

Oral Anti-Infectives for Optometric Practice

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Indications for Oral Antibiotic Use in Primary Eyecare

- Infectious Lid Disease
 - Hordeola, Preseptal Cellulitis, Dacryocystitis
- “Non-Infectious” Lid Disease
 - Meibomian Gland Dysfunction (MGD)
- Ocular manifestations of Systemic disease

Principles of Antibiotic Therapy

- Drug penetration/absorption
- Selective Toxicity
- Spectrum of Activity
- Mechanism of Action
- Microbial Resistance
- Duration of Action/Dosing

Oral Antibiotic Drug Classes

- Penicillins
 - Cephalosporins
 - Tetracyclines
 - Macrolides
 - Fluoroquinolones
 - Sulfonamides
 - Combination meds
- Infectious Lid disease
- MGD
- Second Choice Meds
- Rarely Used in Eyecare
- Second Choice Meds, or suspected MRSA infection

Penicillins & Cephalosporins

- **Drugs of choice for infectious lid disease**
- All bactericidal
- Mechanism of Action: Cell wall inhibitors
- B-lactam ring is the key biochemical component to its effectivity
- **B-lactamase** produced by *Staph* species is mechanism of bacterial resistance.

Penicillin Development

1st Generation Penicillins
 • Mostly Gram +, *Staph* resistance

Penicillin Development

1st Generation Penicillins
 • Mostly Gram +, *Staph* resistance

2nd Generation Penicillins
 • Mostly Gram +, effective against *Staph*

3rd Generation Penicillins
 • Expanded spectrum to Gram (-), *Staph* resistance

4th Generation Penicillins
 • Expanded spectrum to against *Pseudomonas*

Penicillins & Cephalosporins

- | | |
|--|--|
| ➤ 2 nd generation ▪ Limited to gram + ▪ QID dosing | ➤ 1 st generation ▪ Limited to gram + ▪ BID dosing |
| ➤ 3 rd generation ▪ Expanded gram (-) ▪ <i>Staph</i> resistance | ➤ 2 nd generation ▪ Expanded gram (-) |
| ➤ 4 th generation ▪ Antipseudomonal ▪ Mostly IV & IM preps | ➤ 3 rd generation ▪ Antipseudomonal |
| | ➤ 4 th & 5 th generation ▪ Mostly IV & IM preps |

Penicillins & Cephalosporins

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Penicillins & Cephalosporins

- | | |
|--|--|
| | ➤ 1 st generation ▪ cephalexin (Keflex®) |
| ➤ 3 rd generation ▪ amoxicillin w/clavulanate (Augmentin®) | ➤ 2 nd generation ▪ cefprozil |
| | ➤ 3 rd generation ▪ cefdinir |

cephalexin

- Generically available (original trade name of Keflex®)
- Dosage: 500mg PO BID x 10 days
- Well tolerated
- Drug of choice for:
 - Internal or External Hordeolum
- Limited use for Preseptal Cellulitis
 - Due to limited gram (-)/ *H.Flu* coverage

Hordeolum

- **INTERNAL:** Acute Infection of the Meibomian gland
- **EXTERNAL:** Acute Infection of gland of Zeis or Moll
- Likely offending organism of both:
Staph aureus

Preseptal Cellulitis

- Acute infection of the diffuse lid tissue anterior to the orbital septum
- **S&S:** Erythema, edema (may induce ptosis) from canthus to canthus, **warm to touch**, tender/painful

Preseptal Cellulitis

- **Etiology:**
 - Trauma, laceration of the skin
 - Insect bite
 - Spread of localized lid infection (Non-contained hordeolum)
 - Extension of ethmoid sinus infections
- Likely offending organism: *Staph aureus*, *Staph epidermidis*, *Strep*, *H. Flu*

Dacryocystitis

- Infection of the lacrimal sac
- **S&S:** Pain, swelling, redness on lower nasal aspect of lid, tearing
- Likely offending organism: *Staph*, *Strep*, *H. Flu*, & *Pseudomonas*

