Lecture 7

ANTIMICROBIAL AGENTS

Staphylococcus

Penicillium colony

Objectives

- Define antimicrobial, antibiotic, bacteriostatic, bactericidal,
- Discuss the importance of selective toxicity property of antimicrobials,
- Explain spectrum of activity and give examples
- Explain mechanisms of action of clinically used antibiotics
- List major groups of antibiotics and give examples

Antimicrobial agents

- **Antimicrobial** agent is a substance that **kills** or **inhibits** the growth of microorganisms such as bacteria, fungi or viruses.

- Depending on the type of organisms targeted, these substances are also known as **antibacterial**, **antifungal**, **anti-parasitic**, or **antiviral** agents.

Antibiotic

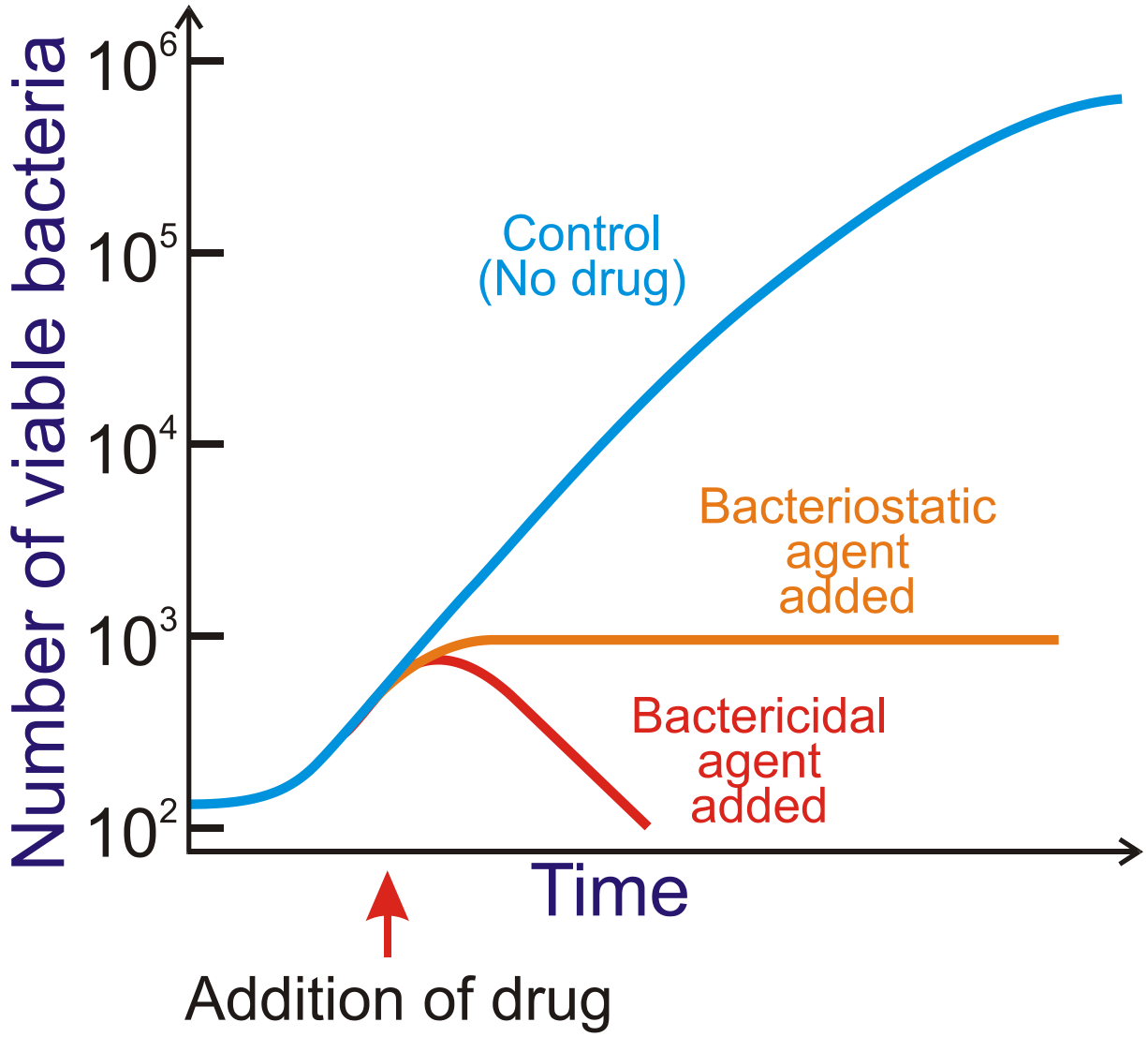
- ***Technically***, antibiotics are only those substances that are produced by one microorganism that kill, or prevent the growth, of another microorganism.

- ***Practically*****:** The term “antibiotic” is often used in medical contexts to refer to all **antibacterial** pharmaceuticals, not just to antibiotics in this narrower sense.

Bacteriostatic vs. bactericidal

- **Bacteriostatic**: Antibiotics do not kill bacteria directly but **inhibit their growth**. This allow the immune system to destroy them more quickly.
- **Bactericidal:** Antibiotics that can **kill** microorganisms.

