



Formula C₁₆H₁₇KN₂O₄S

CHEMOTHERAPY



And Anti-Microbial Drug Resistance

Common Abbreviations

- qd = every day
- bid = twice a day
- tid = three times a day
- qid = four times a day
- hs = at bed time
- ac = before eating breakfast
- pc = after eating a meal; generally 2 hours afterwards
- prn = as necessary
- SGOT = serum glutamate oxaloacetate transaminase, now known as AST, aspartate amino transferase, a liver and heart marker enzyme
- SGPT = serum glutamate pyruvate transaminase, now known as ALT, alanine amino transferase, a liver and heart marker enzyme
- LDH = lactate dehydrogenase; a liver marker enzyme
- AIP = alkaline phosphatase; a liver and bone marker enzyme

- BUN = Blood urea nitrogen, a kidney marker metabolite
- Creatinine = a kidney marker metabolite
- CBC = complete blood count; usually includes RBC count, WBC count, platelet count, hemoglobin, hematocrit, WBC differential; may include MCH, MCHC, MCV and RDW
- qod = every other day
- ad lib = as often as desired
- "c" with a line over it = with
- s = within
- "s" with a line over it = without
- CPK-MB (or CK-MB) = creatine phosphokinase-MB fraction; a heart marker enzyme
- 2° = secondary to; because of; due to
- PT = prothrombin time; a measure of the blood's/body's ability to clot

Introductory Chemotherapy Comments

Definition

- = the use of chemical agents in the treatment of bacterial, or bacteria-like, infections.
- NOT to be confused with cancer chemotherapy.

- In general, drugs are metabolized faster with a high protein and low carbohydrate diet rather than vice versa.
- A drug that has not been ionized will morereadily diffuse from urine back to the blood.
- In some instances, alkaline urinary pH increases tubular reabsorption which reduces renal elimination and increases the duration of action – may lead to toxicity, e.g., imipramine (tricyclic antidepressant [Tofranil] and amphetamine.
- 2-3 g vitamin C qd reduces the pH of urine to \leq 5.5
- Patients taking antacids or diuretics will have alkaline urine, e.g., acetazolamide (Diamox)

- Dysgeusia: loss of taste may be secondary to meds
 - Griseofulvin antifungal
 - Penicillamine anti-arthritic
 - Many antilipemics
 - Phenytoin anticonvulsant
 - Methimazole anti-thyroid
- Antabuse reactions are possible, as well:
 - Flagyl
 - Furazolidone
 - Chlorpropamide
 - Griseofulvin
 - Quinacrine
 - Procarbazine

Best rule: no alcohol while taking medications within 24 hours before use and within 72 hours after last use.

- ASA: 1-3 g = 5 mL blood loss and 2 mg Fe loss
- ASA: absorbed more rapidly with refrigerator cold water on empty stomach
- UTI "may" be due to allergies
- Primary Offenders are:
 - Citrus fruits
 - Tomatoes
 - Pepper
 - Chocolate
 - Grapes
 - Apples
 - Watermelon
- Elimination of these foods reduce UTI sx

General Summary of Selected Medications that are

Involved with/in Skin Sun Sensitization

Generic Name	Trade Name
Azithromycin	Zithromax
Ciprofloxacin	Cipro
Minocycline	Minocin
Ofloxacin	Floxacin
Tetracycline	Achromycin
Isotretinoin	Accutane
Tretinoin	Retin-A
Diphenhydramine	Benadryl
Amitryptyline	Elavil
Trazodone	Desyrel
Daily Ibuprofen	Advil
Daily Naproxen	Aleve

St. John's Wort sensitizes skin to sun, as well.

Microbial Sources of Some Antibiotics

Microorganism	Antibiotic
Bacteria	
Streptomyces spp.	Amphotericin B, Clavulanic acid, Chloramphenicol, Kanamycin, Lincomycin, Oxytetracycline, Erythromycin, Neomycin, Rifampin, Streptomycin, Tetracycline
Micromonospora spp.	Gentamicin
Amycolatopsis	Vancomycin
Bacillus spp.	Polymyxin B
Fungi	
Penicillium spp.	Griseofulvin, Penicillin
Cephalosporium spp.	Cephalosporins

Mechanisms of Antibacterial Drug Action

Five Classes of Antibiotics



Cell Wall Synthesis Inhibitors Examples



Example Cell Wall Synthesis Inhibitors Action Mechanisms



Translation Inhibitors Examples



Example Translation Inhibitors Action Mechanisms

Rib

PABA

TŇF

mes

Tetracycline NOTE: Reduces plasma PT* activity and causes an increased risk of bleed out UNLESS anticoagulants are reduced. Streptomycin/Gentamycin: bind with bacterial ribosomal sub-unit to inhibit translation and cause mis-reading of the mRNA; Chloramphenicol: binds with bacterial ribosomal sub-unit to block peptide bond formation by inhibiting peptidyl transferase; Tetracycline: binds with bacterial ribosomal sub-unit and interferes with amino-acyl tRNA binding. PCN/Cephalosporins: inhibit transpeptidization enzymes involved in the cross-linking of the polysaccharide chains of the bacterial cell wall peptidoglycan; activates lytic enzymes in the cell wall; Bacitracin: inhibits cell wall synthesis by interfering with the action of the lipid carrier that transports wall precursors across the cell membrane; LY121019: on C. albicans (fungus ["yeast"]) causes cell lysis.

> Poly-Myxin-B: binds to cell membrane and disrupts its structure and permeability properties

Rifampin: blocks transcription by inhibiting RNA polymerase (DNAdependent) INH: Disrupts NAD metabolism and functioning; <u>Sulfonamides</u>: inhibits folate synthesis competing for PABA; <u>Trimethoprim</u>: DHFR inhibitor blocks THF synthesis

Nucleic Acid Synthesis/Function Inhibitors Examples



Example Nucleic Acid Synthesis/Function Inhibitors Action Mechanisms



Cell Membrane Disruptors Examples



Example Cell Membrane Disruptors Action Mechanisms



Metabolic Antagonists Examples



Example Metabolic Antagonists Action Mechanisms



Miscellaneous Chemotherapeutic Drugs	
Fungizome IV (Amphotericin B)	Antifungal
Lotrimin (Clotrimazole)	Antifungal
Spectazole (Econazole)	Antifungal
Grisactin (Griseofulvin)	Antifungal
Flagyl; Protostat (Metronidazole)	Antiprotozoal; anti-anaerobic
Monistat (Miconazole)	Antifungal
Mycostatin (Nystatin)	Antifungal
Virazole (Ribavirin)	Antiviral
Vagitrol (Sulfanilamide)	Anti-Candidal
Desenex (Undecylenic acid)	Antifungal (athlete's foot)

β -Lactamase Inhibition



Cephalosporinase v Penicillinase



Penicillinase Cephalosporinase Inactivates "SOME", but Inactivates not with efficiency

Resistance of cephalosporins to cephalosporinase depends on the size of the R' groups (steric hindrance), i.e., the greater the size, the greater the resistance.

Chemotherapy of Some Representative Bacterial Pathogens

Pathogen	Representative Diseases	Drugs of Choice (In approximate order of preference)
G + Bacteria		
S. pneumoniae	Pneumonia	PCN, erythromycin or 3d generation cephalosporin until C&S are back
α-, β-hemolytic Streptococcus	Strep throat, skin infections, rheumatic fever	PCN, cephalexin or amoxicillin (Augmentin)
C. diphtheriae	Diphtheria	Diphtheria anti-toxin, followed by 14 days tx with Erythromycin or PCN

Pathogen	Representative Diseases	Drugs of Choice (In approximate order of preference)
G - Bacteria		
N. gonorrhoeae	Gonorrhea	recently – cefixime, ceftriaxone (#1 choice per CDC), azithromycin, doxycycline – last groups of antibiotics effective (losing cefixime effectiveness) on N. gonnorrhoeae
B. pertussis	Whooping cough	Erythromycin, azithromycin and clarithromycin > 1 MOA; <1 MOA, azithromycin only; > 2 MOA SXT appropriate
E. coli	UTI	Sulfonamides, AMP – multi-resistance is progressing – research continues for more alternatives
K. pneumoniae	Pneumonia, UTI	Cephalosporin, gentamicin for non-drug resistant strains – carbapenems (e.g., Biapenem) last line of tx and Carbapenem Resistant Enterobacteraciae (CRE) on the rise may lead to fatal disease
S. typhi	Typhoid fever	Chloramphenicol, cephtriaxone or AMP
Shigella dysenteriae	Dysentery	AMP, SXT, cephtriaxone, ciprofloxacin or chloramphenicol; TET
V. cholerae	Cholera	Doxycycline for adults; azithromycin for children and pregnant women. 26

Pathogen	Representative Diseases	Drugs of Choice (In approximate order of preference)
AFB		
M. tuberculosis	Tuberculosis	INH + rifampin; pyrazinamide, ethambutol, streptomycin in various combinations for MDRMT; rifapentine; XDRMT tough to treat
Other Bacteria		
T. pallidum	Syphilis	PCN, erythromycin (resistance developing), TET
M. pneumoniae	Walking pneumonia	TET, erythromycin, doxycycline
Rickettsia spp.	Rocky Mtn Spotted Fever	Doxycycline, TET, chloramphenicol, azithromycin, rifampin, nalidixic acid and cipro (fluoroquinolones), fluoroquinolones are up to their 4 th generation of development and most are too toxic for safe use – still use 1 st generation fluro's for tx.

