

What to Prescribe When

Systemic Medications
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Financial Disclosure: Dr. Pizzimenti

I have no relevant financial relationships to disclose and no proprietary interest in any product discussed in this presentation.

Course Goal

To provide clinically useful information about the treatment of ocular conditions using systemic medications.



Questions?



What Pharmacotherapy Means to Optometry

The ability to use pharmaceutical agents has enabled optometrists to become true primary health care providers.

Routes of Drug Administration:

- Alimentary
 - Sublingual
 - Oral ←
 - Rectal
- Parenteral
 - Subcutaneous (SC)
 - Intramuscular (IM)
 - Intravenous (IV)
- Other
 - Inhalation
 - Topical



The Florida Fourteen

The following chart depicts the current **Formulary of Oral Ocular Pharmaceutical Agents**.

The following **ANALGESICS** or their generic or therapeutic equivalents:

1. Tramadol hydrochloride
2. Acetaminophen 300 mg with No. 3 codeine phosphate 30 mg

The following **ANTIBIOTICS** or their generic or therapeutic equivalents:

1. Amoxicillin with or without clavulanic acid
2. Azithromycin
3. Erythromycin
4. Dicloxacillin
5. Doxycycline/Tetracycline
6. Cephalexin (Keflex®)
7. Minocycline

The Florida Fourteen

The following **ANTIVIRALS** or their generic or therapeutic equivalents:

1. Acyclovir
2. Famciclovir
3. Valacyclovir

The following **ORAL ANTI-GLAUCOMA AGENTS** or their generic or therapeutic equivalents, which may not be administered or prescribed for more than 72 hours:

1. Acetazolamide
2. Methazolamide

The Oral Ocular Formulary may only be modified statutorily by the Florida Legislature. The only exception is if any oral ocular pharmaceutical agent listed in the formulary is subsequently determined by the United States Food and Drug Administration (FDA) to be unsafe for administration or prescription, that particular agent will automatically be considered deleted from the oral formulary.

Principles of Pharmacology

- Pharmacokinetics: What the body does to a drug
- Pharmacodynamics: What the drug does to the body
- Always keep in mind contraindications, side effects and drug-drug interactions before starting medication.
- Drug risks vs. benefits
- Be mindful of the age and weight of the patient
 - Consider starting with one half standard dose in the young or elderly
 - Polypharmacy: elderly often on multiple meds – may lead to adverse reactions/interactions

Practice-building Tip

- When Rx-ing for Peds:
- Place a courtesy call and send follow-up letter to pediatrician
- Especially with po meds



Know Your Patient



Remember:

Know your ABCD's of Med Rxing

A = Allergies

B = Body weight

C = Current Medications

D = Diseases

Each patient is unique.



Choosing the Proper Drug Therapy

- Patient considerations
 - Immune system viability
 - Kidney and liver function
 - Pregnant or nursing
 - Age
 - Allergy history
- Safety profile of the drug
- Cost considerations



General Principles

- Drug Metabolism – Most drugs are metabolized by liver enzymes
- Drug Excretion – The kidney is the major route
- Some drugs are excreted after metabolism
- Some drugs are excreted unchanged
- Therefore, **proper liver function is critical for metabolism of medications, and kidney function is essential to drug excretion.**

Normal Vital Signs (Adult)

Temperature (oral): 97.8°F - 99°F

Heart Rate: 60 - 99 beats per minute

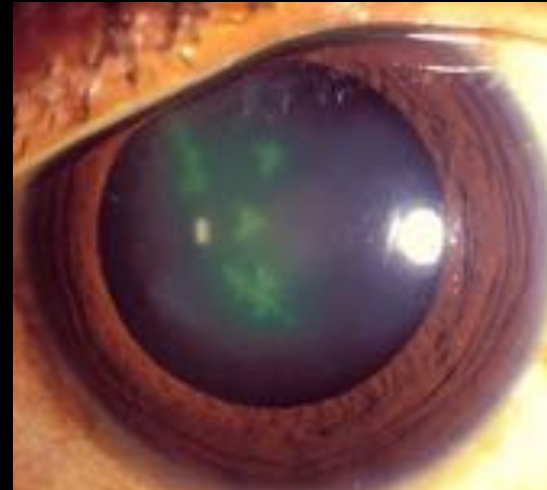
Respiratory Rate: 12 - 16 breaths per minute

Blood Pressure: Less than 120mmHg systolic and less than 80mmHg diastolic

Pulse Oximetry: 95 - 100%

Case

- 64 year-old WM c/o decreased VA OS, watery eye, pain, and photophobia
- Used ATs for relief
- Ocular Hx: Cataract surgery OU, PKP OD 2005
- PMHx: +DM X 19 years
- BCVA: OD 20/20, OS 20/30



Dendritic Keratitis

Herpesviridae

Virus	Ophthalmic manifestations
Herpes simplex virus 1 (HSV-1)	Blepharitis, conjunctivitis, keratitis, anterior uveitis, retinal necrosis (a combination of the above)
Herpes simplex virus 2 (HSV-2)	Same as above
Varicella zoster virus (VZV)	Same as above
Epstein-Barr virus (EBV)	Epithelial and stromal keratitis
Cytomegalovirus (CMV)	Epithelial and stromal keratitis, endothelitis, and retinitis (or a combination of the above)

ANTIVIRALS

Oral Antiviral Agents

- Inhibit viral DNA polymerase without inhibiting normal cellular activity
- Works best if treatment initiated **within 72 hours**
 - *but can be as late as 1 week*
- Pregnancy category B
- Caution in patients with renal disease



Oral Antiviral Drugs

Antiviral Drug	HSV	HZO
Acyclovir	400 mg 5x/day for 1 week	800 mg 5x/day for 1 week
Valacyclovir	500 mg TID for 1 week	1000 mg TID for 1 week
Famciclovir	250 mg TID for 1 week	500 mg TID for 1 week

Special populations, special Rx.



Pregnancy Category B

- Acyclovir (Zovirax®)
- Acute infection - 400 mg PO 5x/day X 7 d
 - HSV Keratitis
 - Dendritic ulcer
 - HSV Blepharodermatitis
 - Lid involvement
- Caution in those with kidney disease



Traditional FDA Use-in-Pregnancy Ratings

Category	Description
A Absolutely safe	No risk in humans or animals
B Probably safe	No evidence of risk in humans or adverse findings in animals. or In the absence of adequate human studies, animal studies show no fetal risk. The chance of fetal harm is remote, but remains a possibility.

<http://www.fda.gov>

Use-in-Pregnancy Ratings

Category	Description
C	Risk can not be ruled out; but the potential benefits may outweigh the potential risk.
Questionably safe	
D	Positive evidence of Risk
X	Contraindicated in Pregnancy

<http://www.fda.gov>

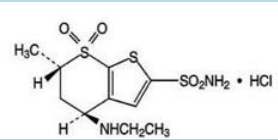
[12/3/14] The FDA published the Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling, referred to as the "Pregnancy and Lactation Labeling Rule"



What Meds Can Be Used During Pregnancy?

- Antibiotics
 - Amoxicillin
 - Amoxicillin/clavulanate
 - Azithromycin
 - Erythromycin
- Antivirals
 - Acyclovir
 - Valacyclovir
- Anti-inflammatory
 - Prednisone
- Analgesics
 - Acetaminophen
 - Ibuprofen
 - Tylenol #3
 - Vicodin





Ocular and Periocular Pain



Pain

- Pain is a feeling triggered in the nervous system.
- It may be sharp or dull.
- Pain may come and go, or it may be constant.
- It may result from various ophthalmic and other causes.



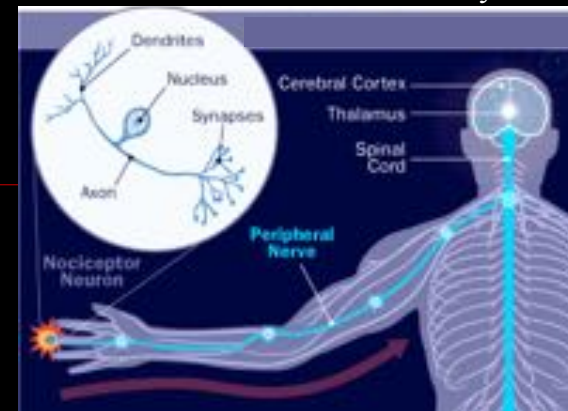
Pain is...

An "unpleasant **sensory** and **emotional** experience associated with actual or potential tissue damage, or described in terms of such damage."

Source: International Association for the Study of Pain



Nociception (from the Latin word for "hurt"), is the process by which a painful stimulus is relayed from the site of stimulation to the central nervous system.



Analgesics...



work either **peripherally** (NSAIDS and aspirin) at the end receptors or **centrally** (opioids and acetaminophen) in the nervous system.