Bacteriostatic / Bactericidal



Selective toxicity

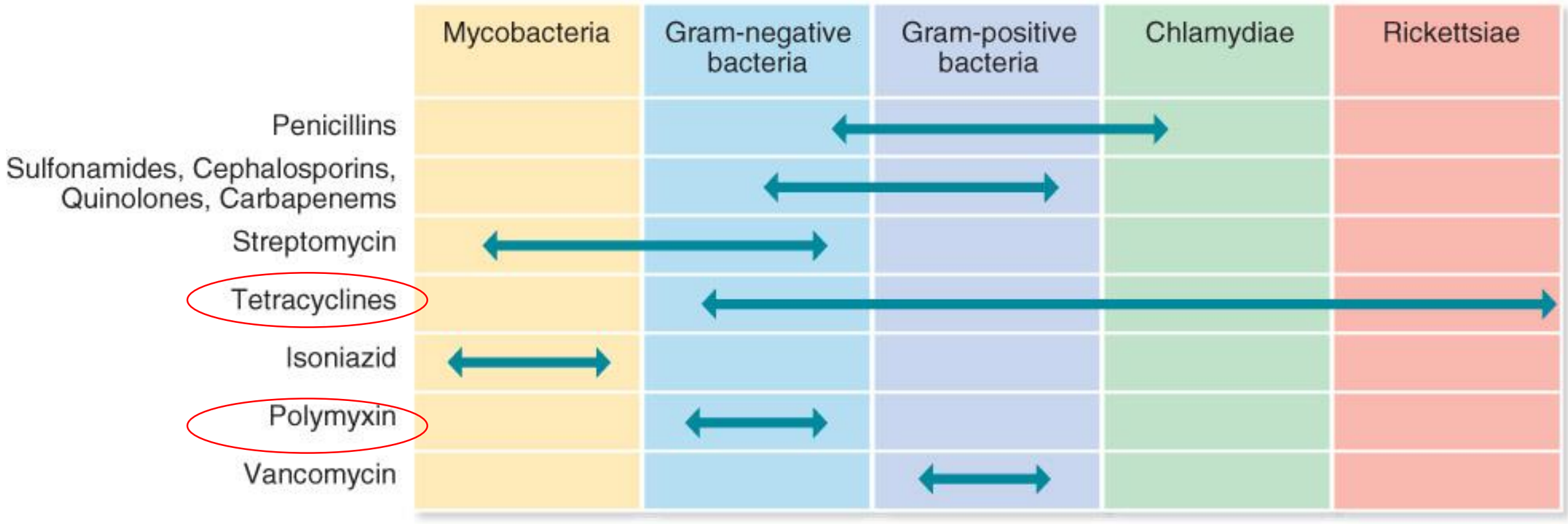
- It is **selective** inhibition of the growth of the **microorganism** without damage to the host.
- Selective toxicity is achieved by exploiting the **differences** between the metabolism and structure of the microorganism and the corresponding features of human cells.
- For example, **penicillin** is an effective antibacterial agents because it prevents the synthesis of **peptidoglycan**, thereby inhibiting the growth of bacterial but not human cells.

Spectrum of Activity

- Refers to the range of microorganisms that a antimicrobial agent can kill or inhibit.

Broad spectrum antibiotics	Narrow spectrum antibiotics:
Antibiotics that are active against **many** types of microorganisms.	Antibiotics that are active against **one** or very **few** types of microorganisms.
e.g. tetracyclines are active against many Gram positive bacteria, Gram negative bacteria, Chlamydia, Rickettsia and Mycoplasma .	e.g. polymixin, active only against Gram negative bacteria