PCN = penicillin; AMOX = amoxicillin;

TET = tetracycline; MDRMT = multi drug-resistant M. tuberculosis

FDA Pregnancy Categories

A: O.k. for use during pregnancy

B: Animal studies show no fetal risk; no comparable studies in women

C: Animal studies show fetal adversity; no comparable studies in women

D: Risk to fetus, but benefits MAY be worth the high risks

X: Absolutely not safe during pregnancy; risks FAR outweigh the benefits

Drugs are not administered during pregnancy UNLESS they are ABSOLUTELY required!

DO NO HARM!!!!!

Antibiotics

GENERIC DRUG NAME: Amikacin

CATEGORY: Aminoglycoside

DRUG TRADE NAME: Amikin

INDICATION/USAGE: Short term therapy due to susceptible G-bacteria: Pseudomonas, E. coli, Proteus, Providencia, Klebsiella, Serratia;

G+: also for Staphylococcal infections (including MRSA) coupled with a β -lactamase inhibitor

PREGNANCY CATEGORY: D

WARNINGS: Use as a last resort in the elderly; Hydrate patient well; Ototoxic (VIII); Nephrotoxic; Avoid using diuretics with amikacin (also VIII); Neurotoxic (numbness, twitching, tingling)

MONITORING TESTS: \downarrow SpG, \uparrow BUN, \uparrow Creatinine, urinary casts, RBC, WBC, or \uparrow urinary albumin, creatinine clearance: Reduce or d/c

COMMENTS: Use with caution in patient's with Parkinson's or myasthenia gravis 2° to ↑ muscle weakness; Derivative of kanamycin

GENERIC DRUG NAME: Amoxicillin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Amoxil

INDICATION/USAGE: G-: H. influenzae, E. coli, P. mirabilis, N. gonorrhoeae

G+: Streptococci (including faecalis), S. pneumoniae and n-PP* Staphylococci

PREGNANCY CATEGORY: B

WARNINGS: Determine other drug allergies; May permit hypercolonization of C. difficile

MONITORING TESTS: ↑SGOT (non-specific finding)

COMMENTS: Stable to gastric acid, therefore, can give with disregard to meals; Analog of PCN; with clavulanic acid = Augmentin

GENERIC DRUG NAME: Amphotericin B CATEGORY: Antifungal Cell Membrane Disrupter DRUG TRADE NAME: Fungizome IV **INDICATION/USAGE:** Apergillosis, candidiasis, systemic histoplasmosis PREGNANCY CATEGORY: B WARNINGS: Do not use if a nursing mother; Give SLOW IV: too fast will put the patient in shock; Wrap IV line with AI foil to protect from light; Do not reconstitute with normal saline MONITORING TESTS: Renal function, Liver panel, Electrolytes (especially Mg²⁺ and K⁺), CBC

COMMENTS: Use ONLY in life-threatening disease and/or invasive disease; Do not use of a precipitate is present; wear gloves while preparing this drug

GENERIC DRUG NAME: Ampicillin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Omnipen-N

INDICATION/USAGE: G-: Shigella, Salmonella, H. influenzae, E. coli, P. mirabilis, N. gonorrhoeae, N. meningitidis, Klebsiella

G+: Streptococci, S. pneumoniae, n-PP staphylococcus

PREGNANCY CATEGORY: B

WARNINGS: Determine other drug allergies; Diarrhea may occur; Thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia been reported (suggestive of sensitization reactions)

MONITORING TESTS: \uparrow SGOT (non-specific); may give false positive reactions for glucose in urine with Clinitest TM, Benedict's or Fehling's solution, NOT with enzymatic testing; Estrogens decrease in pregnancy 2° AMP; \uparrow SGPT, Alkaline phosphatase and LDH; \downarrow CBC; \uparrow BUN and creatinine. Reduce or d/c

COMMENTS: Analog of PCN

GENERIC DRUG NAME: Azithromycin

CATEGORY: Translation inhibitor (macrolide)

DRUG TRADE NAME: Zithromax

INDICATION/USAGE: 1) Bacterial exacerbations of COPD secondary to H. influenzae, M. catarrhalis, S. pneumoniae; 2) Pneumonia secondary to S. pneumoniae or H. influenzae on out-patient basis; 3) Uncomplicated S. aureus infections of the skin; 4) NGU and cervicitis secondary to C. trachomatis; 5) As an alternative in the treatment of S. pyogenes for those sensitive to first-line

regimens

PREGNANCY CATEGORY: B

WARNINGS: 1) Hypersensitivity to macrolides (e.g., erythromycin); 2) S. faecalis and MRSA are resistant/cross-resistant with erythromycin; 3) As with Biaxin; 4) Avoid concomitant antacids; 5) Give one hour before or two hours after meals; 6) May cause vaginitis due to C. albicans over growth; 7) May cause rash

and photosensitivity similar to that seen with tetracyclines

GENERIC DRUG NAME: Bacampicillin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Spectrobid

INDICATION/USAGE: Upper and lower respiratory infections caused by: β-hemolytic Streptococci, S. pyogenes, S. pneumoniae, H. influenzae

UTI: E. coli, P. mirabilis, S. faecalis

Uncomplicated N. gonorrhoeae

PREGNANCY CATEGORY: B

WARNINGS: Determine previous hypersensitivity; Double check cross reactivity with cephalosporins; May be super-infections; False positive urine glucoses by chemical testing, but not be enzymatic testing (see AMP)

MONITORING TESTS: SGOT, CBC, Platelets with diffy

COMMENTS:
GENERIC DRUG NAME: Bacitracin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Bacitracin

INDICATION/USAGE: G+ organisms; specifically staphylococcal infections

PREGNANCY CATEGORY: C

WARNINGS: IM therapy: renal failure; Hydrate patient; Double check intake and output (I/O)

MONITORING TESTS: Albuminuria, azotemia

COMMENTS: Produced by B. subtilis

GENERIC DRUG NAME: Carbenicillin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Geocillin

INDICATION/USAGE: G-: E. coli, P. mirabilis, M.

morganii, P. vulgaris, Pseudomonas

G+: S. faecalis

PREGNANCY CATEGORY: B

WARNINGS: Determine hypersensitivity; May be unsafe for pediatric usage

MONITORING TESTS: ↑SGOT (non-specific)

COMMENTS: PCN analog; Avoid use in nursing mothers; Acid stable

GENERIC DRUG NAME: Cefaclor

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Ceclor

INDICATION/USAGE: G-: H. influenzae, E. coli, P. mirabilis, Klebsiella

G+: S. pneumoniae, Staphylococci, S. pyogenes

PREGNANCY CATEGORY: B

WARNINGS: Determine hypersensitivity; Refrain from use in infants < 1 month of age; May give positive direct Coombs' test; Diarrhea 2° C. difficile

MONITORING TESTS: ↑SGOT, ↑SGPT, ↑Alkaline phosphatase, ↑BUN, ↑Creatinine

COMMENTS: May also give false positive urinary glucose tests with Benedict's, Fehling's and Clinitest Tablets -- NOT with Tes-Tape (enzymatic method); cephalosporin

GENERIC DRUG NAME: Cefoxitin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Mefoxin

INDICATION/USAGE: G-: E. coli, Klebsiella, H. influenzae, Bacteroides, P. mirabilis, P. vulgaris, N. gonorrhoeae

G+: Streptococcus (except faecalis), S. aureus, Clostridium spp., peptostreptococcus

PREGNANCY CATEGORY: B

WARNINGS: Diarrhea 2° C. difficile; Determine hypersensitivity; Refrain from use in infants < 3 months of age; May exacerbate myasthenia gravis

