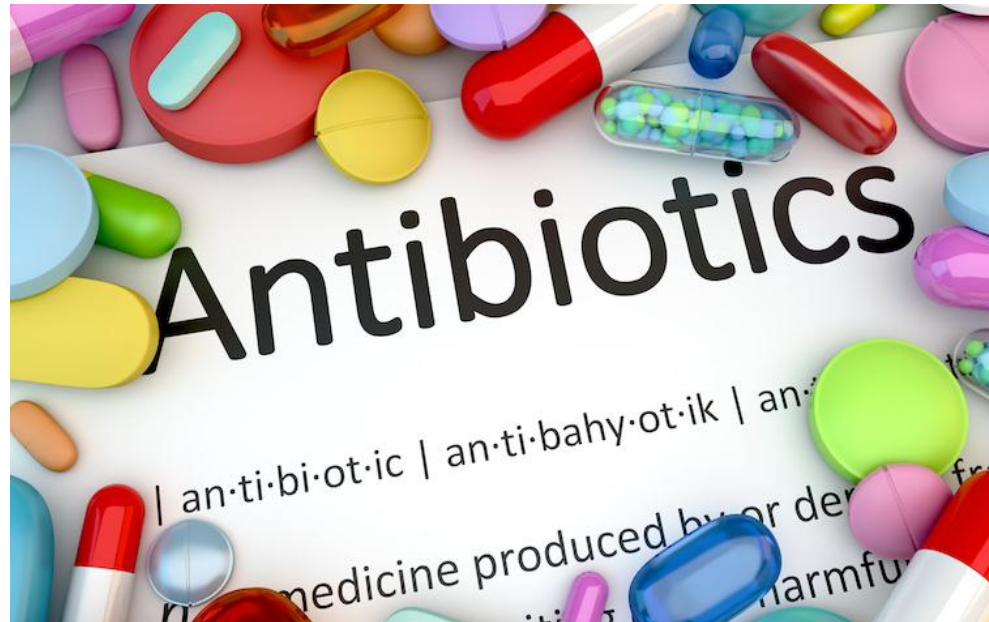




Salih Atakan NEMLI, MD

Antibiotics

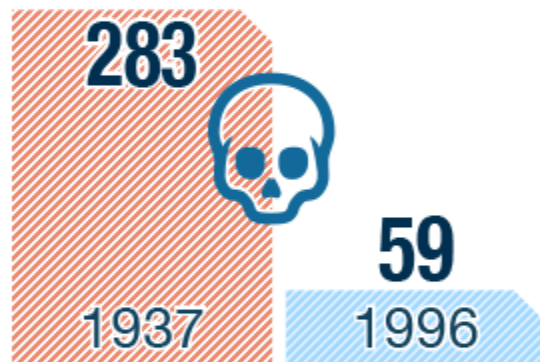


Alexander Fleming

Discovered
1928

REDUCED
INFECTIOUS DISEASE
MORTALITY RATE

Per 100,000 Population



ENABLED MODERN
MEDICINE



PREMATURE
INFANT CARE



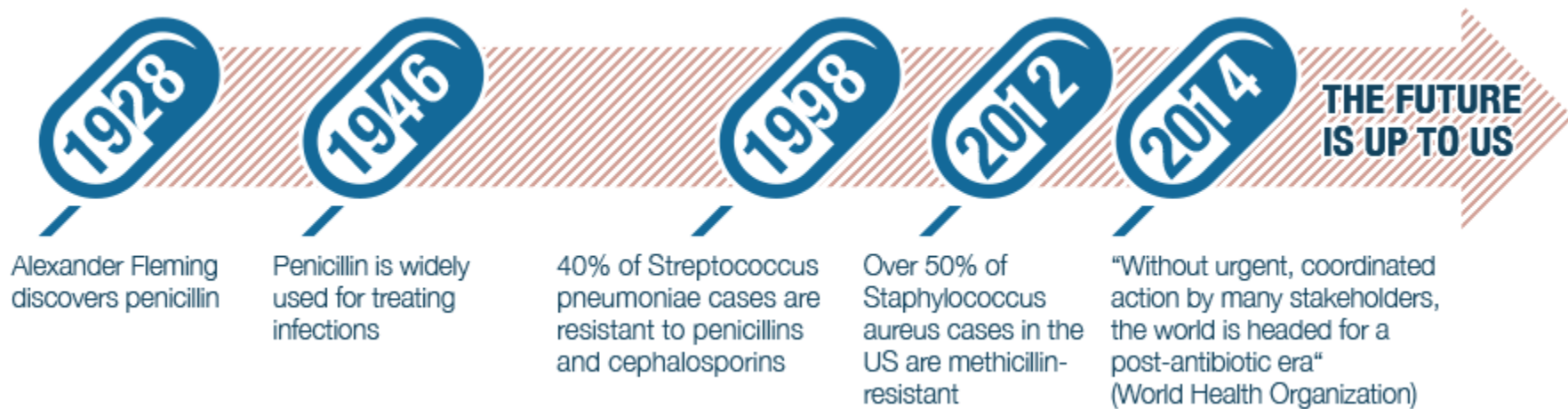
COMPLICATED
SURGERIES



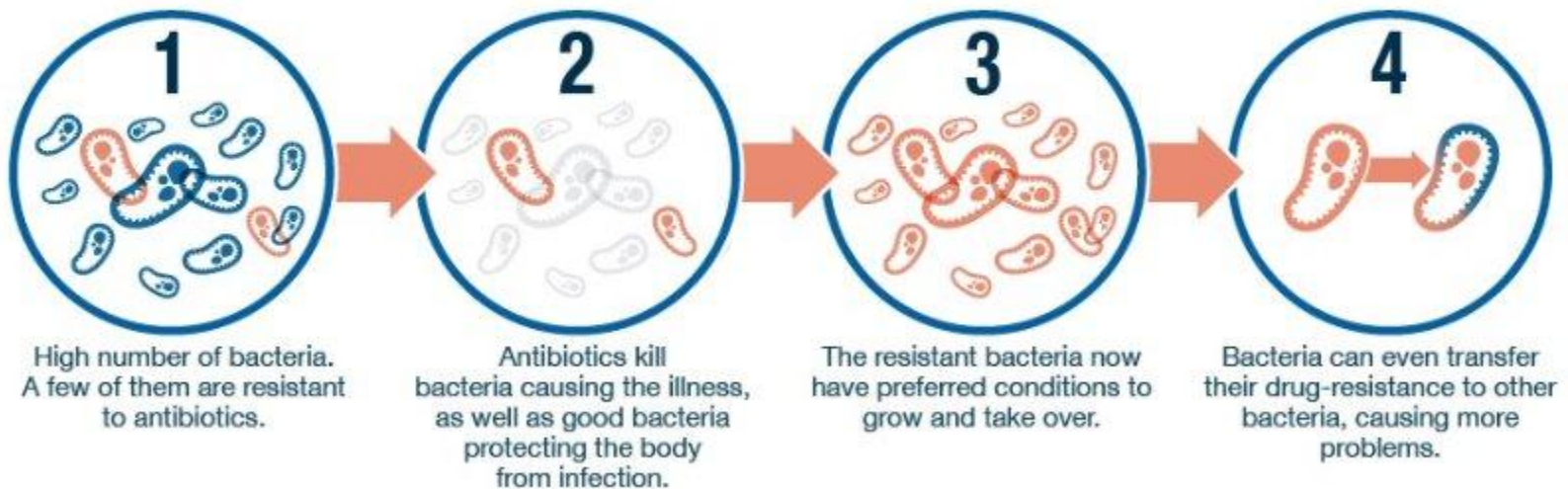
CRITICAL
CARE



ORGAN
TRANSPLANTS



How does antibiotic resistance occur?



