

# Inhibiting Microbial Growth *in vivo*

CLS 212: Medical Microbiology

# Definitions

**Chemotherapy**

**Chemotherapeutic Agent**

**Antimicrobial Agent**

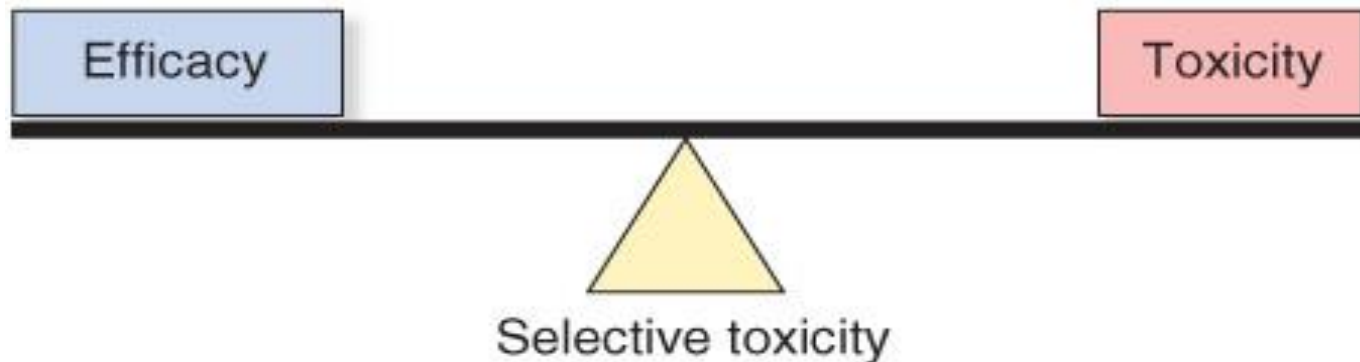
**Antibiotics**



# Definitions

- **Selective Toxicity:**

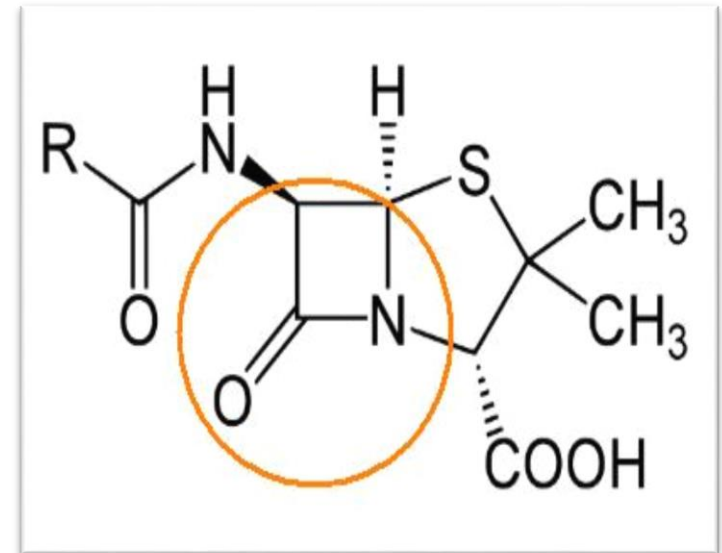
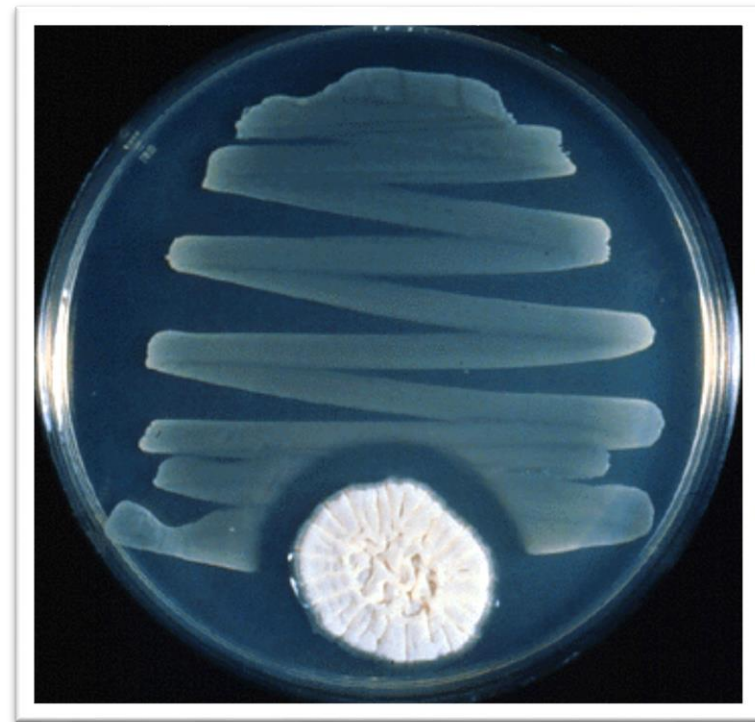
The drug cause greater harm to microorganisms than to the human host.



