Antimicrobial resistance of bacteria

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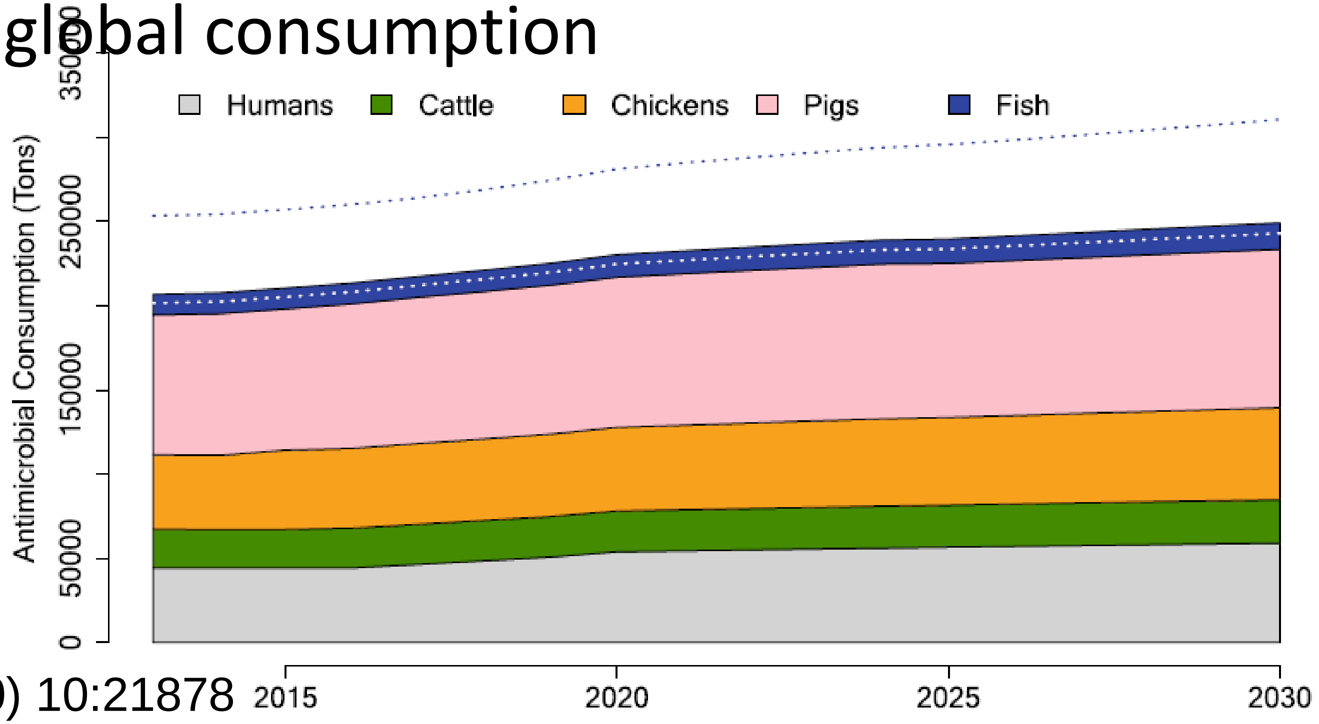
Antimicrobial in aquaculture

- Global antimicrobial consumption in aquaculture in 2017 was estimated at 10,259 tons
- global antimicrobial consumption is projected to rise 33% to 13,600 tons by 2030
- The Asia–Pacific region 93.8% of global consumption
- Africa - 2.3%
- Europe - 1.8%



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- Globally, the most commonly used classes of antimicrobials
  - quinolones (27%),
  - tetracyclines (20%),
  - amphenicols (18%),
  - sulfonamides (14%)
- Proportion of use across sectors remains relatively consistent through 2030
- human use 48,608 tons – 20.5%,
- terrestrial food producing animal use 174,549 tons – 73.7%
- aquatic food producing animal use 13,600 tons 5.7% of global consumption

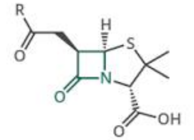
- Increasing use of antimicrobials in humans and food producing animals is driving antimicrobial resistance
- increase treatment failure rates,
- undermining sustainable food animal production and animal welfare.

DIFFERENT CLASSES OF ANTIBIOTICS - AN OVERVIEW

Key: COMMONLY ACT AS **BACTERIOSTATIC AGENTS**, RESTRICTING GROWTH & REPRODUCTION | COMMONLY ACT AS **BACTERICIDAL AGENTS**, CAUSING BACTERIAL CELL DEATH

ß-LACTAMS

MOST WIDELY USED ANTIBIOTICS IN THE NHS



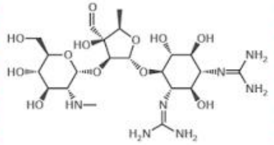
All contain a beta-lactam ring

EXAMPLES
Penicillins (shown) such as amoxicillin and flucloxacillin; *Cephalosporins* such as cefalexin.

MODE OF ACTION
Inhibit bacteria cell wall biosynthesis.

AMINOGLYCOSIDES

FAMILY OF OVER 20 ANTIBIOTICS



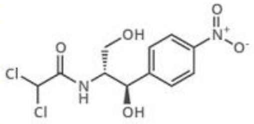
All contain aminosugar substructures

EXAMPLES
Streptomycin (shown), neomycin, kanamycin, paromomycin.

