

## Oral Medications: A Useful Clinical Guide

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### Course Goals

- Keep it real
- One or two things to take home to clinic that you can use!

### The Most Common Scenario

#### Subjective:

- 59 y/o white male presents with c/o OU burning, itching and redness, worse in AM upon awakening. Lids are stuck together in the AM, and OU feel gritty.

### Common Case

- has had recurrent hordeola and chalazia over the past decade, and has been treated on numerous occasions with a regimen of lid hygiene du jour, consisting of combinations of: antibiotic and AB/steroid combo's, ointments, drops, commercially prepared lid scrub towelettes, baby shampoo, cotton swabs, sandpaper, you name it, he's tried it.
- he has been your patient for the past 7 years.

### Common Case



## Most Common

### Objective:

- ☐ VA: OD 20/25; OS 20/30
- ☐ Pupils, EOM's, Confrontation fields: all intact and normal.
- ☐ Lids: symmetrically thickened margins, erythematous, with trichiasis, seborrheic debris, and varying amounts of dried mucous in the lashes.
- ☐ Cornea: inferior 1/3 fine SPK.
- ☐ A/C: deep and quiet.
- ☐ AT & DFE: non-contributory.

## Indication #1

### Assessment:

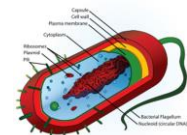
**CHRONIC BLEPHARITIS**

## PO Antibiotics

- Oral Fluroquinolones
  - Topical advantages to fluoro use for the eye and adnexa
- Orals known to cause loose connective tissue damage
  - Tendons
  - Aortic involvement
- ???long term topical complications???
  - Two possible cases reported

## PO Antibiotics: Many Choices

- Penicillins
  - Inhibit bacterial cell wall synthesis
  - **Bactericidal**
  - Contain beta lactam ring necessary for antimicrobial activity
  - Natural selection: some bacteria produce **beta lactamase (penicillinase)** which reduces efficacy of several penicillins



## Penicillins

- Staph aureus and staph epidermidis often produce beta lactamase
- Dicloxacillin and methicillin generally are beta lactamase resistant
- Ampicillin and Amoxicillin have broad spectrum of activity but are not penicillinase resistant

## Penicillins

- Augmentin = amoxicillin + clavulanate
  - **Clavulanate is a penicillinase inhibitor**
- All available in generics and all generics are relatively inexpensive

## Penicillins

- Major side effects are allergic hypersensitivity reactions
- Hypersensitivity reactions range from type IV (most common) to type I (least common)
- Also common is disruption of intestinal flora with resultant upper (more common) GI disruptions



## Penicillin Rx'ing

- Penicillins
  - Pen Vee K 250
    - 1 PO QID
  - Dicloxacillin 500 mg
    - 1 PO BID
  - Amoxicillin/Clavulinate (Augmentin) 500
    - 1 PO BID to TID

## Cephalosporins

- Are derivatives of penicillins
- Interfere with cell wall synthesis
  - Therefore **bactericidal**
- Contain beta lactam group but derived from different amino acids
- Natural selection: some beta lactamases that deactivate penicillins may or may not deactivate cephalosporins

## Cephalosporins

- 4 iterations (generations) of cephalosporins based upon different chemical side chains
  - 1<sup>st</sup> generations more effective against gram +
  - 2<sup>nd</sup> and 3<sup>rd</sup> gens more effective against gram -
  - 4<sup>th</sup> more activity against bacteria resistant to other generations and effective against gram +
- 1<sup>st</sup> generations cost less than 4<sup>th</sup> generation cephalosporins

## Cephalosporins

- Hypersensitivity reactions is common adverse effects with cephalosporins
  - Type IV most common, Type I least common
- Given similar chemical structure to penicillins, 5-10% of patients allergic to penicillins will **cross react** to cephalosporins

## Cephalosporins

- Be judicious in Rx'ing cephalosporins to patients allergic to penicillins. Not contraindicated, but caution is required.
- **In general those with more severe reactions to penicillins are more likely to cross react whereas those with less severe reactions are less likely to do so.**

## Cephalosporins

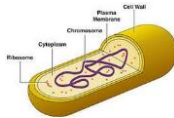
- Commonly disrupt normal intestinal flora with resultant upper and lower (more commonly) GI disturbances
- Can also disrupt bacteria necessary for synthesis of Vitamin K which can result in **impaired clotting**.
  - Judicious use in patients undergoing concurrent post MI, CVA and arrhythmia treatments

