

# Oral Pharmaceuticals in Anterior Segment Disease

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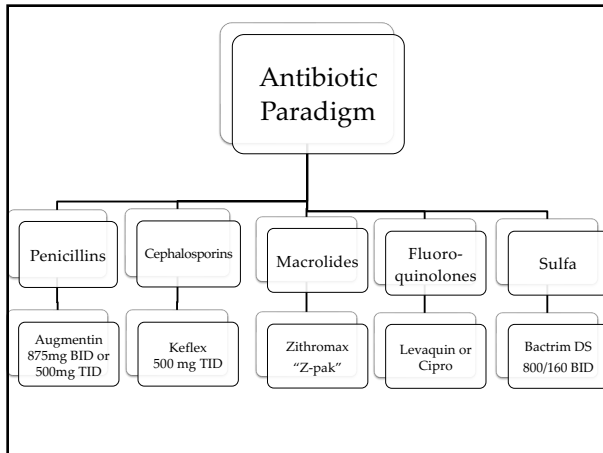
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## Disclosures

- Aerie Pharmaceuticals
- Allergan
- Avellino
- B&L
- Bruder
- Diopsys
- Dompe
- Ellex/LumiBird
- EyePromise
- Horizon
- iCare
- Innova Systems
- Ivantis
- Lumenis
- Nidek
- Novartis
- Ocusoft
- Optovue/Visionix
- Orasis
- Oyster Point
- Reichert
- RVL Pharmaceuticals
- Sight Sciences
- Sun Pharma
- Tarsus
- Thea Pharmaceuticals
- Triad Ophthalmics

All relevant relationships have been mitigated

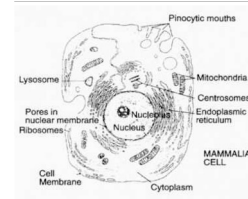
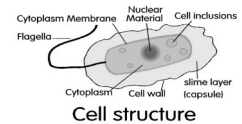
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## Principles of Antimicrobial Therapy

- Structural and biochemical differences exist between humans and microorganisms. Antimicrobial therapy takes advantage of these differences, e.g.
  - Bacterial cell wall
  - Bacterial ribosomes



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## Principles of Antimicrobial Therapy

- Selection of an appropriate antimicrobial requires:
  - knowledge of the organisms identity,
  - its susceptibility,
  - site of infection,
  - safety of agent,
  - cost of therapy, and
  - patient factors.
- Often, the organism is not conclusively identified, and the treatment is empirical.
  - the choice of agents in the absence of confirmatory testing may be guided by known association of a particular organism with an infection in a given clinical setting

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### Overview of Bacterial Infections

A human body diagram with various bacterial infections listed by location:

- Bacterial meningitis**
  - *Streptococcus pneumoniae*
  - *Neisseria meningitidis*
  - *Haemophilus influenzae*
  - *Streptococcus agalactiae*
  - *Listeria monocytogenes*
- Otitis media**
  - *Streptococcus pneumoniae*
- Pneumonia**
  - Community-acquired:
    - *Streptococcus pneumoniae*
    - *Haemophilus influenzae*
    - *Staphylococcus aureus*
  - Atypical:
    - *Mycoplasma pneumoniae*
    - *Chlamydia pneumoniae*
    - *Legionella pneumophila*
  - Tuberculosis
    - *Mycobacterium tuberculosis*
- Skin infections**
  - *Staphylococcus aureus*
  - *Streptococcus pyogenes*
  - *Pseudomonas aeruginosa*
- Sexually transmitted diseases**
  - *Chlamydia trachomatis*
  - *Neisseria gonorrhoeae*
  - *Treponema pallidum*
  - *Ureaplasma urealyticum*
  - *Haemophilus ducreyi*
- Eye infections**
  - *Staphylococcus aureus*
  - *Neisseria gonorrhoeae*
  - *Chlamydia trachomatis*
- Sinusitis**
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
- Upper respiratory tract infection**
  - *Streptococcus pyogenes*
  - *Haemophilus influenzae*
- Gastritis**
  - *Helicobacter pylori*
- Food poisoning**
  - *Campylobacter jejuni*
  - *Salmonella*
  - *Shigella*
  - *Clostridium*
  - *Staphylococcus aureus*
  - *Escherichia coli*
- Urinary tract infections**
  - *Escherichia coli*
  - Other Enterobacteriaceae
  - *Staphylococcus saprophyticus*
  - *Pseudomonas aeruginosa*

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## Principles of Antimicrobial Therapy

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  - cost of therapy, and
  - patient factors.
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## Principles of Antimicrobial Therapy

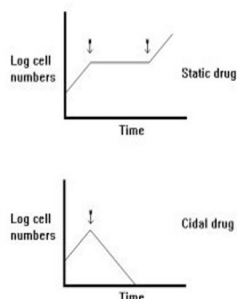
- Adequate levels of the antibiotic must reach the site of infection.
  - different tissues have variable permeability to the drugs.
  - natural barriers to drug delivery exist, such as prostate, CNS, brain and vitreous.
- Patient factors are crucial in drug selection. For example:
  - the status of patient's immune system,
  - kidneys, liver, circulation,
  - age, gender, pregnancy, breast feeding,
  - allergies, etc.

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## Principles of Antimicrobial Therapy

### • Bacteriostatic vs. Bactericidal drugs:

- **bacteriostatic** drugs "arrest" the growth and replication of bacteria thus limiting the spread of infection while the body attacks.
- **bactericidal** drugs kill bacteria at serum concentration levels



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## Principles of Antimicrobial Therapy

- many of the antibiotics are minimally toxic
  - such as penicillins as they interfere with a site unique to bacteria growth
- others are reserved for life-threatening infections because of potential for serious toxicity
  - e.g. chloramphenicol
- cost of therapy also needs to be considered,
  - ie. if similar efficacy is achieved with a generic or less expensive medication (or combo of meds) that may increase compliance.

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## Chemotherapeutic Spectra

- **Narrow-spectrum antibiotics:**
  - act only on a single or a limited group of microorganisms, e.g. isoniazid active only against mycobacteria.
- **Extended-spectrum antibiotics:**
  - effective against gram (+) and significant number of gram (-) bacteria, e.g. ampicillin.
- **Broad-spectrum antibiotics:**
  - effective against wide variety of microbial species (e.g. tetracycline and chloramphenicol).
  - their use can drastically alter the bodies normal flora (and result in superinfections)

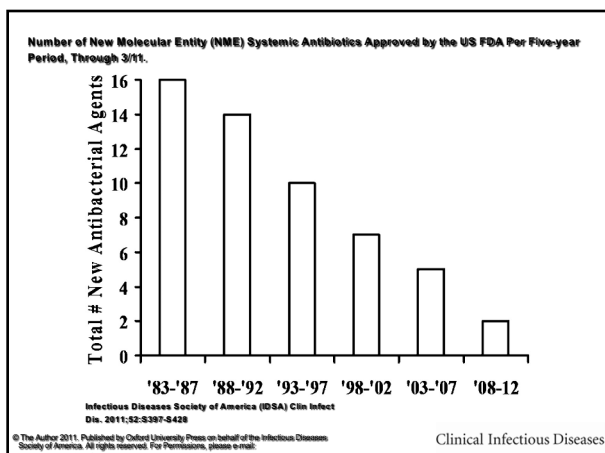
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## Preventing Resistance

- Just one organism, methicillin-resistant Staphylococcus aureus (MRSA), kills more Americans every year (~19,000) than emphysema, HIV/AIDS, Parkinson's disease, and homicide combined
  - most serious MRSA infections, an estimated 85%, are associated with a healthcare exposure, but nearly 14% of the infections are community-associated.
- Almost 2 million Americans per year develop hospital-acquired infections (HAIs), resulting in 99,000 deaths the vast majority of which are due to antibiotic-resistant pathogens
- CDC: *Get Smarts: Know When Antibiotics Work*
  - teaches both the provider and the patient when antibiotics should be used.
- **The IDSA suggests five to seven days is long enough to treat a bacterial infection** without encouraging resistance in adults, though children should still get the longer course
  - this is different than previous guidelines of treating infections from 10-14 days.

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## Shortage of New Antibiotics

- In 2010, in recognition of the need for creative, new ideas to address the antibiotic pipeline problem and a measurable goal by which to gauge progress, IDSA (Infectious Diseases Society of America) launched the “10 × ’20 initiative” .
  - The 10 × ’20 initiative calls for the development of 10 novel, safe and effective, systemic antibiotics by 2020.

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## New Class of Antibiotics

- Fidaxomicin (Dificid) is the first of a new class of antibiotics called macrocycles and was approved by the FDA in May 2011;
  - Optimer Pharmaceuticals
  - it's a narrow-spectrum drug aimed specifically at *Clostridium difficile*,
    - the bacterial, toxin-producing, potentially fatal infection of the gut that occurs when broad-spectrum antibiotics have killed off the other populations of bacteria that normally live in the intestines
  - Fidaxomicin's existing competition is vancomycin
    - as compared against vancomycin, fidaxomicin was “noninferior,” in industry jargon

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## Preventing Resistance

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## Ocular TRUST 3: Ongoing Longitudinal Surveillance of Antimicrobial Susceptibility in Ocular Isolates

- Background:
- Ocular TRUST is an ongoing annual survey of nationwide antimicrobial susceptibility patterns of common ocular pathogens.
- To date, more than 1,000 isolates from ocular infections have been submitted to an independent, central laboratory for in vitro testing.
- Ocular TRUST, now in its third year, remains the only longitudinal nationwide susceptibility surveillance program specific to ocular isolates.