MODE OF ACTION
Inhibit the synthesis of proteins by bacteria, leading to cell death.

CHLORAMPHENICOL

COMMONLY USED IN LOW INCOME COUNTRIES



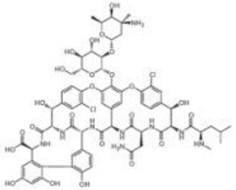
Distinct individual compound

MODE OF ACTION
Inhibit synthesis of proteins, preventing growth.

No longer a first line drug in any developed nation due to increased resistance and worries about safety.

GLYCOPEPTIDES

COMMON 'DRUGS OF LAST RESORT'



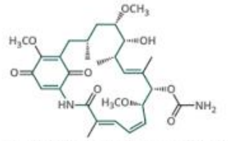
Consist of carbohydrate linked to a peptide formed of amino acids

EXAMPLES
Vancomycin (shown), teicoplanin.

MODE OF ACTION
Inhibit bacteria cell wall biosynthesis.

ANSAMYCINS

CAN ALSO DEMONSTRATE ANTIVIRAL ACTIVITY



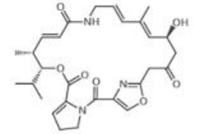
All contain an aromatic ring bridged by an aliphatic chain.

EXAMPLES
Geldanamycin (shown), rifamycin, naphthomycin.

MODE OF ACTION
Inhibit the synthesis of RNA by bacteria, leading to cell death.

STREPTOGRAMINS

TWO GROUPS OF ANTIBIOTICS THAT ACT SYNERGISTICALLY



Combination of two structurally differing compounds, from groups denoted A & B

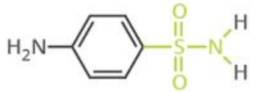
EXAMPLES
Pristinamycin IIA (shown), Pristinamycin IA.

MODE OF ACTION
Inhibit the synthesis of proteins by bacteria, leading to cell death.

DISCOVERY 1930 1940 1950 1960 1970 1980

SULFONAMIDES

FIRST COMMERCIAL ANTIBIOTICS WERE SULFONAMIDES



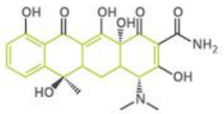
All contain the sulfonamide group

EXAMPLES
Prontosil, sulfanilamide (shown), sulfadiazine, sulfisoxazole.

MODE OF ACTION
Do not kill bacteria but prevent their growth and multiplication. Cause allergic reactions in some patients.

TETRACYCLINES

BECOMING LESS POPULAR DUE TO DEVELOPMENT OF RESISTANCE



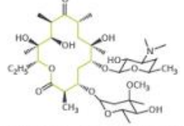
All contain 4 adjacent cyclic hydrocarbon rings

EXAMPLES
Tetracycline (shown), doxycycline, limecycline, oxytetracycline.

MODE OF ACTION
Inhibit synthesis of proteins by bacteria, preventing growth.

MACROLIDES

SECOND MOST PRESCRIBED ANTIBIOTICS IN THE NHS



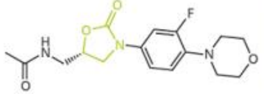
All contain a 14-, 15-, or 16-membered macrolide ring

EXAMPLES
Erythromycin (shown), clarithromycin, azithromycin.

MODE OF ACTION
Inhibit protein synthesis by bacteria, occasionally leading to cell death.

OXAZOLIDINONES

POTENT ANTIBIOTICS COMMONLY USED AS 'DRUGS OF LAST RESORT'



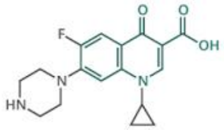
All contain 2-oxazolidone somewhere in their structure

EXAMPLES
Linezolid (shown), posizolid, tedizolid, cycloserine.

MODE OF ACTION
Inhibit synthesis of proteins by bacteria, preventing growth.

QUINOLONES

RESISTANCE EVOLVES RAPIDLY



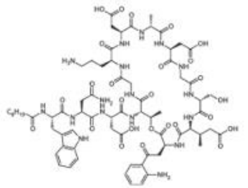
All contain fused aromatic rings with a carboxylic acid group attached

EXAMPLES
Ciprofloxacin (shown), levofloxacin, trovafloxacin.

MODE OF ACTION
Interfere with bacteria DNA replication and transcription.

