Technical session VI

Antimicrobial Resistance

Speaker

Dr Tenzin Wangchuk

Deputy Chief Veterinary Officer
National Veterinary Hospital

JOIN US

Venue: NVH Conference Hall
Date and time: 26/09/25 at 3:15pm

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for a live session

Royal Government of Bhutan
Department of Livestock
National Veterinary Hospital

Antimicrobial Resistance (AMR)

Dr. Tenzin Wangchuk

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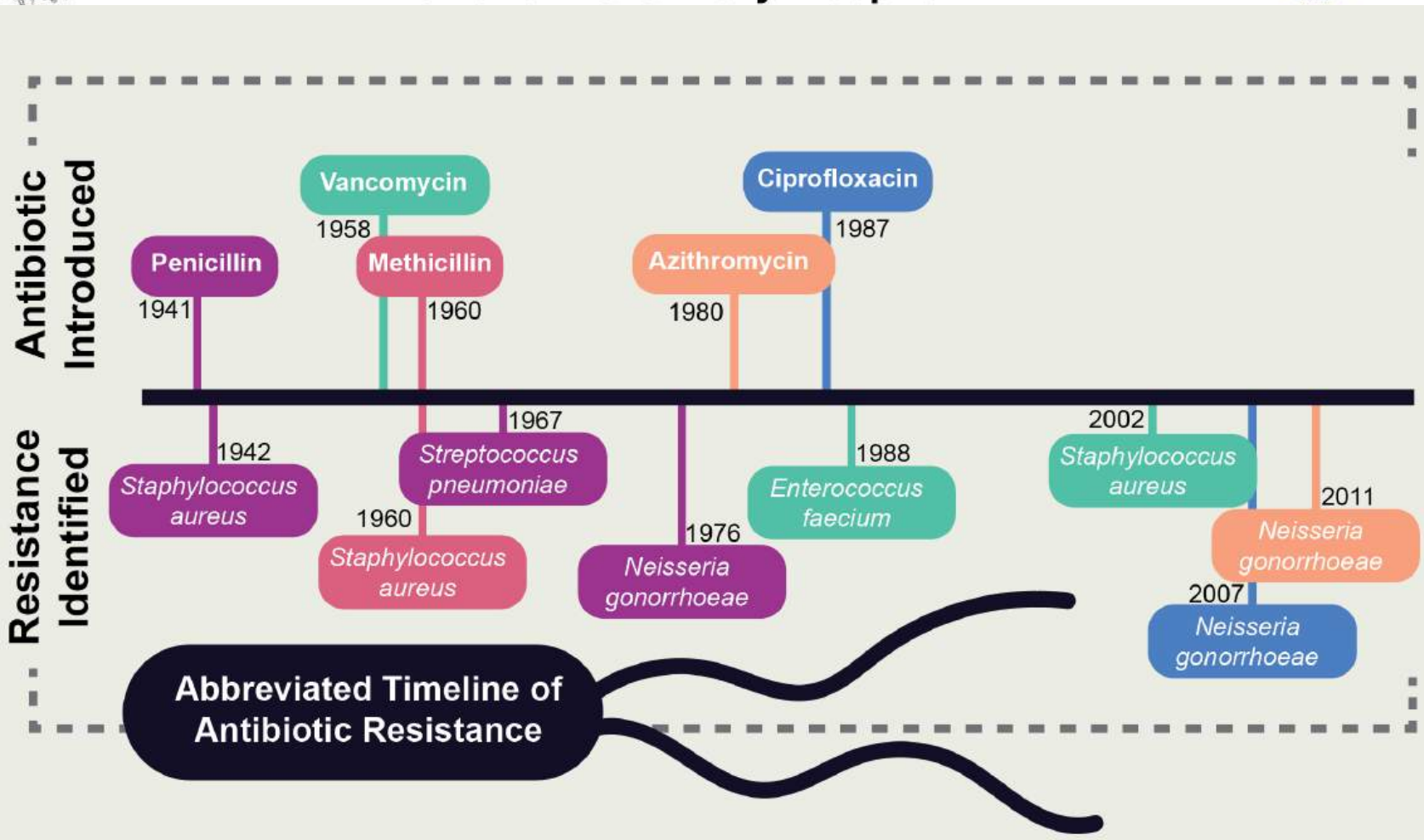


What is AMR?

- AMR occurs when microorganisms no longer respond to medicines
- Leads to treatment failure, prolonged illness, higher mortality
- A One Health challenge affecting humans, animals, and environment

Global Context

- By 2050, AMR could cause 10 million deaths annually (WHO)
- Major economic loss in livestock and food security
- A 'silent pandemic' threatening progress in health and agriculture

AMR in Bhutan

- Bhutan has recognized AMR as a national priority
- National AMR Action Plan (2018–2022; updated 2025)
- Surveillance in livestock via Veterinary Information System (VIS)
- Common antibiotics: Benzathine Penicillin, Enrofloxacin, Amoxicillin, Oxytetracycline
- Challenges: overuse, under-dosing, withdrawal period non-compliance

Drivers of AMR in Animals

- Overuse/misuse of antibiotics without lab confirmation
- Empirical treatment
- Incorrect dosing or duration
- Poor farm biosecurity and hygiene
- Lack of awareness among farmers and Prescribers
- Lack/Poor infection control (IPC)

Consequences of AMR

- Poor treatment response in animals
- Increased cost of treatment
- Risk of zoonotic transmission
- Trade barriers & food safety issues
- Threatens Bhutan’s livestock sustainability

Antimicrobial Stewardship

AMS Objectives

1. Improving Patient Outcomes

2. Reducing AMR

3. Optimizing Cost

4. Infection Prevention and Control

5. Minimize Adverse Effects

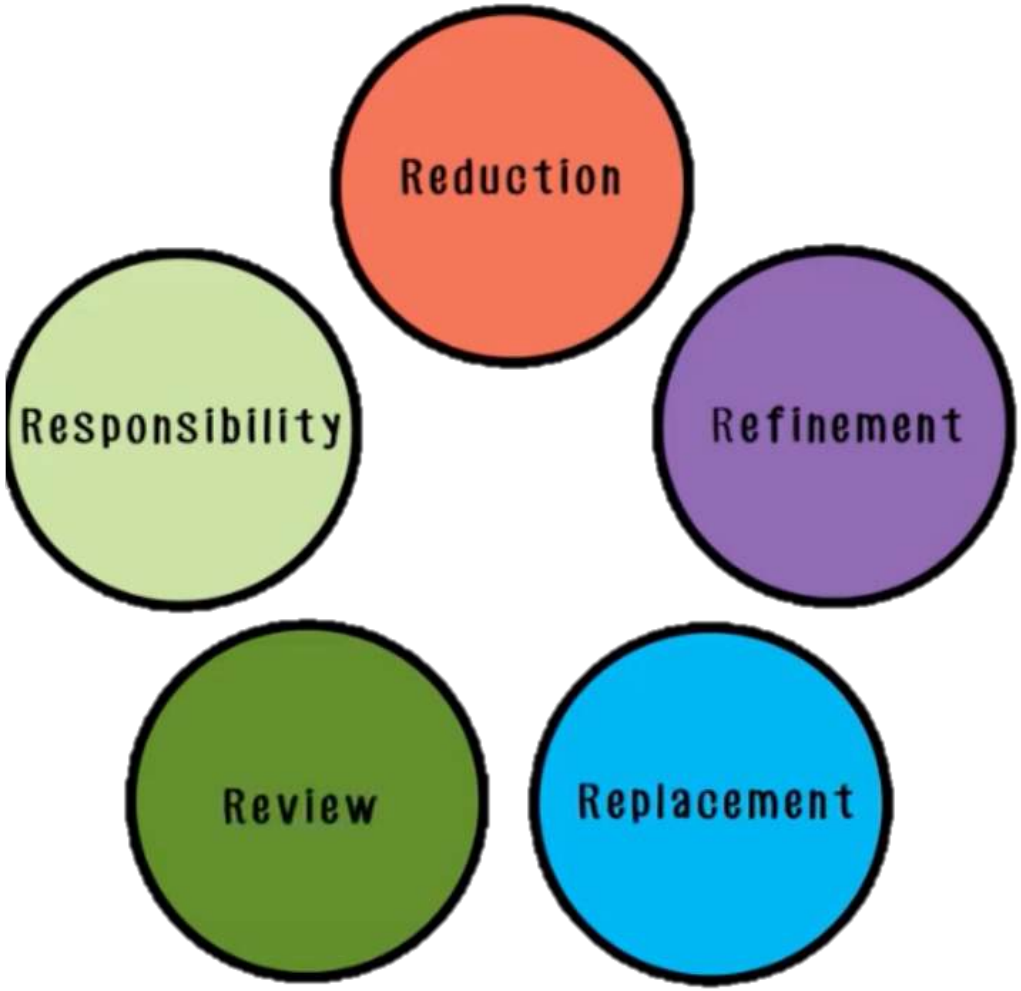
Guiding principles for AMS

1. Education
2. Utilization of guidelines and judicious antimicrobial use
3. Prescription auditing and feedback
4. Delayed prescription
5. Antimicrobial restriction
6. Diagnostic testing
7. Biosecurity