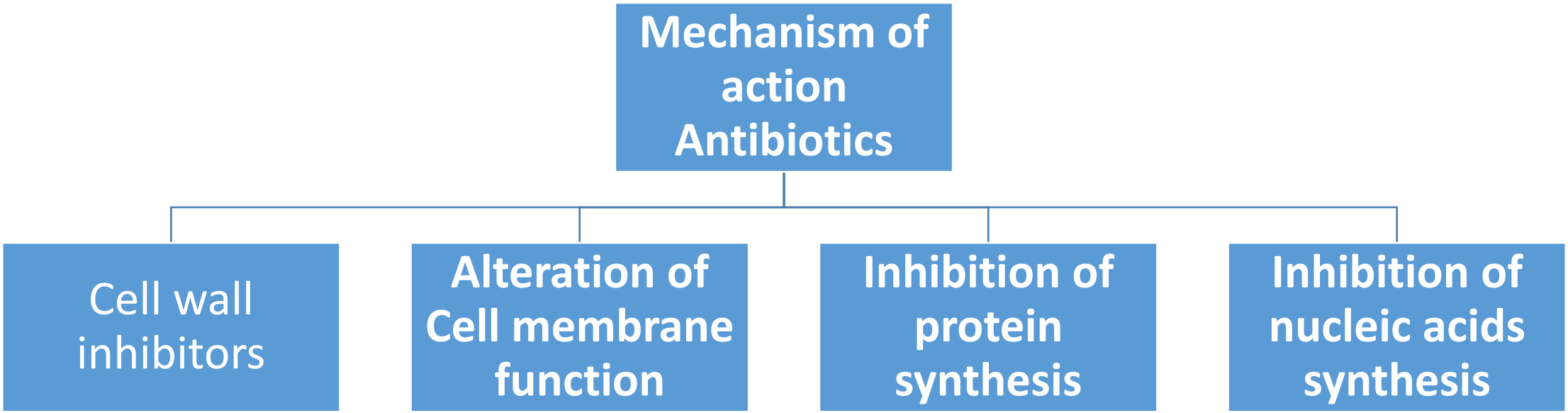
The antimicrobial spectrum of activity

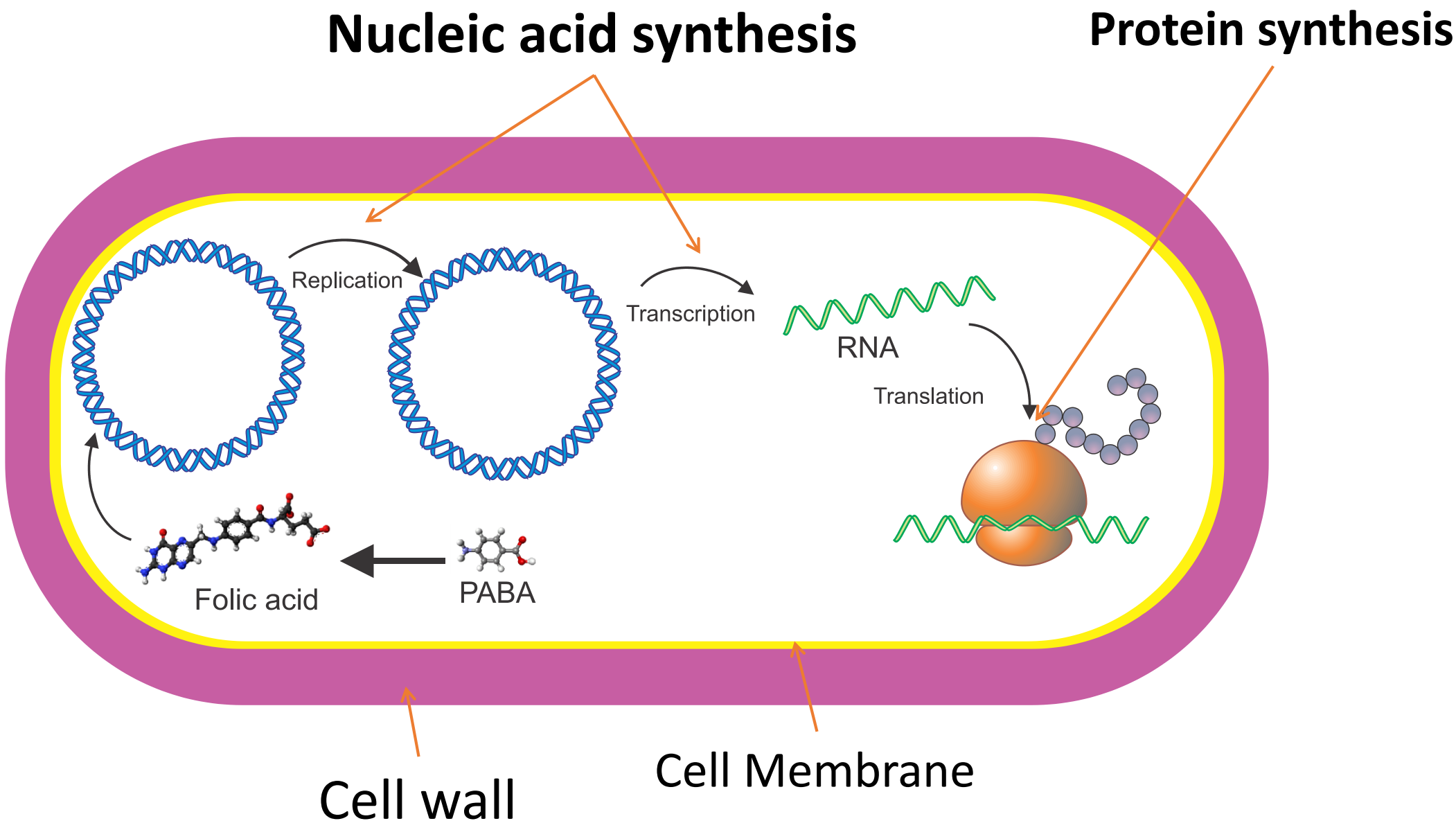


Mechanism of action of clinically used antibiotics:

At the cellular and subcellular levels most antimicrobial agents function in one of 4 major ways:-

1. Inhibition of cell wall synthesis.
2. Alteration of cell membrane permeability.
3. Inhibition of protein synthesis.
4. Inhibition of nucleic acid synthesis.

