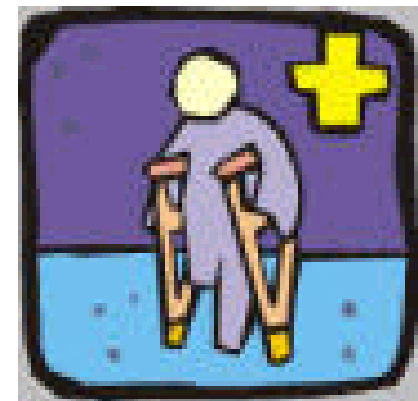


ANTIBIOTIC THERAPY

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Host Factors Affecting Antibiotic Use

- Allergy
- Immune status
 - bactericidal drugs in the immunocompromised host
- Infection site complications
 - BBB, foreign bodies, perfusion
- Age
- Pregnancy and lactation
- Genetics



Inappropriate Antibiotic Prescriptions

Type of Infection	Prescriptions/Year	Percent Inappropriate	Comment
Common Cold	18 Million	100	Abx are ineffective
Bronchitis	16 Million	80	Abx are ineffective except in a few select cases
Sore Throat	13 Million	50	Abx should be used only in cases of confirmed Strep
Sinusitis	13 Million	50	Abx should be withheld for 10 days in the absence of facial pain

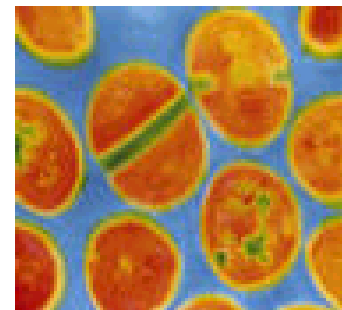
Misuses of Antibiotics

- For treatment of viral infections
- For treatment of FUO
 - except in the immunocompromised host
- In the absence of bacteriologic information
- In inappropriate dosage, patient
- In the absence of other interventions such as drainage, removal of foreign bodies, etc.



Selective Toxicity and Mechanism of Antibiotic Action

- Antibiotics have unique mechanisms of action that make them selectively toxic to bacteria
 - Disruption of bacterial cell walls or inhibition of cell wall synthesis
 - Lethal or nonlethal inhibition of bacterial protein synthesis
 - Inhibition of bacterial nucleic acid synthesis
 - Antimetabolites



Antibiotics and their MOA

DRUG CLASS

EXAMPLES

Cell Wall Synthesis Inhibitors

Penicillins, Cephalosporins,
Vancomycin, Imipenem

Bactericidal Protein Synthesis
Inhibitors

Aminoglycosides

Bacteriostatic Protein Synthesis
Inhibitors

Clindamycin, Erythromycin,
Linezolid, Tetracyclines

Inhibitors of DNA or RNA Synthesis

Fluoroquinolones, Rifampin

Antimetabolites

Sulfonamides, Trimethoprim

Do Antibiotics Promote the Emergence of Resistance?

- YES!!!
- If a drug-resistant organism is present in a population, selective pressure of an antibiotic will cause it to overgrow
- ANY antibiotic MAY promote resistance, but **broad spectrum** agents are the most likely to cause it.

Mechanisms of Antibiotic Resistance

- Production of drug-metabolizing enzymes
- Decreased drug uptake
- Change in drug receptor with decreased binding of antibiotic
- Synthesis of compounds that antagonize the antibiotic



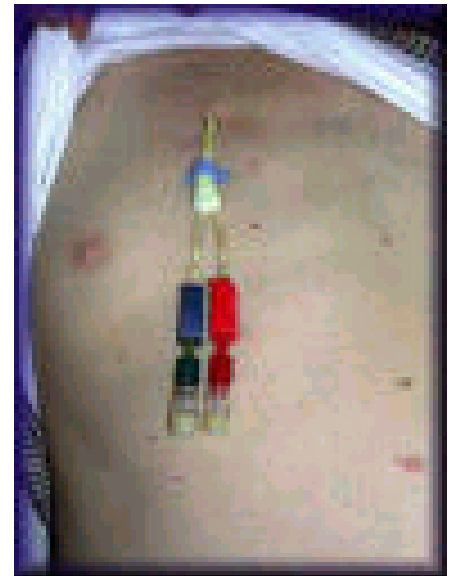
How do Bugs Acquire Resistance?

- Spontaneous mutation
 - occurs to only one drug
- Conjugation
 - mostly occurs between gram-negative bacteria--may occur between normal flora and pathogens
 - extra-chromosomal DNA encoding for resistance (R-factor) is passed from one bacterium to another
 - is responsible for multiple-drug resistant bugs



CDC's Campaign to Prevent Antimicrobial Resistance

- Prevent Infection
 - Vaccinate
 - Remove catheters
- Diagnose and Treat Infections Effectively
 - Target the pathogen
 - Access the experts



CDC's Campaign to Prevent Antimicrobial Resistance

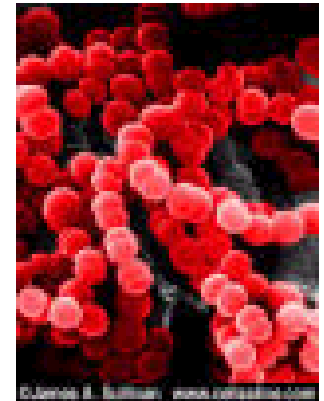
- **Use Antimicrobials Wisely**
 - Practice antimicrobial control
 - Use local data
 - Treat infection, not contamination
 - Treat infection, not colonization
 - Know when to say “no” to Vanco
 - Stop treatment when infection is cured or unlikely
- **Prevent Transmission**
 - Isolate the pathogen
 - Break the chain of contagion

Who Should Receive Antibiotic Prophylaxis?

- Certain surgical patients
 - cardiac, peripheral vascular, orthopedic, GI, hysterectomy
- The severely neutropenic patient
- The patient at risk for bacterial endocarditis
- The patient with recurrent UTIs, severe rheumatic endocarditis

Indications for Antibiotic Combinations

- Initial therapy of severe infection
 - until invading organism(s) is identified
- In mixed infections
 - common in GI, pelvic, brain abscesses
- To prevent emergence of resistance
 - TB, HIV, certain parasites
- To decrease toxicity
- To promote a synergistic effect
 - Ampicillin + Gentamicin; Sulfasoxazole + Trimethoprim

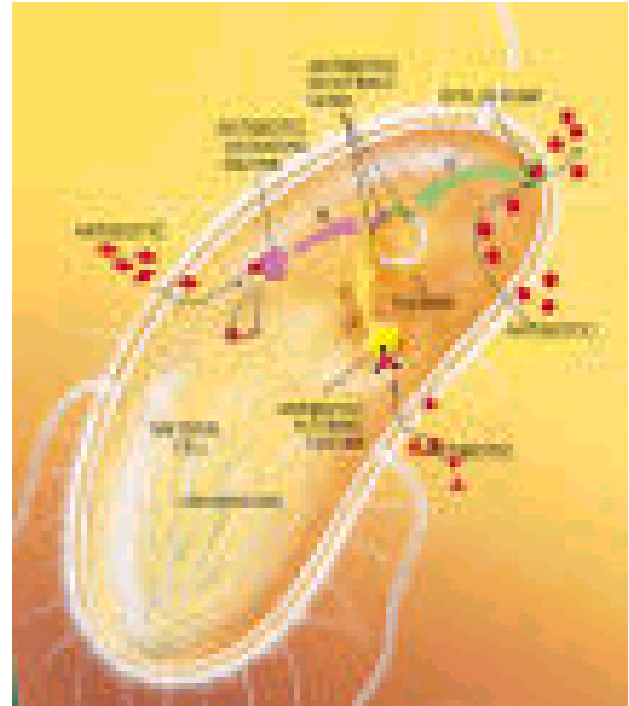


Disadvantages of Antibiotic Combinations

- Increased risk of adverse effect such as allergy or toxicity
- Increased risk of suprainfection
- Increased chance for emergence of drug resistance
- Increased cost

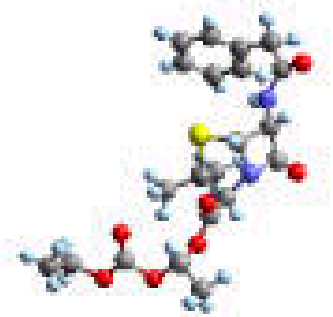
Cell Wall Synthesis Inhibitors

- Penicillins
- Cephalosporins
- Carbapenems
- Aztreonam
- Vancomycin
- Teicoplanin
- Fosfomycin