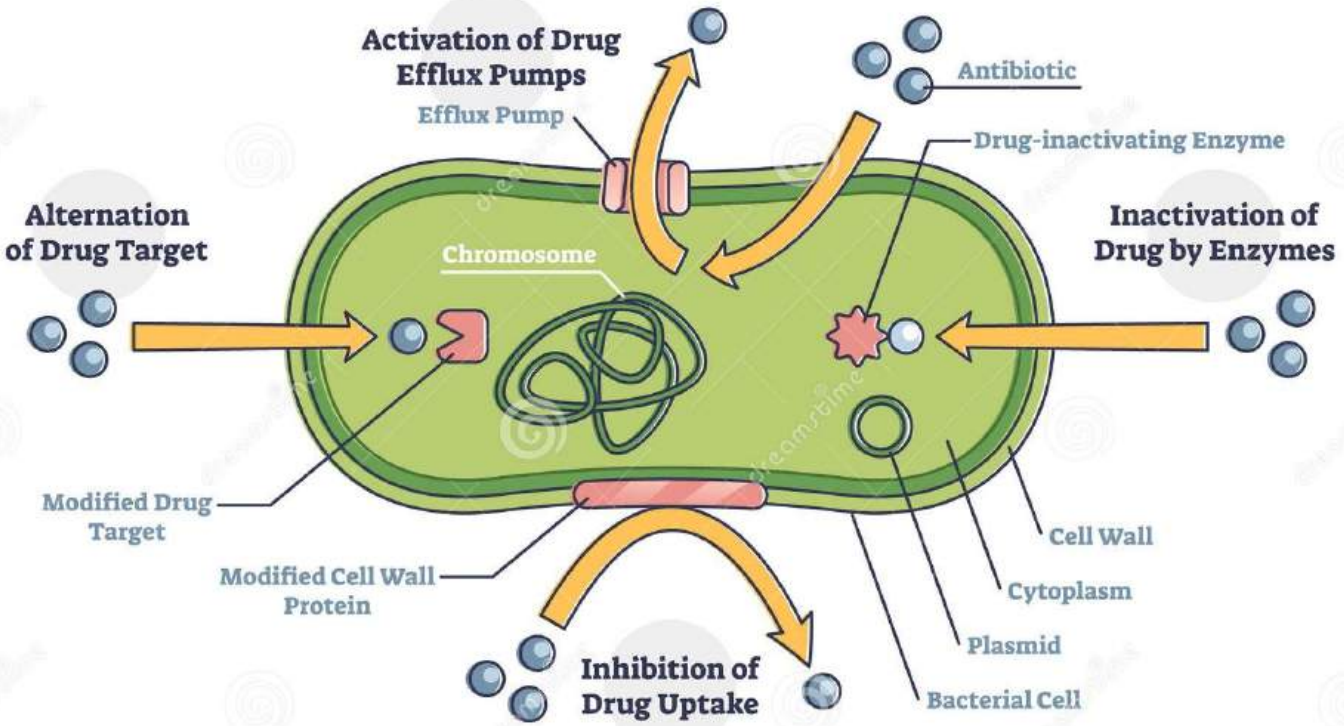
Responsible Use of Antimicrobials

- Five Rs of responsible use:
- 1. Right Drug
- 2. Right Dose
- 3. Right Duration
- 4. Right Route
- 5. Right Reason

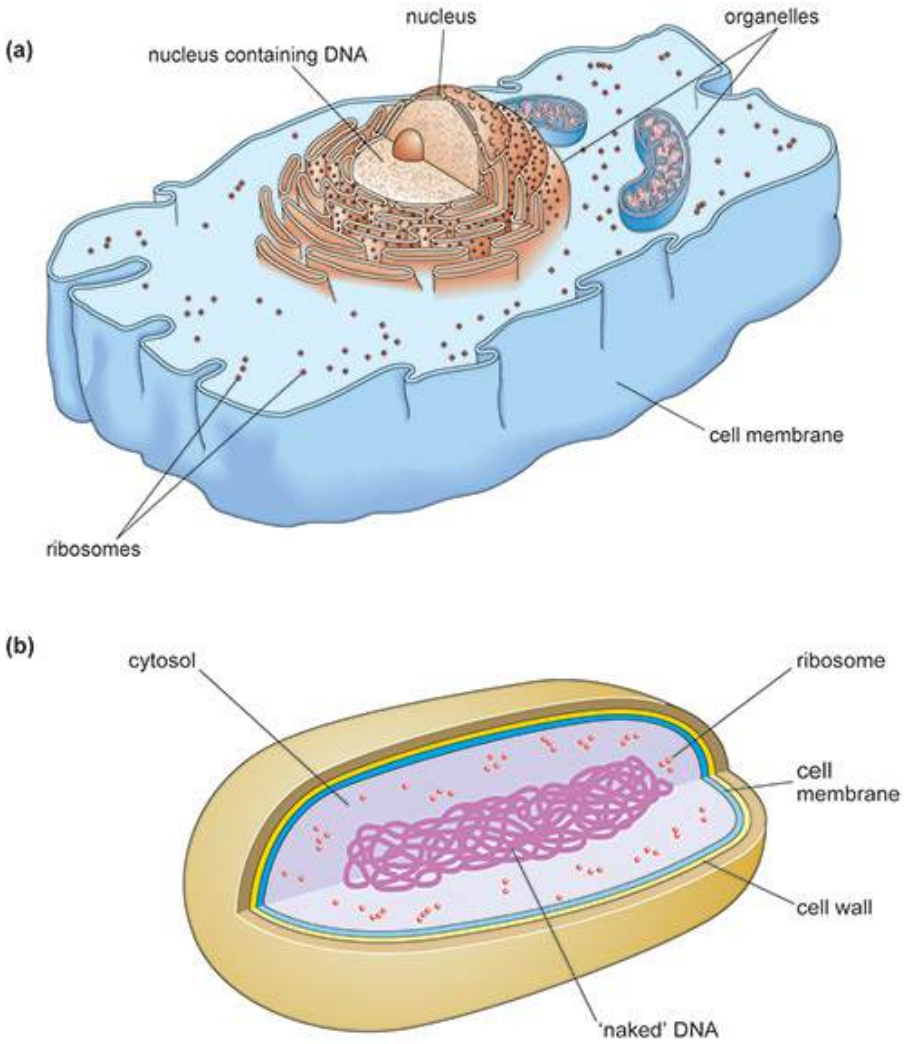
Antimicrobial Stewardship framework (5Rs)



