General Microbiology Course
Lecture 9
(Antibiotics)
2

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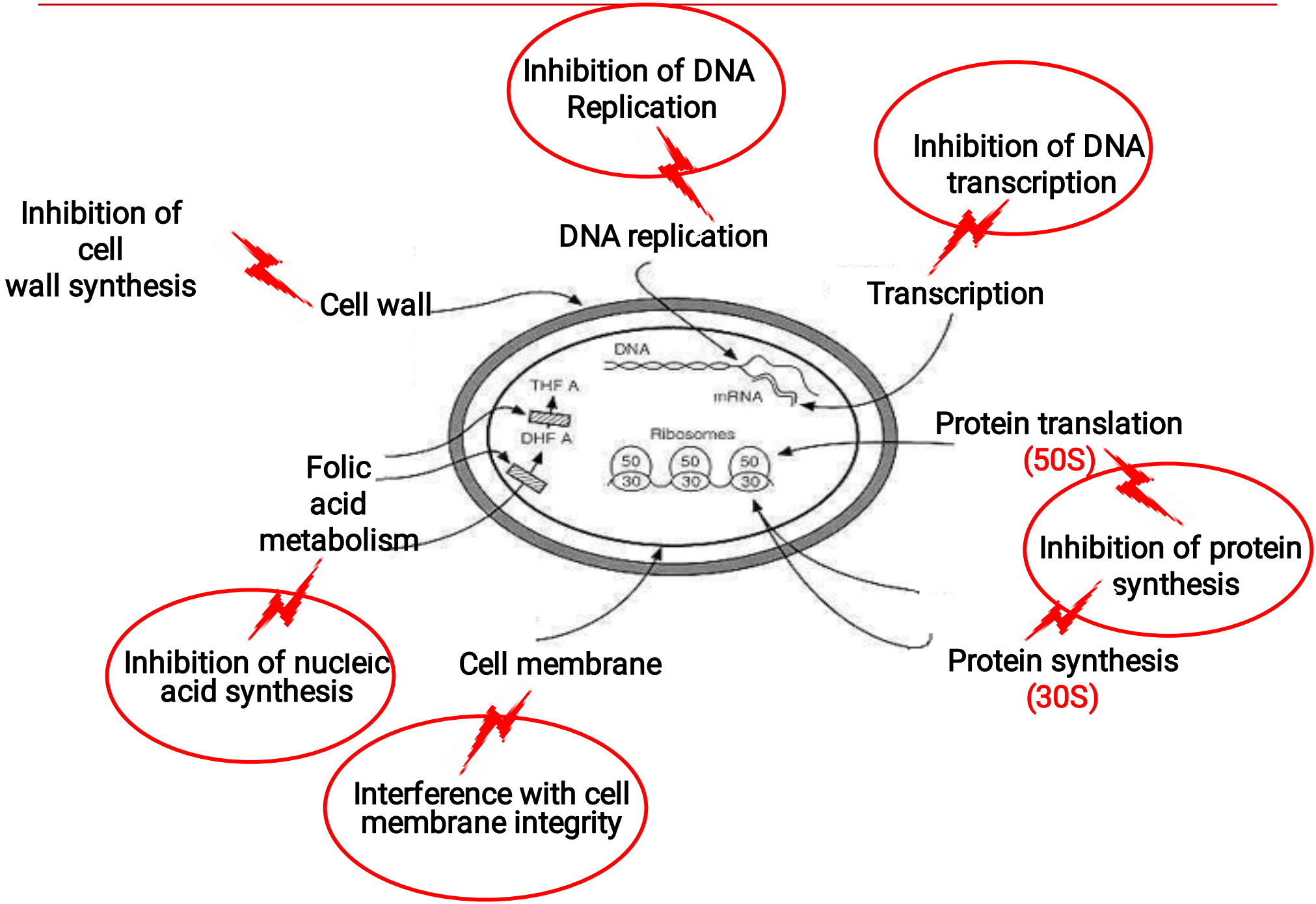
Mechanisms of Action of Antibacterial Drugs



Inhibition of protein synthesis

Antimicrobials that Bind to the 30S Ribosomal Subunit

Aminoglycosides

Streptomycin
Kanamycin
Gentamicin
Tobramycin
Amikacin
Netilmicin
Spectinomycin
neomycin (topical)

Tetracyclines

Minocycline
doxycycline

Inhibition of protein synthesis

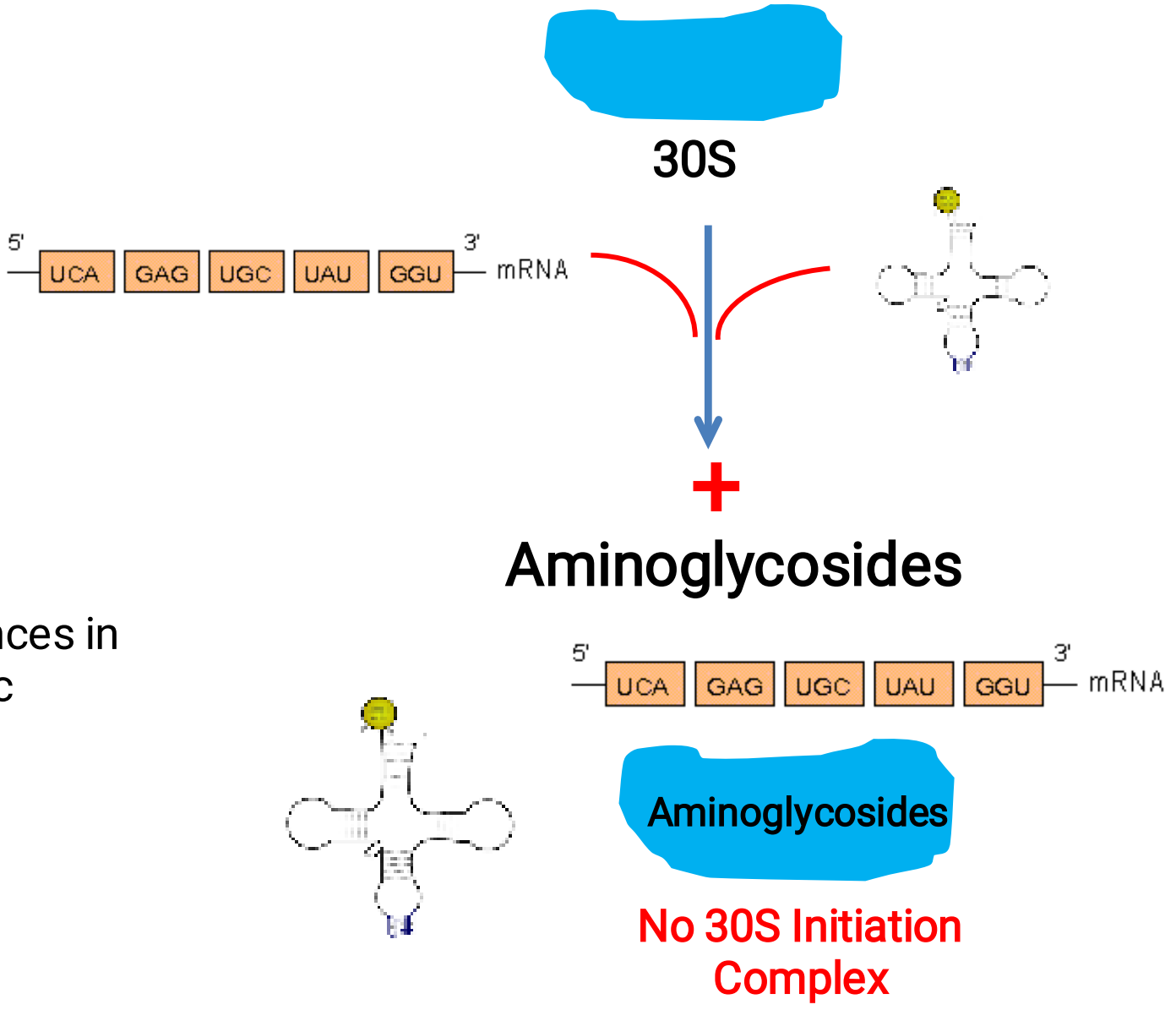
Antimicrobials that Bind to the 30S Ribosomal Subunit

Aminoglycosides

- They irreversibly bind to the 30S and eventually they will freeze the initiation complex (30S-mRNA-tRNA) so that no further initiation can occur.

