

CHAPTER 37

Antibiotics

NDEG 26 A – Pharmacology I
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Antibiotics: Definition

- Medications used to treat bacterial infections
- Ideally, before beginning antibiotic therapy, the suspected areas of infection should be cultured to identify the causative organism and potential antibiotic susceptibilities

Antibiotics: Classes

- Sulfonamides
- Aminoglycosides
- Penicillins
- Quinolones
- Cephalosporins
- Tetracyclines
- Macrolides

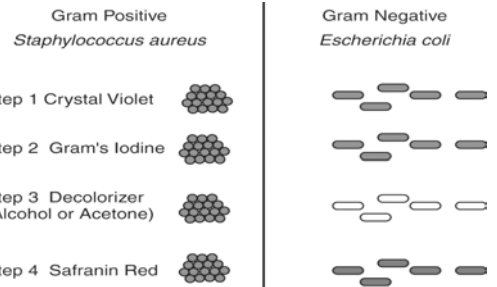


Figure 37-03 Gram-stain morphology of bacteria. The crystal violet of Gram stain is precipitated by Gram iodine and is trapped in the thick peptidoglycan layer in gram-positive bacteria. The decolorizer disperses the gram-negative outer membrane and washes the crystal violet from the thin layer of peptidoglycan. Gram-negative bacteria are visualized by the red counterstain. (From Murray PR et al: *Medical microbiology*, St. Louis, 2002, Mosby.)

Gram-negative bacterial infections are harder to treat because drug molecules have a harder time penetrating the more complex gram-negative cell wall.

Signs and symptoms of infection

- Fever
- Chills
- Sweat
- Redness
- Pain and swelling
- Fatigue
- Weight loss
- ↑ WBC (normal = 4300-10,800 or 5-10K)
- Pus

Empiric therapy: Coverage by a combination of antibiotics such as, clindamycin plus gentamicin, effective against gram-positive, gram-negative and anaerobes, or
A single broad-spectrum antibiotic, such as, imipenem/cilastatin

Receive culture report with sensitivities

If gram-positive only
Continue gram-positive coverage, discontinue gram-negative and anaerobic coverage

If mixed
Continue therapy as initiated

If gram-negative only
Continue gram-negative coverage, discontinue gram-positive and anaerobic coverage

If anaerobic only
Continue anaerobic coverage, discontinue gram-positive and gram-negative coverage

Figure 28.1 Therapeutic strategy in treating patients with an infection of unknown origin.

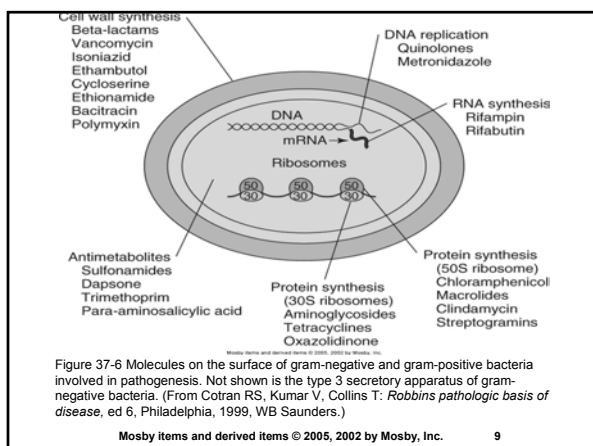
Antibiotic Therapy

- Empiric therapy: treatment of an infection before specific culture information has been reported or obtained
- Prophylactic therapy: treatment with antibiotics to prevent an infection, as in intraabdominal surgery

Antibiotic Therapy (cont'd)

Four common mechanisms of action

- Interference with cell wall synthesis
- Interference with protein synthesis
- Interference with DNA replication
- Acting as a metabolite to disrupt critical metabolic reactions inside the bacterial cell



Actions of Antibiotics

- Bactericidal: kill bacteria
- Bacteriostatic: inhibit growth of susceptible bacteria, rather than killing them immediately; will eventually lead to bacterial death