Go-to Mild-Mod Pain Meds

- MOTRIN, ADVIL (Ibuprofen)
- ALEVE (Naproxen)
- TYLENOL (Acetaminophen)



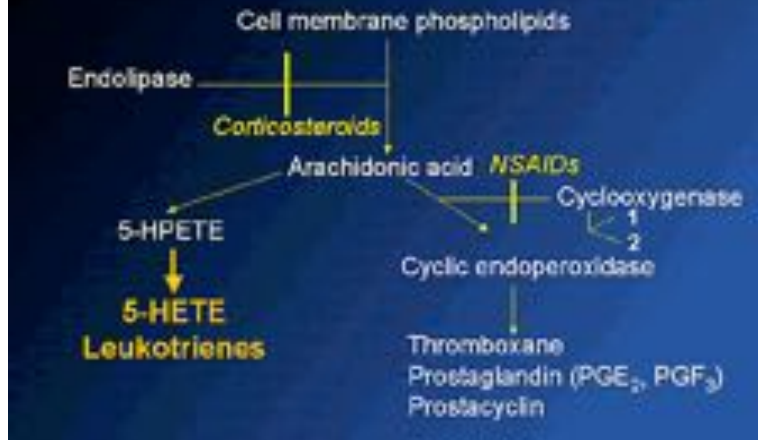
Alternating acetaminophen and ibuprofen: 400 mg of ibuprofen followed 2-4 hours later by 325 mg acet – then repeat.

Analgesics

- NSAIDS primarily used for pain management
 - Advil (Ibuprofen)
 - 200-400 mg q4h for analgesia (OTC dose)



NSAIDs Mechanism of Action



IBUPROFEN

- Miscellaneous information
 - Take with food
 - Avoid alcohol due to gastric irritation / bleeding
 - Overuse may cause rebound
 - 400 mg qid + 325-500mg acetaminophen is comparable to acetaminophen / codeine
 - Tylenol #3
 - May interfere with aspirin's anti-platelet effect
 - Take 30-120 minutes after or 8 hours before aspirin

Naproxen

- 220 mg tabs
- Take 2 tabs the first hour, then 1 tab q8 hours.
- Avoid in children under 12 years old.



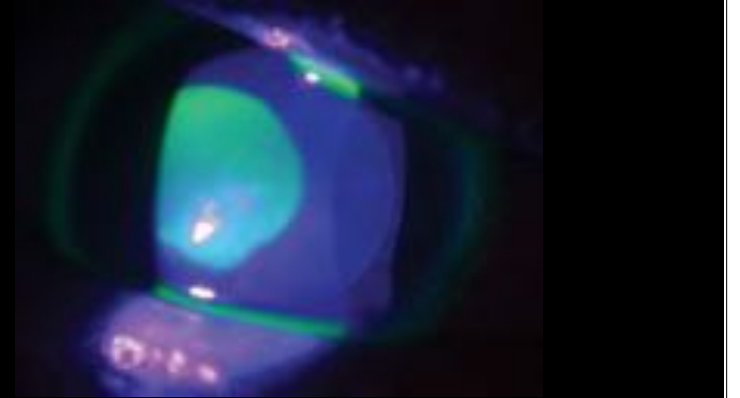
Moderate-Severe Ocular Pain



Large Corneal Abrasion



Recurrent Erosion



Ultram – Tramadol HCL (DEA #)

- CNS agent – reduces the perception of pain

- Equal in effectiveness to Tylenol 3
- Weak opioid receptor binding
- Can be taken w/o regard to meals



- Minimal side effects (constipation, dizziness and nausea)
- **Dosage:** One 50 mg tablet QID or more frequent
 - not to exceed 400 mg / day



The initial dose of ULTRACET is 2 tablets every 4 to 6 hours as needed for pain relief up to a maximum of 8 tablets per day.

Treatment duration should not exceed **5 days**

ULTRACET[®] tab.
(37.5 mg tramadol HCl/325 mg paracetamol)
30 Tablets
For oral administration
SOLD ONLY BY PRESCRIPTION
Store at 25°C in the original package

ULTRACET[®]
(37.5 mg tramadol HCl/325 mg acetaminophen tablets)
100 tablets
Rx only.

Light yellow, coated, capsule-shaped tablet imprinted "04M" and "550".
For dosage and other prescribing information, see package insert.
Dispense in child-resistant container.
Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).
Dispense in light container.
Keep out of reach of children.

Mfg. by: Janssen Ortho, LLC
Gurukul, PA 00778
Mfg. for: Janssen Pharmaceutiek, Inc.
Titusville, NJ 08850

© Janssen 2000 10178002

Control Exp. Date

Opioids

- Hydrocodone/acetaminophen is the most frequently prescribed oral medication in the U.S
- **Tylenol 3 (30 mg codeine with 300 mg acetaminophen)**
 - *category III scheduled drug*
 - *1-2 tabs q4h is usual adult dosage*
- Used for more severe pain management
 - *hydrops*
 - *post-surgical pain*
 - *severe trauma*
 - *severe corneal abrasions/erosions*

Side effects

- Mild adverse effects: itching, rashes, contact dermatitis
- Severe adverse effects: delirium, seizures, cardiotoxicity especially when used with other CNS depressants including alcohol
- **Addiction**/tolerance

The Opioid Epidemic in America

The Research Behind Understanding, Preventing and Treating Addiction



Data from the U.S. National Institute on Drug Abuse indicates:*



Roughly
21-29%
of patients prescribed opioids
for chronic pain misuse them



Between
8-12%
develop an opioid use
disorder



An estimated
4-6%
who misuse prescription
opioids transition to heroin



Approximately
80%
of people who use heroin first
misused prescription opioids

*National Institute on Drug Abuse (2017). Opioid Crisis. Retrieved May 2017.
From <https://www.drugabuse.gov/drug-facts/opioids/opioid-crisis>

Contraindications of Narcotic Analgesics

- Prior addiction
- Renal dysfunction
- Liver dysfunction
- **Use of CNS agents – Tricyclic anti-depressants, phenothiazines, MAO inhibitors, alcohol, benzodiazepines**
- Lung problems - COPD



Important Note:

Long-term opioid use often begins with treatment of acute pain!

A Colleague's Story

CONQUERING OPIOID ADDICTION

An optometrist reveals her personal journey from abuse to recovery in the hopes of helping others

JENNIFER KIRBY, SENIOR EDITOR



On Sept. 30, 2016, Melanie Weiss, O.D., was in handcuffs in the back of a patrol car. Just 15 minutes earlier, she was seeing patients at Weiss Eyecare Clinic, her private practice in Watertown, SD.

"I remember looking at their badges, but I still didn't think I was going to be arrested. Drugs just do not let your mind go to the consequences," recalls Dr. Weiss, who is recovering from opioid addiction. "I honestly thought the detectives were going to say, 'Melanie, you should probably get back to work.' Obviously, that did not happen."

Here, along with related facts regarding opioid abuse, Dr. Weiss discusses her journey from abuse to recovery in the hopes of helping others who are grappling with opioid addiction, be it themselves or someone they know.



Dr. Weiss speaks about her journey through addiction.

pharmacology classes, so I knew what opioids do to the brain, but I also thought, 'I'm smart; I know when to stop.'"

Prescribed two pills every four to six hours, Dr. Weiss divulges she raised it to two and a half, then three, three and a half and on.

"For most people, opioids make them feel sleepy. For me, it was the opposite. I felt like I could go from 6 a.m. until 2 a.m. and be the best eye doctor, the

best boss, the best mom — I have three daughters — and the best wife," she asserts. "Both physically and mentally, the opioids made me feel like I was superwoman."

FACT: Opioids attach to and activate natural opioid receptors located on nerve cells in the brain, among other organs. They work to block pain signals, while delivering surges of dopamine to the brain's reward circuit, creating feelings of euphoria. Long-term opioid users can build up a tolerance, prompting them to increase their dosages and frequency of use. Additionally, opioid use

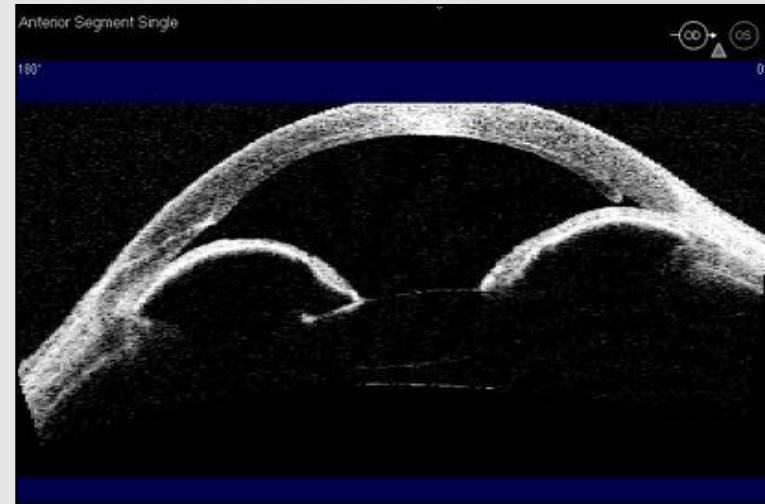
Acute Angle Closure

- Rapid rise in IOP due to blockage of TM
- True ocular emergency!
- Definitive Tx. is w/LPI



AACG Tx: Oral CAIs

- Give two 250mg tablets of Diamox (acetazolamide) as first step in reducing IOP in angle closure, or any other form of acute IOP increase.
 - Since Diamox 500mg Sequels are **time released**, don't use them for acute situations
- The typical dosage of acetazolamide for acute pressure spikes is two 250mg tablets, followed by an additional dose in 3 to 4 hours, if needed.