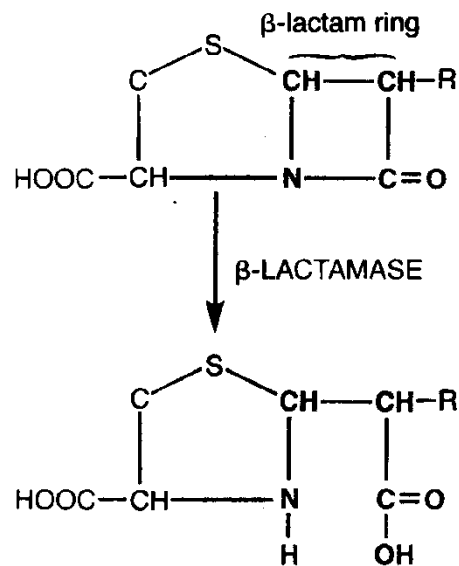
PENICILLINS

- Inhibit transpeptidases necessary for cell wall synthesis and activate autolysis which cleave bonds in the cell wall. These targets are called PBPs: PBP1 and PBP3 are the most crucial targets.
- **Resistance** is due to inability of drug to reach the PBPs or enzymatic inactivation of the drug



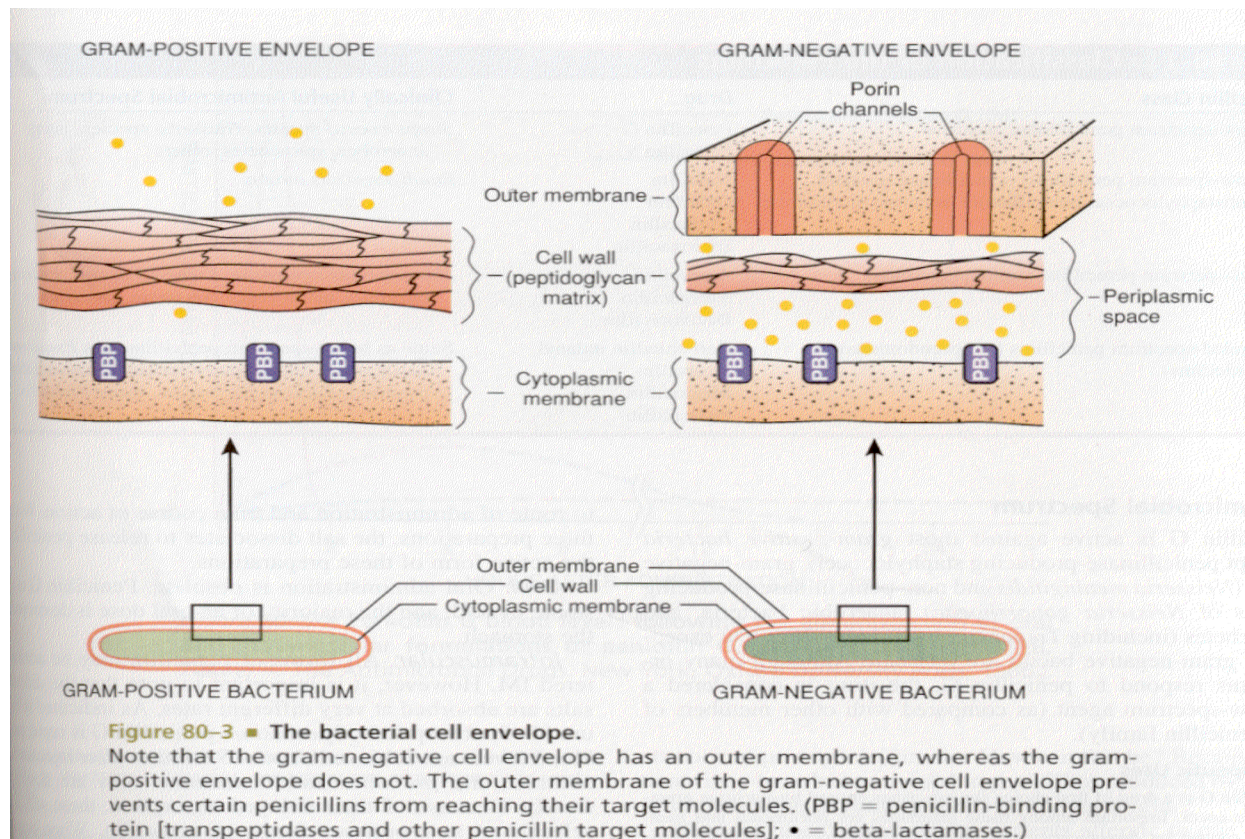
EFFECT OF BETA-LACTAMASE ON PENICILLINS

- The enzyme cleaves open the drug molecule



Bacterial Cell Walls

- Gram positive vs. Gram negative



Penicillins: Antibacterial Spectrum

- Narrow-spectrum penicillinase sensitive
 - Pen G, Pen V
 - Useful for Strep spp., Neisseria spp., many anaerobes, spirochetes
- Narrow-spectrum penicillinase resistant
 - Nafcillin, Oxacillin, Cloxacillin, Dicloxacillin
 - Useful for Staph aureus



Penicillins: Antibacterial Spectrum

- Broad-spectrum penicillins
 - Ampicillin, Amoxicillin, Bicampicillin
 - Useful for *H. influenzae*, *E. coli*, *P. mirabilis*, *N. gonorrhoeae*, enterococci
- Extended-spectrum penicillins
 - Carbenicillin indanyl, Ticarcillin, Mezlocillin, Piperacillin
 - Useful for same as above plus *Pseudomonas*, *Enterobacter* spp., *Proteus*, *Bacterioides fragilis*, many *Klebsiella* spp.

Penicillins: Side Effects and Toxicities

- Pain at IM injection site
- Rare neurotoxicity
- Reactions to procaine and potassium
- ALLERGY: immediate (2-30 min); accelerated (1-72 h); late (days to weeks)
 - Anaphylactic reactions occur with PCNs more than with any other drugs. Incidence is about 0.02%, but mortality is 10%

In the Patient with a PCN Allergy....

- Avoid PCNs entirely
- In cases of a mild allergy, a cephalosporin could be used; if anaphylaxis or severe allergy, avoid a ceph (5-10% cross-sensitivity)
- Vancomycin and Erythromycin may be alternatives
- In life-threatening infections when no alternative will do, give PCN according to a desensitization schedule

Penicillins Combined with a Beta-Lactamase Inhibitor

- These are extended spectrum agents with limited toxicity; useful against *Pseudomonas*
- Ampicillin + sulbactam (Unasyn)
- Amoxicillin + clavulanic acid (Augmentin)
- Ticarcillin + clavulanic acid (Timentin)
- Piperacillin + tazobactam (Zosyn)

CEPHALOSPORINS

- Most widely used antibacterials
- Are beta-lactam antibiotics that bind to PBPs
- Resistance to cephalosporins occurs due to beta-lactamases which cleave open the drugs
- These drugs are grouped into generations, which take into account spectrum of activity, susceptibility to beta-lactamases, and increasing ability to penetrate the CSF

CEPHALOSPORINS

- First Generation
 - Cefadroxil, Cefazolin, Cephalexin, Cephapirin, Cephradine
 - good gram positive coverage
- Second Generation
 - Cefaclor, Cefmetazole, Cefonicid, Cefotetan, Cefoxitin, Cefprozil, Cefuroxime, Loracarbef
 - some gram negative coverage

CEPHALOSPORINS

- Third Generation
 - Cefdinir, Cefditoren, Cefixime, Cefoperazone, Cefotaxime, Cefpodoxime, Ceftazidime, Ceftibuten, Ceftizoxime, Ceftriaxone
 - gram negative aerobes; ceftazidime is effective against Pseudomonas
- Fourth Generation
 - Cefipime
 - broadest spectrum

Cephalosporins: Side Effects and Toxicities

- Allergy
 - maculopapular rash after several days is the most common manifestation
- Increased bleeding tendencies
 - Cefmetazole, Cefoperazone, Cefotetan
- Thrombophlebitis with IV infusion
- Alcohol intolerance
 - Cefmetazole, Cefoperazone, Cefotetan

CARBAPENEMS

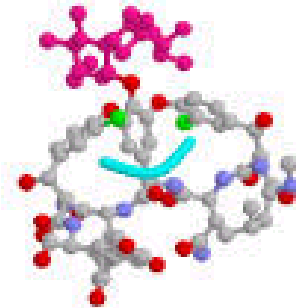
- Broad spectrum beta-lactam antibiotics
- Imipenem, Meropenem, Ertapenem (Invanz)
- **Imipenem (Primaxin)** is the broadest spectrum of any antibacterial
- **Meropenem (Merrem IV)** may be used for bacterial meningitis
- All 3 are relatively safe and well-tolerated

