Antimicrobial Therapy Review 2014

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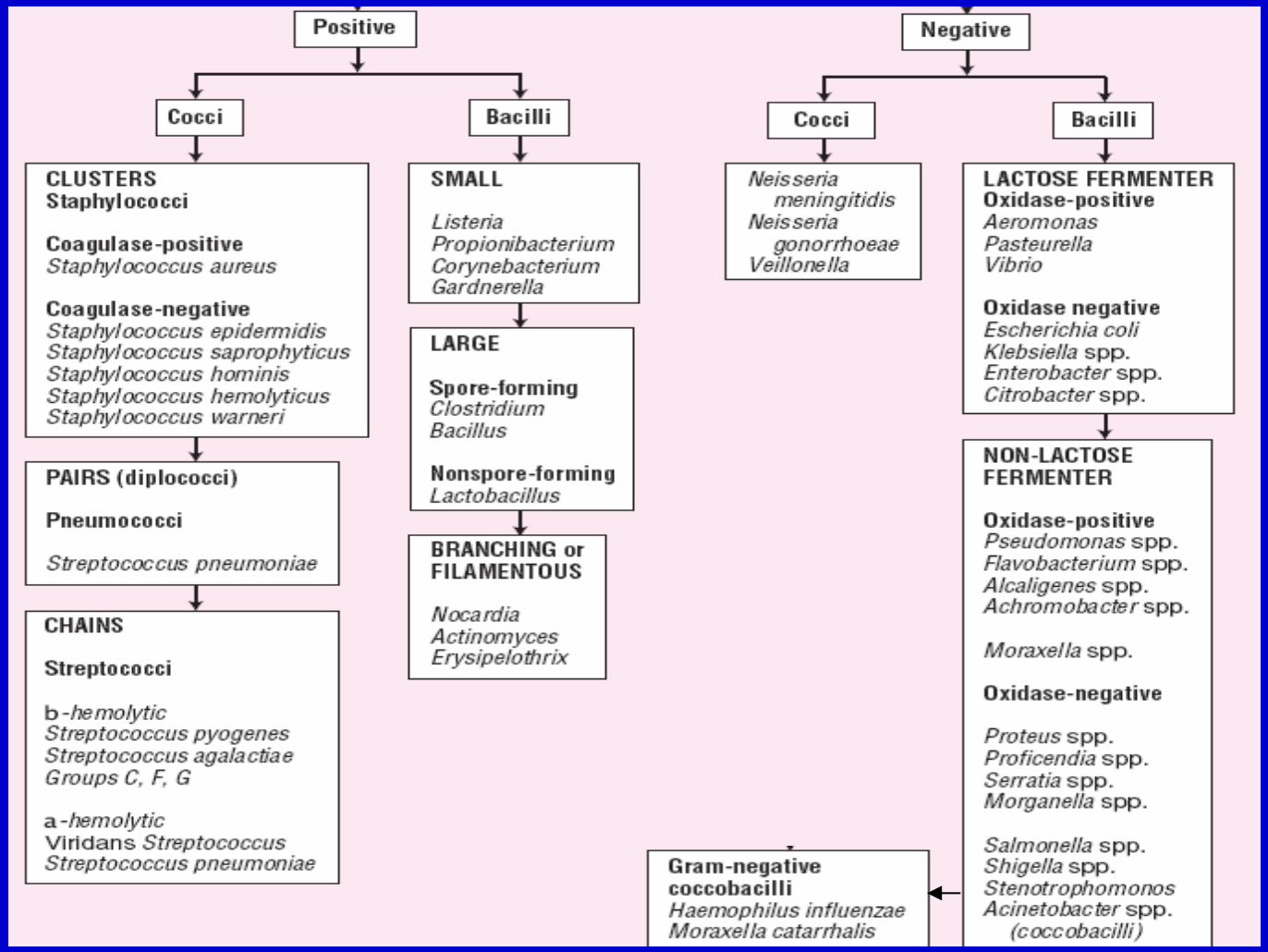
Microbiology: Gram Stain



Identify the Likely Pathogen

- Normal bacterial flora

	Gram-Positive		Gram-Negative	
	Cocci	*Rods*	*Cocci*	*Rods*
Skin	*Staphylococcus* spp. (e.g., *S. epidermidis*) *Streptococcus* spp.	*Corynebacterium* spp. *Propionibacterium* spp.		Enteric bacilli (some sites) *Acinetobacter* spp. (Coccobacilli)
Oropharynx	Streptococci—viridans group Micrococcus	*Corynebacterium* spp.	Neisseria	*Hemophilus* spp.
Gastrointenstinal tract	*Enterococcus* spp. *Peptostreptococcus* spp.	*Lactobacillus, Clostridium*		*Bacteroides* spp. Enteric bacilli (*E. coli, Klebsiella spp.*)
Genital tract	*Streptococcus* spp. *Staphylococcus* spp.	*Lactobacillus* *Corynebacterium* spp.		Enterobacteriaceae *Prevotella* spp.