LIPOPEPTIDES

INSTANCES OF RESISTANCE RARE

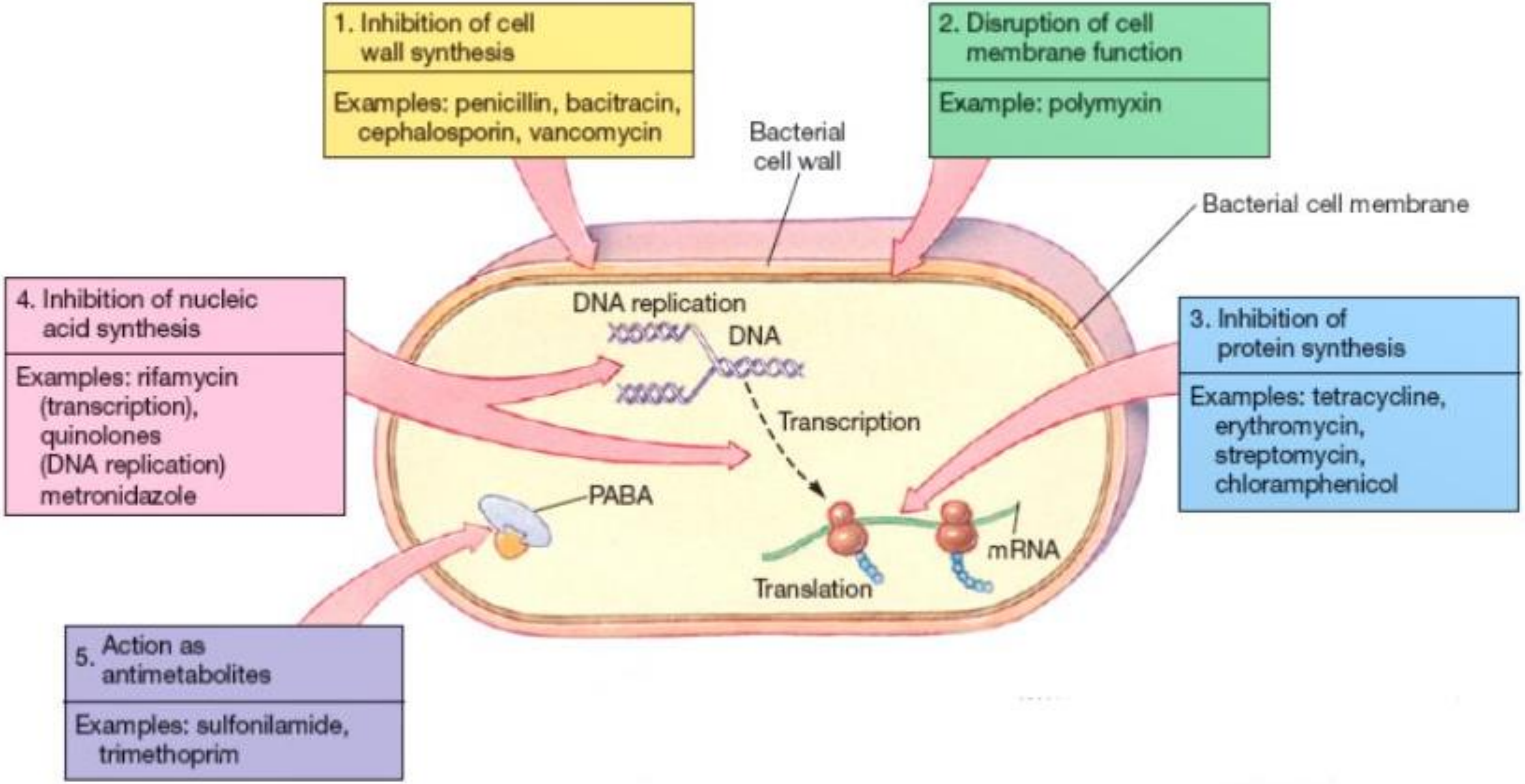


All contain a lipid bonded to a peptide

EXAMPLES
Daptomycin (shown), surfactin.

MODE OF ACTION
Disrupt multiple cell membrane functions, leading to cell death.

Antimicrobial mode of action



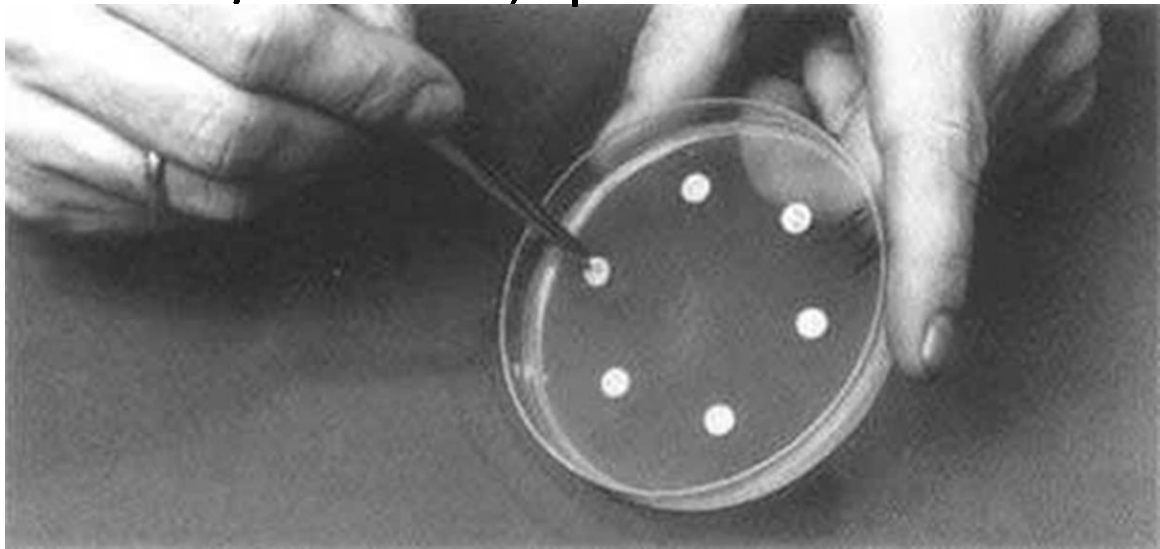
Antibiotic	Acronym	Classes	Disk Load (μg)
Streptomycin	S	Aminoglycosides	10
Neomycin	N		30
Kanamycin	K		30
Gentamicin	CN		30
Ampicillin	AM	Aminopenicillins	10
Florfenicol	FFC	Amphenicols	30
Erythromycin	E	Macrolides	15
Flumequine	FLM	Quinolones	30
Oxacillin	OA	Penicillin	10
Penicillin	P		10
Amoxicillin	AX		20
Oxytetracycline	OT	Tetracyclines	30