-Selectivity due to differences in prokaryotic and eukaryotic ribosomes

-**Resistance** – Common



Inhibition of protein synthesis

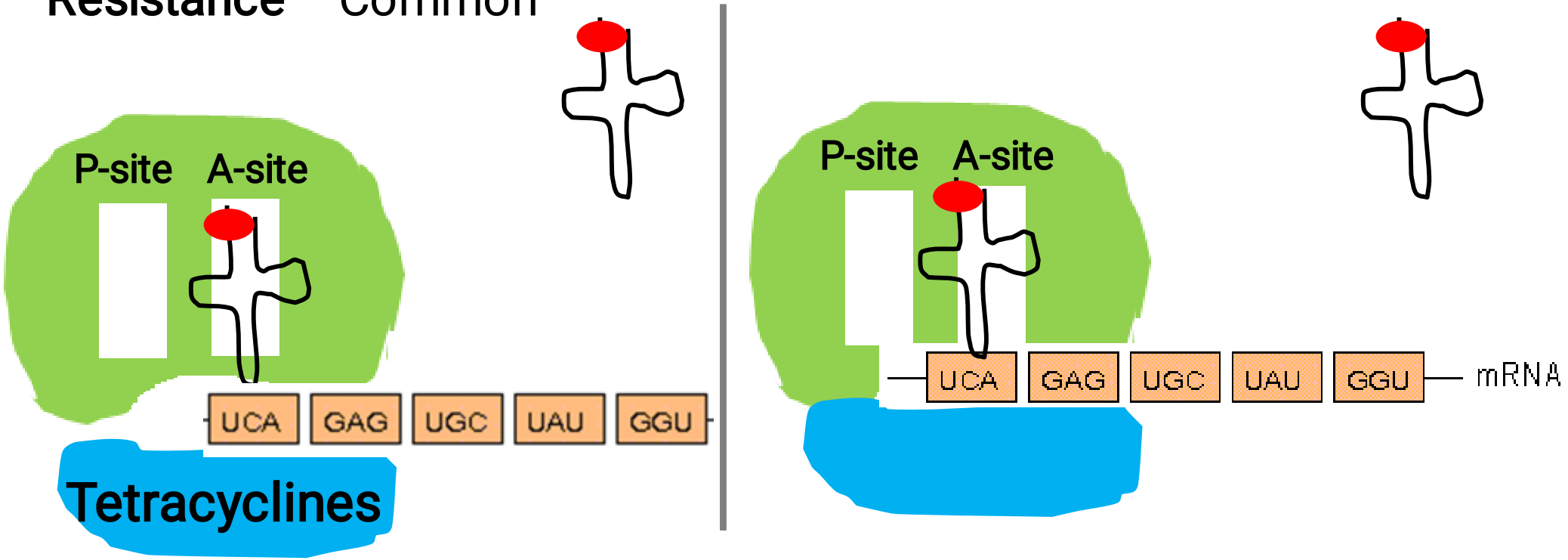
Antimicrobials that Bind to the 30S Ribosomal Subunit

Tetracyclines

Mode of action - The tetracyclines reversibly bind to the 30S ribosome and inhibit binding of aminoacyl-t-RNA to the acceptor site on the 70S ribosome.

