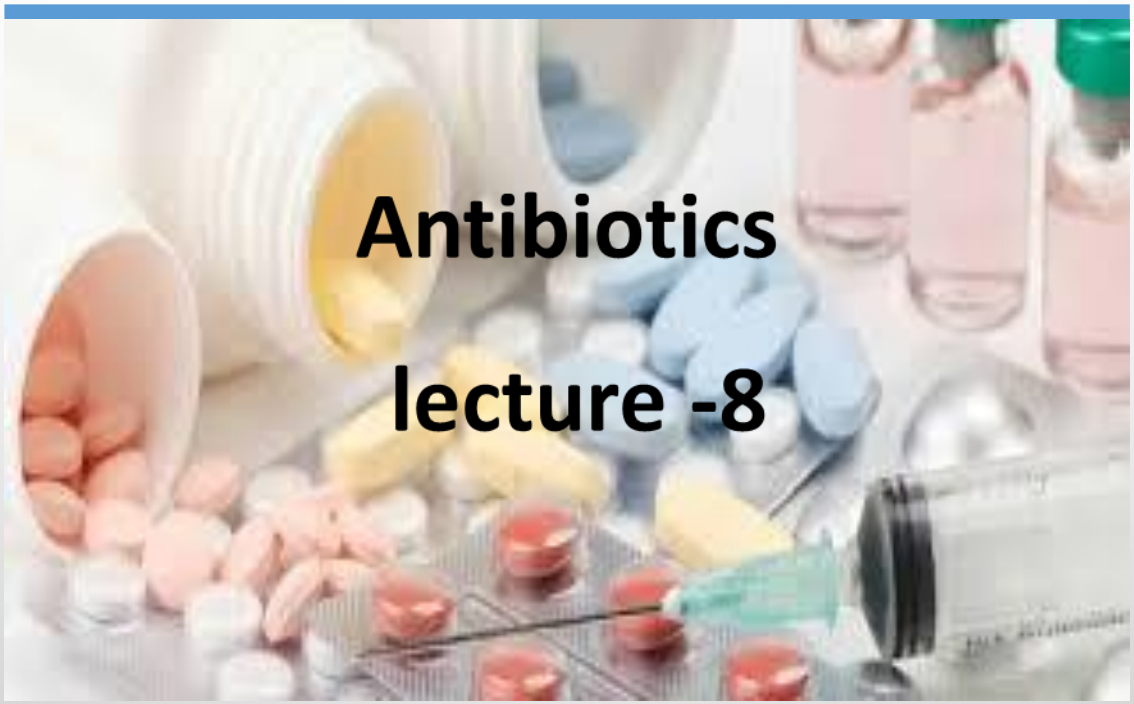
Third stage/ Microbiology



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Objectives

-Recognize the difference between antibiotic & antimicrobial

-know the genral characteristics of antimicrobial drugs

-How to determine the level of antimicrobial activity

-Mechanisms of action of antimicrobial agents

-know the factors that influence the effectiveness of antimicrobial drugs

-Mechanism of antibiotic resistant

Antibiotic & Antimicrobial

***Antibiotic:**

Also known as antibacterial, it is medications that destroy (kill) or slowdown the growth of bacteria.

It can be produced by a microorganism that kills or inhibits the growth of other microorganism.

-Antibiotics are powerful drugs that can treat diseases caused by bacteria BUT they cannot treat viral infections(cold, flu and most coughs)…

***Antimicrobial agent:**

A chemical that kills or inhibits the growth of other microorganism.