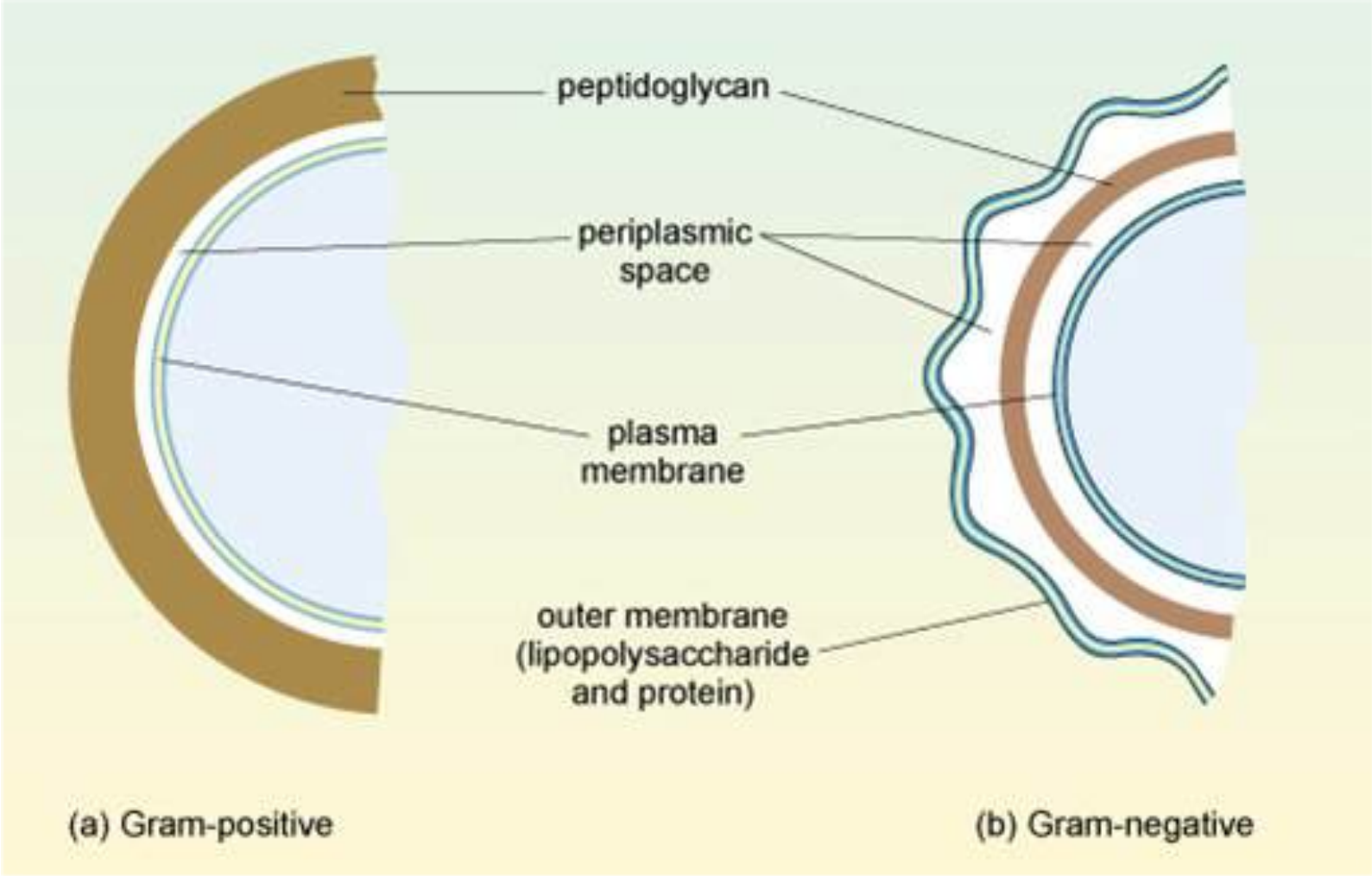
MECHANISMS
OF ANTIBIOTIC RESISTANCE



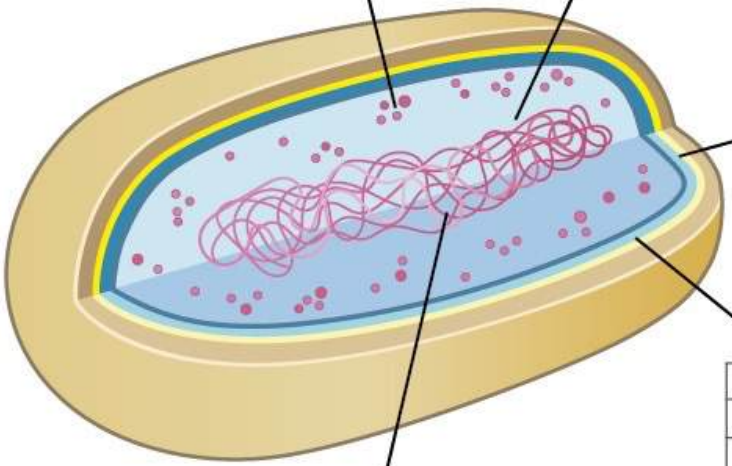
Selective toxicity



Gram-positive and Gram-negative bacteria



1. Antibiotic mode of action



Protein synthesis	
TARGET	**ANTIBIOTIC**
Small ribosome subunit	Aminoglycosides
Large ribosome subunit	Oxazolidinones

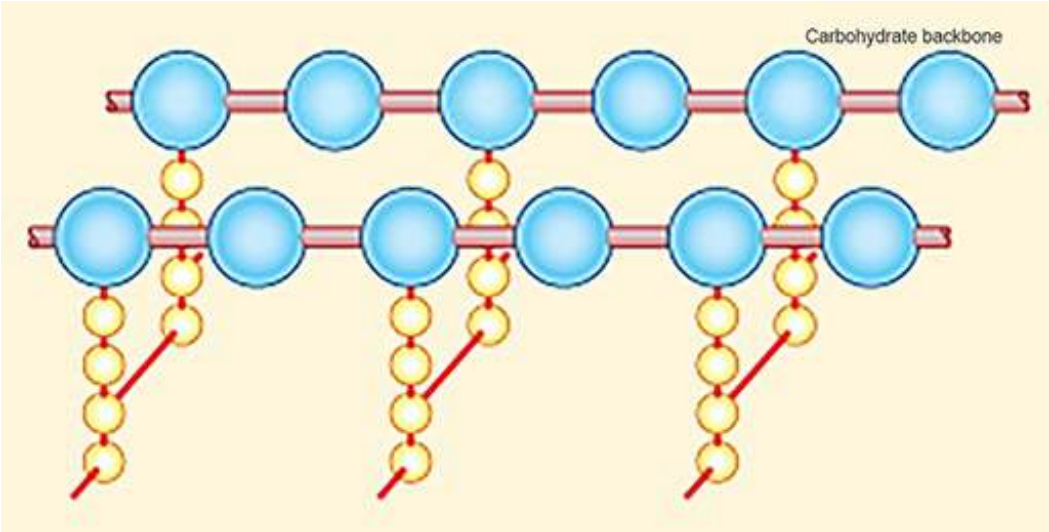
Metabolic reactions	
TARGET	**ANTIBIOTIC**
Folic acid synthesis	Trimethoprim

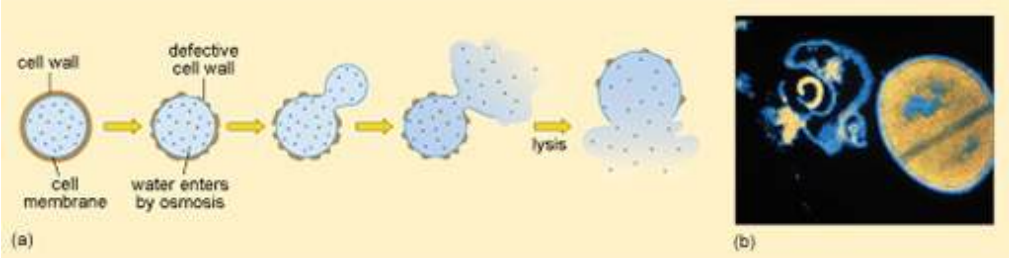
Cell membrane disruptors	
TARGET	**ANTIBIOTIC**
Gram-negative outer membrane and cell membrane	Polymyxins
Gram-positive cell membrane	Daptomycin

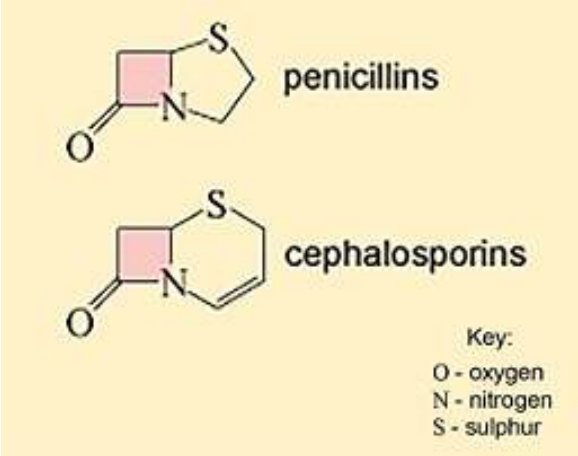
Cell wall synthesis	
TARGET	**ANTIBIOTIC**
Peptidoglycan cross-linking	β-lactams: penicillins cephalosporins

Nucleic acid synthesis	
TARGET	**ANTIBIOTIC**
Enzymes which unwind DNA	Fluoroquinolones
RNA polymerase	Rifamycins