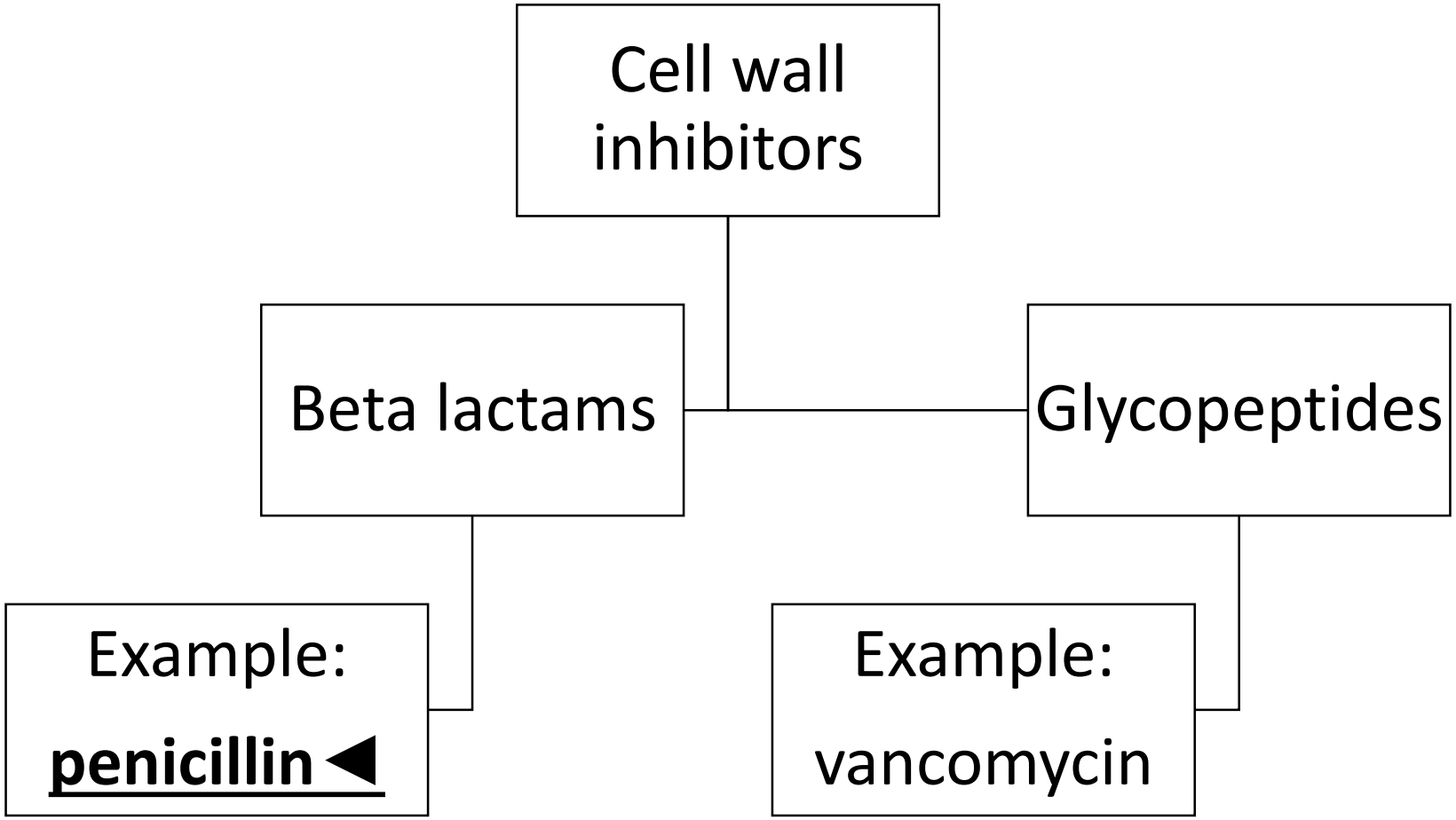

Mechanism of action Antibiotics
Cell wall inhibitors
Alteration of Cell membrane function
Inhibition of protein synthesis
Inhibition of nucleic acids synthesis


Nucleic acid synthesis
Protein synthesis
Replication
Transcription
RNA
Translation
Folic acid
PABA
Cell wall
Cell Membrane

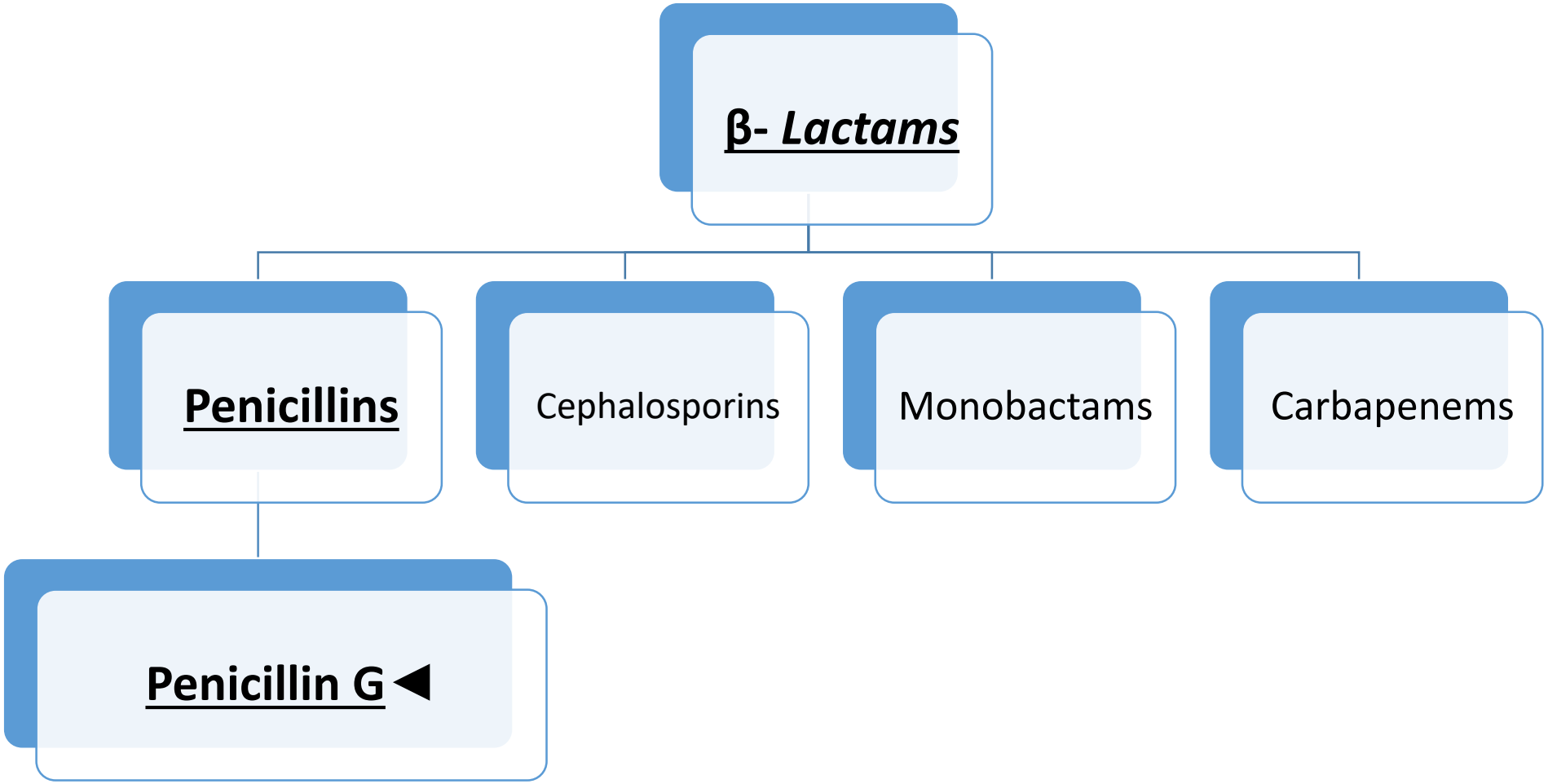
1. Cell wall inhibitors

- Cell wall synthesis inhibitors exert their selective toxicity against bacteria because **humans cells lack cell walls**.
- The cell walls of most bacteria contain a rigid girdle of peptidoglycan, which protects the cell against rupture from hypotonic environments.