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## Ocular Trust 3

- Antimicrobials tested represent six classes of drugs:
  - fluoroquinolones (ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin);
  - dihydrofolate reductase inhibitors (trimethoprim);
  - macrolides (azithromycin);
  - aminoglycosides (tobramycin);
  - polypeptides (polymyxin B); and
  - $\beta$ -lactams (penicillin).
- Staphylococci were classified as methicillin-resistant (MRSA) or methicillin-susceptible (MSSA) based on susceptibility to oxacillin.

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## Ocular Trust 3: Results

- most antimicrobials, except penicillin and polymyxin B, continue to be highly active against MSSA (azithromycin shows only moderate activity)
- with the exception of trimethoprim and tobramycin, less than one-third of MRSA strains are susceptible to ophthalmic antimicrobials
- susceptibility profiles remain virtually identical for the fluoroquinolones, regardless of methicillin phenotype
- S. aureus is more susceptible to the fluoroquinolones than to macrolides, as represented by azithromycin

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## 2015 ARMOR study

- Trimethoprim
  - MRSA 93% susceptible
  - MSSA 97% susceptible
- Clindamycin
  - MRSA 69% susceptible
  - MSSA 93% susceptible
- Azithromycin
  - MRSA 7% susceptible
  - MSSA 57% susceptible
- Levofloxacin
  - MRSA 24% susceptible
  - MSSA 86% susceptible

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## 2015 ARMOR Susceptibility Rates

- **MRSA**
- Vancomycin 100%
- Trimethoprim 93%
- Tobramycin 56%
- Moxi/gatifloxacin 25%
- Besifloxacin N/A\*
- **Pseudomonas**
- Levofloxacin 93%
- Gati/Moxi/Besifloxacin N/A\*
- Tobramycin 97%
- Polymyxin B 89%

\*Had lowest MIC of all antibiotics but unable to determine statistical significance

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## 2018 ARMOR study

- Trimethoprim
  - MRSA 89.7% susceptible
  - MSSA 96.2% susceptible
- Clindamycin
  - MRSA 68.0% susceptible
  - MSSA 92.4% susceptible
- Vancomycin
  - MRSA 100% susceptible
  - MSSA 100% susceptible
- Tobramycin
  - MRSA 50.3% susceptible
  - MSSA 95.2% susceptible
- Azithromycin
  - MRSA 6.5% susceptible
  - MSSA 60.3% susceptible
- Levofloxacin
  - MRSA 21.4% susceptible
  - MSSA 87.9% susceptible
- Moxifloxacin
  - MRSA 23.5% susceptible
  - MSSA 89.1% susceptible
- Gatifloxacin
  - MRSA 21.4% susceptible
  - MSSA 87.5% susceptible

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## 2018 ARMOR study

- Polymyxin B
  - Pseudomonas 95.8% susceptible
- Tobramycin
  - Pseudomonas 96.4% susceptible
- Azithromycin
  - Strep Pneumo 68.6% susceptible
- Levofloxacin
  - Pseudomonas 93.0% susceptible
  - Strep Pneumo 100% susceptible
- Moxifloxacin
  - Pseudomonas N/A
  - Strep Pneumo 100% susceptible
- Gatifloxacin
  - Pseudomonas 91.6% susceptible
  - Strep Pneumo 100% susceptible

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## 2018 ARMOR Susceptibility Rates

- **MRSA**
- Vancomycin 100%
- Trimethoprim 89.7%
- Clindamycin 68.0%
- Tobramycin 50.3%
- Moxifloxacin 23.5%
- Gatifloxacin 21.4%
- Besifloxacin N/A\*
- **Pseudomonas**
- Tobramycin 96.4%
- Polymyxin B 95.8%
- Levofloxacin 93.0%
- Ciprofloxacin 91.7%
- Gatifloxacin 91.6%
- Moxifloxacin N/A\*
- Besifloxacin N/A\*

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## Ocular Trust 3 & ARMOR Results

- For suspected ocular MRSA infection the most effective topical treatment includes (in order):
  - Vancomycin
  - Besifloxacin (Besivance)
  - Polytrim
  - Tobramycin

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## OPHTHALMIC MRSA INFECTIONS IN THE PARKLAND HEALTH AND HOSPITAL SYSTEM, 2000 – 2004

Blomquist, *Trans Am Ophthalmol Soc* 2006;104:322-345

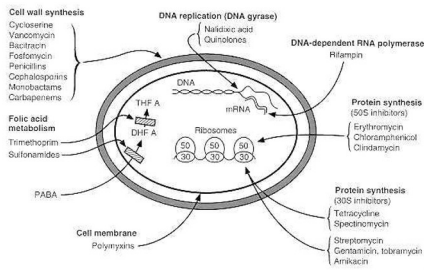
**1 million patients seen in the system from 2000-2004, with 3460 confirmed MRSA infections**  
**- of the total MRSA infections, 1.3% if them were ocular**

Ophthalmic Infection	Percent of Cases
Preseptal cellulitis	42%
Conjunctivitis	21%
Corneal ulcers	10%
Endophthalmitis	8%
Orbital cellulitis	2%
Other: e.g. dacryocystitis	10%

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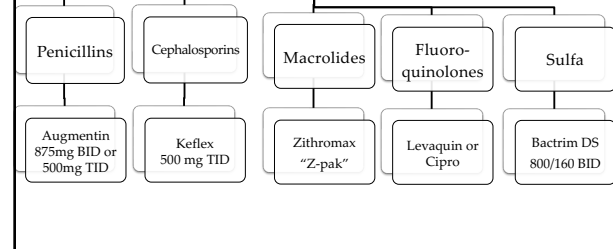
## Sites of Antimicrobial Actions

- Antibiotics can be classified by their chemical structure, the organisms they are effective against or by their site of action.



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## Antibiotic Paradigm



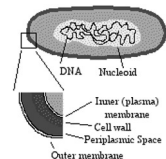
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## Inhibitors of Cell Wall Synthesis

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## Inhibitors of Cell Wall Synthesis

- Human cells do not possess a cell wall like bacteria do
  - it is a very selective way to interfere with bacterial growth.
- To be maximally effective, the inhibitors require actively proliferating bacteria
  - they are ineffective against non-dividing bacteria.
- The most important members of this group are:
  - B-lactam antibiotics and
  - vancomycin.



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## B-Lactam Antibiotics

- This group includes:
  - penicillins.
  - cephalosporins.
  - carbapenems and monobactams.
- B-lactamase inhibitors** are sometimes added in combination to reduce a bacteria's ability to overcome the activity of the antibiotic
  - E.g. potassium clavulanate (clavulanic acid)

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## Penicillins

- Among the most widely effective and least toxic
  - increased resistance has limited their use
  - they are bactericidal
- Interfere with the last step of bacterial wall synthesis, resulting in cell lysis.
- Therapeutic application in gram (+) cocci and bacilli, gram (-) cocci, anaerobic, spirochetes (syphilis).
- The most common side effects include hypersensitivity and diarrhea.**

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## Penicillins

- This group includes the following commonly used members:
  - Amoxicillin** (250/500 tid, 875 mg bid or extended release 775mg qd)
    - treatment of otitis media, sinusitis, and infections caused by susceptible staph/strept involving upper and lower respiratory tract, skin and urinary tract; prophylaxis of infective endocarditis
  - Pediatric dosing:
    - <3 months: oral 20-30 mg/kg/day divided q 12 hrs
    - >3 months: oral 20-50 mg/kg/day divided 8-12 hrs
    - >12 yrs: extended release 775 mg daily

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## Penicillins: Dicloxacillin

- Dicloxacillin (250-500 mg)
  - penicillinase resistant, used in penicillin resistant staph**
  - administer orally at least 1 hour before or 2 hours after meals
  - Dosing:
    - Children <40kg: 12.5-25 mg/kg daily divided
    - Children >40kg: 125-250 mg q 6 hours
    - Adults: 250 mg q 6 hours (QID)

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## Penicillins

Name	Treatment for	Administration
Penicillin G and V	All stages and forms of syphilis	Via IM or IV injection
Ampicillin	Prophylactic use in dental surgery patients Active against haemophilus and salmonella	Adults: - 250-500 mg every 6 hours
Nafcillin	Osteomyelitis, septicemia, endocarditis and CNS infections	IM/IV Adults: - 500 mg every 4-6 hours

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## Penicillins: Augmentin (Amoxi-Clav, Clavulin)

- Augmentin is amoxicillin with potassium clavulanate (clavulanic acid 125 mg).**
- Clavulanate is a B-Lactamase inhibitor which reduces a bacteria's ability to negate the effect of the amoxicillin by inactivating penicillinase (enzyme that inactivates the antibiotic effect).
  - Dicloxacillin can also be used in infections due to penicillinase-producing staph.
- Augmentin (U.S.)
- Amoxi-Clav, Clavulin, Novo-Clavamoxin, Teva-Amoxicillin/Clavulanic Acid (Canada)

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## Penicillins: Augmentin (Amoxi-Clav, Clavulin)

- Kills many bugs, good for both gram (+) and (-)
  - staph, strep, H. flu
- Augmentin is very effective for skin and skin structure infections such as:
  - dacryocystitis,
  - internal hordeola,
  - pre-septal cellulitis.
- Treatment of:
  - otitis media,
  - sinusitis,
  - lower respiratory and urinary infections.
- Given prophylactically to dental surgery patients.