Classes of antibiotics

Gram +

Penicillins

Amoxicillin

Gram + (Strep, Syphilis)

Disrupt synth of peptidoglycan

Macrolides

azithromycin, clarithromycin, erythromycin

Gram +, URTIs (Strep, Staph)

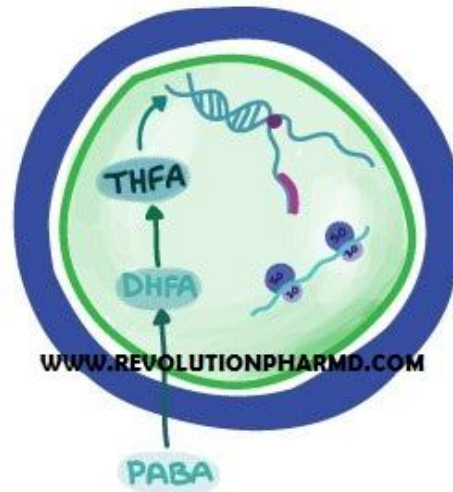
Inhibit protein synth at 50S subunit

Lincosamides

clindamycin

Strep, Staph

Inhibit protein synth at 50S subunit



Gram + and -

Tetracyclines

tetracycline, doxycycline

Broad spectrum (Gram+/-, atypicals)

