18/MHS07/022

PHARMACOLOGY

PHA 206

ASSIGNMENT: List and explain 4 mechanism of antimicrobial resistance.

ANSWER:

**Antimicrobial resistance** (**AMR** or **AR**) is the ability of a microbe to resist the effects of medication that once could successfully treat the microbe. The term **antibiotic resistance** (**AR** or **ABR**) is a subset of AMR, as it applies only to [bacteria](https://en.wikipedia.org/wiki/Bacteria) becoming resistant to [antibiotics](https://en.wikipedia.org/wiki/Antibiotic) Resistant microbes are more difficult to treat, requiring alternative medications or higher doses of antimicrobials. These approaches may be more expensive, [more toxic](https://en.wikipedia.org/wiki/Adverse_effect) or both. Microbes resistant to multiple antimicrobials are called [multidrug resistant](https://en.wikipedia.org/wiki/Multiple_drug_resistance) (MDR). Those considered extensively drug resistant (XDR) or totally drug-resistant (TDR) are sometimes called "superbugs".

**Drug resistance** is the reduction in effectiveness of a medication such as an [antimicrobial](https://en.wikipedia.org/wiki/Antimicrobial) or an [antineoplastic](https://en.wikipedia.org/wiki/Antineoplastic) in treating a [disease](https://en.wikipedia.org/wiki/Disease) or condition. The term is used in the context of resistance that [pathogens](https://en.wikipedia.org/wiki/Pathogen) or cancers have "acquired", that is, resistance has evolved. [Antimicrobial resistance](https://en.wikipedia.org/wiki/Antimicrobial_resistance) and [antineoplastic resistance](https://en.wikipedia.org/wiki/Antineoplastic_resistance) challenge clinical care and drive research. When an organism is resistant to more than one drug, it is said to be [multidrug-resistant](https://en.wikipedia.org/wiki/Multiple_drug_resistance).

The three fundamental mechanisms of antimicrobial resistance are:

(1) enzymatic degradation of antibacterial drugs,

(2) alteration of bacterial proteins that are antimicrobial targets, and

(3) changes in membrane permeability to antibiotics.

Antibiotic resistance can be either plasmid mediated or maintained on the bacterial chromosome. The most important mechanism of resistance to the penicillin’s and cephalosporin’s is antibiotic hydrolysis mediated by the bacterial enzyme beta-lactamase. The expression of chromosomal beta-lactamase can either be induced or stably depressed by exposure to beta-lactam drugs. Methods to overcome resistance to beta-lactam antibiotics include the development of new antibiotics that are stable to beta-lactamase attack and the coadministration of beta-lactamase inhibitors with beta-lactam drugs. Resistance to methicillin, which is stable to gram-positive beta-lactamase, occurs through the alteration of an antibiotic target protein, penicillin-binding protein .

(4) Production of antibiotic-modifying enzymes and synthesis of antibiotic-insensitive bacterial targets are the primary resistance mechanisms for the other classes of antibiotics, including trimethoprim, the sulfonamides, the aminoglycosides, chloramphenicol, and the quinolone drugs. Reduced antibiotic penetration is also a resistance mechanism for several classes of antibiotics, including the beta-lactam drugs, the aminoglycosides, chloramphenicol, and the quinolones.

Antimicrobials show selective toxicity. Suitable targets for antimicrobials to act at include the bacterial cell wall, bacterial protein and folic acid synthesis, nucleic acid metabolism in bacteria and the bacterial cell membrane. Acquired antimicrobial resistance generally can be ascribed to one of five mechanisms. These are production of drug-inactivating enzymes, modification of an existing target, and acquisition of a target by-pass system, reduced cell permeability and drug removal from the cell. Introduction of a new antimicrobial into clinical practice is usually followed by the rapid emergence of resistant strains of bacteria in some species that were initially susceptible. This has reduced the long-term therapeutic value of many antimicrobials. It used to be thought that antibacterial resistance was mainly a hospital problem but now it is also a major problem in the community. Organisms in which resistance is a particular problem in the community include members of the Enterobacteriaceae, including Salmonella spp. and Shigella spp., Mycobacterium tuberculosis, Streptococcus pneumoniae, Haemophilus influenzae and Neisseria gonorrhoeae. Multi-resistant Gram-negative rods, methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci are major causes of concern in the hospital setting. Prevalence of antibacterial resistance depends both on acquisition and spread. Decreasing inappropriate usage of antimicrobials should lessen the rate of acquisition, and spread can be minimised by sensible infection control measures.