

# Pharm 504

## Most Commonly Prescribed Drugs

### Anti-Infectives

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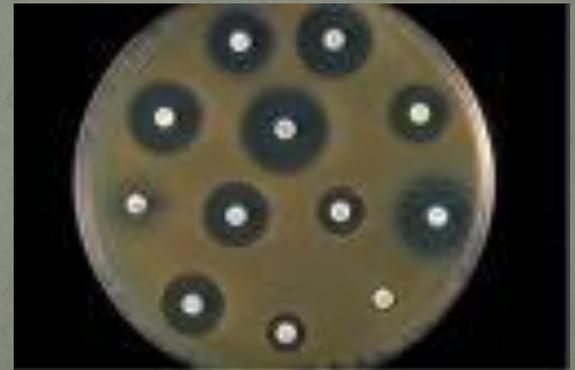
# Objectives

- Identify commonly prescribed anti-infective medications
- Explain common counseling points for each class of anti-infective medications
- Identify the specific counseling points, side effects, and special toxicities of anti-infective medications



# General Terms and Definitions:

- Antibiotic: Substance which works by killing or inhibiting the growth of bacteria
- Antimicrobial – Substance which works by killing or inhibiting the growth of microorganisms such as bacteria, fungi, and protozoa

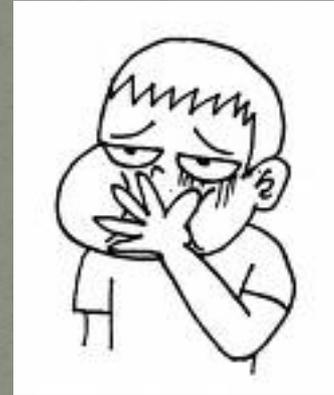


# General Terms and Definitions:

- Bacteriostatic – Substance which inhibits growth of bacteria
- Bacteriocidal – Substance which kills bacteria
- Why is this important?

# General Patient Counseling Points:

- Normal GI and vaginal flora get disrupted with most oral antibiotics, leading to four major side effects:
  1. Nausea
  2. Vomiting
  3. Diarrhea
  4. Yeast Infection
- How can these effects be prevented/minimized?
  - Take with food, constipating foods (cheese, peanut butter), yogurt (probiotics)



# General Patient Counseling Points:

- Relief of symptoms:
  - Usually within 48-72 hours of taking medication
    - Except: Zithromax
- Duration of Therapy:
  - Varies, usually 7 to 14 days
  - Can be as little as 1 day, as long as indefinitely
- Finish course of therapy **EVEN IF FELLING BETTER**
  - Why?  
**reduces risk of developing secondary infection with resistant bacteria**

# General Patient Counseling Points:

- If a dose is missed:
  - Take the dose as soon as you remember
  - If it is almost time for next dose, SKIP missed dose and continue therapy until course is complete
  - Do NOT double up on medication unless indicated by prescriber.



# General Patient Counseling Points:

- Reconstituted Suspension:
  - Shake well
  - Discard any remaining portion after completion of therapy
  - Stability ranges from 10-14 days
  - Refrigeration:
    - Always (eg, amox/clav, cephalexin)
    - Recommended (eg, amox)
    - Ok at room temperature (eg, cefprozil, azithromycin, SMZ/TMP)
- Tablets and Capsules:
  - Keep at room temperature and away from heat/light/moisture

# General Patient Counseling Points:

- Watch out for ALLERGIC reactions to antibiotic

## Classification of allergic reactions to penicillin

Type of reaction	Time course of reaction
Immediate	Within 30-60 minutes of penicillin administration IgE antibodies directed against minor determinants*
Accelerated	Within 1-72 hours of penicillin administration IgE antibodies directed against major determinants**
Delayed	72 hours or more after penicillin administration Type II, III, and IV hypersensitivity; nonimmune reactions

\*Minor determinants ( $\leq 5\%$ ): benzylpenicillin, penicilloate, penilloate, penicilloyl-*n*-propylamine

\*\*Major determinant (95%): penicilloyl hapten moiety conjugated to endogenous protein (Pre-Pen®)

