - Severe prodromal pain
    - Severe rash
    - HZO



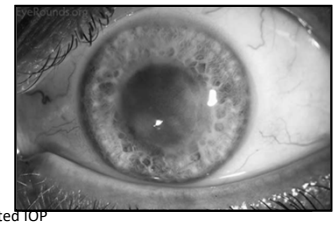
Herpes Zoster Ophthalmicus (HZO)



- 20% of Herpes Zoster cases involve trigeminal n.
- Hutchinson's sign: Tip of nose involved
  - LACK of Hutchinson's sign is not a guarantee that there's no ocular involvement
  - PRESENCE of Hutchinson's sign – look VERY carefully at the eye
- HZO can affect every structure in the eye
  - Skin
  - Conjunctiva
  - Sclera/episclera
  - Cranial nerve involvement
  - Cornea
  - Uvea
  - Retina
  - Optic nerve
- Acute symptoms occur within 1 month of rash



HZO – Corneal Classification



- Similar/same as HSK
- Epithelial (acute)
  - Pseudodentrites
- Stromal (subacute)
  - Nummular
  - With or without ulceration
- Endothelial (subacute)
  - "disciform"
  - Often associated with elevated IOP
- Neurotrophic (chronic)

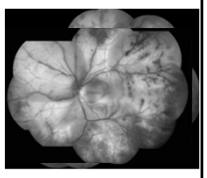
Recurrent and Chronic HZO

- Recurrence: after treating acute disease, HZO can recur
  - 8% at 1 year
  - 17% at 3 years
  - 25% at 5 years
  - 31% at 6 years
- Chronic disease (active disease persisting after 90 days) = 23%
  - Uveitis and elevated IOP are significant risk factors for developing chronic disease
  - Often involves posterior segment

HZO – Posterior Segment Involvement

- Tends to affect immunocompromised patients
- Acute Retinal Necrosis (ARN)
  - Focal retinal necrosis in peripheral retina with rapid progression
  - Prominent vitritis and anterior chamber reaction
  - Very poor visual outcome
- Progressive Outer Retinal Necrosis (PORN)

Need aggressive VERY HIGH DOSE antivirals, retinal referral



HZO - Management

- Goal of management:
  - Shorten disease course
  - Provide analgesia
  - Prevent complications
- DISEASE IS NOT LIMITED TO SURFACE – SYSTEMIC THERAPY IS REQUIRED!!!
  - Reduce viral shedding from skin lesions
  - Reduce incidence and severity of complications

HZO Management - ACUTE

- Oral antiviral therapy 7-10 days
  - Valacyclovir 1g 3x/d
  - Famciclovir 500mg 3x/d
  - Acyclovir 800mg 5x/d
- Oral steroid can reduce duration of pain; consider in patients without immune suppression or diabetes with quick taper
- Topical therapy:
  - Topical antiviral therapy is NOT indicated
  - Topical lubricants
  - Cycloplegia
  - Topical corticosteroid therapy – cornea, uvea
    - VERY, VERY SLOW TAPER
  - Topical astringent (Domboro's solution) to skin, cool compresses

Zoster Eye Disease Study (ZEDS)

- RCT to determine whether prolonged suppressive valcyclovir treatment reduces complications of HZO including chronic eye disease and PHN
- Rationale:
  - Recent recognition of *infectious* nature of HZO complications and chronic dz in immunocompetent patients
  - Known benefit of suppressive antiviral therapy in HSV
- Treatment plan: 1g/day valacyclovir for 1 year
  - Follow every 3 months x 18 months
  - New or worsening keratitis or iritis
  - Secondary objectives:
    - Does treatment persist beyond 12 months
    - Does treatment reduce incidence, severity, and duration of PHN (12m, 18m)

HZO – A special problem

- Cataract Surgery
  - Study involving 38 patients with recurrent HZO pre-cataract surgery
  - HZO recurred in 40% of patients after cataract surgery
  - Most common in patients with shorter period of quiescence preceding cataract surgery and in patient with increased number of recurrences
  - ***consider oral antivirals at therapeutic dose

Zoster – a few last things

- Zoster (all types) is a MAJOR risk factor for stroke
  - Greater after HZO
- Zoster (all types) is a trigger for GCA
  - New evidence that more sections of TA are needed in biopsy
  - PCR for VZV 74%
  - Antiviral therapy may benefit standard steroid therapy
- ZOSTER VACCINE