AZTREONAM

- (Azactam): Beta-lactam called a monobactam
- Narrow spectrum, effective only against gram negatives.
- Safe for patients with other beta-lactam allergies
- Must be given parenterally

VANCOMYCIN

- Reserved for serious infections
 - AAPMC (second choice to metronidazole), MRSA, serious infections in the PCN-allergic patient
- Binds to precursors for cell wall synthesis, but is not a beta-lactam
- Adverse effects include ototoxicity (at plasma levels > 30ug/mL), rashes, thrombophlebitis; no cross-reactivity in the PCN-allergic patient

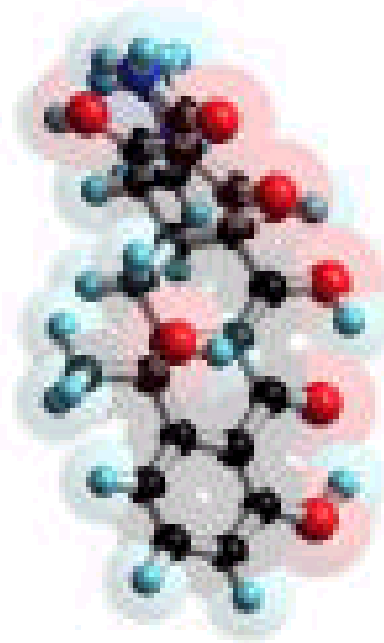


TEICOPLANIN AND FOSFOMYCIN

- **Teicoplanin (Targocid)** is not a beta-lactam, but disrupts cell wall synthesis
- Narrow spectrum with activity against gram positives only
- **Fosfomycin (Monurol)** disrupts cross-linking of cell wall peptidoglycan strands
- Useful as single dose therapy for UTIs

BACTERIOSTATIC INHIBITORS OF PROTEIN SYNTHESIS

- Tetracyclines
- Macrolides
- Clindamycin
- Chloramphenicol
- Linezolid
- Dalfopristin/Quinupristin
- Spectinomycin



TETRACYCLINES

- Tetracycline, Oxytetracycline (Terramycin), Demeclocycline (Declomycin), Methacycline (Randomycin), Doxycycline (Vibramycin), and Minocycline (Minocin)
- All are broad-spectrum drugs that suppress bacterial growth by binding to the 30S ribosomal subunit. This prevents binding of tRNA to the mRNA-ribosome complex, so amino acids cannot be added to protein chains

TETRACYCLINES

- Therapeutic uses of Tetracyclines include:
 - Infectious diseases: rickettsia, Chlamydia trachomatis, brucellosis, cholera, Mycoplasma pneumonia, Lyme disease, anthrax, Helicobacter pylori
 - Treatment of acne: PO and topically
 - Peptic ulcer disease
 - Periodontal disease

Tetracyclines: Side Effects and Toxicities

- GI irritation: NVD, esophageal ulceration
- Staining of teeth: avoid during pregnancy, avoid from ages 4 mos to 8 years
- Suprainfection: AAPMC, Candida
- Hepatotoxicity
- Renal toxicity
- Photosensitivity



MACROLIDES

- Erythromycin

- Binds to the 50S ribosomal subunit and blocks the addition of amino acids to the protein chain
- Has activity against most gram positives and some gram negatives
- Is a drug of choice in the PCN-allergic patient, for whooping cough, and for Legionnaire's disease

Erythromycin: Side Effects and Toxicities

- GI side effects are common: NVD
- Cholestatic hepatitis: caused by erythromycin estolate, usually develops 10-20 days after treatment is started. Symptoms reverse when drug is discontinued.
- Suprainfection



Drug Interactions With Erythromycin

- Erythromycin inhibits cyp450, raising levels of many drugs
- Erythromycin elevates levels of theophylline, carbamazepine, and warfarin--monitor patients *closely*.
- Erythromycin antagonizes binding of chloramphenicol and clindamycin--do not combine.

Other Macrolides

- **Clarithromycin (Biaxin)**: good for skin and soft tissue infections, *H. pylori*, respiratory tract infections, and in PCN-allergic patients
- **Azithromycin (Zithromax)**: Uses as above, and as a DOC for *Chlamydia trachomatis*
- **Dirithromycin (Dynabac)**: Uses as above, and CAP caused by pneumococci

OTHER BACTERIOSTATIC INHIBITORS OF PROTEIN SYNTHESIS

- **Clindamycin (Cleocin)**

- Used for gram - and + anaerobes and gram + aerobes. Is a preferred drug for abdominal and pelvic infections caused by *B. fragilis*.
- Main adverse effect is antibiotic-associated pseudomembranous colitis (AAPMC)
 - Suprainfection of the GI tract with *C. difficile*. Causes profuse, watery diarrhea (+/- mucus and blood) that develops within 1 week of treatment to 4-6 weeks after. To treat, d/c the clindamycin and give metronidazole or vancomycin.

OTHER BACTERIOSTATIC INHIBITORS OF PROTEIN SYNTHESIS

- **Chloramphenicol (Chloromycetin)**
 - Broad spectrum agent limited to use against serious infections (CNS) when other drugs fail.
 - Most serious toxicity is fatal aplastic anemia and bone marrow suppression. In children <1 year, causes gray baby syndrome.

OTHER BACTERIOSTATIC INHIBITORS OF PROTEIN SYNTHESIS

- Linezolid (Zyvox)
 - Has activity against VRE and MRSA
 - Also active against *E. faecium*, *E. faecalis*, *Staph. epidermidis*, *Staph. aureus*, and *S. pneumoniae*
 - Adverse effects can include myelosuppression so CBC should be done weekly

OTHER BACTERIOSTATIC INHIBITORS OF PROTEIN SYNTHESIS

- **Dalfopristin/Quinupristin (Synercid)**
 - Used for VR *E. faecium*, MRSA, MRSE, and drug-resistant *Strep pneumo*.
 - Hepatotoxicity is major adverse reaction--measure liver enzymes and bilirubin twice the first week and once weekly thereafter.
 - Inhibits CYP3A4 so many drug interactions