Oral CAIs: Neptazane

- The typical dosage for methazolamide (Neptazane) is 25mg bid, stepping up to 50mg bid as needed.
- Methazolamide is usually well-tolerated and carries a much reduced risk of renal calculi (kidney stones) compared to acetazolamide.

Oral CAIs

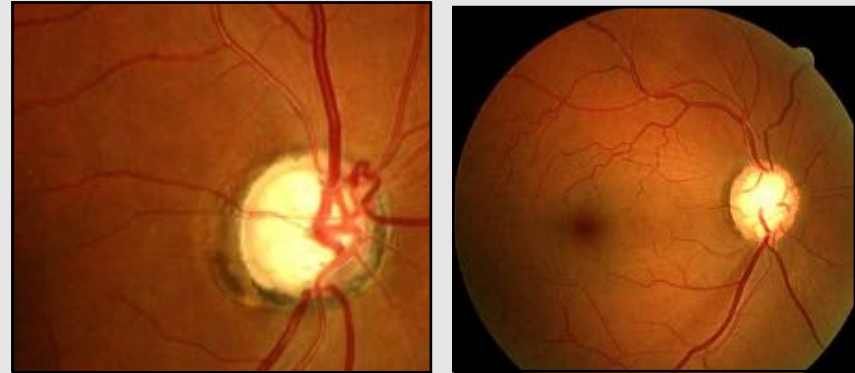


Oral CAIs

- Ocular side effects:
 - idiosyncratic sulfonamide-related transient angle-closure, myopia and choroidal thickening, but these are rare
- Systemic side effects:
 - GI upset, paresthesias, diuresis, metabolic acidosis, malaise, anorexia, metallic taste, tingling of fingers, renal calculi, and potassium depletion, especially with **prolonged** use.
 - Avoid in sickle cell patients

• Open Angle Glaucoma

• Angle Closure Glaucoma



Oral CAIs

- Potassium depletion is more likely if the patient is also taking a hydrochlorothiazide diuretic, digitalis or a corticosteroid. Potassium levels should be monitored in these circumstances.
- More severe reactions, such as renal stones, blood dyscrasias or Stevens-Johnson syndrome, are possible but uncommon.
- **Contraindications for Diamox and Neptazane include sulfa allergies or a history of renal stones or renal failure.**
- Care should be exercised if a patient is susceptible to metabolic acidosis, is a brittle diabetic, has hepatic insufficiency, or has chronic obstructive pulmonary disease with acidosis.
- Note: simultaneous regular aspirin use can lead to CAI accumulation and toxicity.

INFECTIOUS DISEASE



Bacterium



Virus



Protozoan



Fungus



Helminth

The 5 Classes of Micro-organisms

- 538 types of **bacteria**
- 208 types of **viruses**
- 317 types of **fungi**
- 57 types of **protozoa** (parasites)
- 287 types of **helminths** (worms)

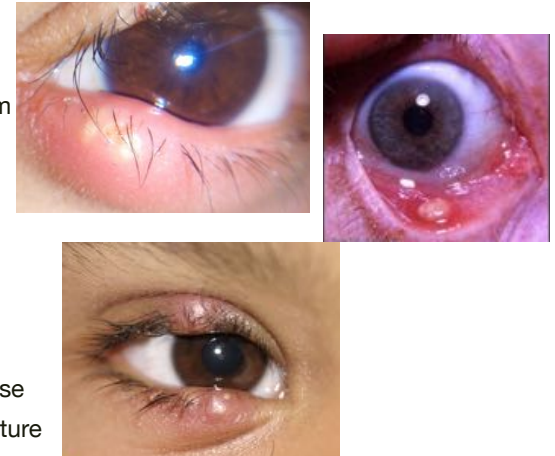
These organisms differ from human eukaryotic cells.

Drugs target these differences.

Drugs affect the microbe without affecting the host.

Ocular Uses of Antibiotics

- Bacterial keratitis
- Canaliculitis
- Chalazion/Hordeolum
- Preseptal cellulitis
- Chlamydia
- Dacryocystitis
- Dacryoadenitis
- Lyme disease
- Eyelid lacerations
- Ocular surface disease
- Orbital blow-out fracture



Antibacterial Terminology:

- Bacteriostatic – stops the growth / replication of the bacteria
- Bactericidal – kills the bacteria



What is your plan?

Treat or turf?

If you treat bacterial infection...

- Bacteriostatic – stops the growth / replication of the bacteria

versus

- Bactericidal – kills the bacteria

Treat to kill.

Choosing the Proper Drug Therapy

- **Efficacy** of Antibiosis
 - **MIC** = minimum inhibitory concentration
 - Lowest concentration that inhibits visible growth (growth-stopping)
 - Measures **bacteriostatic** activity of antimicrobials.
 - **MBC** = minimum **bacteriocidal** concentration
 - Lowest concentration that kills the microbe

Systemic Tx. For MRSA

■ Bactrim (trimethoprim/ sulfamethoxazole)

- 1-2 tabs
- q12h x 1 wk
- Kills ocular, systemic MRSA
 - **Not** one of the FL Fourteen



Antibiotic/Antimicrobial Resistance (ABR/AMR)

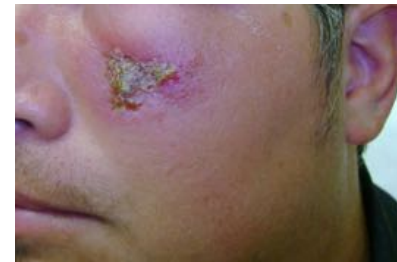
- Antibiotics are vital life and vision saving medicines.
- ABR/AMR is both a global and local problem.
 - In the US, about 2 million people
 - 23,000 people die as a result
 - *The World Health Organization (WHO) has identified AMR as 'one of the biggest threats to global health'.*
 - About 700,000 die people each year worldwide



MRSA – The Superbug

- **Methicillin-resistant Staphylococcus Aureus**
- A strain of staph that's resistant to the broad-spectrum antibiotics commonly used to treat it.
- **MRSA can be fatal.**
- Most MRSA infections occur in hospitals or other health care settings, such as nursing homes and dialysis centers.
- It's also known as **health care-associated MRSA, or HA-MRSA.**
- Older adults and people with weakened immune systems are at high risk of HA-MRSA.
- Health care providers also at risk.

MRSA Ophthalmic Complications



Over 80% of MRSA strains are resistant to **all fluoroquinolones**, a class of antibiotics that has been a mainstay in for the past two decades.



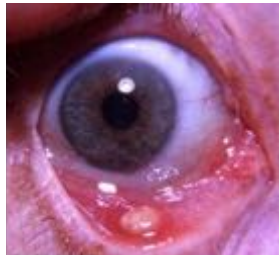
Case Example

- 24 year-old WM c/o painful “bump” on lower left eyelids X 2-3 days
- Med Hx: Unremarkable
- BCVA: OD 20/20, OS 20/20
- Pupils: -APD
- EOM: Full OD/OS
- CVF: FTFC OD/OS

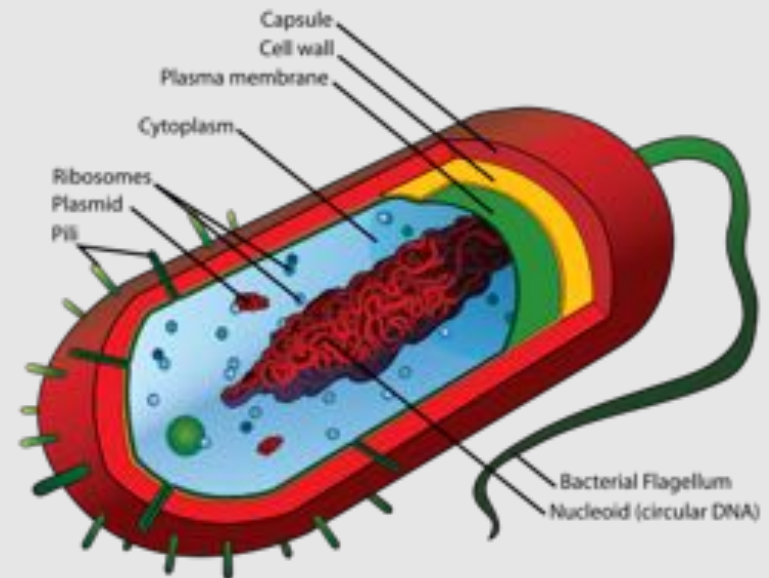


Hordeolum

- *Staphylococcus aureus* is a common cause of hordeolum
- **External hordeolum** involves infection of the glands of Zeis or Moll
- **Internal hordeolum** arises from infection of the meibomian glands