## Cephalosporin Rx'ing

- Cephalosporins
  - Cephalexin (Keflex) 250/500
    - 1 PO QID (250) or BID to TID (500)
  - Cefaclor (Ceclor) 250
    - 1 PO TID
  - Cefadroxil (Duracef) 500
    - 1 PO BID
  - Cefprozil (Cefzil) 500
    - 1 PO QD

## Macrolides

- These drugs are chemically have a large macrolide ring onto which are attached various sugars
- Interfere with bacterial ribosomal protein synthesis
  - **Bacteriostatic**
  - Can be bactericidal in higher doses



## Macrolides

- Generally effective against gram + and some gram – bacteria
- Effective against chlamydia
- **Erythromycin also has anti inflammatory properties, making it a good alternative when tetracyclines are contraindicated**

## Macrolides

- Generally safe
- Most common side effects are on GI tract
  - Nausea, vomiting, diarrhea
  - Some are enteric coated to reduce these effects (EES 400)

## Macrolide Rx'ing

- Erythromycin 250
  - 1 PO QID
- Erythromycin ethylsuccinate (EES 400)
  - GI friendly enteric coated filmtab
  - 1 PO TID
- Erythromycin Delayed (ERYC) 250
  - 1 PO QID

## Macrolide Rx'ing

- Clarithromycin (Biaxin) 500
  - 1 PO BID to TID
- Azithromycin (Zithromax, Z-Pak, TriPak)
  - Z-Pak: 500mg day 1 and 250mg day 2-5
  - TriPak: 500mg X 3 days
  - Single Dose: 1GM (reserve for chlamydia)

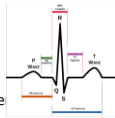
## Azithromycin vs Erythromycin

- Increased absorption rates
- Longer half life
- Better tolerance
- Less frequent dosing
- Better compliance



## Macrolides and Big Macs

- Statins have interactions with multiple medications
  - Including macrolide antibiotics
- Torsades de Pointes
  - Prolonged QT interval
  - A form of V-fib induced by toxic levels of macrolides
- Macrolides interfere with cytochrome P450 thereby prevent metabolism



[Statin toxicity from macrolide antibiotic coprescription: a population-based cohort study.](#) AM Patel, S Shariff, DG Bailey... - Annals of Internal Medicine 2013 - Am Coll Physicians

## Tetracyclines

- Are the preferred antibiotics for **chronic** lid diseases such as:
  - Meibomitis
  - Chronic blepharitis
  - **Recurrent** chalazia/hordeola
    - Acute hordeola better treated with macrolides, cephalosporins or penicillins
  - RCE's
    - More later

## Tetracyclines Preferred for Chronic Lid Diseases

### •WHY?

## Tetracyclines Preferred for Chronic Lid Diseases

- In addition to anti bacterial properties, they also have anti inflammatory properties
- Multiple mechanisms of action
  - Inhibit pmn's
  - Inhibit MMP's
  - Inhibit collagenase

## Tetracyclines

- **They inhibit** lipase production by staph epidermidis
  - Results in enhanced metabolism of meibomian gland secretions resulting in more stable tear film
- **Anti microbial properties are limited** by a high resistance rate

## Tetracyclines

- Tetracycline:
  - **Not greatly absorbed** from the digestive tract
  - **Bind** to calcium containing foods such dairy products
  - Best if taken on an empty stomach

## Tetracyclines

- Tetracycline
  - Tends to accumulate in calcium reservoirs in the body
    - Bone and teeth
  - Can cause delayed bone growth and discolored teeth in children

## Tetracyclines

- Tetracycline, Doxycycline, Minocycline
  - More problems with tetracycline, less with minocycline
- GI toxicity a common problem
- Photosensitivity
- Tinnitus and vertigo
- IH can occur, but still exceedingly rare
  - More pronounced with minocycline

## Tetracycline Problems

- **Tetracycline** is cleared through **the kidney**
  - Can raise BUN
  - Aberrant lab studies
  - Cautious use in impaired renal function patients
- **Doxycycline** is cleared through **the GI tract**
  - Can be used in patients with impaired renal function
- Enhances Coumadin activity