$$\text{Chemotherapeutic index} = \frac{\text{Toxic dose}}{\text{Therapeutic dose}}$$

# Penicillin

- It is the first antibiotic discovered by Fleming
- Bactericidal
- Natural antibiotic
- Narrow spectrum (G +ve).
- Inhibit cell wall synthesis by interfering with the synthesis and cross linking of peptidoglycan.
- Destroyed by gastric acid. and by  $\beta$ -lactimase.
- Cause allergic reaction lead to anaphylactic shock



# Antimicrobial Agents



## Antibacterial Agent

Drugs used to treat bacterial infections.

## Antifungal Agent

Drugs used to treat fungal infections.

## Antiprotozoal Agent

Drugs used to treat protozoal infections.

## Antiviral Agent

Drugs used to treat viral infections.

# Antibiotics



- Are primarily antibacterial agents and are used to treat bacterial diseases.

## Natural Antibiotics:

- Are produced by certain molds and bacteria usually living in the soil.
- **Penicillin and cephalosporin** are examples of antibiotics produced by molds.
- **Bacitracin, erythromycin and chloramphenicol** are examples of antibiotics produced by bacteria.

## Semisynthetic Antibiotics

e.g. semisynthetic penicillin such as ampicillin and carbenicillin

## Synthetic Antibiotic

chemically designed in the lab

# Ideal Qualities of Antimicrobial Agent

## Characteristics of a good Drug:

1. Kill or inhibit the growth of pathogens.
2. Cause no damage to the host.
3. Cause no allergic reaction in the host.
4. Stable to store in solid or liquid form.
5. Stay in target tissues for a long time to be effective.
6. Kill the pathogen before they become resistant to it.

# How Antimicrobial Agents Work

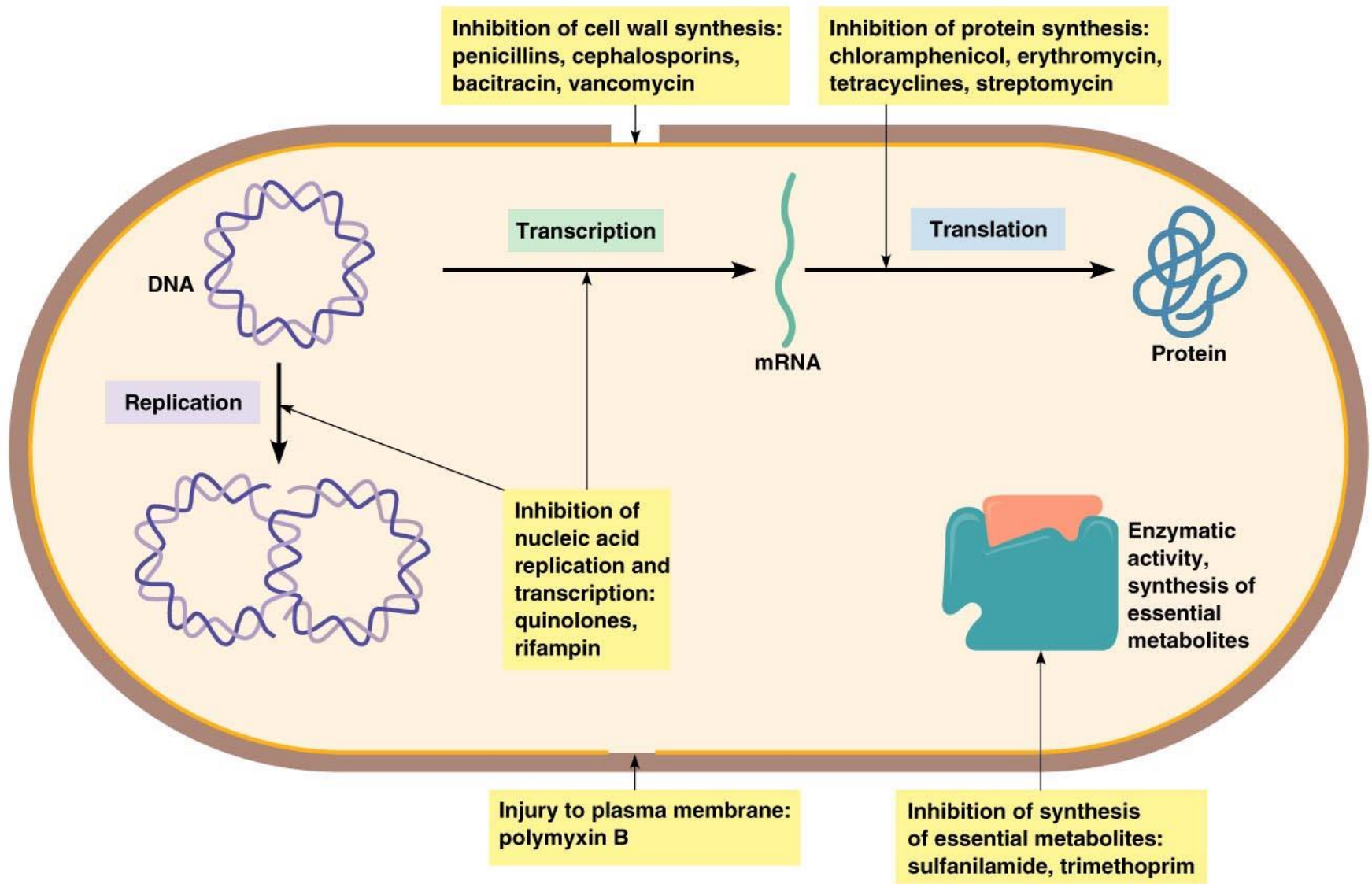
- The antimicrobial agent must target a metabolic process or structure present in the pathogen and not in the host.