MONITORING TESTS: ↑SGOT, ↑SGPT, ↑LDH, ↑Alkaline phosphatase with jaundice; ↑BUN, ↑Creatinine

COMMENTS: Cephalosporin; Nephrotoxicity increases with combined aminoglycoside therapy

GENERIC DRUG NAME: Cephalexin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Keflex

INDICATION/USAGE: G+: S. pneumoniae, S. pyogenes (PCN drug of choice, but may use Keflex), Staphylococci

G-: M. catarrhalis, H. influenzae, P. mirabilis, K. pneumoniae

PREGNANCY CATEGORY: B

WARNINGS: Determine hypersensitivity; May be cross allergenicity with PCN's and cephalosporins; Diarrhea, 2° C. difficile; May have positive direct Coombs'; False positive reactions for glucose by reductive methods (chemical), NOT with enzyme

MONITORING TESTS: As per other cephalosporins

COMMENTS: In overdose: GI decontamination not necessary UNLESS 5-10X the dose has been ingested GENERIC DRUG NAME: Cephalothin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Keflin

INDICATION/USAGE: G+: S. pneumoniae, Staphylococci, S. pyogenes, S. viridans

G-: Klebsiella, H. influenzae, E. coli, P. mirabilis, Salmonella, Shigella

PREGNANCY CATEGORY: B

WARNINGS: Determine hypersensitivity; Diarrhea 2° C. difficile; False positive urine glucoses; Refrain from giving to nursing mothers

MONITORING TESTS: \uparrow SGOT, \uparrow AIP (Alkaline phosphatase), \uparrow BUN, \downarrow creatinine clearance

COMMENTS: Cephalosporin; NOT recommended for meningitis; Do NOT mix with aminoglycosides: 1 nephrotoxicity; Over dose may cause seizures

GENERIC DRUG NAME: Chloramphenicol

CATEGORY: Translation Inhibitor

DRUG TRADE NAME: Chlormycetin

INDICATION/USAGE: S. typhi, H. influenzae (especially meningitis), Rickettsia

PREGNANCY CATEGORY: X

WARNINGS: Aplastic anemia with death after local application has been reported; Aplastic anemia terminating in leukemia been reported; Must be given topically (eye) or IV or p.o.: IM ineffective

MONITORING TESTS: Liver panel, CBC with diffy, Urine dipstick for Hgb

COMMENTS: Depression common; NOT to be used trivially: DANGEROUS

GENERIC DRUG NAME: Ciprofloxacin

CATEGORY: Nucleic Acid Synthesis Inhibitor

DRUG TRADE NAME: Cipro

INDICATION/USAGE: G-: E. coli, K. pneumoniae, P. mirabilis, P. aeruginosa, H. influenzae, H. parainfluenzae, P. vulgaris, S. marcescens, C. jejuni, S. flexneri or sonnei

G+: S. pneumoniae, S. aureus, S. pyogenes, S. faecalis

PREGNANCY CATEGORY: C

WARNINGS: Refrain from use in GROWING children and pregnant/lactating women (2° arthropathies); May cause seizures, psychosis; Do NOT mix with theophylline; Diarrhea 2° C. difficile; Preferred dose 2 hours pc; Take fluids po ad lib; Refrain from antacids, Fe and Zn; Until patient knows how reacts to drug, refrain from operating machinery; Reduce caffeine intake

MONITORING TESTS: ↑SGOT, ↑SGPT, ↑AIP, ↑LDH, ↑Bilirubin, Eosinophilia, ↑BUN, ↑Creatinine

COMMENTS: With overdose: induce vomiting or gastric lavage; H₂ antagonists do not affect bioavailability of ciprofloxacin 44

GENERIC DRUG NAME: Clarithromycin

CATEGORY: Translation inhibitor (macrolide; erythromycin "substitute")

DRUG TRADE NAME: Biaxin

INDICATION/USAGE: M. pneumoniae (primary atypical pneumonia); MAC (mix with other drugs); S. pyogenes (tonsillitis); S. pneumoniae (acute maxillary sinusitis); M. catarrhalis; uncomplicated S. aureus infections

PREGNANCY CATEGORY: C

WARNINGS: 1) May increase effects of carbamazepine, Dilantin, theophylline, terfenadine, digoxin, coumadin, ergotamines, cyclosporine; 2) Do not use with patients on terfenadine who have cardiac arrhythmias; 3) Do not use on patients with electrolyte imbalances; 4) Do not give if patient has known hypersensitivity to macrolides; 5) May inhibit the action of AZT; 6) May cause N/V; 7) May cause cephalalgia; 8) May cause ventricular arrhythmias, including torsades de pointes (a very rapid ventricular tachycardia characterized by a strange QRS complex: it looks sort of twisted; may stop itself or develop into ventricular fibrillation)

MONITORING TESTS: GPT (ALT); GOT (AST); AIP; LDH; Bilirubin; BUN;

creatinine: with elevations of these, d/c or "manipulate the dosage" of the drug

Clarithromycin

 Torsade de pointe – many spellings – "twisted points" about isoelectric line of EKG; a rapid v tach with a changing QRS complex; usually self-limiting, may, however, change into v fib – looks like a "twisted ribbon"



GENERIC DRUG NAME: Clavulanic acid

CATEGORY: β-Lactamase Inhibitor

DRUG TRADE NAME: Clavulanic acid

INDICATION/USAGE: with PP-bacteria

PREGNANCY CATEGORY: B

WARNINGS: Determine hypersensitivity

MONITORING TESTS:

COMMENTS: Coupled with amoxicillin = Augmentin

GENERIC DRUG NAME: Clindamycin

CATEGORY: Translation Inhibitor

DRUG TRADE NAME: Cleocin

INDICATION/USAGE: Streptococci, Staphylococci, Pneumococci

PREGNANCY CATEGORY: B

WARNINGS: Diarrhea 2° C. difficile (Fatal colitis); Exacerbates effects of neuromuscular blocking agents; Refrain from using ointment with preemie infants (contains benzyl alcohol = allergen); Use may result in "yeast" hypergrowths

MONITORING TESTS: For chronic use: Liver panel, Kidney panel and CBC

COMMENTS: Antagonized by erythromycin; acne treatment; reserve for PCN-allergic patients; derivative of lincomycin

GENERIC DRUG NAME: : Clotrimazole

CATEGORY: Antifungal

DRUG TRADE NAME: Lotrimin

INDICATION/USAGE: Tinea pedis, Tinea cruris, Tinea corporis (Trichophyton, Epidermophyton, Microsporum)

PREGNANCY CATEGORY: B

WARNINGS: Keep out of eyes; Determine hypersensitivity

MONITORING TESTS: prn with dx

COMMENTS: pedis = foot; capitis = scalp; corporis = non-hairy part of body; cruris = groin; unguium = finger/toe nails; versicolor = pale tan fungal infection on upper trunk/arms that does not tan in sun -- fluoresces under Wood's light (UV light at 365 nm)

GENERIC DRUG NAME: C	Colistin
----------------------	----------

CATEGORY: Cell Membrane Disrupter

DRUG TRADE NAME: Coly-Mycin S

INDICATION/USAGE: E. coli, Shigella, P. aeruginosa, Klebsiella

PREGNANCY CATEGORY: C

WARNINGS: Double check renal function before therapy with this drug

MONITORING TESTS: BUN, creatinine, Creatinine clearance

COMMENTS: Oral suspension and topical suspension for ears

GENERIC DRUG NAME: Dicloxacillin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Pathocil

INDICATION/USAGE: PP-Staphylococci and non-PP Staphylococci

PREGNANCY CATEGORY: B

WARNINGS: Determine Hypersensitivity; p.o. 1° ac or 2° pc

MONITORING TESTS: BUN, Creatinine, SGOT, SGPT: With elevations, reduce or d/c

COMMENTS: Derivative of PCN; absorption delayed after meal

```
GENERIC DRUG NAME: Econazole
```

CATEGORY: Antifungal

DRUG TRADE NAME: Spectazole

INDICATION/USAGE: Same as clotrimazole, wider spectrum

PREGNANCY CATEGORY: C

WARNINGS: Keep out of eyes

MONITORING TESTS: prn with dx

COMMENTS:

GENERIC DRUG NAME: Erythromycin

CATEGORY: Translation Inhibitor

DRUG TRADE NAME: Ilotycin

INDICATION/USAGE: S. pyogenes, S. pneumoniae, M. pneumoniae, B. pertussis, E. histolytica, PID (2° N. gonorrhoeae), S. aureus, T. pallidum*, L. pneumophila

