

Course: Drug discovery

Introduction to Antimicrobial drugs

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Antimicrobial Drugs

- Chemicals used to treat microbial infections
- Before antimicrobials, large number of people died from common illnesses
- Now many illnesses easily treated with antimicrobials
- However, many antimicrobial drugs are becoming less useful

Antimicrobial Drugs

- Different types of antimicrobial drugs:
 - Antibacterial drugs
 - Antifungal drugs
 - Antiparasitic drugs
 - Antiviral drugs

Features of Antimicrobial Drugs: Antimicrobial Action

- **Bacteriostatic:** Inhibit growth of microorganisms
- **Bactericidal:** Kill microorganism

Features of Antimicrobial Drugs: Spectrum of Activity

- Antimicrobial medications vary with respect to the range of microorganisms they kill or inhibit
- Some kill only limited range : **Narrow-spectrum antimicrobial**
- While others kill wide range of microorganisms: **Broad-spectrum antimicrobial**

	Mycobacteria	Gram-negative bacteria	Gram-positive bacteria	Chlamydiae	Rickettsiae
Penicillins					
Sulfonamides, Cephalosporins, Quinolones, Carbapenems					
Streptomycin					
Tetracyclines					
Isoniazid					
Polymyxin					
Vancomycin					

Features of Antimicrobial Drugs: Effects of Combining Drugs

- Combinations are sometimes used to fight infections
- **Synergistic**: action of one drug **enhances** the activity of another or *vice versa*.
- **Antagonistic**: activity of one drug **interferes** with the action of another.

Features of Antimicrobial Drugs: Adverse Effects

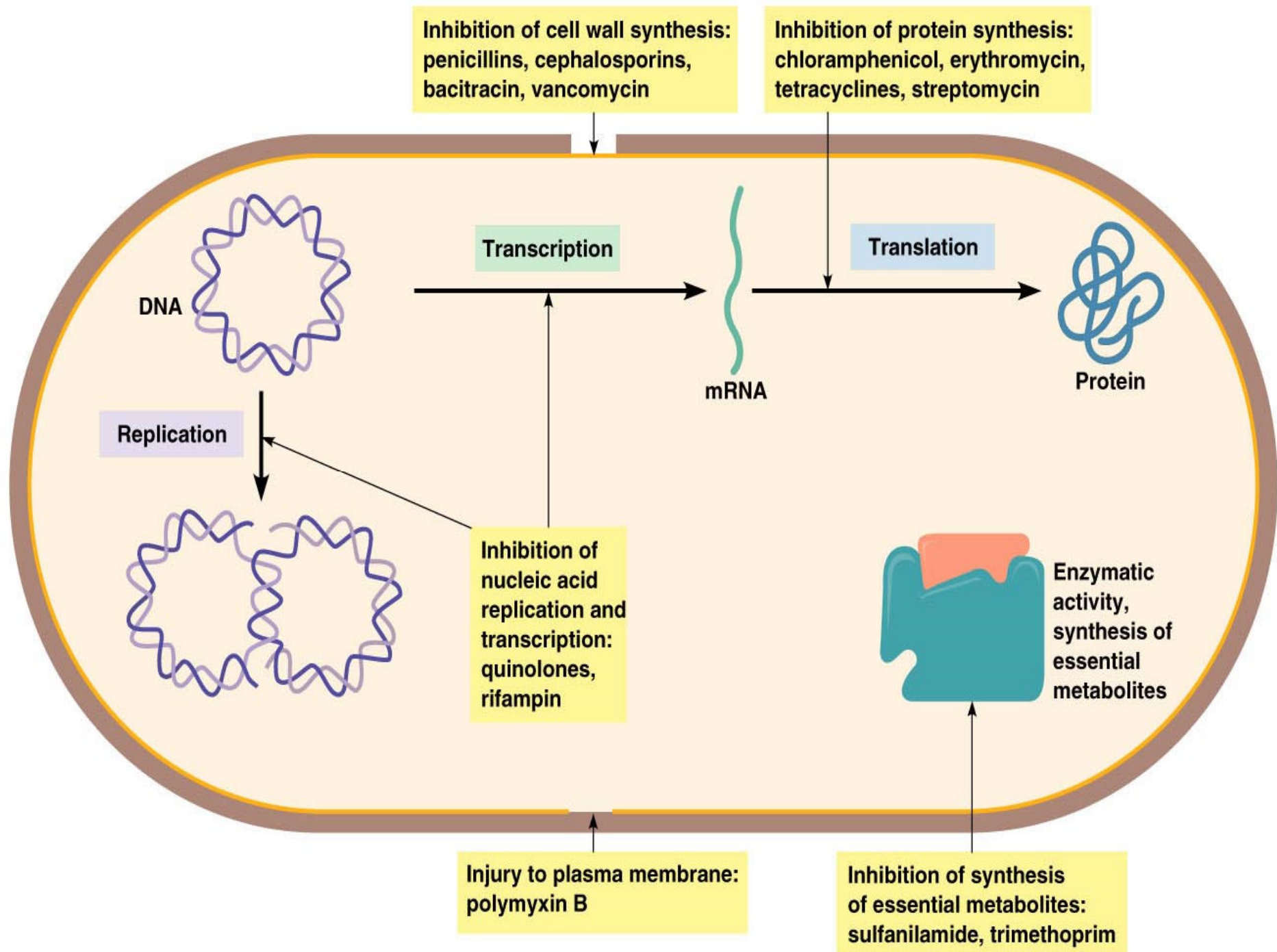
1. **Allergic Reactions:** some people develop hypersensitivities to antimicrobials
2. **Toxic Effects:** some antimicrobials toxic at high concentrations or cause adverse effects
3. **Suppression of normal flora:** when normal flora killed, other pathogens may be able to grow to high numbers