Antibiotics: Sulfonamides

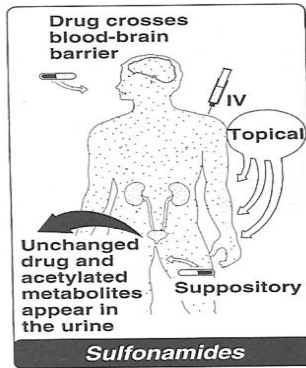
One of the first groups of antibiotics

- sulfadiazine
- sulfamethoxazole
- sulfisoxazole

Sulfonamides: Mechanism of Action

- Bacteriostatic action
- Prevent synthesis of folic acid required for synthesis of purines and nucleic acid – FOLATE ANTAGONIST ANTIMETABOLITE
- Do not affect human cells or certain bacteria—they can use preformed folic acid

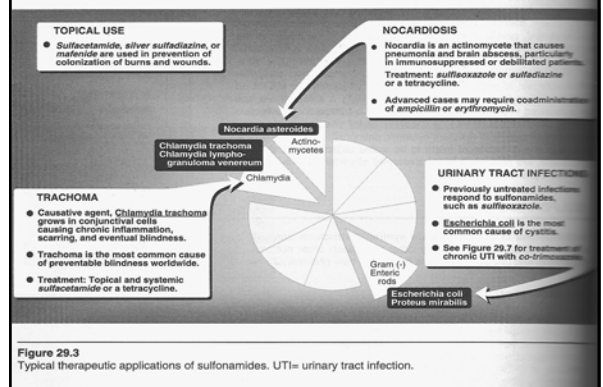
Sulfonamides: Distribution and Route



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Sulfonamides: Indications



Sulfonamides: Combination Products

- trimethoprim/sulfamethoxazole (Bactrim, Septra)
 - Used to treat UTIs, PCP, otitis media, other conditions
- erythromycin/sulfisoxazole (Pediazole)
 - Used to treat otitis media
- sulfisoxazole (Gantrisin)
 - Used to treat otitis media, UTIs, other conditions

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Sulfonamides: Side Effects

Body System	Effect
Blood	Hemolytic and aplastic anemia, thrombocytopenia
Integumentary	Photosensitivity, exfoliative dermatitis, Stevens-Johnson syndrome, epidermal necrolysis

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Sulfonamides: Side Effects



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Sulfonamides: Side Effects (cont'd)

Body System	Effect
GI	Nausea, vomiting, diarrhea, pancreatitis
Other	Convulsions, crystalluria, toxic nephrosis, headache, peripheral neuritis, urticaria

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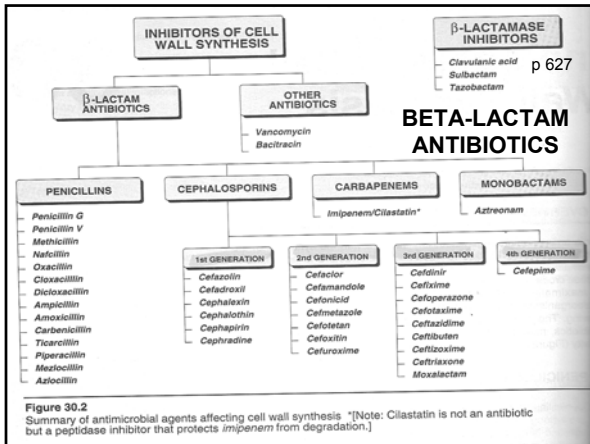


TABLE 37-2

PENICILLINS CLASSIFICATION

Subclass	Generic Drug Names	Description
Aminopenicillins	amoxicillin, ampicillin, bacampicillin	Have an amino group attached to their penicillin nucleus structure that enhances their activity against gram-negative bacteria compared with natural penicillins.
Extended-spectrum agents	piperacillin, ticarcillin, carbenicillin	Have wider spectra of activity than that of all other penicillins.
Natural penicillins	penicillin G, penicillin V	Though many modifications of the original natural (mold-produced) structure have been made, these are the only 2 in current clinical use. Penicillin G is the injectable form for IV or IM use; penicillin V is a PO dosage form (tablet and liquid).
Penicillinase-resistant agents	cloxacillin, dicloxacillin, nafcillin, oxacillin	Stable against hydrolysis by most staphylococcal penicillinases (enzyme that normally break down the natural penicillins).