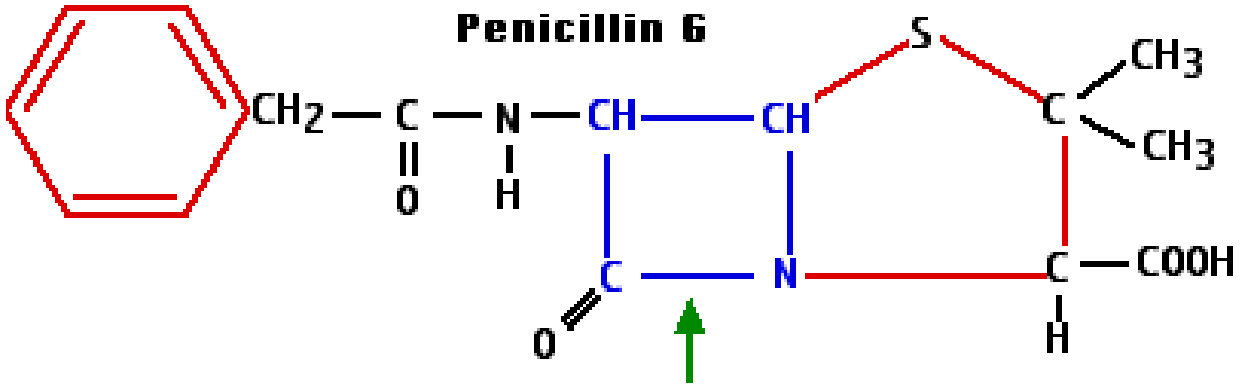
1. Cell wall inhibitors



β- *Lactams*


β- Lactams
Penicillins
Cephalosporins
Monobactams
Carbapenems
Penicillin G◄

The Beta-Lactam antibiotics



The beta-lactams get their name from the characteristic beta-lactam **ring structure** that they all share.

Resistance to beta lactam antibiotics

There are 2 main modes of bacterial resistance to β-lactams

- The organism produce penicillin **destroying enzyme** (**β-lactamases**)
- The organism alter the **targets** for penicillin action as a result of chromosomal mutation.

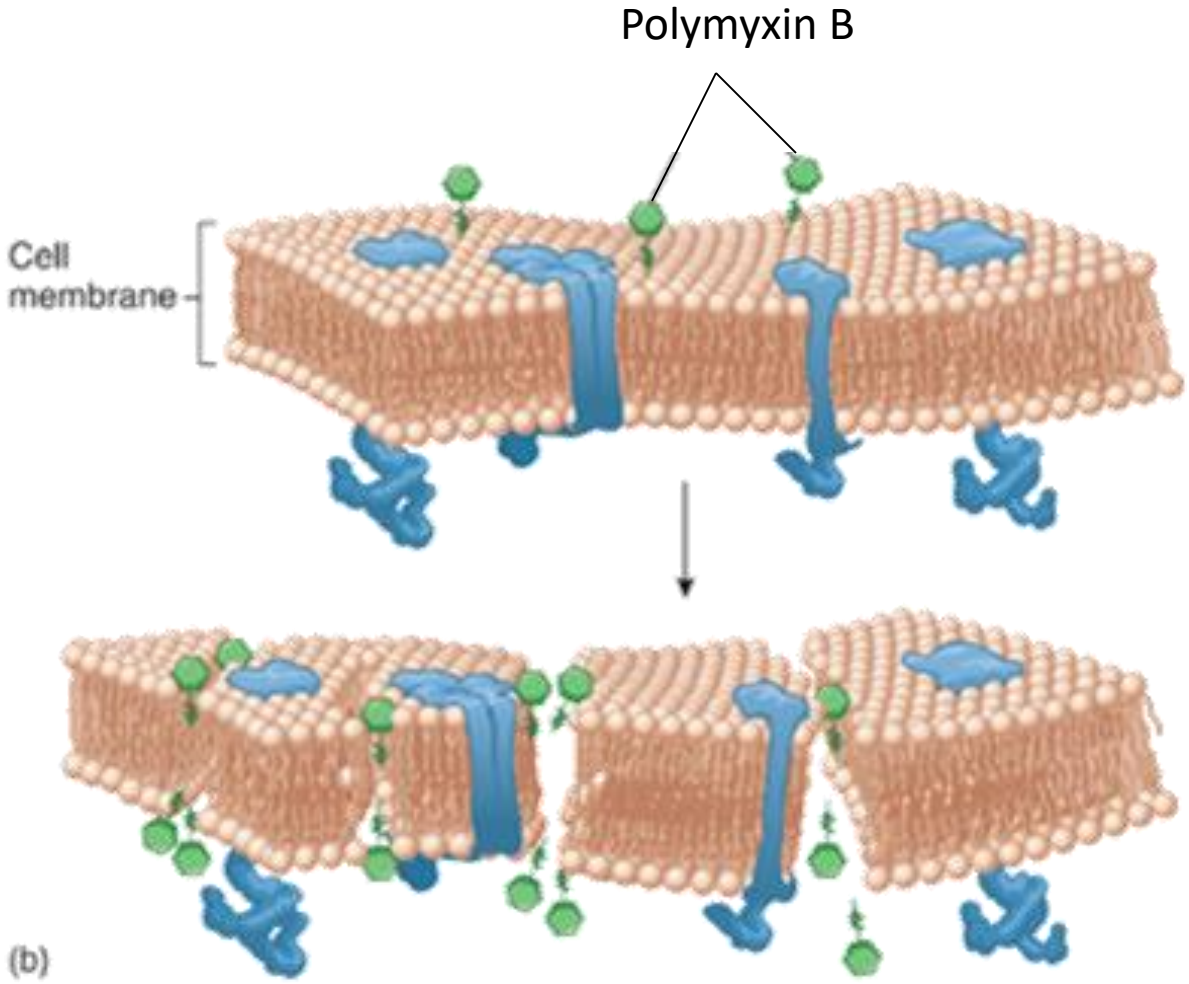
Antimicrobial action through inhibition of cell membrane function

- The plasma membrane separates the interior of all cells from the outside environment.
- Disrupting the plasma membrane results in bacterial cell death due to leakage of cell contents.