This term include antibiotics and chemically synthesized drugs

*General Characteristics of Antimicrobial Drugs:

1-Selective toxicity with minimum side effects

***Antimicrobial drug should cause greater harm to microorganisms than the host**

– Therapeutic dose

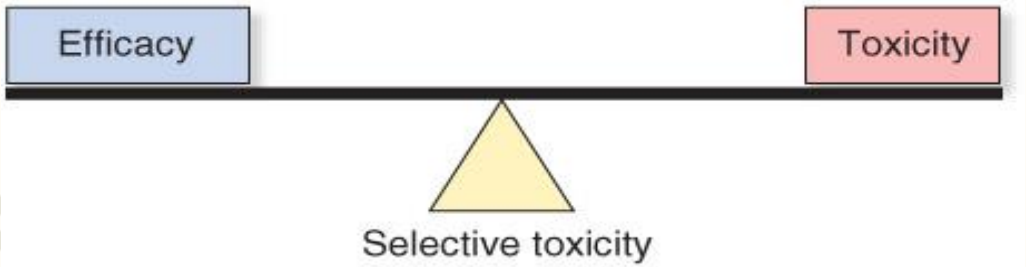
The drug level required for clinical treatment of a particular infection

– Toxic dose

The drug level at which the agent becomes too toxic for the host (produces undesirable side effects).

– Therapeutic index

The ratio of toxic dose to therapeutic dose:
the larger **therapeutic index** the better.



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

2-Broad spectrum activity

(activity against a wide variety of pathogens)
is more desirable than narrow spectrum activity.