Inhibit protein synth at 30S subunit

Cephalosporins

Disrupt synth of peptidoglycan

1st: Gram + (Keflex)

2nd: Gram - > Gram + (Cefzil)

3rd: Gram - >> Gram +, Pseudomonas (Ceftriaxone)

4th: Pseudomonas (Cefepime)

5th: MRSA (Zeftera)

Fluoroquinolones

Ciprofloxacin (Gram -)

Levofloxacin/Moxifloxacin (Gram +)

Broad spectrum

Inhibit DNA gyrase or topoisomerase

Sulfonamides

Trimethoprim-sulfamethoxazole (TMP-SMX)

UTIs (E coli, S. saprophyticus)

Work together to inhibit enzyme tetrahydrofolic acid (THFA) needed for thymidine synth (and DNA)

Carbapenams

meropenem

Broad spectrum

Disrupt synth of peptidoglycan

Nitrofurans

macrobid

UTIs (E coli, S. saprophyticus)

Damage DNA

Metronidazole

Flagyl

Anaerobes, protozoa

Disrupts DNA

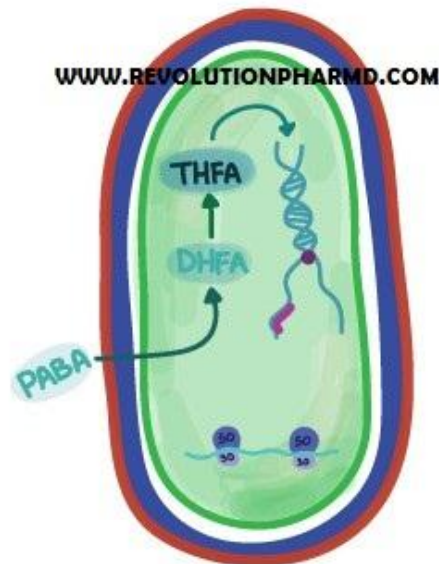
Gram -

Aminoglycosides

streptomycin, tobramycin, gentamicin

Gram -, Pseudomonas

Inhibit protein synth at 30S subunit



Cell Wall Synthesis

Beta Lactams

Penicillins
Cephalosporins
Carbapenems
Monobactams

Vancomycin
Bacitracin

Cell Membrane

Polymyxins

Folate synthesis

Sulfonamides
Trimethoprim



Nucleic Acid Synthesis

DNA Gyrase

Quinolones

RNA Polymerase

Rifampin

50S

30S

50S subunit

Macrolides
Clindamycin
Linezolid
Chloramphenicol
Streptogramins

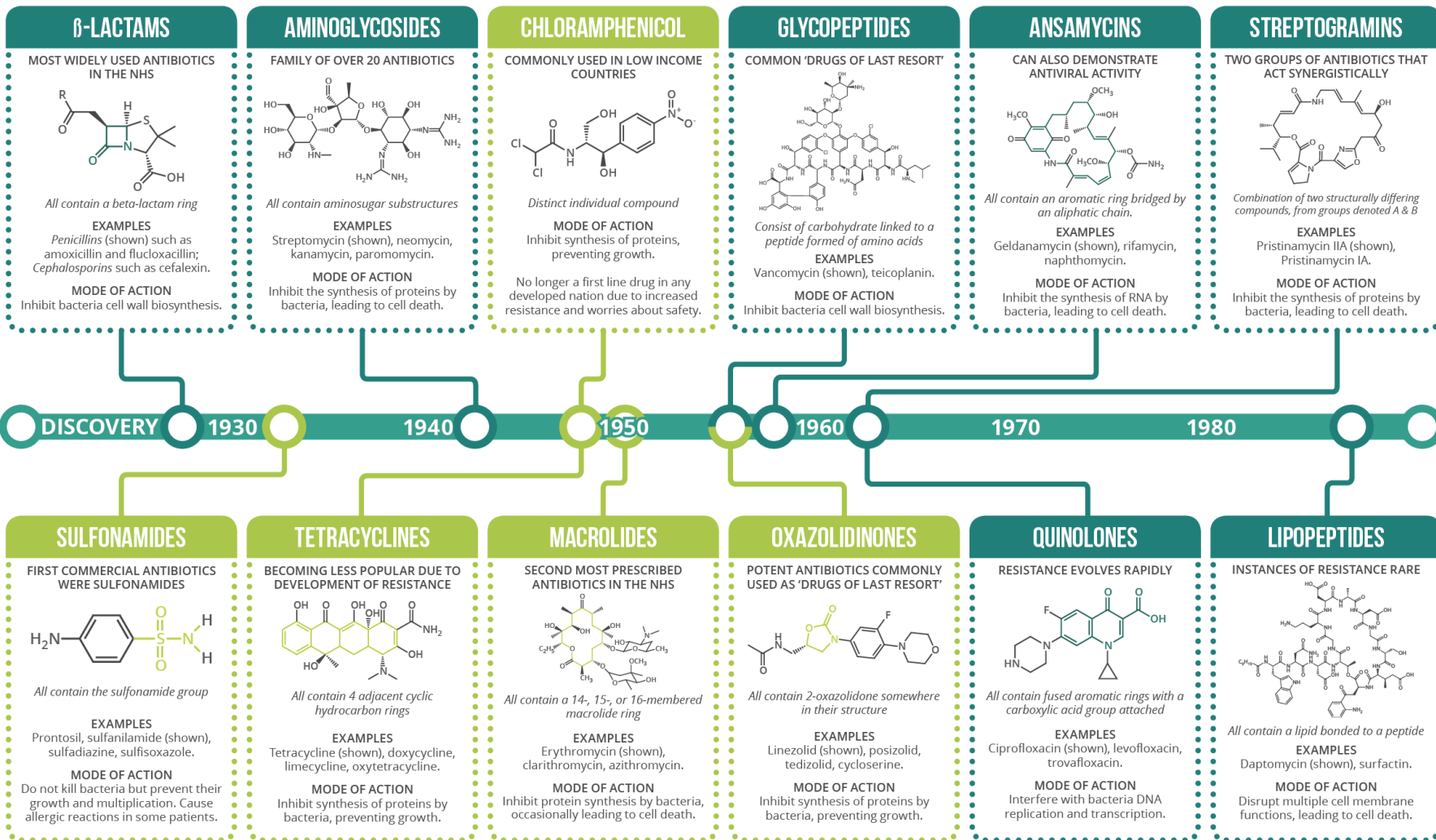
30S subunit

Tetracyclines
Aminoglycosides

Protein Synthesis

DIFFERENT CLASSES OF ANTIBIOTICS - AN OVERVIEW

Key: ● COMMONLY ACT AS BACTERIOSTATIC AGENTS, RESTRICTING GROWTH & REPRODUCTION ● COMMONLY ACT AS BACTERICIDAL AGENTS, CAUSING BACTERIAL CELL DEATH