Examples:

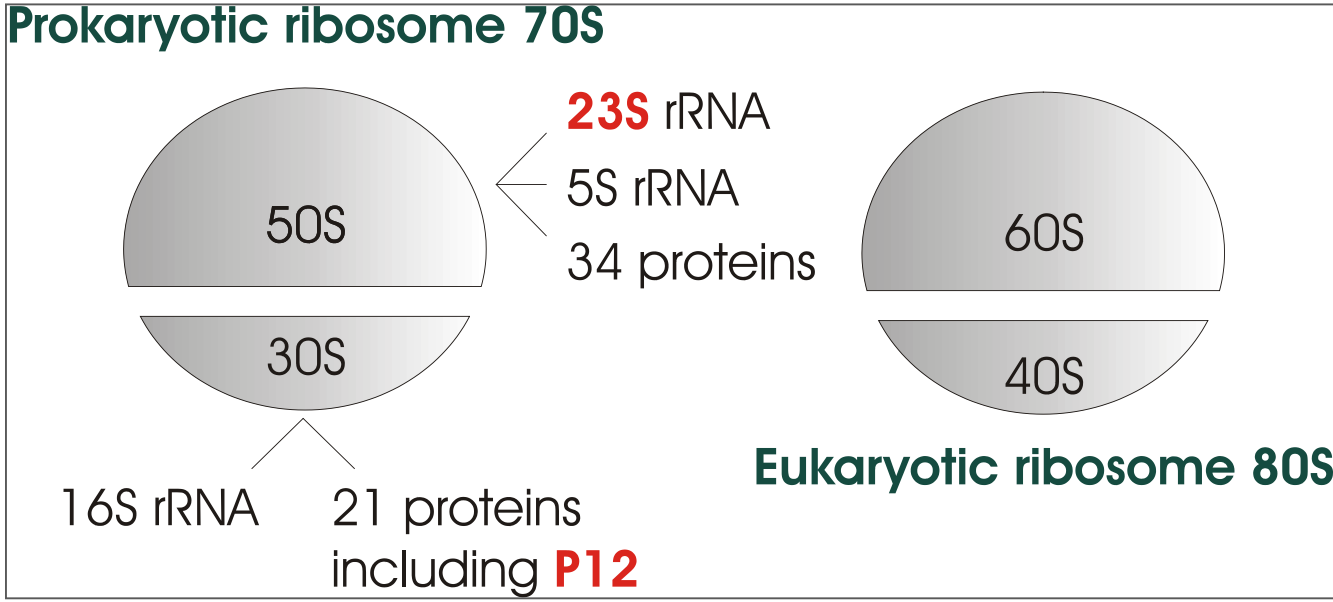
- **Polymyxins (antibacterial)◄**
- Nystatin (antifungal).
- Amphotericin B (antifungal).

Membrane disruption (leakage) is lethal to the cell



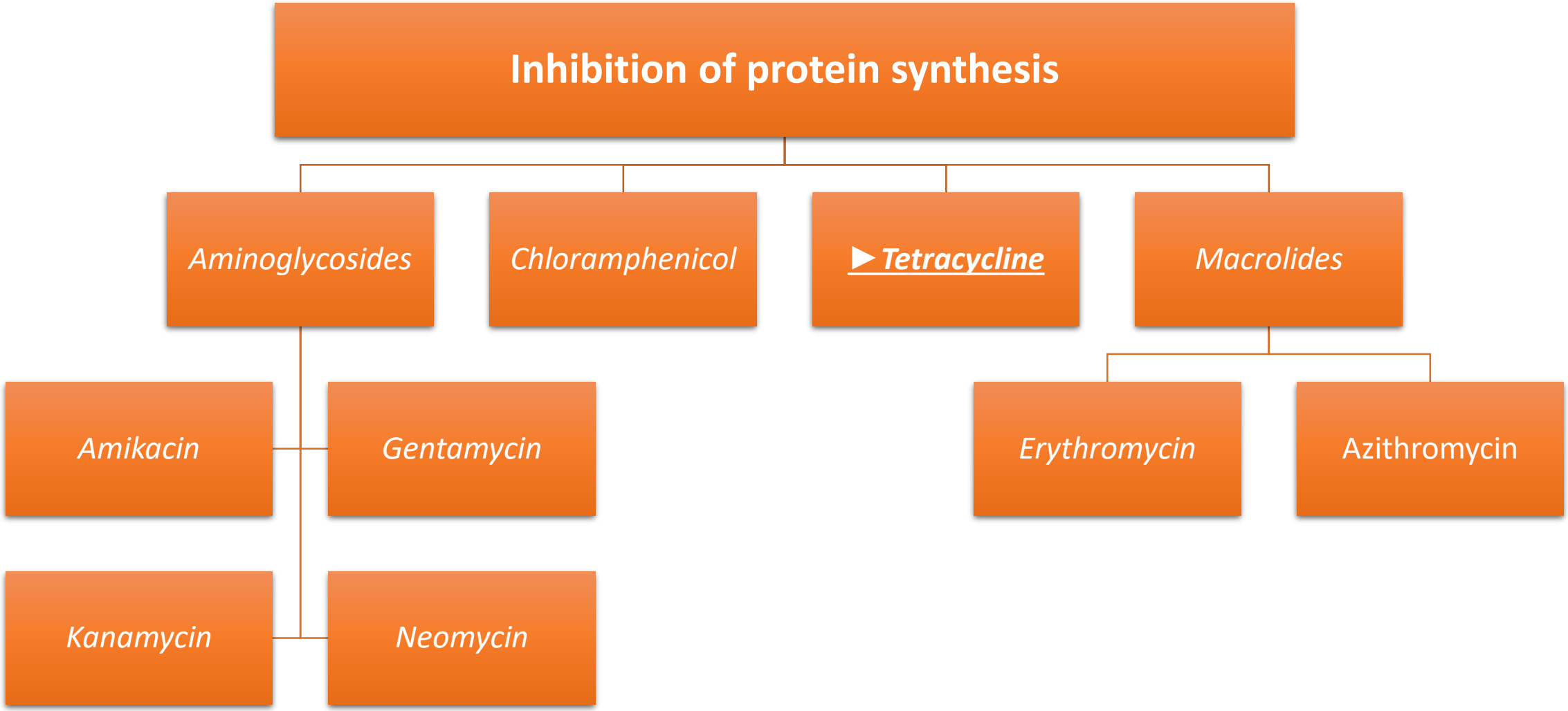
Antibacterial action through inhibition of protein synthesis

- Antibiotics that inhibit protein synthesis take advantage of the fact that the **bacterial ribosome** and the **eukaryotic ribosome** differ structurally.
- Bacteria have 70S ribosomes, whereas Eukaryotic cells have 80S ribosomes.