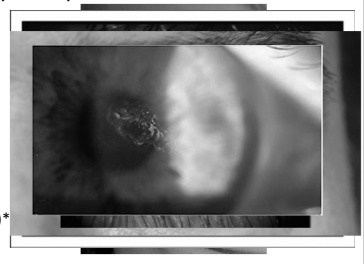
Zoster vaccination

- 51% decrease in incidence of HZO
- 66% decrease in PHN

- CDC recommends at age 50 (never too late!)
  - LIVE virus (Zostavax): one dose
  - RZV (Shingrix): two dose**
  - American Academy of Ophthalmology recommends RZV for patients 50 and older without contraindications
  - Episodes of zoster keratitis/uveitis in HZO patients 2-5 weeks after vaccination
    - Recommend observe 4-6 weeks after vaccine

Antibacterial Therapy in Eye Care

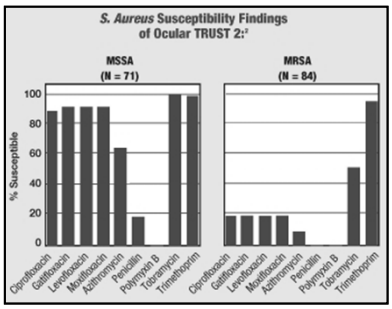
- Ophthalmic indications for systemic antibacterial medication:
  - Lid infection
    - Acute (hordeolum, preseptal cellulitis)
    - Chronic (Meibomian gland dysfunction, ocular rosacea)*
  - Adult Inclusion Conjunctivitis
  - Recurrent corneal erosion (RCE)*



Antibacterial Therapy in Eye Care

- What organisms are most common?
  - Staph, strep
- What drugs work best?
  - Ocular Trust Data
    - 50 centers across USA, all ocular isolates sent to single reference lab for culture/sensitivity testing
      - 2006: 16.8% of staphylococcal isolates were MRSA
      - 2008: 48.1% of staphylococcal isolates were MRSA

Ocular Trust Data



2020 ARMOR Study

2020 ARMOR SURVEILLANCE DATA: MIC_{90} COMPARISONS FOR STUDY ISOLATES

	S. aureus		MRSA		CoNS		MRCoNS	
	2015 (n=1169)	2020 (n=2189)	2015 (n=493)	2020 (n=765)	2015 (n=992)	2020 (n=1765)	2015 (n=493)	2020 (n=871)
Besifloxacin*	0.25	1	2	2	0.25	2	4	4
Vancomycin	1	1	1	1	2	2	2	2
Trimethoprim*	2	4	2	2	32	>128	>128	>256
Moxifloxacin*	1	4	1	16	1	16	32	32
Gatifloxacin	2	4	16	16	2	16	32	32
Ofloxacin	8	>8	>8	16	8	>8	>8	32
Ciprofloxacin	8	128	256	256	8	64	64	64
Tobramycin*	1	128	>265	256	4	16	16	32
Azithromycin	>512	>512	>512	>512	>512	>512	>512	>512

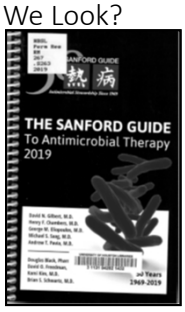
* Denotes the four antibiotics we use most routinely, given their proven efficacy and relatively low resistance profile.

As a reminder, the lower the MIC_{90}, the more potent the anticipated efficacy.

CoNS = coagulase-negative *Staph.* species, of which the majority are *Staph. epidermidis*.

Sources: Asbell PA, et al. JAMA Ophthalmol. 2015;133(12):1445-1454.
Asbell PA, et al. JAMA Ophthalmol. Published Online April 9, 2020.

Where Else Should We Look?

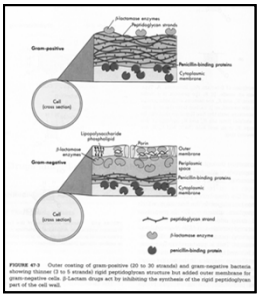


Commonly prescribed antibacterial agents

- Penicillins
  - Dicloxacillin
  - Amoxicillin/clavulanic acid (Augmentin)
- Cephalosporins
  - Cephalexin (Keflex)
- Macrolides ("erythromycins")
  - Azithromycin
- Tetracyclines
  - Doxycycline
  - Minocycline
- Sulfonamides
  - Sulfamethoxazole/trimethoprim