## Tetracycline Rx'ing

- Tetracycline 250
  - 1 PO QID
- Doxycycline (Vibramycin) 100
  - 1 PO BID
- Minocycline 50
  - 1 PO BID
  - **Almost 100% absorption**
  - **Extended half life** in prolonged dosages
  - **Safe in renal compromised** patients

## Minocycline

- Has extended MIC bioavailability
- MIC levels measured in lids remain elevated for weeks after medication discontinued
  - Chronic therapy (4-8 weeks) can result in extended MIC levels

• **Reduces recurrence rates**

## Minocycline

- **Minocycline and Neuroprotection**
  - Minocycline has been clinically implicated in offering potential neuroprotection for:
    - Cerebral ischemia
    - Traumatic brain injury
    - Degenerative brain diseases
  - Research being conducted looking at minocycline role in Retinal Ganglion Cell (RGC) death

## Minocycline

- **Minocycline and Neuroprotection**
  - Current investigations in animal models
  - Minocycline found to delay RGC apoptosis in both transected optic nerves and induced glaucoma
  - Proposed Mechanisms
    - Inhibits microglial activity
    - Inhibits matrix metalloproteinase activity
    - Inhibits release of oxygen free radicals
  - Net-Net:
    - To be determined
    - Look at Alphagan several years ago

## Clinical Uses of Antibiotics

- **Lid disease**
  - Separate into acute conditions or chronic conditions
- **Acute conditions include:**
  - Hordeola
  - Preseptal cellulitis
  - Acute infections
  - Lid lacerations

## Acute Lid Conditions

- **No real need to use tetracyclines**
- **Penicillins**
  - Pen Vee K, 250
    - 1 PO QID
  - Amoxicillin 250
    - 1 PO QID
  - Amoxil 5/125 oral suspension
    - 1 tsp BID to TID
    - Great flavors

## Acute Lid Conditions

- Augmentin (amoxicillin and clavulinate) 500
  - 1 PO BID to TID
- Available as Augmentin 250, 500 or 875
  - Each dose includes 125mg clavulinate
    - 250/125 or 500/125
    - **Doubling the dose of Augmentin 250 is not the same as Augmentin 500**
- Augmentin 875
  - 1 PO BID

### Acute Lid: Cephalosporins

- Several to choose from:
- Keflex (cephalexin) 500
  - 1 PO BID to TID
- Cheap, well tolerated, generics available

### Acute Lid: Macrolides

- Several to choose from:
- Biaxin 500
  - 1 PO BID to TID
- EES-400
  - 1 PO TID
  - Cheap, generics available, well tolerated
  - No need to use azithromycin as half life is long and you need immediate relief

### Chronic Lid Conditions

- These are best served by treating with tetracyclines
  - Chronic or recalcitrant blepharitis
  - Chronic meibomitis
  - Recurrent chalazia
- Treatment is not for 7-10 days; it is for 30-60 days
  - Eliminate condition
  - Reduce recurrence rate

### Chronic Lid = Tetracyclines

- Resistance is high to tetracycline
- Doxycycline 100
  - 1 PO BID X 30-60 Days
- Minocycline 50
  - 1 PO BID X 30-60 Days

### Chronic Lid AB Therapy

When Rx'ing PO antibiotics for several weeks duration, GI toxicity can become a problem

- Especially lower GI
- AAB (Antibiotic Associated Diarrhea)
- ~1/3 of patients on long term AB's will experience AAB
- Probiotics are recommended
  - Replenish natural GI flora with non pathogenic flora
  - \*\*Limited data...mixed results\*\*
  - \*\*Which probiotics??\*\*



Hempel S, Newberry S, Maher A, et al. Probiotics for the prevention and treatment of antibiotic-associated diarrhea. JAMA. 2012;307: 1959-1969.

### Chronic Lid AB Therapy

- For your female patients...yeast infections can be an issue
- Rx Diflucan as well for these individuals



## Diflucan

- Fluconazole
- Anti-fungal approved for treatment of:
  - Vaginal candidiasis
  - Oropharyngeal candidiasis
- Vaginal candidiasis dosing  
150 mg qd as a single dose
- Very effective, no compliance issues
- Other topical treatments available but multiple doses over several days

## Tetracyclines Safe Long Term Use?

- Tetracyclines and Breast Cancer
  - JAMA 2004;29:827-835
  - Cumulative lifetime use of tetracycline for > 50 days doubles risk of developing breast cancer

## Tetracyclines Safe Long Term Use?

- Antibiotics and Breast Cancer
  - Retrospective study of 5000 breast cancer patients vs 26291 female controls
  - Number of days cumulative on AB's ranged to 500+ days
  - Data did not support higher incidence of cancer
  - Net/Net: long term AB use *may* have long term consequence, but probably not increased CA rate

• Garcia and Gonzalez-Perez, American J. Epidemiology 2005 Apr 1;161(7):616-9  
• Kay, Jick, Journal of Epidemiology 2005 Sep;116(5):688-90.