- Aminoglycosides (Gentamycin , Amikacin, , Kanamycin, Neomycin),
- **Tetracycline**◄,
- Macrolides (Erythromycin, azithromycin)
- Chloramphenicol.

(3) Antibacterial action through inhibition of protein synthesis:-

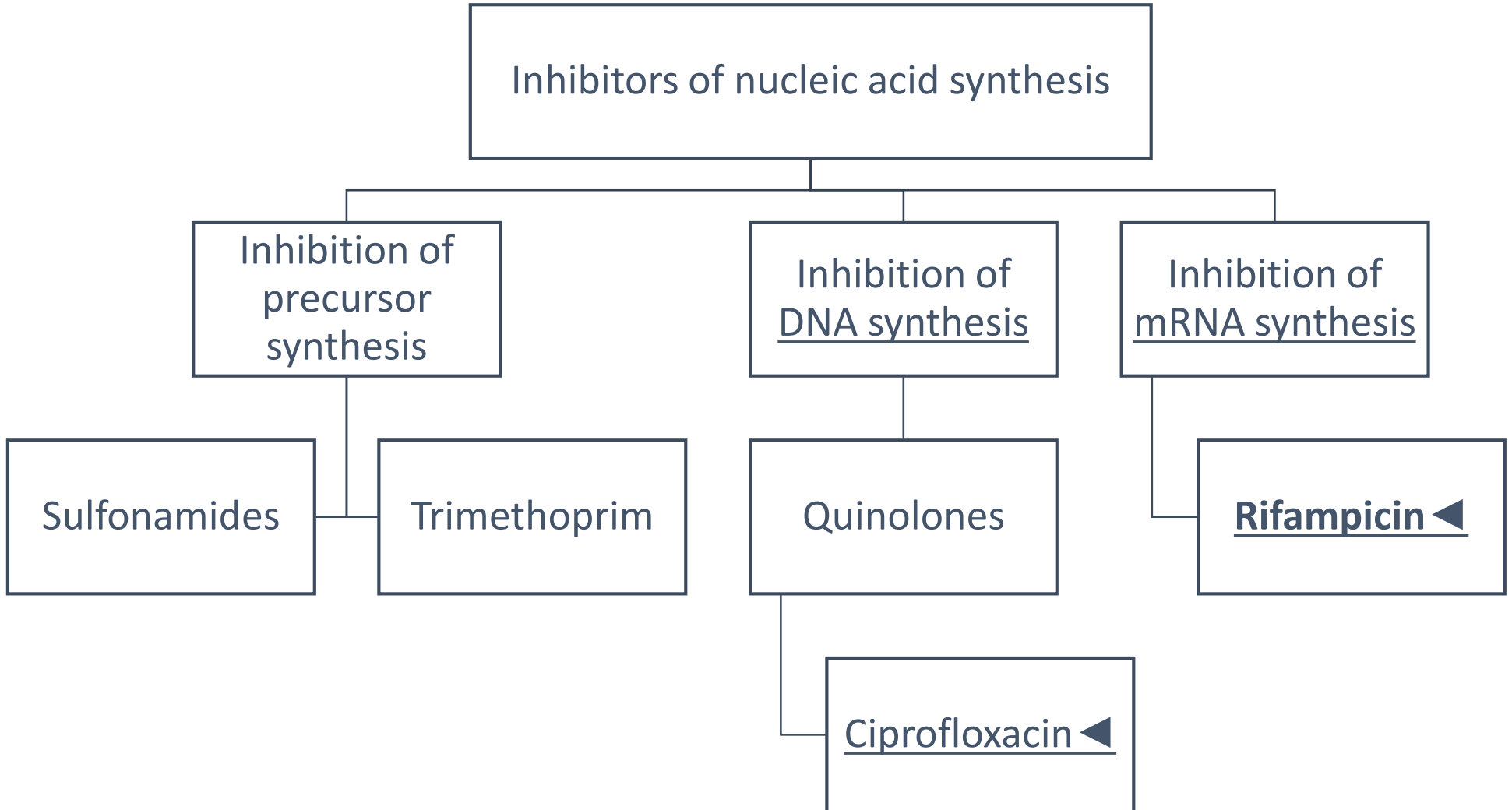


Antimicrobial action through inhibition of nucleic acid synthesis

Nucleic acid synthesis can be inhibited at the level of:

- Inhibition of nucleic acid precursors → Example : Sulfonamides
- Inhibition of DNA synthesis (replication) → Example : **ciprofloxacin**.◄
- Inhibition of mRNA synthesis (transcription) → Example: **rifampicin**.◄

Antimicrobial action through inhibition of nucleic acid synthesis



Quizzes

1. Which statement is accurate for Penicillin G?

A. It inhibits DNA synthesis.

B. It inhibits protein synthesis.

C. It act through inhibition of cell membrane function.

D. It inhibit cell wall synthesis.

1- Which statement is accurate for Tetracycline?

A. It inhibits DNA synthesis.

B. It inhibits protein synthesis.

C. It act through inhibition of cell membrane function.

D. It inhibit cell wall synthesis.

3- Which statement is accurate for Rifampicin?

A. It inhibits mRNA synthesis.

B. It inhibits protein synthesis.

C. It act through inhibition of cell membrane function.

D. It inhibit cell wall synthesis.

4- Polymyxins act through:

a) It inhibits DNA synthesis.

b) It inhibits protein synthesis.

c) It act through inhibition of cell membrane function.

d) It inhibit cell wall synthesis.

5- Quinolones (e.g. ciprofloxacin) act through:

a) It inhibits DNA synthesis.

b) It inhibits protein synthesis.

c) It act through inhibition of cell membrane function.

d) It inhibit cell wall synthesis.

6. Tetracycline is

A. Broad spectrum antibiotic

B. Narrow spectrum antibiotic

7. True or False

1. Bactericidal antibiotic is an antibiotic that inhibit the growth of bacteria.
2. Bactericidal antibiotic is an antibiotic that kill bacteria.
3. Bacteriostatic antibiotic is an antibiotic that inhibit the growth of bacteria
4. Bacteriostatic antibiotic is an antibiotic that kill bacteria.
5. Broad spectrum antibiotic is active against few types of microorganisms
6. Polymyxin is a broad spectrum antibiotic.