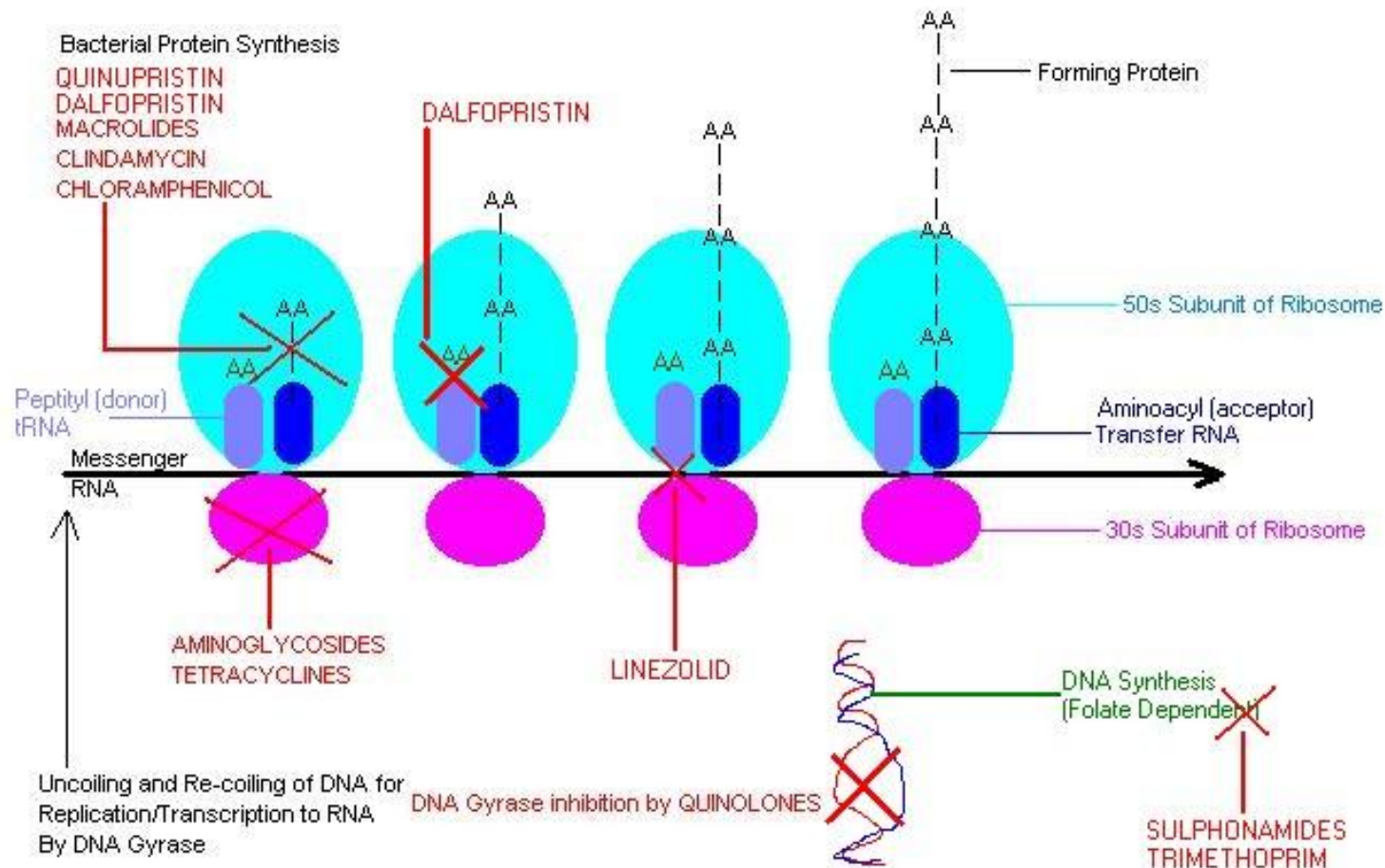
AMINOGLYCOSIDES

- Bactericidal inhibitors of protein synthesis
- Narrow-spectrum agents effective against aerobic gram negative bacilli
- All must be administered parenterally
- Most commonly used ones are gentamicin, tobramycin, and amikacin

AMINOGLYCOSIDES

- MOA: Bind to the 30S ribosomal subunit
 - inhibit protein synthesis
 - terminate protein synthesis
 - cause production of abnormal proteins secondary to misreading of genetic code
 - all are bactericidal even after serum levels have dropped below the bactericidal concentration (PAE)

Mechanism of Action of AGs



AMINOGLYCOSIDES

- Bugs become resistant to AGs via transfer of R factors which encode enzymes that inactivate the drugs
 - Amikacin is the least likely to induce resistance
- AGs work against *E. coli*, *K. pneumoniae*, *S. marcescens*, *P. mirabilis*, and *P. aeruginosa*

Aminoglycosides: Side Effects and Toxicities

- **Ototoxicity:** AGs can damage both hearing and balance. Damage is related to persistently elevated trough levels of drug. Usually irreversible.
 - Risk is increased in renal impairment, with concurrent use of ethacrynic acid, and administration of high doses for >10 days
 - First sign of cochlear damage is high-pitched tinnitus
 - First sign of vestibular damage is headache

Aminoglycosides: Side Effects and Toxicities

- **Nephrotoxicity**: AGs damage proximal renal tubule cells, and damage present as acute renal failure. Symptoms are proteinuria, casts in the urine, elevated serum creatinine and BUN, and production of dilute urine. This is reversible upon d/c of the drug.
- **Neuromuscular blockade**
- **Hypersensitivity**
- Monitor trough levels 2 and 12 hours after dosing in patients getting these drugs once a day

Aminoglycosides: Considerations

- **Tobramycin (Nebcin):** Often used in nebulized form for CF patients
- **Amikacin (Amikin):** Broadest spectrum, least likely to induce resistance; should be reserved for cases of AG resistance
- **Netilmicin (Netromycin):** Similar to gentamicin
- **Neomycin:** Most ototoxic and nephrotoxic
- **Kanamycin (Kantrex):** Resistance is common
- **Streptomycin:** Rarely used
- **Paromomycin (Humatin):** Used for GI infestations of tapeworms and amebiasis

ANTIMETABOLITES

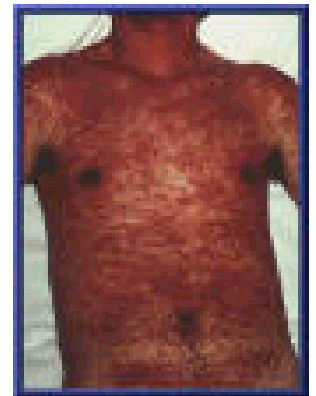
- **SULFONAMIDES and TRIMETHOPRIM**
- Broad spectrum antibiotics that block the synthesis of folic acid
- When used together, a synergistic effect on bacterial growth results
- Resistance is less when both are used together; resistance to sulfonamides occurs via R factors or spontaneous mutation

SULFONAMIDES

- Sulfisoxazole, Sulfadiazine, Sulfamethizole (Thiosulfil Forte), Sulfamethoxazole (Gantanol),
- Sulfacetamide, Silver Sulfadiazine and Mafenide (topical)
- Uses include UTIs, nocardiosis, burns, superficial eye infections

Sulfonamides: Side Effects and Toxicities

- Hypersensitivity reactions: rash, drug fever, photosensitivity, Stevens-Johnson syndrome
- Hemolytic anemia: seen in patients with G-6-PD deficiency
- Kernicterus: do NOT give to infants < 2 mos or in late pregnancy, breastfeeding
- Renal damage from crystalluria



Stevens-Johnson Syndrome



TRIMETHOPRIM

- Rarely used alone--only for acute, uncomplicated UTIs due to susceptible organisms
- Well-tolerated, some GI upset.
- Rarely causes megaloblastic anemia, thrombocytopenia, and neutropenia in patients with folate deficiency
- **TMP-SMZ (Bactrim)** is used for UTIs and *Pneumocystis carinii* infections

DRUGS THAT DISRUPT BACTERIAL NUCLEIC ACID SYNTHESIS

- **Fluoroquinolones:** inhibit bacterial DNA gyrase so that DNA cannot be supercoiled. Bactericidal.
- **Metronidazole:** Breaks DNA strands and inhibits DNA synthesis. Bactericidal.

FLUOROQUINOLONES

- Broad spectrum antibiotics used for bone and soft tissue infections, UTIs, respiratory tract infections, GI infections, and prevention of anthrax.
- Drugs include Ciprofloxacin (Cipro), Ofloxacin (Floxin), Lomefloxacin (Maxaquin), Sparfloxacin (Zagam), Moxifloxacin (Avelox), Gemifloxacin (Factive), Norfloxacin (Noroxin), Levofloxacin (Levaquin)

Fluoroquinolones: Side Effects and Toxicities

- Mild GI side effects
- CNS side effects including dizziness, headache, restlessness. Seizures are a rare SE.
- Tendon rupture (usually of the Achilles tendon) is a rare SE, but d/c at first sign of tendon pain
- Do not use in children < 18 years of age
- May elevate levels of warfarin and theophylline



Achilles Tendon Rupture



METRONIDAZOLE

- **Metronidazole (Flagyl):** Used to treat anerobic bacterial infections of CNS, abdominal organs, skin, joints, soft tissues, and genitourinary tract, and protozoal infections. Also used as a prophylactic antibiotic for colorectal surgery, abdominal surgery, vaginal surgery. May be used in combination to treat *H. pylori*.

Metronidazole: Side Effects and Toxicities

- GI side effects are common and include nausea, dry mouth, metallic taste.
- Urine may turn a darker color
- Avoid use during first trimester of pregnancy
- Causes a disulfiram-like reaction with alcohol
- Lower doses of warfarin when used with Metronidazole

Summary: Antibiotic Update

- The “old rules” apply
 - Right Drug
 - Right Dose
 - Right Duration
 - Right Patient
 - Right Time

Summary: Antibiotic Update

- Alert patient to anticipate side effects
- Monitor for drug interactions
- Encourage Compliance
 - Better therapeutic response
 - Decreased chance for emergence of resistance

Emerging Antibiotic Resistance: Bugs as Moving Targets

WHY ARE BACTERIA BECOMING RESISTANT?

- Inappropriate prescribing
- Overuse of broad spectrum drugs
- Lack of patient education (demand!!)
- Agricultural/animal use

ANTIBIOTIC RESISTANCE

- CDC estimates that as many as 50% of prescriptions are unnecessary
- Most prescriptions are written for ambulatory respiratory tract infections
- Cost of treating resistant infections is \$30 billion

Emerging Drug Resistance

- The prevalence of antimicrobial resistant pathogens is rapidly increasing
- Discovery and development of new drugs active against these organisms have slowed dramatically
- So far resistance has developed to all antimicrobial agents

Penicillin-Resistant Streptococcus

Who Gets Pneumococcal Disease?