Features of Antimicrobial Drugs: Resistance to Antimicrobials

- Some microorganisms inherently resistant to effects of a particular drug
- Other previously sensitive microorganisms can develop resistance through spontaneous mutations or acquisition of new genes (usually plasmids).

Mechanisms of action of Antibacterial Drugs

1. Inhibit cell wall synthesis
2. Inhibit protein synthesis
3. Inhibit nucleic acid synthesis
4. Inhibit plasma membrane synthesis
5. Inhibit synthesis of essential metabolites



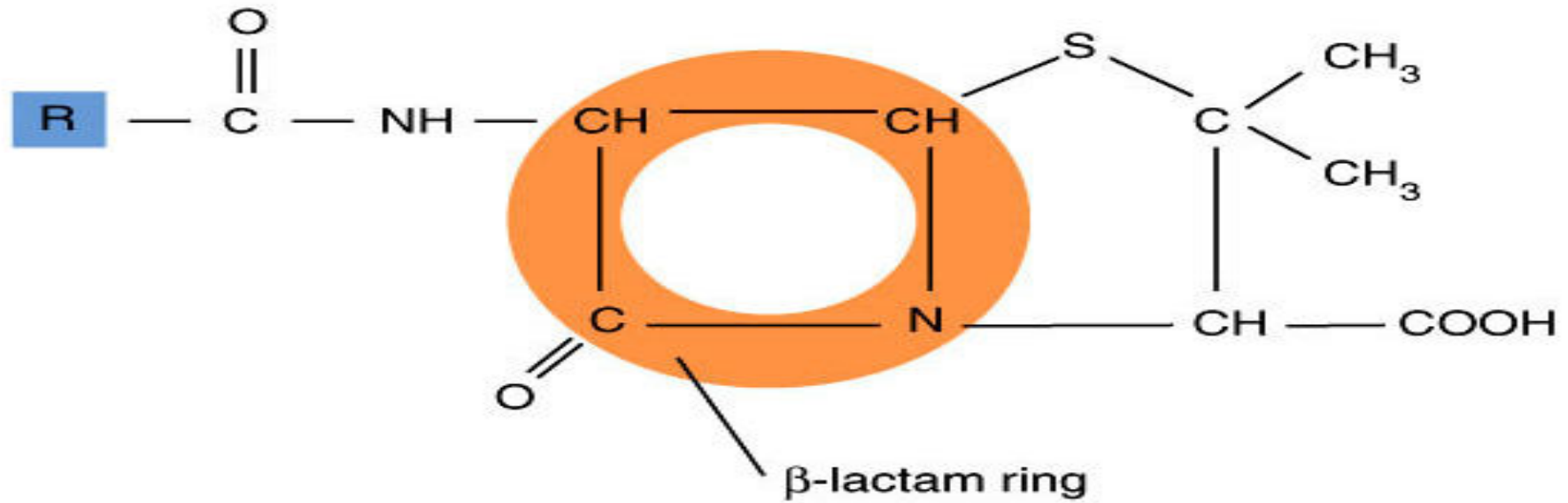
Inhibition of Cell Wall Synthesis: β -Lactam Drugs

- Irreversibly inhibit enzymes involved in the final steps of cell wall synthesis
- These enzymes mediate formation of peptide bridges between adjacent stands of peptidoglycan
- β -lactam ring similar in structure to normal substrate of enzyme
- Drug binds to enzyme, competitively inhibit enzymatic activity