8. Fill in the spaces:

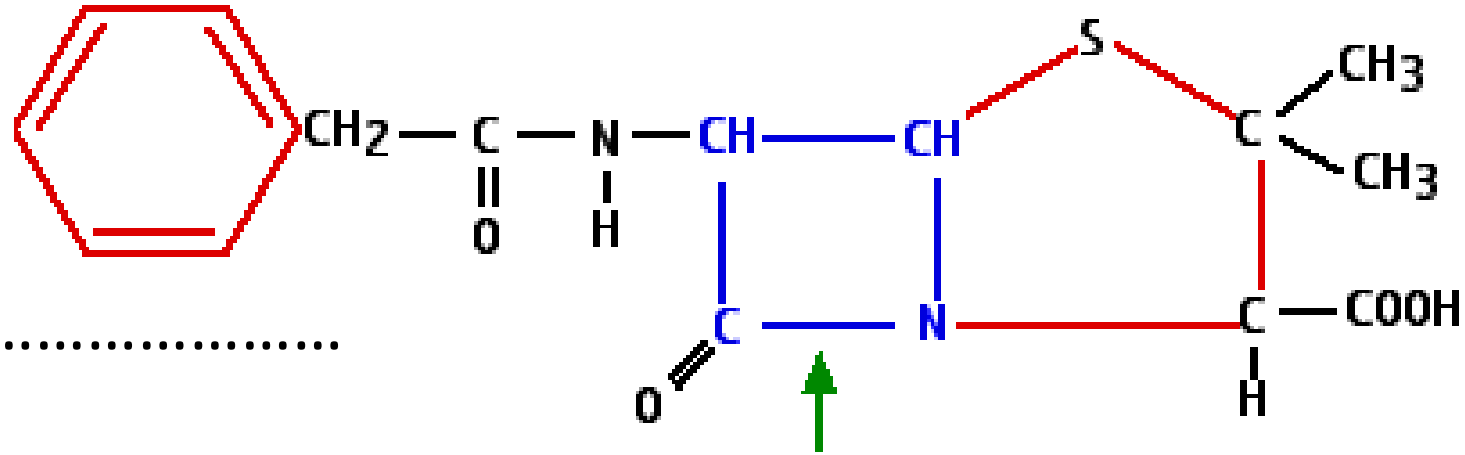
Mechanisms of action of antibiotics :

1. ……
2. ……
3. ……
4. ……

9. Connect

Polymyxins	Inhibition of Cell wall synthesis
Rifampicin	Inhibition Protein synthesis
Penicillin G	Inhibition of DNA synthesis
Tetracycline	Inhibition of Cell membrane function
Ciprofloxacin	Inhibition of mRNA synthesis

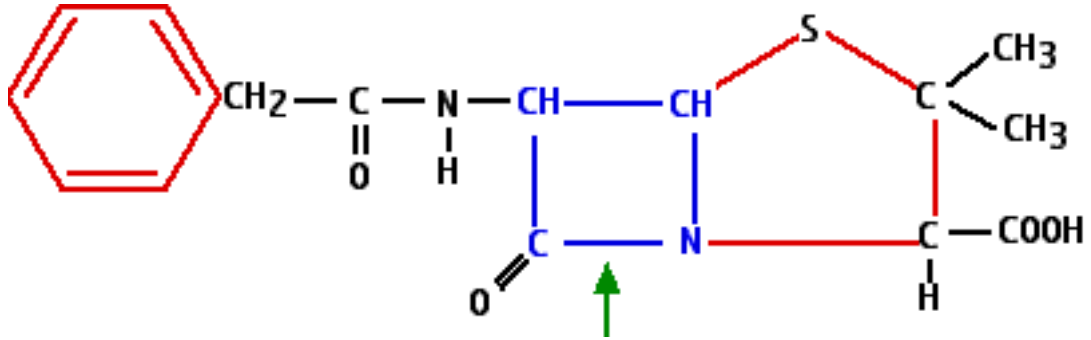
10. Study the following figure and select the correct answer:



The type of this antibiotic ……

- ☐ aminoglycoside,
- ☐ beta lactam antibiotic,
- ☐ tetracycline,
- ☐ vancomycin

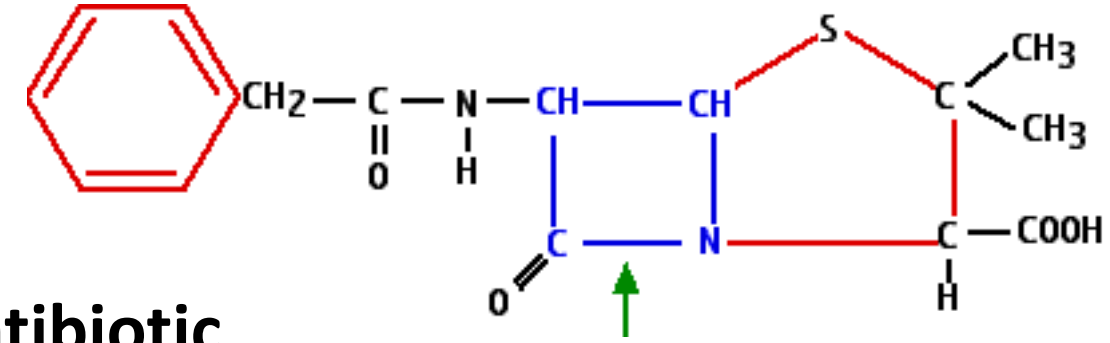
11. Study the following figure and select the correct answer:



This antibiotic act on ……

- ☐ Cell wall synthesis,
- ☐ Cell membrane function,
- ☐ Protein synthesis,
- ☐ Nucleic acid synthesis

12. Study the following figure and select the correct answer:



Bacteria can resist the action of this antibiotic through production of: _____

- ☐ Peptidase enzyme,
- ☐ Beta lactamase enzyme
- ☐ Acetyltransferase enzyme