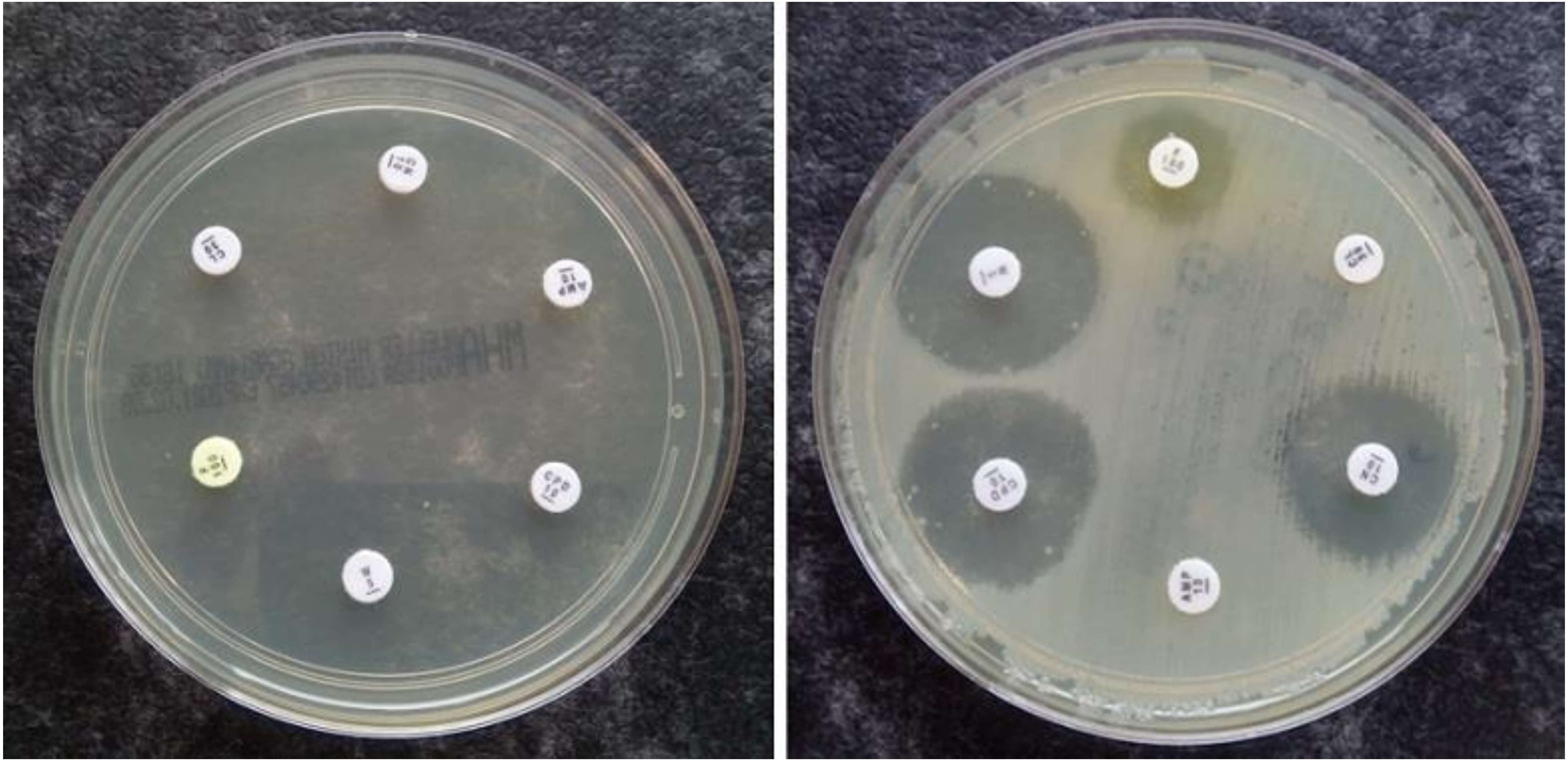
Antibiotic Susceptibility Testing

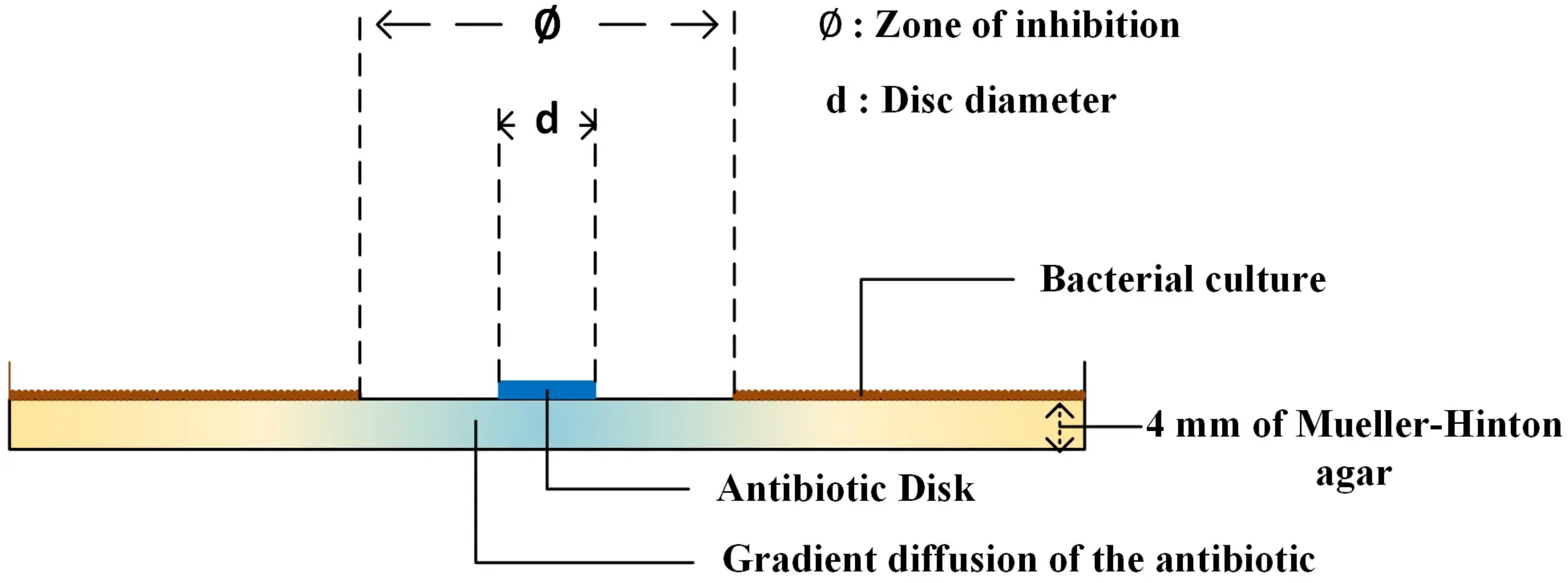
- The Antibiotic Susceptibility Testing is an in vitro test of the sensitivity of a bacteria
- Guide the clinician in the choice of an antibiotic to treat a bacterial infection and to use the data for monitoring bacterial resistance to antibiotics.

Principle

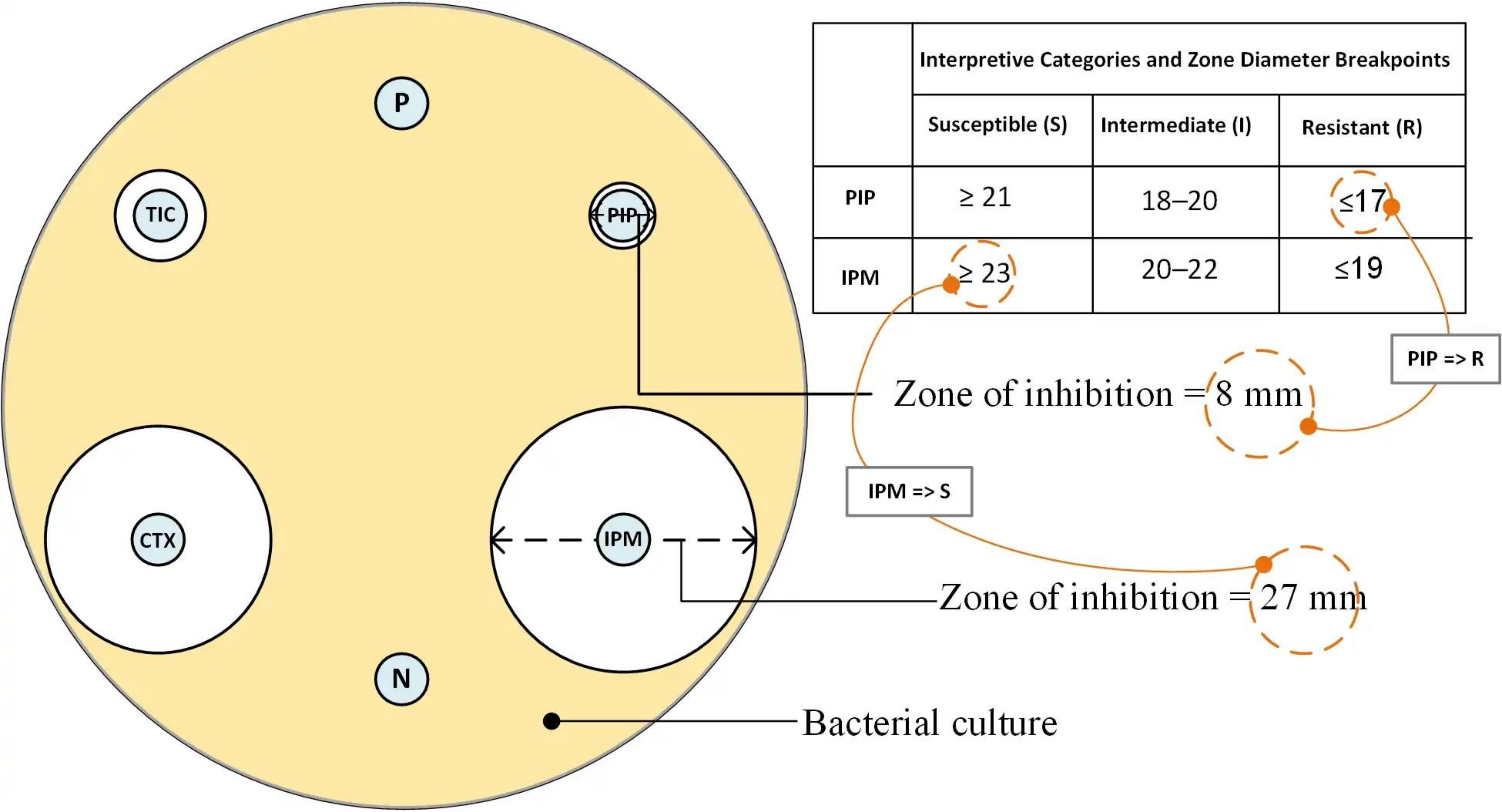
- A standardized inoculum of bacteria (usually 0.5Mcf) is dabbed onto the surface of a dish of Mueller-Hinton (MH) agar .
- Filter paper discs impregnated with antimicrobial agents are placed on the agar.
- After overnight incubation, the diameter of the zone of inhibition is measured around each disc.
- By referring to the tables of the CLSI standard / EUCAST, qualitative report of
  - sensitive (S),
  - intermediate (I)
  - resistan (R).