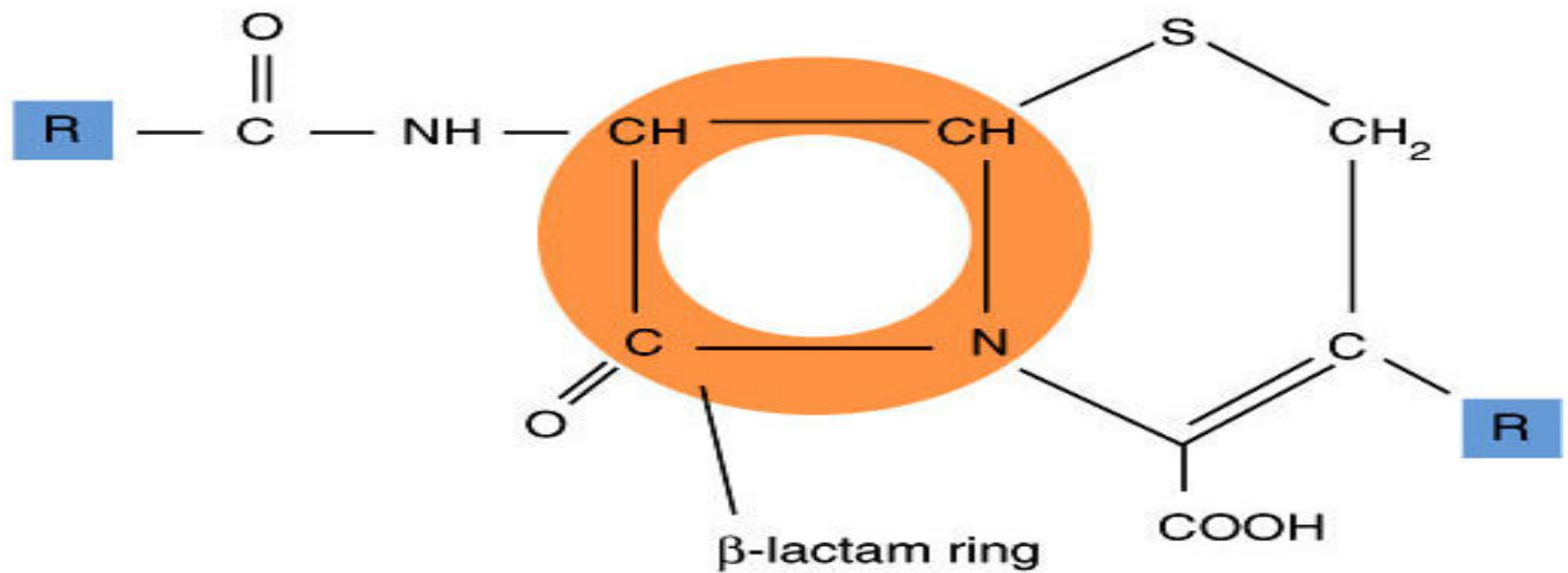
β -Lactam Drugs

- Some bacteria produce β -lactamase-enzyme that breaks the critical β -lactam ring
- β -lactam drugs include: penicillins and cephalosporins

(a) Penicillin



(b) Cephalosporin



Penicillins (Benzylpenicillin)

- Acid-labile.
- Gram+ bacteria.
- So, take phenoxymethylpenicillin.
- Large V_d , but penetration into brain: poor, except when the meninges are inflamed.
- Broad spectrum penicillins: **amoxicillin** and **ampicillin** are more hydrophilic and therefore, are active against gram-bacteria.

Cephalosporins

- Used for treatment of meningitis, pneumonia, and septicemia.
- Same mech and p'col as that of pens.
- May → allergic rxn and cross-reactivity to pen.
- Similar to pens in broad-spectrum antibacterial activity.

Cedadroxil (for UTI) in case of antibact resist.

Cefuroxime (prophylactic in surgery) – Resistant to inactivation by β -lactamases and used in severe infections (others ineffective).

Ceftazidime – wide range of activity against gram- including *Pseudomonas aeruginosa*), but is less active than cefurozime against gram+ bact (*S. aureus*).

Used in meningitis (CNS-accessible) caused by gram-bacteria.

Vancomycin

- Not well absorbed orally.
- Inhibits peptidoglycan formation.
- Active against most gram+ organisms.
- I.v. treatment for septicemia or endocarditis caused by MRSA.
- Used for pseudomembranous colitis (superinfection of the bowel by *Clostridium difficile* – produces a toxin that damages the colon mucosa)

A collage of various biological structures. At the top left is a green, multi-lobed virus-like particle. Next to it is a blue, elongated, spindle-shaped microorganism. To the right is a pink, spherical virus with many surface proteins. Below the green virus is a yellow, star-shaped microorganism with many long, thin filaments. In the center is a blue, spherical, textured cell. To its right is a green, elongated, segmented microorganism. Below the yellow star-shaped microorganism is a yellow, spherical, textured cell. To its right is a red, oval-shaped cell. At the bottom left is a dark blue, spherical, textured cell. In the center bottom is a green, spherical, textured cell. To its right is a red, oval-shaped cell. At the bottom right is a brown, elongated, textured microorganism. On the far right is a DNA double helix structure.