# Symptoms of Allergic Reaction

## Non Anaphylaxis

- Erythema- red skin
  - Pruritis- itchy skin
  - Raised skin/hives
- 
1. Stop antibiotic
  2. Call Pharm.D or MD
  3. Can take antihistamine (diphenhydramine)
  4. Notify all health care providers of allergy

## Anaphylaxis

- Immediate symptoms (5-60 minutes)
  - hives, swelling of mucosal membranes (tightness of throat, chest)
  - reduced BP, organ compromise
- 
1. Stop antibiotic
  2. Call 911
  3. If take antihistamine, take note of when and how much (EMT needs to know when to give Epi-Pen)
  4. Notify all health care providers of allergy

# What about antibiotics and birth control?



- Hypothesis:
  - Antibiotics may interfere with flora responsible for metabolism and absorption of oral contraceptives
  - MOST antibiotics have been found NOT to produce this effect
  - Pharmacists continue to counsel on this due to liability reasons; it is noted in the drug interactions of many antibiotics.



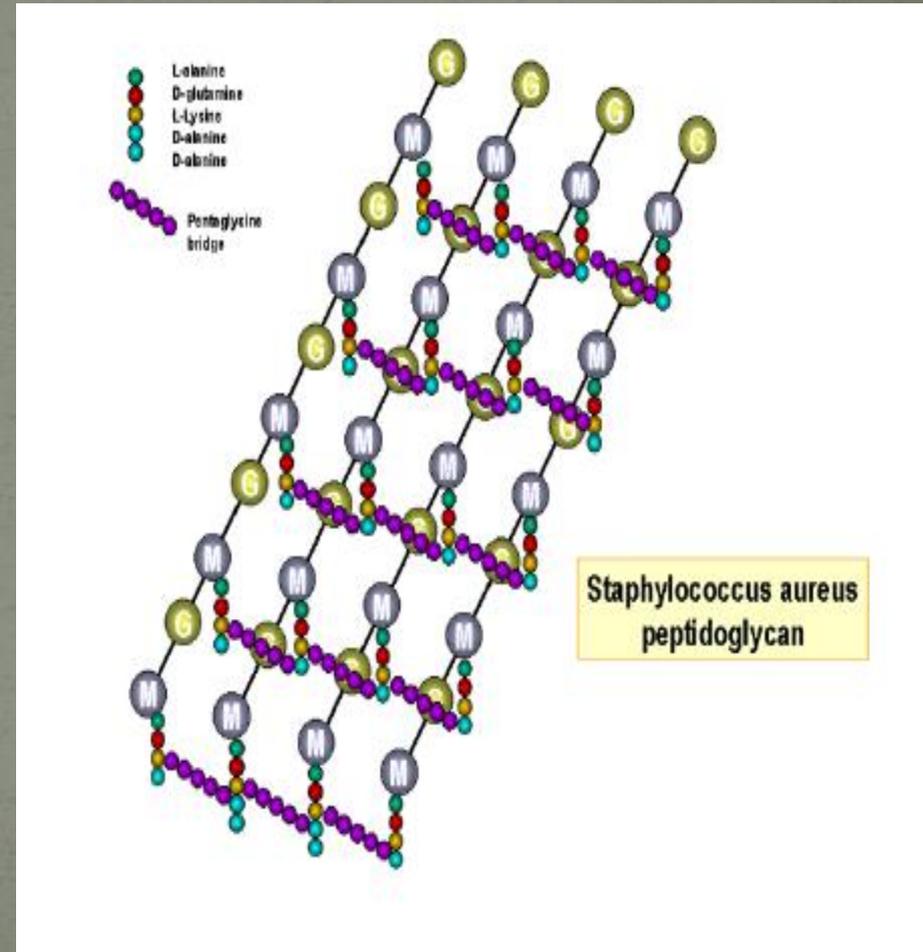
# $\beta$ – lactam antibiotics

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Penicillins and Cephalosporins

# Mechanism of Action

- Inhibits bacterial cell wall synthesis via acetylation of transpeptidase enzyme
- LAYMAN's terms: faulty cell wall synthesis leads to HOLES in cell wall of bacteria
- Bactericidal