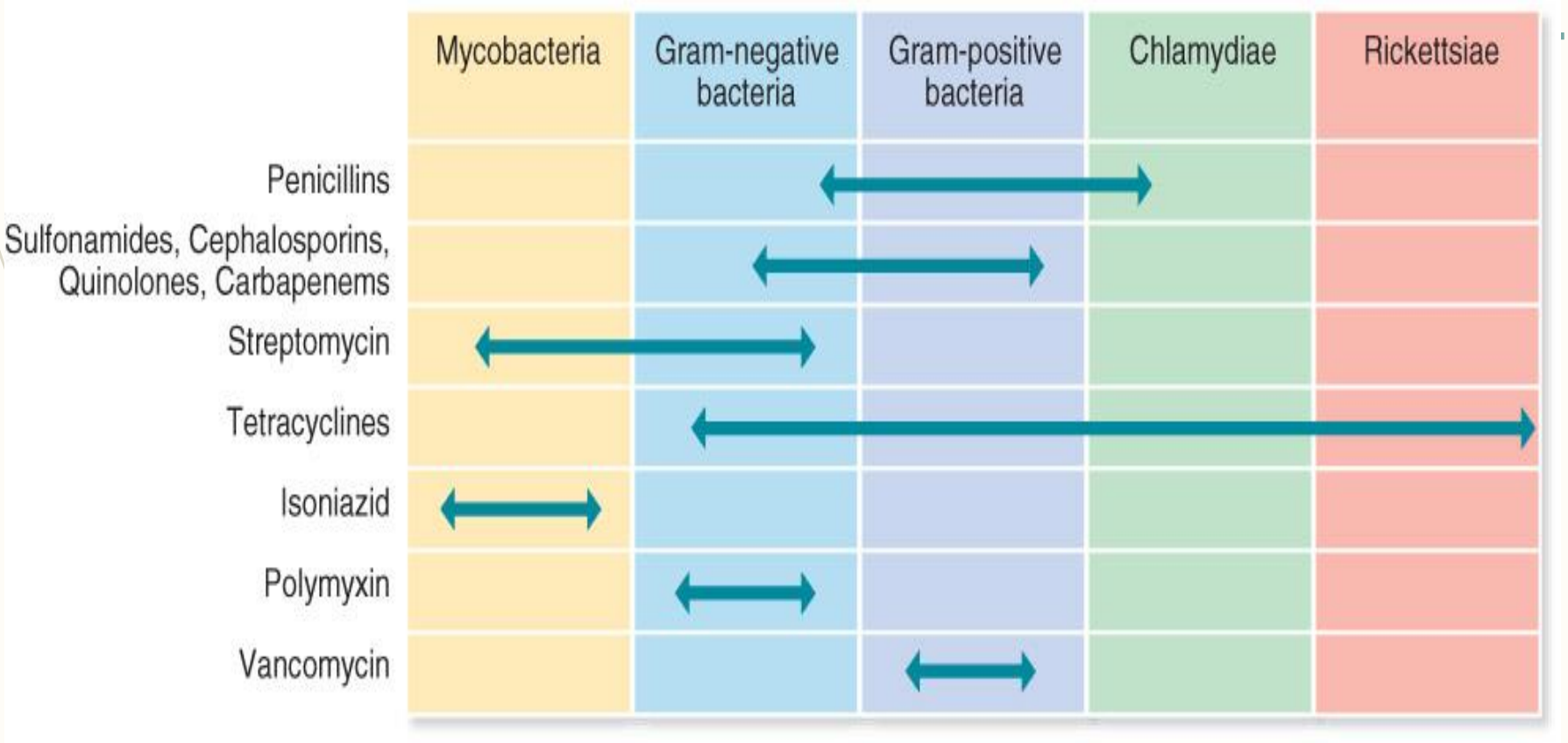
3- Drug can be cidal or Static

Bacteriocidal (able to kill)
Bicteriostatic (able to inhibit growth)

4- Antimicrobial agents can occur

- naturally or
- be synthetic or
- semi- synthetic **(chemical modifications of naturally occurring antibiotics)**

Antibiotic spectrum of activity



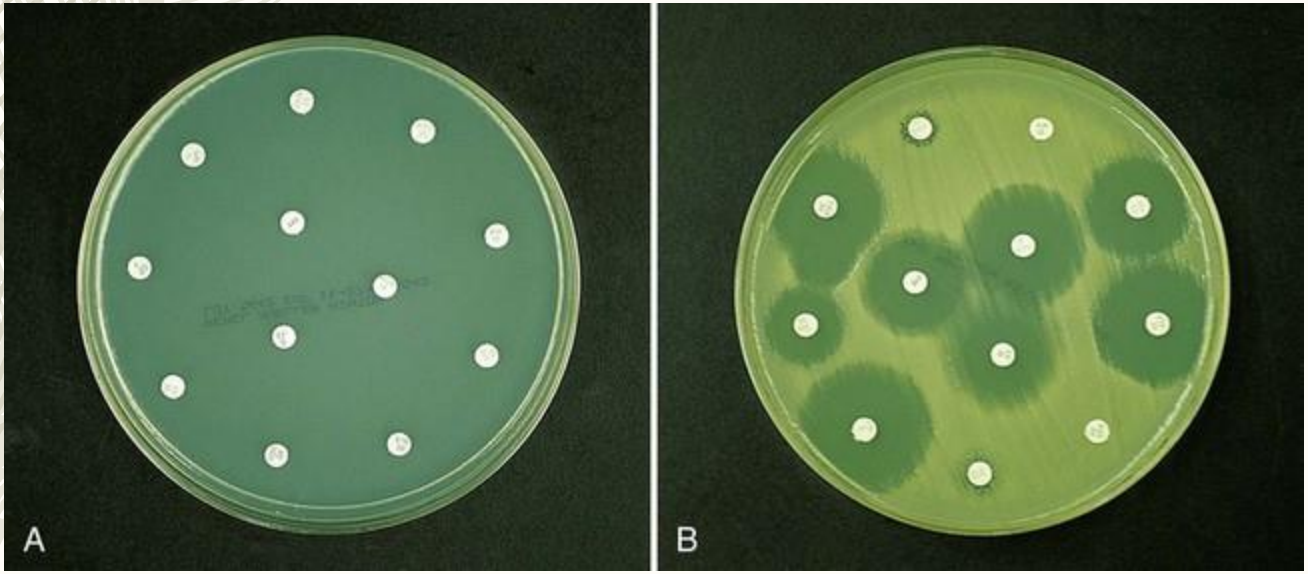
* Determining the Level of Antimicrobial Activity

Dilution susceptibility tests

– The lowest concentration of the antibiotic resulting in no microbial growth is the minimum inhibitory concentration (MIC)

Disk diffusion tests

– disks saturated with specific drugs are placed on agar plates inoculated with the test organisms.