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## Penicillins: Augmentin (Amoxi-Clav, Clavulin)

- Pregnancy Category B\*\*\*
- It has low:
  - GI upset,
  - allergic reaction and anaphylaxis.
- Serious complications include:
  - anemia,
  - pseudomembranous colitis and
  - Stevens-Johnson syndrome.

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## Penicillins: Augmentin (Amoxi-Clav, Clavulin)

### Adults:

- 250-500 mg tab q 8hr (tid) (also available in chewable tablets and suspension)
- or 875 mg q 12hr (bid)
- 1000 mg XR: q12 hr and not for use in children <16

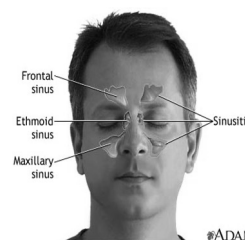
### Peds:

- <3 mos 30mg/kg/day divided q12hrs using suspension
- >3 mos 30-60mg/kg/day divided q12hrs (otitis media 90mg for 10 days)

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## Sinusitis Red Eye

- Sinus infections (rhinosinusitis), are an inflammation of the nasal and sinus passages that can cause uncomfortable pressure on either side of the nose and last for weeks
- The increase in mucus creates pressure in the sinuses that leads to pain.
- The sinuses surround the ocular region
  - pressure from sinuses may feel like eye pressure.
  - swollen sinuses and nasal membranes can push against ocular nerves resulting in pain.
- Most develop during or after a cold or other upper respiratory infection, but allergens and environmental irritants may also trigger them



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## Sinusitis Treatment

- The infection is likely bacterial and should be treated with antibiotics if:
  - symptoms last for 10 days without improvement, or
  - include fever of 102 degrees or higher,
  - nasal discharge and facial pain lasting three to four days
- Because of increasing resistance to the antibiotic amoxicillin – the current standard of care – the ISDA recommends Augmentin
- Augmentin 250/500 TID for 5-7 days for adults, 10-14 days for children

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## Penicillins: Hordeola:

- **Internal** are secondary to a staph infection of the meibomian glands
- **External** are an infection of the Zeis or Moll glands
  - Patients present with tenderness and swelling of affected area.
- Standard treatment includes:
  - good lid hygiene with warm compresses and lid washes
  - Augmentin 500/125 mg TID or 875/125 mg BID
  - Dicloxacillin 250 mg po QID for 7-10 days.
  - may consider topical AB ung on external hordeolum.



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## Penicillins: Dacryocystitis

- infection of the lacrimal sac usually secondary to an obstruction.
- in pediatric patients:
  - the obstruction usually resolves by age 9-12 months.
  - many pediatric ophthalmologists will wait until after this age to probe the ducts to free the obstruction.



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## Penicillins: Dacryocystitis

- Treatment includes:
  - **Augmentin** 500/125 mg (500 mg amoxicillin/125 mg clavulanic acid) TID
    - or 875/125 mg BID for 7 days or
  - **Dicloxacillin** 250 mg po QID.



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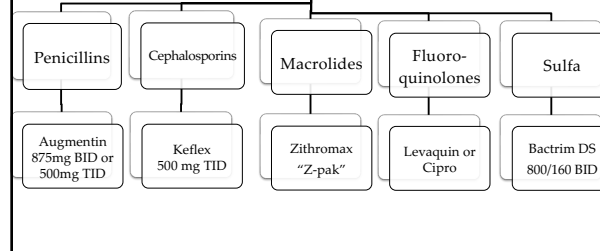
## Penicillins: Preseptal Cellulitis

- Infection and inflammation located anterior to the orbital septum and limited to the superficial periorbital tissues and eyelids.
  - usually follows periorbital trauma or dermal infection (suspect staph sp in trauma).
  - eyelid swelling, redness, ptosis, pain and low grade fever.
- Tx:
  - **Augmentin 500/125 mg TID**
    - or 875/125 mg BID for 7 days or
  - if moderate to severe IV Fortaz (ceftazidime) 1-2 g q8h.



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## Antibiotic Paradigm



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## Cephalosporins

- Closely related structurally and functionally to the penicillins,
  - have the same mode of action,
  - affected by the same resistance mechanisms.
  - tend to be more resistant to B-lactamases.
- classified as 1st, 2nd, 3rd, and 4th generation based largely on their bacterial susceptibility patterns and resistance to B-lactamases.
- Should be avoided or used with caution in patients who are allergic to penicillin (apprx 10% x-reaction with penicillin allergy has been reported but thought to be much closer to the 1-2%)
  - allergic response without allergy to penicillin is 1-2%.
- Typically administered IV or IM, **poor oral absorption.**

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## Cephalosporins

- 1st generation:
  - cephalexin (Keflex)\*\*\* 500 mg BID-QID
  - cefadroxil (Duricef)\*\*\*
  - cefazolin (Ancef)
- 2nd generations:
  - cefaclor (Ceclor)\*\*\* 500 mg TID
  - cefprozil
  - cefuroxime (Ceftin, Zinacef) 250 mg BID
  - cefotetan
  - cefoxitin
- Duricef, Keflex, Ceclor (all orally administered) are effective against most gram positive pathogens and especially good for skin and soft tissue infections.

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## Cephalosporins

- 3rd generation:
  - cefnir,
  - cefixime,
  - cefotaxime (Claforan),
  - ceftazidime (Fortaz),
  - cefibuten,
  - ceftizoxime,
  - ceftriaxone (Rocephin IM/IV).
- 4th generation:
  - cefepime
- *Duricef, Keflex, Ceclor* (all orally administered) are effective against most gram positive pathogens and especially good for skin and soft tissue infections.

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## Cephalosporins

- **Keflex (cephalexin):**
  - treatment of respiratory, GI, skin and skin structure, and bone infections as well as otitis media
  - good for gram (+)\*\*\*
  - not good for H. flu\*\*\*\*
  - Adults: 250-1000 mg every 6-8 hours (TID-QID)
    - - typical dosing 500 every 6-8 hours
  - Children: 25-100 mg/kg/day divided 6-8 hours
- Pregnancy category B\*\*\*

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## Cephalosporins: Dacryocystitis

- Dacryocystitis Tx:
  - Keflex 250-500 mg po TID-QID,
- In febrile cases:
  - IV cefazolin (Ancef) 1g q8h or
  - IV cefuroxime (Zinacef) 1.5g q8h.



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## Cephalosporins: Dacryoadenitis

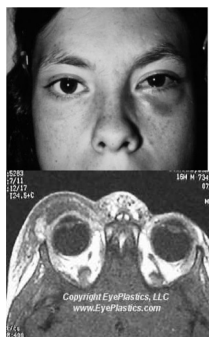
- An inflammation or infection of the lacrimal gland.
  - S&S include:
    - swelling of lid,
    - pain in area of swelling,
    - excess tearing or discharge and swelling of lymph nodes.
- maybe secondary to viral or bacterial infection
- Tx:
  - *Keflex (cephalexin) 250-500mg po TID-QID,*
  - *for more severe cases IV cefazolin(Ancef) 200mg/kg divided into 3 doses.*



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## Cephalosporins: Preseptal Cellulitis

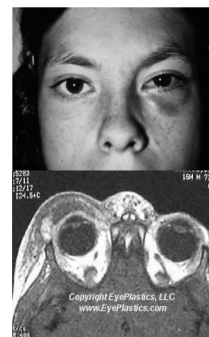
- infection and inflammation anterior to the orbital septum and limited to the superficial periorbital tissues and eyelids.
  - Signs and Symptoms include:
    - eyelid swelling,
    - redness,
    - ptosis,
    - pain and
    - low grade fever.



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## Cephalosporins: Preseptal Cellulitis Treatment

- Tx:
  - Mild:
    - Keflex (cephalexin) 500 mg TID
    - Ceclor (cefactor) 250-500mg q8h
  - Moderate to severe:
    - IM Rocephin (ceftriaxone) 1-2 grams/day or
    - IV Fortaz (ceftazidime) 1-2 g q8h.



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## Cephalosporins: Orbital Cellulitis

- infection and inflammation within the orbital cavity producing orbital S&S.
- most commonly secondary to ethmoid sinusitis.
- Staph and Strept most common isolates.
- Signs and Symptoms include:
  - decreased VA,
  - pain,
  - red eye,
  - HA,
  - diplopia,
  - bulging eye,
  - APD,
  - EOM restriction,
  - lid swelling and
  - fever (generally 102 degrees F or higher)



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## Cephalosporins: Orbital Cellulitis

### Treatment

#### \*\*\*IV Antibiotics for 7-10 days:\*\*\*

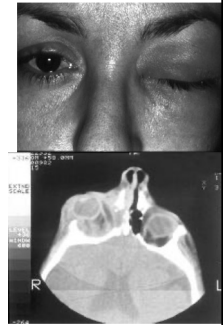
- IV Ceftriaxone (Rocephin) 50 mg/kg/Q12h/day **OR**
- IV Cefotaxime (Claphoran) 50 mg/kg/Q6h/day

#### PLUS

- IV clindamycin 40 mg/kg/day in 3 doses

#### IF PATIENT HAS A PENICILLIN ALLERGY

- IV vancomycin 30 mg/kg/day in 3 doses infused over 90 minutes
- Oral treatment 2-3 weeks post IV:
  - Amoxicillin-clavulanate 875 mg/125 mg PO q12h or
  - Cefpodoxime 200 mg PO q12h or
  - Cefdinir 600 mg/day PO q 12h



56

## Vancomycin/Bacitracin

- Vancomycin and bacitracin both inhibit cell wall synthesis.
- Vancomycin is increasingly important as it is effective against multiple drug-resistant organisms (such as MRSA/MRSE and enterococci)
  - used in patients who have penicillin allergies
  - often considered the drug of last resort, though overuse has brought about resistance.
- Bacitracin is active against a wide variety of gram (+) organisms
  - restricted to topical use due to its potential for nephrotoxicity.