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Table 37-02 Penicillins classification

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Penicillins

- Bacteria produce enzymes capable of destroying penicillins
- These enzymes are known as beta-lactamases
- As a result, the medication is not effective

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Penicillins (cont'd)

- Chemicals have been developed to inhibit these enzymes:
 - Clavulanic acid
 - Tazobactam
 - Sulbactam
- These chemicals bind with beta-lactamase and prevent the enzyme from breaking down the penicillin

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Penicillins (cont'd)

- Penicillin-beta-lactamase inhibitor combination drugs
 - ampicillin + sulbactam = Unasyn
 - amoxicillin + clavulanic acid = Augmentin
 - ticarcillin + clavulanic acid = Timentin
 - piperacillin + tazobactam = Zosyn

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Penicillins: Mechanism of Action

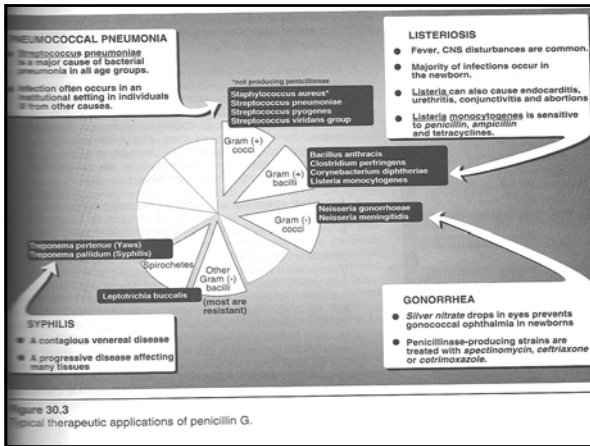
- Penicillins enter the bacteria via the cell wall
- Inside the cell they bind to penicillin-binding protein
- Once bound, normal cell wall synthesis is disrupted
- Result: bacteria cells die from cell lysis
- Penicillins do not kill other cells in the body

Does not penetrate into the CNS unless meninges are inflamed

Mostly unchanged drug appears in the urine

Penicillin

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Penicillins: Adverse Effects

- Allergic reactions occur in 0.7% to 8% of cases
 - Urticaria, pruritus, angioedema
- 10% of allergic reactions are life threatening
 - 10% of these are fatal

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Penicillins: Side Effects

- Common side effects
 - Nausea, vomiting, diarrhea, abdominal pain
- Other side effects are less common

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Cephalosporins

- Semisynthetic derivatives from a fungus
- Structurally and pharmacologically related to penicillins
- Bactericidal action
- Broad spectrum
- Divided into groups according to their antimicrobial activity

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Cephalosporins

- 1st generation
- 2nd generation
- 3rd generation
- 4th generation

Therapeutic advantages of selected cephalosporins

First Generation

- Cefazolin
- Cefadroxil
- Cephalexin
- Cephadrine
- Cephadrine

This first-generation parenteral cephalosporin has a longer duration of action and a similar spectrum of action compared to other first-generation drugs. Good penetration into bone.

Prototype of first-generation oral cephalosporins. Oral administration twice daily is effective against pharyngitis.

Mosby

Cephalosporins: First Generation (cont'd)

- Used for surgical prophylaxis, URIs, otitis media
 - cefazolin (Ancef and Kefzol): IV or PO
 - cephalexin (Keflex): PO

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Cephalosporins

Second Generation

Associated with serum sickness.

→ **Cefactor**
Cefamandole
Cefonicid
Cefmetazole
Cefotetan

→ **Cefoxitin**
Cefuroxime
Cefuroxime axetil

Shows good activity against anaerobes, particularly *Bacteroides fragilis*. Useful in patients with intraabdominal sepsis, and against gynecologic sepsis including pelvic inflammatory disease.