Ø
d
Ø : Zone of inhibition
d : Disc diameter
Bacterial culture
4 mm of Mueller-Hinton agar
Antibiotic Disk
Gradient diffusion of the antibiotic



	Interpretive Categories and Zone Diameter Breakpoints		
	Susceptible (S)	Intermediate (I)	Resistant (R)
PIP	≥ 21	18–20	≤17
IPM	≥ 23	20–22	≤19

What does the test result mean?

- Susceptible — likely, but not guaranteed to inhibit the pathogenic microbe
- Intermediate — may be effective at a higher dosage, or more frequent dosage
- Resistant — not effective at inhibiting the growth of the organism in a laboratory test

- These categories are based on the minimum inhibitory concentration (MIC)
- Results may be expressed as the MIC, in units such as micrograms/milliliter

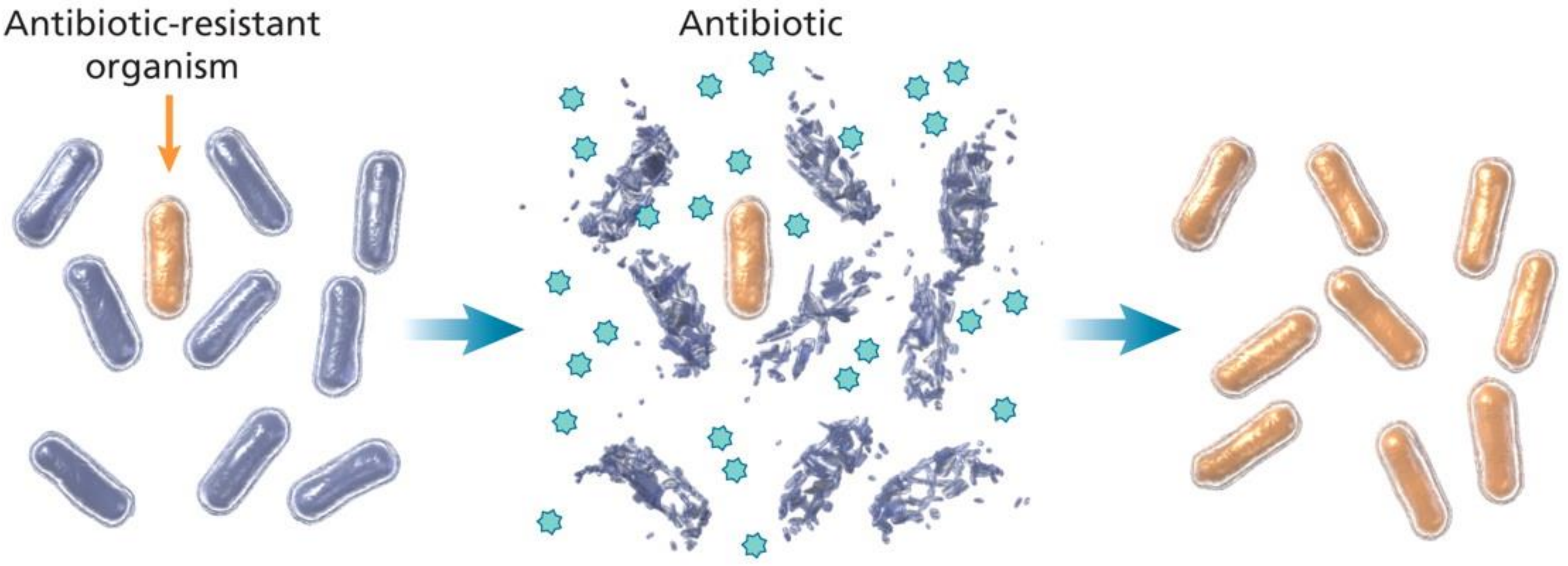
Strains	St	K	AMP	FFC	S	E	OA	FLM	P	AX	N	OT	CN
Italian	S	10	95	75	0	40	25	35	80	90	5	95	100
	I	55	0	0	35	40	0	0	0	5	75	0	0
	R	35	5	25	65	20	75	65	20	5	20	5	0
Turkish	S	15	100	90	0	40	0	0	100	100	1	95	100
	I	30	0	5	10	55	0	0	0	0	4	5	0
	R	55	0	5	90	5	100	100	0	0	15	0	0
Spanish	S	0	100	90	0	15	0	0	100	100	0	100	100
	I	0	0	10	0	80	0	0	0	0	25	0	0
	R	100	0	0	100	5	100	100	0	0	75	0	0
Greek	S	0	0	40	0	0	0	0	0	0	0	100	100
	I	0	0	60	0	100	0	0	0	0	0	0	0
	R	100	100	0	100	0	100	100	100	100	100	0	0
Total	S	21.25	0	23.75	11.25	65	0	0	0	1.25	31.25	1.25	100
	I	6.25	73.75	75	0	27.5	6.25	8.75	70	72.5	2.5	97.5	0
	R	72.5	26.25	1.25	88.75	7.5	93.75	91.25	30	26.25	66.25	1.25	0