Anti-Infective Agents

Antibiotics:

Sulfonamides

Penicillins

Cephalosporins

Tetracyclines

Aminoglycosides

Quinolones

Macrolides

Antibiotics

- 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

- **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 intra-abdominal surgery

Antibiotics

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

Types of Bacteria

- Aerobic bacteria
needs oxygen to survive
- Anaerobic bacteria
survives in the absence of oxygen

How Antibiotics Work

- Block protein formation

How Antibiotics Work

- Block protein formation
 - Macrolides
 - Tetracyclines
 - Aminoglycosides

How Antibiotics Work

- Block protein formation
- Inhibit cell wall formation
- Interfere with DNA formation

How Antibiotics Work

- Block protein formation
- Inhibit cell wall formation
- Interfere with DNA formation
 - Nalidixic acid

How Antibiotics Work

- Block protein formation
- Inhibit cell wall formation
- Interfere with DNA formation
- Prevent folic acid synthesis

How Antibiotics Work

- Block protein formation
- Inhibit cell wall formation
- Interfere with DNA formation
- Prevent folic acid synthesis
 - Sulfonamides

Sulfonamides

One of the first groups of antibacterial agents

- sulfadiazine
- sulfamethizole
- sulfamethoxazole
- sulfisoxazole

Sulfonamides: Mechanism of Action

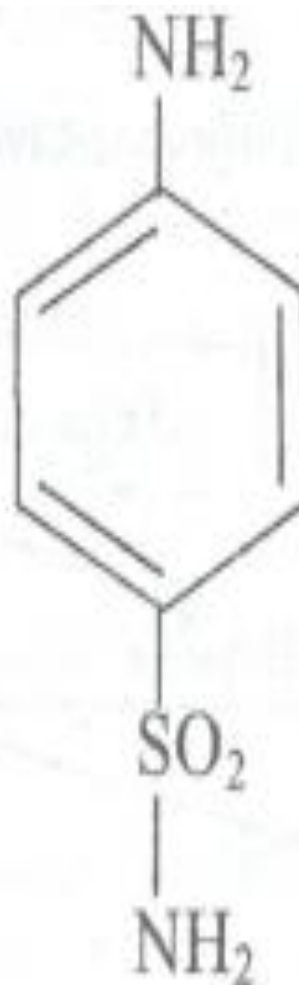
- Bacteriostatic action
- Prevent synthesis of folic acid required for synthesis of purines and nucleic acid
- Does not affect human cells or certain bacteria—they can use preformed folic acid