- Leading cause of illness in young children , illness and death in the elderly and or immunocompromised
 - 3,000 cases of meningitis
 - 50,000 cases of bacteremia
 - 500,000 cases of pneumonia
 - 7 million cases of otitis media

Pneumococcal Disease

- Invasive Disease (bacteremia)
 - 15-30 cases per 100,000 pop
 - rates higher for
 - children < 2 years old (160 cases)
 - adults > 65 years
 - > African Americans, American Indians & Alaskan Natives

PCN Resistant Strep

- Function of altered (PBPs) penicillin-binding proteins
 - Transpeptidases
 - involved in cell wall synthesis
 - Level of resistance directly related to the number of PBPs involved
 - Most common serotypes
 - 6, 14, 19 & 23

PCN Resistant Strep

- Risk factors for acquisition of Resistant Strep
 - Previous antimicrobial therapy
 - Day care center attendance
 - Hospitalization
 - Caucasian

Pneumococcal Disease

Risk Factors in Adults

- Chronic cardiovascular disease
 - » i.e., congestive heart failure, cardiomyopathy
- Chronic pulmonary disease
 - » i.e., COPD, emphysema
 - » e.g., Asthma (steroids)
- Chronic liver disease
 - » i.e., cirrhosis, EtOh
- Diabetes mellitus
- Asplenia, Sick cell
- Immunosuppressed
 - congenital (CGD)
 - HIV-1
 - Leukemia, lymphoma
 - Multiple myeloma
 - Hodgkins
 - Transplantation
 - chemotherapy
 - chronic renal failure, nephrotic syndrome

Pneumococcal Disease

Mortality

- 40,000 deaths annually in US
 - Meningitis or Bacteremia
 - Elderly
 - Underlying medical conditions
 - Immunocompromised
 - Splenectomy
 - Overall cases-fatality rates among adults
 - 30-40% elderly
 - 36% adult inner-city

PCN Resistant Strep

- Treatment
 - Empiric (risk factors & susceptibility unknown)
 - Ceftriaxone/ Cefotaxime
 - Quinolones
 - When to add Vancomycin
 - Meningitis
 - Septic Shock
 - History of bacterial sepsis
 - WBC <5000, >30,000, neutropenia

PCN Resistant Strep

- Treatment P.O.
 - Quinolones
 - Gram positive activity
 - Levofloxacin
 - Moxifloxacin
 - Quinolone resistance
 - Increasing (adults)
 - 2.6% > 65 years old
 - » highest per capita use
 - Associated with PCN resistance

MRSA and VISA

Methicillin-Resistant *Staphylococcus aureus*

- Resistance is conferred by the chromosomal *mecA* gene, which encodes an altered PBP (2A)
 - Resistance to all beta-lactams including cephalosporins
 - Continue to produce beta-lactamase
 - Reservoir for resistance: quinolones, tetracyclines, sulfonamides, chloramphenicol, macrolides, gentamicin

Who Gets Methicillin-resistant *Staphylococcus aureus*?

- MRSA continues to increase
 - Nosocomial isolates
 - 2.4% 1975
 - 29% 1991
 - 50% 1997
 - Persists in 87.5% of hospitals once introduced
 - Vancomycin remains the drug of choice for serious infections

Who Gets Methicillin-resistant Staphylococcus aureus?

- Community-acquired MRSA
 - Many community-acquired MRSA cases were from long-term care facilities, IVDU, recent admissions or surgery, risk factors for hospital exposure and acquisition.
 - Recently CA MRSA infection in patients without risk factors
 - Pediatric hospitals
 - Day care centers
 - Athletes
 - Minority communities (urban& rural)
 - High mortality

Methicillin-resistant *Staphylococcus aureus*

- In hospitalized patients, about 1/3 of colonized patients develop an infection.
- To avoid spread of MRSA: hand-washing and glove use
- Vancomycin can be used, unless VISA....

Vancomycin-Resistant *Staphylococcus aureus*

- First reported from Japan 1997
- Three cases from US
 - Older diabetic men
 - Peritonitis in ESRD
 - MRSA bacteremia
 - 12 - 18 weeks of Vancomycin therapy
- Intermediate resistance
 - thicker extracellular matrices
- Good news: no colonization in contacts
- Rx: ? Linezolid (Zyvox) and Quinupristin/Dalfopristin (Synercid)

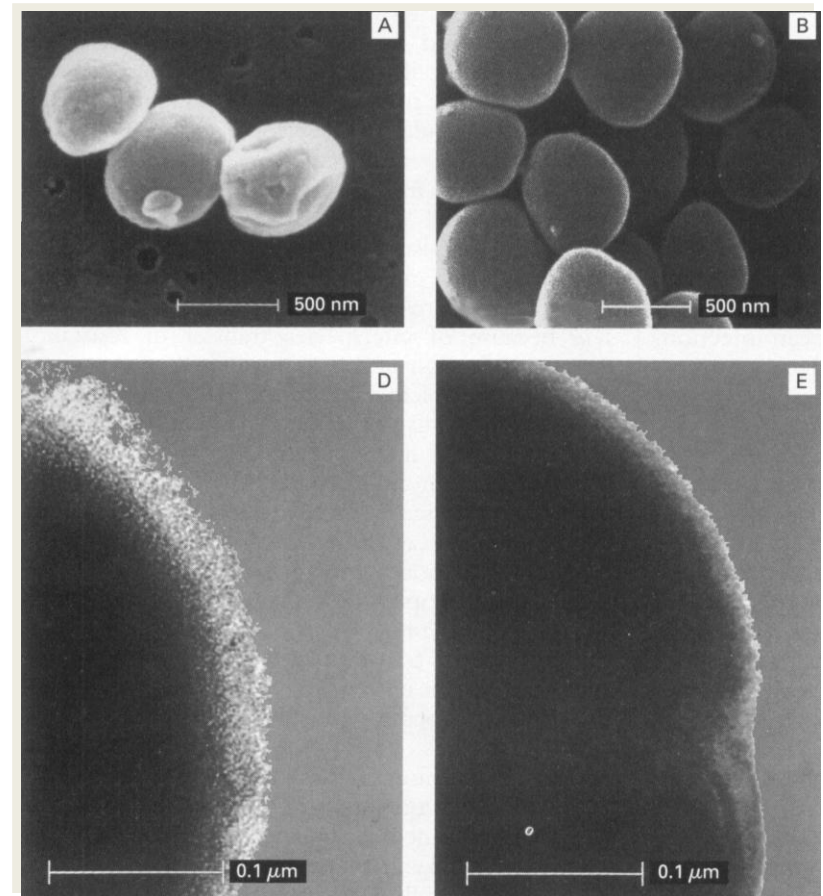
Vancomycin Resistant *Staphylococcus aureus*

Electron Micrographs *S. aureus* isolates

A & D VISA

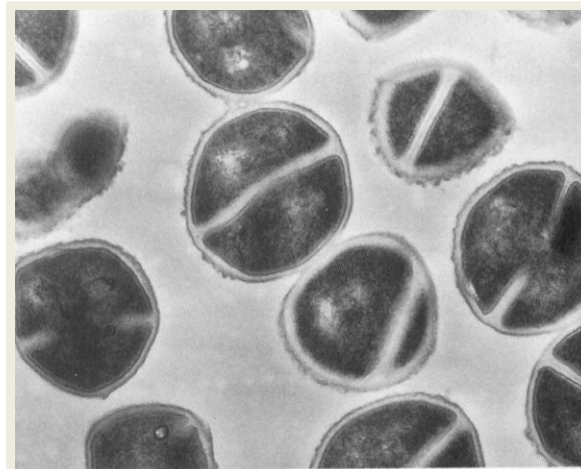
B & E MRSA

**Layer of extracellular
material in VISA**

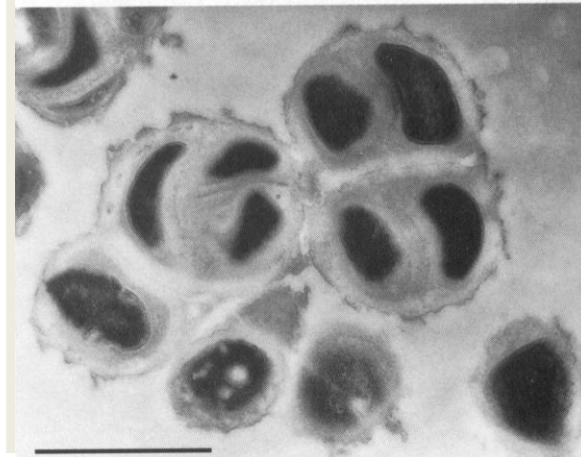


Vancomycin Resistant *Staphylococcus aureus*

**Electron
Micrographs**



MSSA



VISA

Vancomycin-Resistant Enterococcus

Vancomycin-Resistant Enterococcus

- Normally, vancomycin binds with high affinity to the D-ala-D-ala terminus of pentapeptide precursor, blocking cross-linking necessary for strengthening the peptidoglycan layer

Vancomycin-Resistant Enterococcus

- Mechanism of resistance
 - Ligase with altered substrate specificity
 - Dehydrogenase which creates a pool of D-lactate
 - Dipeptidase which reduces the pool of D-alanine
- Abnormal peptidoglycan precursors terminating in D-ala-D-lac with low affinity for vancomycin

Where Did Vancomycin-Resistant Enterococcus Come From?