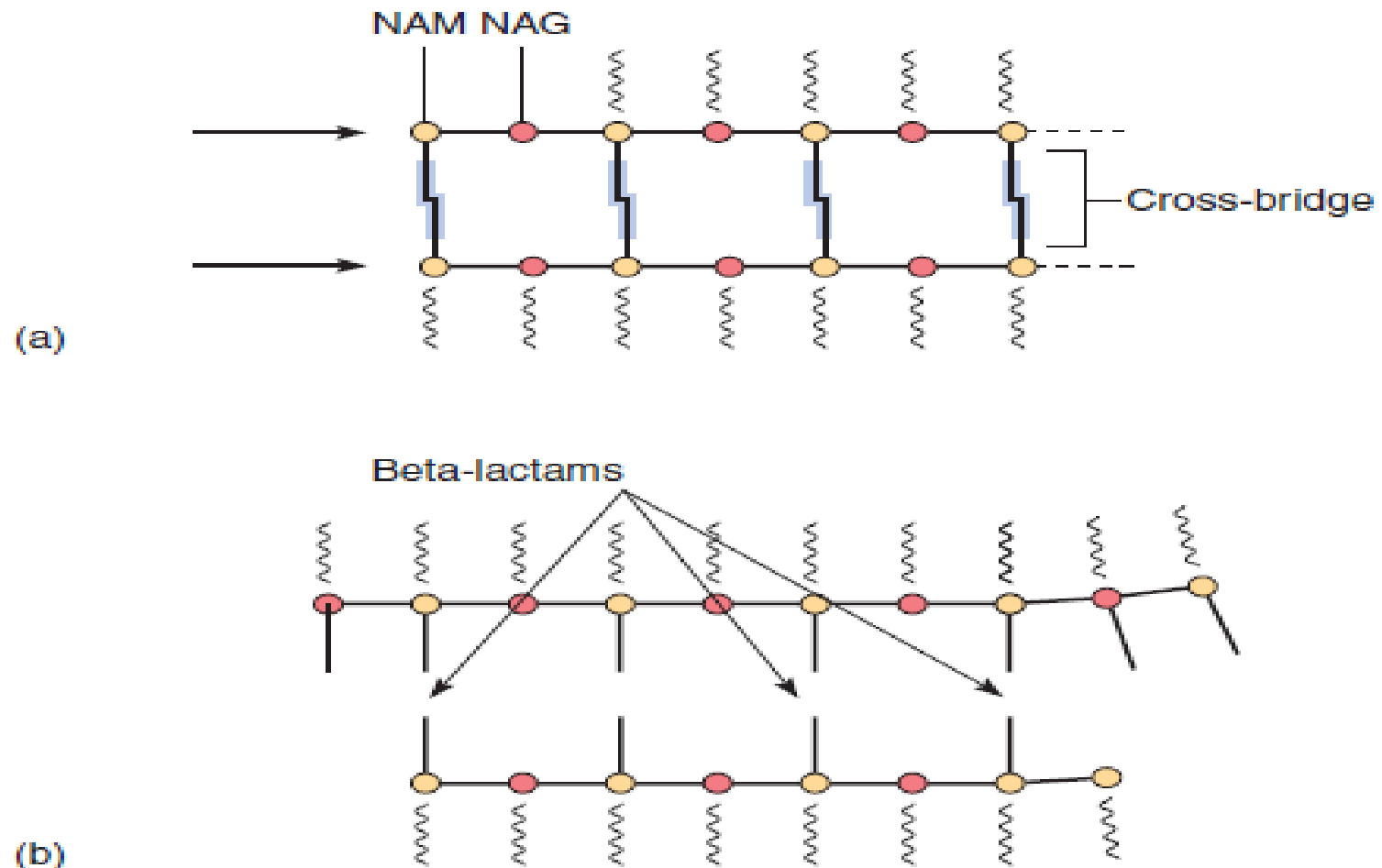
## (A) Classification of Antibacterial Agents:

### **(1) Based on mechanisms of action (Target site) of antibiotics are:**

1. Inhibition of the cell wall synthesis (production).
2. Damage to the cell membrane.
3. Inhibition of the nucleic acid synthesis (DNA or RNA).
4. Inhibition of protein synthesis.
5. Inhibition of enzyme activity.