Human cells do not have a cell wall; bacterial cells do



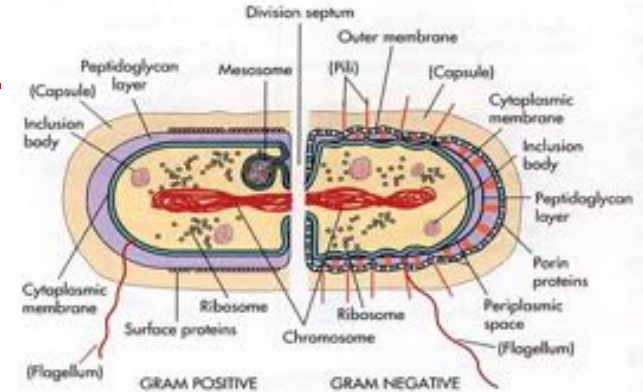
Oral Antibiotics

Five main classes:

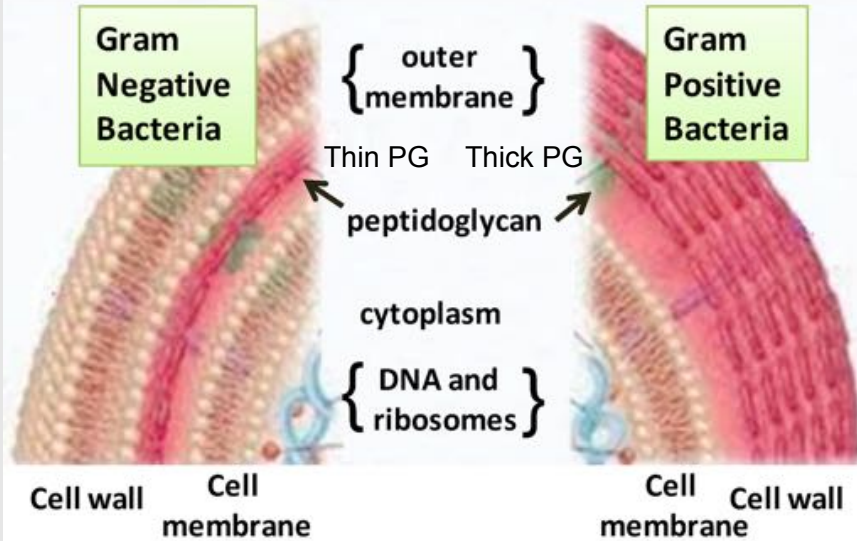
- Penicillins
- Cephalosporins
- Macrolides
- Tetracyclines
- Fluoroquinolones

The trend in oral antibiotic Rx-ing is to simplify dosing and administration ...QD or BID

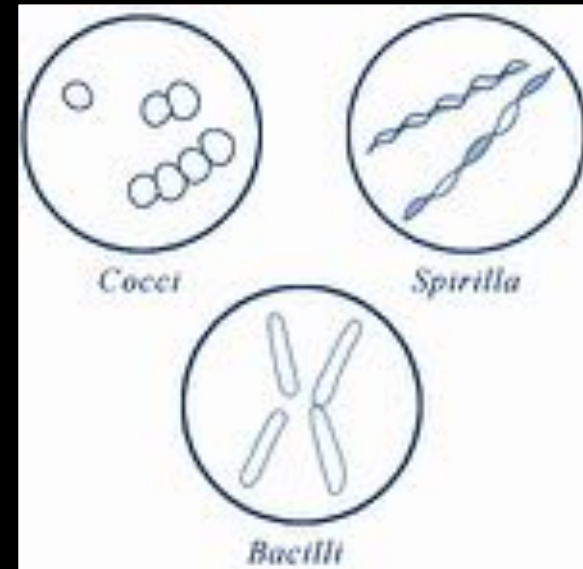
Gram + vs Gram -



- Gram-positive cell walls contain a **thick** layer of **peptidoglycan** that encircles the cell.
- Gram-negative cell walls contain a **thin** layer of peptidoglycan between the cytoplasmic membrane and the outer membrane.

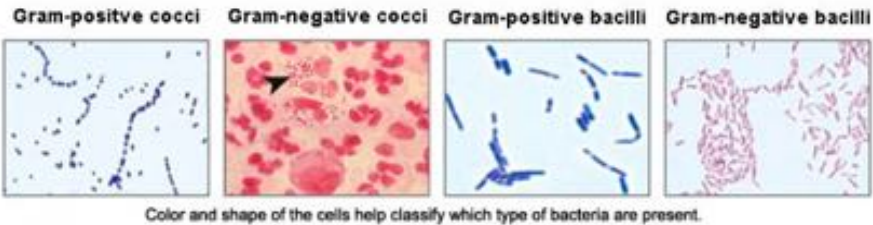


Bacterial genome consists of a single chromosome of circular DNA located in the nucleoid

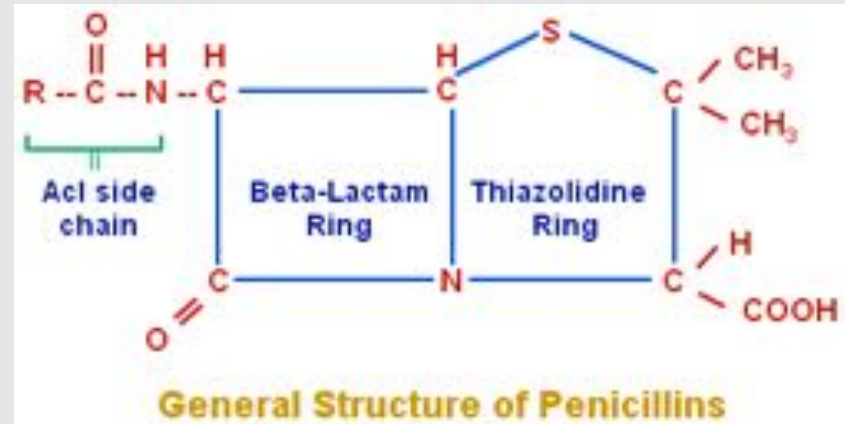


Fortunately, most infections of the eye/adnexa are caused by gram + organisms (staph and strep).

However...



Most staphylococcal bacteria produce an enzyme called Penicillinase ...which inactivates penicillins and some cephalosporins



Penicillins

Bactericidal with relatively low toxicity

Mechanism of Action:

- Inhibits the last step in formation of bacterial cell wall, thus exposing the cell membrane, causing lysis

Natural Penicillins:

- Penicillin G or V
- Gram + except for Staphylococcal
- Penicillin G is IV only drug of choice for syphilis
- Penicillin V is oral used for Strep infections

Penicillins

GROUP I: Ample Spectrum

Generic Name

Trade Name

Amoxicillin

Amoxil®

Ampicillin

Omnipen®

Bacampicillin

Spectrobid®

Carbenicillin Indanyl

Pyopen®,

Geogen®,

Geocillin®

Mezlocillin

Mezlin®

Piperacillin*

Pipracil®

Ticarcillin

Ticar

Amoxicillin

- Dosage

- Adults: 125-875 mg
BID-TID x 7-10 d
- Eg. Preseptal
cellulitis: 500 mg TID
x 10 days
- Children: 20-40 mg/kg
TID x 7-10 d



Prescribing for Children



Step 1: Convert pounds to kilograms by dividing # lbs by 2.2

Step 2: Multiply kilograms by dosage recommendation.

Step 3: Divide daily milligram total by number of doses per day.

Step 4: Choose from available manufactured doses.

Step 5: Write prescription.

Prescribing for Children



Example; 50 lb child Amoxicillin 20 mg/kg TID

Step 1: Convert pounds to kilograms by dividing by 2.2

$$50/2.2 = 23 \text{ kg}$$

Step 2: Multiply kilograms by dosage recommendation.

$$23 \text{ kg} \times 20 \text{ mg/kg} = 460 \text{ mg}$$

Step 3: Divide daily milligram total by number of doses per day.

$$460/3 = 153 \text{ mg}$$

Step 4: Choose from available manufactured doses.

Closest is 125 mg/5 ml.

So, we can write our prescription for amoxicillin 125mg 5ml. We need 5ml TID, so every eight hours (15 ml per day) for 10 days.

So, 15ml/day x 10 days = 150ml bottle.

Final Prescription

Dr. Jane Smith
2020 Main Street
Miami, FL 12345
(305) 123-4567

Name: Laura Fernandez
Address: 4000 Avenue A

Age: 7
Date: 10-15-2016

Rx: Amoxicillin 125/5 #150ml
1 tsp (5 ml) q8h x 10 days

Refills—ZERO

Jane Smith, O.D.