## Lid Treatment Caveat

- Important to treat both internally and externally
  - Internally: oral antibiotics
  - Externally: Lid hygiene, AB or AB/Steroid ointments
    - Ilotycin
    - Gentamycin
    - Tobramycin
    - TobraDex

## Azasite

- Topical azithromycin
- Prolonged half life
- Product literature stresses penetrability
- Expensive
- Nice marketing
- Better alternatives

## PO Antibiotics for Lid Disease and Adjacent Involvement

- With concurrent sinusitis, otitis media:
  - *Minocycline*
  - *EES 400*
    - 1 PO TID x 7-14 days
  - *Augmentin 500 BID, 850 BID or 1000XL BID x 7-10 days*

## PO Antibiotics for Lid Disease and Adjacent Involvement

- With upper respiratory infection

- **Biaxin 500mg**

- 1 PO BID x 1-2 weeks

- **Zithromax**

- Z-Pack (250mg)
  - 1 PO BID x 1 D then QD x 4 D
- Tripak: (500mg)
  - 1 PO QD x 3 D

- **Cipro 250**

- 1 PO TID x 1-2 weeks

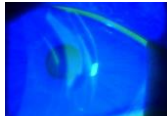
## Another Common Indication

The Case of:  
Cat Scratch Red Eye

## Corneal Injury

### Subjective:

- 36 year old white female with history of recurrent corneal erosion
- Erosions recur about every 3-4 months, and increasing
- repeatedly properly managed with hypertonics, BCL's with no resolution
- after explaining options, you both decide to proceed with corneal debridement and stromal micropuncture.
- Meds: OC's. NKDA.



## Corneal Injury

### Objective:

- VA: OD 20/25; OS 20/20
- Pupils: PERRLA; (-) RAPD; EOM's intact.
- Cornea OD: epithelial basement membrane defect, present since original corneal insult.
- A/C: trace cell and flare OD; deep and quiet OS.
- DFE: not performed.
- no contraindications to epithelial debridement and stromal micropuncture.

## Corneal Injury

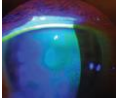
### Assessment:

RCE


## Indication #2

- Ocular Pain Management
- Recurrent Corneal Erosions

### Considerations in the Management of Corneal Pain



- differentiation necessary between 'corneal' pain and 'uveitic' pain.
- the size of the corneal epithelial defect is NOT a good indicator of the amount of pain that should be experienced.




### Considerations in the Management of Corneal Pain:

- differentiation between "fresh" pain vs "old" pain
- Recent ictus vs several days duration
- Management: BCL or Pressure Patch???

### Ocular Pain Management

- Multi faceted problem
- Multifaceted solutions
  - MUST control/prevent anterior uveitis
- **Acute** pain and **Chronic** pain are DIFFERENT and are managed differently



Recommendations for Management of Acute Pain

Acetaminophen

↓ ineffective

Add nsNSAIDs/coxibs

↓ ineffective



Add opioids

(Generally short acting agents at regular intervals; avoid oral for acute management unless other management)

### Anyone Use a Pressure Patch?

### Considerations in the Management of Corneal Pain

- ☐ BCL vs Pressure Patching
- ☐ Either can be used, but for specific situations
- ☐ BCL generally if:
  - Shorter time since ictus
  - Smaller defect
  - Minimal uveitic response
- ☐ Pressure patch OK if:
  - Larger defect of longer duration
  - Anterior chamber cooking
  - Low risk of fungal origin

### Considerations in the Management of Corneal Pain

- Several arguments in favor of BCL vs patching:
  - Donnenfeld et al Ophthalmology 1995
    - No differences in healing time, photophobia,tearing
    - Pain reduced with topical NSAID
  - Corneal Abrasion Patching Group
    - Ophthal, 1997
      - NSAID helpful in reducing pain of 'new' non infected, non CL abrasions
  - Literature search generally shows no difference
- Like patients show no compromise to healing with patching.