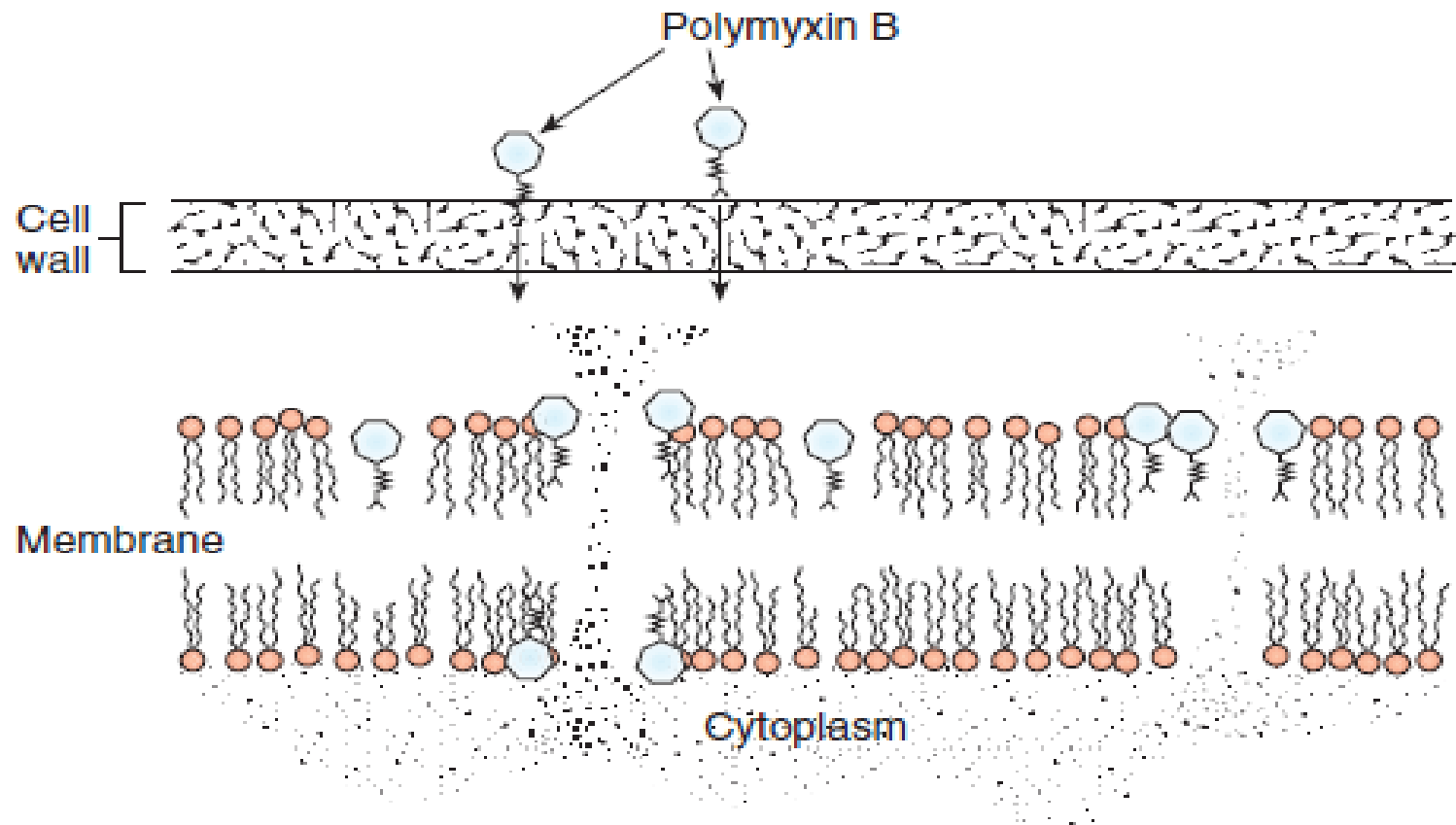


**FIGURE 12.4**

**The mode of action of beta-lactam antibiotics on the bacterial cell wall.**

**(a)** Intact peptidoglycan has chains of NAM (N-acetyl muramic acid) and NAG (N-acetyl glucosamine) glycans cross-linked by peptide bridges.