# Penicillins

## Penicillin VK (Veetids®)

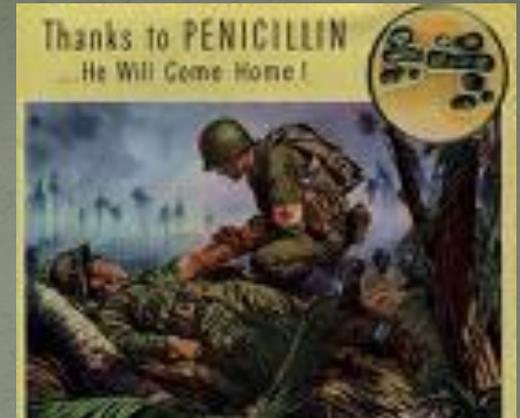
- tablets (250mg, 500mg)
- oral suspension (125mg, 250mg per 5ml)

## Amoxicillin (Amoxil®, Trimox®)

- capsules (250mg, 500mg)
- oral susp (50mg, 125mg, 200mg, 250mg, 400mg per 5ml)
- chewable tablets (125mg, 200mg, 250mg, 400mg)
- tablets (500mg, 875mg)

## Amoxicillin/Clauvulanic acid (Augmentin®)

- tablets (250/125mg, 500/125mg, 875/125mg, XR 1000/62.5mg)
- chewable tablets (125/31.25mg, 200/28.5mg)
- oral susp (125/31.25mg, 200/28.5mg, 250/62.5mg, 400/57mg, 600/42.9mg per 5ml)



# Penicillins: Indications

## Amoxicillin:

- **Acute otitis media (AOM) and acute bacterial sinusitis (ABS)**, pharyngitis, upper and lower respiratory infection (URI & LRI), community Acquired Pneumonia (CAP), urinary tract infections (UTIs), and gonorrhea.

## Penicillin:

- **Pharyngitis, AOM, syphilis**

## Amox/clav:

- **Recurrent AOM (beta-lactamase producing strains)**, sinusitis, CAP, URI, LRI, UTIs, skin structure infections

# Amoxicillin/Clavulanic Acid

- What does clavulanic acid do?
  - Inhibits  $\beta$ -lactamase enzymes which bacteria produce to destroy Penicillins
    - Inhibits or slows down the inactivation of the  $\beta$ -lactam ring thus enhancing effectiveness of amoxicillin
- What is the most common side effect?
  - Stomach upset/diarrhea

# Penicillins- Patient Info

## Administration:

- PCN: Preferably without food, 1 hour before or 2 hours after a meal with a FULL glass of water. Usually QID dosing
- Amox: Preferably without food, 1 hour before or 2 hours after a meal with a FULL glass of water. Usually BID or TID dosing.
- Amox/clav: Take WITH food to enhance absorption and decreases stomach upset/diarrhea. Usually BID or TID dosing.

## Side Effects:

- All can cause N/V/D and yeast infections

## Cautions/Contraindications:

- Report any RASH or shortness of breath



# Cephalosporins

## 1<sup>st</sup> generation: Cephalexin (Keflex<sup>®</sup>)

- capsules (250mg, 500mg, 750mg)
- oral suspension (100mg, 125mg, 250mg per 5ml)
- tablets (250mg, 500mg)

## 2<sup>nd</sup> generation: Cefuroxime (Ceftin<sup>®</sup>)

- tablets (250mg, 500mg)
- oral suspension (125mg, 250mg per 5ml)

## 3<sup>rd</sup> generation: Cefdinir (Omnicef<sup>®</sup>)

- capsules (300mg)
- oral suspension (125mg or 250mg per 5ml)

Greater gram (-) coverage with newer generations

# Cephalosporins- Indications

- Cephalexin: **Impetigo and mild cellulitis**, LRI, URI, UTI, skin and skin structure infections (tx and prophylaxis), bone and joint infections from gm (+) bacteria
- Cefuroxime: **Pharyngitis, tonsillitis**, AOM, LRI, UTI, impetigo, gonorrhea
- Cefdinir: **CAP**, sinusitis, pharyngitis, skin infections, chronic bronchitis, otitis media in children