*Mechanisms of Action of Antimicrobial Agents

1• **Inhibition of cell wall synthesis**

2• **Inhibition of protein synthesis**

3• **Inhibition of nucleic acid synthesis**

4• **Disruption of cell membranes**

5• **Inhibition of metabolic activities**

1• Inhibition of cell wall synthesis

Stop synthesis of wall by preventing cross linking of peptidoglycan units.

-Beta lactam containing antibiotics such as penicilin and cephalosporins.

-Vancomycin

-Cycloserine

2• Inhibition of protein synthesis

-Aminoglycosides (streptomycin, neomycin,Gentamicin, and kanamycin)

-Tetracyclines

-Macrolides (Erythromycin, Azthromycin)

-Chloramphenicol

3• Inhibition of nucleic acid synthesis

Stop DNA replication in :

-Qunilones and fluoroquinolones(such as ciprofloxacin)

-Rifampicin

OR

Stop RNA synthesis in :

-Metronidazole

4• Disruption of cell membranes

Inhibition of functions of cellular membrane (the cytoplasmic membrane).

-Polymyxin can selectively combine with phosphatide in the cell membrane and cause the increase of membranous permeability. As a result, some important materials will outflow from bacterial cells and result in death of bacteria

5• Inhibition of metabolic activities (Antimetabolites)

A drug mimics the normal metabolite, and acts as a competitive inhibitor. The process happened when enzyme of cell recognizes the drug instead of the normal metabolite (pathway stops).

-Sulfonamides (Sulpha drugs) and trimethoprim

(inhibit folic acid synthesis).