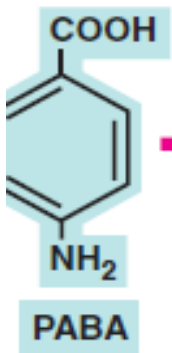
**(b)** The beta-lactam antibiotics block the peptidases that link the cross-bridges between NAMs, thereby greatly weakening the cell wall meshwork.



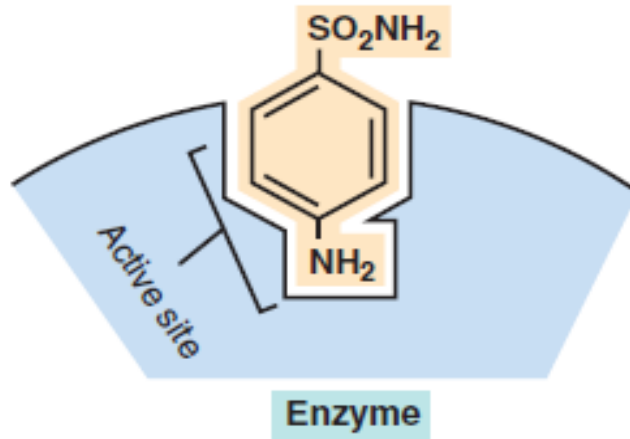
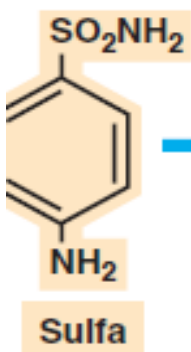
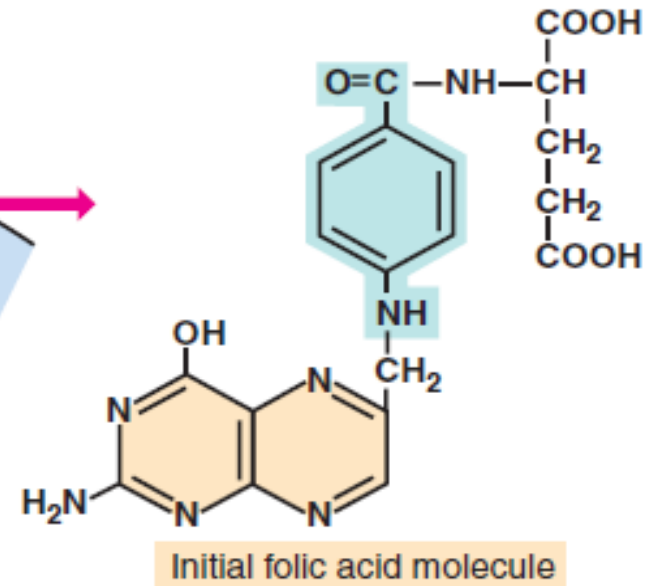
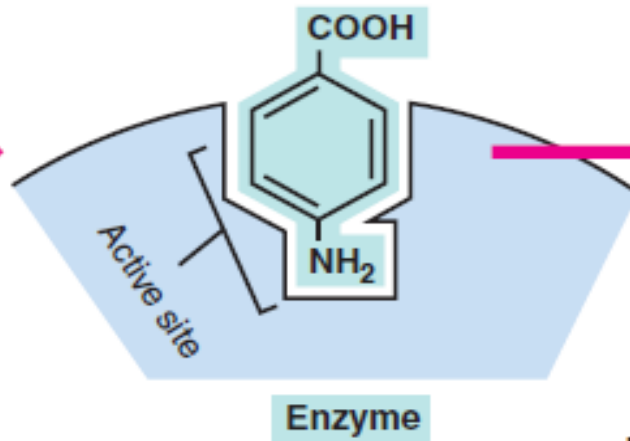
**FIGURE 12.8**

**The detergent action of polymyxin.** After passing through the cell wall of gram-negative bacteria, polymyxin binds to the cell membrane and forms abnormal openings that cause the membrane to become leaky.