Augmentin®

- Generically available as combination of amoxicillin & clavulanate
- Dosage: 875mg PO BID x 10 days
- **LARGE tablets:** Alternative 500mg PO TID
- Drug of choice for:
 - Preseptal Cellulitis
 - Dacryocystitis
 - Internal or External Hordeolum
 - All pediatric lid infections

Pediatric Dosing of Augmentin®

- PDR Peds dosing (AGE >3mos): 25mg/kg/day in 2 divided doses
(2.2 lbs=1 kilogram)
- EXAMPLE: 50lb=22.7kg x 25mg=567.5mg/day in 2 divided doses
Rx: 300mg PO q 12hrs
- **CLARK'S RULE:** General Rule *to approximate* Pediatric Dosing based on weight:
Ped dose=Adult dose x weight (lbs.)/150
- EXAMPLE: 875mg q12hrs x 50lbs/150lbs= 291.6mg
Rx: 300mg PO q 12hrs

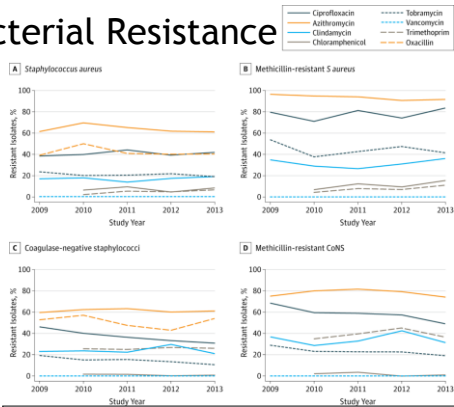
cefprozil

- Generically available (original trade name of Cefzil® has been discontinued)
- Dosage: 250-500mg PO BID x 10 days
- Alternative to Augmentin as drug of choice for:
 - Preseptal Cellulitis
 - Dacryocystitis
 - Internal or External Hordeolum
 - All pediatric lid infections

Penicillins & Cephalosporins

- **SIDE EFFECTS:**
 - Hypersensitivity: Type I anaphylaxis, can be fatal
 - Stevens Johnson Syndrome
 - Nausea, diarrhea
 - For broader spectrum agents can lead to superinfection of pseudomembranous colitis from *Clostridium difficile*
 - Can alter effectiveness of oral contraception
- **CONTRAINDICATIONS:**
 - Hypersensitivity to any in class**
 - Cross reactivity between drugs between PCN & CEPH classes is mostly limited to 1st generation CEPHs
 - Hemophilia (Ceph) due to Vit K deficiency

Bacterial Resistance



Asbell PA, Sanfilippo CM, et al. Antibiotic Resistance Among Ocular Pathogens in the United States Five-Year Results From the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) Surveillance Study. *JAMA Ophthalmol.* 2015;133(12):1445-1454.

Alternative Therapy 1

When treating an infectious lid disease in the presence of a Penicillin and Cephalosporin allergy, consider:

- **ADULTS: levofloxacin (Levaquin®)**
500mg PO QD x 10days

Oral Fluoroquinolones

- Systemic Side Effects of oral fluoroquinolones:
 - Nausea
 - HA, dizziness, sleep disturbance
 - binds positively charged ions (like Ca⁺ and Mg⁺) to damage cartilage so oral forms are contraindicated in children
 - can cause tendon rupture in elderly

Oral Fluoroquinolones

- Contraindications
 - Age < 18
 - Pregnant and Nursing Mothers
 - Myasthenia Gravis
 - Concurrent use of antacids, iron, zinc
 - Concurrent use of Coumadin
 - Concurrent use of anti-arrhythmia drugs