Bacteria by Site of Infection

Mouth
Peptococcus
Peptostreptococcus
Actinomyces

Skin/Soft Tissue
Staph. aureus
Strep. pyogenes
Staph. epidermidis
Pasteurella

Bone and Joint
Staph. aureus
Staph. epidermidis
Streptococci
N. gonorrhoeae
Gram-negative rods

Abdomen
E. coli, Proteus
Klebsiella
Enterococcus
Bacteroides spp

Urinary Tract
E. coli, Proteus
Klebsiella
Enterococcus
Staph. saprophyticus

Upper Respiratory
S. pneumoniae
H. influenzae
M. catarrhalis
Strep. pyogenes

Lower Respiratory Community
Strep. pneumoniae
H. influenzae
K. pneumoniae
Legionella pneumophila
Mycoplasma, Chlamydia

Lower Respiratory Hospital
K. pneumoniae
P. aeruginosa
Enterobacter spp
Serratia spp
Staph. aureus

Meningitis
Strep. pneumoniae
N. meningitidis
H. influenza
Group B Strep.
E. coli
Listeria

Adapted from: Lee M. Basic skills in interpreting laboratory data, 3rd edition. 2004. p508.

Aerobic Gram-Positive Bacteria

- *Streptococcus*
- *Enterococcus*
- *Staphylococcus*
- *Cornybacterium*
- *Listeria*

Aerobic Gram-Negative Bacteria

- *Enterobacteriaceae (E. coli, Klebsiella, Enterobacter, Citrobacter, Proteus, Serratia, Salmonella, Shigella, Morganella, Providencia)*
- *Pseudomonas*
- *Helicobacter*
- *Haemophilus*
- *Legionella*
- *Moraxella*
- *Neisseria*

Anaerobic Bacteria

- Gram-Positive
- *Peptococcus*
- *Peptostreptococcus*
- *Clostridia*
- *Propionibacterium acnes*

- Gram-Negative
- *Bacteroides*
- *Fusobacterium*

Atypicals

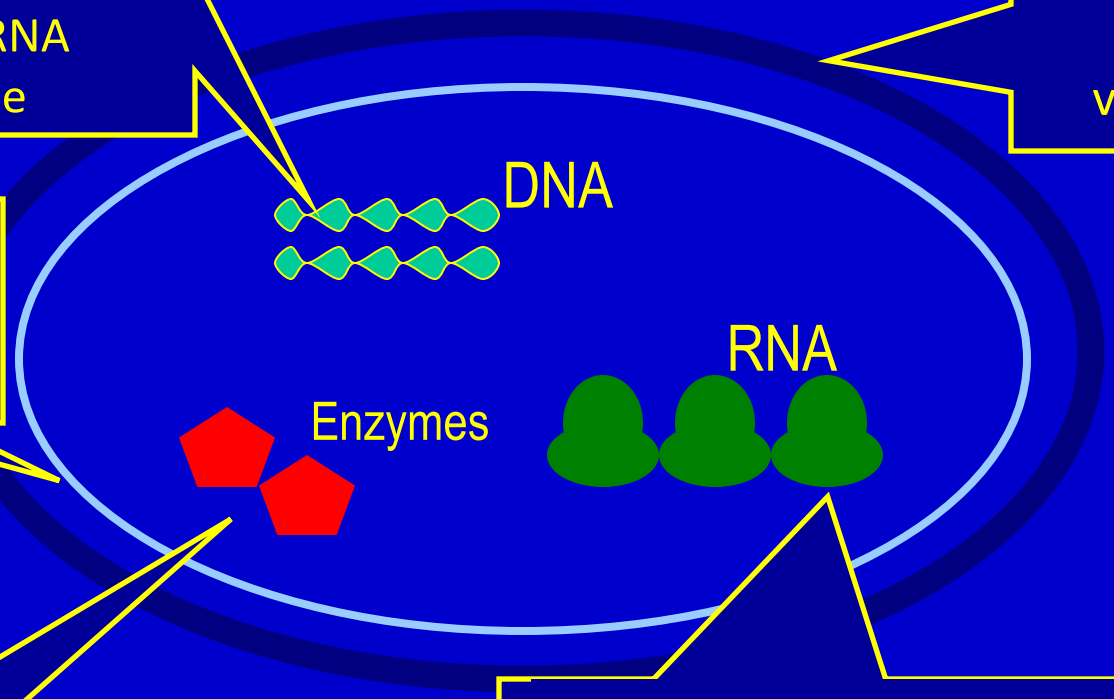
- *Chlamydia*
- *Chlamydophila*
- *Rickettsiae*
- *Mycoplasma*
- *Spirochetes* (Syphilis, Lyme disease)
- *Mycobacterium*