PREGNANCY CATEGORY: B

WARNINGS: Hepatic dysfunction; May potentiate theophylline toxicity; May elevate digoxin levels; Potentiates anticoagulant activity

MONITORING TESTS: Liver panel

COMMENTS: Acid labile: 1° ac or 2° pc; *for PCN-allergic patients; interferes with fluorimetric catecholamine determination in urine

GENERIC DRUG NAME: Ethambutol

CATEGORY: Metabolic Antagonist

DRUG TRADE NAME: Myambutol

INDICATION/USAGE: Mycobacterial infection

PREGNANCY CATEGORY: \mathbf{X}

WARNINGS: Not for use in children < 13 YOA; Couple with INH [+streptomycin]; Determine hypersensitivity; Causes ophthalmopathology (color, etc); Requires 100% compliance

MONITORING TESTS: Uric acid (gout), Liver panel

COMMENTS: Hydrate patient well

GENERIC DRUG NAME: Furazolidone

CATEGORY: Metabolic Antagonist

DRUG TRADE NAME: Furoxone

INDICATION/USAGE: Broad spectrum; specifically, bacterial or protozoal diarrhea

PREGNANCY CATEGORY: C

WARNINGS: Stop alcohol intake during and thru 4 days after therapy; MAOI's, tyramine containing foods to be d/c'd; Nasal decongestants to be d/c'd; Keep from infants < 1 month of age (2° hemolytic anemia)

MONITORING TESTS: CBC with diffy; plasma Hgb

COMMENTS: Observe people with Mediterranean, Near-Eastern and African origin for hemolysis (is reversible when therapy stopped)

```
GENERIC DRUG NAME: Gentamicin
```

CATEGORY: Aminoglycoside/Translation Inhibitor

DRUG TRADE NAME: Garamycin

INDICATION/USAGE: P. aeruginosa, Proteus, E. coli, Klebsiella, Serratia, Staphylococcus

PREGNANCY CATEGORY: C

WARNINGS: Potentially nephrotoxic; Ototoxic; As with Amikacin

MONITORING TESTS: As per Amikacin, plus, Ca²⁺, Na⁺ and K⁺

COMMENTS: See Amikacin for cautions

GENERIC DRUG NAME: Griseofulvin

CATEGORY: Anti-fungal -- binds to keratin

DRUG TRADE NAME: Grisactin

INDICATION/USAGE: Very broad spectrum; wider than Econazole

PREGNANCY CATEGORY: Do NOT prescribe for pregnant women or women contemplating pregnancy

WARNINGS: Determine hypersensitivity; MAY be cross reactive with PCN (2° from penicillium spp.); Causes photosensitivity; Decreases activity of warfarin anticoagulants; Barbiturates decrease griseofulvin activity; No alcohol with griseofulvin; Griseofulvin may increase estrogen metabolism and DECREASE effectiveness of OCP activity and result in pregnancy

MONITORING TESTS: Liver panel; Renal panel

COMMENTS: po vs topical (other three anti-fungals)

GENERIC DRUG NAME: Isoniazid

CATEGORY: Metabolic Antagonist

DRUG TRADE NAME: INH

INDICATION/USAGE: M. tuberculosis

PREGNANCY CATEGORY: Undetermined, but is embryocidal in rats and rabbits

WARNINGS: Fatal hepatitis; Do not give with liver disease; Stop alcohol use; Double check vision regularly (before and during therapy); 100% compliance required

MONITORING TESTS: SGOT, SGPT, Bilirubin, UA (For bilirubin), CBC with diffy

COMMENTS: Can cause gynecomastia

GENERIC DRUG NAME: Kanamycin

CATEGORY: Aminoglycoside/Translation Inhibitor

DRUG TRADE NAME: Kantrex

INDICATION/USAGE: E. coli, Proteus, K. pneumonia, S. marcescens -- MAY be used for Staphylococcus, but NOT drug of choice

PREGNANCY CATEGORY: D

WARNINGS: Ototoxicity; Nephrotoxicity; Neurotoxicity; See also Amikacin

MONITORING TESTS: See Amikacin

COMMENTS: See Amikacin

CATEGORY: Translation Inhibitor

DRUG TRADE NAME: Lincocin

INDICATION/USAGE: Streptococcus, Staphylococcus -- reserve for PCN-allergic patients -- primarily G+ bacteria including C. tetani and C. perfringens

PREGNANCY CATEGORY: B or C – both exist – err on side of caution

WARNINGS: Diarrhea 2° C. difficile (opiates and Lomotil worsen the condition); Determine hypersensitivity; Is also a neuromuscular blocker (like Clindamycin)

MONITORING TESTS: Liver/Renal panels, CBC

COMMENTS: *NOTE:* The injection contains benzyl alcohol, which has been associated with a fatal gasping syndrome in infants.

GENERIC DRUG NAME: Methicillin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Staphcillin

INDICATION/USAGE: PP-Staphylococci

PREGNANCY CATEGORY: B

WARNINGS: Determine hypersensitivity; Do not concurrently give TET (antagonizes); Hydrate patient well; Avoid use in infants

MONITORING TESTS: UA, BUN, Creatinine, SGOT, SGPT, C and S useful

COMMENTS: Penicillinase resistant PCN; May depress bone marrow activity

GENERIC DRUG NAME: Metronidazole

CATEGORY: Anti-protozoal; anti-anaerobic agent

DRUG TRADE NAME: Flagyl; Protostat

INDICATION/USAGE: ORAL: T. vaginalis; E. histolytica, Bacteroides, Clostridia; IV: Bacteroides, Clostridia

PREGNANCY CATEGORY: B

WARNINGS: Seizures have been reported; NO alcohol (Antabuse effect); Reduce doses for patients with hepatic disease; Increases activity of warfarin anticoagulants; May cause Li toxicity; Interferes with assays for SGOT, SGPT, LDH, TGS, Hexokinase (glucose) activity; Use ONLY for amebiasis in children; May have metallic taste in mouth; May flatten T-wave

MONITORING TESTS: EKG, CBC, Platelets, UA

COMMENTS: Treat BOTH partners for T. vaginalis; Give slow IV drip; Keep away fro AI containing IV supplies (needles, cannulas); IV solutions need to be neutralized \rightarrow CO2 produced = relieve gas pressure in container; Do NOT refrigerate neutralized solution: it PRECIPITATES!!!!!!

Flagyl Add-on

- May leave a metallic taste in mouth
- Flagyl + food delays absorption but decreases gastric irritation
- Add to Tetracycline page:
- Do NOT take with Fe or Zn

GENERIC DRUG NAME: Miconazole

CATEGORY: Anti-fungal

DRUG TRADE NAME: Monistat

INDICATION/USAGE: Vulvovaginal candidiasis, Trichophyton, Epidermophyton

PREGNANCY CATEGORY: **Do NOT use vaginally in first trimester;**

Otherwise: C

WARNINGS: Refrain from use when nursing; Keep out of eyes; Determine hypersensitivity; Increases Coumarin activity; Do not give rifampin at same time (Lowers miconazole levels); Do not give concurrently with cyclosporine (elevates cyclosporine levels)

MONITORING TESTS: CBC, Electrolytes, Lipids, Platelets

COMMENTS:Sold OTC as Micatin

GENERIC DRUG NAME: Mupirocin

CATEGORY: Translation inhibitor

DRUG TRADE NAME: Bactroban Ointment

INDICATION/USAGE: Impetigo secondary to S. aureus; b-hemolytic

Strep, S. pyogenes

PREGNANCY CATEGORY: B

WARNINGS: 1) Hypersensitivity to drug or ointment base: d/c; 2) Burning, itching, contact dermatitis: d/c; 3) Do NOT use in eyes! or on mucous membranes; 4) Temporarily d/c if nursing as not known if it crosses into milk

MONITORING TESTS: Observe for dermal reactions; observe BUN and creatinine in patients with questionable renal function: with elevations, d/c

GENERIC DRUG NAME: Nafcillin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Unipen

INDICATION/USAGE: PP and non-PP Staphylococci

PREGNANCY CATEGORY: B

WARNINGS: Determine hypersensitivity; Diarrhea 2° C. difficile; Do not give with TET; Decreases effects of warfarin; Decreases cyclosporine levels; Causes positive Sulfosalicylic (protein) reaction, but NOT with dipstick; NO approved neonatal/pediatric IV regimens; Bone marrow depression may occur

MONITORING TESTS: PT, Liver panel, Renal Panel

COMMENTS:

GENERIC DRUG NAME: Nalidixic Acid

CATEGORY: Quinolone; Nucleic Acid Synthesis Inhibitor

DRUG TRADE NAME: NegGram

INDICATION/USAGE: UTI 2° majority of Proteus, Klebsiella, E. coli

PREGNANCY CATEGORY: NOT for use in first trimester; Refrain from using prior to delivery of baby; Otherwise B

WARNINGS: Brief convulsions; ↑ IC pressure: in very old or very young; Antagonized by Nitrofurantoin; May increase oral anticoagulant activity; Cause false positive urinary glucose tests chemically, but not enzymatically

MONITORING TESTS: CBC, Renal and Liver panels

COMMENTS: Use with caution in patients with liver disease and renal disease; photosensitivity may occur; Do NOT use in prepubertal children (Arthropathy 2° cartilage destruction)

GENERIC DRUG NAME: Nitrofurantoin

CATEGORY: Metabolic Antagonist (BROAD antagonism)

DRUG TRADE NAME: Furadantin

INDICATION/USAGE: UTI 2° E coli, S. faecalis, S. aureus and various strains of Klebsiella and Proteus

PREGNANCY CATEGORY: B

WARNINGS: Pneumonitis (with > 6 months' therapy) or fibrosis been observed; Hemolytic anemia similar to Primaquine) been induced: watch Mediterraneans, Near-Easterners and African-Americans; Do NOT give with magnesium trisilicate (decreases absorption); Hepatitis may occur

MONITORING TESTS: G-6-PDH, CBC with Diffy, Liver Panel, Renal Profile

COMMENTS: Do not give with renal impairment

GENERIC DRUG NAME: Novobiocin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Albamycin

INDICATION/USAGE: Treatment of SERIOUS S. aureus infections resistant to less toxic antibiotics

PREGNANCY CATEGORY: C

WARNINGS: Induces resistant strains of S. aureus RAPIDLY; Rapidly sensitizing (IgE): d/c; Do NOT use in neonates/preemies; May induce "pseudojaundice" (Yellowish discoloration of the skin not due to bile pigments; Pseudojaundice can occur with excessive ingestion of foods rich in beta-carotene (e.g., squash, melons, and carrots). Unlike true jaundice, carotenemia does not result in scleral icterus or elevation of the bilirubin level.)

MONITORING TESTS: CBC with diffy, Liver panel, platelets

COMMENTS:

GENERIC DRUG NAME: Nystatin

CATEGORY: Antifungal Cell Membrane Disrupter

DRUG TRADE NAME: Mycostatin

INDICATION/USAGE: Intestinal candidiasis, vulvovaginal candidiasis, mucocutaneous candidiasis

PREGNANCY CATEGORY: C (Oral suspension) -- A (Vaginal tablets)

WARNINGS: Determine hypersensitivity; Generally well tolerated by all ages

MONITORING TESTS: prn with dx

COMMENTS: Watch patient for diarrhea

GENERIC DRUG NAME: Penicillin G with Potassium (PenGK)

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Pentids

INDICATION/USAGE: Tablets: Mild/moderate infections: Group A Streptococci (URI), S. pneumoniae, Staphylococci

Injection: Severe infections: S. pneumoniae, Staphylococci, Clostridia, E. coli, Salmonella, Shigella, P. mirabilis, P. multocida

PREGNANCY CATEGORY: B

WARNINGS: Determine hypersensitivity; Positive Coombs' test after many IV doses; For syphilis: have examination q 6 mo X 2-3 years; Antagonized by TET and erythromycin (slows rate of bacterial growth)

MONITORING TESTS: With prolonged therapy: Renal Profile, Liver Panel, CBC with Diffy and Reticulocyte count, K⁺

COMMENTS:

GENERIC DRUG NAME: Penicillin V with Potassium (PenVK)

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: V-Cillin K

INDICATION/USAGE: Streptococcal infections (mild/moderate) URI and Scarlet fever and erysipelas; S. pneumoniae including otitis media; Staphylococci

PREGNANCY CATEGORY: B

WARNINGS: Determine hypersensitivity; po X 10 d!!!!!!!!!!!!; As per other PCN's

MONITORING TESTS: Gram Stains, C and S, per other PCN's

COMMENTS:
GENERIC DRUG NAME: Polymyxin B

CATEGORY: Cell Membrane Disrupter

DRUG TRADE NAME: Aerosporin

INDICATION/USAGE: P. aeruginosa, H. influenzae meningitis, E. coli UTI, K. pneumoniae

PREGNANCY CATEGORY: C

WARNINGS: IM therapy ONLY in hospital; Reduce dosage in renal damage; Respiratory paralysis 2° neuromuscular blockade may occur; Bactericidal to ALL G- EXCEPT Proteus; Do NOT mix with curare-like drugs

MONITORING TESTS: Renal panel. urine albumin; with *†*BUN, d/c

COMMENTS: May decrease sperm count and motility

GENERIC DRUG NAME: Probenecid

CATEGORY: Tubular Transport Blocker

DRUG TRADE NAME: Benemid

INDICATION/USAGE: Adjuvant treatment with PCN; to increase plasma levels of PCN and to decrease transport of PCN out of system

PREGNANCY CATEGORY: B

WARNINGS: Use carefully in patients with ulcers; Do NOT use with PCN with renal impairment; Use with care in NIDDM (may cause hypoglycemia); False increases in theophylline levels may occur

MONITORING TESTS: As with PCN; Uric acid (Probenecid is also uricosuric)

COMMENTS: Hydrate patient well to excrete urate with 3-7.5 g NaHCO₃ qd to stop urate from precipitating in urine

GENERIC DRUG NAME: Pyrazinamide

CATEGORY: Metabolic Antagonist/Antimycobacterial

DRUG TRADE NAME: Pyrazinamide

INDICATION/USAGE: M. tuberculosis ONLY after INH, Streptomycin and PASA have been tried and FAILED

PREGNANCY CATEGORY: Avoid its use – C – both out there

WARNINGS: 100% compliance required; Use when can test liver enzymes (SGPT and SGOT) before and every 2-4 weeks with treatment; Couple with at least one other anti-TB drug

```
MONITORING TESTS: Liver profile, uric acid: d/c if acute gouty arthritis flares; CBC, PT, PTT
```

GENERIC DRUG NAME: Ribavirin

CATEGORY: Antiviral aerosol

DRUG TRADE NAME: Virazole

INDICATION/USAGE: Severe LRI 2° RSV in hospitalized infants and young children; Document diagnosis with immunofluorescence or ELISA before or during the first 24° of treatment

Not indicated

PREGNANCY CATEGORY:

adults; X

WARNINGS: Do not use Ribavirin with ventilatory equipment (may precipitate and interfere with appropriate ventilation); Use special equipment (SPAG-2: Small Particle Aerosol Generator – for more info: http://www.nemc.org/RespCare/ribagrap.htm)

MONITORING TESTS: CBC and diffy and reticulocyte count

COMMENTS: Treat early in course of disease for optimal therapy; Do NOT use bacteriostatic water for reconstitution

in

GENERIC DRUG NAME: Rifampin

CATEGORY: Nucleic Acid Synthesis Inhibitor -- anti-tubercular

DRUG TRADE NAME: Rifadin

INDICATION/USAGE: All forms of TB in conjunction with at least one other drug

PREGNANCY CATEGORY: C

WARNINGS: Produces liver dysfunction; may be fatal; Twice weekly doses work better than qd; Monitor for 100% compliance; May cause urine, feces, saliva, spit, sweat and tears to turn reddish-orange or brown; May discolor soft contact lenses; May decrease effectiveness of OCP's; Inhibits assays for Folate and B12 determinations; May reduce activity of anticoagulants, cardiac glycosides, analgesics, diazepam, theophylline to name a few; Diabetes may be more difficult to regulate

MONITORING TESTS: SGPT (ALT), SGOT (AST), Bilirubin, CBC

GENERIC DRUG NAME: Silver sulfadiazene

CATEGORY: Cell Membrane/Wall Disrupter

DRUG TRADE NAME: Silvadene

INDICATION/USAGE: Prevention and treatment of wound sepsis in 2d and 3d degree burns, specifically, Pseudomonas

PREGNANCY CATEGORY: B

WARNINGS: Fungal growth about eschar may occur; May cause hemolysis in patients with G-6-PDH deficiency