Structure



Action



Folic acid synthesis  
cannot be  
completed

# Antibacterial Agents

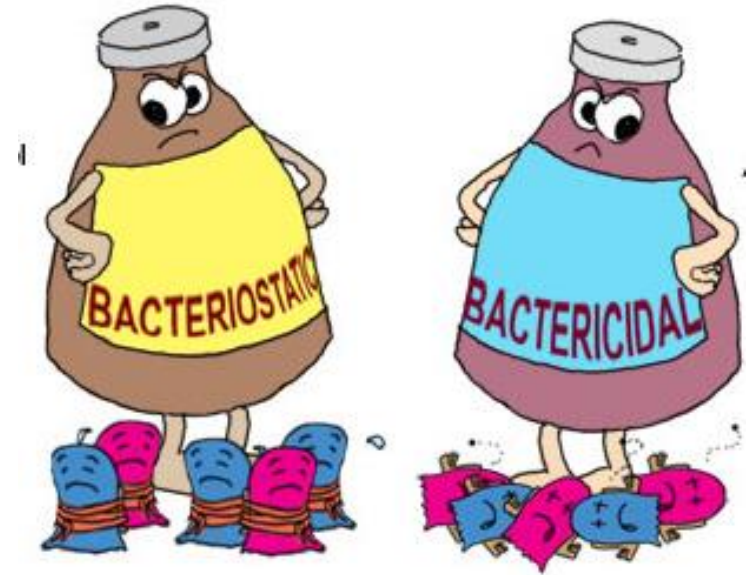
## (2) Based on activity of the drug:

### Bacteriostatic Agent

- Stop bacteria from growing and multiplying.
- Used **only** in healthy people.

### Bactericidal Agents

- Kill the bacteria.
- Used in healthy and immunocompromised people.



# Antibacterial Agents

## 3- Based on the Antibiotic effect spectrum:

### ➤ Narrow-spectrum Antibiotics

e.g. **vancomycin** work

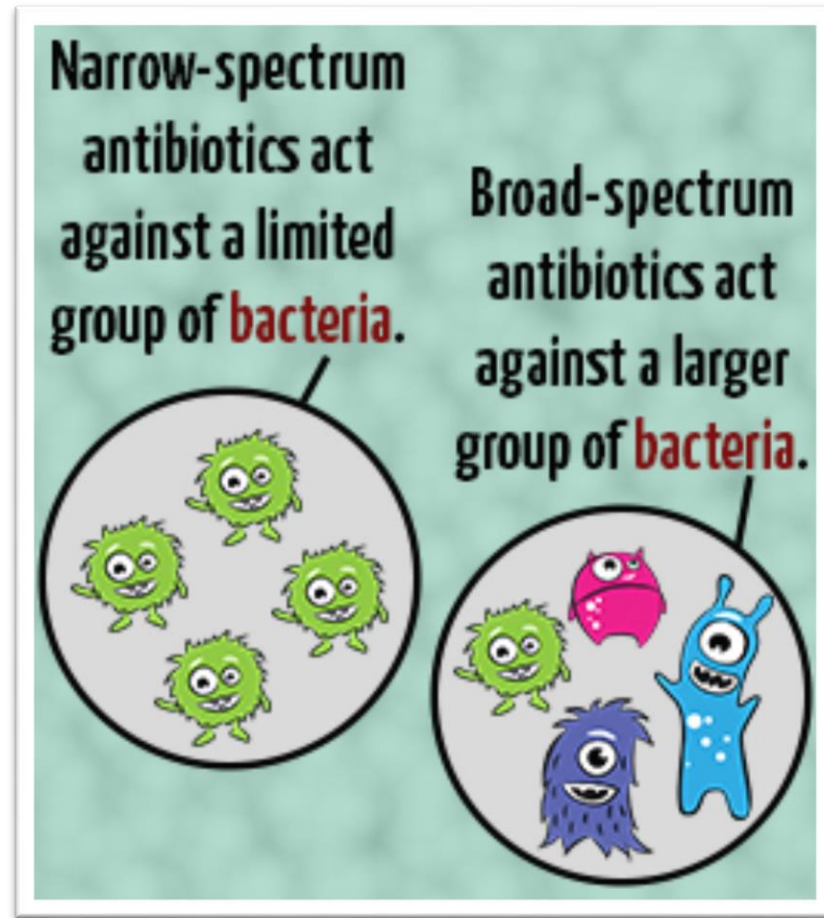
on Gram positive bacteria only.

**colistin** work

on Gram negative bacteria only.

### ➤ Broad-spectrum Antibiotics

e.g. **Ampicillin**.