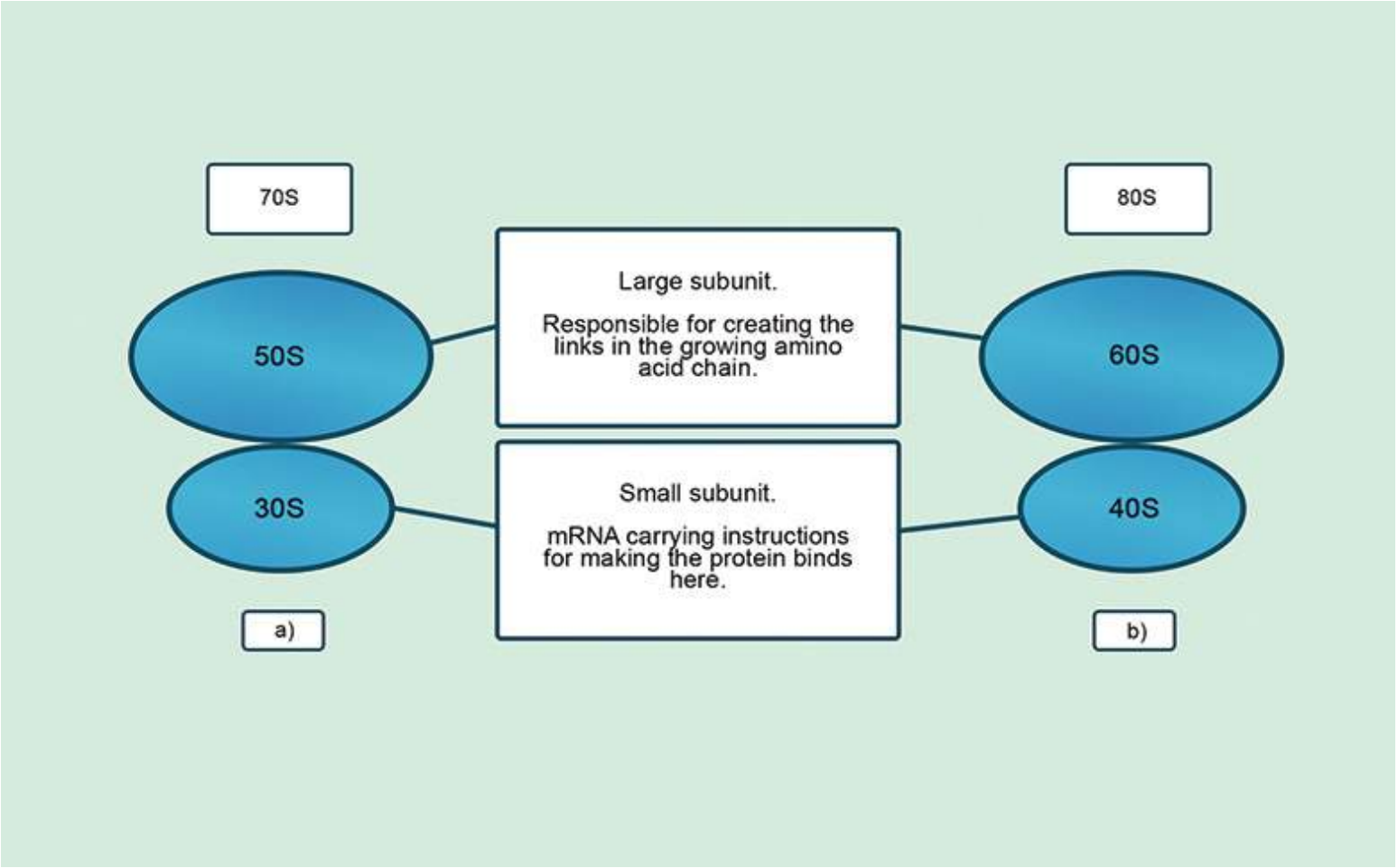
1.1. Inhibitors of Cell Wall Synthesis





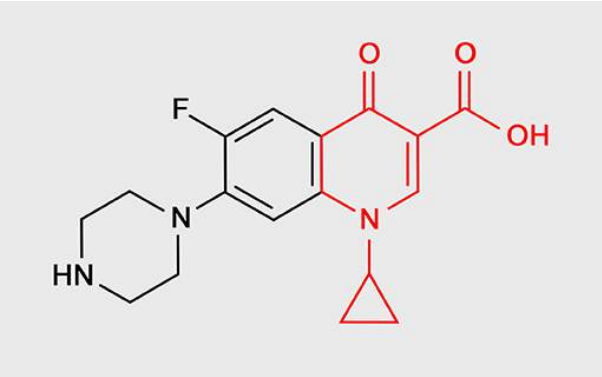


1.2. Inhibitors of Protein Synthesis



1.3. Inhibitors of Nucleic Acid Synthesis

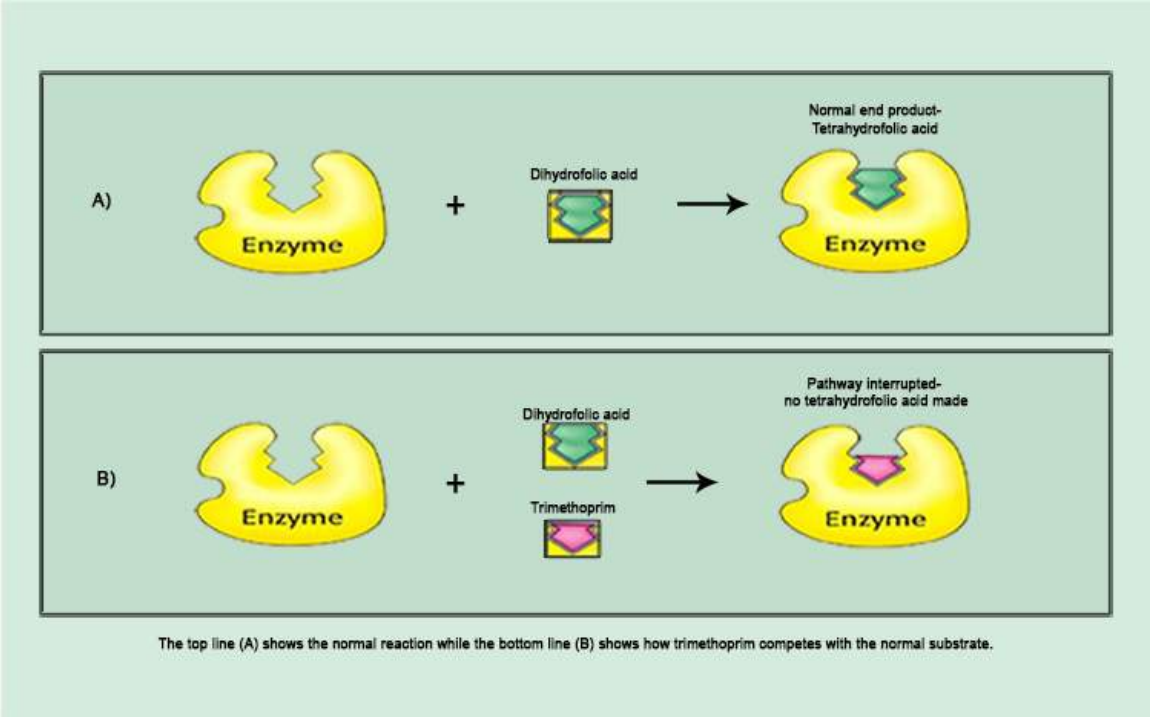
- Fluoroquinolones such as ciprofloxacin and levofloxacin specifically inhibit bacterial enzymes that unwind the DNA double helix, separating the two strands so that the DNA can be copied.
- If the strands of DNA do not unwind and separate, bacterial **replication** is blocked.



The fluoroquinolone called ciprofloxacin. Fluoroquinolones all contain the chemical structure highlighted in red

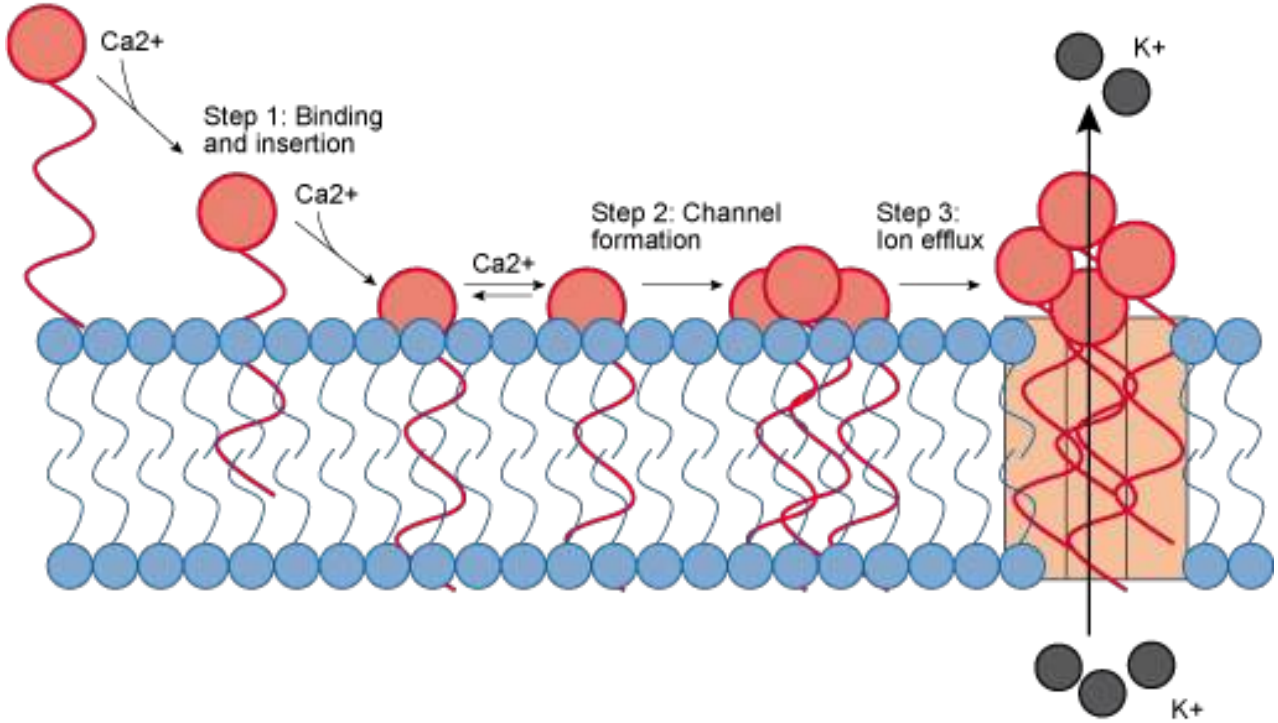
1.4 Inhibitors of Metabolic Reactions

Fig. shows the folic acid pathway. Trimethoprim prevents the enzyme dihydrofolate reductase reacting with the intermediate compound dihydrofolic acid, thereby blocking the pathway at the point shown.