This prototype second-generation parenteral cephalosporin has a longer half-life than similar agents. It crosses the blood-brain barrier and can be used for community-acquired bronchitis or pneumonia in the elderly and for patients who are immunocompromised.

Oral administration twice daily. Well absorbed. Active against β -lactamase-producing organisms.

- Good gram-positive coverage
- Better gram-negative coverage than first generation

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Cephalosporins: Second Generation (cont'd)

- cefoxitin (Mefoxin): IV and IM
 - Used prophylactically for abdominal or colorectal surgeries
 - Also kills anaerobes
- cefuroxime (Kefurox and Ceftin): PO
 - Surgical prophylaxis
 - Does not kill anaerobes

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Cephalosporins:

Third Generation

These cephalosporins contain the methylthio tetraazole side chain and can cause hypoprothrombinemia and bleeding problems as well as a disulfiram effect, that is, an intolerance to ingested ethanol.

→ **Cefdinir**
Cefprozime

→ **Cefoperazone**
Cefotaxime
Ceftazidime
Ceftibuten

→ **Ceftriaxone**

producing organisms.

Oral dosing once daily.

Good penetration into CSF.

Active against *Pseudomonas aeruginosa*.

Longest half-life of any cephalosporin (8-8 hrs) permits once a day dosing. High and CSF. Effective against genital, anal and pharyngeal penicillin-resistant *Neisseria gonorrhoeae*. Drug excreted in bile and may be used in patients with renal insufficiency. Good penetration into bone.

Fourth Generation

Cefepime

- Most potent group against gram-negative
- Less active against gram-positive

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Cephalosporins: Third Generation (cont'd)

cefixime (Suprax)

- Only oral third-generation agent
- Best of available oral cephalosporins against gram-negative
- Tablet and suspension

ceftriaxone (Rocephin)

- IV and IM, long half-life, once-a-day dosing
- Easily passes meninges and diffused into CSF to treat CNS infections

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Cephalosporins: Third Generation (cont'd)

- ceftazidime (Ceptaz, Fortaz, Tazidime, Tazicef)
 - IV and IM forms
 - Excellent gram-negative coverage
 - Used for difficult-to-treat organisms such as *Pseudomonas* spp.
 - Eliminated renally instead of biliary route
 - Excellent spectrum of coverage

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Cephalosporins: Fourth Generation

- cefepime (Maxipime)
 - Newest cephalosporin agents
 - Broader spectrum of antibacterial activity than third generation, especially against gram-positive bacteria
- cefdinir
- cefditoren pivoxil

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Cephalosporins: Side Effects

Similar to penicillins

Carbapenems

- Very broad-spectrum antibacterial action
- Reserved for complicated body cavity and connective tissue infections
- May cause drug-induced seizure activity
imipenem-cilastatin (Primaxin)
- Used for treatment of bone, joint, skin, and soft tissue infections; many other uses

Monobactams

aztreonam (Azactam)

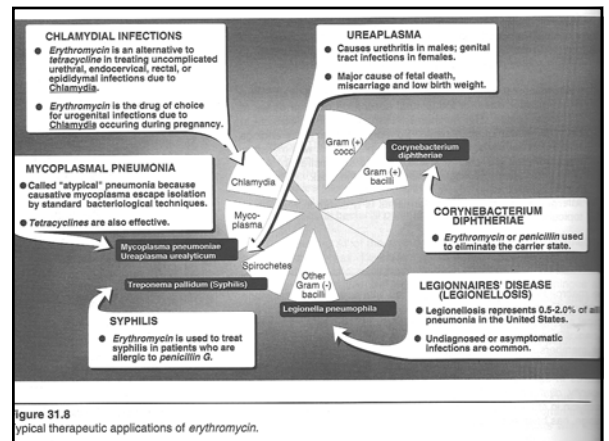
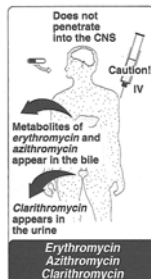
- Synthetic
- Primarily active against aerobic gram-negative bacteria (*E. coli*, *Klebsiella*, *Pseudomonas*)
- Bactericidal
- Used for severe systemic infections and UTIs