# Cephalosporins- Patient Info

## *Administration:*

- Cephalexin: Preferably without food, 1 hour before or 2 hours after a meal with a FULL glass of water. Usually QID dosing
- Cefuroxime: without regard to food (unless suspension). Usually BID dosing
- Cefdinir: without regard to food. No IRON supplements or ANTACIDS within 2 hours of dose
- Some suspensions must be taken with food to increase bioavailability
- N/V/D, less than PCNs

# Cephalosporins- Cross sensitivity

## Cross sensitivity with PCN allergies

- Older studies display a 5-10% risk of cross sensitivity
- It is believed that risk is much lower (0.5%) due to old studies which had PCN contaminated samples
- Cephalexin and Cefuroxime do have same chemical structures that can cause allergic reaction

## Pt. counseling

- There is a small chance of cross sensitivity
- Look for signs of allergy and preferably take 1<sup>st</sup> dose with someone watching

# Macrolide antibiotics

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Azithromycin, Clarithromycin



# Macrolides

Azithromycin (Zithromax<sup>®</sup>, Z-pak<sup>®</sup>, Tri-pak<sup>®</sup>, Zmax<sup>®</sup>)

- tablets (250mg, 500mg, 600mg)
- oral suspension (100mg, 200mg per 5ml; single dose 1gm packets, single dose 2gm ER)

Clarithromycin (Biaxin<sup>®</sup>, Biaxin XL<sup>®</sup>)

- tablets (250mg, 500mg, XR 500mg)
- oral suspension (125mg, 250mg per 5ml)

# Macrolides- Indications

Azithromycin: URI/LRI, **chlamydia**, sinusitis, COPD, AOM, prevention of disseminated *Mycobacterium avium* complex in advanced HIV patients, CAP, skin infection, PID, gonorrhea

Clarithromycin: **pharyngitis**, sinusitis, bronchitis, CAP, skin infection, AOM, adjunct therapy with omeprazole to treat *H. pylori*

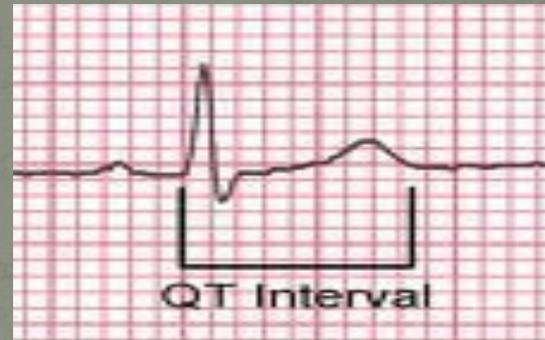
# Macrolides- Patient Info

## Administration:

- Azithromycin-without regard to food, Usually QD dosing
  - **do not take antacids within one hour of administration.**
  - Z-Pak (5 days), Tri-Pak (3 days), Zmax (1 dose)
  - Long  $t_{1/2}$
  - What are the advantages and disadvantages ?
- Clarithromycin- take Biaxin XL with food, otherwise without regard. Usually BID dosing
  - Metallic taste
  - Possible sun sensitivity
  - Avoid grapefruit juice

## Cautions/Contraindications:

- Both: potential for QT prolongation, caution with arrhythmias



# Fluoroquinolone antibiotics

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Ciprofloxacin, Levofloxacin, Moxifloxacin

# Mechanism of Action

- Binds DNA gyrase and topoisomerase IV enzymes, creating a ternary complex and inhibiting DNA replication and transcription
  - LAYMAN's terms: Inhibits DNA replication of bacteria by inhibiting enzymes in bacterial cell.
- Bacteriocidal

# Fluoroquinolones

## Ciprofloxacin (Cipro<sup>®</sup>, Cipro XR<sup>®</sup>)

- tablets (250mg, 500mg, 750mg; XR 500mg, 1000mg)
- oral suspension (250mg, 500mg per 5ml)
- ophthalmic solution (0.3%)

## Levofloxacin (Levaquin<sup>®</sup>)

- tablets (250mg, 500mg, 750mg)
- oral solution (25mg/ml)

## Moxifloxacin (Avelox<sup>®</sup>)

- tablets (400mg)

