



Project: Technical assistance to improve implementation of food safety standards and disease crisis preparedness

Training course: Antimicrobials and antimicrobial resistance

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Date:

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- Antimicrobial/Antibiotic - definitions
- Use of antimicrobials
- Antimicrobial resistance - definitions
- Antimicrobials - origin
- Antimicrobials classification
 - Antimicrobial classes
 - Bactericidal vs Bacteriostatic

What is antibiotic/antimicrobial



- An antibiotic is a substance produced by a microorganism, that has the capacity, to selectively inhibit or kill other microorganisms (Paul Vuillemin, 1941)
- Antimicrobial is a broader term - referring to any substance that can affect microbial life, including synthetic and semisynthetic compounds and substances without selective toxicity (e.g., biocides)
- An antimicrobial agent means a naturally occurring, semi-synthetic or synthetic substance that exhibits antimicrobial activity (kill or inhibit the growth of micro-organisms) at concentrations attainable in vivo. Anthelmintics and substances classed as disinfectants or antiseptics are excluded from this definition. (OIE)

What is antibiotic/antimicrobial



- EU legal framework definitions
- ‘antimicrobial’ means any substance with a direct action on micro-organisms used for treatment or prevention of infections or infectious diseases, including antibiotics, antivirals, antifungals and anti-protozoals;
- ‘antibiotic’ means any substance with a direct action on bacteria that is used for treatment or prevention of infections or infectious diseases;
- ‘antimicrobial resistance’ means the ability of micro-organisms to survive or to grow in the presence of a concentration of an antimicrobial agent which is usually sufficient to inhibit or kill micro-organisms of the same species.



- **Therapeutic use:**

To treat sick animals

- **Prophylactic / Metaphylactic use:**

To prevent infection in animals

- **Growth promoters** (used as a supplement in animal feed in sub therapeutic concentrations, which is prohibited in the EU):

To improve feed utilization, production and enhance economic returns to farmers

Control of chronic diseases in intensively-reared animals





- Real world - clinical definition

Resistance is the ability of a bacterial strain to survive or grow during antimicrobial treatment

- Research - genetic definition

Resistance is defined by the presence of a genetic change (mutation or gene) = resistance determinant

- Laboratory - microbiological definition:

Resistance is the ability to survive or grow in higher antibiotic concentrations than most other bacterial strains of the same species

"antimicrobial resistance" means the ability of micro-organisms

of certain species to survive or even to grow in the presence of a given concentration of an antimicrobial agent, that is usually sufficient to inhibit or kill micro-organisms of the same species;

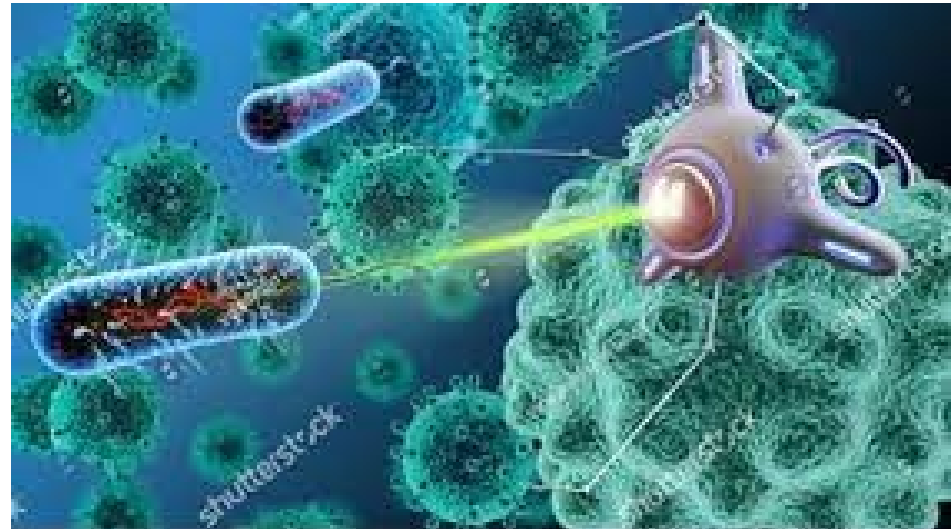
(Directive 2003/99)