MONITORING TESTS: CBC with diffy, retic count, Renal Profile

GENERIC DRUG NAME: Spectinomycin

CATEGORY: Translation Inhibitor

DRUG TRADE NAME: Trobicin

INDICATION/USAGE: Acute gonococcal urethritis and proctitis in men and acute gonococcal cervicitis and proctitis in women

PREGNANCY CATEGORY: B

WARNINGS: Diluent contains benzyl alcohol which may cause fatal "gasping syndrome" in infants; Determine hypersensitivity; Use 20 g needle; Treat both partners; Patients treated with Spectinomycin need "STS" after 3 months' treatment

MONITORING TESTS: CBC, Renal profile, Liver profile

COMMENTS: Spectinomycin will not work for gonorrhea of the throat, syphilis, colds, flu, or other virus infections; IM use ONLY; Do NOT use in mixed VD's: masks symptoms/signs of syphilis [with gonorrhoeae] and it progresses

GENERIC DRUG NAME: Streptomycin

CATEGORY: Translation Inhibitor

DRUG TRADE NAME: Streptomycin

INDICATION/USAGE: All forms of M. tuberculosis; Y. pestis, P. tularensis, H. influenzae, K. pneumoniae, E. coli, Proteus, S. faecalis, S. viridans

PREGNANCY CATEGORY: **D** -- **May cause ototoxicity in fetus**

WARNINGS: May cause ototoxicity in fetus; Double check hearing in adults; May cause renal dysfunction; May get dizzy

MONITORING TESTS: Renal panel, Audiometry prn, CBC with diffy and platelets

COMMENTS: May need to alkalinize urine 2° \uparrow uricouresis 2° Streptomycin therapy to decrease precipitation

GENERIC DRUG NAME: Sulfamethoxazole and Trimethoprim (SXT)

CATEGORY: Metabolic Antagonists

DRUG TRADE NAME: Bactrim and Septra

INDICATION/USAGE: E. coli, P. mirabilis, P. vulgaris, S. pneumoniae, H. influenzae, PCP

PREGNANCY CATEGORY: C

WARNINGS: Use with care in geriatric patients; Do NOT use for Group A - β -hemolytic Streptococci; Hydrate patient to prevent crystalluria; May interfere with creatinine determination (\uparrow about 10%); Do not use in infants < 2 months of age

MONITORING TESTS: CBC, Renal profile, UA

COMMENTS: May elevate body temperature

GENERIC DRUG NAME: Sulfanilamide

CATEGORY: Metabolic Antagonist

DRUG TRADE NAME: Vagitrol

INDICATION/USAGE: Vulvovaginitis 2° Candida albicans

PREGNANCY CATEGORY: C

WARNINGS: Determine hypersensitivity; Vaginal applicators use with care in 3d trimester

MONITORING TESTS: CBC with diffy and prn dx

GENERIC DRUG NAME: Tetracycline

CATEGORY: Translation Inhibitor

DRUG TRADE NAME: Tetracycline

INDICATION/USAGE: Rickettsia, M. pneumoniae, Chancroid, Y. pestis, Bacteroides, E. coli, Shigella, H. influenzae, Klebsiella; when PCN contraindicated, used for N. gonorrhoeae, T. pallidum, Clostridia, B. anthracis

PREGNANCY CATEGORY: Do NOT use in

pregnancy

WARNINGS: Do not use with Streptococcus; Affects tooth and bone development: last half of pregnancy to about 8 YOA: DO NOT give to patient; Causes photosensitivity: stay out of sun; Patients on anticoagulants may need to have drug decreased 2° reduced PT activity 2° TET; Use for 10 days!!!!!!!!!!!; Antagonistic to PCN

MONITORING TESTS: PT, prn with dx

COMMENTS: Do not give with antacids; No dairy products; take with full glass of water 1°ac or 2°pc

GENERIC DRUG NAME: Tobramycin

CATEGORY: Translation Inhibitor

DRUG TRADE NAME: Tobrex

INDICATION/USAGE: Topically optically: Staphylococci, S. pneumoniae, P. aeruginosa, H. influenzae

Injection: P. aeruginosa, Klebsiella, Serratia, E. coli, Proteus, S. aureus

PREGNANCY CATEGORY: D

WARNINGS: Ototoxic and nephrotoxic; Do NOT use in preemie/neonate; Do not give concomitantly with strong diuretics; Do not "mix" with neuromuscular blockers (cholines, curares) 2° respiratory paralysis; Use with great care in myasthenia gravis; See other Aminoglycosides

MONITORING TESTS: Ca²⁺, Mg²⁺, Na⁺, Renal Panel, CBC with Diffy

GENERIC DRUG NAME: Undecylenic Acid

CATEGORY: Antifungal

DRUG TRADE NAME: Desenex

INDICATION/USAGE: Athlete's foot; Microsporum (skin) ringworm; jock itch

PREGNANCY CATEGORY: Compound undecylenic acid topical preparations have not been shown to cause birth defects or other problems in humans.

WARNINGS: Apply liberally into new shoes (dust cloud); Destroy old shoes; Wear cotton socks; Wear shoes that breathe

MONITORING TESTS: prn dx

GENERIC DRUG NAME: Vancomycin

CATEGORY: Cell Wall Synthesis Inhibitor

DRUG TRADE NAME: Vancocin

INDICATION/USAGE: Infections by MRSA (IV therapy) and C. difficile (po therapy)

PREGNANCY CATEGORY: C

WARNINGS: Slow IV NOT LESS THAN 60 minutes for infusion; May cause ototoxicity; Do not give with cholestyramine or colestipol (binds drug); Nephrotoxic

MONITORING TESTS: CBC with diffy, Renal panel, Audiometry

COMMENTS: Do NOT give concomitantly with anesthetics: causes H_1 problems; adjust doses in geriatric patients DOWN

Interactions between Nutrients and Drugs:

An Introduction

Various nutrients interact with medications

- 1) Achromycin V, a tetracycline, is not to be taken with antacids, Fe, Zn, Ca, Mg, dairy products, urinary alkalinizers or food since they all reduce absorption. This drug also reduces the effectiveness of oral contraceptives.
- 2) Furoxone is not to be taken with tyramine-containing foods (wines, aged meats like genoa sausages, pepperoni).
- 3) Azulfidine reduces the concomitant absorption of folate, so they must be given separately at different times.
- 4) Cefobid is to be taken without EtOH. No EtOH is to be taken until 72 hours after the last dose.
- 5) Cipro is not to be taken with concomitant antacids, Fe and Zn.

- 6) Flagyl has already been discussed above.
- 7) Noroxin is not to be taken with antacids or minerals; it potentiates the effects of caffeine.
- 8) Fulvicin P/G potentiates EtOH effects; reduces oral contraceptive effecetiveness.
- 9) Macrobid or Macrodantin are not to be taken with magnesium trisilicate.
- Dysgeusia is the loss of taste. This can occur due to taking numerous medications. A few follow that cause this obnoxity: griseofulvin (antifungal), penicillamine (antiarthritic) many antilipemics, phenytoin (anticonvulsant) and methimazole (antithyroid).

Drugs Causing Primary Nutrient MALABSORPTION

Drug	Use	Nutrients Lost	Action
Cholestyramine	Bile resin	Fat, A, D, K, B ₁₂ , Fe	Binds bile salts and nutrients
Colchicine	Treat gout	Fat, B ₁₂ , Pro-A, Lactose, Na ⁺ , K ⁺	Enzyme damage; ↓cell reproduction
Methyl DOPA	Antihypertensive	B ₁₂ , folate, Fe	??????
Neomycin	Antibiotic	Fat, B ₁₂ , N, lactose, sucrose, Na ⁺ , K ⁺ , Fe ²⁺ , Ca ²⁺	Binds bile salts; ↓ pancreatic lipase
KCI	K ⁺ replacement	B ₁₂	↓ileal pH

Drug	+	Alcohol/food	=	Effect
Chlorpropamide (oral hypoglycemic)	+	alcohol	=	SOB, headache, flushing
ADH inhibitors (Disulfiram, metronidazole)	+	alcohol, alcohol- containing foods	I	Belly and chest pain, flushing, headache, N/V
Tolinase, Orinase (oral hypoglycemics)	+	alcohol, sugar, sweets	H	Confusion, weakness, irrational behavior, unconsciousness
MAO inhibitors (antidepressants)	+	Cheese, red wine, chicken, liver	II	CVA, ↑BP, headache
Isoniazid (anti-TB)	+	Yeast (foods high in tyramine)	=	N/V, restlessness