The top line (A) shows the normal reaction while the bottom line (B) shows how trimethoprim competes with the normal substrate.

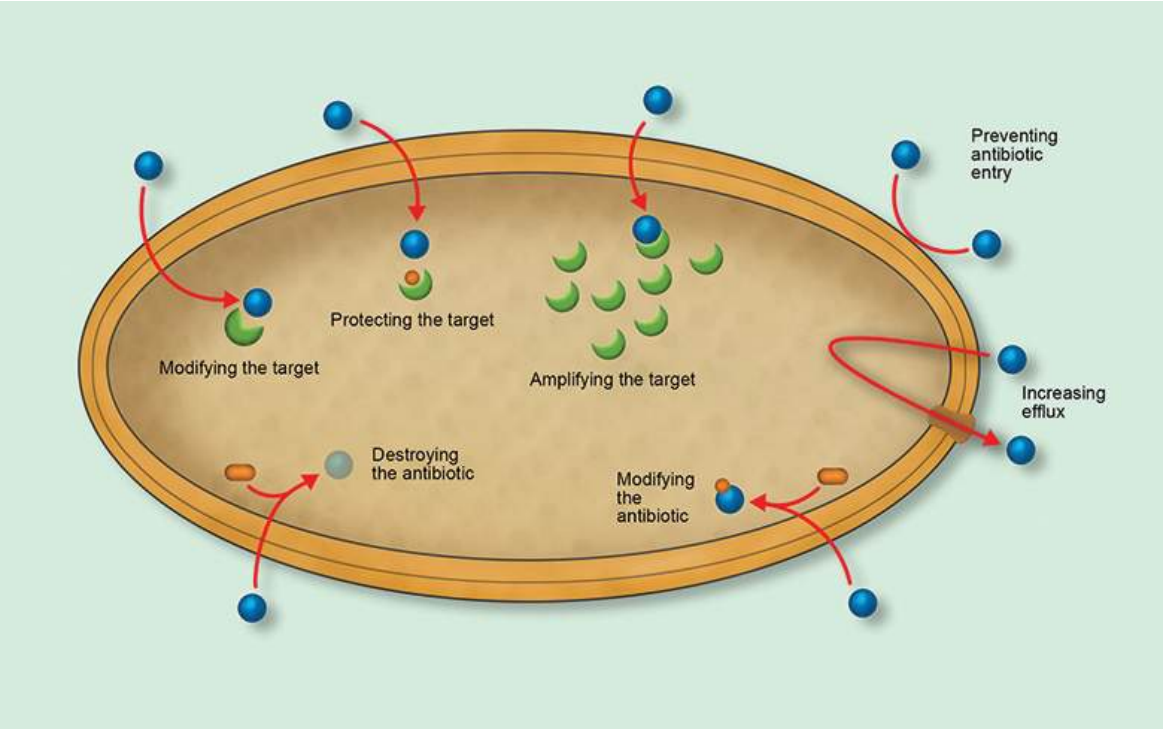
1.5 Inhibitors of Cell Membrane Function



Daptomycin (red) forms a complex with calcium which inserts into the cell membrane (blue) creating a pore like structure which allows ions (black) to leak out of the cell.

Polymyxins, such as colistin, are another group of cell membrane inhibitors that are used to target Gram-negative cells

2. How do bacteria become resistant to antibiotics?



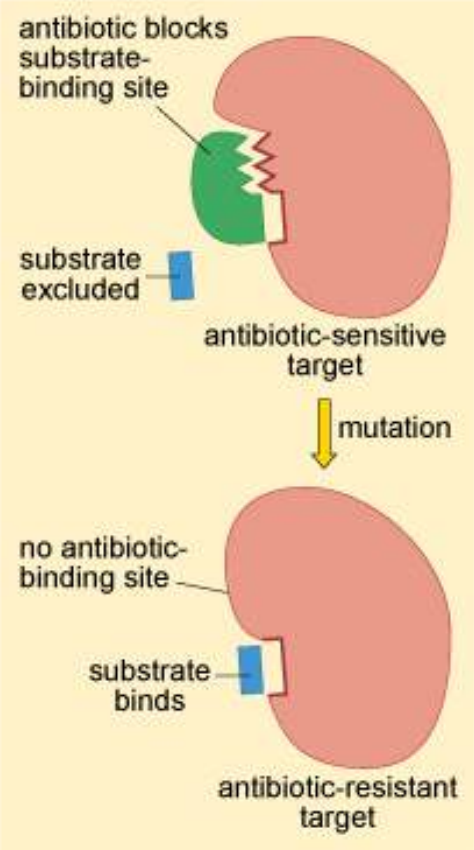
- Antibiotic resistance is the ability of bacteria to resist the action of antibiotics so that they survive exposure to antibiotics that would normally kill them or stop their growth.

•Modifying the antibiotic target

•Destroying or modifying the antibiotic

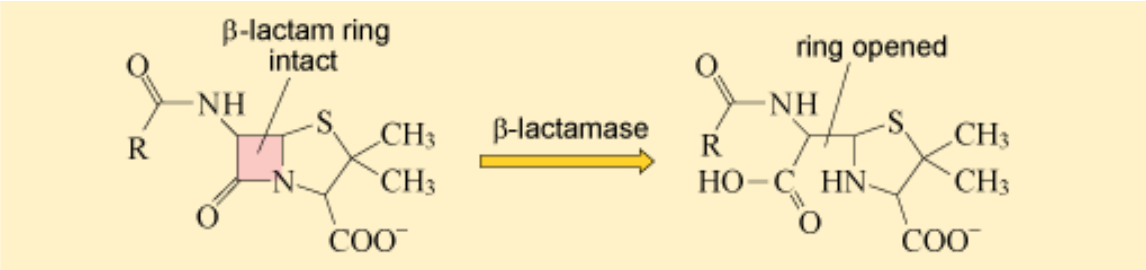
•Preventing the antibiotic from reaching its target.

2.1. Modifying the Antibiotic Target



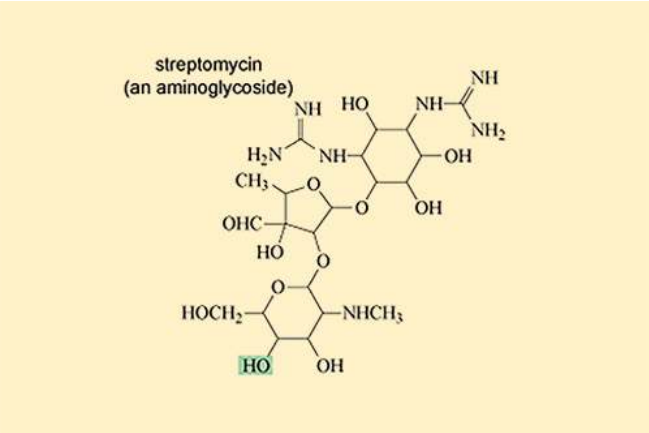
Changes to the structure of the target that prevent efficient antibiotic binding but still enable the target to carry out its normal function will confer antibiotic resistance

2.2. Destroying or Modifying the Antibiotic Molecule



β-lactamases deactivate the β-lactam ring of β-lactam antibiotics, preventing them from binding to their target

In the 1980s, a new group of β-lactamase enzymes were detected in Europe that hydrolyze a wider range of β-lactams. These enzymes are known as extended spectrum β-lactamase (ESBL).



Aminoglycoside-modifying enzymes add bulky chemical groups to the exposed hydroxyl (–OH) and amino ($–NH_2$) groups of the antibiotic, thus preventing it from binding to its target.

2.3. Preventing entry, increasing exit

- Bacteria can prevent antibiotics from reaching their target by decreasing the permeability of their outer membrane or by actively transporting antibiotics out of the cell .
- Both decreased porin expression and increased efflux pump expression have been reported in antibiotic-resistant clinical **isolates**. For example, *P. aeruginosa* strains that overexpress multidrug-resistant efflux pumps, which transport a wide range of antibiotics, have been isolated from patients .