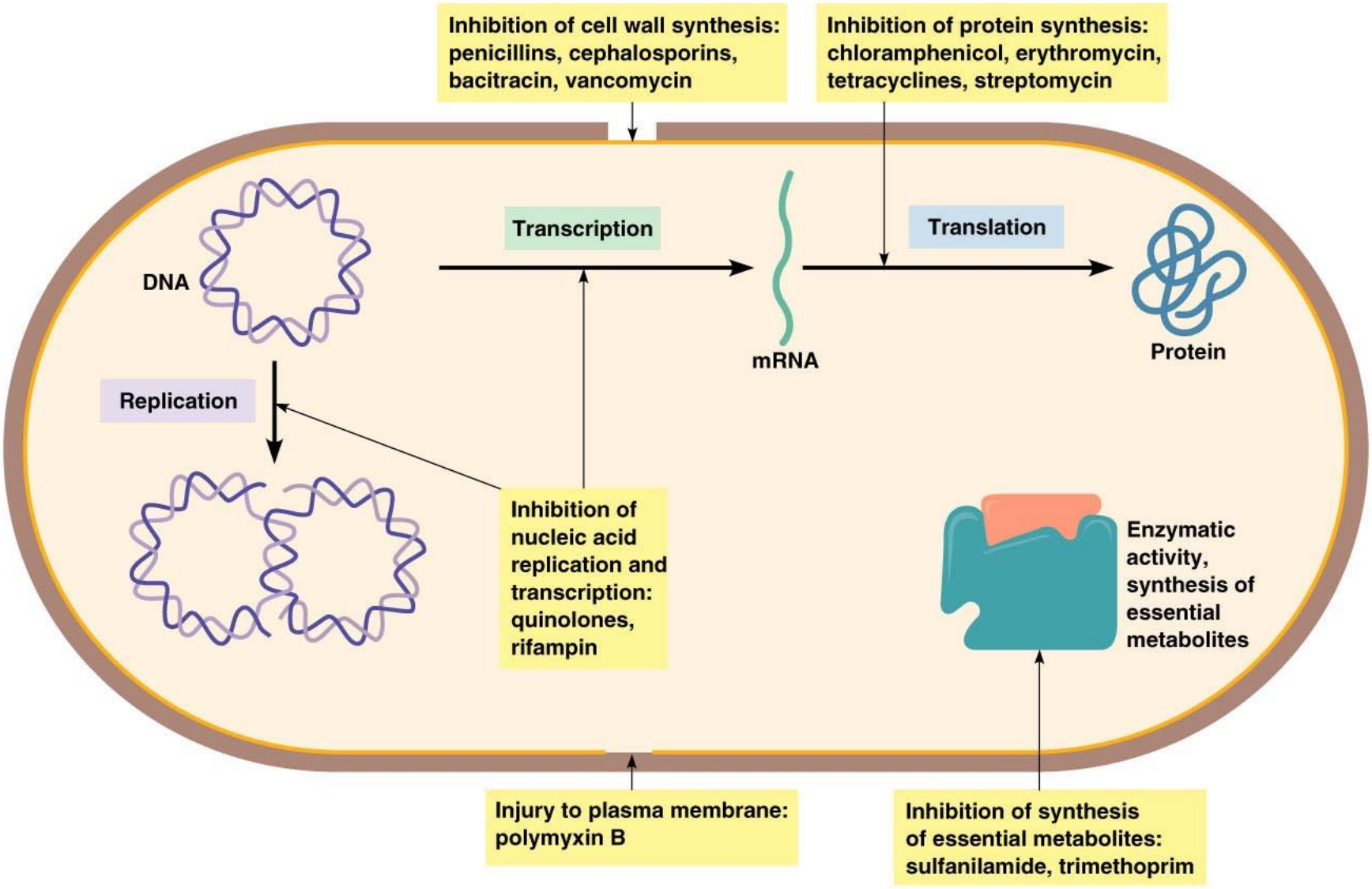


Figure 20.2

Factors Influencing the Effectiveness of Antimicrobial Drugs

1- Factors influencing a drug's ability to reach the site of Infection.

2- Factors influencing drug concentration in the body.

3- The nature of the pathogen

1- Factors influencing a drug's ability to reach the site of Infection:

a– Mode of administration

- **Oral**
- **Topical**
- **Parenteral (injection)**

b– Susceptibility to various body defense mechanisms

(e.g., penicillin is rapidly degraded in the stomach, but the penicillin derivative ampicillin is more acid stable)

2- Factors influencing drug concentration in the body.

Drug concentration must exceed the pathogen's MIC for the drug to be effective.

This will depend on

a– **Amount of drug administered**

b– **Route of administration**

c– **Speed of uptake**

d– **Rate of clearance (elimination) from the body**

3- The nature of the pathogen

This includes:

a- Inherent susceptibility of the pathogen and the presence of its active growth .

b- Drug resistance (This has become an increasing problem)

Bacteria had developed a number of mechanisms to protect themselves from the action of antibiotics.

Mechanisms of Antibiotic Resistance

- **Enzymatic destruction of drug**
- **Prevention of penetration of drug**
- **Alteration of drug's target site**

.Chemical modification of the drug

1-Enzymatic Destruction (inactivation) of the drug

Antibiotic hydrolysis by bacterial cellular enzymes result in stopping its effectiveness. An example: penicillinases and other beta lactamases.

2-Prevention of penetration of drug

Alterations that affect permeability which can involve a decreased influx or an increased efflux from the bacterial cell.

3-Alteration of the drug‘s target site through mutation.

An example is streptomycin resistance.

Streptomycin binds to bacterial ribosome and acts through prevention of protein synthesis. In resistant bacteria ,alteration of a single amino acid in bacterial ribosomal protein will prevent streptomycin binding to ribosome and thus will not affect bacterial protein synthesis.

4-Chemical modification of drug:

By acetylation, phosphorylation or adenylation of the antibiotic by bacteria results in inactivation of the antibiotic.

Thank you

Recap

-Recognize the difference between antibiotic & antimicrobial

-Know the genral characteristics of antimicrobial drugs

-Know how to determine the level of antimicrobial activity

- Know the mechanisms of action of antimicrobial agents

-Know the factors that influence the effectiveness of antimicrobial drugs

- Know the mechanism of antibiotic resistant