Mechanisms of Action

Inhibit DNA synthesis:
Quinolones → DNA gyrase
Rifamycins → DNA-dependent RNA polymerase

Inhibit cell wall synthesis: Beta-lactams: PCN, Ceph, vancomycin

Inhibit cell membrane:
Polymyxins



Inhibit folate:
SMX/TMP

Inhibit ribosomal protein synthesis:
AGs, tetracyclycin → 30S
Clindamycin, macrolides→ 50S

Major classes of antibiotics

- Cell wall active agents
  - β-lactams
    - Penicillins
    - Cephalosporins
    - Carbapenems
    - β-latam/β-lactamase inhibitor combinations
  - Monobactam
    - Aztreonam
  - Glycopeptide
    - Vancomycin
- Protein synthesis inhibitors
  - Macrolides
  - Clindamycin
  - Streptogramins
  - Aminoglycosides (AG)
  - Tetracyclines
  - Tigecycline
  - Oxazolidinones
    - Linezolid

Major classes of antibiotics

- Interfere with DNA synthesis
  - Sulfonamides and trimethoprim
  - Fluoroquinolones (FQ)
  - Rifamycins
- Miscellaneous
  - Metronidazole
  - Polymixin

Penicillins

- MOA: beta-lactams; bind to penicillin binding protein to inhibit cell wall synthesis
- Spectrum: gram-positives, gram-negatives, anaerobes
- AEs: hypersensitivity, GI, hematological, seizures
- DIs: oral contraceptives

Natural Pencillins

- Gram-positives
  - Enterococcus, *Treponema pallidum*, Streptococcal species (pyogenes, pneumoniae [resistance]), Enterococcus (combined with aminoglycoside), *Neisseria meningitidis*, *Borrelia burgdorferi*, anaerobes above diaphragm
- Penicillin G
  - Aqueous: IV
  - Procaine: IM
  - Benzathine: IM
- Indications
  - Streptococcal infections
  - Syphilis

Cost: $-$$ Freq: Q6-8H

- Penicillin VK: PO
  - Best on empty stomach
- Indications
  - Pharyngitis (Strep.)
  - Erysipelas

www.nlm.nih.gov/medlineplus

Antistaphylococcal Penicillins

- Staphylococcal and fair Streptococcal activity
- Not available anymore
  - Methicillin
  - Oxacillin
  - Cloxacillin
- Methicillin-susceptible *Staphylococcus aureus* (MSSA)
- Nafcillin: IV
- Effective for penicillinase producing organisms
- Drug of choice: MSSA

- Dicloxacillin: PO
  - Erratic absorption
  - Rate and extent ↓ by food
  - Skin and skin structure infections (SSSIs)
- Indications
  - Osteomyelitis, septicemia, endocarditis, and CNS infections
  - Caused by susceptible strains of staphylococci species

Cost: $-$$ Freq: Q6-8H

Amino Penicillins
(ampicillin, amoxicillin)

- Spectrum: Streptococcal species, Enterococci, Listeria, *Enterobacteriaceae*, *Borrelia burgdorferi*, *H. pylori*
- Indications: respiratory tract infections, Lyme, GI ulcers, endocarditis prophylaxis
- Drug of choice: Lyme disease, *H. pylori* , *S. pneumoniae*, *Proteus mirabalis*
- Mononucleosis – erythematous rash

Extended-Spectrum Penicillin (piperacillin, mezlocillin, ticarcillin, azlocillin)

- Spectrum: extended gram-negative coverage including *Pseudomonas aeruginosa*
- Indications: serious infections
- Intravenous only – inpatient treatment