Antimicrobial resistance

- Antimicrobial resistance is not a new phenomenon.
- In nature, microbes are constantly evolving in order to overcome the antimicrobial compounds produced by other microorganisms.
- Human development of antimicrobial drugs and their widespread clinical use has simply provided another selective pressure that promotes further evolution.
- Several important factors can accelerate the evolution of drug resistance.
  - overuse and misuse of antimicrobials,
  - inappropriate use of antimicrobials,
  - subtherapeutic dosing,
  - noncompliance with the recommended course of treatment.

- When antibiotics were first introduced in the 1900’s, it was thought that we had won the war against microorganisms.
- It was soon discovered however, that the microorganisms were capable of developing resistance to any of the drugs that were used
- Apparently most pathogenic microorganisms have the capability of developing resistance to at least some antimicrobial agents.

- The advent of antimicrobial resistance has added significantly to the impact of infectious diseases, in number of infections, as well as added fish treatment costs.
- Even though we have a very large number of antimicrobial agents from which to choose for potential infection therapy, there is documented antimicrobial resistance to all of these, and this resistance occurs shortly after a new drug is okayed for use.



Population of bacteria with a subset of antibiotic-resistant organisms.

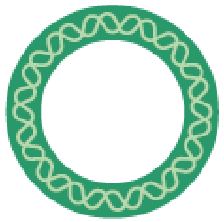
In the presence of an antibiotic, susceptible strains are killed; the resistant strain survives.

The resistant strain proliferates and may be capable of causing a new infection.

Antibiotic resistance moves from bacteria to bacteria

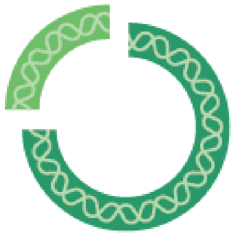
- Any antibiotic use can lead to antibiotic resistance
- Antibiotics kill bacteria, but the resistant survivors remain
- Resistance traits can be inherited generation to generation
- They can also pass directly from bacteria to bacteria by way of mobile genetic elements

Mobile Genetic Elements



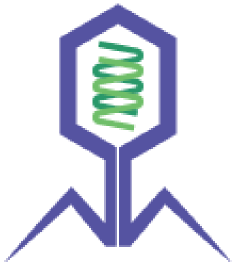
Plasmids

Circles of DNA that can move between cells.