- First recognized in mid-1980s
- Principally a nosocomial phenomenon in ICU
- 6 years from the first descriptions to entrenched nosocomial pathogens
- 3-fold increase in 2 years, east - west coast
- Increase from ICU to wards

WHO GETS VRE?

- Nosocomial--in urine of patients with indwelling catheters
- Immunocompromised
- Patients on prolonged antibiotic courses
- PREVENT SPREAD by isolating patients, hand washing, gloves, gowns
- Colonization may last >3 months!

WHO GETS VRE?

- Risk factors for acquisition
 - Prolonged hospitalization
 - ICU and wards
 - Need for intrahospital transfer to another ward
 - Need for post-liver transplant re-exploration
 - Enteral tube feedings

WHO GETS VRE?

- Risks for bacteremia
 - Poor APACHE II score
 - Bone marrow transplant
 - Hematologic malignancy
 - Multiple antibiotics
 - Parenteral vancomycin
 - Third generation cephalosporins
 - Oral vancomycin

Outsmarting Vancomycin-Resistant Enterococcus

- Treatment of VRE
 - Major challenge
 - usually multiresistant
 - Ampicillin + gentamicin (E.faecalis)
 - Chloramphenicol
 - Doxycycline
 - Quinolones
 - Nitrofurantoin (UTIs)
 - Teicoplanin
 - Oxazolidiones (Zyvox)
 - Streptogramins (E. faecium)(Synercid)

Outsmarting Vancomycin-Resistant Enterococcus

- Invasive VRE infections:
- Use Zyvox for *E. faecium* and *E. faecalis*.
- Synercid may be effective against *E. faecium*.
- Doxycycline and Chloramphenicol may be effective.

Outsmarting Vancomycin-Resistant Enterococcus

- Eradication of GI Colonization
 - decrease risk of infection
 - decrease VRE reservoir
 - decrease cost & inconvenience of infection control
- High failure rates
- High relapse rates
 - 66% with long term follow up

Recommendations for the Use of Vancomycin

- APPROPRIATE
 - Treatment of serious infections due to beta-lactam resistant gram + pathogens
 - Treatment of infections due to gram + pathogens in patients allergic to beta-lactams
 - AAPMC which fails to respond to 2 X Flagyl, or if severe and life-threatening
 - Prophylaxis for endocarditis or implantation of prosthetics for patients at high risk for MRSA or MRSE

Recommendations for the Use of Vancomycin

- INAPPROPRIATE
 - Routine surgical prophylaxis
 - Empiric for neutropenic fever unless suspect line infection
 - Treatment for a single positive blood culture of a coag-neg Staph
 - Prophylaxis for IV catheters
 - Selective decontamination of GI tract
 - Eradication of MRSA colonization

Recommendations for the Use of Vancomycin

- INAPPROPRIATE
 - Primary treatment of AAPMC
 - Routine prophylaxis for dialysis patients
 - Treatment of infections due to beta-lactam-sensitive gram + in patients with renal failure
 - Continuous empiric use in patients with negative cultures

NOSOCOMIAL INFECTIONS

Nearly 5% of all patients admitted to an acute care hospital will acquire a new infection.

2 million nosocomial infections each year

39% Urinary Tract

17% Surgical

7% Bacteremias

18% Pneumonias

NOSOCOMIAL INFECTIONS

- These infections cost \$4.5 billion annually
- 88,000 patients die from them each year
- 70% of infections are due to organisms resistant to at least 1 drug
- Over the past 20 years, there has been a 36% increase in nosocomial infections

Nosocomial Infections: ICU

- ICU-acquired infections
 - Risk factors
 - Length of stay
 - Mechanical ventilation
 - Trauma
 - Catheterization
 - Most common types of infection
 - Pneumonia, Septicemia

NOSOCOMIAL PNEUMONIA

Nosocomial pneumonias are the most common fatal nosocomial infection

Estimated 15% of all hospital-associated deaths are directly related to hospital acquired pneumonias

Mortalities from nosocomial pneumonias = 20-50%

NOSOCOMIAL PNEUMONIA

ETIOLOGIES

PERCENT

Pseudomonas aeruginosa

50-70%

Enterbacteriaceae

Staphylococcus aureus

15-30%

Anaerobic

20-30%

H. influenzae

10-20%

Pneumococcus

10-20%

Legionella

4%

Viral

CMV, Influenzae, RSV

10-20%

Aspergillus

1%

Changing Resistance

- Gram-negatives
 - Nosocomial
 - Klebsiella
 - Enterobacter
 - E. coli
 - Citrobacter
 - Serratia
 - Pseudomonas
 - Acinetobacter

Mechanism of Resistance

Cephalosporins	-----	Extended-spectrum beta-lactamases, chromosomal cephalosporinases
Beta-lactamase Inhibitors	-----	Hyperproducers of beta-lactamases, resistance to inhibitors, chromosomal cephalosporinases
Quinolones	-----	Alterations in DNA topoisomerase, efflux /permeab.
Carbapenems	-----	Zinc metalloenzymes, other beta-lactamases

NOSOCOMIAL PNEUMONIA

Mortality is high although bacteremia occurs in less than 10% of nosocomial pneumonia cases

Mortality associated with aerobic gram negative bacillary pneumonias higher than gram positive or viral pneumonias.

Pseudomonas = 70% mortality

Other gram negative bacilli = 30%

WHO IS AT RISK FOR A NOSOCOMIAL PNEUMONIA?

Predisposing Factors for Hospital Acquired Pneumonia

- Intubation
- ICU
- Antibiotics (change colonization)
- Surgery (especially with intubation)
- Chronic lung disease
- Advanced age (>60)
- Immunosuppression

PATHOGENESIS

⇒ **Most cases due to aspiration of upper airway flora**

⇒ **Few cases due to bacteremia**

Risks for gram negative colonization

- 1. More advanced degree of illness**
- 2. Longer duration of hospitalization**
- 3. Prior or concomitant use of antibiotics**
- 4. Intubation**
- 5. Azotemia**
- 6. Underlying pulmonary disease**

SOURCE OF GRAM NEGATIVE BACILLI

- Enterobacteriaceae - GI Tract
 - Enterobacter
 - Citrobacter
 - Klebsiella
 - Proteus
 - Serratia
- Non-Enterobacteriaceae - Environmental
 - Pseudomonas
 - Acinetobacter
- May get GI colonization with Pseudomonas first
- Role of acidification on colonization not clear

TREATMENT

Complicated by:

- Necrosis and hemorrhage
- Debilitated hosts
- High MICs of gram negative bacilli
- **Antimicrobial resistance**
 - Choice determined by hospital susceptibilities

Treatment of Nosocomial Pneumonia

- Empiric
 - Combination therapy
 - Beta-lactam + aminoglycoside
 - Piperacillin + gentamicin
 - Ceftazidime + gentamicin
 - Cefepime + gentamicin
 - Once daily dosing for aminoglycosides

Empiric Antibiotics for Infectious Diseases

Antibiotic Classes

- Beta-lactams

- Penicillins
 - ampicillin, amoxicillin
 - nafcillin, dicloxacillin
 - piperacillin, ticarcillin
- Cephalosporins
 - cefazolin, cephalexin
 - cefuroxime, cefpodoxime
 - cefoxitin, cefotetan
 - ceftriaxone, cefotaxime
 - ceftazidime, cefepime
- Monobactam
 - aztreonam
- Carbapenem
 - imipenem
 - meropenem

- Combinations

- amoxicillin/clavulanate
- ampicillin/sulbactam
- piperacillin/tazobactam

- Glycopeptides

- vancomycin
- teicoplanin

- Macrolides

- erythromycin
- clarithromycin
- azithromycin

- Lincosamides

- clindamycin

Antibiotic Classes

- Aminoglycosides

- gentamicin
- tobramycin
- amikacin

- Quinolones

- norfloxacin
- ciprofloxacin
- ofloxacin
- levofloxacin
- gemifloxacin
- moxifloxacin

- Sulfonamides

- trimethoprim + sulfamethoxazole

- Tetracyclines

- tetracycline
- doxycycline
- minocycline

- Nitroimidazoles

- metronidazole

Antibiotic Classes

- Linezolid
 - Zyvox
- Streptogramins
 - Synercid
- Daptomycin
 - Cubicin

Newer Antibiotics for Gram-positive Infections

- **Quinupristin-dalfopristin (Synercid)**
 - Combination of 2 compounds
- **Mechanism of action**
 - Protein synthesis inhibitor
- **Spectrum of activity (VRE infections, skin & soft tissue infections with Staph or Strep)**
 - MRSA & MSSA
 - VRE (*E. faecium* only)(FDA indication)
 - VISA & VRSA
- **Toxicity**
 - Venous irritation
 - Elevates conjugated bilirubin
 - Severe arthralgias and myalgias
 - Pregnancy category B
- **IV formulations only, 7.5 mg/kg q 8 hours**