Macrolides

- erythromycin (E-mycin, E.E.S, others)
- azithromycin (Zithromax)
- clarithromycin (Biaxin)

Macrolides: Mechanism of Action

- Prevent protein synthesis within bacterial cells
- Bacteria will eventually die



Macrolides: Indications

- Strep infections
 - *Streptococcus pyogenes*
(group A beta-hemolytic streptococci)
- Mild to moderate URI
 - *Haemophilus influenzae*
- Spirochetal infections
 - Syphilis and Lyme disease
- Gonorrhea, *Chlamydia*, *Mycoplasma*

Macrolides: Side Effects

GI effects, primarily with erythromycin

- nausea, vomiting, diarrhea, hepatotoxicity, flatulence, jaundice, anorexia
- Newer agents, azithromycin and clarithromycin: fewer side effects, longer duration of action, better efficacy, better tissue penetration

Tetracyclines

- Broad-spectrum
- Obtained from cultures of *Streptomyces*
- Bacteriostatic—inhibit bacterial growth
- protein synthesis inhibitor
- Stop many essential functions of the bacteria

Tetracyclines (cont'd)

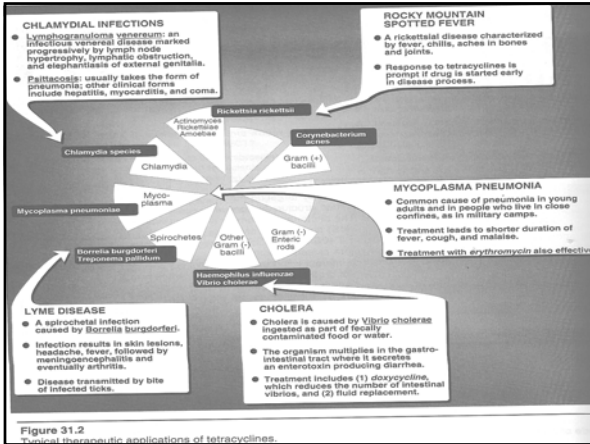
- Bind to Ca^{2+} and Mg^{2+} and Al^{3+} ions to form insoluble complexes
- Thus, dairy products, antacids, and iron salts reduce absorption of tetracyclines

Tetracyclines

- demeclocycline (Declomycin)
- oxytetracycline
- tetracycline
- doxycycline (Doryx, Vibramycin)
- minocycline

Tetracyclines: Indications

- Wide spectrum
 - Gram-negative, gram-positive, protozoa, *Mycoplasma*, *Rickettsia*, *Chlamydia*, syphilis, Lyme disease
- demeclocycline is also used to treat SIADH, and pleural and pericardial effusions



Tetracyclines: Side Effects

Strong affinity for calcium

- Discoloration of permanent teeth and tooth enamel in fetuses and children
- May retard fetal skeletal development if taken during pregnancy

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Tetracyclines: Side Effects (cont'd)

Alteration in intestinal flora may result in:

- Superinfection (overgrowth of nonsusceptible organisms such as *Candida*)
- Diarrhea
- Pseudomembranous colitis

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Tetracyclines: Side Effects (cont'd)

May also cause:

- Vaginal moniliasis
- Gastric upset
- Enterocolitis
- Maculopapular rash

Figure 31.3
Effect of antacids and milk on the absorption of tetracyclines.