Structure of sulfonamides

para-Aminobenzoic acid



sulfonamide



Classification of sulfonamides (accordingly to duration of action)

- **Short action:** streptocid, sulfadimezine, aethazole, norsulfazole, urosulfan, sulfizoxazole, sulfacyl-sodium
- **Medium duration of action:** sulfamethoxazole (is a part of co-trimoxazole)
- **Longlasting action:** sulfadimethoxyn, sulfapirydazin, sulfamonomethoxyn
- **Super longlasting action:** sulfalen, sulfadoxyn (is a part of fansidar)

Sulfonamides: sulfamethoxazole

Therapeutic Uses

Trimethoprim - sulfamethoxazole

- Used to treat UTIs, *Pneumocystis carinii* pneumonia, ear infections, bronchitis, gonorrhea, etc.

Co-trimoxazole = Bactrim (trimethoprim + sulfamethoxazole)



Sulfonamides: Side Effects

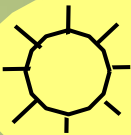
<u>Body System</u>	<u>Effect</u>
Blood	Hemolytic and aplastic anemia, thrombocytopenia
Integumentary	Photosensitivity, exfoliative dermatitis, Stevens-Johnson syndrome, epidermal necrolysis

Sulfonamides: Side Effects

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

Sulfonamides' Dispensing Issues

- Avoid the sun
- Maintain adequate fluid intake



**Avoid
SUN EXPOSURE**



**TAKE WITH
FLUIDS**

Classes of Antibiotics

- Sulfonamides
- Penicillins
- Cephalosporins
- Tetracyclines
- Macrolides
- Ketolides
- Quinolones
- Streptogramins
- Aminoglycosides
- Cyclic Lipopetides

Antibiotics: Penicillins

- Natural penicillins
- Penicillinase-resistant penicillins
- Aminopenicillins
- Extended-spectrum penicillins

Antibiotics: Penicillins

Natural penicillins

- penicillin G, penicillin V potassium

Penicillinase-resistant penicillins

- cloxacillin, dicloxacillin, methicillin, nafcillin, oxacillin

Antibiotics: Penicillins

Aminopenicillins

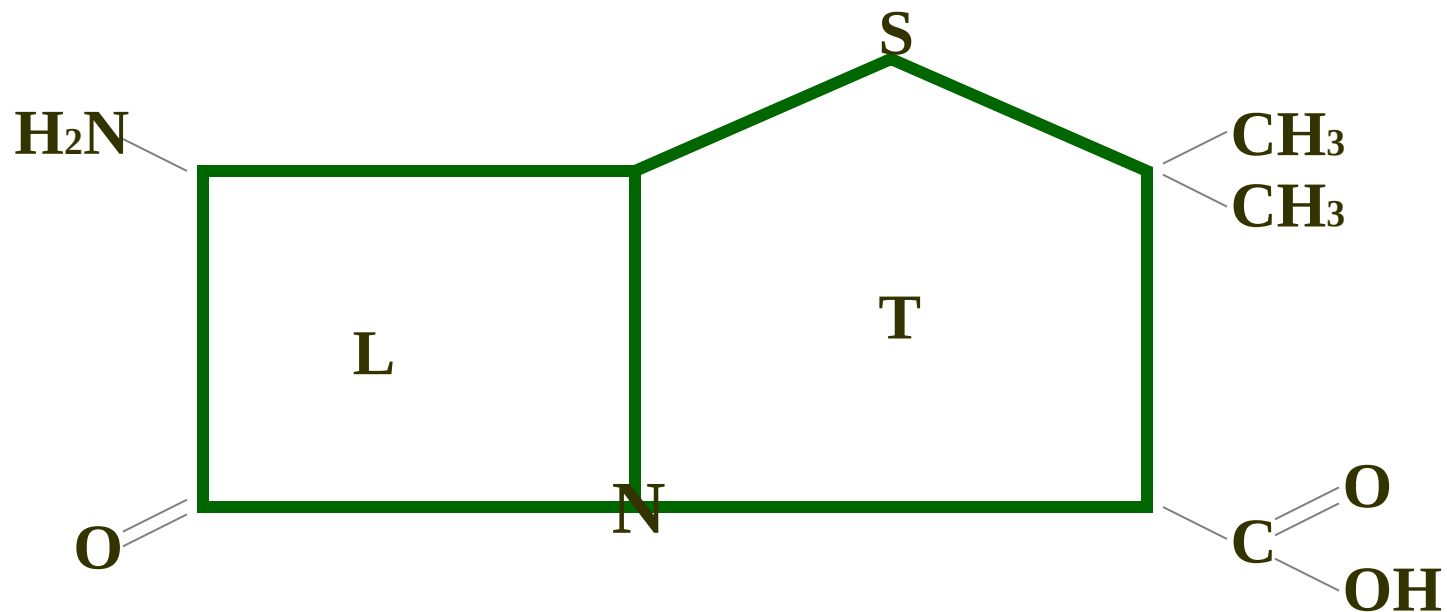
- amoxicillin, ampicillin, bacampicillin