Classification of antimicrobials



- Based on chemical structure
- Based on target organisms
 - Antiviral
 - Antibacterial
 - Antifungal
 - Antiparasitic
- Based on antimicrobial activity
 - Bactericidal
 - Bacteriostatic
- Spectrum of activity
 - Narrow
 - Broad
- NB: Sulfonamides are both antibacterial and antiparasitic

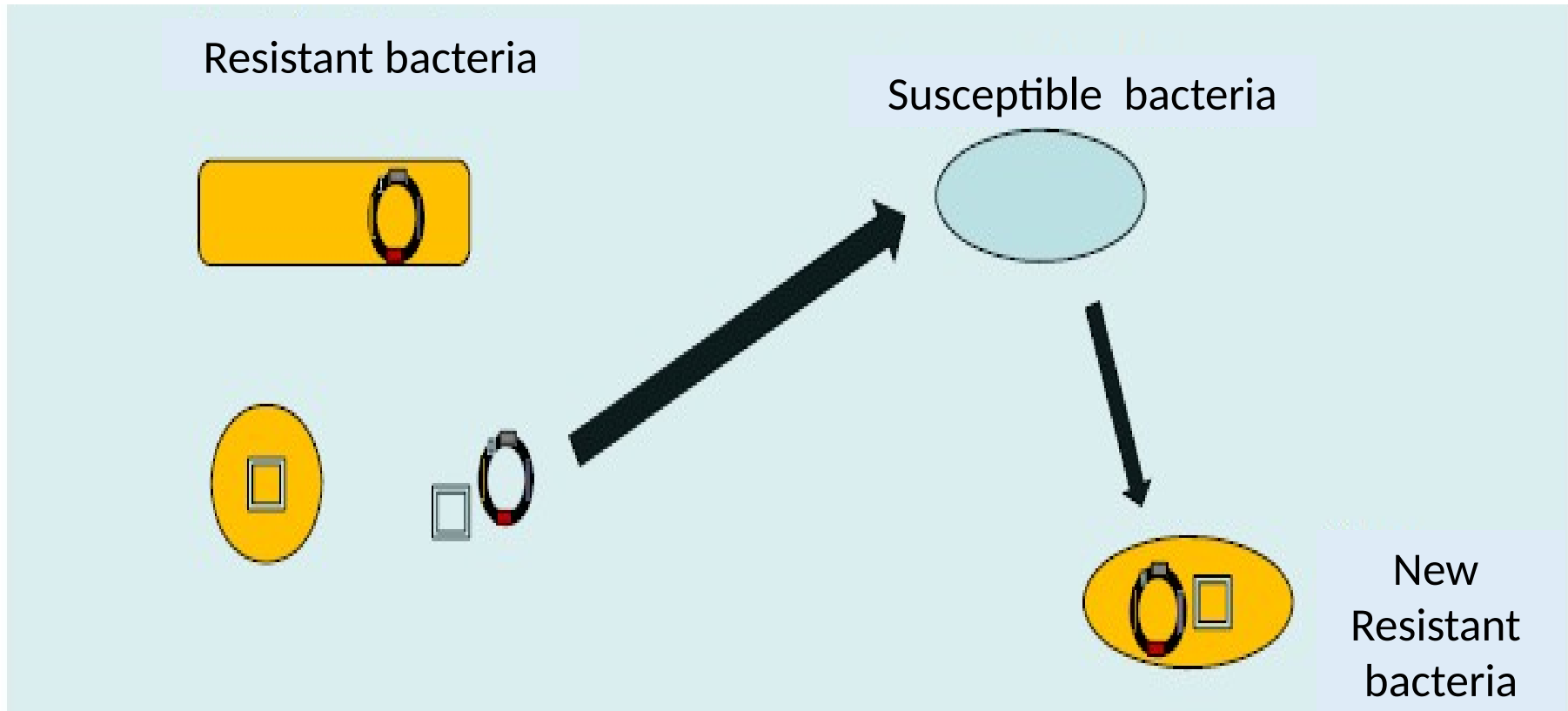
- Inhibition of cell wall synthesis
- Inhibition of DNA synthesis
- Inhibition of protein synthesis
- Inhibition of folic acid synthesis
- Disruption of osmotic integrity



