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QUESTION: LIST AND EXPLAIN 4 MECHANISM OF ANTIMICROBIAL RESISTANCE.

The three **fundamental mechanisms** of antimicrobial resistance are:

 (1) Enzymatic degradation of antibacterial drugs

 (2) Alteration of bacterial proteins that are antimicrobial targets.

 (3) Changes in membrane permeability to antibiotics.

 [4]The inactivation or modification of the antibiotic;

 Antibiotic resistance can be either plasmid mediated or maintained on the bacterial chromosome. The most important mechanism of resistance to the penicillins and cephalosporins is antibiotic hydrolysis mediated by the bacterial enzyme beta-lactamase.

**Enzymatic degradation of antibacterial drugs**: While hydrolysis is especially important clinically, particularly as applied to beta-lactam antibiotics, the group transfer approaches are the most diverse and include the modification by acyltransfer, phosphorylation, glycosylation, nucleotidylation, ribosylation, and thiol transfer. A unique feature of enzymes that physically modify antibiotics is that these mechanisms alone actively reduce the concentration of drugs in the local environment; therefore, they present a unique challenge to researchers and clinicians considering new approaches to anti-infective therapy.

**Alteration in the target sites of antibiotics is a common mechanism of resistance**: Examples of clinical strains showing resistance can be found for every class of antibiotic, regardless of the mechanism of action. Target site changes often result from spontaneous mutation of a bacterial gene on the chromosome and selection in the presence of the antibiotic. Examples include mutations in RNA polymerase and DNA gyrase, resulting in resistance to the rifamycins and quinolones, respectively. In other cases, acquisition of resistance may involve transfer of resistance genes from other organisms by some form of genetic exchange (conjugation, transduction, or transformation). Examples of these mechanisms include acquisition of the mecA genes encoding methicillin resistance in Staphylococcus aureus and the various van genes in enterococci encoding resistance to glycopeptides.

**Changes in membrane permeability to antibiotics**

Due to their outer membrane, Gram negative bacteria are the only germs which can resist antibiotics by a mechanism of reduced permeability. This outer hydrophobic membrane allows hydrophilic molecules to pass only through its aqueous pores. The transmembrane pores have a trimere structure with a monomere component acting as an aqueous channel. Mean pore diameter is 1 to 1.2 nm. Changes in the absolute number of pores or in qualitative function reduce the diffusion of antibiotics entering the cell. This mechanism of reduced permeability can lead to cross resistance to several families of antibiotics. It is difficult to determine the clinical incidence since such resistances are not always detected.

**The inactivation or modification of the antibiotics**

Antibiotic-inactivating enzymes can accomplish this task by one of two means: by eradicating the essential reactive center of the antibiotic or by modifying the drug in a manner that impairs target binding.

How bacteria resist antibiotics

There are two main ways for bacteria to withstand the effects of an antibiotic:

1. To stop the antibiotic from reaching its target at a high enough concentration
2. To modify or bypass the target that the antibiotic acts on