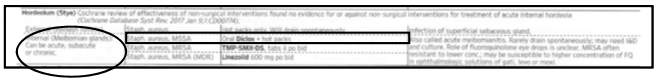
Penicillins

- Inhibit bacterial cell wall synthesis
- Generally gram (+) spectrum
  - Increasing resistance, often due to beta-lactamase production
- Pregnancy Category "B"
- Common adverse effects: GI upset, nausea, vomiting
- Hypersensitivity: rash, anaphylaxis



Penicillins

- Dicloxacillin
  - In same class as methicillin ("methicillin resistant" includes dicloxacillin)
  - Good against strep, MSSA
  - Ineffective against MRSA
  - Adult dose: 250mg qid



Penicillins

- Augmentin (amoxicillin + clavulanic acid)
  - Amoxicillin alone is highly sensitive to beta-lactamase enzyme
  - Clavulanic acid is a beta-lactamase inhibitor
- Augmentin effective against many *Staph* species, *H.flu*
  - Adult dose: 500-875mg (each has 125mg clavulanic acid) BID
  - Pedi dose: 25-45mg/kg/day (divided q12h)
- Generic is very inexpensive, readily available

Cephalosporins

- Mechanism of action *very* similar to that of penicillins
- Similar spectrum of activity (earlier generations)
- Require intact beta-lactam ring; susceptible to beta-lactamase
- Significant emerging resistance

- Cross-reactivity with PCN (1-10%); inquire about PCN reaction
- Vitamin K absorption alteration – contraindicated in hemophilia and bleeding disorders

Cephalosporins

- Cephalexin (Keflex) – 1st generation
  - Adult dose: 250mg qid –OR – 500mg BID x 7-14 days
  - Pedi dose: 25-50mg/kg/d, divided doses

- **Disulfiram-like reaction**

Macrolides

- Erythromycin, clarithromycin, azithromycin: inhibit protein synthesis
- Can be used in place of tetracyclines for children and pregnant/lactating women
- Pregnancy category B

- Azithromycin:
- Primary use in eyecare is adult inclusion conjunctivitis
  - Dose: single 1-gram dose (four 250-mg tabs or two 500mg tabs taken together)

Inclusion conjunctivitis (adult) Usually unilateral & concomitant genital infection	Chlamydia trachomatis	**Azithro** 1 gm once	**Doxy** 100 mg po bid x 7 days	Oculogenital disease. Diagnosis NAAT. Urine NAAT for both GC & Chlamydia. Treat sexual partner. May need to repeat dose of azithro.

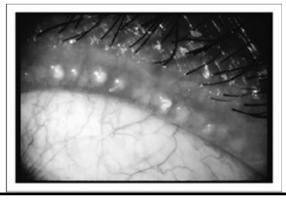
  - May be used in lieu of doxycycline for MGD/chronic lid disease patients

Clinical science

Oral azithromycin versus doxycycline in meibomian gland dysfunction: a randomised double-masked open-label clinical trial

Mohsen Bahmani Kashkouli,[1] Ali Jalili Fazel,[1] Victoria Kiavash,[1] Marzieh Nojomi,[2] Leila Ghiasian[3]

Kashkouli MB, *et al. Br J Ophthalmol* 2015;**99**:199–204. doi:10.1136/bjophthalmol-2014-305410



ABSTRACT

Background/aims To assess the efficacy and safety of oral azithromycin compared with oral doxycycline in patients with meibomian gland dysfunction (MGD) who had failed to respond to prior conservative management.

Methods 110 patients (>12 years old) with MGD were randomly assigned to receive either oral 5-day azithromycin (500 mg on day 1 and then 250 mg/day) or 1-month doxycycline (200 mg/day). They also continued eyelid warming/cleaning and artificial tears. A score comprising five symptoms and seven signs (primary outcome) was recorded prior to treatment and at 1 week, and 1 and 2 months after treatment. Total score was the sum of both scores at each follow-up. Side effects were recorded and overall clinical improvement was categorised as excellent, good, fair or poor based on the percentage of change in the total score.

Results Symptoms and signs improved significantly in both groups (p=0.001). While improvement of symptoms was not different between the groups, bulbar conjunctival redness (p=0.004) and ocular surface staining (p=0.01) were significantly better in the azithromycin group. The azithromycin group showed a significantly better overall clinical response (p=0.01). Mild gastrointestinal side effects were not significantly different between the groups except for the second visit, when the doxycycline group had significantly more side effects (p=0.002).