2.2 Intrinsic and acquired resistance

- There are two ways in which bacteria can have these resistance mechanisms:
- intrinsic (or inherent) resistance
- acquired resistance.

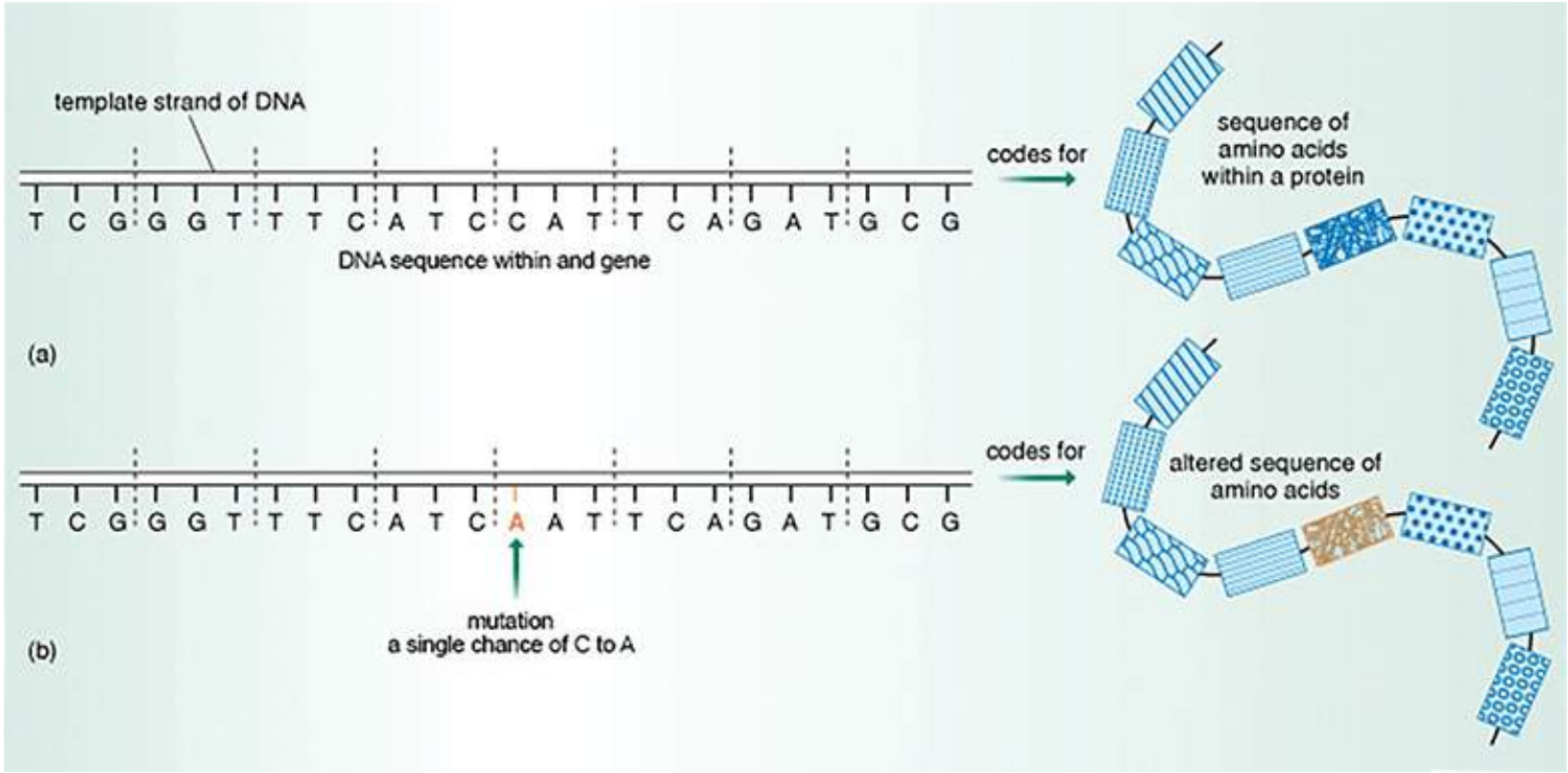
2.3 Multidrug Resistance (MDR)

- Bacteria can acquire multiple resistance mechanisms, making them resistant to multiple antibiotics.
- This is known as multidrug resistance (MDR). MDR bacteria are often known as ‘superbugs’ (although it is important to note that being resistant does not make bacteria more pathogenic, just that it will be harder to treat) and they are a major concern because they severely limit available treatment options.
- There are two primary mechanisms that can cause bacteria to acquire resistance to multiple antibiotics, and even to multiple types of antibiotic, at the same time. One is preventing the antibiotics from reaching their target in the bacterial cell; this has been covered already in Section 2.1.3: changes in the numbers of the same porins or efflux pumps on the bacterial cell wall can affect the concentration of antibiotics in many species of bacteria.

3.1 How do mutations lead to resistance?

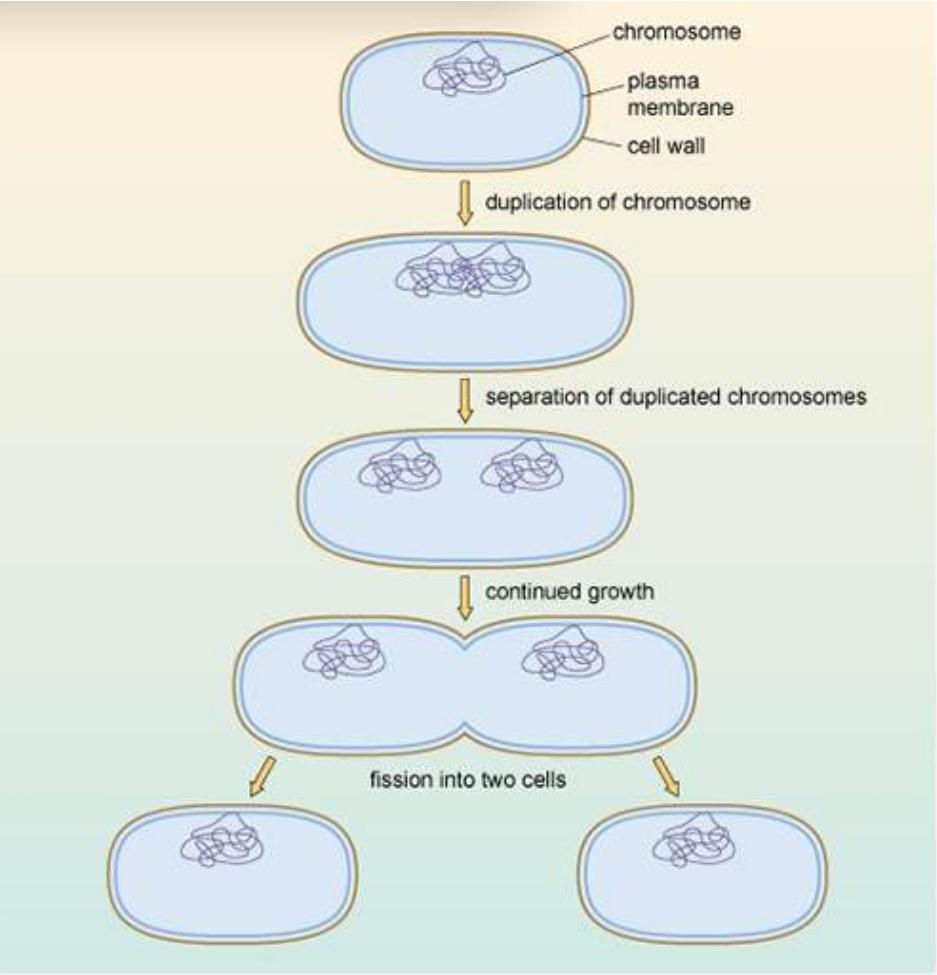
- A bacterium can develop antibiotic resistance through **genetic mutations** that are permanent changes in the deoxyribonucleic acid (DNA) sequence that makes up a **gene**. Perhaps the best example of acquisition of resistance by mutation is *Mycobacterium tuberculosis*, where resistance to all therapeutic agents is caused by mutation.
- genetic information, encoded by DNA, is converted into proteins that are required for the structure and function of bacteria.