Alternative Therapy 1

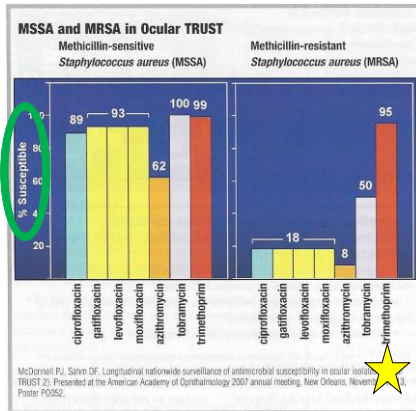
When treating an infectious lid disease in the presence of a Penicillin and Cephalosporin allergy, consider:

- **< AGE 18: azithromycin (Zithromax®) 500mg PO QD x 3days or 10mg/kg PO QD x 3 days**

Alternative Therapy 2

When treating an infectious lid disease with the suspicion of MRSA infection:

- **trimethoprim & sulfamethoxazole (Bactrim®) 160/800mg PO BID x 10days**
- **Side Effects: widespread GI effects, Stevens Johnson syndrome**
- **Contraindications: known hypersensitivity, pregnant/nursing mothers, blood dyscrasias**



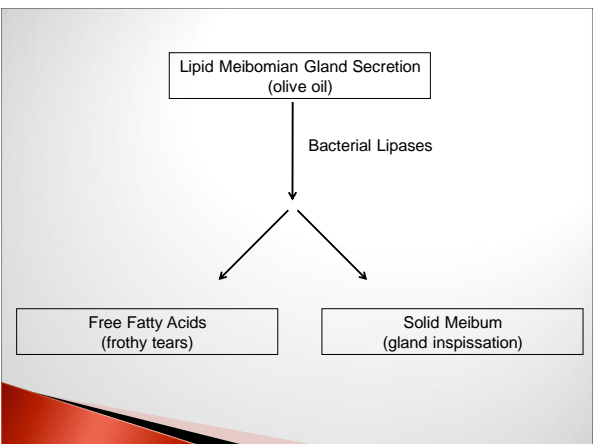
Alternative Therapy 3

When treating a non-resolving or culture positive for *Pseudomonas* dacryocystitis:

- **cefdinir 300mg PO BID x 10days**

Meibomian Gland Dysfunction

- **“Non-Infectious” Lid Disease**
- **Pathophysiology: lipid dysregulation**
- **Staph and Strep overgrowth leads to increased bacterial lipase activity**
- **Lipases breakdown normal meibomian lipid production into:**
 - **inflammatory, free fatty acids**
 - **solid lipid components**



MGD Drug of Choice

- Meibomian Gland Disease/Acne Rosacea/Chalazion
 - Initial Dosing Regime:
doxycycline monohydrate 100mg PO QAM x 30d
 - Maintenance Dosing:
doxycycline monohydrate 20-50 PO QAM x 30d

Tetracycline Drug Class

- Side Effects:
 1. GI upset (but depends on formulation)
 2. Reflux esophagitis
 3. Irregularities in bone growth and tooth development
 4. Photosensitivity/sunburn
 5. Potentiates effects of Coumadin
 6. Yeast infections and altered effectiveness of oral contraceptives
 7. Idiopathic Intracranial Hypertension (IIH) aka Pseudotumor Cerebri

Tetracycline Drug Class

Contraindications:

- Pregnant/nursing mothers
- Children under age of 8-12
- Patients on Coumadin

Other Ophthalmic Uses of Doxycycline

- Corneal healing:
 - Tx of RCE and resolving corneal ulcers by inhibiting matrix metalloproteinases (MMPs) that impair corneal healing
 - Dosage: 50mg PO QD x6-8wks
- Uveitis secondary to Lyme Disease: at MIC of 100mg PO BID x14-21 days

Doxycycline Formulations

- Generically available in 20,50,75,100 & 150mg (50,75,100,150,200mg ER)
 - 100mg monohydrate tablet ~\$22/mo
- Brand name formulations:
 - Acticlate® (75, 150mg) ~\$958/mo
 - Avidoxy® (100mg)
 - Doryx® (50, 200mg) ~\$361-1,315/mo
 - Monodox® (50, 75, 100mg) ~\$587/mo
 - Oracea® 40mg PO QAM (30mg+10mg ER) ~\$610/mo
 - Vibramycin® (100mg) ~\$365/mo