Conclusions Although both oral azithromycin and doxycycline improved the symptoms of MGD, 5-day oral azithromycin is recommended for its better effect on improving the signs, better overall clinical response and shorter duration of treatment.

Azithromycin – Important Cardiac Warning

- Prolonged cardiac repolarization and QT interval, imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen with treatment of macrolides, including azithromycin…Practitioners should consider the risk of QT prolongation, which can be fatal when weighing the risks and benefits of azithromycin for at-risk groups including:
  - Patients with known prolongation of the QT interval, a history of torsades de pointes, congenital long QT syndrome, bradyarrhythmias, or uncompensated heart failure
  - Patients on drugs known to prolong the QT interval
  - Patients with ongoing proarrhythmic conditions such as uncorrected hypokalemia or hypomagnesemia, clinically significant bracycardia, and in patients receiving antiarrhythmia drugs
  - Elderly patients

Doxycycline

- One of the tetracycline drugs (inhibit protein synthesis)
- Good activity against atypical organisms (chlamydia)
- In addition to antibacterial properties, has anti-seborrheic and anti-inflammatory, anti-collagenase properties
- CONTRAINDICATION:
  - Do not use in children under 8 years of age
  - Pregnancy Category "D"

Doxycycline

- Dosing: WIDE range of dosing depending on condition
  - Adult inclusion conjunctivitis: 100mg BID x 7 days
  - Antibacterial (lid disease): 100mg BID
  - Chronic lid disease: 100mg BID x 2-4 weeks, then 50mg BID x 2-4 weeks, then as low as 20mg BID x 3-6 months (variations)
  - Rosacea: 50-100mg/day x 2-6 weeks
  - Recurrent corneal erosion/corneal ulcers: 50-100mg BID x 4-6 weeks
- <u>IMPORTANT PRESCRIBING ISSUES</u>:
  - Take prior to or with meal
  - Take with full glass of water
  - Remain upright for at least 30 minutes after taking
- Minocycline = alternative; 50mg BID (lid disease); may cause dizziness & vertigo

Sulfonamides

- Inhibit production of folic acid by bacteria
- Sulfonamide antibiotic (sulfamethoxazole) = commonly reported antibiotic allergy
  - Rash
  - Stevens-Johnson syndrome (most common verified cause of SJS)

Sulfamethoxazole/Trimethoprim

- Bactrim DS, Septra, generic
  - Effective against MRSA

Hordeolum (Stye) Cochrane review of effectiveness of non-surgical interventions found no evidence for or against non-surgical interventions for treatment of acute internal hordeola (*Cochrane Database Syst Rev.* 2017 Jan 9;1:CD007476).

External (eyelash follicle):	Staph. aureus	Hot packs only. Will drain spontaneously	Infection of superficial sebaceous gland.
Internal (Meibomian glands):	Staph. aureus, MSSA	Hot Packs + foil patch	Also called acute meibomianitis. Rarely drain spontaneously; may need I&D
Can be acute, subacute or chronic.	Staph. aureus, MSSA	**TMP-SMX-DS**, tabs 1 po bid	Or culture. Role of fluoroquinolone eye drops is unclear. MRSA often
	Staph. aureus, MRSA (MDR)	**Linezolid** 600 mg po bid	Resistant to lower conc.; may be susceptible to higher concentration of FQ

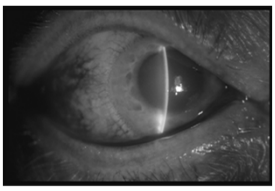
- Dose: 1 DS tab BID x 1 week
- Drug of choice in cases of suspicion of MRSA (ex: healthcare worker)

Glaucoma – Carbonic Anhydrase Inhibitors

- Effectively reduce intraocular pressure by decreasing aqueous production
- Poor tolerability when given for chronic care
  - Paresthesia
  - "Symptom complex"
  - Anorexia
  - Metallic taste, taste perversion
- Contraindications:
  - Severe hepatic disease, renal insuffiency
  - Caution in reported hypersensitivity to sulfonamide antibiotics (likely little crossover)

Carbonic Anhydrase Inhibitors

- Acetazolamide (Diamox)
  - 250mg tabs or 500mg sustained-release capsules (Sequels)
  - Up to 1000 mg per day for chronic use
  - In urgent situation: 500mg (two 250-mg tabs)
- Methazolamide (Neptazane)
  - 25-50mg TID-QID (better tolerated than acetazolamide for chronic use)