Extended-spectrum penicillins

- piperacillin, ticarcillin, carbenicillin, mezlocillin

Antibiotics: Penicillins

- First introduced in the 1940s
- Bactericidal: inhibit cell wall synthesis
- Kill a wide variety of bacteria
- Also called “beta-lactams”



Nucleus of penicillin molecule
L – beta-lactame ring, T – thiazolidine ring

Antibiotics: Penicillins

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

Antibiotics: Penicillins

- 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

Antibiotics: Penicillins

- Penicillin-beta-lactamase inhibitor combination drugs:
 - ampicillin + sulbactam
 - amoxicillin + clavulanic acid
 - ticarcillin + clavulanic acid
 - piperacillin + tazobactam

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.

Penicillins: Therapeutic Uses

- Prevention and treatment of infections caused by susceptible bacteria, such as:
 - gram-positive bacteria
 - Streptococcus, Enterococcus, Staphylococcus species

Penicillins: Adverse Effects

- Allergic reactions occur in 0.7% – 8% of treatments
 - urticaria, pruritus, angioedema
- 10% of allergic reactions are life-threatening
- 10% of these are fatal

Penicillins: Side Effects

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

Penicillins' Dispensing Issues

- Take on an empty stomach
 - Food slows absorption
 - Acids in fruit juices or colas could deactivate the drug