Food Effect On Drug Absorption		
Absorption \downarrow by Food	Absorption Delayed by Food	
Amoxicillin, Ampicillin, ASA, Isoniazid, I-DOPA, Pen-G [V(K)], phenobarbital, tetracycline	Tylenol, ASA, Cephalexin, Digoxin, Furosemide, Sulfanilamide, Sulfasoxazole	

Nutrient/Drug Interactions		
Drug Name	Class/Indication	Comment
Achromycin V	TET antibiotic	antacids, Fe, Zn, Ca, Mg, Dairy products, urinary alkalinizers and food ↓ absorption ALSO: ↓'s OCP Activity
Furoxone	Antimicrobial	AVOID: tyramine- containing foods
Azulfidine	Salicylate- sulfonamide	↓'s folate absorption given concomitantly
Cefobid	cephalosporin	AVOID: EtOH for AT LEAST 72° after dose
Cipro	quinolone	AVOID: concomitant antacids, Fe and Zn

Nutrient/Drug Interactions		
Drug	Class/Indication	Comment
Flagyl	nitroimidazole	AVOID: EtOH during and AT LEAST 24° after use
Noroxin	quinolone	AVOID; concomitant antacids and minerals; potentiates caffeine
Fulvicin P/G	griseofulvin	potentiates EtOH; OCP activity \downarrow 'd
OCP's	OCP's	antacids and antibiotics may inhibit absorption

Nutrient/Drug Interactions			
Drug	Class/Indication	Comment	
Macrobid or Macrodantin	antibiotic	AVOID: Mg trisilicate	

Anti-Microbial Drug Resistance

Terms and Definitions

- Genotype: genetic organization
- Phenotype: expression of the genotype
- Both discussed in BIOL 190, 191, 208, 223, 224

New Terms and Definitions

- Selection: phenotypic variation due to genotype, e.g., bacterium with gene for resistance to TET can be distinguished from bacterium lacking the gene by growing in media with TET (agent of selection).
- Expression: selection of the gene requires this; observed by phenotype
- Bacteriophage: viruses associated with prokaryotes
- Lytic phages: make many numbers/copies of themselves as they LYSE their host cell
- Temperate phages: enter non-lytic prophage state; nucleic acid replication of phage linked to hoist cell DNA replication
- Lysogenic: prophage infected bacteria; due to a physiological signal that can initiate lytic cycle and cause bacterial death
- Prokaryotic DNA replication: linked to the cell membrane (mesosomes); this provides sepatation of the membrane which binds the DNA to "hold it" in place for replication
- Two ends of DNA: 5' and 3': 5' = phosphate end (P) and 3' = -OH end

New Terms and Definitions

- Plasmid: small circles of DNA about 6-7 kilobase pairs long; amenable to genetic manipulation and introduction into cells (primarily prokaryotes); carry genes associated with special functions; many carry the genes that mediate their transfer from 1 organism to another BESIDES the gene[s] that cause DNA enlargement, reduction or rearrangement;
- insertion sequences are on RTF (Resistance Transfer Factor) genes in plasmids.

Prokaryotic DNA Replication



Recombination Mechanisms

- DNA is double stranded for recombination and for replication, too – in case you missed it in the Prokaryotic DNA Replication model.
- Legitimate Recombination: occurs due to donor DNA and recipient DNA being closely similar; a.k.a. Homologous Recombination; occurs because genes have a common ancestry.
- Illegitimate Recombination: Dis-similar DNA sequences recombined by enzyme mediation; a.k.a. Non-Homologous Recombination; codes for its own enzymes to cause integration.
- rec recombination: <u>rec</u>iprocal recombination, i.e., as donor gives to recipient, recipient transfers a homologous sequence to the donor.

Genetic Material Transfer Mechanisms

- Interstrain transfer of DNA in prokaryotes is ubiquitous and leads to the biggest contribution to the genetic diversity of prokaryotic organisms. This genetic transfer is typically a transfer of small genetic fragments from a donor genome to a recipient organism.
- What are some Mechanisms of Transfer?

Conjugation

Energy and nucleotides from donor cell make new DNA strand; physically moved to recipient cell; recipient cell completes the DS DNA synthesis in a complimentary manner; in transcription: only 1 strand is transcribed in a specific region of the genome



Conjugation

 Plasmids are most frequently transferred; these plasmids are "selftransmissible" because the have the "tra" (transfer) genes; Transfer through sex pilus; conjugation involved in transferring R factors (resistance factors).



Enzymes Directed by R Factors

- 1. β -lactamase against PCN's
- 2. Chloramphenicol acetylase against chloramphenicol
- 3. Streptomycin phosphotransferase against streptomycin
- 4. Streptomycin adenylate synthetase against streptomycin and spectinomycin
- 5. Kanamycin phosphotransferase against kanamycin, neomycin B, paromomycin
- 6. Kanamycin acetyl transferase against kanamycin and neomycin B
- 7. Gentamycin adenylate synthetase against gentamycin and kanamycin

Transduction

- Donor DNA is in a phage; transferred by phage infective process.
- Phage-mediated recombination: temperate phages are the preferred form for genetic transfer; this is due to the fact that infection of the bacteria is done under conditions that favor bacteriolysis, hence temperate phages are used to favor recombinant strain survival; generally limited to genetic engineering.
- Generalized transduction: transfer of any of a number of genetic sequences
- Specialized transduction: transfers specific DNA sequences from the phage to bacteria.



Transformation

 Direct uptake of DNA from a donor by recipient; naturally doesn't happen very often; "forced transformation" is a laboratory process; unusual process with bacteria; requires competence factors for direct DNA uptake at a specific time in the growth cycle; can be forced under laboratory conditions.

Elementary Transcription and Translation

- Once mRNA has been synthesized (transcription) and matured in the nucleus (or nucleoid as in prokaryotic cells), it is ready for transport through the nuclear envelope (in eukaryotes) into the cytosol to bind to ribosomes.
- tRNA, then, transports the necessary amino acids to the mRNA-ribosomal complex to continue the process of protein synthesis (translation).
- How is it that the two RNA's code for the amino acids?
- The genetic code is based upon triplets, i.e., a set of three nucleotides in sequence that code for a single amino acid.
- Each triplet in mRNA is called the codon.
- Each triplet in tRNA is called the anti-codon and is read complimentarily to the codon.

Listed below in the table is an incomplete list of codons for some of the amino acids:

Triplet Code (Codon with Amino Acid NOT Inclusive)				
UAA = <u>Stop</u>	CAC = His	CUA = Leu		
AAG = Lys	UAC = Tyr	CGA = Arg		
AAC = Asn	AGA = Arg	UGG = Trp		
GAA = Glu	AGC = Ser	UGC = Cys		
GAU = Asp	GGG = Gly	ACA = Thr		
CAA = GIn	AUA = lle	GCA = Ala		
CCC = Pro	UUU = Phe	AUG = Met (Start)		
GUG = Val				

Note that, in some instances, the difference between amino acids is one (1) nucleotide in the triplet, e.g.,

- mRNA sequence: AUG-CAC-AGA-CCC-UGC-UAA
- •
- amino acid sequence:

```
(Start) Met-His-Arg-Pro-Cys-Stop
```

•

- If you alter this sequence by placing an "A" after 9 bases, the new sequence is:
- mRNA sequence: AUG-CAC-AGA-ACC-CUG-CUA-A____
- New amino acid sequence:

(Start) Met-His-Arg-Thr-Leu-Leu-----

Mutations

- One shift, one base change alters the whole protein after the insertion of the "A".
- A *mutation* is any change that presents in the DNA of a cell.
- Mutations are chance activities and occur spontaneously in all nuclear material.
- Mutations are neither good nor bad (like emotions) and are simply a natural occurrence of cellular activities.

 Mutations can not be predicted, nor can the effects be predicted - caveat: some ARE predictable, i.e., the ones we recognize and have studied extensively.

- Those compounds that interact with DNA and increase the frequency with which bases are altered or which causes the likelihood of mutation are called *mutagens*.
- Most mutations impair cell function rather than increase useful cell functions, therefore, mutations are though of as being harmful.
- Even with incredible minimal exposure to mutagens, there is still a small likelihood that a gene may mutate.
- This is called a *spontaneous mutation*.
- The frequency of spontaneous mutations vary greatly between genes and organisms.
- When this frequency increases, it is assumed that some mutagen is causing it.

The table, below, summarizes different types of mutations.