Corticosteroids

- Corticosteroids have widespread actions that affect pathways involving inflammation, angiogenesis, oxidative stress, and apoptosis
- Disrupt the inflammatory pathway by immobilizing arachidonic acid, downregulating multiple cytokine pathways, stabilizing mast cells, inhibiting leukocyte interaction
- Decrease capillary permeability, decrease fibroblast and collagen formation (slow/delay healing)

Corticosteroid Therapy

- Consider risk:benefit ratio
  - Topical, injected, and sustained release steroids:
    - Cataract
    - Elevated IOP/glaucoma
    - Secondary infection
    - Skin thinning
  - Systemic steroids:
    - Hyperglycemia/diabetes
    - Osteoporosis
    - Systemic hypertension
    - Gastritis
    - Depression
    - Insomnia
    - Weight gain

Contraindications to Systemic Steroid Use

- Peptic ulcer disease, psychosis, pregnancy
- Osteoporosis
- Renal failure
- Congestive heart failure
- Hypertension
- Diabetes
- Epilepsy
- TB (and other infections)
- Herpes simplex keratitis

"PORCH DETH"

Systemic Steroids – the Drugs

- Prednisone most commonly prescribed (most flexibility in dosing)
  - 40mg/day for 3-7 days, then stop (no taper)
- Methylprednisolone comes in convenient 6-day "dose pak", good for compliance when short-term therapy is desired
  - 4mg methylpred equiv to 5mg prednisone
- **TAKE WITH MEAL FOR BEST TOLERABILITY**!

- With prolonged therapy, must be concerned about adrenal suppression; taper steroid slowly to allow the adrenal system to rebound
  - Reduce dose by approximately 10% every 3-4 days

Systemic Steroids – When/Why?

- Typically used for ***severe*** inflammation of posterior segment, orbit, and optic nerve
  - Scleritis
  - Uveitis
  - Inflammatory orbital pseudotumor
  - GCA****
    - 80-100mg while waiting for biopsy
    - Involve patient's PCP – they will be on long-term steroid
  - Optic Neuritis (**always** IV FIRST, followed by oral)
  - Thyroid Eye Disease

Systemic Steroids – When/Why?

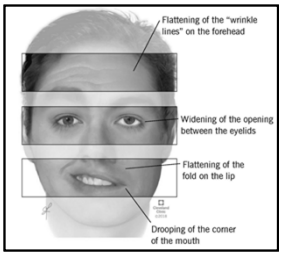
- Can be used for severe dermatologic manifestations:
  - Periocular insect bite
  - Acute allergic blepharodermatoconjunctivitis
  - Poison ivy dosing: 60mg/day x 5 days with a taper

Update: Bell's Palsy

- Bell's Palsy: benign, self-limiting inflammatory condition caused by HSV infection
  - CN VII passes through bony canal in temporal bone; inflammation produces a compresses neuropathy
- Differential:
  - Infectious (lyme, HZV)
  - Auto-immune (Guillain-Barre, sarcoidosis)
  - Tumor
  - Stroke

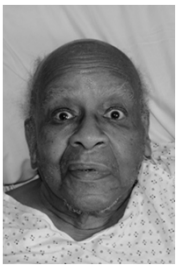
Bells Palsy

- Diagnosis:
- **HISTORY IS KEY**
  - Acute onset that progresses to complete facial hemiparesis within 72 hours
  - Often preceded by postauricular pain, dysgeusia, and hyperacusis
  - ***More slowly progressive paralysis: suspect malignancy
- Exam –
  - Gross exam:
    - Tumor in parotid or submandibular gland, neck
    - External auditory canal (vesicular eruption – Ramsay Hunt syndrome (HZV)
  - ALL branches of facial nerve
    - Temporal/frontal
    - Zygomatic
    - Buccal
    - Marginal mandibular
    - Cervical
  - Neuro-imaging if not complete, or if timing does not fit Bell's



Bells Palsy vs Stroke

- Timing
- Structures involved
- Other symptoms



Bell's Palsy - Treatment

- Oral prednisone
  - 50-60 mg/day for 10 days, followed by taper for 5 days (taper by 10mg/day)
- Oral antivirals
  - Evidence has NOT been clearly established
  - Some recommend Valacyclovir 500mg BID x 7d along with oral steroids
- PROTECT ocular surface: lubricants, patch, tape, etc. while waiting for recovery
- Non-resolving: may need plastics consultation (ex: lid weight)

Thank You For Your Attention!

Questions?
Email me: dmarrelli@uh.edu