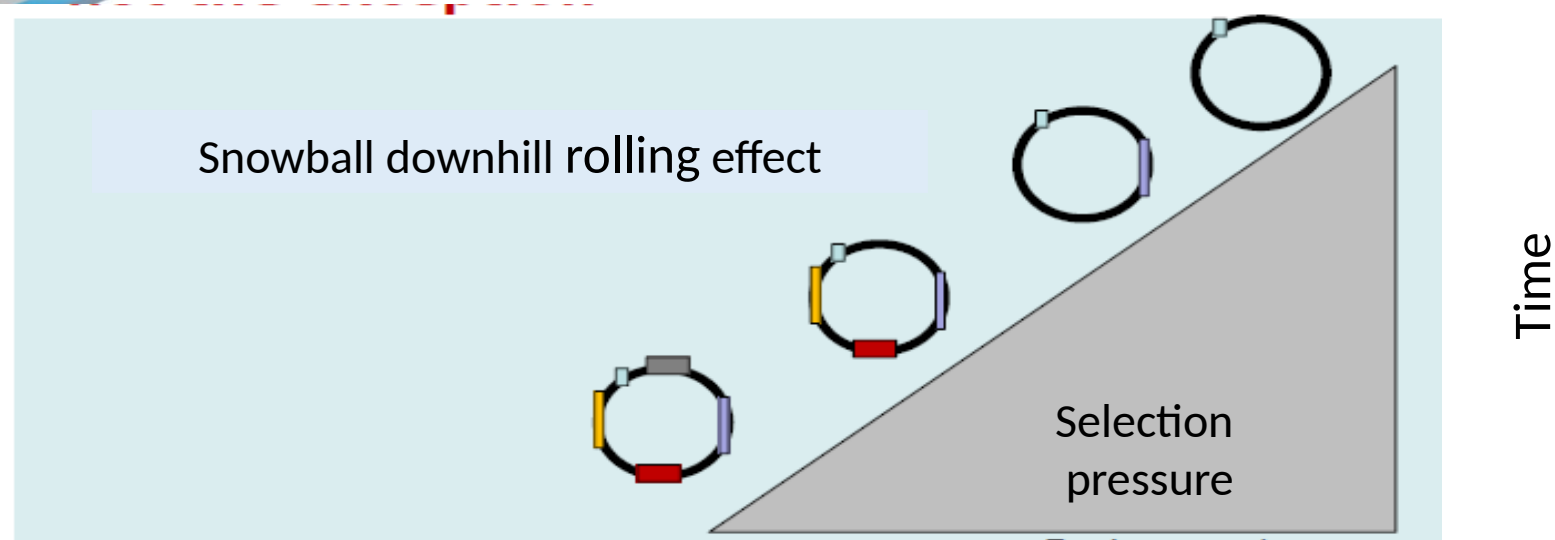


- Resistance can occur in three ways:
 - Natural resistance
 - Genetic mutation
 - Transfer from other microorganisms
- Antibiotics fight bacteria. But bacteria resist and find new ways to survive. Their protective strategies are called stability mechanisms
- Bacteria which prove to be capable of resisting the action of antimicrobial substances, survive and reproduce, whereas susceptible microorganisms die or their growth is suppressed.