Spectrum of activity - Broad spectrum; Useful against intracellular bacteria

Resistance – Common

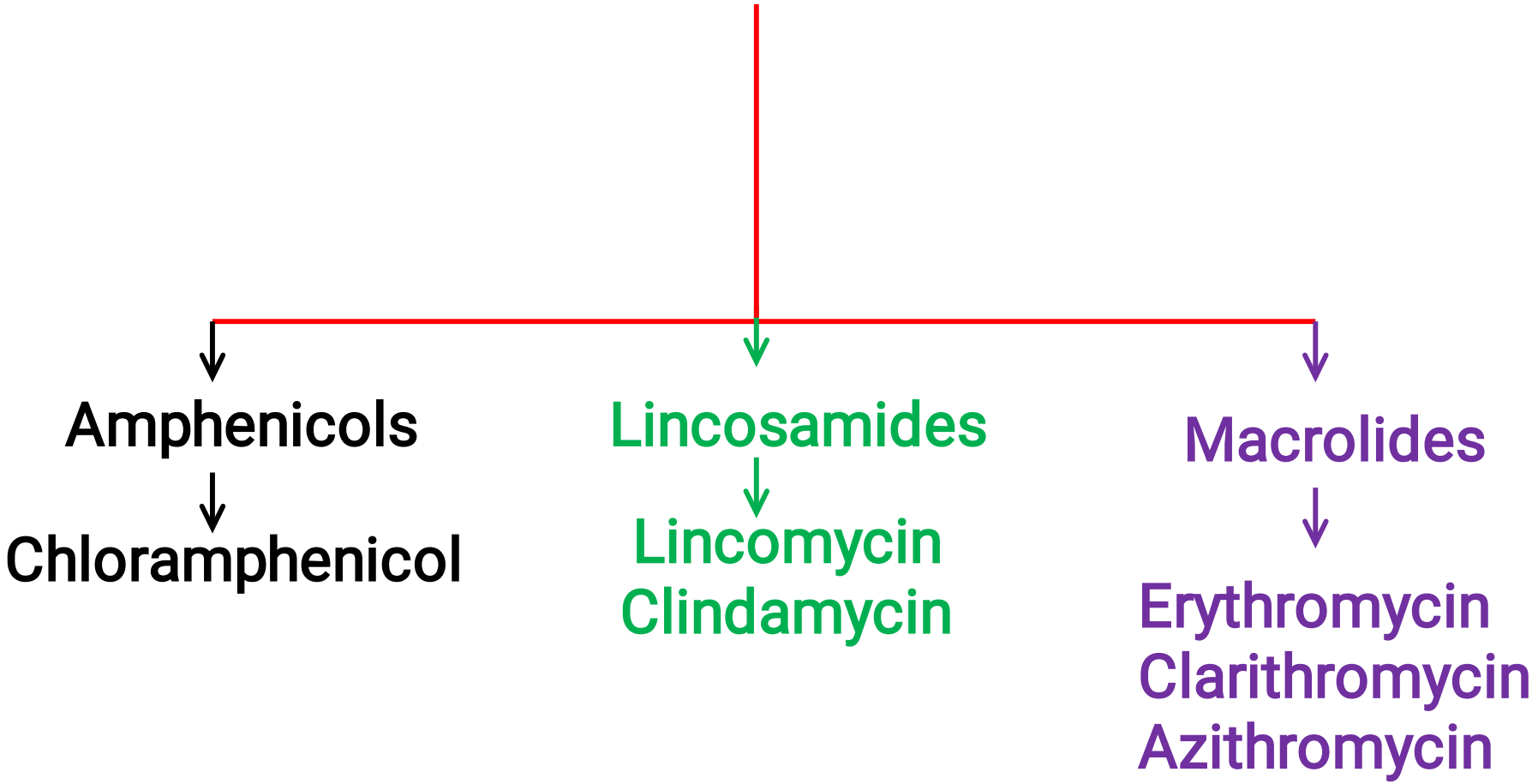


70S Initiation Complex

Antimicrobials that Bind to the 50S Ribosomal Subunit

Inhibition of protein synthesis

Antimicrobials that Bind to the 50S Ribosomal Subunit

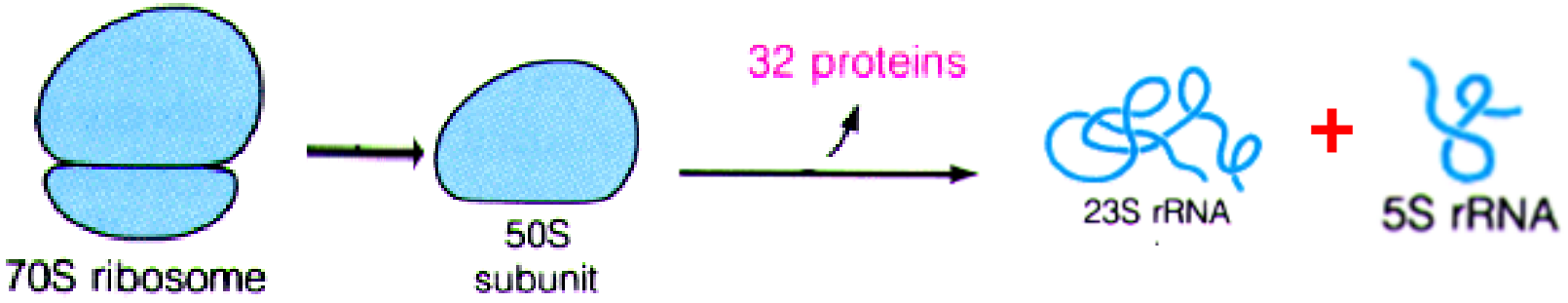


Inhibition of protein synthesis

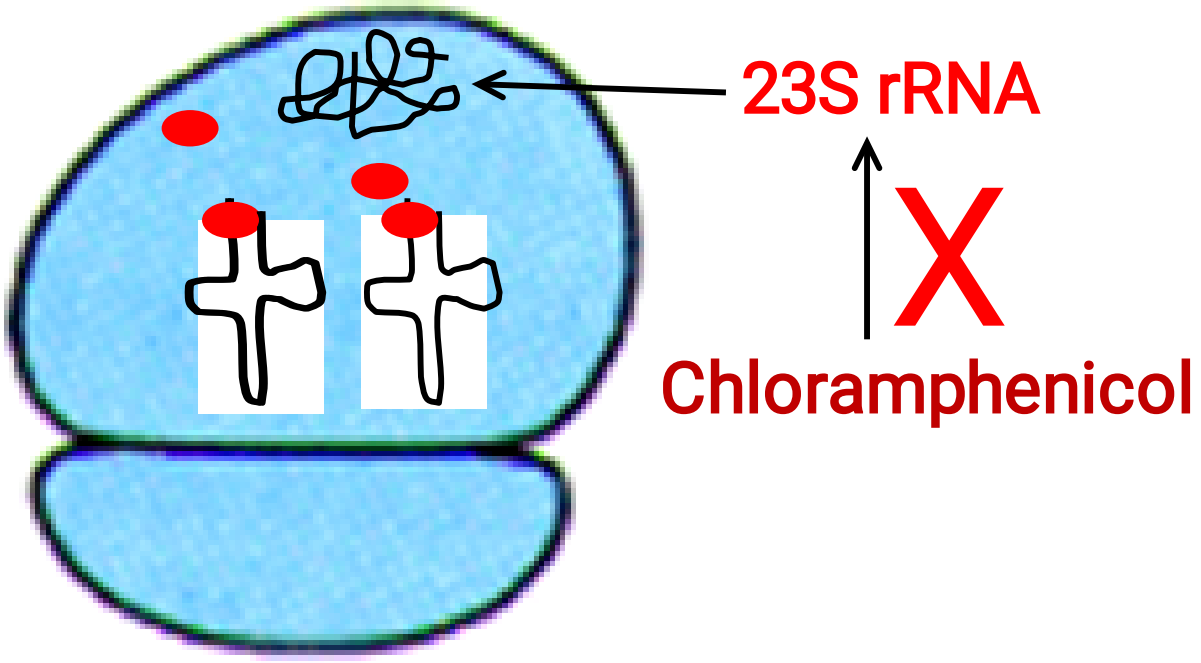
Antimicrobials that Bind to the 50S Ribosomal Subunit

Amphenicols and Lincosamides

Mode of action - These antimicrobials bind to the 50S ribosome and inhibit peptidyl transferase activity of the 23S rRNA.



- **Resistance** - Common

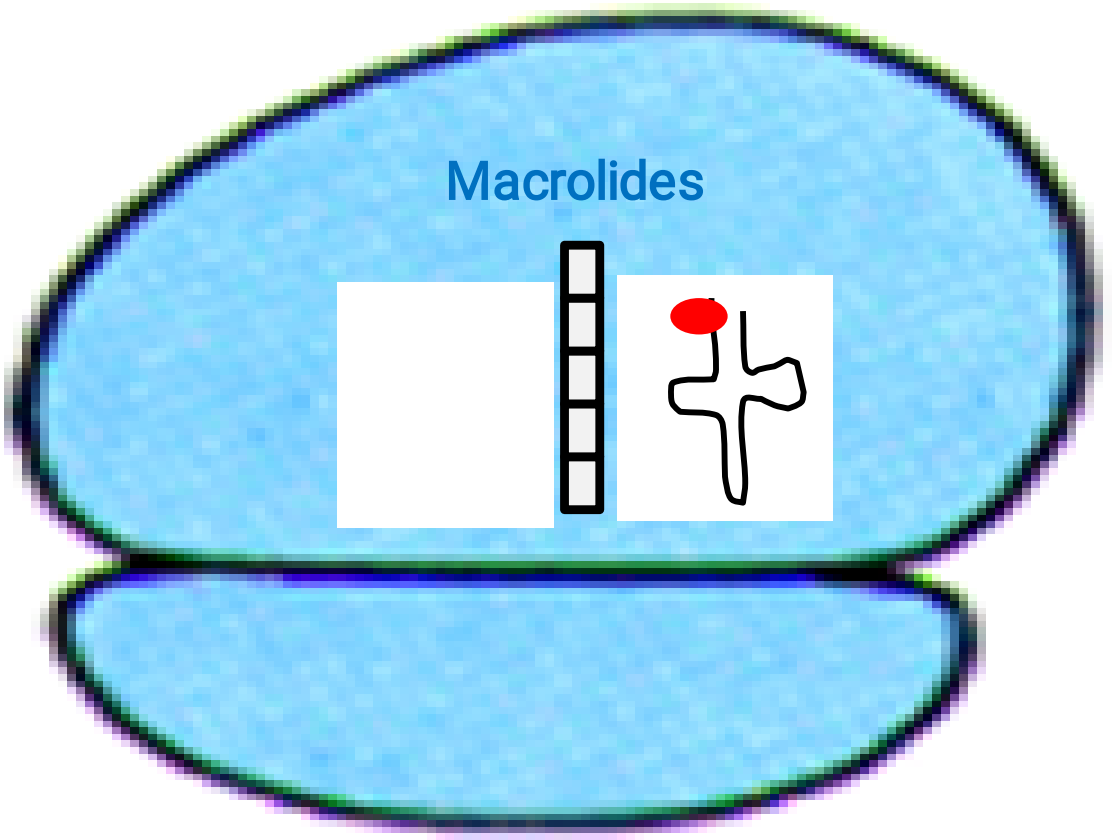


Inhibition of protein synthesis

Antimicrobials that Bind to the 50S Ribosomal Subunit

Macrolides :erythromycin, clarithromycin, azithromycin

- **Mode of action** - The macrolides inhibit translocation.
- **Spectrum of activity**: Gram-positive bacteria, *Mycoplasma, Legionella*
- **Resistance:** common



Inhibitors of RNA Synthesis

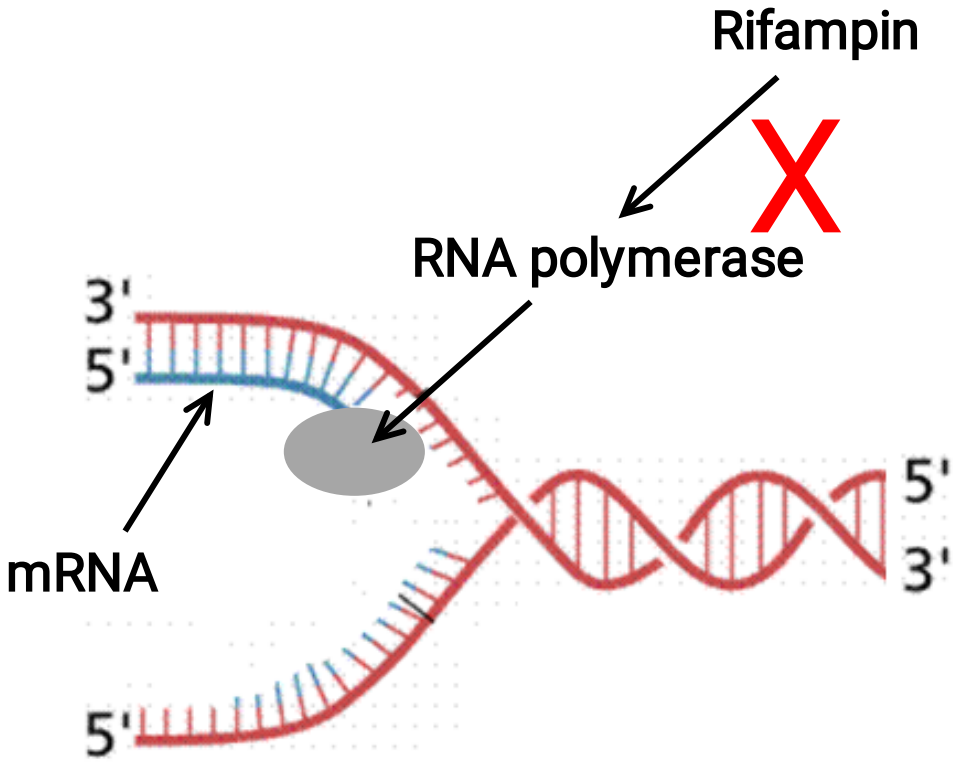
Rifamycins group:

Rifampin, Rifampicin, Rifabutin

Selectivity due to differences between prokaryotic and eukaryot RNA polymerase

Mode of action: these antimicrobials bind to DNA-dependent RNA polymerase and inhibit initiation of mRNA synthesis.