3.2 Genetic mutations and protein structure



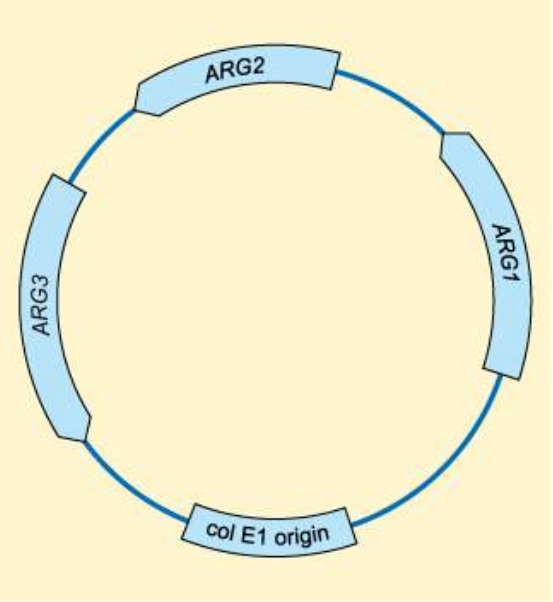
Small changes, or mutations, in the DNA sequence within a gene can alter the amino acid sequence of the protein it encode

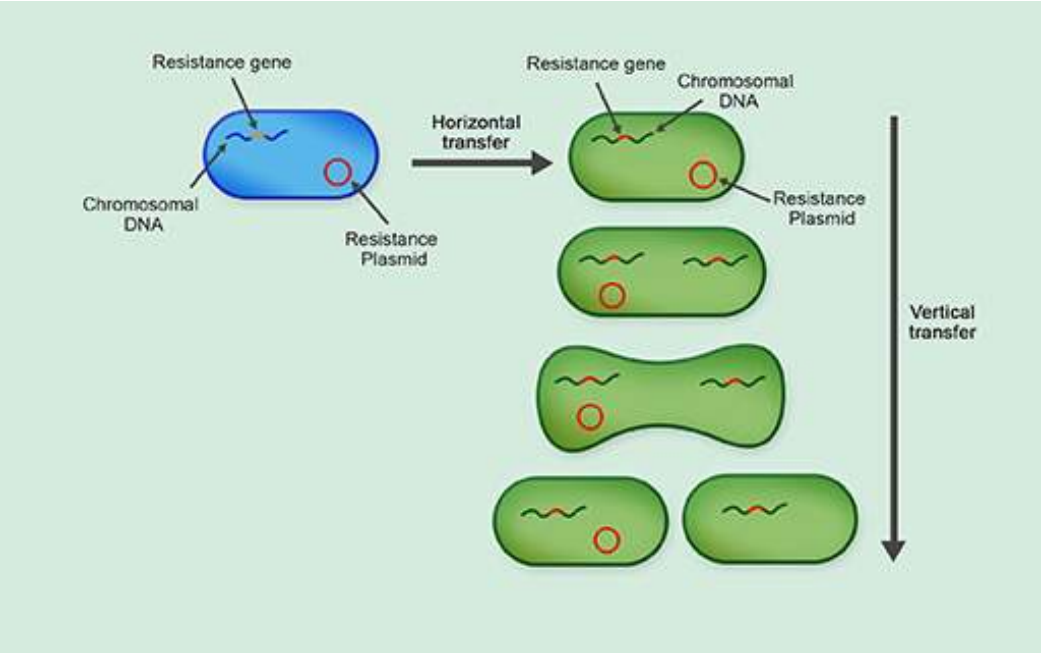
3.3 Transmission of mutations by vertical gene transfer



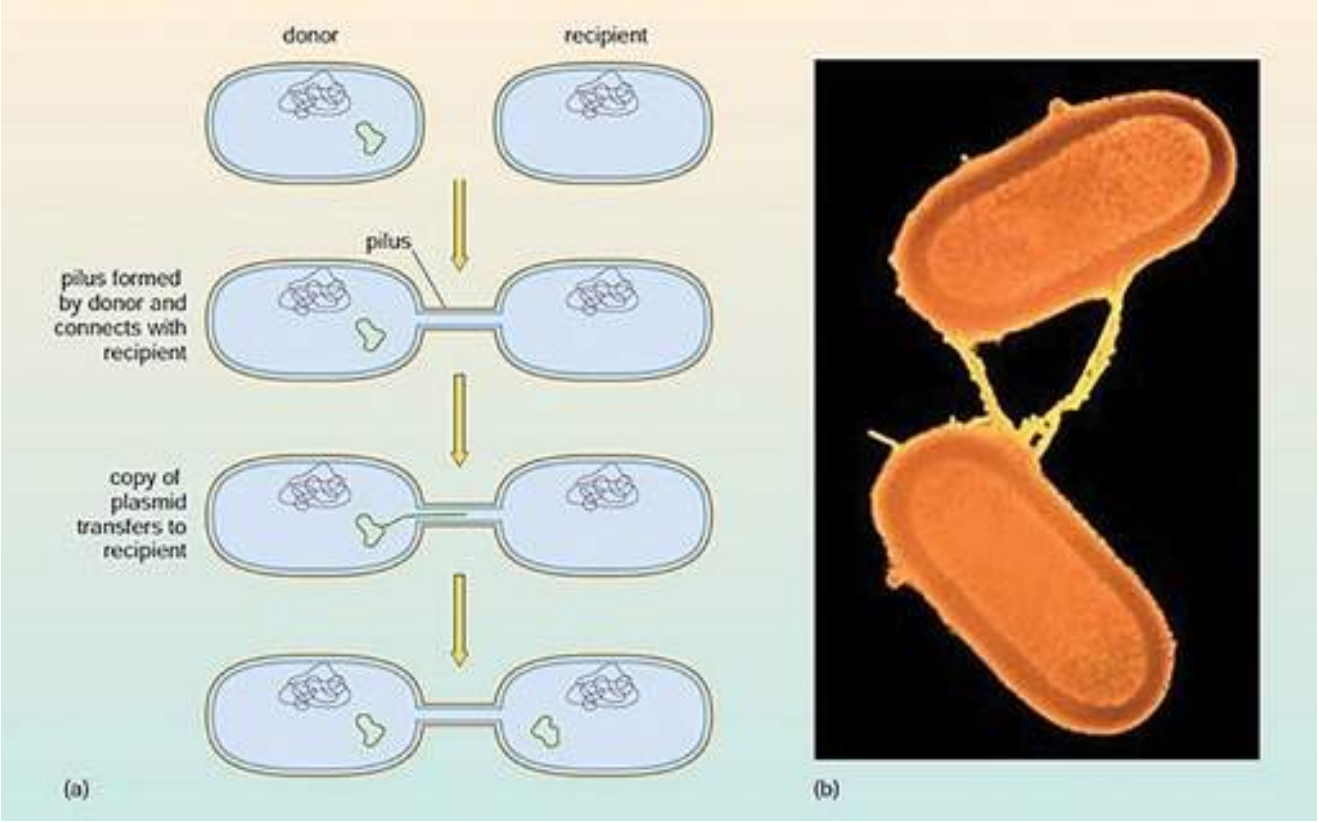
3.2.1 Plasmids

- A **plasmid** is a small, circular piece of DNA that often carries genes associated with a specific function: for example, antibiotic resistance





3.2.2 Conjugation

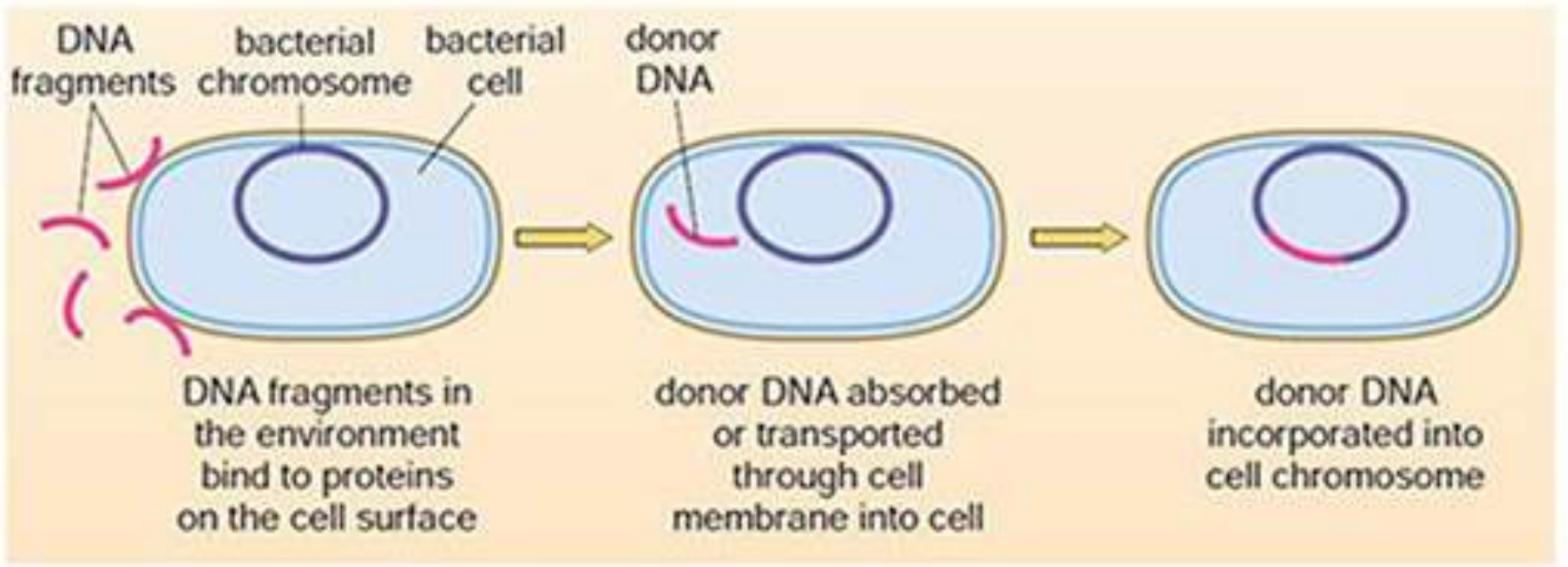


In the process of conjugation, plasmids are transferred between two contacting bacteria via a hollow tube or pilus

Since antibiotic resistance genes are often located on plasmids, conjugation can result in the transfer of antibiotic resistance from one bacterium to another.