Newer Antibiotics for Gram-positive Infections

- Linezolid (Zyvox)
- Mechanism of action
 - Protein synthesis inhibitor
- Spectrum of activity (nosocomial pneumonia, CAP, skin & soft tissue infection including DM foot infection (not osteomyelitis))
 - MRSA & MSSA (FDA indication)
 - VRE (FDA indication)
 - VISA & VRSA
- Toxicity
 - Increase LFTs
 - Skin rash
 - Myelosuppression, especially thrombocytopenia
 - Pregnancy category C
- IV and PO formulations
 - 600 mg q12

Newer Antibiotics for Gram-positive Infections

- Daptomycin (Cubicin)
- Mechanism of action
 - Binds to cell membrane and depolarizes it , inhibits DNA, RNA and Protein synthesis (Bacteriocidal)
- Spectrum of activity: for treatment of complicated skin and soft tissue infections with MRSA, Strep spp, vancomycin susceptible E. faecalis
 - Not for the treatment of pneumonia
 - MRSA & MSSA (FDA indication)
 - VISA & VRSA
- Toxicity
 - Constipation
 - Myopathy (increases in creatinine phosphokinase, need to stop the drug if increase 5 times the upper limit of normal)
 - Pregnancy category B
- Adjustments for renal impairment are needed
- IV formulation only
 - 4 mg/kg q24

Newer Antibiotics for Gram-positive Infections

- How to Use?
- First line therapy
 - Synercid or Zyvox for Vancomycin resistant enterococcus
- Alternative therapies for serious infections with Staph or Strep
 - Where Serious allergies, intolerance or treatment failures to Beta-lactams, Clindamycin or Vancomycin have occurred.
 - ?Vancomycin-resistant Staphylococcus ?

Antibiotic Side Effects, Toxicity and Other Problems

- PCN

- Allergic reactions (1-5%)
- Anaphylaxis (.004-.015%)
- Cross reaction
 - 3-7% PCN to Ceph
- Prolonged high dose
 - granulocytopenia
 - interstitial nephritis

- Cephalosporins

- Allergic reactions (1-3%)
- Cefotetan
 - 3-methylthiotetrazole side chain: disulfiram-like reaction (etoh) and hemostasis (hypoprothrombinemia)

- Carbapenems (Imipenem)

- Allergic reactions with PCN
- Seizure with high doses

- Vancomycin

- Red-man syndrome
- nephrotoxicity when used with aminoglycosides

Antibiotic Side Effects, Toxicity and Other Problems

- **Macrolides**

- GI complaints: cramping, diarrhea
- Drug interactions

- **Aminoglycosides**

- Nephrotoxicity
- Ototoxicity

- **Quinolones**

- GI and CNS complaints
- Seizure with high doses

- **Sulfonamides**

- Allergic reactions
- Stevens-Johnson

- **Tetracyclines**

- Photosensitivity

- **Metronidazole**

- Disulfiram-like reaction with etoh
- CNS (seizure) and neuropathy

Infectious Disease Problems

- Skin and Soft Tissue
- Upper Respiratory Tract Infection
- Lower Respiratory Tract Infection
- Gastrointestinal
- Urinary Tract Infection
- Central Nervous System
- Blood Stream Infection
- STDs

Skin & Soft Tissue Infections

- Staph.aureus, Strep.pyogenes
 - impetigo, erysipelas, lymphangitis
 - cellulitis, surgical wound infection
 - pyomyositis, necrotizing fasciitis
- cefazolin, cephalexin
- nafcillin, dicloxacillin
- clindamycin
- vancomycin
- amox/clav, amp/sulbactam
- duration: 10 days

Skin & Soft Tissue Infection

- Bite Wounds

- Staph & Strep, (including microaerophilic), Eikenella (animal bites: Pasteurella), Bacteroides, Prevotella, Fusobacterium, Peptostreptococcus

- Treatment

- Clean, debride and tetanus shot
- amox/clavulanate, ampicillin/sulbactam

Upper Respiratory Tract Infections

- Pharyngitis

- Grp A Strep
- PCN x 10 days

- Otitis Media

- Pneumococcus
- H. influenzae
- Moraxella catarrhalis
- Amoxicillin
 - Augmentin
- Macrolides
- Cephalosporins
 - cefuroxime, cefodoxime
 - cefixime, ceftriaxone

- Sinusitis/Bronchitis

- Pneumococcus
- H. influenzae
- Klebsiella
- Moraxella
- Staph aureus
- Anaerobes
- TMP/SMX
 - Amoxicillin
 - Augmentin
 - Macrolides
 - Cephalosporins
 - Quinolones

Community Acquired Pneumonia

- Typical

- acute onset
- symptoms < 1 week
- productive cough
- short of breath
- chest x-ray
 - lobar infiltrates

- Atypical

- insidious onset
- symptoms > 1week
 - 2-3 weeks usually
- nonproductive cough
- dyspnea on exertion
 - then SOB
- chest x-ray
 - interstitial infiltrates

Community Acquired Pneumonia

- Typical

- Streptococcus pneumoniae
- Haemophilus influenzae
- Moraxella catarrhalis
- Klebsiella pneumoniae
 - E. coli, Serratia marcescens, Pseudomonas aeruginosa
- Staphylococcus aureus
- Aspiration / anaerobic
 - lung abscess

- Atypical

- Mycoplasma pneumoniae
- Chlamydia pneumoniae
- Legionella pneumophila
- Influenza A & B
 - Parainfluenza, Adenovirus
- TB, miliary
- fungal
 - Histoplasma capsulatum
 - Blastomyces dermatitidis
 - Coccidioides immitis
- Pneumocystis carinii

Empiric Treatment of CAP

- Typical CAP

- Problem

- PCN resistance or Pneumococcus
 - 2-8% high R
 - 10-25% intermed. R
 - Macrolide resistance
 - 20-30% R

- Ceftriaxone or Cefotaxime

- Alternatives
 - Vancomycin
 - Clindamycin
 - Quinolones
 - levofloxacin, gemiflox or moxiflox

- Atypical CAP

- Problem

- diagnosis

- Erythromycin

- Clarithromycin
- Azithromycin

- Alternatives

- quinolones

Urinary Tract Infection

- Cystitis and Uncomplicated Pyelonephritis
 - E.coli (80-90%), S.saprophyticus, Proteus, Klebsiella, Enterococcus, Pseudomonas
- Complicated UTIs
 - E.coli (25-35%), Enterococcus (22%), Pseudomonas (20%), S. epidermidis (15%) Mixed (10%), Proteus, Klebsiella
- Catheter-Associated UTI
 - E.coli (24%), Yeast (28%), Mixed(11%), Pseudomonas, Enterococcus, Proteus, Klebsiella

Urinary Tract Infection

- **Diagnosis:**

- Clean catch, in & out catheterization
- pyuria, leukocyte esterase, hematuria
- >100,000 bacterial colonies

- **Treatment**

- Empiric

- Cystitis: TMP/SMX, quinolone 5-7 days
- Pyelonephritis: 14 days
- Catheter: remove or change to new catheter, if urosepsis: Piperacillin plus gentamicin and follow up on culture results

Meningitis

- Most common:
 - Streptococcus pneumoniae, Neisseria meningitidis and Haemophilus influenzae
- very young, very old or immunocompromised
 - Listeria monocytogenes
- seizure
 - focal brain lesion, syphilis or Herpes simplex

Meningitis

- **Diagnosis:**

- Fever, Headache & stiff neck
- Altered mental status, seizure or focal neurological deficits
- CSF pleocytosis

- **Treatment:**

- Ceftriaxone 2 grams iv q12 hr
 - add vancomycin (if suspect PCN Resistance)
 - add ampicillin (if suspect Listeria)
 - add acyclovir (if suspect Herpes)
 - add Metronidazole (if suspect brain abscess)

Gastrointestinal

- Gastroenteritis

- Shigella
- Salmonella
- enterotoxigenic E. coli
- Campylobacter

- HYDRATION

- TMP/SMX
- quinolones

- C. difficile Colitis

- Metronidazole (PO/IV)
- Vancomycin (PO)