How resistance to antimicrobial drugs arises



How resistance to antimicrobial drugs arises



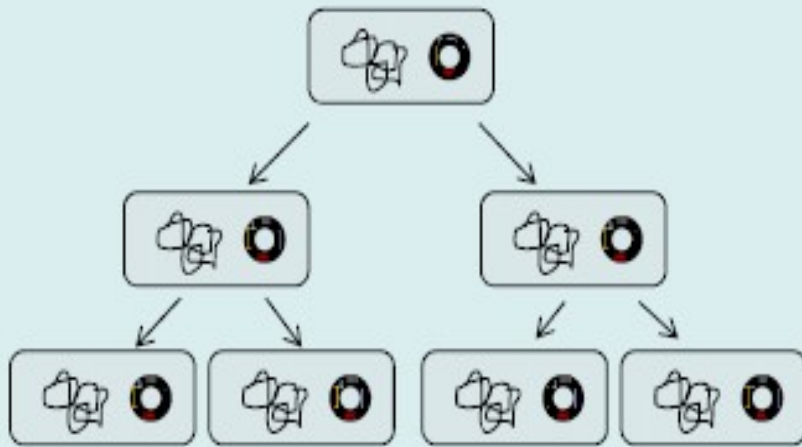
2000 years ago: eat this plant

- 300 years ago: drink this potion
- 1941: that potion is poison - take this penicillin
- 1947: Oops! The germs are resistant - take this streptomycin
- 1948: Oops! The germs are now resistant - take this new drug
- 60 years later! Oops !!!: eat this plant...
- It has been estimated that by 2050, 10 million worldwide deaths could result from antibiotic resistance, making it deadlier than cancer.

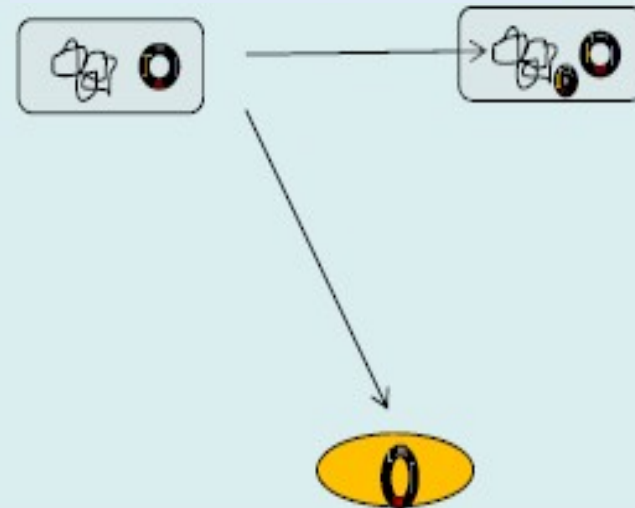
Environment

- Chromosomes or plasmids

Vertical



Horizontal



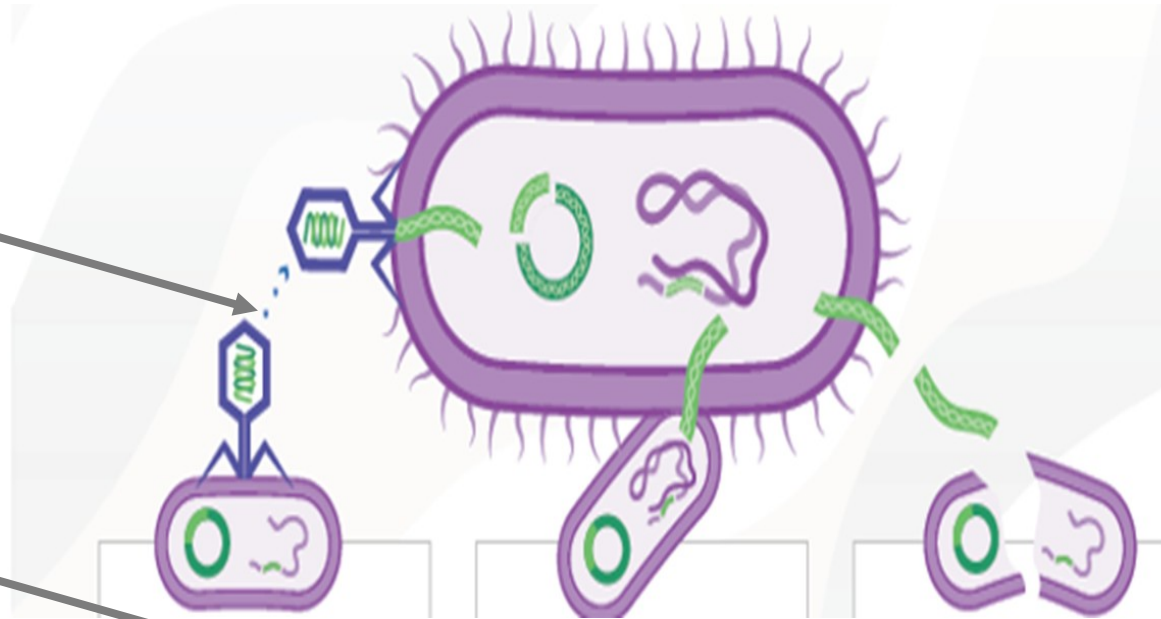


- Resistance genes can be directly transmitted from bacteria to bacteria through mobile genetic elements
- Plasmids - circles of DNA that can move between cells
- Transposons - small bits of DNA that can enter the cell's DNA and change it. They can move from chromosomes (which carry all the genes necessary for the survival of bacteria) to plasmids and vice versa
- Phages - viruses that attack microbes and can transfer DNA , etc bacteria to bacteria