57

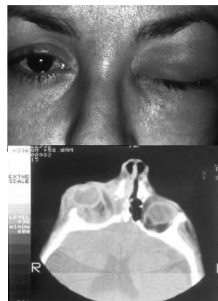
## Vancomycin

- Vancomycin is typically administered systemically as an infusion due to its poor oral absorption
  - complications are minimized when it is administered at less than 10 mg/min
    - topical fortified vancomycin can be compounded (25-50 mg/ml) (Vancocin HCl 2.5% Ophthalmic Drops)
- Complications include:
  - anaphylaxis (hypotension, wheezing, dyspnea, urticaria, pruritis),
  - upper body flushing,
  - pain secondary to muscle spasm, nausea, diarrhea, headache.
  - typically the most serious complication is nephrotoxicity but it is an infrequent complication.

58

## Vancomycin

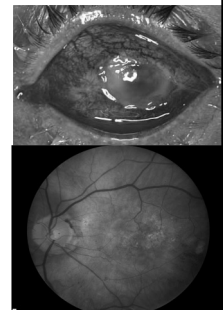
- Orbital Cellulitis:** Infection and inflammation within the orbital cavity producing orbital S&S.
  - decreased VA, pain, red eye, HA, diplopia, bulging eye, APD, EOM restriction, lid swelling and fever.
- IV ceftriaxone (Rocephin) 50 mg/kg/Q12h/day **OR**
- IV cefotaxime (Claforan) 50 mg/kg/Q6h/day *plus*
- IV vancomycin 30 mg/kg/day in 3 doses infused over 90 minutes (penicillin allergy) or IV clindamycin 40 mg/kg/day in 3 doses



59

## Vancomycin

- Endophthalmitis:** intraocular infection involving anterior/posterior segments usually secondary to postoperative infection.
  - present with pain, photophobia, discharge, red eye, decreased VA, proptosis, corneal edema, injection, KP's, AC reaction, vitritis, etc.
- Intravitreal vancomycin 1 mg/0.1ml and ceftazidime 2.25 mg/0.1 ml (or amikacin),
- subconj vancomycin 25mg and ceftazidime 100mg (gentamicin) and dexamethasone 12-24mg,
- topical fortified vancomycin and ceftazidime 50mg/ml/hr, topical steroid and cycloplegic



60

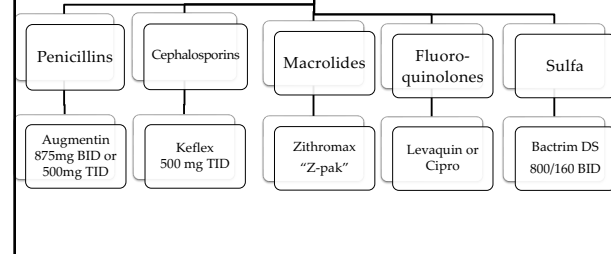
## Bacitracin

- Due to nephrotoxicity, ***bacitracin not used as a systemic med.***
- Bacitracin useful for bacterial lid disease (staph blepharitis)
  - has a low rate of allergy and toxicity.
- **Primarily gram + activity** so usually found in combination with a gram - compound
  - e.g. polymixin B (Polysporin).



61

## Antibiotic Paradigm



62

## Protein Synthesis Inhibitors

63

## Protein Synthesis Inhibitors

- These antibiotics work by targeting the bacterial ribosome.
  - they are structurally different from mammalian ribosomes,
  - in higher concentrations many of these antibiotics can cause toxic effects.
- This group includes:
  - (a) tetracyclines, (b) aminoglycosides, (c) macrolides,
  - (d) chloramphenicol, (e) clindamycin, (f) quinupristin/dalfopristin and (g) linezolid

64

## Aminoglycosides

- Previously were mainstay treatment for infections due to aerobic gram (-) bacilli.
  - due to serious associated toxicities, they have been replaced by safer antibiotics such as 3rd gen cephalosporins, fluoroquinolones, cilastin.
- Effective in the treatment of infections suspected of being due to aerobic gram (-) bacilli including Pseudomonas.
  - usually combined with B-lactam or vancomycin for anaerobic bacteria. They are bacteriocidal!
- Can have severe adverse effects including ototoxicity, nephrotoxicity, delay in nerve conduction, and skin rash.

65

## Aminoglycosides

- This group includes:
  - **Gentamicin**
  - Neomycin
  - Streptomycin
  - **Tobramycin**
  - Amikacin

66

## Aminoglycosides: Ocular Indications

- Systemic aminoglycosides not commonly indicated for ocular conditions
  - amikacin has been used for endophthalmitis IV and intravitreal
- Topical preparations are widely used as single agent preparations, in combination with other antibiotics as well as in combination with steroids.

67

## Macrolides

- Erythromycin was the first of these drugs, as an alternative to penicillin. Bacteriostatic.... though at [higher] maybe cidal
- Macrolides bind to the bacterial ribosome and inhibit protein synthesis.
  - have same spectrum of action as penicillins so are used in those patients who are allergic to that group.
- **Resistance to erythromycin is becoming a serious clinical problem.**
- Adverse effects include:
  - mild-moderate epigastric distress, jaundice, ototoxicity and contraindicated in patients with hepatic disease.
  - No renal adjustment
- Pregnancy Category B\*\*\*

68

## Macrolides

- This group includes:
  - Erythromycin (125 or 250 mg cap, enteric coated) dosing 250mg q 6h or 500 q12h
  - Clarithromycin (Biaxin)
  - **Azithromycin (Z-pak)**- 500mg first day, then 250 mg for next 4 days
    - 10 mg/kg day 1, then 5 mg/kg after that
  - **Azithromycin (Tri-pack)**- 500 mg/day X 3 days
    - 10 mg/kg daily X 3 days
  - Azithromycin 1g PO single dose for.....
    - Chlamydia
  - Telithromycin

69

## Macrolides

- Azithromycin (Z-pak) is active against respiratory infections due to H. influenzae and Moraxella. Also covers staph & strep
  - it is a costly medication (generic now available),
  - now a preferred therapy for urethritis by chlamydia.
  - excellent for soft tissue infections.
  - use with caution in patients with impaired liver function and no controlled studies for use in pregnancy.
- Adverse effects include:
  - mild-moderate epigastric distress, jaundice, ototoxicity and contraindicated in patients with hepatic disease.
  - No renal adjustment
- Pregnancy Category B\*\*\*

70

## Recent New Report

- A study published in a recent addition of the New England Journal of Medicine, found patients prescribed Z-Pak were more likely to die than those prescribed amoxicillin.
- The results were especially pronounced for those who died of heart attacks
- Patients on azithromycin had two and a half times the odds of dying from a cardiovascular than did patients on amoxicillin.
- FDA Recommendation: those patients on azithromycin should continue taking their medication

Azithromycin and the Risk of Cardiovascular Death. Wayne A. Ray, Ph.D., Katherine T. Murray, M.D., Kashi Hall, B.S., Patrick G. Arbogast, Ph.D., and C. Michael Stein, M.B., Ch.B. N Engl J Med 2012; 366:1881-1890/23

71

## Macrolide: Hyperacute Conjunctivitis

- Hyperacute conjunctivitis:
  - usually secondary to gonorrhea or chlamydia.
  - profuse purulent discharge, pain, redness, chemosis, positive nodes.
- Tx: **Azithromycin (Zithromax)**
  - 1 gram single oral dose.
    - concurrent use of ocular lavage and topical fluoroquinolone (e.g. cipro//moxi/besi/gatifloxacin q1-2 hrs).



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### Macrolides: Adult Inclusion Conjunctivitis

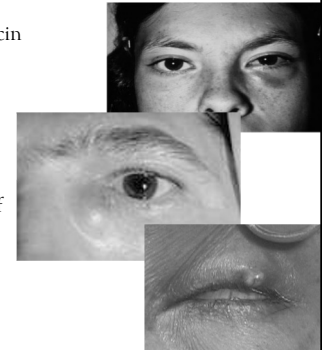
- Adult Inclusion Conjunctivitis:
  - occurs in sexually active adults presenting with ocular irritation, watering, mucopurulent discharge and positive nodes.
  - follicles inferior fornix, mixed papillary/follicular on upper lid, subepithelial infiltrates, SPK.
- Inclusion conjunctivitis:
  - Azithromycin 20 mg/kg (1 gram for adult) as a single dose or
  - 500 mg first day then 250 mg daily for 4 days,
  - erythromycin 250 mg po QID for 14 days.