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Aminoglycosides

- gentamicin (Garamycin)
- kanamycin
- neomycin
- streptomycin
- tobramycin
- amikacin (Amikin)
- netilmicin

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TABLE 37-10 AVAILABLE AMINOGLYCOSIDE ANTIBIOTICS		
Origin	Aminoglycoside Product	Description
Natural	gentamicin	All chemically derived from <i>Streptomyces</i> spp. by a fermentation process
	kanamycin	
	neomycin	
	paromomycin	
	streptomycin	
	tobramycin	
Semisynthetic	amikacin	Chemical derivative of kanamycin
	netilmicin	Structurally related to gentamicin

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Table 37-10 Available aminoglycoside antibiotics

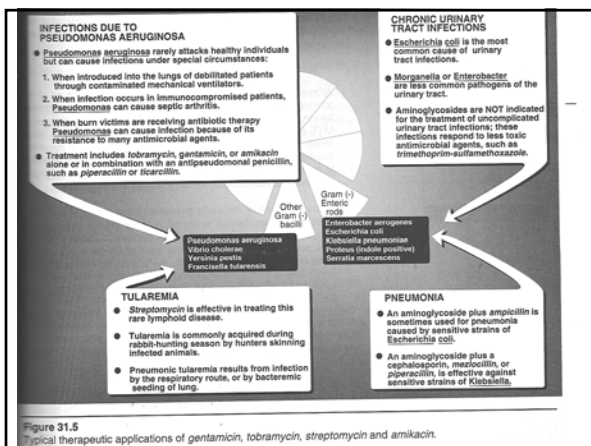
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Aminoglycosides

- Natural and semisynthetic
- Produced from *Streptomyces*
- Poor oral absorption; no PO forms
- Very potent antibiotics with serious toxicities
- Bactericidal; prevents protein synthesis
- Kill mostly gram-negative; some gram-positive also

Aminoglycosides: Indications

- Used to kill gram-negative bacteria such as *Pseudomonas* spp., *E. coli*, *Proteus* spp., *Klebsiella* spp., *Serratia* spp.
- Often used in combination with other antibiotics for synergistic effect



Aminoglycosides: Indications (cont'd)

- All aminoglycosides are poorly absorbed through the GI tract, and given parenterally
- Exception: neomycin
 - Given orally to decontaminate the GI tract before surgical procedures
 - Also used as an enema for this purpose

Aminoglycosides: Agents

- Three most common (systemic): gentamicin, tobramycin, amikacin
- Cause serious toxicities
 - Nephrotoxicity (renal failure)
 - Ototoxicity (auditory impairment and vestibular [eighth cranial nerve])
- Must monitor drug levels to prevent toxicities

Aminoglycosides: Side Effects

- Ototoxicity and nephrotoxicity are the most significant
 - Vertigo
 - Headache
 - Paresthesia
 - Neuromuscular blockade
 - Dizziness
 - Skin rash
 - Fever
 - Superinfections

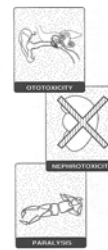


Figure 31.7
Some adverse effects of aminoglycosides.

Quinolones

- ciprofloxacin (Cipro)
- lomefloxacin (Maxaquin)
- norfloxacin (Noroxin)
- ofloxacin (Floxin)
- levofloxacin (Levaquin)
- gatifloxacin (Tequin)

Quinolones

- Excellent oral absorption
- Absorption reduced by antacids
- First oral antibiotics effective against gram-negative bacteria

Quinolones: Mechanism of Action

- Bactericidal
- Effective against gram-negative organisms and some gram-positive organisms
- Alter DNA of bacteria, causing death
- Do not affect human DNA

Quinolones: Indications

- Lower respiratory tract infections
- Bone and joint infections
- Infectious diarrhea
- Urinary tract infections
- Skin infections
- Sexually transmitted diseases
- Anthrax

Quinolones: Side Effects

<u>Body System</u>	<u>Effects</u>
CNS	Headache, dizziness, fatigue, depression, restlessness
GI	Nausea, vomiting, diarrhea, constipation, thrush, increased liver function studies

Quinolones: Side Effects (cont'd)

<u>Body System</u>	<u>Effects</u>
Integumentary	Rash, pruritus, urticaria, flushing, photosensitivity (with lomefloxacin)
Other	Fever, chills, blurred vision, tinnitus

Other Antibiotics

- clindamycin (Cleocin)
- dapsone
- linezolid (Zyvox)
- metronidazole (Flagyl)
- nitrofurantoin (Macrochantin)
- quinupristin and dalbapristin (Synercid)