## Considerations in the Management of Corneal Pain

- 4 hours duration
- PLAN:
  - BCL
  - cycloplegic
  - Topical AB Q2H
  - NSAID BID/QID
- ◆ 4 days duration
- ◆ PLAN:
  - ◆ Pressure patch
  - ◆ 1% atropine
  - ◆ AB ung
  - ◆ Oral analgesic

Why manage differently????

## Analgesics: Either Peripheral or Central NS Action

- Peripheral
  - Prevent formation of pain mediators and release of inflammatory cascade at site
  - Aborts first steps of the inflammatory cascade
  - Effective in mild to moderate pain of ACUTE onset
- ◆ Central
  - ◆ Block the afferent stimulation of the pain receptors
  - ◆ Centrally act to mute the sensation of pain, once it is established
  - ◆ Effective in moderate to severe pain once inflammatory cascade has begun

## Analgesics

- ◆ Non-Narcotics
  - ◆ NSAIDS
  - ◆ Salicylates
    - ◆ ASA/APAP
  - ◆ Peripheral nervous system action
  - ◆ Interrupt inflammatory cascade
- ◆ Narcotics
  - ◆ Numerous choices
  - ◆ Addictive potential
  - ◆ Central nervous system action
  - ◆ Mute the sensation of pain

## Use Refractive Surgery as a Template

- PRK, E-Lasik, PTK (surface ablations)
  - Trauma induced in controlled environment
  - Eye is anesthetized prior to trauma
  - Intraoperative NSAIDS (topical) used
  - Cycloplegia rarely needed-no uveitis
  - Patient discharged on AB's, topical NSAIDS, and BCL
- Patients do remarkably well
- Why?
  - **Inhibition of the initial steps in the inflammatory cascade**



## Acute Corneal Trauma

- Very similar inflammatory process as surface ablation patient on presentation
- Recent onset of injury
- BCL and topical NSAID's instituted relatively soon
- In addition, cycloplegic used
- Stunts initial inflammatory cascade

## Friday/Monday Trauma

- These injuries have been present for a while prior to presentation
- Uveitis cooking
- OK to pressure patch with AB ung
- Cycloplege
- Rx oral analgesic, probably centrally acting narcotic

## What about Orals?

- Useful in moderate to severe ocular pain
- Usually needed in injuries of longer:
  - Time since ictus
  - Duration of healing
- Many to choose from

## Non-Narcotic Analgesics

- SALICYLATES:
  - Aspirin
  - Acetaminophen
- GI ulcerations (ASA)
- Increased bleeding times
- Liver toxicity (APAP)

## Non-Narcotic Analgesics

- NON SALICYLATES: NSAIDS
- Ibuprofen (Motrin, Advil)
- Naproxen (Naprosyn, Aleve)
- Indomethacin (Indocin)
- Piroxicam (Feldene)
- Oxaprozin (Daypro)
- Celecoxib (Celebrex)
- Generally better GI tolerance than ASA
- Variable degrees of anti inflammatory properties



## Narcotic Analgesics

- Codeine
- Hydrocodone
- Oxycodone

## Narcotic Analgesics

- Drowsiness and somnolence common
- Nausea
- Vomiting
- Constipation
- Respiratory depression
- Addictive potential is real

## Rx'ing Analgesics

- Use a step care approach
  - Not too much...not too little
- Remember comfortable eyes heal faster
- If you're going to use an oral analgesic, you need to cycloplegic as well
- Begin with non narcotics and use narcotics PRN

### Rx'ing Analgesics

- Mild pain:
- 500 mg Acetaminophen + 600 ibuprofen
  - QID to Q4H
- 500 mg Acetaminophen + 800 ibuprofen
  - QID to Q4H

### Rx'ing Analgesics

- Moderate Pain
- Tylenol #3 (300 APAP + 30 mg codeine)
  - 2 PO stat then 1 q4-8h prn pain
- Tylenol #4 (300 APAP + 60 mg codeine)

### Rx'ing Analgesics

- Moderate to severe pain: Oxycodone
- Percodan (4.5 mg oxycodone + ASA)
  - 1 or 2 PO stat then 1 q4-8h prn pain
- Percocet (4.5 mg oxycodone + APAP)
  - 1 or 2 PO stat then 1 q 4-8h prn pain