GROUP II: Penicillins and Beta Lactamase Inhibitors

Generic Name

Amoxicillin + Clavulanic Acid

Ampicillin-Sulbactam*

Benzylpenicillin

Cloxacillin

Dicloxacillin

Methicillin

Oxacillin

Penicillin G

Penicillin V

Piperacillin + Tazobactam*

Ticarcillin + Clavulanic Acid

Nafcillin

Trade Name

Augmentin®

Unasyn®

Benpen®

Tegopen®, Coxapen®

Dycill®, Dynapen®,

Pathocil®

Staphcillin®

Prostaphilin®, Bactocil®

Wycellin®

Pen-Veek®, Beepen-VK®

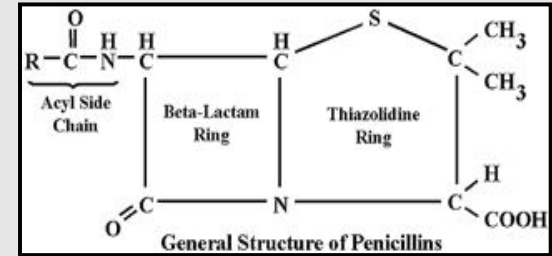
Zozyn®

Timentin®

Unipen®, Nafcil®

Penicillinase Resistant Penicillins

- AKA **Staphylococcal Penicillins**
- Very large R group- C and H attached to molecule
- Methacillin
- Naphcillin
- Cloxicillin
- **Dicloxacillin**

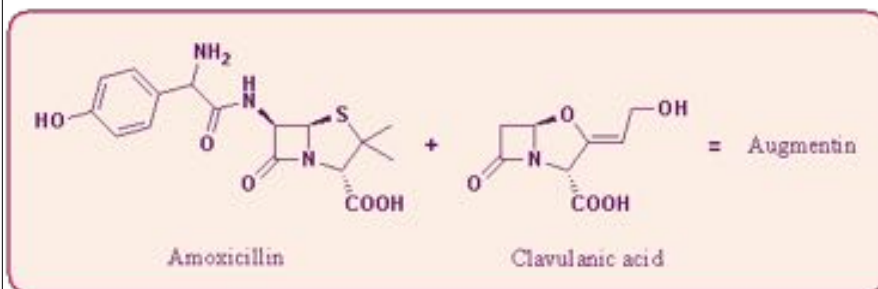


- **Dicloxacillin (Dynapen)** – excellent choice for treatment of internal hordeolum, preseptal cellulitis, dacryocystitis, orbital blow out fractures

Typical Adult Dose: 250-500 mg QID X 7-10 d
For children: 12.5-25 mg/kg QID X 7-10 d

Augmentin: Amoxicillin + Clavulanic Acid

- Clavulanic Acid
– A beta-lactamase inhibitor with some AB activity



GROUP II: Penicillins and Beta Lactamase Inhibitors

- Augmentin = Amoxicillin/clavulanic acid (inhibits beta lactamase)
- Amoxicillin is a pro-drug of Ampicillin

Typical Adult Dose:
500 mg BID or TID X 1 week to 10 days

Augmentin

- Dosage

- Adults: 125-875 mg
 BID-TID x 7-10 d
- Eg. Preseptal
 cellulitis: 500 mg TID
 x 10 days
- Children: 20-40 mg/kg
 TID x 7-10 d



Penicillins

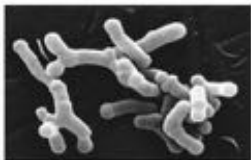
Side Effects



- Diarrhea may occur from increased GI motility
- May occur from a disruption of natural GI flora that is a barrier to infection/aids in carbohydrate digestion

Probiotics vs antibiotics

- Antibiotics
 - damage commensal microflora.
 - can increase the occurrence of resistant bacteria
 - can have adverse side effects
- Probiotics
 - can be used in adjunction to antibiotics to restore the commensal microflora



Penicillins: Side Effects

- Diarrhea is the most common SE
 - ~35% get **Antibiotic Associated Diarrhea (AAD)**,
 - Pseudomembranous Colitis**; 17% of cases = fatal
- Take **probiotics** for prevention and treatment
- Also common are nausea, vomiting, upset stomach
- Allergy 5%** - from degraded beta lactams. Rash, swelling, itch
- Anaphylaxis**- within min - hours, throat. Epinephrine Tx.
- The Penicillins are Category B

Penicillins: Contraindications

- Penicillins are contraindicated in patients who have had serious allergic reactions to them.
 - True penicillin allergy prevalence is actually no greater than 5%.



Anaphylaxis

EMERGENCY

- Ana (*without*) phylaxis (*protection/guard*)
- A serious systemic (multisystem) allergic reaction.
- Rapid in onset
 - *Acute onset of an illness (minutes to several hours)*
 - *The result of a re-exposure to an antigen that elicits an IgE mediated response.*
- **May cause death**
 - *Death can occur in **minutes**, usually due to closure of airways*

Sampson et al. Second symposium on the definition and management of anaphylaxis. J Allergy Clin Immunol 2006;117:391-7)

Severe antibiotic Reaction.....



Steven Johnson Syndrome

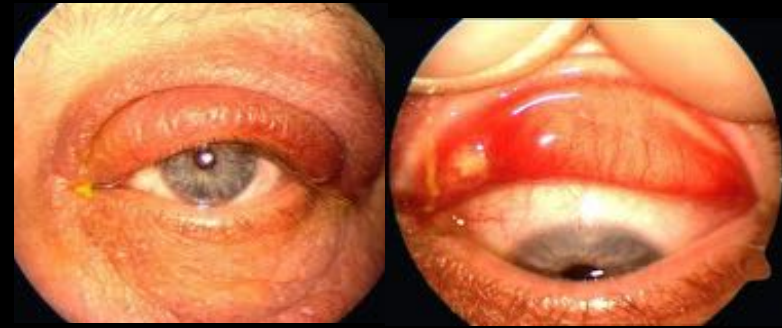
Avoid Drug Resistance

- Don't Rx antibacterial for non-bacterial infection
- Rx full dose, and avoid intermittent use
- Complete the full course of therapy
- Do not taper antibiotic below therapeutic dose

Case

- 55 y/o W M
- CC: LUL red, tender, irritated x 3 days
- Oc Hx: + choroidal nevus, DM w/no DR
- Med Hx: DM x 6yrs, HTN, heart disease, dyslipidemia
- BVA: 20/20-1, 20/20-1
- FROM, FTFC OD OS, No APD
- SLE: see photo

Internal Hordeolum: infection of meibomian gland w/Preseptal Cellulitis



External Hordeolum: infection of glands of Zeiss/Moll

What are you going to do?

- Make sure it is not **orbital** cellulitis!
- **Warning signs:** absence of lid crease, + red, pain, blurred vision, headache, double vision, warmth, proptosis, pain w/ eye movement, restricted motility, fever, decreased periorbital sensation





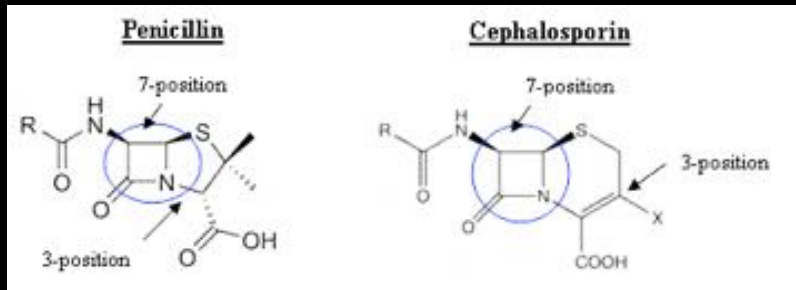
Orbital Cellulitis

Cephalexin

- Brand names
 - Keflex, Biocef, Keftab, Zartan
 - Generic
- Mechanism
 - Inhibits bacteria cell wall synthesis
 - Bactericidal against gram + and gram -
- Uses
 - Hordeola
 - Preseptal cellulitis
 - *S. Aureus*, streptococci, *haemophilus influenzae*



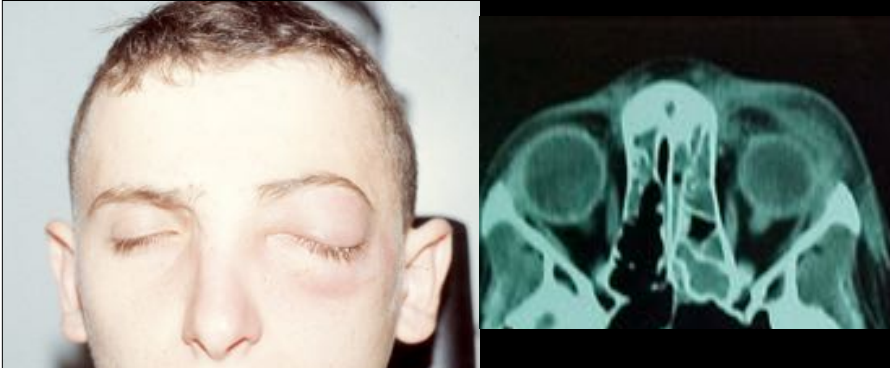
Cephalexin: similar to Penicillins



Preseptal Cellulitis



ORBITAL CELLULITIS



Acknowledgement: Dr. M. Dufek

Cephalexin

- Dosing
 - Adults: 250-500 mg QID x 7-14 days
 - Children: 25-50 mg/kg QID x 7-14 days

- Other uses
 - Dacryocystitis
 - Dacryoadenitis
 - Blow-out fracture



Cephalexin

- Side effects
 - GI disturbances
 - Hypersensitivity reaction
 - Diarrhea, Pseudomembranous colitis
- Contraindications
 - Cephalosporins share slight **cross-allergenicity with penicillins**, therefore...
 - Avoid in patients w/Hx of **life threatening** reactions to penicillin (2-4%)



Cephalexin

- Pregnancy / nursing
 - **Category B**
 - Presumed safe based upon animal studies
- Children
 - OK over age 5
 - 25-50 mg/kg/day divided into 4 doses
 - 7-14 days