β-Lactamase Inhibitors

- Enhanced activity versus β-lactamase producing bugs
- Penicillin plus β-Lactamase Inhibitor
  - Ampicillin-Sulbactam (Unasyn®) & Amoxicillin-Clavulanic Acid (Augmentin®)
    - Added Staphylococcal (NOT MRSA), gram-negative, (NOT Pseudomonas) & anaerobic activity
  - Ticarcillin-Clavulanic Acid (Timentin®) & Piperacillin-Tazobactam (Zosyn®)
    - MSSA, Acinetobacter spp, Bacteroides fragilis
- Indicated for wide range of infections, respiratory tract infections, animal bites, skin infections
- AE: clavulanate→diarrhea

http://www.bmb.leeds.ac.uk/mbiology/ug/ugteach/gene2020/lactamase.gif

Cephalosporins

- Spectrum of activity
  - Activity broadens as generation of cephalosporins progresses
  - Gram (+) → gram (+) and gram (-)
  - Gram (+) activity generally decreases with each generation and gram (-) activity increases with generation
  - **No *enterococcus spp or listeria* activity**
  - Cefoxitin and cefotetan vs. anerobes
  - Ceftazidime, cefoperzone, and cefepime vs. *Pseudomonas*
  - 3rd generation better CSF penetration
- Renal elimination
- Ceftriaxone- Dual hepatic and renal elimination

Cephalosporins

	Agents	Spectrum of Activity
First Generation **SSSIs,UTIs,Periop prophylaxis**	Cefadorxil (Duricef) PO Cefazolin (Ancef) IV Cephalexin (Keflex) PO	Gram (+), ↑↑MSSA Some gram (-) (no CNS penetration)
Second Generation (primarily used for abdominal surgery prophylaxis)	Cefuroxime (Ceftin) IV/PO Cefotetan IV Cefoxitin IV	Decreased *S. aureus* Enhanced gram (-) Cefoxitin and cefotetan vs. anaerobes
Third Generation	Cefdinir (Omnicef) PO Cefpodozime (Vantin) PO Cefotaxime (Claforan) IV Ceftazidime (Fortaz) IV Ceftibuten (Cedax) PO Ceftrixone (Rocephin) IV	Decreased gram (+) Better gram (-) Ceftazidime vs. *Pseudomonas*
Fourth Generation (good CNS penetration)	Cefepime (Maxipime) IV	Like 3rd generation Active vs. *Pseudomonas, MSSA*

Cephalosporins

- MOA: beta-lactams - inhibit cell wall synthesis
- Spectrum: gram-positive, gram-negative
- 1st, 2nd, 3rd, and 4th generation
- AEs: cross-sensitivity with penicillins, GI, hematologic, serum sickness
- DIs: some have decreased absorption with decreased GI acidity

First Generation Cephalosporins

- Oral: cephalexin (Keflex), cephradine (Velosef), cefadroxil (Duricef)
- Parenteral: cefazolin (Ancef, Kefzol)
- Spectrum: gram-positives (staph and strep), limited gram-negatives, oral anaerobes
- Indications: skin infections, alternative for strep, pre-op prophylaxis

Second Generation Cephalosporins

- Oral: cefaclor (Ceclor), cefprozil (Cefzil), cefuroxime (Ceftin)
- Parenteral: cefuroxime (Zinacef), *cefoxitin (Mefoxin), cefotetan (Cefotan)*

- *Methylthiotetrazole (MTT) side chain: hypothrombinaemia, alcohol intolerance (flushing, tachycardia, N/V, hypotension, dyspnea)*

Second Generation Cephalosporins

- Spectrum:
  - less gram-positive and more gram-negative
  - anaerobes – some cover *B. fragilus* (cefoxitin, cefotetan)
- Indications: respiratory tract infections, UTIs, Lyme, skin infections
- Drug of choice: cefuroxime – Lyme disease and *Moraxella catarrhalis*

Third Generation Cephalosporins

- Oral: cefixime (Suprax), cefpodoxime (Vantin), cefdinir (Omnicef), ceftibuten (Cedax), cefditoren (Spectracef)
- Parenteral: ceftriaxone (Rocephin), ceftazidime (Fortaz), cefotaxime (Claforan)