### Rx'ing Analgesics

- Moderate to severe pain: Hydrocodone
- Vicodin, Vicodin ES, Vicodin HP (potency)
  - 5 mg hydrocodone + 500 APAP
  - 7.5 mg hydrocodone + 750 APAP
  - 10 mg hydrocodone + 660 APAP
- Typically Vicodin = QID to Q3H
- Vicodin ES and HP usually QID MAX

### Rx'ing Analgesics

- Moderate to severe pain: Hydrocodone
- Lortab 2.5/500, 5/500, 7.5/500 or 10/500
  - 1 PO q3-8h prn pain

### Rx'ing Analgesics

- One of more common symptoms associated with severe eye pain is nausea
- One of the most common side effects of narcotic analgesics is nausea and vomiting

## Rx'ing Analgesics + Nausea

- Mepergan Fortis (50mg meperidine + 25 mg promethazine)
  - 1 PO q4-6h prn pain **NO MORE!!!**
- Compazine (5 or 10 mg)
  - Orally in addition to other narcotic
  - 25mg suppository
- Phenergan (promethazine)
  - 25 mg to QID



## Rx'ing Analgesics: Ultram

- Ultram (Tramadol) narcotic-like action
  - NSAID that works on opioid receptors in brain
  - Less dependence, less respiratory effects
  - 50 or 100mg up to TID



## So What about our Patient in this case: RCE with debridement

- Given we are initiating the trauma in a controlled environment:
  - BCL
  - Topical NSAID
  - Topical AB
  - Cycloplege

## Back to our case of RCE

- What about RCE and Doxycycline?
  - Does this work? Why sometimes and not other times???
  - ....it depends on *why* someone is eroding

## Two Types of RCE

- Mechanical/structural disruptions of the basement membrane
  - BM defect prohibits good adhesion of basal epithelial cells
- Physiological disruptions of the basement membrane
  - Biochemical process
  - Collagenase and matrix metalloproteinases are the culprits
  - More chronic **re-inflammations**



## RCE & Cyclines

- Where did the Collagenase come from?
  - Lid microbes!
  - Blepharitis!!!!
- Collagenase disrupts bio-integrity of BM, thereby preventing cellular adhesion
  - Similar in clinical appearance to DLK
- Cyclines inhibit collagenase

## RCE & Cyclines

- What are matrix metalloproteinases?
  - Proteolytic enzymes released from ocular tissues that can degrade components of the extracellular matrix.
  - Induced during wound healing and are believed to play a role in extracellular matrix remodelling.
- Cyclines inhibit MMPs

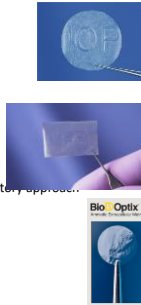
## RCE & Cyclines

Lid Appearance and timing of recurrences are the keys to management

- If recurrences are spread out between times of corneal integrity, etiology is usually mechanical
  - Debridement, stromal micropuncture, PTK
- If recurrences are contiguous with ictus, then need to look at the lids
  - Hypertonic + doxycycline 100mg BID X 4 weeks
  - THEN proceed to AMG

## Amniotic Membrane Grafts

- Several manufacturers
  - Ambiodisc, Prokera, BioD Optix (sunny-up)
- 3 layers of inner most placental tissue
  - Epithelium
  - Basement membrane
  - Stroma
    - Downregulates inflammatory cascade
- Useful in those RCE's that are more chronic in nature
- Chronic-inflammatory= recurrence=need for anti inflammatory approach.



## Another Common Oral Med

- The case of:
  - I got sucked into this one.

## Case with a Twist

### Subjective:

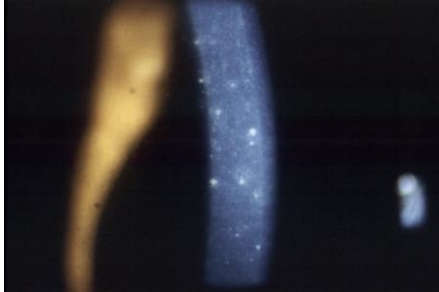
- ☑ 57 y/o new patient, presents with a long history of recurrent anterior uveitis OS
  - Episodes typically flare up once Q12 months, and have always been controlled with Tobradex TID for 7-10 D.
- ☑ Currently self medicating with no relief.
- ☑ +III cell and + II flare; all else normal.
- ☑ Rx 1% atropine HS and Pred Forte Q2H while awake, and schedule a follow-up for 2-3 days.