Penicillins/Cephalosporins

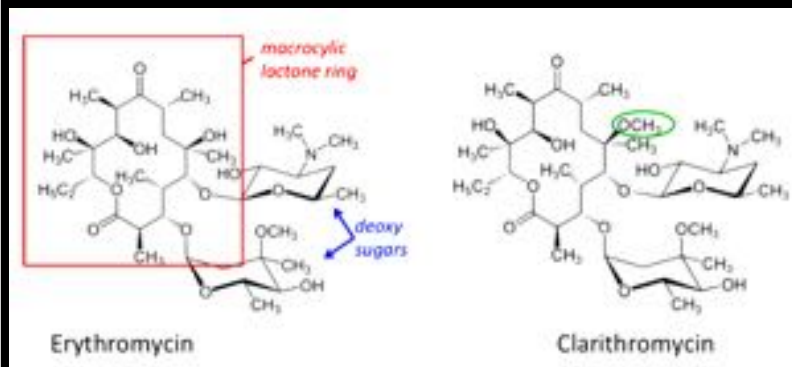
Adverse Reactions:

- Hypersensitivity reactions
~ 5% (rash, angioedema, anaphylaxis)
- Diarrhea
- Nausea
- Vomiting
- Keflex: **Sulfa cross-sensitivity in 15% of cases**

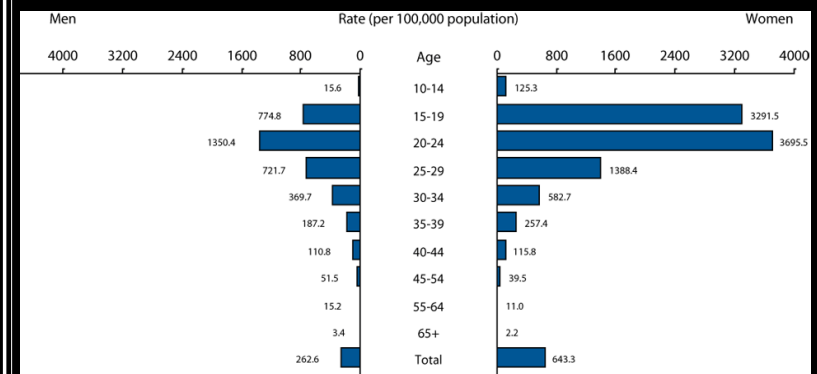
Macrolides

- Chemically made of a large macrolide ring onto which are attached various sugars
- **MOA: Interfere with bacterial ribosomal protein synthesis**
 - **Bacterial ribosomes are structurally different from mammalian**
 - Bacteriostatic (in general)
 - Can be bactericidal in higher doses

Macrolide Structure



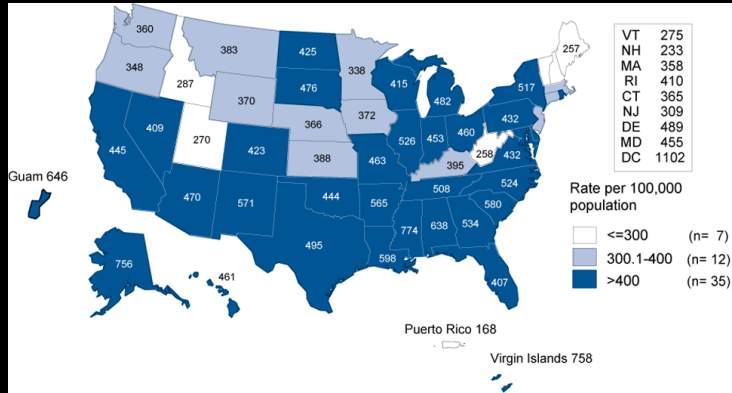
Chlamydia Statistics



As many as 25% of men with chlamydia have no symptoms. In men, chlamydia may produce symptoms similar to gonorrhea.

About 70% of women with chlamydia have no symptoms

Chlamydia Statistics



One can get chlamydia with gonorrhea or syphilis, so if you have one STD you must be screened for other sexually transmitted infections as well. All sexual contacts should be screened for chlamydia.

Macrolides

Generic Name

Azithromycin*
 Clarithromycin*
 Clindamycin
 Dirithromycin
 Erythromycin

Lincomycin
 Troleandomycin

Trade Name

Zithromax®
 Biaxin®
 Cleocin®
 Dynabac®
 E-mycin®,
 Benzamycin®
 Lincocin®
 Tao®

Azithromycin (Zithromax)

- Drug of choice for Chlamydia
 - 1 gram either as a single dose or once weekly x 3 wks
- Z-PAK
- New Zithromax Tripak
 - Three 500 mg tablets
 - For adults



Z-PAK



Macrolides: Dosing

Erythromycin (E-Mycin) 500mg BID x 1week (mainly gram +)

Azithromycin (Zithromax) Two 250 mg tabs on day 1, then one 250 mg tab QD x 4 days (Z-Pak)

Clarithromycin (Biaxin) 250 mg or 500 mg BID x 7 days (gram +)

- Chlamydia – single dose 1000 mg Azithromycin

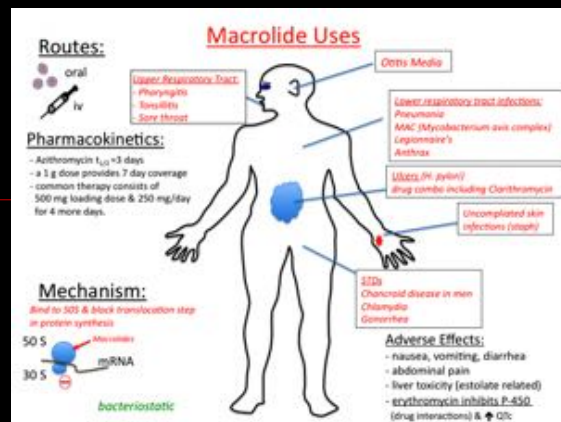
Important Note:

- Consider an oral fluoroquinolone over macrolides if penicillin allergy because macrolides are bacteriostatic.

Macrolides

- Generally effective against **gram +** (and some gram –) bacteria
- Effective against **chlamydia**
- Also have **anti-inflammatory** properties, so good alternative for MGD when tetracyclines are contraindicated.

Indications



Macrolides

- Generally safe
- Most common SEs are on **GI tract**
 - Nausea, vomiting, diarrhea
 - Some are enteric coated to reduce these effects (**EES 400**)
 - Can cause an **elongated QT interval**, leading to abnormal heart rhythm.



Macrolide Rx'ing

- Clarithromycin (Biaxin) 500
 - 1 PO BID to TID x 1 week
- Azithromycin (Zithromax, Z-Pak, TriPak)
 - Z-Pak: 500mg day 1 and 250mg day 2-5
 - Children: 10 mg/kg day 1, 5 mg/kg day 2-5
 - TriPak: 500mg X 3 days

Macrolides: Disadvantages

- Use with caution in patients with known liver dysfunction, cardiac issues
- Limited activity against Hemophilus
- Increasing resistance and limited spectrum
- Azithromycin and Erythromycin = Category B
- Clarithromycin, dirithromycin, troleandomycin = Category C

Chronic Lid AB Therapy

- When Rx'ing PO antibiotics for several weeks duration, GI toxicity can become a problem
- Yeast infections also become common in female patients
- May need to Rx po Diflucan, probiotics

Systemic Tx. For MRSA

- Bactrim (trimethoprim/
sulfamethoxazole)
 - 1-2 tabs
 - q12h x 1 wk
 - Kills ocular, systemic MRSA
 - Not one of the FL Fourteen

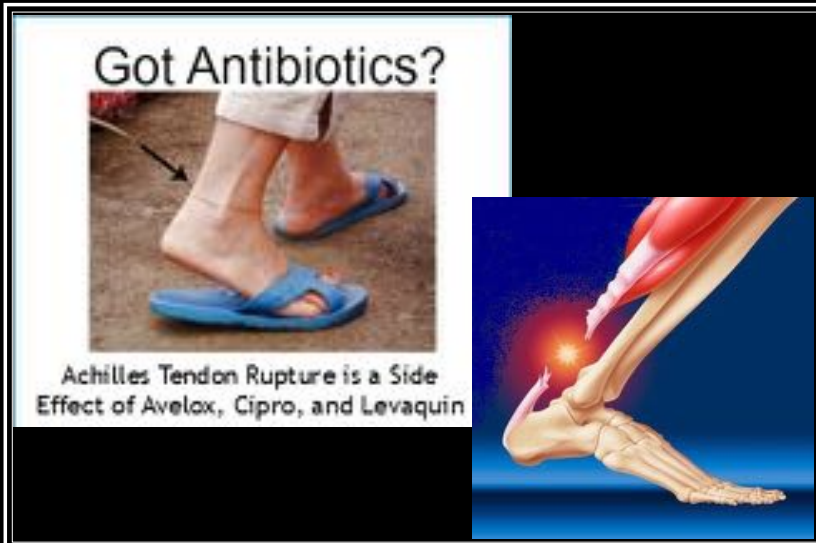


Fluoroquinolones:

- Inhibit enzyme called DNA gyrase
- Bactericidal
- Not related chemically to the penicillins or cephalosporins
- Excellent oral absorption – skin infections and STD
- Ciprofloxacin (Cipro) 500 mg BID X 1 week
- Levofloxacin (Levaquin) 500 mg QD X 1 week ****
- Ofloxacin (Floxin) 400 mg BID X 1 week
- Norfloxacin (Noroxin) 400 mg BID x 1 week

Fluoroquinolones:

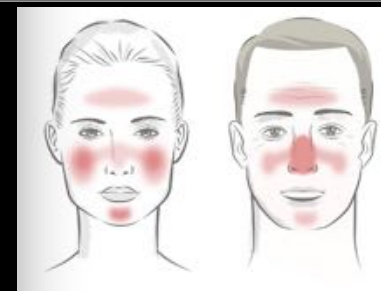
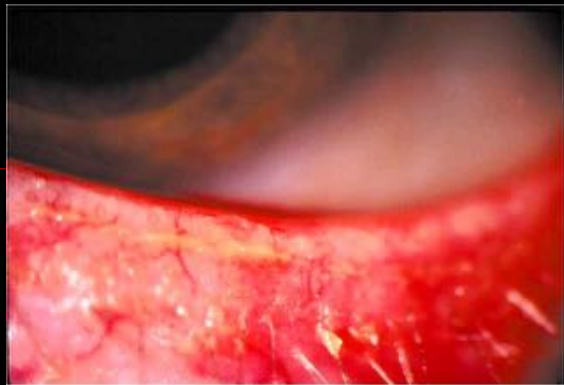
- All drugs in this class have been associated with convulsions.**
- Fluoroquinolones are classed category C
- The Fluoroquinolones are well tolerated by patients and are relatively safe. They do not affect human DNA
- Nausea, vomiting, diarrhea, and abdominal pain are some of the common side effects reported
- Should not be used in kids under 15 years old



CASE: 61 Y/O WM

- CC: red, burning, sandy feeling, crusty OU
- Oc Hx: LEE 2 yrs, unremarkable
- Med Hx: Rosacea x many years
- BVA: 20/20-1, 20/20-1
- FROM, FTFC OD OS, NO APD
- SLE: see photo
- IOP: 12/12 @ 9:40am
- DFE: unremarkable OU

61 Y/O WM



Rosacea
What is your plan?

Azithromycin 1% sol

- AzaSite® (Akorn)
- Macrolide AB
 - Broad-spectrum
 - Anti-inflammatory?
- Approved for children >1 y/o
- Approved for **bact conj only**.



Azithromycin Ophthalmic Sol.

- Dosing
- 1 drop bid for first two days
- then 1 drop once daily for next five days.



Is topical Tx. enough for mod/
severe rosacea-associated MGD
and ant bleph?



Rosacea: Clinical Signs



Lissamine Green Staining

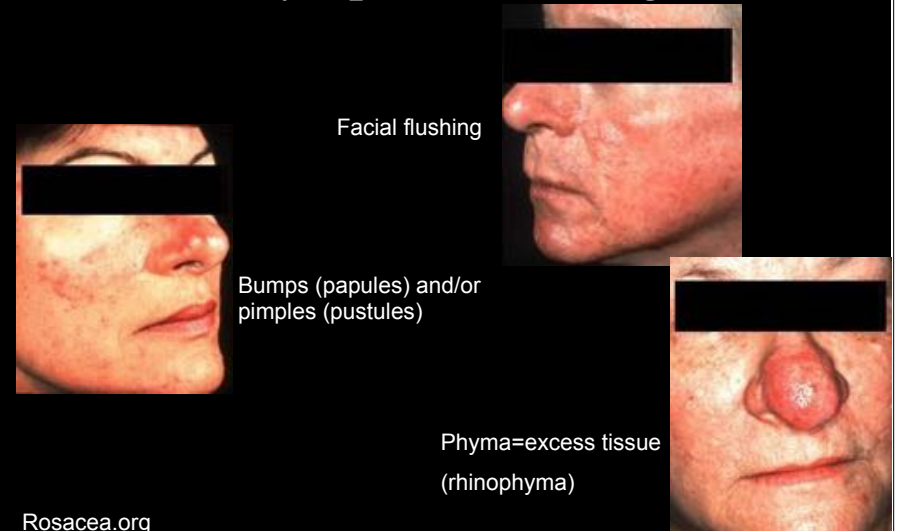


Doxycycline

- Brand names
 - Adoxa, Doryx, Monodox, Oracea, Periostat, Vibramycin, Doxy-100, Vibra-tabs
 - Generic
- Mechanism
 - Inhibits protein synthesis
 - Restores lipid production
 - Effective against gram + and gram -
- Uses
 - Blepharitis
 - Meibomianitis, Hordeola
 - Preseptal Cellulitis
 - Dacryocystitis/adenitis



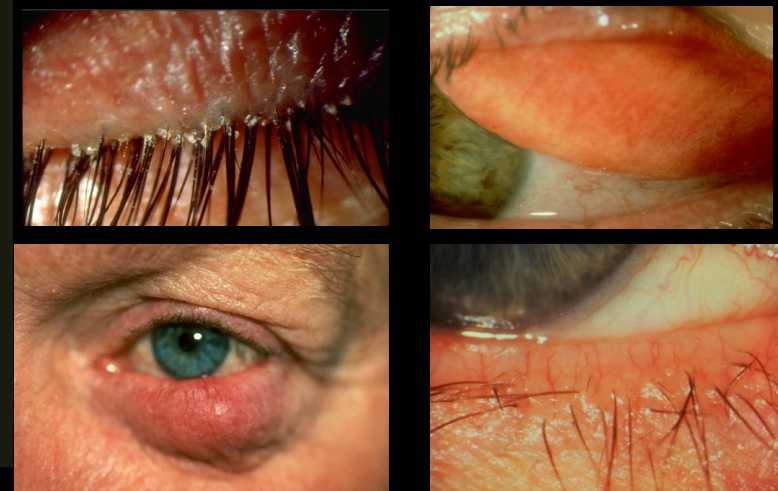
Rosacea Symptoms and Signs



Common Case



Ocular Rosacea



Doxycycline- the “triple duty” drug

- Anti-seborrheic
 - MGD/ Rosacea
- Anti-infective
 - Similar indications to Ceclor or Keflex
- Anti-inflammatory/anti-collagenase
 - Corneal ulcers, erosions, abrasions
 - Severe ocular surface inflammatory disease
 - Contraindicated in pregnant women and kids under age 8
- Side- Effects
 - GI Upset
 - Nausea, diarrhea, pseudomembranous colitis
 - For nausea, administer with food
 - Tooth discoloration, bone deformity
 - Photosensitization
 - Pseudotumor cerebri



Doxycycline Dosing

- For MGD: 100-200 mg first day, then 50-100 mg a day for up to 21 days
- For Chlamydia: 100 mg BID x 7+ days
 - *Azithromycin 1 g 1 dose is preferred by some, but not all authorities*
- For ancillary treatment of corneal abrasion, ulcers, erosions: 50-100 mg QD

Pediatric Dosage Calculation

- **Clark's Rule**

$$\text{Pediatric Dose} = \text{Adult Dose} \times \text{Weight (kg)} / 70$$

Or

$$\text{Adult Dose} \times \text{Weight (lb)} / 150$$

- Pediatric Dosage Calculation By Age

Age	Percent of Adult Dose
>12	100%
6-12	50%
2-6	25%

Doxycycline

- Dosing for bleph/MGD
 - 100 mg qd-bid for 2-6 weeks, then taper slowly
 - Some need 20-50 mg/d indefinitely

- Other Ophthalmic Uses

- Recurrent corneal erosion
- Chlamydia/trachoma
- Lyme disease
- Bartonella Neuroretinitis



The Tetracyclines

- Generally bacteriostatic, though higher doses may be bactericidal.