Oral Antibiotics to treat Ocular Manifestations of Systemic Disease

- Rocky Mountain Spotted Fever
 - Doxycycline 100mg BID x10 days
- Lyme Disease
 - Doxycycline 100mg BID x10-21 days
- Chlamydia
 - Azithromycin 1000mg PO (single dose)
- Syphilis
 - IM penicillin

Oral Antiviral Agents in Eyecare

Formulations

- Zovirax® (acyclovir)
- Valtrex® (valacyclovir)
- Famvir® (famciclovir)

All available generically

Oral Antiviral Agents in Eyecare

Effective Against DNA viruses

- Mechanism: inhibit DNA polymerase, but only activated by viral kinases
- Spectrum of Activity: HSV-1, HSV-2, VZV
- Side Effects: nausea, diarrhea, HA
 - acyclovir and famciclovir contain lactose
 - valacyclovir is lactose-free
- Contraindications: Renal insufficiency since it is cleared thru the kidneys

Oral Antiviral Agents for Zoster

Dosages:

- Zovirax® (acyclovir): 800mg 5x/d x 7d
- Valtrex® (valacyclovir): 1000mg TID x 7d
- Famvir® (famciclovir): 500mg TID x 7d

Oral Antiviral Agents for Simplex

Dosages:

- Zovirax® (acyclovir): 400mg 5x/d x 7d
- Valtrex® (valacyclovir): 500mg TID x 7d
- Famvir® (famciclovir): 250mg TID x 7d

Oral Antiviral Agents in Treating Ocular Herpes Simplex

- Clinical Uses when Herpes Simplex manifests as:
 - a) Blepharodermatitis
 - b) Uveitis
 - c) When a topical antiviral agent is contraindicated
 - d) Recurrent disease/recurrence prevention**

**special dosing per HEDS II

- e) ***Localized standard of care when treating stromal herpetic disease

Oral Antiviral Agents in Treating Ocular Herpes Simplex

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**special dosing per HEDS II

- e) ***Localized standard of care when treating stromal herpetic disease

Herpetic Eye Disease Study (HEDS I)

- Aim 1: In Tx of stromal herpetic disease, does adding topical steroids to topical antiviral improve outcome
 - → YES
- Aim 2: In Tx of stromal herpetic disease, does adding oral acyclovir to topical steroids & topical antiviral improve outcome
 - → NO***
- Aim 3: In Tx of simplex uveitis, does adding oral acyclovir to topical steroids & topical antiviral improve outcome
 - → YES

Herpetic Eye Disease Study (HEDS II)

- Aim 1: In Tx of simplex epithelial keratitis, does adding oral acyclovir to topical antiviral prevent stromal or uveitis
 - → NO
- Aim 2: In Tx of simplex epithelial keratitis, does adding oral acyclovir to topical antiviral prevent recurrences
 - → YES
- Aim 3: Study the role of external factors in the induction of recurrence of simplex keratitis → No published results yet

Oral Antiviral Agents for Simplex

Dosages for Simplex Recurrence Prevention (HEDS II):

- Acyclovir 400mg BID for 1 year
- Valtrex 500mg QD for 1 year
- Famvir 250mg BID for 1 year

Oral Antifungals

- Nystatin (oral)
- Ketoconazole (oral)
- Fluconazole (oral)[Diflucan®]
- Voriconazole** (IV/oral)
 - ** is DOC for systemic fungal infections
 - 200mg PO BID treated until approximately 2 weeks after resolution

Antimicrobial Best Practices

- Only prescribe when indicated
- Use the right drugs for the right bugs
- Avoid sublethal dosing
- Have patients continue their course of Tx for the full duration to ensure that all microbes are killed

Thank You!