- Hepatobiliary

- enteric gram neg
- enterococcus
- anaerobes

- Ceftriaxone
- Ampicillin/sulbactam
- Cefoxitin

- Catastrophic GI

- Polymicrobial
- Cefoxitin
- Amp/sulbactam
- Amp + gent + metronidazole

Endocarditis

- 85% gram pos
 - Streptococcus
 - S.viridans
 - Staphylococcus
 - Staph aureus
 - Enterococcus
- IVDA
 - Staph aureus
 - Pseudomonas
 - Candida
- Treatment
 - Nafcillin + gentamicin
- Viridans strep
 - PCN + gent
 - 2 - 4 weeks
- Staph aureus
 - Nafcillin + gent
 - 4 - 6 weeks
- Enterococcus
 - Ampicillin + gent
 - 6 weeks

Nosocomial Infections

- Nosocomial Pneumonia

- Pseudomonas, Acinetobacter, Enterobacter, Staphylococcus
- Piperacillin + gentamicin

- Nosocomial UTI (catheter)

- Gram negatives, Candida and non-candidal yeasts, Staphylococcus spp
- Piperacillin or quinolone +/- gentamicin

- Nosocomial Fever

- Line-related
- Staph epi, Staph aureus (MRSE & MRSA), Candida and non-candidal yeasts, gram negatives
- Change catheter, Vancomycin (if septic)

STDs

- Urethritis / Cervicitis
 - Nongonococcal urethritis (NGU)
 - Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma genitalium (?HSV, ?Trichomonas vaginalis)
 - Doxycycline 100mg bid x 7 days or Azithromycin 1gram single dose
 - Erythromycin 500mg qid x 7 days
 - Ofloxacin 300mg bid x 7 days
 - Refractory: Metronidazole 2 gram single dose

STDs

- Urethritis / Cervicitis
 - Gonococcal Urethritis
 - Mucopurulent
 - N.gonorrhoeae
 - Cefixime 400mg or Ciprofloxacin 500mg or Ofloxacin 400mg orally in a single dose or Ceftriaxone 125mg IM in a single dose
 - **PLUS** Doxycycline 100mg bid x 7days or Azithromycin 1 gram, unless using Ofloxacin (bid x 7day) regimen.
 - GC pharyngitis
 - same as above but Cefixime is **not** effective
 - Disseminated GC
 - Ceftriaxone or Cefotaxime IV for 7 - 14 days

STDs

- Vaginal Discharge

- Bacterial Vaginosis (not a STD)

- white, noninflammatory discharge, clue cells, pH >4.5, fishy odor (+/- 10% KOH)
 - Prevotella sp., Mobiluncus sp, Gardenerella vaginalis, Mycoplasma hominis replacing Lactobacillus sp (H2O2)
 - Metronidazole 500mg bid x 7 days
 - Clindamycin cream 2% or Metronidazole gel 0.75% intravaginally qhs x 7 days

STDs

- Vaginal Discharge

- Trichomoniasis

- malodorous, yellow-green discharge with irritation
 - Trichomonas vaginalis protozoan

- Metronidazole 2 grams orally single dose or 500 mg bid x 7 days

- Vulvovaginal Candidiasis

- white discharge with pruritis +/- burning
 - Candida albicans and other spp.

- Topical azole antifungals x 3-14 days or Fluconazole 150mg orally in single dose

STDs

- Pelvic Inflammatory Disease (PID)

- Inflammatory disorder of the upper female genital tract (endometritis, salpingitis, tubo-ovarian abscess, pelvic peritonitis).
- *N. gonorrhoeae*, *C. trachomatis*, anaerobes, *G.vaginalis*, *H. influenzae*, enteric gram neg. rods, *Streptococcus agalactiae*, *M. hominis*, *U.urealyticum*
- Lower abdominal, adnexal, cervical motion tenderness +/- temp/discharge/ESR/CRP or
- Histopath/ultrasound/laparoscopic

STDs

- Pelvic Inflammatory Disease (PID)
 - Parenteral Regimen
 - cannot r/o surgical abdomen, pregnant, N/V, immunodeficiency or tubo-ovarian abscess
 - Cefotetan or Cefoxitin 2grams iv Plus Doxycycline
 - Clindamycin iv Plus gentamicin
 - 14 day treatment
 - Oral Regimen
 - Ofloxacin 400mg bid x14 days Plus Metronidazole 500mg bid x 14 days

STDs

- Syphilis

- Primary & Secondary Syphilis

- Benzathine penicillin G 2.4 mill U im x 1 week
 - PCN allergy: Doxycycline 100 mg bid x 2 weeks

- Latent Syphilis → Tertiary Syphilis

- Benzathine penicillin G 7.2 mill U im weekly x 3weeks

- Neurosyphilis

- Aqueous penicillin G 18-24 mill U iv x 10-14 days

STDs

- Ulcers

- Chancroid

- Multiple painful ulcers, no syphilis, adenopathy
 - *H. ducreyi*

- Azithromycin 1 gram x 1 or Ceftriaxone 250mg im or Ciprofloxacin 500mg bid x 3 days or erythromycin 500mg qid x 7 days

- Herpes Simplex

- Painful ulcer(s), positive culture for HSV
 - Acyclovir 400mg tid or Famciclovir 250mg tid or Valacyclovir 1 gram bid x 7-10 days

STDs

- Ulcers

- Granuloma Inguinale (Donovanosis)

- Painless, progressive, ulcerative lesions without lymphadenopathy (tropical/developing areas), negative culture but donovan bodies on biopsy

- Trimethoprim-sulfamethoxazole DS bid x 3 weeks or Doxycycline 100mg bid x \geq 3 weeks

- Lymphogranuloma Venereum

- ulcer, tender lymphadenopathy, proctocolitis/fistulas/strictures

- Chlamydia trachomatis

- Doxycycline 100mg bid x 21 days or Erythromycin 500mg qid x 21days

TIPS FOR USING ANTIBIOTICS

JUDICIOUS ANTIBIOTIC USE IN COMMON INFECTIONS

- OTITIS MEDIA
 - One-third of cases are viral
 - Antibiotics can be deferred for 48 h in mild cases
 - Amoxicillin, TMP/Sulfa are most appropriate
 - If no clinical improvement within 48-72 h, change antibiotics

JUDICIOUS ANTIBIOTIC USE IN COMMON INFECTIONS

- ACUTE BRONCHITIS
 - Most cases are self-limiting, and/or viral
 - Consider antibiotics for patients with COPD, symptoms suggestive of pneumonia, or symptoms lasting longer than 10 days

JUDICIOUS ANTIBIOTIC USE IN COMMON INFECTIONS

- PHARYNGITIS

- Most cases are self-limiting--only 12% are caused by group A Strep
- Penicillin is still drug of choice
- Determine that Strep is the causative agent

JUDICIOUS ANTIBIOTIC USE IN COMMON INFECTIONS

- COLDS AND ACUTE SINUSITIS
 - Most cases are viral
 - Green or yellow discharge are NOT indicative of bacterial infection
 - Defer treatment unless temp is $>39^{\circ}\text{C}$, facial pain/swelling, or cough with purulent rhinorrhea for >7 -10 days

PREVENTION OF RESISTANCE?

- Prevention
 - Education
 - Appropriate use of antibiotics
 - Diagnosis
 - Surveillance (ICU)
 - Interrupting Transmission
 - Mechanical device
 - Person-person
 - Barrier precautions
 - Isolation

PREVENTION OF RESISTANCE?

- Prevention
 - Modify Host Risks
 - Enteral-tube feeding
 - » prevent aspiration
 - Gastric colonization
 - » Gastric pH
 - » unresolved issues
 - Vaccination
 - » pneumococcal
 - Avoid prophylactic systemic antibiotics

PREVENTION OF RESISTANCE ?

- Targeted therapy
- Combination therapy
- Reverse underlying pathology
- Remove catheters/foreign bodies

GUIDELINES TO PREVENT THE SPREAD OF ANTIBIOTIC RESISTANCE

- Wash hands
- Do not accede to patient demands for unnecessary antibiotics
- Make an accurate diagnosis
- Defer antibiotics for self-limited infections
- Avoid prescribing antibiotics over the phone

GUIDELINES TO PREVENT THE SPREAD OF ANTIBIOTIC RESISTANCE

- Do not use broad spectrum agents as “freebies”
- Isolate hospitalized patients infected with or colonized by resistant organisms
- Revise treatment regimens
- Use local epidemiologic data
- Educate patients about taking full course of antibiotics
- Use shorter courses when possible

Abbreviated Antibiotic Courses

- Use of antibiotics for more than 7 days in children increased risk of colonization or infections with Penicillin-resistant Strep pneumo 3-fold.
- Antibiotic prophylaxis >48 h for CV surgery doubles the risk of colonization or infection with antibiotic-resistant gram negative bacilli or enterococci
- Higher doses, shorter courses?
- One step ahead.....