Other Antibiotics (cont'd)

- vancomycin
 - Natural, bactericidal antibiotic
 - Destroys cell wall
 - Treatment of choice for MRSA, and other gram-positive infections
 - Must monitor blood levels to ensure therapeutic levels and prevent toxicity
 - May cause ototoxicity and nephrotoxicity

Other Antibiotics

- vancomycin (cont'd)
 - Should be infused over 60 minutes
 - Monitor IV site closely
 - Redman's syndrome may occur
 - Decreased BP, flushing of neck and face
 - Antihistamine may be ordered to reduce these effects
 - Ensure adequate hydration (2 L fluids/24 hr) if not contraindicated to prevent nephrotoxicity

Antibiotics: Nursing Implications

- Before beginning therapy, assess drug allergies; hepatic, liver, and cardiac function; and other lab studies
- Be sure to obtain thorough patient health history, including immune status
- Assess for conditions that may be contraindications to antibiotic use or that may indicate cautious use
- Assess for potential drug interactions

Nursing Implications

It is **ESSENTIAL** to obtain cultures from appropriate sites **BEFORE** beginning antibiotic therapy

Nursing Implications

- Patients should be instructed to take antibiotics exactly as prescribed and for the length of time prescribed; they should not stop taking the medication early when they feel better
- Assess for signs and symptoms of superinfection: fever, perineal itching, cough, lethargy, or any unusual discharge

Nursing Implications

For safety reasons, check the name of the medication carefully because there are many agents that sound alike or have similar spellings

Nursing Implications

- Each class of antibiotics has specific side effects and drug interactions that must be carefully assessed and monitored
- The most common side effects of antibiotics are nausea, vomiting, and diarrhea
- All oral antibiotics are absorbed better if taken with at least 6 to 8 ounces of water

Nursing Implications

Sulfonamides

- Should be taken with at least 2000 mL of fluid per day, unless contraindicated
- Due to photosensitivity, avoid sunlight and tanning beds
- These agents reduce the effectiveness of oral contraceptives
- Oral forms should be taken with food or milk to reduce GI upset

Nursing Implications

Penicillins

- Any patient taking a penicillin should be carefully monitored for an allergic reaction for at least 30 minutes after its administration
- The effectiveness of oral penicillins is decreased when taken with caffeine, citrus fruit, cola beverages, fruit juices, or tomato juice

Nursing Implications

Cephalosporins

- Orally administered forms should be given with food to decrease GI upset, even though this will delay absorption
- Some of these agents may cause a disulfiram (Antabuse)-like reaction when taken with alcohol

Nursing Implications

Macrolides

- These agents are highly protein-bound and will cause severe interactions with other protein-bound drugs
- The absorption of oral erythromycin is enhanced when taken on an empty stomach, but because of the high incidence of GI upset, many agents are taken after a meal or snack

Nursing Implications

Tetracyclines

- Milk products, iron preparations, antacids, and other dairy products should be avoided because of the chelation and drug-binding that occurs
- All medications should be taken with 6 to 8 ounces of fluid, preferably water
- Due to photosensitivity, avoid sunlight and tanning beds

Nursing Implications

Aminoglycosides

- Monitor peak and trough blood levels of these agents to prevent nephrotoxicity and ototoxicity
- Symptoms of ototoxicity include dizziness, tinnitus, and hearing loss
- Symptoms of nephrotoxicity include urinary casts, proteinuria, and increased BUN and serum creatinine levels

Nursing Implications

Quinolones

- Should be taken with at least 3 L of fluid per day, unless otherwise specified
- Intake of alkaline foods and drugs, such as antacids, dairy products, peanuts, and sodium bicarbonate should be limited

Nursing Implications

Monitor for therapeutic effects

- Improvement of signs and symptoms of infection
- Return to normal vital signs
- Negative culture and sensitivity tests
- Disappearance of fever, lethargy, drainage, and redness

Monitor for adverse reactions