Third Generation Cephalosporins

- Spectrum: less gram-positive and more gram-negative
  - *P. aeruginosa*: ceftazidime, cefoperazone
- Indications: respiratory tract infections, skin infections, UTIs, gonorrhea (cefixime or ceftriaxone but increasing resistance)
- Drug of choice: gonorrhea (cefixime, ceftriaxone)

Fourth/Fifth Generation Cephalosporins

- Cefepime (Maxepime) – parenteral
  - gram-positive and gram-negative activity
  - increased stability to beta-lactamases and activity against *Pseudomonas aeruginosa*
- Ceftaroline (Teflaro)- parenteral
  - gram-positive and gram-negative activity
  - **activity against MRSA and resistant *S. pneumoniae***
  - no activity against *Pseudomonas aeruginosa*

Monobactam: Aztreonam (Azactam®)

- Spectrum of activity
  - Excellent gram (-) including *Pseudomonas*, *Citrobacter spp*, *Enterobacteriaceae*, *P. aeruginosa*, *Serratia spp*
  - Poor gram (+) and anaerobes
- Renal elimination
- IV formulation
- No cross sensitivity with PCN/cephalosporins
  - Cross reactivity with ceftazidime allergy due to side chain
- Indications
  - UTIs
  - Intra-abdominal infections
  - LRTIs
  - SSSI
  - Genitourinary infections
  - Sepsis

Carbapenems

- Broadest spectrum of activity of all antibiotics
- Spectrum of activity
  - Excellent gram (+), gram (-), anaerobes
  - **No** MRSA, MRSE, *stenotrophomonas* and poor *Enterococcus* coverage
  - No *Pseudomonas* coverage with **ertapenem**
  - DOC for infections caused by extended-spectrum b-lactamase (ESBL)–producing gram-negative m.o.
- Indications
  - Lower respiratory tract infections
  - Intra-abdominal infections
  - Bacterial sepsis
  - UTI
  - Bone and Joint infections
  - Skin and skin structure infections
  - Endocarditis
  - Polymicrobial infections
  - Bacterial meningitis

Carbapenems

- Imipenem/cilastatin (Primaxin®)
  - Cilastatin: No instrinic antibacterial activity, blocks effect of dehydropeptidase enzyme
- Meropenem (Merrem®)
- Ertapenem (Invanz®)
  - IV, IM; once daily
- Doripenem (Doribax®)
  - Better in vitro activity versus GNB
- Renal elimination
- Precipitates seizure activity
  - Imipenem > meropenem > ertapenem = doripenem (?)
  - *Risk factors*: underlying CNS pathology and ↓renal function
- Cross sensitivity with PCNs <1%

Fluoroquinolones

- norfloxacin (Noroxin)
- ciprofloxacin (Cipro)
- ofloxacin (Floxin)
- lomefloxacin (Maxaquin)
- levofloxacin (Levaquin)
- gemifloxacin (Factive)
- moxifloxacin (Avelox)

Fluoroquinolones

- MOA: bind to and inhibit topoisomerases II & IV
- Good tissue penetration
- Spectrum: gram-positives (issues of resistance), gram-negatives (cipro - *P. aeruginosa*, gonorrhea resistance), atypicals (chlamydia, mycoplasma), some have anaerobic coverage - gemifloxacin
- Indications: respiratory tract infections, skin infections, UTIs, anthrax, traveler's diarrhea

Fluoroquinolones Adverse Events

- GI
- CNS
- Cartilage toxicity (no peds)
- Tendinitis and tendon rupture – black box warning
- Photosensitivity
- QT prolongation
- Hypo/hyperglycemia
- Rash
- Exacerbation of myasthenia gravis

Fluoroquinolones Drug Interactions

- Theophylline
- Warfarin
- Divalent/trivalent cations - chelation
- Drugs affecting QT interval
- Drugs affecting blood glucose

Macrolides

- Agents: erythromycin, clarithromycin (Biaxin), azithromycin (Zithromax)
- Oral/parenteral
- MOA: inhibit protein synthesis
- Azithromycin half-life = 2-4 days

Macrolides

- Spectrum: gram-positives, some gram-negatives (depends on agent), atypicals (mycoplasma, chlamydia, Rickettsia, *Borrelia burgdorferi*)
  - Note increasing pneumococcal resistance

Macrolides

- Indications: respiratory tract infections, Lyme, GI ulcers (clarithro), MAC (azithro & clarithro), chlamydia STDs, skin infections
- Drug of choice: community-acquired pneumonia, chlamydia, mycoplasma, *H. pylori* (clarithromycin)