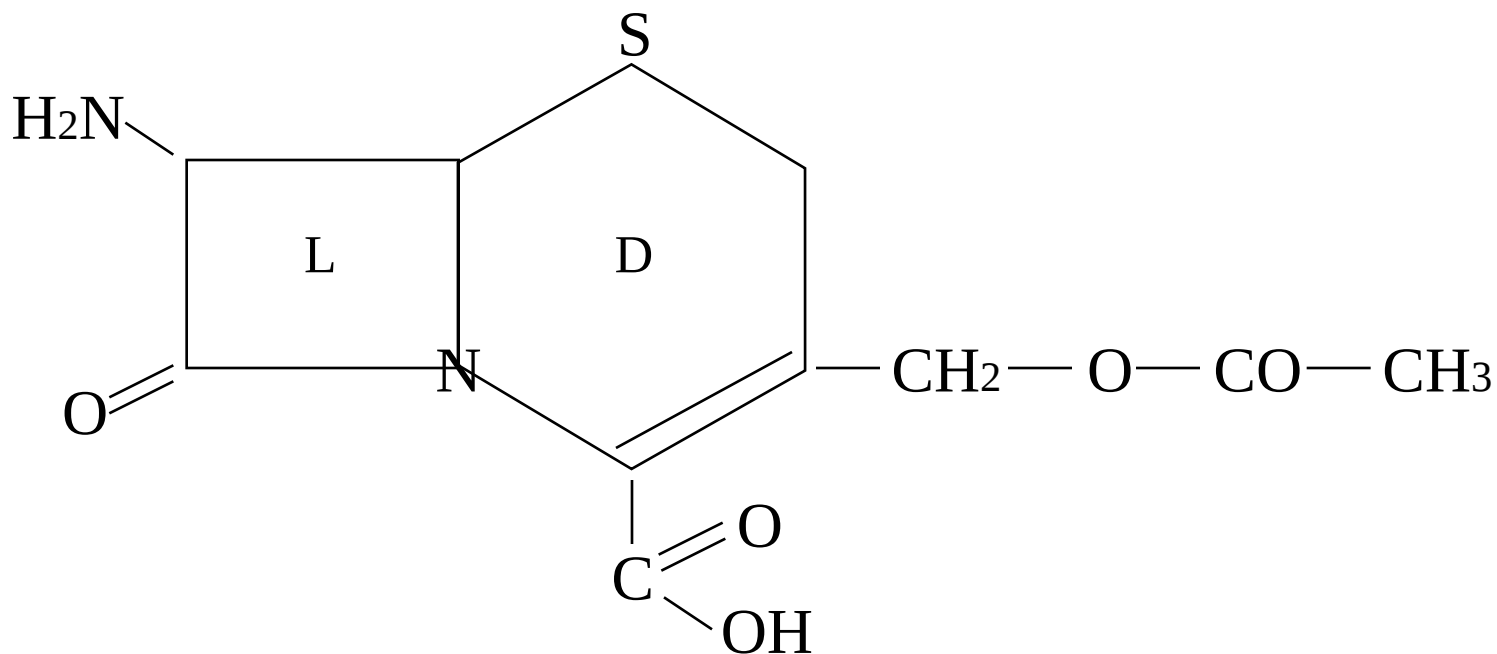
**Take on an
empty stomach**

Penicillin Resistance

- Penicillinase-resistant penicillins work against gram-positive aerobes
- Extended-spectrum penicillins are more resistant to gram-negative bacteria
- Penicillin combinations improve effect

Antibiotics: Cephalosporins

- First Generation
- Second Generation
- Third Generation
- Fourth Generation



Structure of cephalosporins

L – beta-lactame ring, D – dihydrothiazine ring

Antibiotics: Cephalosporins

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

Cephalosporins: First Generation

- cefadroxil
- cephalexin
- cephradine
- cefazolin
- cephalothin
- cephapirin
 - Good gram-positive coverage
 - Poor gram-negative coverage

Cephalosporins

- First-generation
 - Similar to penicillinase-resistant penicillins with greater gram-negative coverage
 - Used for
 - community-acquired infections
 - mild to moderate infections

Cephalosporins: First Generation

cefazolin

(Ancef and Kefzol)

IV and PO

cephalexin

(Keflex and Keftab)

PO

used for surgical prophylaxis, URIs, otitis media

Cephalosporins: Second Generation

- cefaclor
 - cefprozil
 - cefamandole
 - cefoxitin
 - cefuroxime
 - cefonicid
 - ceforanide
 - cefmetazole
 - cefotetan
- Good gram-positive coverage
 - Better gram-negative coverage than first generation

Cephalosporins

- Second-generation
 - Increased activity, especially against *Haemophilus influenzae*
 - Used for
 - Otitis media in children
 - Respiratory infections
 - UTIs

Cephalosporins: Second Generation

Cefoxitin
(Mefoxin)
Ceftin)

IV and IM

Used prophylactically for
prophylaxis
abdominal or colorectal
surgeries
Also kills anaerobes

cefuroxime
(Kefurox and

PO

Surgical

Does not kill
anaerobes

Cephalosporins: Third Generation

- cefixime
 - cefpodoxime proxetil
 - cefoperazone
 - cefotaxime
 - ceftizoxime
 - ceftriaxone
 - ceftazidime
 - moxalactam
- Most potent group against gram-negative
 - Less active against gram-positive

Cephalosporins

- Third-generation
 - Active against a wide spectrum of gram-negative organisms
 - Long half-life, so once-a-day dosing for some
 - Used for
 - Ambulatory patients
 - Children (dosing before or after school)

Cephalosporins: Third Generation

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

Cephalosporins: Third Generation

ceftazidime (Ceptaz, Fortaz, Tazidime, Tazicef)

- IV and IM
- Excellent gram-negative coverage
- Used for difficult-to-treat organisms such as *Pseudomonas* spp
- Eliminated renally instead of biliary route
- Excellent spectrum of coverage

Cephalosporins: Fourth Generation

cefepime (Maxipime)

- Newest cephalosporin agents.
- Broader spectrum of antibacterial activity than third generation, especially against gram-positive bacteria.

Antimicrobial spectrum of cephalosporins

<i>Generation of cephalosporins</i>	<i>Active towards</i>		<i>Stability towards beta-lactamase</i>	
	Gram-positive bacteria	Gram-negative bacteria	Staphylo cocci	Gram-negative bacteria
I	+++	+/-	++	-
II	++	+	++	+/-
III	+	+++	+	+
IV	++	+++	++	++

Cephalosporins

Alert the Pharmacist if a patient allergic to penicillins is receiving a cephalosporin prescription.