Resistance: Common



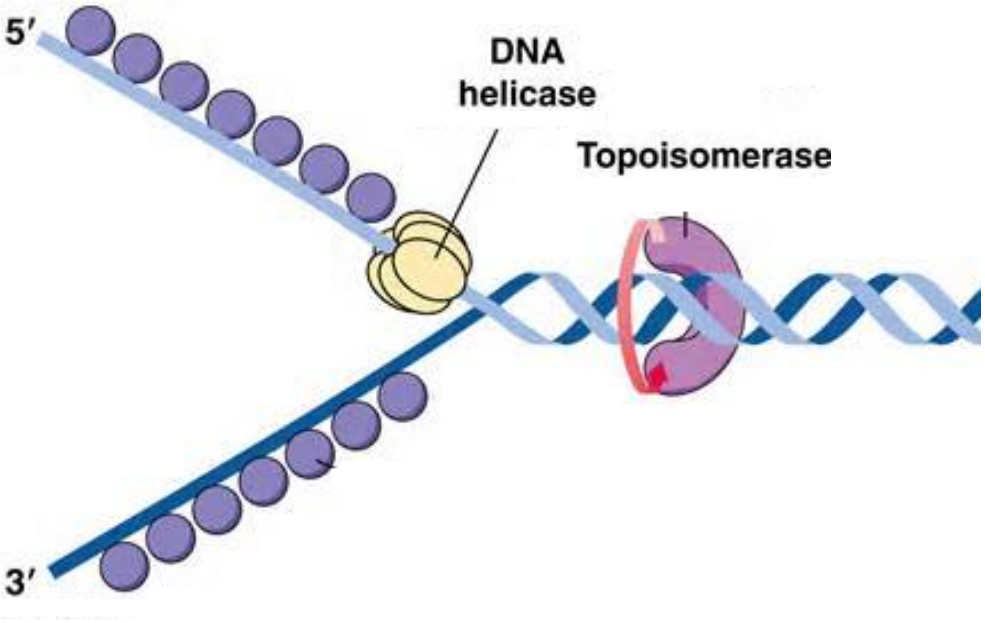
Inhibitors of DNA Synthesis

Fluoroquinolones:

nalidixic acid, ciprofloxacin, ofloxacin, norfloxacin, levofloxacin.

Mode of action - These antimicrobials bind to the A subunit of DNA gyrase (topoisomerase) and prevent supercoiling of DNA, thereby inhibiting DNA synthesis.

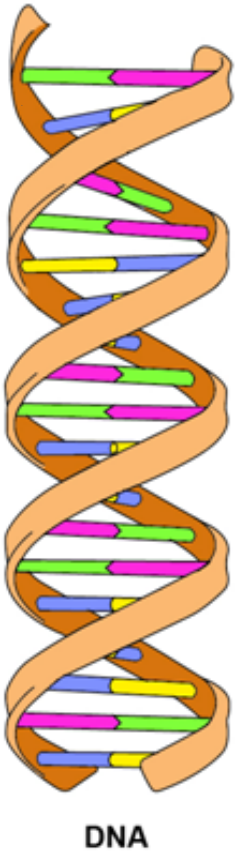
Resistance - Common for nalidixic acid



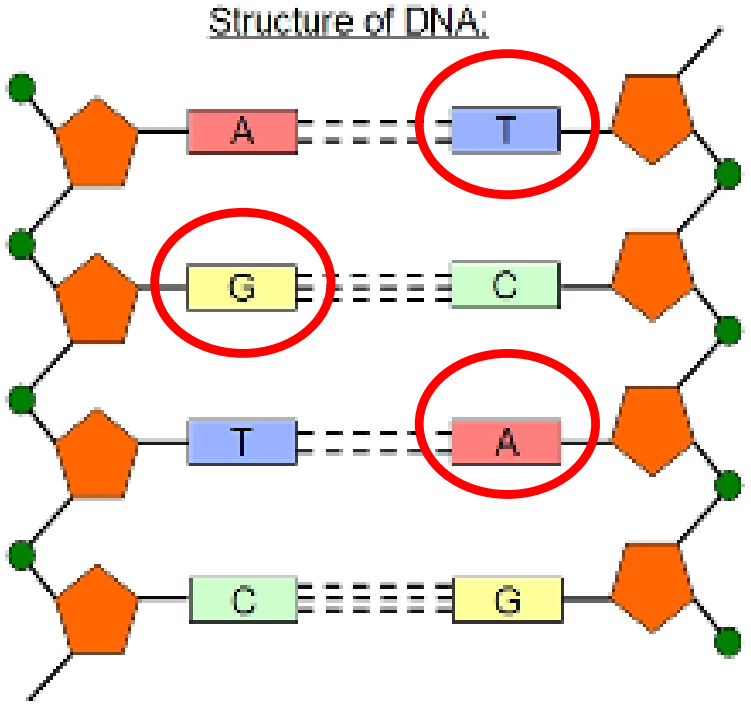
Inhibition of nucleic acid synthesis

Nucleic acid synthesis is inhibited by:

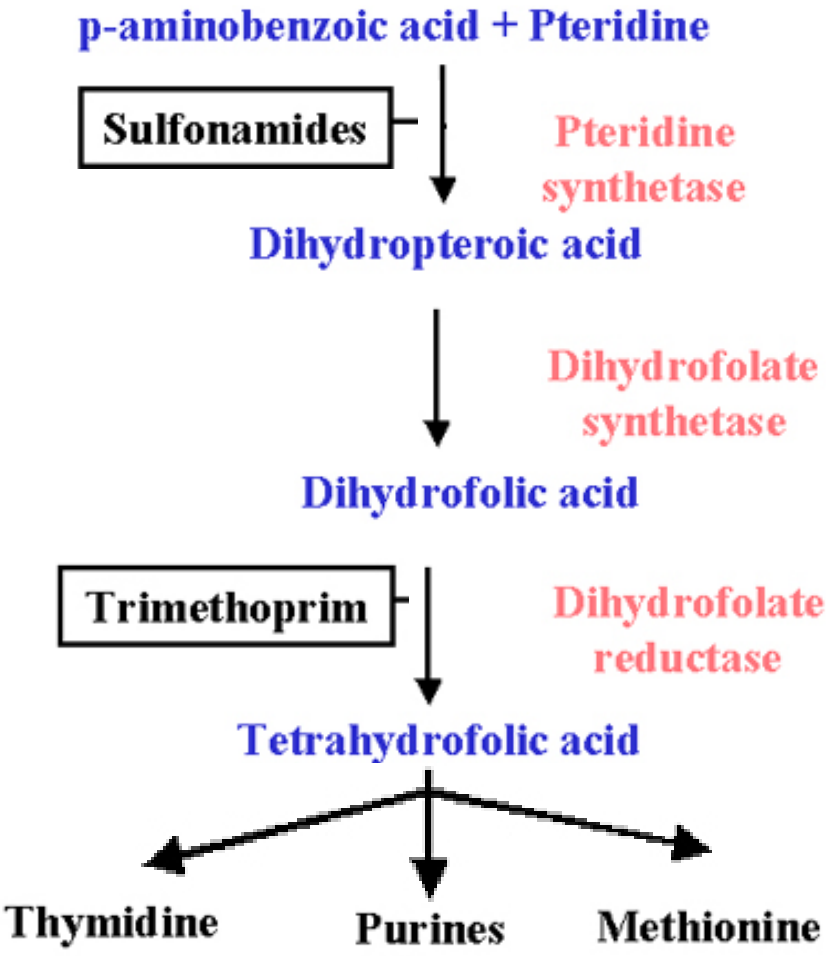
1. **Trimethoprim**
2. **Sulfonamide group:** Sulfamethoxazole, Sulfadiazine Sulfathiazole, Sulfamerazine



DNA



Purine: adenine & guanine
Pyrimidine: cytosine & thymine



(Amino Acid)