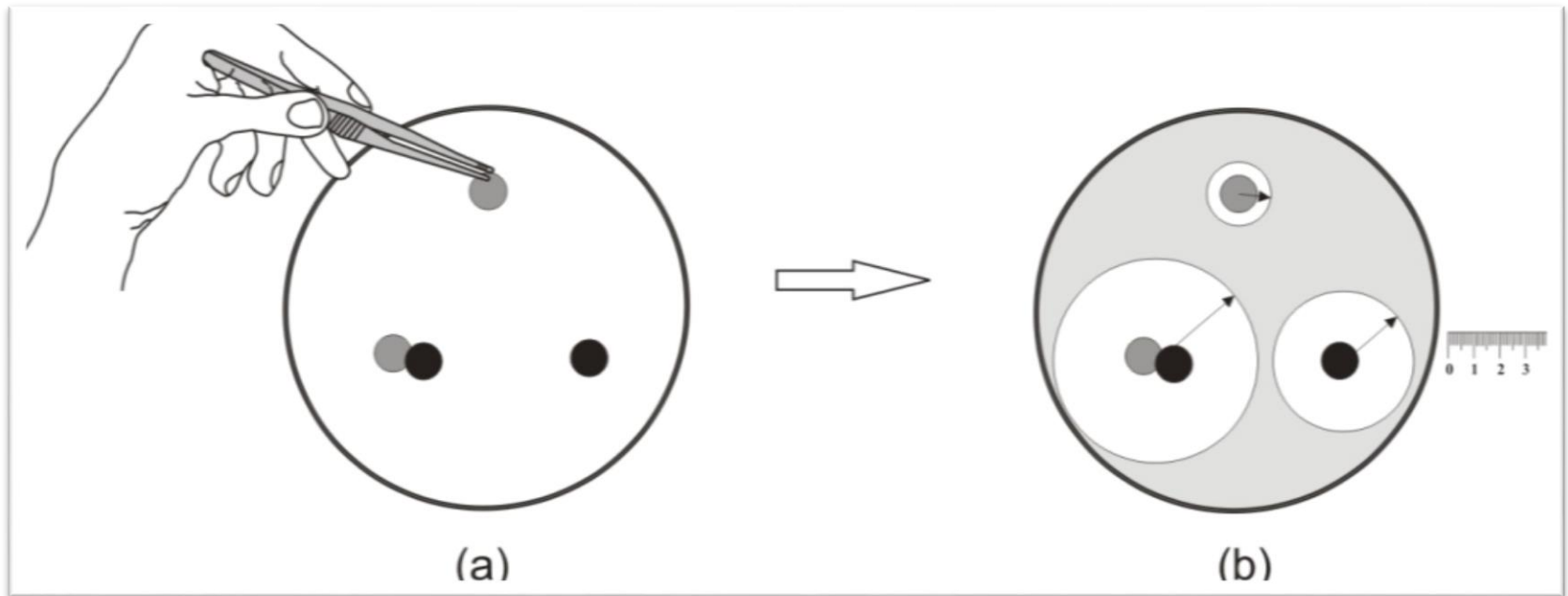


# Multidrug Therapy

- The simultaneous use of two or more drugs to kill all the pathogens and prevent resistant pathogens from growing.

e.g. Treatment of Tuberculosis (Tb)- 4 drugs are used.

## Synergism Vs Antagonism



# Antifungal and Antiprotozoal Agents

- Antimicrobial drugs against fungal and protozoal pathogens are difficult to use because they are eukaryotic cells like our cells so they tend to be toxic to the patient.
- **Mechanisms of action of Antifungal Agents are:**
  1. Binding to cell membrane sterols
  2. Inhibiting sterols synthesis.
  3. Inhibiting nucleic acid synthesis.

**e.g.** Amphotericin B

- **Mechanisms of action of Antiprotozoal Agents are:**
  1. Inhibiting nucleic acid synthesis.
  2. Inhibiting protozoal metabolism.

**e.g.** Metronidazole



# Antiviral Agents

- Until recent years there were no drugs for the treatment of viral diseases.
- Antiviral drugs are specially very difficult to produce because viruses are intracellular pathogens.
- Only few drugs have been found to be effective in certain viral diseases. They work by inhibiting viral replication within cells.

e.g.

**Acyclovir** for the treatment of HSV.

“cocktail” of drugs including **lamivudine** for HIV.

# Resistance of Bacteria

## Intrinsic Resistance

Some bacteria have natural resistance to some drugs because the drug cannot enter the bacterial cells or the bacteria doesn't have the target site specific to the drug.