# Fluoroquinolones- Indications

- Ciprofloxacin: infectious diarrhea, UTI treatment and prophylaxis, LRI, bone and joint infections, anthrax post-exposure prophylaxis. **No longer for gonorrhea!**
- Moxifloxacin: acute sinusitis, bronchitis, CAP, skin infection
- Levofloxacin: similar to cipro, w/ greater gm (-) activity, CAP, sinusitis, bronchitis, skin infections

# Fluroquinolones- Patient Info

## Administration:

- All take with or without food
- Ciprofloxacin: usually BID dosing
- Levofloxacin and Moxifloxacin: usually QD dosing
- ALL: Avoid concurrent use of antacids, iron supplements, metal cations, separate by 2 hours
  - Avoid dairy and antacids 2 hrs before and 6 hrs after with Ciprofloxacin

## Side Effects

- Sun sensitivity
- Headache
- Dizziness
- Dyspepsia (indigestion)
- Ciprofloxacin increases effects of caffeine



# Fluoroquinolones-Patient Info cont.

## Cautions/Contraindications

**Tendon Toxicity-** potential of tendon rupture on all patients but most likely to those with weak composition (elderly) and those who have high stress into the tendons (basketball players), should always keep in mind although **VERY RARE**



Do not use in <18, pregnancy, lactation

Caution in patients with seizure or CNS disorders. Concurrent NSAID use may lower seizure thresholds.

Moxifloxacin: may prolong QT interval

# Tetracycline antibiotics

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Doxycycline, Minocycline, Tetracycline

# Mechanism of Action

- Binds competitively to the 30s ribosomal subunit thus inhibiting bacterial protein biosynthesis
  - LAYMAN's terms: slows down cell growth by inhibiting protein synthesis
- Bacteriostatic

# Tetracyclines

Doxycycline (Vibramycin<sup>®</sup>, Vibra-Tabs<sup>®</sup>)

- capsules (50mg, 100mg)
- tablets (100mg)

Minocycline (Minocin<sup>®</sup>)

- capsules/tablets (50mg, 100mg)

Tetracycline (Sumycin<sup>®</sup>, Panmycin<sup>®</sup>)

- capsules (250mg, 500mg)

# Tetracyclines- Indications

- Doxycycline and minocycline: **acne and skin infections**, PID, urethritis, cervicitis, STDs (Chlamydia, gonorrhea, syphilis), urinary tract infectious disease
- Tetracycline: **severe acne**, mycoplasma, chlamydia, rickettsia, gonorrhea/syphilis in PCN allergic pts, chlamydia

# Tetracyclines – Patient Info

## *Administration:*

- Doxycycline and minocycline: Preferably without food, but can take with food if GI upset occurs. Usually BID dosing.
- Tetracycline: Take on an empty stomach. Usually QID dosing.
- Avoid concurrent use of antacids, iron preps, multivitamins, and dairy products.

# Tetracyclines-Patient Info cont.

## *Side effects:*

- Sun sensitivity, HA, dyspepsia, teeth discoloration, dizziness



## *Caution/contraindications:*

- Not usually recommended in children <8 and in pregnancy. Binds to cations and can turn teeth/nails yellow, decreases bone growth.

- Expired Tetracycline produces toxic metabolites
  - What do you tell patients?

# Lincosamide antibiotics

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Clindamycin

# Mechanism of Action

- Binds reversibly to the 50s ribosomal subunit at the 23s portion of the subunit thus inhibiting bacterial protein biosynthesis
  - LAYMAN's terms: slows down cell growth by inhibiting protein synthesis
- Bacteriostatic antibiotic, but is bactericidal in high concentrations

# Lincosamides

Clindamycin (Cleocin<sup>®</sup>, Clindagel<sup>®</sup>)

- capsules (75mg, 150mg, 300mg)
- topical gel (1%), vaginal cream (2%)
- oral suspension (75mg/5ml)

## *Indications*

- **anaerobic infections of the upper GI tract, intra-abdominal infections**, respiratory tract infections, bacterial vaginosis, PID, Pneumocystis carinii pneumonia, bacterial vaginosis, Necrotizing faeciitis
- Topical preparations used primarily for acne

# Lincosamides- Patient Info

## *Administration*

- Take with full glass of water, without regard to meals. Usually QID dosing.