Interference with cell membrane integrity

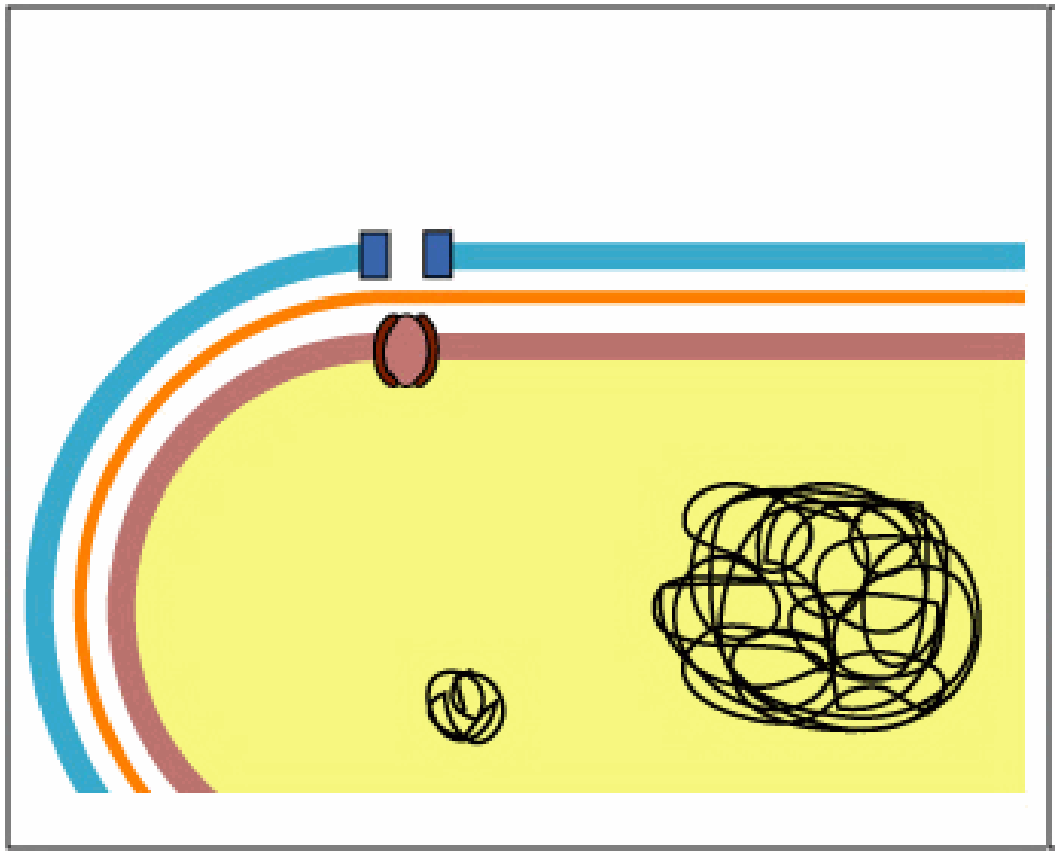
- Polymyxin B: binds to membrane of Gram negative bacteria and alters permeability
- This leads to leakage of cellular contents and cell death
- These drugs also bind to eukaryotic cells to some extent, which limits their use to topical applications

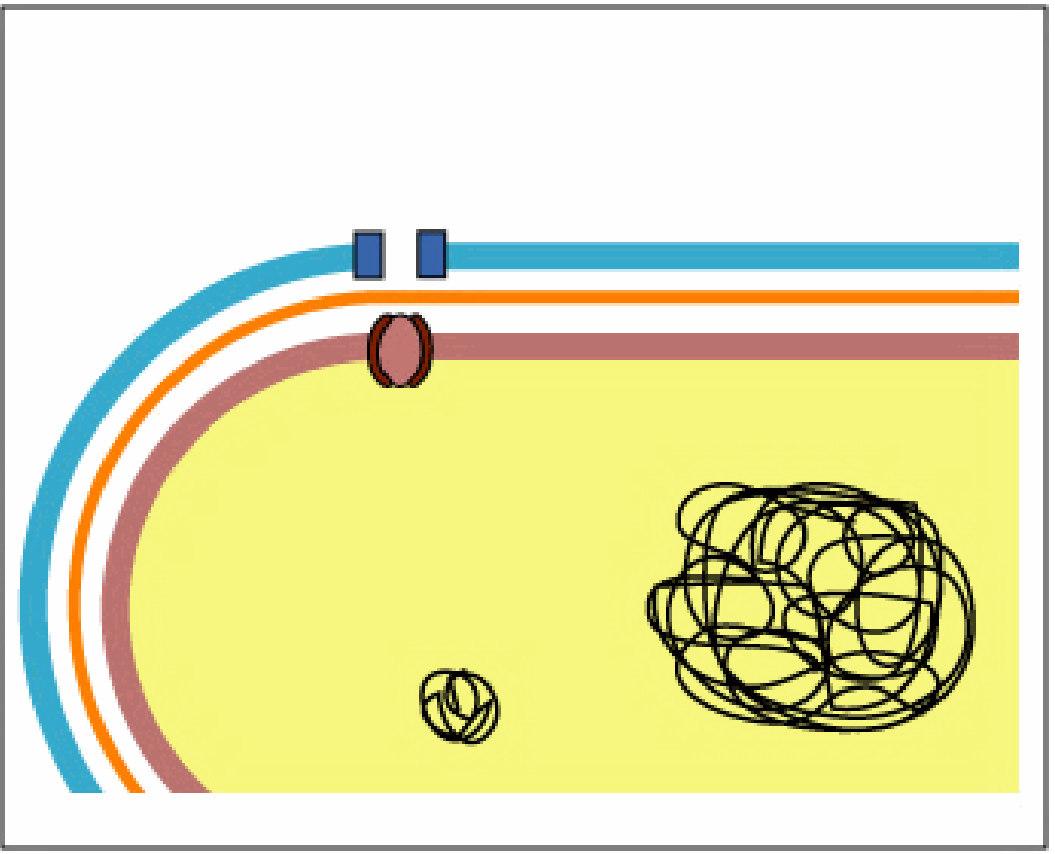
Antimicrobial Drug Resistance Principles and Definitions

- Resistance can arise by mutation or by gene transfer (*e.g.* acquisition of a plasmid)
- Resistance provides a selective advantage
- Resistance can result from single or multiple steps

Antimicrobial Drug Resistance Principles and Definitions

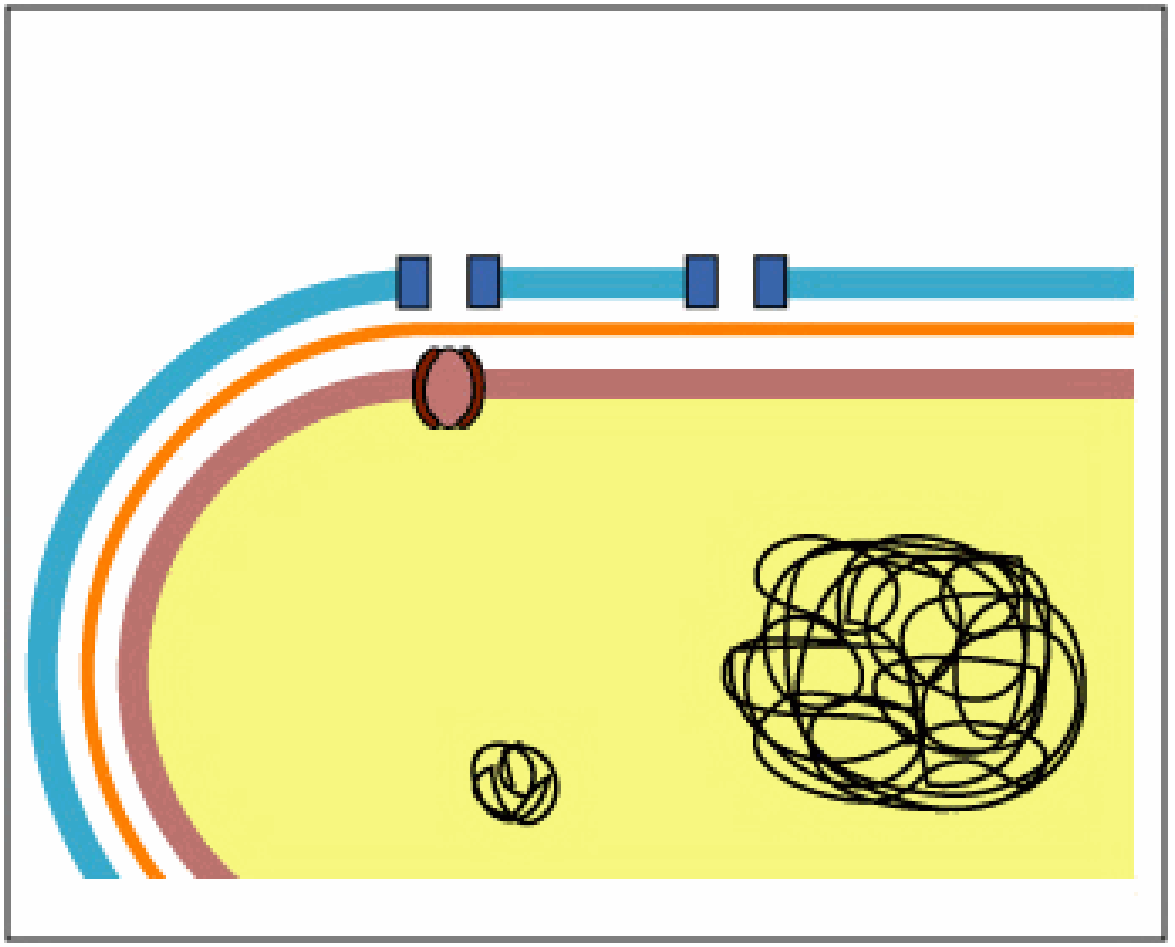
- Altered permeability
  - Altered influx
    - Gram negative bacteria