Type of Mutation	Example	
Wild type ("normal")	DNA is in cell nuclei.	
Point	DNA is in cell nuclei (NO period)	
Insertion	DNA is NOT in cell nuclei.	
Gene duplication	DNA is in <mark>IN</mark> cell nuclei.	
Gene duplication with point mutation	DNA is in <u>A</u> N cell nuclei.	
Chromosome duplication	DNA is in cell nuclei. <mark>DNA is in cell nuclei.</mark>	
Translocation	DNA is cell nuclei in.	
Inversion	DNA is in cell <u>ielcun</u> .	
Frameshift*	DN Ai sin cel lnu clei.	

*removal of or insertion of bp sequences that alter the reading of the DNA sequence.

- In terms of mutations of hereditary and somatic forms, when the mutation is passed onto the offspring it is said to be inherited, hereditary, genetic for lower organisms.
- For MAN there are two sort of mutations:
 - <u>hereditary</u>, which occurs ONLY in sex cells: sperm and ova (includes BRCA-1 and BRCA-2); and
 - <u>somatic</u> mutation, which consists of most mutations.
- These occur in all other cells.
- Somatic mutations are NOT hereditary and are NEVER passed onto progeny.
- Hence, there is a genetic and an environmental element involved in cancer.
- It is of significant interest that mutation, aging and cancer are tightly linked by somatic mutations.

Six Mechanisms of Antimicrobial Drug Resistance

- 1. Enzymatic Production
- 2. Permeability Changes
- 3. Evolve Different Target/Receptor for Drugs
- 4. Change Metabolic Pathways
- 5. Change the Enzyme Just a Little Bit
- 6. Just Naturally that Way

Enzymatic Production

 β-lactamase production in Staph, Strep, Haemophilus and Moraxella makes them resistant to PCN's – require an inhibitor if one desires to use PCN's: Clavulanic Acid, e.g., Augmentin = Amoxicillin and Clavulanic acid.

Permeability Changes

 Drug simply can not get across the cell membrane; if drug can't get in cell, cell is resistant, converesely, if CAN get in the cell, cell is susceptible, e.g., TET: Strep have innate barrier to aminoglycosides (translation inhibitors).

Evolve Different Target/Receptor for Drugs

Make ineffective PBP, alter some parts of a ribosome

Change Metabolic Pathways

 E.g., PAS with PABA in folate synthesis: will use already formed folate instead of synthesizing their own folate – if unavailable, cell dies.

Change the Enzyme Just a Little Bit

• Still has the same function, but the inhibitory site is slightly altered



- 1. <u>ES</u> Normal Lock-n-Key post-Induced Fit, as well
- 2. <u>Competitive inhibition</u> of an enzyme, i.e., an inhibitor specific to this enzyme COMPETES with the substrate for the active site of this enzyme. It is reversible; will block S from binding. One example of this sort of inhibition is carbamoyl choline that competitively inhibits acetylcholinesterase.
- 3. <u>Uncompetitive inhibition</u>: this sort of inhibition involves covalently bound inhibitor and inactivates the enzyme irreversibly. Two examples of this sort of inhibitor are nerve gas and organophosphates that inhibit acetylcholinesterase. Organophosphate poisoning may be reversed by injecting a drug called 2-PAM. Valium and atropine are useful to treat muscle spasms and breathing difficulties, as well.
- 4. <u>Noncompetitive inhibition</u>. Note that the inhibitor does NOT bind to the active site of the enzyme, rather it has its own unique binding site. When a noncompetitive inhibitor binds to an enzyme, it causes the enzyme to change shape and shuts off its activity reversibly by not allowing S to bind completely. This sort of inhibition is also referred to as allosteric inhibition and plays major roles in metabolic regulation. An example of a noncompetitive inhibitor is aspirin. Aspirin inhibits cyclooxygenase, which is the main enzyme in prostaglandin biosynthesis. Prostaglandins mediate pain, inflammation, blood pressure, gastric mucous secretion, blood clotting, labor and delivery, to name a few.

Just Naturally that Way

• May be bacteria's natural defense against other microbes that produced that agent

Origin of Anti-Microbial Resistance

- Two Origins for Consideration:
- 1. Non-Genetic
 - 1. Metabolically inactive bacteria may be resistant, but the daughter cells are susceptible; host defense can protect against bacteria remaining after infection, but daughter cells will be fully susceptible to the antibiotic after multiplication
 - 2. Bacteria may lose the target for the drug due to drug administration and remain as "persisters" for many generations; as the cells regain the target, they regain susceptibility to the antibiotic, e.g., cell wall synthesis inhibitors

Origin of Anti-Microbial Resistance

- Two Origins for Consideration:
- Genetic most drug resistance microorganisms occur this way
 - 1. Chromosomal resistance: SPONTANEOUS mutation in a gene that regulates the organism's susceptibility to the drug; the drug holds down growth of the susceptible organisms, but selects for the resistant organism; spontaneous mutation is very infrequent; chromosomal mutants are primarily resistant to the drugs due to a change in drug-binding receptor or due to the loss of a drug binding protein (dBP).
 - 2. Extrachromosomal resistance: R factors (Resistance factors) from plasmids; control synthesis of hydrolytic enzymes, e.g., PCN'ase and cephalosporinase; control synthesis of drug altering enzymes; control active transport across membrane
 - 1. Transduction not of great importance
 - 2. Transformation used in the lab
 - 3. Conjugation is the primary manner in which MDR occurs
 - 4. Transposition: plasmid to plasmid short DNA transfer; intra-bacterial plasmid DNA to bacterial DNA transfer; questionable influence

Cross Resistance between Drugs

 Bacteria resistant to one drug may cause resistance to another if have acommon mechanism of action, e.g., PCN'ase and cephalosporinase

Practical Drug Resistance Reduction Applications

- 1. Keep high enough [drug] in the tissues to stop reproduction of original pathogens and first generation pathogens
- 2. Give two drugs at once that do not contribute to cross resistance, i.e., drug combinations. The idea is to let the two drugs prolong the appearance of resistant mutants, e.g., Drug 1 and 2: 1 blocks 2 and 2 blocks 1 while 1 and 2 kill pathogens susceptible to 1 and 2, respectively.
 - 1. Sulfonamide is bacteriostatic (DHF synthesis inhibitor); PCN is bactericidal these drugs antagonize each other at first with time, they act synergistically.
 - 2. Synergy: combined effect is greater than the sum of each part, Drug A has X activity, Drug B has Y activity together, their activity is greater than the sum of X and Y; e.g., PCN with translation inhibitor (e.g., erythromycin) is more effective since there is decreased cell wall synthesis (PCN) and the other drug (Erythromycin) goes to the site of inhibition easily.
 - 3. Additive effect: combined effect is NOT greater than the sum of each part.
 - 4. Antagonism: one drug blocks the other drug from doing its job, e.g., bacteriostatic vs bactericidal, if stop growth, can't kill it.
- 3. Do not use drugs of last defense or drugs of common/agricultural use too readily: their value decreases rapidly and increases resistant strains; resistant mutants are far more likely to show up in large populations of bacteria than small populations of bacteria, e.g., "power drugs" no longer effective in some infections) next slide:

Bacterium	Drug resistant to	Drug in use
N. gonorrhoeae	PCN, sulfonamide, NOW Spectinomycin	1st Spectinomycin; 2d Ceftriaxone
N. meningitidis	Sulfonamides, 1% of colonies to Rifampin	PCN for treatment; Rifampin for prophylaxis
Staphyloccus	PSN, Methicillin, Vancomycin	Vancomycin; Dicloxacillin (PCN'ase resistant)
S. pneumoniae	PCN (due to PBP)	? treatment is difficult in meningitis
Gram negative Enterics	TET (from animal feed) → drug resistant nosocomial infections, too	Whatever works
M. tuberculosis	INH and rifampin (MDR MT)	Streptomycin, ethambutol, pyrazinamide – in combination 129

Practical Drug Resistance Reduction Applications, Cont'd

- 4. Use C & S data whenever possible
- 5. Prescribe narrow spectrum drugs whenever possible
- 6. With prophylactic use, use for shortest time possible and when it is proven to be of value
- 7. Hand washing and aseptic technique to decrease transmission of the beasts
- 8. Use isolation procedures when necessary
- 9. Infection control!

Key Infection Control Elements in Some Health Care Institutions

- Frequent and thorough hand washing. Hand washing for at least 10 seconds with liquid soap and running water.
- 2. Wearing gloves when you expect to have contact with blood, secretions, mucous membranes, non-intact skin or moist body substances.
- 3. Changing gloves between patients
- 4. Using other appropriate barriers (personal protective equipment [PPE])

Prokaryotic Drug Dependence

• Some drug resistant microbes require that same drug for their growth. Probably not important in human infections.