Macrolides

- AEs: GI (stimulates GI motility), ototoxicity, prolong QT, cholestatic jaundice (erythro), taste (clarithromycin), phlebitis (erythro)

- DIs: inhibit cytochrome P450

Ketolides
(telithromycin - Ketek)

- MOA: protein synthesis inhibitor
- Spectrum: gram-positive, gram-negatives, atypicals, some anaerobes
- AEs: **hepatic dysfunction (contraindicated in peds)**, contraindicated in patients with myastenia gravis, GI, vision problems, QT prolongation
- DIs: inhibits CYP3A4

Tetracyclines
(tetracycline, doxycycline, minocycline)

- MOA: protein synthesis inhibitors
- Spectrum: *Propionibacterium acnes*, *H. pylori*, *Rickettsia*, *Chlamydia*, *Mycoplasma*, *Borrelia burfdorferi*, *Treponema pallidum*, community-acquired MRSA

Tetracyclines
(tetracycline, doxycycline, minocycline)

- Indications: acne, respiratory tract infections, Lyme, GI ulcers (tetracycline), Rocky Mountain Spotted Fever, chlamydia, community-acquired MRSA
- Drug of choice: community-acquired pneumonia, chlamydia, mycoplasma, Lyme disease

Tetracyclines

- AEs: photosensitivity, deposition in teeth and bones (no peds & pregnancy), GI, vestibular reactions (minocycline), hepatotoxicity
- DIs: chelation with divalent and trivalent cations, OCs, warfarin

Glycylcyclines (tigecycline-Tygacil)

- Parenteral
- MOA: protein synthesis inhibitor
- Spectrum: gram-positive, gram-negatives, anaerobes, atypicals
- Indications: alternative agent
- AEs: GI, photosensitivity, tooth discoloration (no peds or pregnancy)

Aminoglycosides
(gentamicin, tobramycin, amikacin)

- Parenteral only
- MOA: protein synthesis inhibitors
- Spectrum: aerobic gram-positives and negatives (*P. aeruginosa)*
- Indications: generally gram-negative infections in hospital
- AEs: nephrotoxicity, ototoxicity, neuromuscular blockade

Sulfonamides

- MOA: inhibit folic acid synthesis
- Indications: TMP/SMX (Bactrim, Septra): respiratory tract infections, UTIs, PCP, community-acquired MRSA
- Drug of choice: uncomplicated UTI, *H. influenza* respiratory tract infections
- AEs: GI, hypersensitivity, bone marrow suppression, photosensitivity
- DIs: OCs, warfarin, sulfonylureas

Metronidazole (Flagyl)
Tinidazole (Tindamax)

- Oral/parenteral
- Spectrum: anaerobes (*Bacteroides*, *C. difficile*) and parasites (Trichomonas, Giardia, Entamoeba), *H. pylori*
- Drug of choice: trichomonas, *C. difficile*, *H. pylori*
- AEs: metallic taste, GI, CNS, dark brown urine
- DIs: alcohol, warfarin

Clindamycin

- MOA: inhibit protein synthesis
- Spectrum: gram positive and anaerobes
- MRSA – community-acquired
- Alternative agent in penicillin allergic patients
- AEs: GI – pseudomembranous colitis

Fidaxomicin (Dificid)

- Oral
- MOA: inhibits protein synthesis
- Spectrum: *C. difficile*
- Not systemically absorbed
- AEs: nausea, vomiting

Rifampin

- MOA: inhibits RNA synthesis
- Indications: TB, eradication of nasal carriage of *H. flu*, *Meninogococcus*, *Staphylococcus*, additional agent for resistant infections
- AEs: orange-red body fluids, hepatotoxicity, GI, flu-like symptoms
- DI: induces cytochrome P450

Methicillin-Resistant *S. aureus*

- Vancomycin
- Linezolid (Zyvox)
- Dalfprostin/quinupristin (Synercid): IV, arthralgias, inhibits CYP450
- Daptomycin (Cubicin): IV, increased CPK (monitor weekly)
- Telavancin (Vibativ): IV, taste disturbances, N/V, foamy urine, nephrotoxicity
- Others: tigecycline, ceftaroline
- Community: SMX/TMP, clindamycin, tetracycline