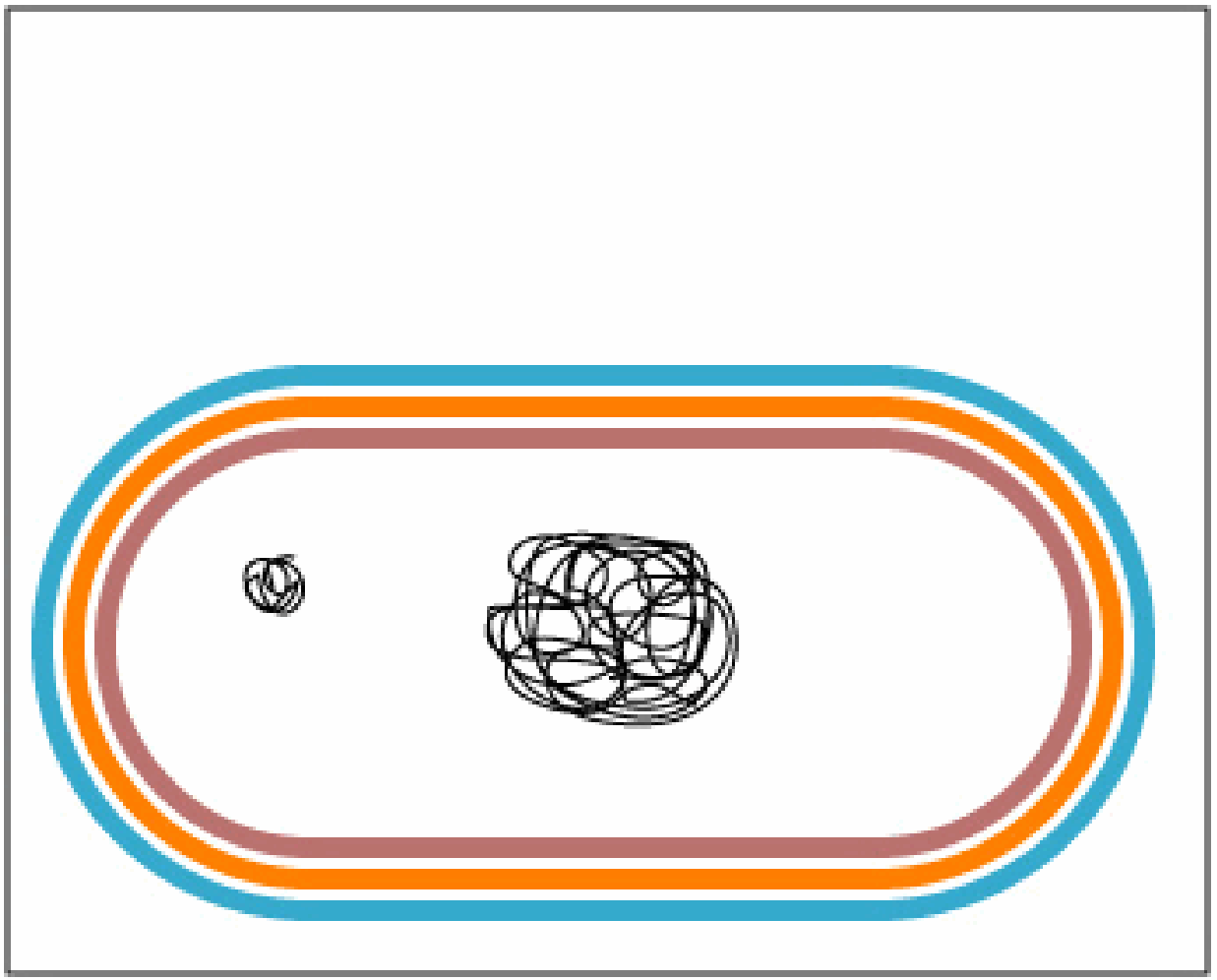
Antimicrobial Drug Resistance Principles and Definitions

- Altered permeability
  - Altered efflux
    - tetracycline



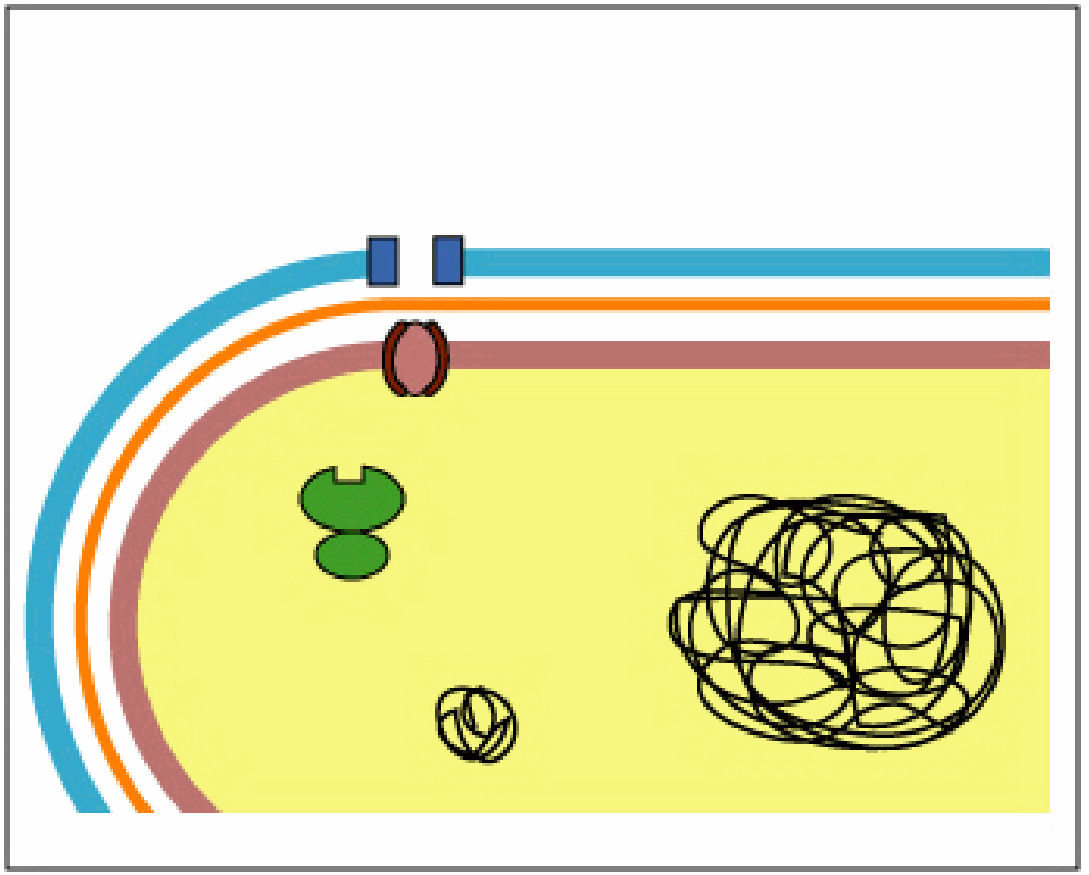
Antimicrobial Drug Resistance Principles and Definitions