## *Side Effects*

- **DIARRHEA 20-30% greater risk of pseudomembraneous colitis (PMC) cause by *C. difficile***
- Topical preparations: skin irritation, peeling



## *Caution/contraindications:*

- Higher risk of PMC in pts with liver or kidney disease because of increased half-life: thus dosage reduction in renal/hepatic impairment.
- **[U.S. Black Box Warning]:** Can cause severe and possibly fatal colitis. Discontinue drug if significant diarrhea, abdominal cramps, or passage of blood and mucus occurs.

# Nitroimidazole antibiotics

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Metronidazole

# Mechanism of Action

- Antibiotic is reduced by electron-transport proteins of susceptible bacteria to unstable intermediate compounds which bind to DNA causing DNA strand breakage and cell death
  - LAYMAN's terms: forms toxic compounds which cause bacterial cell death
  - Exact mechanism not well understood
- Bacteriocidal/ Anti-protozoal

# Nitroimidazole

Metronidazole (Flagyl<sup>®</sup>, Flagyl ER<sup>®</sup>, Metrogel<sup>®</sup>)

- tablets (250mg, 500mg, ER 750mg)
- capsules (375mg)
- topical: cream, gel, vaginal gel

## *Indications:*

- **DOC for C. Difficile Associated Diarrhea (CDAD);** Bacterial vaginosis, anaerobic bacterial infections, adjunct in treating H. pylori, skin and skin structure infections, other unique infections (acute intestinal amebiasis, liver abscess amebiasis), trichomoniasis
- Topical: **acne, rosacea**, vaginal yeast infections

# Nitroimidazoles: Patient Info

## *Administration:*

- Take with food or milk. Usually BID dosing.

## *Side Effects:*

- Metallic taste, discoloration of urine (dark brown, rare), dysuria, dry mouth
- More serious: convulsive seizures, peripheral neuropathy
- Topical: skin irritation, pruritis, burning

# Nitroimidazoles: Patient Info cont.

- DO NOT DRINK ALCOHOL!!
- Disulfiram/Antabuse reaction
  - Reaction between EtOH and MTZ
  - SEVERE N/V, abdominal cramping
- What do we tell patients? Which items should they be careful with?
  - Avoid during treatment and 2-3 days after
    - Alcohol
    - Mouthwash
    - Cough Medications containing EtOH



# Sulfonamides antibiotics

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Sulfamethoxazole and trimethoprim (SMZ/TMP)

# Mechanism of Action

- Sulfamethoxazole- is a competitive antagonist of PABA which inhibits bacterial synthesis of dihydrofolic acid.
- Trimethoprim- blocks production of tetrahydrofolic acid by inhibiting the enzyme dihydrofolate reductase
  - LAYMAN's terms: slows down cell cycle of bacteria by inhibiting formation of folic acid in bacterial cells
- Bacteriostatic

# Sulfonamides

- Sulfamethoxazole/Trimethoprim (Bactrim<sup>®</sup>, Septra<sup>®</sup>)
- tablets: single strength (400mg/80mg); double strength (800mg/160mg)
- oral suspension (200mg/40mg per 5ml)

## *Indications*

- **DOC for uncomplicated UTI, AOM, traveler's diarrhea, bronchitis, pneumocystis carinii pneumonia (PCP) treatment and prophylaxis, acute exacerbation of COPD, traveler's diarrhea**

# Sulfonamides- Patient Info

## *Administration:*

- Preferably on an empty stomach with a full glass of water. If GI upset, ok with food. Usually BID dosing
- SHAKE SUSPENSION WELL!!  
Keep at room temperature.