## Case with a Twist

- Patient presents 7 days later reporting that initially, the eye was feeling much better, but in the past 48 hrs comfort and vision have dropped off considerably.



## Case with a Twist



## Case with a Twist

**Objective:**

- VA OD 20/20, OS 20/200 (OD uninvolved).
- Cornea: Thick KP's on endothelial surface, +II stromal edema, deep folds in Descemet's, and the *largest epithelial dendrite you've ever seen*.
- A/C: +III cell and flare, pupil dilated, and iris and all posteriorly difficult to view.
- Pupils: (-) APD OS by inverse Marcus-Gunn testing.
- DFE: not the greatest of views, but no evidence of any form of chorioiditis or retinopathy.

## Case with a Twist

**Assessment:**

**MARKED ANTERIOR UVEITIS  
with  
OVERLYING HSV KERATITIS**

## Case with a Twist

- dichotomy of treatment of HSV keratitis *and* uveitis.
- of the two conditions, HSV must be the primary concern due to the high likelihood of corneal scarring and the possibility of perforation. Therefore, if any medication has to be deleted from this regimen, it would have to be the steroids and not the antivirals.

## Tackle the Two Entities

- Uveitis
  - Must be managed aggressively
  - 1% atropine on BID to QID basis
  - Topical steroids?
    - Yes, but judiciously as uveitis is raging
- HSVK
  - Topical Viroptic/Zirgan
  - Oral antivirals

## Oral Anti-Virals

- Acyclovir
  - First available and most studied
  - A guanosine analog which interferes with viral DNA synthesis
- Famciclovir (Famvir)
  - A prodrug of penciclovir
- Valacyclovir (Valtrex)
  - Prodrug of acyclovir

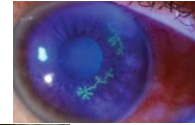
## Oral Anti-Virals

- Famvir and Valtrex are better absorbed and have higher bioavailability
  - Less frequent dosing
- All 3 are generally well tolerated in the GI system
- Most common side effects are GI upset, headache, and rash

## Oral Anti-Virals

- RX schedule will differ significantly on whether treating:

- HSVK
- VZV (HZO)



## HSVK and Oral Anti-Virals

- the role of Zovirax in the management of HSV keratitis is well documented.
- Herpes Eye Disease Study (HEDS)
  - Looked at oral antiviral (+ Viroptic) and HSV keratitis
  - Looked at management of acute disease and prevention of recurrence

## HSVK and Oral Anti-Virals

- HEDS: Acute Disease management
  - Acyclovir and Epithelial disease (-?)
  - Acyclovir and Stromal Disease (+)
  - Acyclovir and Iridocyclitis (+)

## HSVK and Oral Anti-Virals

- Should oral antivirals be used as primary treatment on all epithelial HSV?
  - NO
- Primary Treatment Indicators:
  - Significant visual impairment likely
  - Monocular patients
  - Extenuating circumstances

## Rx'ing Antivirals for HSVK

- Dosage is for duration of *severe* disease
  - Acyclovir: 200 mg 5 times daily
    - (Or 400 mg 5 times daily if necessary)
  - Valtrex: 1gm QD (up to T1D is OK)
  - Famvir: 500mg TID
- Dosage maintained until significant resolution of the HSVK is seen
- Supplements topical Viroptic/Zirgan

## HSVK Recurrence Prophylaxis

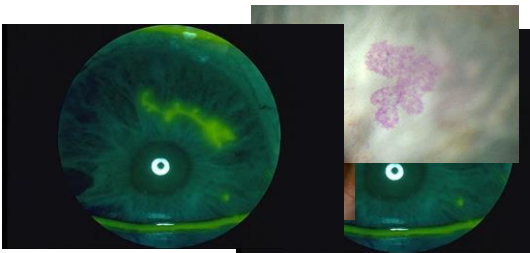
- HEDS: (Acyclovir Prevention Trial) Recurrence rates with long term treatment
  - Acyclovir responsible for overall 41% reduction in recurrence of HSV
  - Acyclovir and epi recurrence
    - 11% vs 9%
  - Acyclovir and Stromal recurrence
    - 13% vs 8%
- **Dosage to reduce recurrence:**
  - Acyclovir 400mg BID up to 12 months

## Typical Management of Severe HSVK

### Plan:

- 1% atropine QD to BID.
- Pred Forte QID while awake.
- Viroptic/Zirgan while awake.
- Valtrex (valacyclovir) 1 gm. QD - or -
- Zovirax (acyclovir) 200 mg. caps, 1 PO 5X daily.
- Follow-up q24h until a "comfortable" level of resolution has been reached.