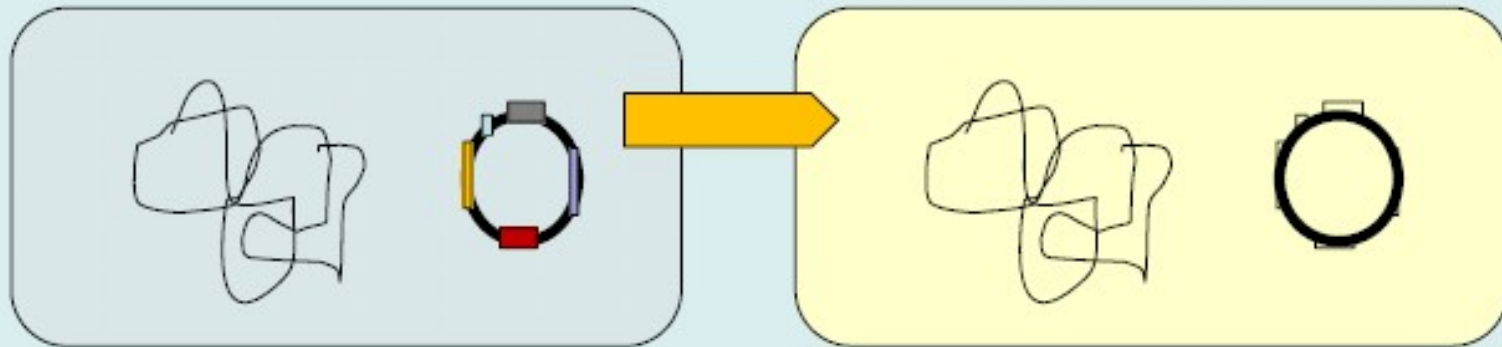


How it works

- Transduction - Resistance genes can be transmitted from one bacterium to another through phages
- Conjugation - Genes sustainability can be transmitted between bacteria when they combine
- Transformation - Resistance genes released by nearby living or dead bacteria, may be selected by other bacteria.