Vancomycin

- Inhibits cell wall synthesis – binds to peptidoglycan precursor and prevents cross-linking of peptidoglycan strands
- Parenteral: MRSA – drug of choice, also other staph and strep infections and *Enterococcus faecalis*
- Oral – not absorbed - *C. difficile* treatment
- AEs: red man's syndrome, thrombophlebitis, nephrotoxicity, ototoxicity
- Trough concentrations: 10-20 mg/L

Linezolid (Zyvox)

- Oral/Parenteral
- Oxazolidinone
- Inhibit protein synthesis
- MRSA, enterococci, streptococci
- AEs: myelosuppression (monitor CBC), GI, neuropathy
- Drug interactions: inhibit monoamine oxidase (MAO)– not with tyramine (aged cheeses, sausage, beer), SSRIs, pseudoephedrine

UTIs

- Nitrofurantoin
- Fosfomycin
- Methenamine
- All have some GI effects

- Recommended treatment for uncomplicated UTI is TMP/SMX

Herpes Viruses

- Acyclovir (Zovirax), famciclovir (Famvir), valacyclovir (Valtrex)
- Herpes simplex (first episode, treatment/suppression of recurrences, decrease transmission)
- Herpes zoster – varicella (speed healing, decrease pain & neuralgia)
- Severe infection→acyclovir
- AEs: GI, headache

Influenza

- Zanamivir (Relenza) and oseltamivir (Tamiflu)
  - Influenza A and B treatment and prevention
  - Influenza A resistance to oseltamivir
  - Zanamivir – inhaled – bronchospasm
  - Oseltamivir – nausea, vomiting, HA

- Amantadine and rimantadine
  - Influenza A treatment and prevention (due to resistance issues not currently recommended)
  - AEs: GI, CNS (less with rimantadine)

CMV

- Ganciclovir (Cytovene), valganciclovir (PO, Valcyte) – bone marrow suppression
- Foscarnet (Foscavir) –nephrotoxicity, electrolytes, bone marrow suppression
- Cidofovir (Vistide) – nephrotoxicity, neutropenia
- Fomivirsen (Vitravene) – ocular toxicity

Hepatitis B

- Interferon alpha
- Nucleos(t)ide analogues (lamivudine, adefovir, entecavir, telbivudine, tenofovir)
- All treatment decrease HBV DNA levels and have been associated with HBeAG loss/seroconversion, decreases in ALT, and improvements in liver histology

Hepatitis B

- Inteferon (SC)
  - 4 m - 1 y treatment duration
  - AEs: many, including flu-like symptoms, bone marrow suppression, and psychiatric symptoms
- Nucleos(t)ide analogues (oral)
  - Greater and faster decline in HBV DNA levels than with interferon
  - Resistance issues (low with tenofovir and entecavir)
  - Minimum treatment duration: at least 1 year
  - Minimal side effects – HA, GI

Hepatitis C

- Recommended treatment:
  - peg interferon + ribavirin + telaprevir x 12 wks then interferon + ribavirin x 12-36 wks (depends on HCV-RNA at 4 and 12 wks and prior therapy status)
  - peg interferon + ribavirin x 4 wks then bocepravir is added and all 3 continued for 24 to 44 wks (peg interferon + ribavirin continued another 12 weeks in some patients)
  - peg interferon + ribavirin x 24 - 48 wks

Hepatitis C

- ribavirin: hemolytic anemia, teratogenic
- boceprevir (Victrelis) – fatigue, nausea, headache, taste distortion, anemia, neutropenia (monitor CBC weeks 4, 8, 12), cytochrome P450 inhibition
- teleprevir (Incivek) – rash, itching, anemia (monitor Hb), nausea, vomiting, diarrhea, fatigue, taste distortion, itching, hemorrhoids, and anal or rectal irritation and pain, cytochrome P450 inhibition

Antifungals

- Polyenes: amphotericin – *wide spectrum*
- Azoles: ketoconazole (Nizoral), fluconazole (Diflucan), itraconazole (Sporonax), voriconazole (Vfend), posaconazole (Noxafil) – *spectrum varies from one agent to the other*
- Terbinafine (Lamisil) – *dermatophyte infections*
- Flucytosine – *only as part of combination therapy*
- Echinocandins: caspofungin (Cancidas), micafungin (Mycamine), anidulafungin (Eraxis) – *candida and aspergillosis*
- Griseofulvin