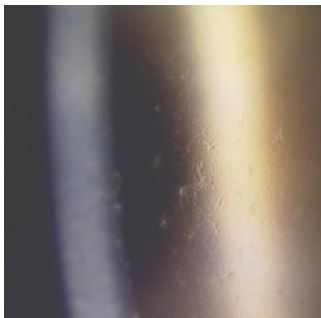
## Identifying HSV Keratitis Early



## Identifying HSV Keratitis Early

- On initial presentation, look for:
  - Epithelial staining (RB or LG)
  - *Raised* epithelial defect
  - **Underlying stromal haze/wbc migration**
  - **Endothelial irregularities underlying epi defect: Micro KP's**

## Identifying HSVK Early



## VZV/HZO and Oral Anti-Virals

- H. Zoster and Antivirals
  - Initiation of oral antivirals ideally made within 48-72 hrs of onset of disease
  - Aimed at reducing the duration of dermatological involvement
  - **\*\*significantly reduced post herpetic pain\*\***

## Zoster Eye Disease Study: ZEDS

- Expected completion date: 2020
- Simple concept: Long term low dose antivirals are beneficial in reducing long term complications for HSK.
- Same for Zoster?



## Zoster Eye Disease Study: ZEDS

- Multi center placebo controlled randomized study
- Primary Outcome: Does 12 mo continued use of 1gm valacyclovir reduce rates of:
  - Keratitis (epi, stromal or endo)
  - Uveitis
- Secondary Outcome: Does 12 mo continued use of 1gm valacyclovir reduce rates of PHN

## Rx'ing Anti-Virals for VZV

- Dosages:
  - Acyclovir 800mg tabs
    - 1 PO 5x daily x 7-10 D
  - Valtrex 1 gm
    - 1 PO TID x 7-10 D
  - Famvir 500mg
    - 1 PO TID x 7-10 D

## H. Zoster Anti viral Therapy

- Adjunctive therapy includes pain management:
  - Narcotics
    - Percodan, Percocet, Vicodin
  - Anti-convulsant, nerve modulators
    - Gabapentin (Neurontin)
    - Pregabalin (Lyrica)

## Post Herpetic Neuralgia

- Neurontin (100, 300, 400, 600, 800 mgs)
  - Indicated for the management of post herpetic neuralgia
  - Ramped up; tapered down
  - Dosage increased until pain reduced
    - 300 mg day 1; 600 day 2; 900 day 3
  - Effective dose is 900-1800mg/day
  - Discontinuation of the medication should be gradual over one week minimum
  - Renal clearance; cautions with renal insufficiency

## Post Herpetic Neuralgia

- Lyrica (pregabalin)
  - Approved for
    - Post herpetic neuralgia
    - Diabetic neuropathy
    - Fibromyalgia
    - Seizures
    - Typical dosage is 50-100mg TID; max 600mg/d
    - Renal clearance; adjust dose in decreased renal function

## Post Herpetic Neuralgia

- Most problematic issue associated with Zoster
- Quick onset of anti-viral treatment essential
- Neurontin/Lyrica beneficial
- Botox beneficial
  - Blocks release of ACH—muscular paralysis
  - Blocks nociceptive neuropeptides involved in chronic inflammatory pain



## Oral Antiviral Caveats

- Herpes Simplex Keratitis
  - If early and epithelial only, Zigan/Viroptic
- Acceptable to use oral antivirals when:
  - Primary stromal involvement
  - Complicated primary cases (monocular, etc)
  - Reduction in recurrence rates desired
- Continue to use topicals
- Continue to use cycloplegics
- Minimize topical steroids

## Oral Antiviral Caveats

- Primary Herpes Simplex Keratitis
  - Acyclovir: 200mg (or 400) 5 times daily
  - Famvir: 500mg TID
  - Valtrex: 1gm QD to TID
- Co-medicate with topical Viroptic/Zigan and cycloplegic
- D/C oral on resolution of majority of disease, and maintain therapy with topical

## Oral Antiviral Caveats

- Herpes Simplex Keratitis Chronic Suppressive Therapy
  - 400mg acyclovir BID X 6-12 months

Thank you from Wilmington NC