## Acquired Resistance

### 1. Chromosomal Mutation

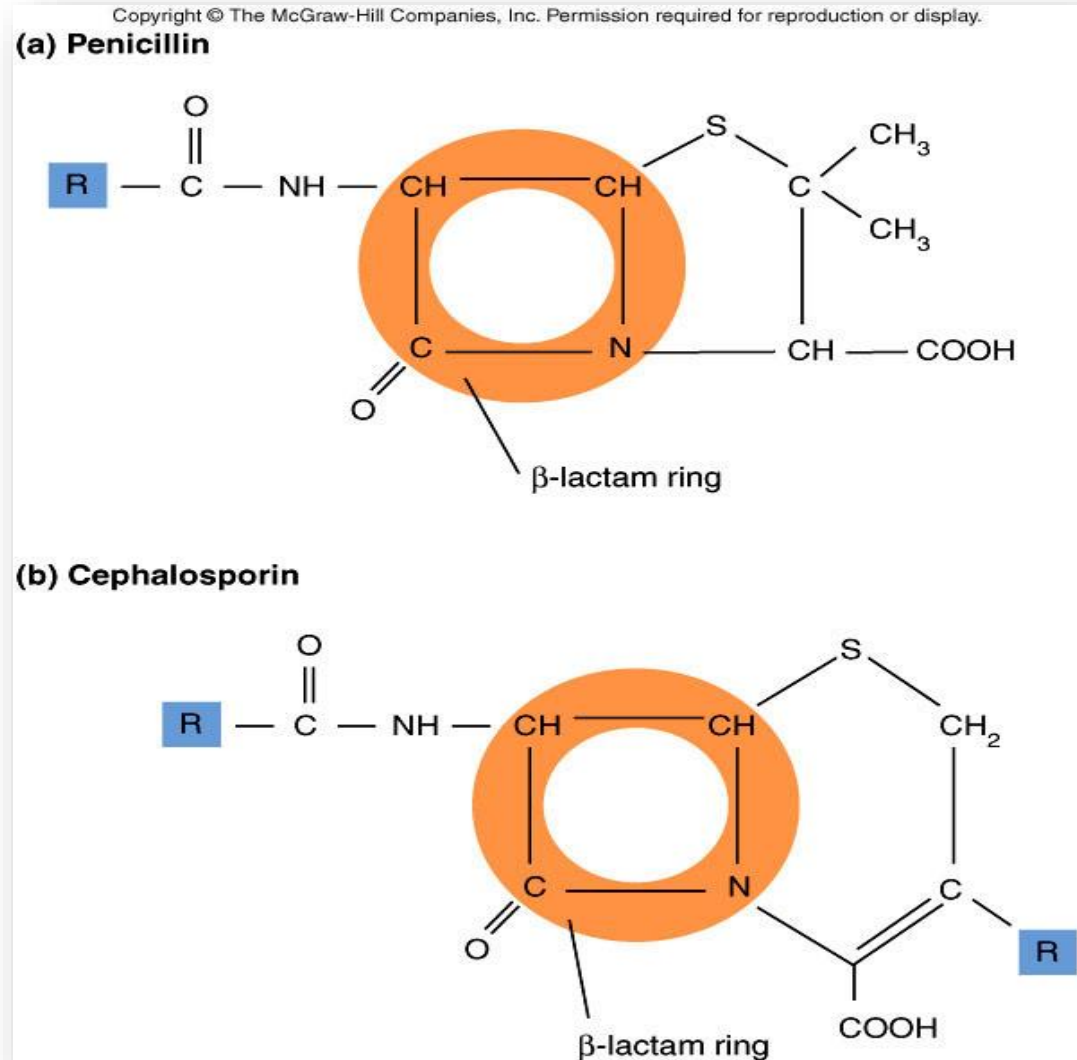
As cells replicate, spontaneous mutations occur at a relatively low rate. Such mutation can alter the binding site at which the antibiotic binds. As a result the antibiotic cannot enter the bacterial cell.

### 2. Gen Transfer

Genes encoding resistance to antibiotic can spread to different strains, species, and even genera. Ex. Plasmids.

# $\beta$ -Lactam Drugs

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



# Antimicrobial Resistance (Superbugs)

- When microorganisms (mainly bacteria) become resistant to one or more antimicrobial agent.
- They make it difficult to treat the disease.
- The worst resistance is **Multidrug Resistance**= resistance to many different antimicrobial drugs.
- **Examples:**
  - a) **MRSA**:Methicillin Resistant *Staphylococcus aureus*.
  - b) **VRSA**:Vancomycin Resistant *Staphylococcus aureus*.
  - c) **MRTB**: Multi-drug Resistant *Mycobacterium tuberculosis*.
  - d)  $\beta$ -Lactamase resistant *Streptococcus pneumoniae*.

Note: some viruses, fungi , parasites have also shown resistance.

**When penicillin G was first introduced, <3% of *Staphylococcus aureus* strains were resistant to it.**

**Now 90% or more are resistant to it!**

# Slowing Down Emergence and Spread of Antimicrobial Resistance.

1. **Responsibilities of Physicians:** must work to identify microbe and prescribe suitable antimicrobials, must educate patients
2. **Responsibilities of Patients:** need to carefully follow instructions
3. **Educate Public:** must understand appropriateness and limitations of antibiotics; **antibiotics not effective against viruses**
4. **Global Impacts:** organism that is resistant can quickly travel to another country
  - in some countries antibiotics available on non-prescription basis
  - antibiotics fed to animals can select for drug- resistant organisms

# Chapter (9)

**Chemotherapeutic Agent**

**Antimicrobial Agent**

**Antibiotics**

**Semisynthetic Antibiotics**

**Narrow-spectrum Antibiotics**

**Broad-spectrum Antibiotics**

**Synergism**

**Antagonism**