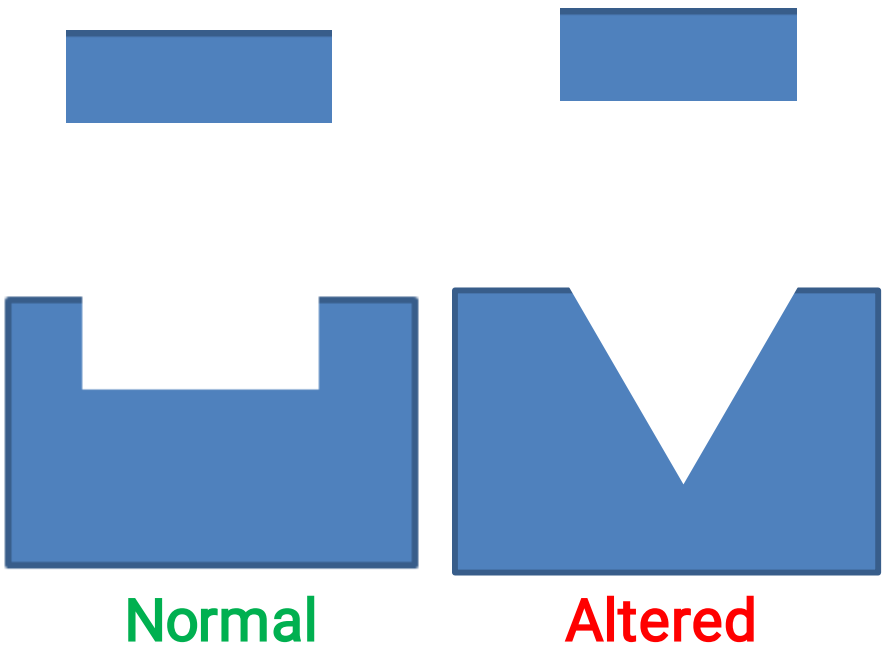
- Inactivation
  - Beta-lactamase



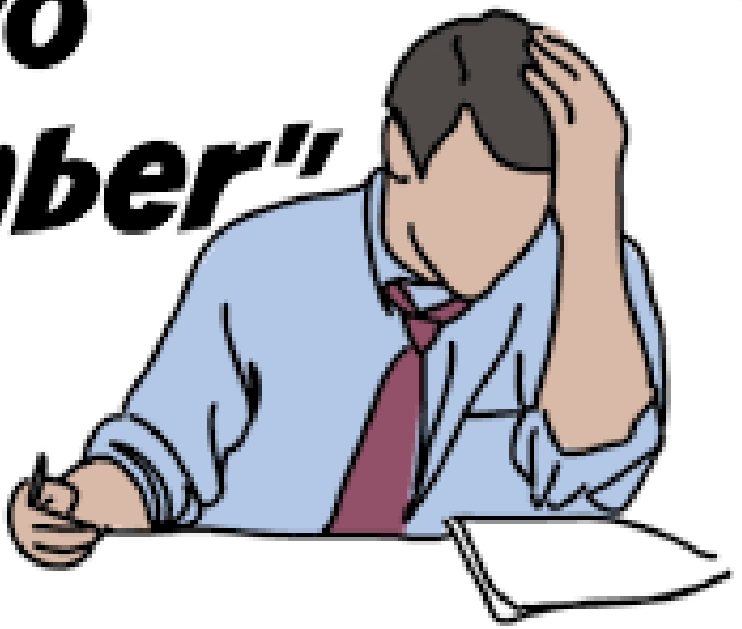
Antimicrobial Drug Resistance Principles and Definitions

- Altered target site
  - Penicillin binding proteins
  - RNA polymerase
  - 30S ribosome

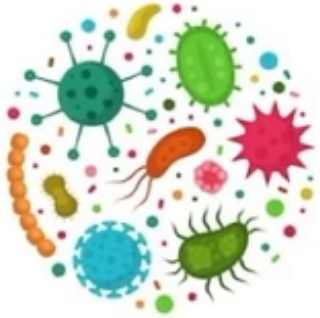




"How to Remember"



Antibiotic Classes



- Mnemonic to remember main antibiotic classes
- Tricks to remember the names of antibiotics in each class
- Trick to remember gram coverage of each antibiotic class.
- Trick to remember mechanism of action of each antibiotic class.

Antibiotic Classes

Mnemonic	Groups	Medication Names	Gram Coverage	Mechanism of Action
Antibiotics	Aminoglycosides	Streptomycin Gentamicin	Gram (-)	Inhibit Protein Synthesis (30s)
Can	Cephalosporins	Ceftriaxone Cefepime	Gram (+)/(-)	Inhibit Cell Wall Synthesis
Terminate	Tetracyclines	Tetracycline Doxycycline	Gram (+)/(-)	Inhibit Protein Synthesis (30s)
Protein	Penicillins	Ampicillin Amoxicillin	Gram (+)/(-)	Inhibit Cell Wall Synthesis
Synthesis	Sulfonamides	Sulfasalazine Sulfamethoxazole	Gram (+)/(-)	Inhibit Folate Synthesis
For	Fluoroquinolones	Ciprofloxacin Levofloxacin	Gram (+)/(-)	Inhibit DNA Replication
Microbial	Macrolides	Azithromycin Erythromycin	Gram (+)	Inhibit Protein Synthesis (50s)
Cells	Carbapenems	Meropenem Ertapenem	Gram (+)/(-)	Inhibit Cell Wall Synthesis
Like	Lincosamides	Clindamycin	Gram (+)	Inhibit Protein Synthesis (50s)
Germs	Glycopeptides	Vancomycin	Gram (+)	Inhibit Cell Wall Synthesis

Antibiotics classes Mnemonic

Antibiotic **C**an **T**erminate **P**rotein **S**ynthesis **F**or **M**icrobial **C**ells **L**ike **G**erms

1. **A**minoglycosides
2. **C**ephalosporins
3. **T**etracyclines
4. **P**enicillins
5. **S**ulfonamides
6. **F**luoroquinolones
7. **M**acrolides
8. **C**arbapenems
9. **L**incosamides
10. **G**lycopeptides

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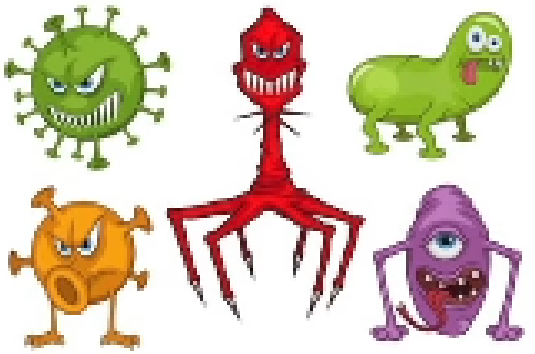
Germs	Glycopeptides	Vancomycin	Gram (+)	Inhibit Cell Wall Synthesis

Antibiotics classes Medication Names

1. Aminoglycosides	• Mycin
2. Cephalosporins	• Cef/Ceph
3. Tetracyclines	• Cylines
4. Penicillins	• Cillins
5. Sulfonamides	• Sulfa
6. Fluoroquinolones	• Floxacin
7. Macrolides	• Thromycii
8. Carbapenems	• Penem
9. Lincosamides	• Mycin
10. Glycopeptides	• In (Mycin)



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Cells	Carbapenems	Meropenem Ertapenem	Gram (+)/(-)	Inhibit Cell Wall Synthesis
Like	Lincosamides	Clindamycin	Gram (+)	Inhibit Protein Synthesis (50s)
Germs	Glycopeptides	Vancomycin	Gram (+)	Inhibit Cell Wall Synthesis

Antibiotics classes

Gram Coverage

1. AmiNoglycosides
2. Cephalosporins
3. Tetracyclines
4. Penicillins
5. Sulfonamides
6. Fluoroquinolones
7. Macrolides
8. Carbapenems
9. Lincosamides
10. Glycopeptides

1. Gram (-)=NO
2. Gram (+)(-)
3. Gram (+)(-)
4. Gram (+)(-)
5. Gram (+)(-)
6. Gram (+)(-)
7. Gram (+)
8. Gram (+)(-)
9. Gram (+)
10. Gram (+)

G L A M

Glycopeptides
Lincosamides
AmiNoglycosides
Macrolides

Antibiotic Classes

Mnemonic	Groups	Medication Names	Gram Coverage	Mechanism of Action
Antibiotics	Aminoglycosides	Streptomycin Gentamicin	Gram (-)	Inhibit Protein Synthesis (30s)
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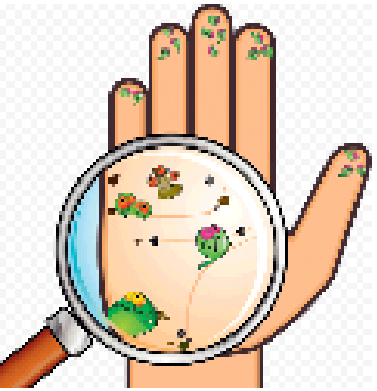
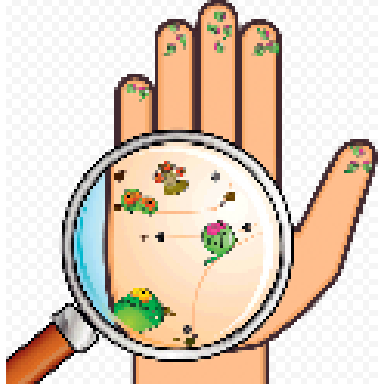


Antibiotics classes

Mechanism of Action



1. Aminoglycosides	1. Inhibits Protein Synthesis	P
2. Cephalosporins	2. Inhibits Cell Wall Synthesis	C
3. Tetracyclines	3. Inhibits Protein Synthesis	P
4. Penicillins	4. Inhibits Cell Wall Synthesis	C
5. SulFOnamide	5. Inhibits Folate = Letters FoF	
6. Fluoroquinolones	6. Inhibits DNA Replication	D
7. Macrolides	7. Inhibits Protein Synthesis	P
8. Carbapenems	8. Inhibits Cell Wall Synthesis	C
9. Lincosamides	9. Inhibits Protein Synthesis	P
10. Glycopeptides	10. Inhibits Cell Wall Synthesis	C

MALT

Macrolides
Aminoglycosides
Lincosamides
Tetracyclines

↓

Inhibits Protein Synthesis

Queen Elizabeth Fears DNA Test Could Damage British Monarchy?