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### Macrolides: Ocular Indications

- Erythromycin or Azithromycin can be used as alternative treatment in patient with:
  - internal hordeola,
  - pre-septal cellulitis,
  - dacryocystitis
- remember high incidence of staph resistance with Erythromycin



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### Chloramphenicol

- Active against a wide range of gram (+) and (-) organisms.
  - because of its toxicity, its use is restricted to life-threatening infections for which no alternative exists.
- Bacteriocidal and bacteriostatic depending on the organism.
- Adverse effects include hemolytic and aplastic anemia.

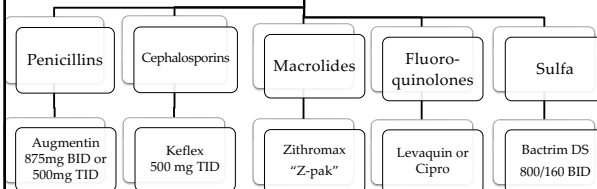
75

### Chloramphenicol: Ocular Indications

- Systemic treatment rarely used for ocular conditions.
- Available in solution 0.5% and ointment 1% (Chloroptic)
  - generally not used in the US but commonly used abroad (Europe and Australia).
- Effective against most ocular bacterial infections but because of potentially fatal complications should only be used as a last resort.

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### Antibiotic Paradigm



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### Inhibitors of Nucleic Acid Synthesis/Function

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## Inhibitors of Nucleic Acid Synthesis/Function.

- The fluoroquinolones are the main group of antibiotics that act in this fashion.
  - they enter the bacterium via passive diffusion and once inside the cell inhibit the replication of bacterial DNA by interfering with the action of DNA gyrase and topoisomerase IV during bacterial growth and reproduction.
- Norfloxacin was the first member of this group and has been rapidly followed by newer generations of drugs which offer greater potency, a broader spectrum and a better safety profile.
  - unfortunately, their overuse has already led to the emergence of resistant strains.

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## Inhibitors of Nucleic Acid Synthesis/Function.

- All the fluoro are bactericidal, with activity becoming more pronounced as the serum [drug] increases.
  - in general, they are effective against gram(-) bacteria including pseudomonas and haemophilus, and have good activity against some gram (+) organisms such as strep.
- Common practice to classify the fluoro into “generations” with nalidixic acid being 1st generation.

80

## Inhibitors of Nucleic Acid Synthesis/Function.

- Ciprofloxacin is the most frequently used fluoro in the US.
  - effective against many systemic infections, with the exception of serious infections caused by methicillin-resistant Staph aureus, the enterococci and pneumococci.
  - it is used in treating infections caused by enterobacteria (ex. travelers diarrhea) and drug of choice for anthrax prophylaxis.
  - has good activity against pseudomonas, and may have synergistic activity with B-lactams.
  - Typical dose - 500 mg BID X 1 week
- Levofloxacin (Levaquin) also commonly used
  - typical dose - 500 mg QD X 1 week
- Resistance has developed due to mutations in both gyrase and topoisomerase.

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## Inhibitors of Nucleic Acid Synthesis/Function.

- The fluoroquinolones are generally very well tolerated though some of the most common adverse reactions include:
  - GI upset,
  - CNS problems (HA and dizziness),
  - phototoxicity,
  - liver toxicity, nephrotoxicity, and
  - connective tissue problems
    - risk of tendon ruptures/tendonitis\*\*\* therefore....
  - Contraindicated:
    - < 18 years old
    - > 65 years old (relative contraindication)
  - Pregnancy category C\*\*\*

82

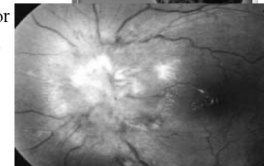
## Ocular Indications

- Hyperacute conjunctivitis (chlamydia): Oral or IM fluoroquinolone (only indicated if unable to use cephalosporin)
- Cat Scratch Disease: ciprofloxacin 500-750 mg po q 12h for 10-14 days.
- Orbital cellulitis: IV ciprofloxacin
- Majority of the use of fluoroquinolones in ocular use is in the form of topical drops and ointments. Used in all forms of infections and prophylaxis in ocular surgeries.

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## Fluoroquinolone: Cat-Scratch Disease

- Cat-scratch disease (Parinaud's): infection with Bartonella
  - resulting in granulomatous conjunctivitis with associated preauricular lymphadenopathy,
  - neuroretinitis,
  - focal chorioretinitis.
- Tx: e.g. oral ciprofloxacin 500 mg or gatifloxacin or moxifloxacin 400mg,
  - IV fluoroquinolone.
  - concurrent use of ocular lavage and topical fluoroquinolone (e.g. cipro//moxi/gatifloxacin q1-2 hrs).

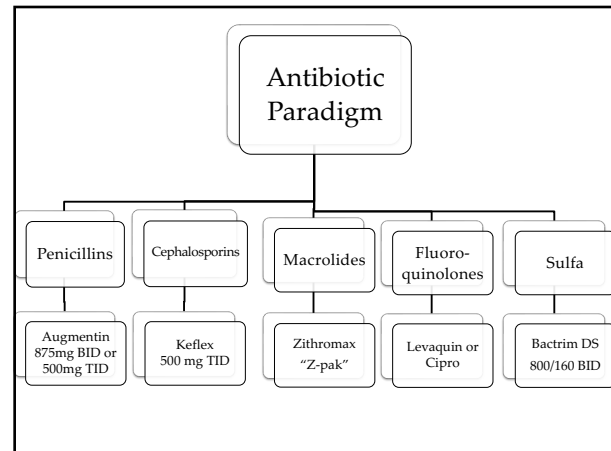


84

## Ocular Fluoroquinolones

- Besivance (besifloxacin 0.6%) is strictly an ophthalmic preparation with no systemic counterpart
  - thought to possibly reduce chance of resistance development
  - has DuraSite as vehicle so forms a gel-like liquid on the eye increasing contact time
  - animal data has shown possible increased activity for MRSA

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## Inhibitors of Metabolism

87

## Inhibitors of Metabolism

- Folic acid is required for the synthesis of precursor molecules for RNA, DNA and other compounds necessary for cellular growth.
  - in the absence of folic acid, cells cannot grow or divide.
- (a) Sulfonamides and (b) trimethoprim are folic acid antagonists and interfere with an infecting bacteria's ability to divide.
- Compounding the two has made a synergistic compound used for effective treatment of a variety of bacterial infections.

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## Sulfonamides

- Sulfa drugs are seldom prescribed alone except in the developing countries, where they are used because of their low cost and efficacy in certain infections such as trachoma.
- With the combination with trimethoprim, co-trioxazole there was a renewed interest in the sulfa drugs.
- Sulfa drugs are bacteriostatic,
  - active against selective enterobacteria in the urinary tract.
  - resistance exists in those bacteria that don't synthesize folic acid and in any PABA producing bacteria (purulent producing bacteria).

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## Sulfonamides

- Adverse effects include:
  - hypersensitivity reactions such as rashes,
  - angioedema,
  - Stevens-Johnson syndrome are fairly common.
  - may also result in nephrotoxicity, hemolytic anemia,
  - drug potentiation
    - Ex. increased effect of hypoglycemic effect of tolbutamide or anticoagulant of warfarin

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## Sulfonamides: Ocular Indications

- No common indications for systemic sulfonamides (sulfadiazine is sometimes used as adjunct therapy in toxoplasmosis Tx) though topical preparations do exist.
- Sulfa's have limited use due to resistance and allergic reactions
  - used more by non-ophthalmic providers.
- Available in combination with steroids
  - ex. Blephamide

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## Trimethoprim and Pyrimethamine

- Similar antibacterial spectrum as sulfonamides, though has a 20-50 fold more potent effect than the sulfonamides.
- Trimethoprim maybe used on its own to treat acute UTI's and in the treatment of bacterial prostatitis (fluoroquinolones preferred though) and vaginitis
  - been found to be an effective treatment option for MRSA
- Pyrimethamine is used for prophylaxis and Tx of malaria.
- Resistance does exist, and adverse affects include several blood anemias which can be reversed by administering folic acid.

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## Trimethoprim: Ocular Indications

- Combined with sulfa (Bactrim/Septera) indicated for MRSA suspected infections
- Trimethoprim is found in combination with polymixin B in a topical eye drop.
  - Trimethoprim has both gram +/- activity but not effective against pseudomonas so Polymixin B is added.
- Low rate of allergic and toxic reactions, and approved for children >2 months.