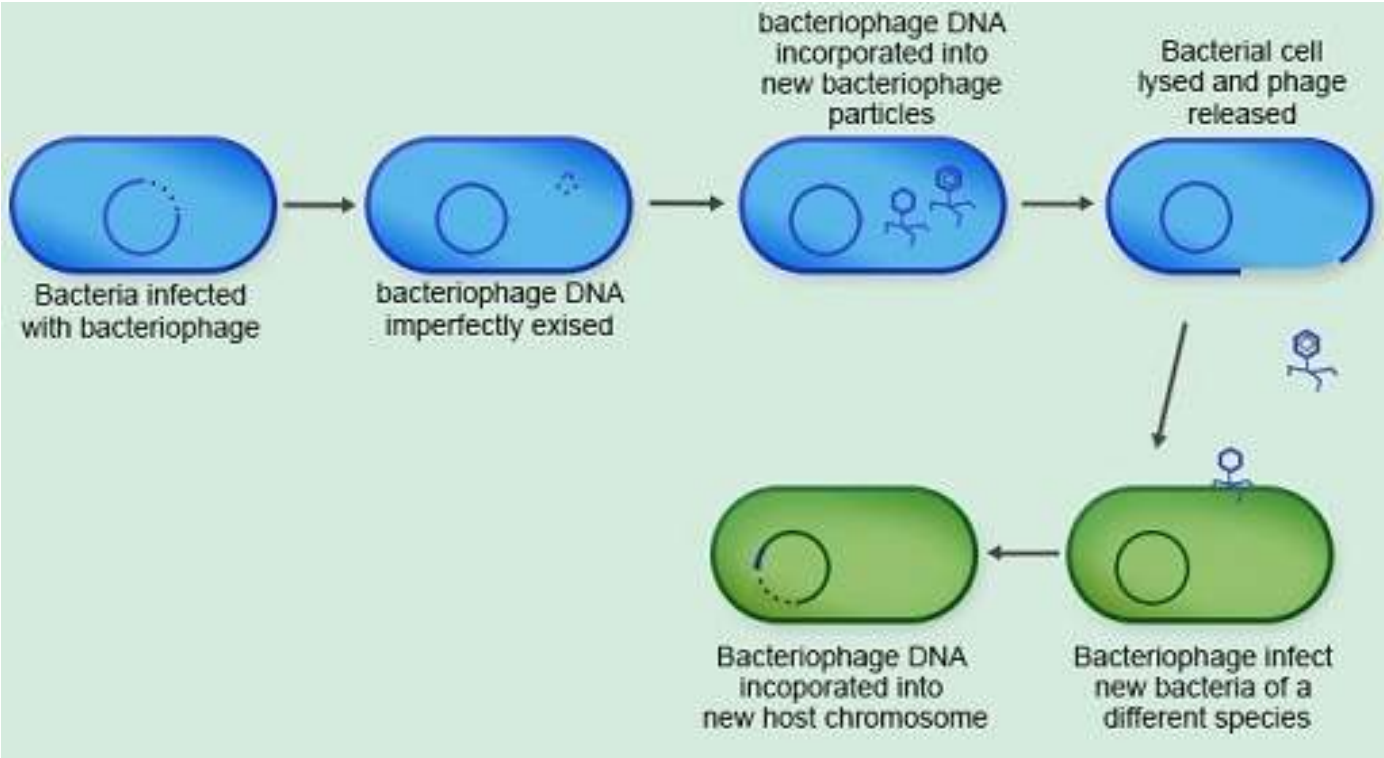
3.2.3 Transformation

- In contrast to conjugation, the process of transformation allows bacteria to take up DNA from their environment (for example, from a lysed bacterium) across the cell wall. This DNA can then be incorporated into the genome of the bacterium

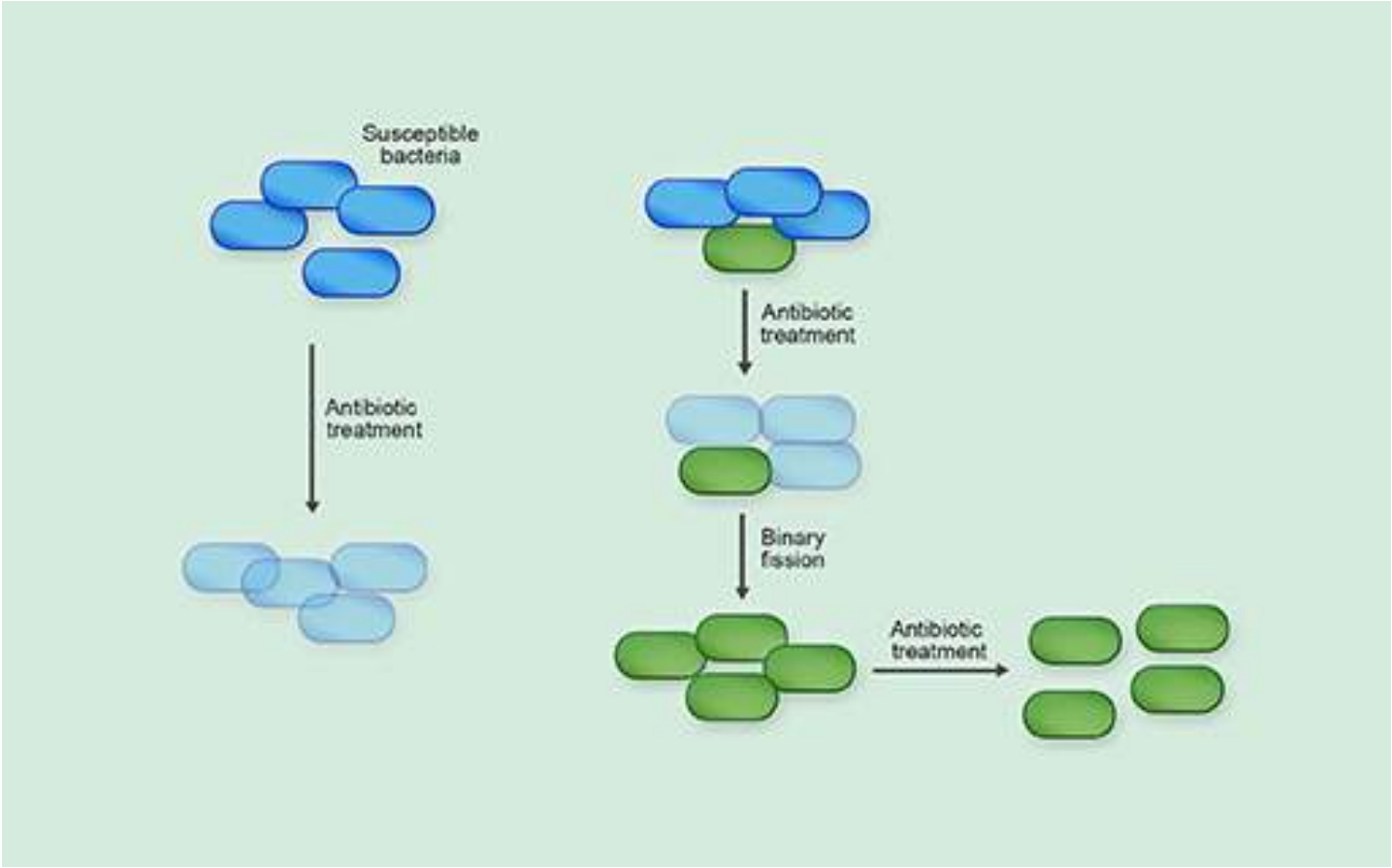


3.2.4 Transduction

- The final mechanism of horizontal gene transfer you will look at is **transduction**. In this process, transfer of DNA from one bacterial cell to another is mediated by a **virus**.



3.3 Evolving resistance to antibiotics



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