Examples

- Doxycycline
- Meropenem
- Sulfamethoxazole

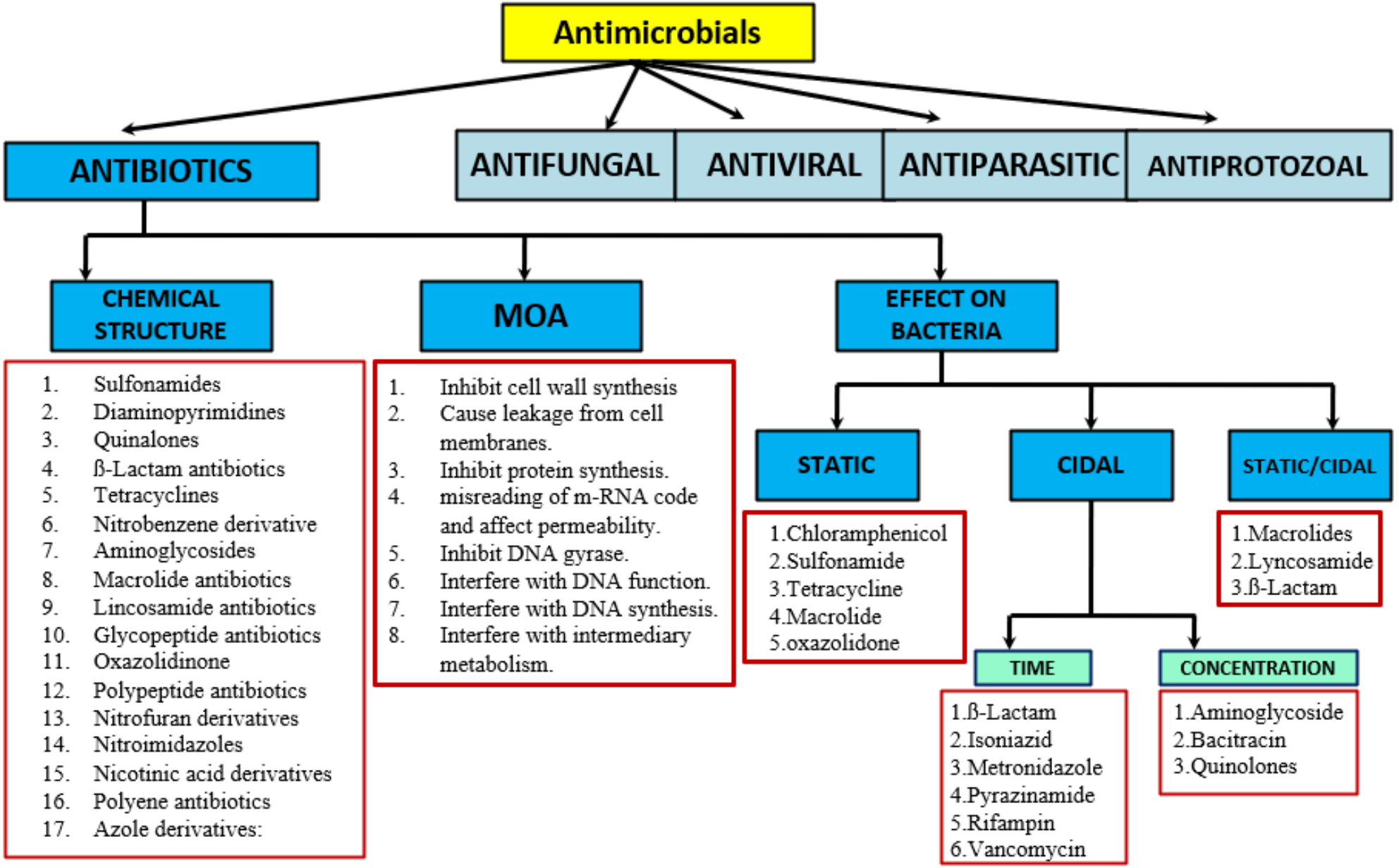
MALT Inhibits Protein Synthesis

G L A M Gram (+) Gram (-)

Mnemonic	Groups	Medication Names	Gram Coverage	Mechanism of Action
Antibiotic				
Can				
Terminate	Tetracycline	Doxycycline	Gram (+)(-)	Inhibits Protein Synthesis
Protein				
Synthesis	SulFOnamide	Sulfamethoxazole	Gram (+)(-)	Inhibits Folate
For				
Microbial				
Cells	Carbapenem	Meropenem	Gram (+)(-)	Inhibits Cell Wall Synthesis
Like				
Germs				

Antibiotic Classes

Antibiotics	Aminoglycosides	Streptomycin Gentamicin	Gram (-)	Inhibit Protein Synthesis (30s)	Bacteremia, Abdominal Infections
Can	Cephalosporins	Ceftriaxone Cefepime	Gram (+)/(-)	Inhibit Cell Wall Synthesis	Skin, Urinary, Resp. Infections
Terminate	Tetracyclines	Tetracycline Doxycycline	Gram (+)/(-)	Inhibit Protein Synthesis (30s)	Lyme Disease, PID, STIs
Protein	Penicillins	Ampicillin Amoxicillin	Gram (+)/(-)	Inhibit Cell Wall Synthesis	ENT, Skin, Urinary Infections
Synthesis	Sulfonamides	Sulfasalazine Sulfamethoxazole	Gram (+)/(-)	Inhibit Folate Synthesis	UTIs, Burns, Eye Infections
For	Fluoroquinolones	Ciprofloxacin Levofloxacin	Gram (+)/(-)	Inhibit DNA Replication	Respiratory & Urinary Infections
Microbial	Macrolides	Azithromycin Erythromycin	Gram (+)	Inhibit Protein Synthesis (50s)	Pneumonia, Sinus, ENT, STIs
Cells	Carbapenems	Meropenem Ertapenem	Gram (+)/(-)	Inhibit Cell Wall Synthesis	Urinary, Abdom. Infections
Like	Lincosamides	Clindamycin	Gram (+)	Inhibit Protein Synthesis (50s)	Skin, Bone, Lung Infections
Germs	Glycopeptides	Vancomycin	Gram (+)	Inhibit Cell Wall Synthesis	MRSA, Skin, Endocarditis


Antimicrobials
ANTIBIOTICS
ANTIFUNGAL
ANTIVIRAL
ANTIPARASITIC
ANTIPROTOZOAL
CHEMICAL STRUCTURE
MOA
EFFECT ON BACTERIA
1. Sulfonamides
2. Diaminopyrimidines
3. Quinalones
4. ß-Lactam antibiotics
5. Tetracyclines
6. Nitrobenzene derivative
7. Aminoglycosides
8. Macrolide antibiotics
9. Lincosamide antibiotics
10. Glycopeptide antibiotics
11. Oxazolidinone
12. Polypeptide antibiotics
13. Nitrofuran derivatives
14. Nitroimidazoles
15. Nicotinic acid derivatives
16. Polyene antibiotics
17. Azole derivatives:
1. Inhibit cell wall synthesis
2. Cause leakage from cell membranes.
3. Inhibit protein synthesis.
4. misreading of m-RNA code and affect permeability.
5. Inhibit DNA gyrase.
6. Interfere with DNA function.
7. Interfere with DNA synthesis.
8. Interfere with intermediary metabolism.
STATIC
CIDAL
STATIC/CIDAL
1.Chloramphenicol
2.Sulfonamide
3.Tetracycline
4.Macrolide
5.oxazolidone
1.Macrolides
2.Lyncosamide
3.ß-Lactam
TIME
CONCENTRATION
1.ß-Lactam
2.Isoniazid
3.Metronidazole
4.Pyrazinamide
5.Rifampin
6.Vancomycin
1.Aminoglycoside
2.Bacitracin
3.Quinolones