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## Co-Trimoxazole (Bactrim/Septera)

- Combination of trimethoprim and sulfamethoxazole
  - shows greater antimicrobial activity than equivalent quantities of either drug alone.
- Has broader spectrum of action than the sulfa's and is effective in treating:
  - UTIs and respiratory tract infections
  - often considered for treatment of MRSA skin infections\*\*\*\*

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## Co-Trimoxazole (Bactrim/Septera)

- Resistance is more difficult because has to develop resistance to both drugs.
- Adverse effects include:
  - severe potential for dermatologic reactions,
    - Stevens Johnson Syndrome
  - GI upset,
  - blood disorders, and
  - drug potentiation.
- Pregnancy category C\*\*\*

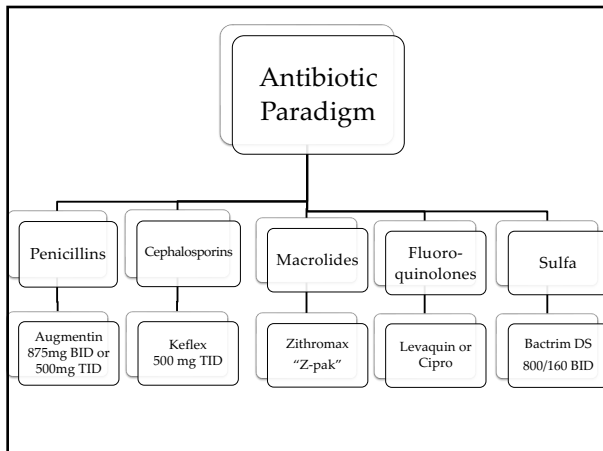
95

## Co-Trimoxazole (Bactrim/Septera)

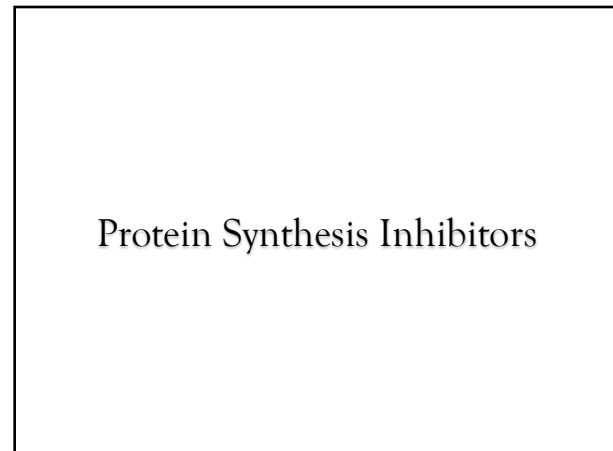
- Available:
  - Bactrim/Septera tablets:
    - contains 80 mg trimethoprim and 400 mg sulfamethoxazole
    - dosing 2 tablets every 12 hours (BID)
  - Bactrim DS/Septera DS (Double Strength)
    - contains 160 mg trimethoprim and 800 mg sulfamethoxazole
    - Dosing 1 tablet every 12 hours (BID)

96





97



98

## Protein Synthesis Inhibitors

- These antibiotics work by targeting the bacterial ribosome.
  - they are structurally different from mammalian ribosomes,
  - in higher concentrations many of these antibiotics can cause toxic effects.
- This group includes:
  - (a) tetracyclines, (b) aminoglycosides, (c) macrolides,
  - (d) chloramphenicol, (e) clindamycin, (f) quinupristin/dalfopristin and (g) linezolid

99

## Tetracyclines

- Nonresistant strains concentrate this antibiotic intracellularly resulting in inhibition of protein synthesis.
- Broad spectrum, bacteriostatic,
  - effective against gram (+) and (-) bacteria and against non-bacterial organisms
  - widespread resistance has limited their use.
- Drug of choice for Rocky Mountain Spotted Fever, Cholera, Lyme disease, mycoplasma pneumonia, and chlamydial infections.
- Side effects include gastric discomfort, phototoxicity, effects on calcified tissues, vestibular problems, pseudotumor.

100

## Tetracyclines

- This group includes:
  - Tetracycline (250mg - 500 mg cap BID-QID) needs to be taken 1 hour before or 2 hours after a meal.
  - Minocycline (100 mg cap BID)
  - Doxycycline (20mg - 100 mg cap or tab BID)

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## Tetracyclines: Acne Rosacea

- Acne rosacea:
  - affects females > males after 30 with peak incidence 4-7th decade of Celtic/Northern European descent. Males more disfigured.
- 4 subtypes with classic signs of flushing, papules or pustules usually in crops, telangiectasia.
  - secondary ocular complications (85% of patients) and often precede other skin manifestations include erythema, itching and burning.
- Mainstay oral Tx is Oracea (40 mg in morning) or
  - tetracycline 500 mg po BID or doxycycline 50 mg po BID or minocycline 100 mg po BID for 4-12 wks.
  - NOTE: Oracea is subantimicrobial therapy.



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## Acne Rosacea Treatments

Oral Antibiotics	Topical Treatments	Non-Prescription
Erythromycin	metronidazole (Metrogel)	Rosacea-Lid III
Tetracycline	BenzaClin (Clindamycin 1% & benzoyl peroxide 5%)	ZenMed
Doxycycline	BenzaMycin (Erythromycin 3% & benzoyl peroxide 5%)	Neova Therapy
Minocycline	tretinoin (Retin-A)	Kinerase
	Clindamycin 1% lotion/gel	Rosacare
	Plexion Cleanser/Lotion (Sulfa 10% & sulfur 5%)	

[www.internationalrosaceaafoundation.org](http://www.internationalrosaceaafoundation.org)

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## Tetracyclines: Adult Inclusion Conjunctivitis

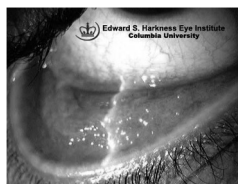
- occurs in sexually active adults
- women are more susceptible than men.
- usually transmitted through hand-to-eye spread of infected genital secretions.
- incubation period is one to two weeks
- Signs and Symptoms:
  - ocular irritation, watering, mucopurulent discharge and positive nodes
  - often a unilateral disease but can involve both eyes
  - follicles inferior fornix, mixed papillary/follicular on upper lid, subepithelial infiltrates, SPK.



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## Tetracyclines: Adult Inclusion Conjunctivitis Treatment

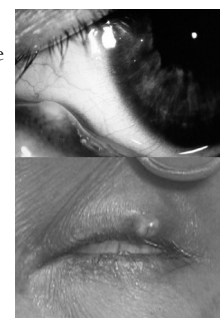
- If left untreated, resolves spontaneously in 6-18 months
- can be treated topically with tetracycline, erythromycin, and fluoroquinolones
  - due to the high prevalence of concomitant genital tract infection, systemic antibiotic therapy is recommended
- Mainstay oral treatment is:
  - Doxycycline 100 mg po BID for 7-10 days.
  - Topical AB therapy is done concurrently.



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## Tetracyclines: Hordeola

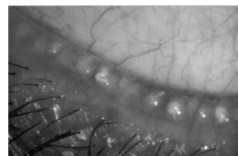
- Internal are secondary to a staph infection of the meibomian glands, while external are an infection of the Zeis or Moll glands. Px present with tenderness and swelling of affected area.
- Standard treatment includes:
  - good lid hygiene with warm compresses and lid scrubs in conjunction with
  - doxycycline 50-100 mg po BID for 2-3 weeks.
  - may consider topical AB ung on external hordeolum.



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## Tetracyclines: Meibomian Gland Dysfunction

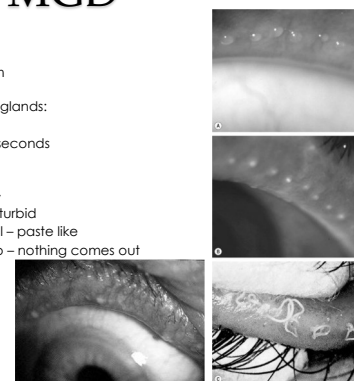
- Meibomian gland dysfunction:
  - also referred to as meibomitis and patients experience dry eye problems secondary to increased evaporation of the tears.
  - signs include noticeable capping of the glands and frothing of tear film.
- Standard treatment includes:
  - good lid hygiene with warm compresses and lid scrubs in conjunction with
  - doxycycline 50 mg po BID for 2-3 months.
    - Erythromycin ung (Ilotycin) can also be used externally.



107

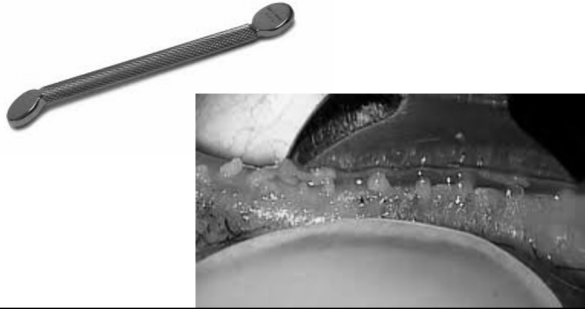
## MGD

- Signs:
  - Frothy or foamy tear film
  - Thickened lid margins
  - Express the meibomian glands:
    - Mastroda paddle
      - Hold for 10-15 seconds
    - Wet Q-tip
  - Ideal scenario – oily
  - Slightly abnormal – turbid
  - Extremely abnormal – paste like
  - Worst case scenario – nothing comes out
- Red eyes
- Reduced TBUT
- Scarring of the eyelid
- Telangiectasia
- Capped glands



108

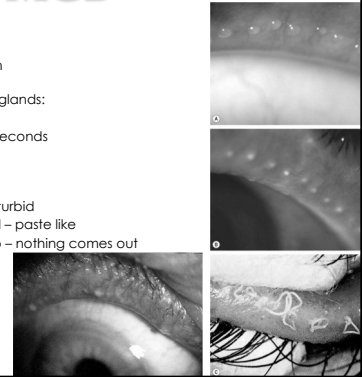
## Mastroda Paddle



109

## MGD

- Signs:
  - Frothy or foamy tear film
  - Thickened lid margins
  - Express the meibomian glands:
    - Mastroda paddle
      - Hold for 10-15 seconds
    - Wet Q-tip
  - Ideal scenario – oily
  - Slightly abnormal – turbid
  - Extremely abnormal – paste like
  - Worst case scenario – nothing comes out
- Red eyes
- Reduced TBUT
- Scarring of the eyelid
- Telangiectasia
- Capped glands