Cephalosporins Side Effects

- Share side effects of penicillin
- Few may initiate unique toxic reactions
- Lower frequency of toxicity than many other antibiotics

Complications, caused by cephalosporins

- Irritation of mucous membrane of digestive tract, infiltrates after intramuscular introduction , phlebitis after intravenous introduction
- Disbacteriosis, superinfection
- Allergic reactions, including cross allergy with penicillins
- Granulocytopenia (in case of treatment during more than 2 weeks)
- Hemorrhages (inhibition of synthesis of factors of blood coagulation in liver) – cephalosporins III
- Nephrotoxicity (accumulation in epithelial cells of kidney canalicules)
- Encephalopathy (hyperreflexia, судоми, coma)

Cephalosporins

All of the cephalosporins look alike when written in the generic form. Watch for dosing and indications for use.

Antibiotics: Tetracyclines

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

Antibiotics: Tetracyclines

- Natural and semi-synthetic
- Obtained from cultures of *Streptomyces*
- Bacteriostatic—inhibit bacterial growth
- Inhibit protein synthesis
- Stop many essential functions of the bacteria

Antibiotics: Tetracyclines

- 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: Therapeutic Uses

- 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

Therapeutic Uses of Tetracyclines

- Acne
- Chronic bronchitis
- Lyme disease
- *Mycoplasma pneumoniae* infection
- *Rickettsia* infection
- Some venereal diseases, such as *Chlamydia* infection
- Traveler's diarrhea

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

Tetracyclines: Side Effects

Alteration in intestinal flora may result in:

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

Tetracyclines: Side Effects

May also cause:

- Vaginal moniliasis
- Gastric upset
- Enterocolitis
- Maculopapular rash

Tetracyclines' Dispensing Issues

- Avoid antacids to avoid chelation with minerals
- Photosensitization
- To be avoided by pregnant women and children
- Expired drugs are dangerous

**Do not take with
ANTACIDS**



**Avoid
SUN EXPOSURE**

Antibiotics: Aminoglycosides

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

Aminoglycosides

- Natural and semi-synthetic
- Produced from Streptomyces
- Poor oral absorption; no PO forms
- Very potent antibiotics with serious toxicities
- Bactericidal
- Kill mostly gram-negative; some gram-positive also

Aminoglycosides

- 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

- 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

- Headache
- Paresthesia
- Neuromuscular blockade
- Dizziness
- Vertigo
- Skin rash
- Fever
- Superinfections

Antibiotics: Quinolones

- ciprofloxacin (Cipro)
- enoxacin (Penetrex)
- lomefloxacin (Maxaquin)
- norfloxacin (Noroxin)
- ofloxacin (Floxin)

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: Therapeutic Uses

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

Quinolones: Side Effects

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

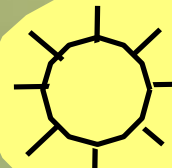
Quinolones: Side Effects

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

Quinolones' Dispensing Issues

- Not to be given with theophylline
- Antacids interfere with absorption
- Avoid exposure to sun

**Do not take with
ANTACIDS**



**Avoid
SUN EXPOSURE**

Antibiotics: Macrolides

- erythromycin
- azithromycin (Zithromax)
- clarithromycin (Biaxin)
- dirithromycin
- troleandomycin
 - bactericidal action

Erythromycin Formulations

Macrolides: Therapeutic Uses

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

Macrolides' Dispensing Issues

Although most antibiotics should be taken on an empty stomach, erythromycins usually cause severe GI distress, so should be taken with food



**TAKE WITH
FOOD**

Antibiotic Dispensing Issues

Warning!

- Mix exactly as directed by manufacturer
- Swab counting tray with alcohol between drugs to prevent cross-contamination

Antibiotic Side Effects

- Most antibiotics should be taken on an empty stomach to attain faster absorption
- Examples of exceptions
 - nitrofurantoin (Macrobid, Macrochantin)
 - cefuroxime (Ceftin, Zinacef)



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.

Antibiotics: Nursing Implications

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

Antibiotics: 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.

Antibiotics: Nursing Implications

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

Antibiotics: 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.

Antibiotics: Nursing Implications

Sulfonamides

- Should be taken with at least 2400 mL of fluid per day, unless contraindicated.
- Due to photosensitivity, avoid sunlight and tanning beds.
- These agents reduce the effectiveness of oral contraceptives.

Antibiotics: 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.

Antibiotics: 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 an Antabuse-like reaction when taken with alcohol.

Antibiotics: 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.

Antibiotics: 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.

Antibiotics: 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.