## *Side Effects:*

- Sun sensitivity is common, diarrhea, dizziness, dark colored urine/stool, fever
- Allergies: RASH (~10%),  
Urticaria

## *Caution/contraindications:*

- Patients with impaired hepatic/renal function, folate deficiency, interactions with diuretics, hypoglycemic meds.
- Pregnancy, lactation, infants <2 months

# Nitrofuran antibiotics

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Nitrofurantoin

# Mechanism of Action

- A Prodrug that is reduced by nitrofuran reductase: the metabolites damage bacterial DNA by attacking ribosomal proteins, DNA, and other processes.
- Also may interfere with carbohydrate metabolism in bacteria.
  - LAYMAN's terms – drug metabolites inside bacteria inhibit DNA synthesis and other processes
- Bacteriocidal

# Nitrofuran

## Nitrofurantoin (Macrobid<sup>®</sup>; Macrochantin<sup>®</sup>)

- Macrochantin Capsule, macrocrystal (25mg, 50 mg, 100 mg)
- Macrobid Capsule, macrocrystal/monohydrate (100 mg)
- oral suspension (25 mg/5 mL)

## *Indications*

- Prevention and treatment of uncomplicated UTI

# Nitrofuran- Patient Info

## *Administration:*

- Take with food to enhance absorption. Usually QID dosing.

## *Side effects:*

- Don't take Mg salts, which may decrease effectiveness
- Urine may turn dark yellow or brown

## *Caution/contraindications:*

- Renal impairment and pregnancy at term, also for dialysis patients.
- Infants < 1months
- Contraindicated in G6PD-deficient patients

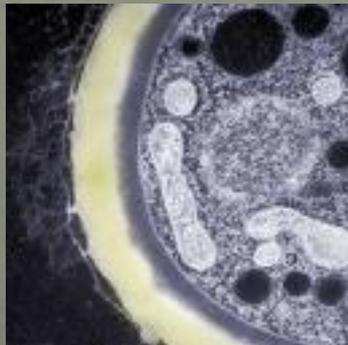
# Antifungals

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Fluconazole, Ketoconazole, Nystatin, Terbinafine

# Mechanism of Action

- Fluconazole- inhibition of CYP<sub>450</sub> enzyme dependent ergosterol synthesis
- Ketoconazole and Terbinafine- impair synthesis of ergosterol
- Nystatin- binds to sterols in cell membrane and changes permeability
  - LAYMEN's terms: prevents proper production of fungal cell wall



# Antifungals

## Fluconazole (Diflucan<sup>®</sup>)

- tablets (50mg, 100mg, 150mg, 200mg)
- oral suspension (10mg, 40mg per 5ml)

## Ketoconazole (Nizoral<sup>®</sup>)

- tablets (200mg)
- shampoo and cream (2%)

## Nystatin (Bio-Statin<sup>®</sup>)

- tablets (500,000 units USP)
- oral suspension (100,000 units USP per ml)

## Terbenafine (Lamisil<sup>®</sup>)

- capsules (250mg)
- shampoo, cream, spray (1%)

# Antifungals- Indications

- Fluconazole and Ketoconazole: **Treatment of oropharyngeal and esophageal candidiasis, systemic candidal infections including UTI, peritonitis, and pneumonia**

- Ketoconazole: **tinea infections and seborrheic dermatitis (topical)**

- Nystatin: **oral candidiasis, non-esophageal mucous membrane GI candidiasis**



- Terbenafine: **onychomycosis of toenail/fingernail due to dermatophytes, ringworm, athlete's foot**

# Antifungals- Patient Info

## *Administration:*

- Take with food if GI upset
- Oral therapy is usually LONG term
- Ketoconazole: separate from antacids by 2 to 4 hours. Usually BID dosing.
- Fluconazole and terbinafine: usually QD dosing.
- Nystatin usually QID dosing

## *Side effects:*

- HA, dizziness, changes in taste, N/V/D

## *Caution/contraindications:*

- Severe liver disease
- [US Black Box Warning]
  - Azoles (especially ketoconazole) have many interactions with drugs since MOA involves P450 enzymes (i.e. warfarin, phenytoin, benzodiazepines, cimetidine). Adjust dose in dialysis patients

# Questions?

- Quiz next week:
  - Know common counseling points for all antibiotics
  - Know the different allergic reactions and what steps patients should take
  - Know all anti-infective classes, MOA, and examples of drugs in each class
  - Know any special counseling points, side effects, or toxicities for drugs (look for things in all CAPS)
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