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## MGD

- Treatment:
  - Mild-moderate cases:
    - Warm compresses
      - 40 degrees Celsius
      - 5 minutes of heat minimum
        - 10-15 is better
    - Lid hygiene
    - AT's
      - Lipid based tears
        - Systane Balance, Refresh Optive Advanced, Ocusoft Retaine
  - Moderate-severe disease (tear osmolarity > 330)
    - Theratears, Oasis tears
  - Lotemax ung at night
    - Wonderful for patients with morning complaints
    - Wouldn't use during the day

111

## MGD

- Treatment:
  - Mild-moderate cases:
    - Warm compresses
      - 40 degrees Celsius
      - 5 minutes of heat minimum
        - 10-15 is better
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112

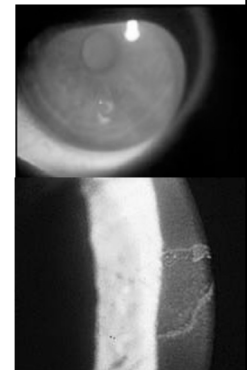
## MGD - treatment

- Tetracyclines
  - Doxy
    - 50 mg BID X 1-3 months
    - 50 mg QD X 1-2 months
  - Minocycline
    - 50mg BID
  - Periostat
    - Approved for gingivitis
    - 20 mg Doxy
  - Can't give to:
    - Children < 12
    - Women pregnant or wanting to become pregnant
    - Breastfeeding
    - Pregnancy category D
  - Side effects:
    - Teeth discoloration
    - Bone problems
    - GI upset\*\*\* #1 reason why people can't take tetracyclines
    - Photosensitivity - sunburn
    - Dairy products and ant-Acids neutralize it
    - Mild dizziness/vertigo – minocycline mostly, very rare with doxy

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## Tetracyclines: Recurrent Corneal Erosion

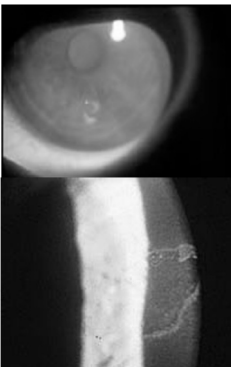
- RCE:
  - repeated, spontaneous disruption of corneal epi.
  - patient experiences foreign body sensation, photophobia, blepharospasm, decreased VA and lacrimation upon waking.
  - History of trauma usually reported or EBMD



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### Tetracyclines: Recurrent Corneal Erosion

- For recalcitrant RCE's treatment includes:
  - Fresh Kote TID
  - Muro ung qhs
  - Steroid QID
  - treat with doxycycline 50 mg po BID for 2-3 months.
    - or Azasite BID
  - if recurrence still happen, consider stromal puncture of affected area.



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## Doxycycline in a kid???

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### No Visible Dental Staining in Children Treated with Doxycycline for Suspected Rocky Mountain Spotted Fever

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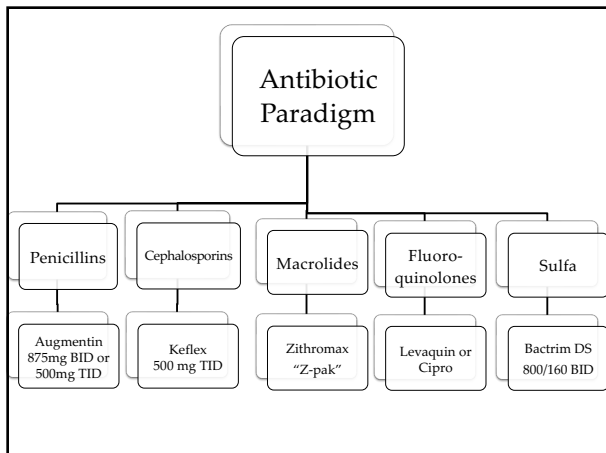
**Objective** To evaluate whether cosmetically relevant dental effects occurred among children who had received doxycycline for treatment of suspected Rocky Mountain spotted fever (RMSF).

**Study design** Children who lived on an American Indian reservation with high incidence of RMSF were classified as exposed or unexposed to doxycycline, based on medical and pharmacy record abstraction. Licensed, trained dentists examined each child's teeth and evaluated visible staining patterns and enamel hypoplasia. Objective tooth color was evaluated with a spectrophotometer.

**Results** Fifty-eight children who received an average of 1.8 courses of doxycycline before 8 years of age and who now had exposed permanent teeth erupted were compared with 213 children who had never received doxycycline. No tetracycline-like staining was observed in any of the exposed children's teeth (0/58; 95% CI 0%-5%), and no significant difference in tooth shade ( $P = .20$ ) or hypoplasia ( $P = 1.0$ ) was found between the 2 groups.

**Conclusions** This study failed to demonstrate dental staining, enamel hypoplasia, or tooth color differences among children who received short-term courses of doxycycline at <8 years of age. Healthcare provider confidence in use of doxycycline for suspected RMSF in children may be improved by modifying the drug's label. (*J Pediatr* 2015;166:1246-51).

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## Herpes Zoster



- Nearly 1 million Americans develop shingles each year
- Ocular involvement accounts for up to 25% of presenting cases
- Over 50% incur long term ocular damage

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## Herpes Zoster

\*\*\*Varicella-Zoster Virus\*\*\*


- Herpes DNA virus that causes 2 distinct syndromes
  1. Primary infection – Chicken pox (Varicella)
    - Usually in children
    - Highly contagious\*\*\*
    - Very itchy maculopapular rash with vesicles that crust over after ≈ 5 days
    - 96% of people develop by 20 years of age
    - Vaccine now available

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## Herpes Zoster

- Herpes DNA virus that causes 2 distinct syndromes
  2. Reactivation – Shingles (Herpes Zoster)
    - More often in the elderly and immunosuppressed (AIDS)
      - Systemic work-up if Zoster in someone < 40
    - Can get shingles anywhere on the body
    - Herpes Zoster Ophthalmicus (HZO)
      - Shingles involving the dermatome supplied by the ophthalmic division of the CNV (trigeminal)
        - 15% of zoster cases



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## Herpes Zoster

- Symptoms:
  - Generalized malaise, tiredness, fever
  - Headache, tenderness, paresthesias (tingling), and pain on one side of the scalp\*\*\*
    - Will often precede rash
  - Rash on one side of the forehead
  - Red eye
  - Eye pain & light sensitivity

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## Herpes Zoster

- Signs:
  - Maculopapular rash -> vesicles -> pustules -> crusting on the forehead
  - Respects the midline\*\*\*
  - Hutchinson sign
    - rash on the tip or side of the nose\*\*\*
  - Classically does not involve the lower lid
  - Numerous other ocular signs



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## Herpes Zoster

- Other Eye Disease (Acute):
  - Acute epithelial keratitis (pseudodendrites)
  - Conjunctivitis
  - Stromal (interstitial) interstitial keratitis
  - Endotheliitis (disciform keratitis)
  - Neurotrophic keratitis



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## Herpes Zoster

- Other Eye Disease (Acute):
  - Episcleritis
  - Scleritis
  - Anterior uveitis
  - IOP elevation
  - Refinitis
  - Choroiditis
  - Neurological complications (nerve palsies)
  - Vascular occlusion
- Treat the complications just like as if they were primary conditions

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## Herpes Zoster

- Treatment:
  - Treat the complications just like as if they were primary conditions
  - Oral antivirals – must be started within 72 hours of symptoms\*\*
    - Acyclovir 800mg 5x/day x 7-10 days
    - Valtrex 1000mg 3x/day X 7-10 days
    - Famciclovir 500mg 3x/day X 7-10 days
  - Topical ointment to skin lesions to help prevent scarring
    - Bacitracin, erythromycin

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## Antiviral Agents for Herpes Virus

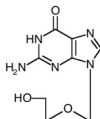
- All current antivirals are nucleoside analogs.
- All available agents are virustatic – they act against replicating viruses only.
- Three Primary Oral Medications:
  - Acyclovir (Zovirax)
  - Valacyclovir (Valtrex)
  - Famciclovir (Famvir)



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## Acyclovir (Zovirax)

- Purine analogue to guanine.
- Selective for viral DNA, thus minimally toxic to host cell.
  - Phosphorylated by virally-encoded thymidine kinase and cellular enzymes, yielding acyclovir triphosphate, which competitively inhibits viral DNA polymerase.
  - Specific for HSV-1, HSV-2, and VZV.



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## Acyclovir (Zovirax)

- Available in:
  - IV Formulation
  - 200-mg capsules,
  - 400 and 800 mg tablets
  - 200 mg/teaspoon oral suspension for children
- Poor oral bioavailability
  - 10-30% gets absorbed
  - Short ½ life of 2 – 3 hours
- Eliminated via the kidneys – need to alter dose patients with renal issues.