Antifungals - AEs

- Amphotericin: nephtrotoxicity, electrolytes, anemia, flu-like symptoms
- Azoles: hepatotoxicity, QT prolongation, ketoconazole-decreased cortisol & testosterone, voriconazole-vision
- Terbinafine: hepatotoxicity
- Echinocandins: histamine-mediated reactions, hepatotoxicity, GI, HA, fever, phlebitis, hypokalemia, bone marrow suppression
- Griseofluvin: GI, HA, hepatotoxicity
- Flucytosine: bone marrow suppression, GI, hepatitis

Antifungals – Drug Interactions

- Azoles inhibit cytochrome P450
- Ketoconazole & itraconazole require GI acidity for absorption
- Rifampin increases clearance of azoles

Bugs and Drugs of Choice

- **MSSA**: a penicillinase-resistant penicillin
- **MRSA serious**: vancomycin
- **Community acquired MRSA**:
  - uncomplicated: clindamycin, TMP/SMX, tetracycline, linezolid
  - complicated: vancomycin, daptomycin, linezolid, televancin, clindamycin

Bugs and Drugs of Choice

- ***Streptococcus pyogenes*:** penicillin V or G
  - penicillin allergic – clindamycin or macrolide
- ***Streptococcus pneumoniae*:** penicillin V or G or amoxicillin

Bugs and Drugs of Choice

- ***Moraxella catarrhalis:*** cefuroxime
- ***Neisseria gonorrhoeae:*** ceftriaxone, cefixime + azithromycin or doxycycline
- ***Neisseria meningitidis:*** penicillin G
- ***Clostridium difficile:*** metronidazole, vancomycin, fidaxomicin

Bugs and Drugs of Choice

- ***E coli* or *Klebsiella pneumoniae*:** ceftriaxone, cefepime, cefotaxime
- ***Proteus mirabilis*:** ampicillin
- ***Haemophilus influenza*** URI: TMP/SMX
- ***Helicobacter pylori*:** PPI + clarithromycin + amoxicillin or metronidazole

Bugs and Drugs of Choice

- ***Chlamydia:*** macrolides and tetracyclines
- ***Mycoplasma pneumoniae:*** macrolide or tetracycline
- ***Borrelia burgdorferi:*** doxycycline, amoxillin, cefuroxime axetil
- ***Treponoma pallidum:*** penicillin G, benzathine penicillin

Drug Interactions - Overview

- Macrolides, dalfopristin/quinupristin,– inhibit cytochrome P450
- Rifampin – induces cytochrome P450
- Fluoroquinolones and Tetracyclines – chelated by divalent and trivalent cations
- Fluoroquinolones – some interact with theophylline
- Linezolid – monoamine oxidase inhibitors
- Alcohol – metronidazole, cefotetan
- Oral contraceptives

Adverse Events Overview

- Photosensitivity – SMP/TMX, tetracyclines, fluoroquinolones, tigecycline
- Rash – multiple agents (fluoroquinolones*)
- QT prolongation – macrolides, fluoroquinolones, telithromycin
- Red man syndrome – vancomycin
- Nephrotoxicity and ototoxicity – vancomycin and aminoglyocides

Adverse Events - Overview

- Seizures – penicillin, fluoroquinolones, carbapenems
- Mononucleosis – erythematous rash – amoxicillin
- Bone marrow suppression – SMP/TMX, linezolid
- *C. difficile* infections – all (clindamycin*)
- GI – multiple agents (clavulanate*)

Adverse Events - Overview

- Taste disturbance – clarithromycin, metronidazole, tinidazole, telavancin
- Tendonitis – fluoroquinolones
- Orange-red fluids – rifampin
- Contraindicated in pediatrics: tetracyclines, fluoroquinolones, tigecycline, telithromycin TMP/SMX (neonates)

Antifungal Efficacy Summary

- **Gold standard: amphotericin B**
- Aspergillosis: *voriconazole, amphotericin*, posaconazole, itraconazole, echinocandins
- Blastomycosis: *itraconazole, amphotericin*, fluconazole
- Candidemia: *fluconazole, echinocandin, amphotericin*, voriconazole
- Coccidiomycosis: *itraconazole, fluconazole, amphotericin*

Antifungal Efficacy Summary

- Cryptococcosis:
  - meningeal or severe nonmeningeal: amphotericin + flucytosine
  - nonmeningeal mild to moderate: *fluconazole*
  - chronic suppression: *fluconazole*, amphotericin, itraconazole
- Histoplasmosis: *amphotericin*, *itraconazole*, fluconazole
- Sporotrichosis: *itraconazole*, *amphotericin* fluconazole