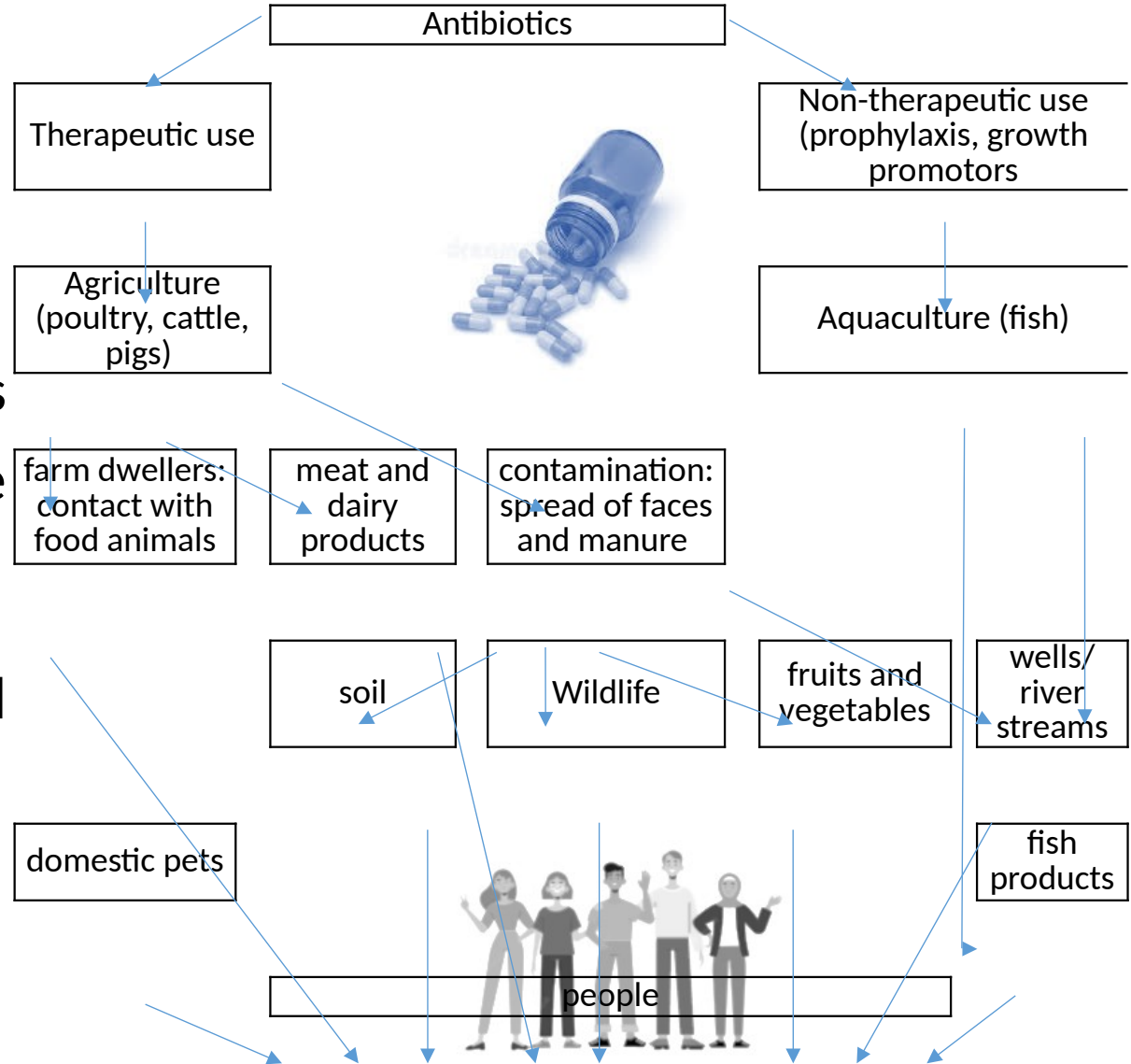
- Acquired resistance may appear due to:
 - mutations of bacterial DNA or
 - discovery of resistance genes through the horizontal transfer of genes during the transfer of DNA one bacterium to another





Factors contributing to AMR

- Inappropriate use of therapeutic antimicrobial drugs
- Use of antimicrobial drugs for non-therapeutic purposes
- Contamination of the environment with antimicrobial drugs
- The increase in world trade and travel contributes to the spread of AMR between countries and regions



Bacteria producing enzymes



- Beta-lactamases of the extended spectrum (BLRS, extended spectrum betalactamases, ESBL) combine a large number of bacterial enzymes capable to mediate resistance III-IV generation cephalosporins (e.g., ceftazidime, cefotaxime, and ceftriaxone)
- Carbapenemases are bacterial enzymes capable to mediate resisting all types of beta-lactam antibiotics, including carbapenems (for example, imipenem, meropenem, ertapenem, doripenem)
- AmpC beta-lactamases (AmpC) are enzymes capable to mediate resisting penicillins, second- and third-generation cephalosporins, and cefamycins.



- Necessary common actions - due to severe health consequences in case of ineffective treatment, deaths and physiopathological consequences and costs
- AMR is a complex problem that affects all aspects of society and life it is controlled by many interrelated factors, therefore single, isolated actions have limited influence

ONE HEALTH APPROACH !!!

Joint efforts from all parties that can contribute

- One Health: is a term used to describe a principle which recognises that human and animal health are interconnected, that diseases are transmitted from humans to animals and vice versa and must therefore be tackled in both. The One Health approach also encompasses the environment, another link between humans and animals and likewise a potential source of new resistant microorganisms. This term is globally recognised, having been widely used in the EU and in the 2016 United Nations Political Declaration on AMR.



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THANK YOU FOR YOUR ATTENTION



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