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## Acyclovir Side Effects

- Side Effects Include:
  - Nausea and Vomiting
  - Abdominal Pains
  - Skin Rash and Photosensitivity
  - Headaches, dizziness, and confusion
- Rarely causes seizures, coma, anemia, renal failure, and hepatitis – More with IV Medication.
- Caution must be used in elderly, immunocompromised, pregnant/nursing, and patients with renal or liver disease.
  - Pregnancy Category B

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## Acyclovir Topical (Zovirax) NOT ophthalmic!!!

- Available as both a 5% Cream and 5% ointment
  - Cream approved for treatment of herpes labialis (Cold Sores) only.
  - Ointment approved for treatment of genital herpes only.
- No studies have shown improved resolution of eyelid infections with the use of antiviral topicals at this time.

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## Valacyclovir (Valtrex)

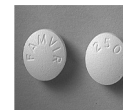
- Pro-drug of acyclovir
  - After absorption, valacyclovir is 95% converted to acyclovir.
  - Provides greater oral bioavailability (3-5X better than Acyclovir) thus less frequency of dosing is required.
- Available in 500 mg and 1 g tablets



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## Famciclovir (Famvir)

- Pro-drug of penciclovir
  - Penciclovir is only available as topical for cold sores.
- After absorption, famciclovir is rapidly converted by intestinal and liver tissues to penciclovir.
  - Penciclovir is structurally similar to acyclovir but with much longer half-life.
- Available in 125 mg, 250 mg, and 500 mg **film-coated** tablets (taken without meals).



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## Herpes Zoster

- Prevention:
  - Zostivax vaccine
    - Live attenuated herpes virus
    - Only given to people who know they had chicken pox as a child\*\*\*
    - Only studied in patients > 60 yo
      - 51% reduction in incidence of HZ
      - 60% reduction in symptom severity in those who got HZ
      - 66.5% reduction in post-herpetic neuralgia

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## Shingrix Vaccine

- Shingrix is a non-live vaccine given intramuscularly in two doses.
- 38,000 patients in a phase III clinical trial
  - >90% efficacy sustained over 4 years

Shingles (Herpes Zoster) Vaccination Information for Healthcare Providers



On October 20, 2017, the U.S. Food and Drug Administration (FDA) licensed Shingrix® for adults aged 50 years and older to prevent shingles.

On October 25, 2017, the Advisory Committee on Immunization Practices (ACIP) voted that Shingrix® is:

- recommended for healthy adults aged 50 years and older to prevent shingles and related complications
- recommended for adults who previously received the current shingles vaccine (Zostavax®) to prevent shingles and related complications
- the preferred vaccine for preventing shingles and related complications

Once approved by the CDC director, these ACIP recommendations will be published in the *Morbidity and Mortality Weekly Report*. At that time, the recommendations will become official policy.

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## Shingrix vs. Zostivax

- |  |   |
|--|---|
| <ul style="list-style-type: none"> <li>• Shingrix:           <ul style="list-style-type: none"> <li>○ <u>Efficacy in preventing shingles:</u></li> <li>○ 96.6% effective in 50-59 year olds</li> <li>○ 97.4% effective in 60-69 year olds</li> <li>○ &gt; 70 year olds               <ul style="list-style-type: none"> <li>• 97.6% in year 1</li> <li>• 84.7% in years 2-4</li> </ul> </li> <li>○ <u>Efficacy in preventing PHN</u> <ul style="list-style-type: none"> <li>• 91.2% in &gt; 50 year olds</li> <li>• 88.8% in &gt; 70 year olds</li> </ul> </li> <li>○ More cost effective</li> <li>○ Lasts longer</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>□ Zostivax:           <ul style="list-style-type: none"> <li>▪ <u>Efficacy in preventing shingles:</u></li> <li>▪ 70% effective in 50-59 year olds</li> <li>▪ 64% effective in 60-69 year olds</li> <li>▪ &gt; 70 year olds               <ul style="list-style-type: none"> <li>○ 38%</li> </ul> </li> <li>▪ <u>Efficacy in preventing PHN</u> <ul style="list-style-type: none"> <li>○ 65.7% in 60-69 year olds</li> <li>○ 66.8% in &gt; 70 year olds</li> </ul> </li> </ul> </li> </ul> |
|--|---|

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## Herpes Zoster

- Post-herpetic Neuralgia
  - Constant or intermittent pain that persists for more than one month after the rash has healed
  - Older patients with early severe pain and larger area are at greater risk
  - Can be so severe that it leads to depression & suicide
  - Improves with time
    - Only 2% of pts affected 5 years out
  - Tx:
    - Cool compresses
    - Topical capsaicin ointment or lidocaine cream
    - Analgesics (Tylenol 3, Vicoden)
    - Amitriptyline 25mg PO TID
    - Neurotin (Gabapentin)

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## Fungal Keratitis

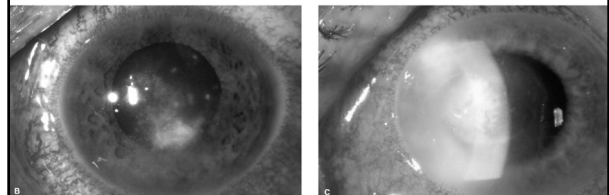
- Sx's:
  - Gradual onset of pain
  - Irritation/grittiness
  - Photophobia
  - Blurred vision
  - Watery or mucopurulent discharge

H/O cornea infection diagnosed as bacterial\*\*  
H/O vegetative trauma, CL abuse, chronic steroid use

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## Fungal Keratitis

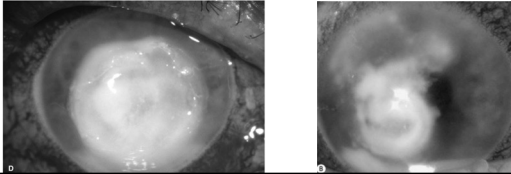
- Signs:
  - Gray-white stromal infiltrate with indistinct "fluffy" or "feathery" borders/margins
  - Often surrounded by fingerlike satellite lesions in the adjacent stroma



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## Fungal Keratitis

- Signs:
  - Epithelial defect overlying the ulcer
    - However can be quite small and sometimes is not present
  - Infiltrates may progressively enlarge and extend into deeper tissue
    - Necrosis, thinning and perforation can occur



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## Fungal Keratitis

- Tx:
  - Pts may require hospitalization
  - Topical meds:
    - Natamycin 5% (for filamentous fungi)\*
    - Amphotericin B 0.15% (for Candida)\*
    - Both q1h around the clock initially and then tapered over 6-12 weeks
  - Orals meds:
    - Voriconazole 200 mg BID
    - Itraconazole
    - Fluconazole
  - Cycloplegics (homatropine BID)
  - Surgical (PKP or DALK)

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## Oral Antifungals

- Ketoconazole – pregnancy category C
  - First successful broad spectrum antifungal that could be administered orally
  - Effective against filamentous and yeast fungi
  - Dosing:
    - 200-400 mg daily
  - Main side effects: GI upset, itching, dizziness, hepatotoxicity, papilledema

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## Oral Antifungals

- Fluconazole – pregnancy category C
  - Excellent oral bioavailability (about 90%) and 24+ hour half life
  - Effective against yeast, becoming less effective against Aspergillus
  - Dosage:
    - 100-200 mg daily
  - Main side effects (one of the best tolerated oral antifungals): GI upset and rash

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## Oral Antifungals

- Voriconazole – pregnancy category D
  - Drug of choice for Aspergillus infections, but also effective against Fusarium
  - Excellent oral bioavailability
  - Dosing:
    - 200 mg BID
  - Main side effects: rash, visual changes\*, fever, N&V, GI upset, HA

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## Acanthamoeba Keratitis

- Sx's:
  - Severe pain\*\*
  - Redness
  - Tearing
  - Decreased vision
  - Photophobia
  - Minimal discharge

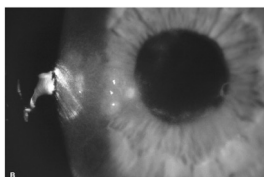
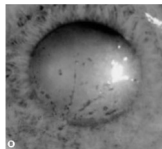
These sx's tend to develop over a period of weeks.\*\*  
H/O CL hygiene problems and swimming in lenses\*\*

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## Acanthamoeba Keratitis

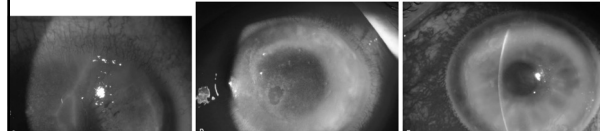
- Signs:
  - Epithelial or subepithelial infiltrates appearing as pseudodendrites early on
  - Patchy anterior stromal infiltrates can also appear early



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## Acanthamoeba Keratitis

- Signs:
  - Radial keratoneuritis\*\*
    - Perineural infiltrates seen during the first 1-4 weeks
  - Gradual enlargement and coalescence of the infiltrates to form a ring infiltrate\*\*
    - Inflammation in the cornea doesn't look that bad\*\*
  - Corneal thinning, melting, perforation, scleritis, hypopyon



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## Acanthamoeba Keratitis

- Tx:
  - Topicals:
    - PHMB 0.02% drops q1h
    - Chlorhexidine 0.02% q1h
      - Fine line agents can be given separately or together
    - Propamidine 1% (Brolene) q1h
  - Orals:
    - Voriconazole 200 mg BID
    - Itraconazole 200-400 mg QD
  - Cycloplegics (homatropine BID)
  - Topical steroids??
  - Pain control
  - Surgery

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Thank you for  
your attention!

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