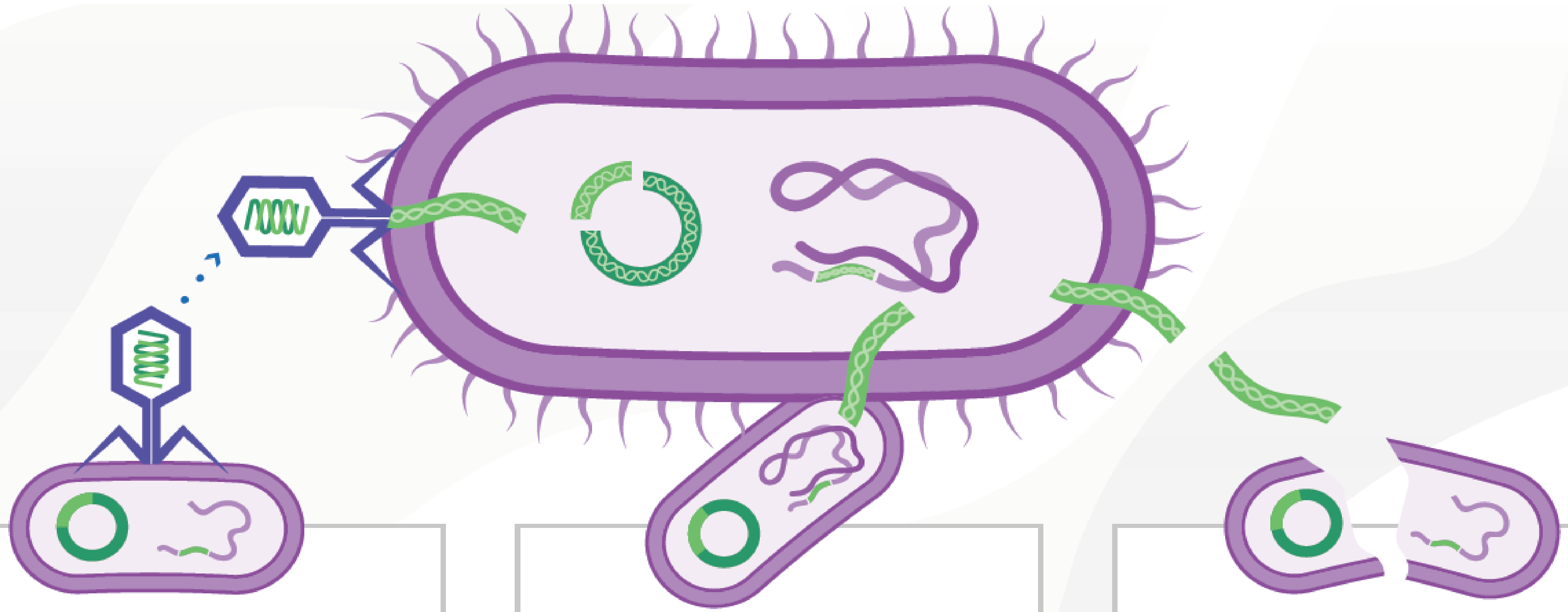
Transposons

Small pieces of DNA that can go into and change the overall DNA of a cell. These can move from chromosomes (which carry all the genes essential for germ survival) to plasmids and back.



Phages

Viruses that attack germs and can carry DNA from germ to germ.



Transduction

Resistance genes can be transferred from one germ to another via phages.

Conjugation

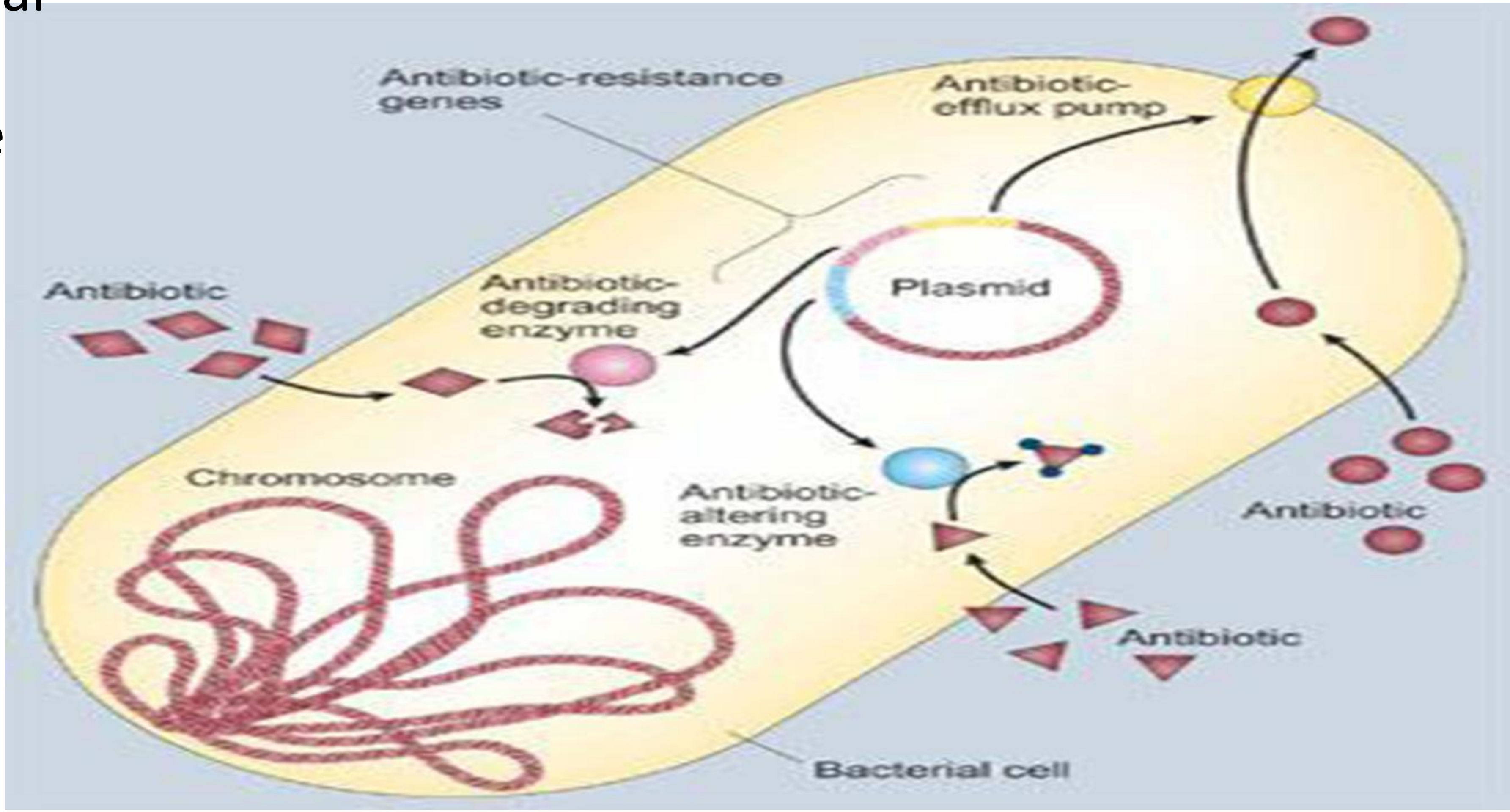
Resistance genes can be transferred between germs when they connect.

Transformation

Resistance genes released from nearby live or dead germs can be picked up directly by another germ.

Mechanisms of Resistance

- Enzymatic inhibition
- Alteration of bacterial membranes
- Rapid ejection of the drug [efflux] or reduced drug influx.
- By pass of antibiotic inhibition.
- Alteration of target sites



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