Tetracyclines

- When longer-term therapy is needed:
 - Periostat (doxycycline hyclate)
 - 20mg tab
 - Qd or bid
 - Initially developed for periodontitis
 - Now available as **generic**.
 - Oracea (doxycycline monohydrate)
 - \$\$\$

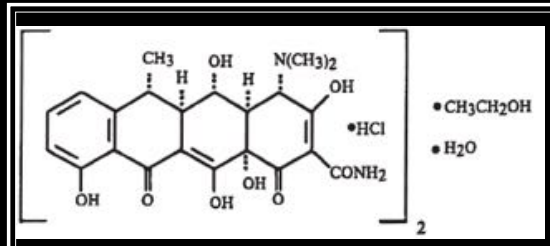


Periostat

©2004 GSM

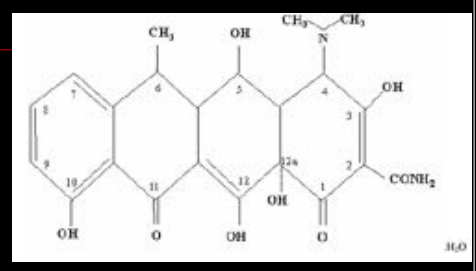


Oracea



Periostat
(doxycycline hyclate)

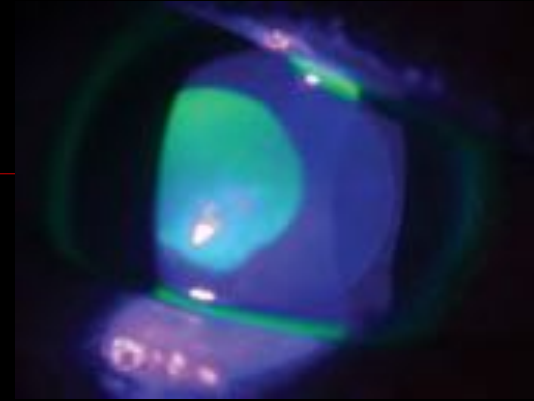
Oracea
(doxycycline monohydrate)



Oracea

- FDA approved in 4/2006 Oracea (doxycycline, CollaGenex Pharmaceuticals) to treat inflammatory rosacea in adults.
 - 1st drug approved for Papulopustular Rosacea only
 - Contains **30mg of immediate-release medication and 10mg delayed-release medication** in capsule
 - Exhibits anti-inflammatory and not antimicrobial properties, so no drug resistance issues

Recurrent Erosion

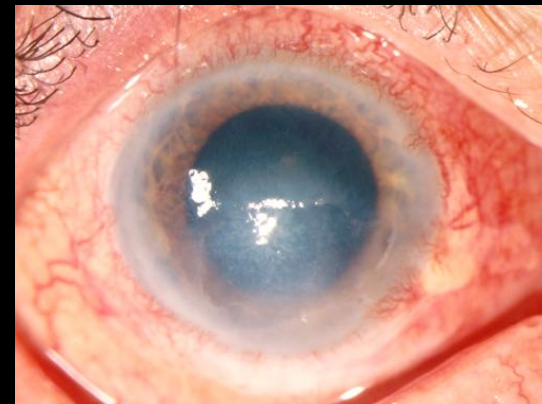


PO Doxy for RCE

Wang L, Tsang H, Coroneo M. Treatment of recurrent corneal erosion syndrome using the combination of oral doxycycline and topical corticosteroid. Clin Exp Ophthalmol. 2008 Feb;36(1):8-12.

- ◆ In one study, patients with RCE received 50mg oral doxycycline BID and topical fluorometholone 0.1% TID for at least 4 wks.
- ◆ After eight weeks of treatment, 71% of the subjects were symptom free.
- ◆ Further, 73% of patients denied any symptoms suggestive of relapse at either 6 or 12 months, respectively.

Chemical Burn



- ❖ Oral doxycycline (100 mg po bid) may be used in the acute phase of chemical burns involving the cornea
- ❖ Reduces collagenase activity and sterile ulceration
 - This activity is independent of its antimicrobial properties
 - Probably due to chelation of zinc at active site of the enzyme
 - Inhibits neutrophil (PMN leukocyte) and MMP (matrix metalloproteinase) activity

Side Effects



Doxycycline

- Side effects (all Tetracyclines)
 - Photosensitivity
 - **Pseudotumor cerebri**, blood dyscrasias
 - Decreased bone growth, teeth discoloration
- Contraindications (all Tetracyclines)
 - Under age 8
 - **Pregnancy Category D**
 - Nursing
 - Liver dysfunction



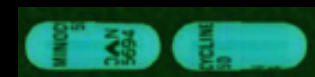
Combination Therapy



Cleeravue-M Kit
50mg **minocycline**
tabs
+
SteriLid



Thera tears
linalool and tea tree
oil kill **Demodex**



Doxycycline

- Children
 - OK over age 8 (12)
 - 1-2 mg/kg Q12-24 h. Duration not to exceed 5 d
- Miscellaneous information
 - Take **with** or without food
 - With food may reduce absorption by 20%
 - Without food may cause GI irritation

Doxycycline

- Do not take with dairy or calcium
- Take at least 2 hrs before lying down
- Avoid antacids
- Oral contraceptives may not work

Minocycline



Minocycline

- Has **extended MIC** bioavailability
 - Adults: 50-100 mg BID x 1-6 wks
 - Children over age 8 (12): 50 mg Q12h not to exceed 5 d
- MIC levels measured in lids remain elevated for weeks after medication is d/c
 - Chronic therapy (4-8 weeks) can result in extended MIC levels

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

Moderate-severe Ocular Pain



Systemic Steroids: Side Effects

- Weight gain
- PSC
- IOP rise
- Central Serous Chorioretinopathy

Bonus Case



Case Example



Differential Diagnosis

- a. Diffuse Episcleritis
- b. Bacterial Conjunctivitis
- c. Diffuse Anterior Scleritis

Differential Diagnosis

- a. Diffuse Episcleritis
- b. Bacterial Conjunctivitis
- c. Diffuse Anterior Scleritis

Persistent History

- Are you certain that you've never had previous episode or medical problem?
- Patient then reported a history of long-standing Rheumatoid Arthritis
- Observation of hand joints

Scleritis



What is your plan?

Treatment for Scleritis

- NSAIDS
- Systemic steroids
- Immunosuppressive therapy
- Topical steroids???

**ANTI-
INFLAMMATORIES**

NSAIDS

- **Ibuprofen**
 - 800 mg q4h for anti-inflammatory activity
 - Suppresses inflammatory cascade by inhibiting COX pathway
- Used for mild inflammation with additional benefit of analgesia
 - Moderate-severe episcleritis
 - Ocular surface injuries
 - Mild scleritis
 - Many others
- Side effects and contraindications
 - peptic ulcers
 - bleeding disorders



Corticosteroids

- **Prednisone**
 - Dosing varies widely, 5 mg – 100 mg / day depending on tapering, severity of symptoms, body weight, degree of vascularization of target tissue, etc.
 - 20-40 mg/day typical for mild-moderate disease (mild scleritis)
 - 80-100 mg/day may be necessary for severe scleritis and related conditions



Side effects and contraindications

- Psychosis
- GI/Peptic ulcers
- Diabetes- hyperglycemia
- Fluid retention (moon face)
- Hypertension
- Immunosuppression
- Chronic renal failure
- Increase IOP
- Cataracts (PSC)

Oral Corticosteroid Considerations

- Accurate diagnosis is essential
- Indicated for acute inflammatory eye, orbital and eyelid conditions
- Pregnancy category C
- Dose paks available
 - – 24 mg, 30 mg, 60 mg with taper
- Best taken with meals
- Short term rarely has ocular side effects

Actual Plan

- Prednisone 60mg po q day x 2 weeks
- Followed by 5 wk taper
- PCP/Rheumatology referral for complete physical
 - CBC (including differential + platelets)
 - ANA, CRP
 - Rheumatoid arthritis diagnostic panel

s/p 2 wks 60 mg po Pred



s/p 2 more wks on po Pred



Serology Results

- CRP 2.41 H < .8 mg/dL
- RF 39 H < 14 IU/mL
- **Cyclic Citrullinated Peptide Antibody (Anti-CCP)**
 - Highly specific for RA w/+ RF
 - Predictive of progressive joint destruction
 - > 59 is strong +; MP was out of range (>60)

Prednisone

- Brand names
 - Orasone, Meltasone, Medrol
 - Generic
- Mechanism
 - Suppresses leukocyte migration, capillary permeability
 - Reduces activity and volume of lymphatic system
- Common Ophthalmic Uses
 - Scleritis, Severe Uveitis, Orbital Inflammatory Pseudotumor



Prednisone

- Side effects
 - Reduced immunity, adrenal insufficiency
 - Secondary diabetes
 - Cushing's disease
 - Slow wound healing
 - Weight gain
 - Mood swings
 - Cataract, IOP rise
- Contraindications
 - Serious infections, fungal infections
 - Brittle diabetics



Prednisone

- Pregnancy / nursing
 - **Category C**
- It is not known whether Prednisone is harmful to an unborn baby.
 - Caution to those lactating
- Children
 - Generally OK; check with Peds
- Miscellaneous information
 - Take with food, taper as needed
 - Medrol dose packs for short term, low dose Tx.
- Tapering steroids too quickly may cause **adrenal insufficiency**, resulting in symptoms including headache, fatigue, joint and muscle pain, weight loss, hypoglycemia and fever, which may range from mild to life-threatening.**



Alternative Pharmacotherapies

- Systemic NSAIDs
- Indications: scleritis, uveitis
- **Indomethacin 25mg qid** until significant improvement, then tid until complete resolution.
 - Less side effects than steroids
- Ibuprofen 400-600mg qid

The “Systemic Seven”

Top systemic Drugs used in Optometry



Access and Assistance

- Rebate programs
- GoodRx.com
- Lower-priced options
 - Polytrim
 - Maxitrol
 - Acyclovir
 - Pred sodium phosphate 1% sol



Remember Your ABCDs

of Med Prescribing:

A = Allergies

B = Body weight

C = Current Medications

D = Diseases



Conclusions

- The ability to prescribe therapeutic agents has enabled optometry to establish itself as a true primary health care profession.
- “With great power comes great responsibility.”
 - Uncle Ben in Spiderman
- Prescribe wisely!



Thank you!

Joe

pizzimen@uiwtx.edu

