**ONUH UGOCHINYERE NZUBECHUKWU.**

**16/MHS01/206. (CARRY OVER)**

**PHA 302- PHARMACOLOGY AND TOXICOLOGY. (ASSIGNMENT).**

A protein synthesis inhibitor is a substance that stops or slows the growth or proliferation of cells by disrupting the processes that lead directly to the generation of new proteins.

**AMINOGLYCOSIDES- INTRODUCTION**:

The aminoglycosides are bactericidal agents that are used for the treatment of serious infections. They are not used as single agents because of concerns about the emergence of resistance. In addition they have a very narrow therapeutic to toxic ratio (i.e. the serum level needed to be effective as a therapeutic agent is close to the level where drug toxicity is encountered).

**CHEMICAL STRUCTURE:**

Consist of at least two amino sugars linked by glycosidic bonds to an aminocyclitol ring

**MECHANISM OF ACTION:**

A rapidly bactericidal agent with multiple mechanisms of action. The primary target is the 30S ribosome causing premature chain termination and RNA codon misreading. In addition causes leakage of the outer membrane of Gram negatives. The basis for the bactericidal activity is not completely understood.

**MECHANISM OF RESISTANCE:**

The principal means of resistance is aminoglycoside modifying enzymes. These enzymes such as the adenyltransferases or phosphotransferases modify the aminoglycoside rendering them ineffective. The genes for these enzymes are often plasmid borne and as a result are readily transferred among different bacterial species. An additional mechanism of resistance is diminished uptake of the aminoglycoside via mutations in the electrochemical gradient.

**ANTIBACTERIAL SPECTRUM:**

Aminoglycosides have a somewhat limited spectrum of activity. They are active against Enterobacteriaceae, pseudomonas species, and Gram positive bacteria including staphylococci and streptococci. Some of the aminoglycosides are active against mycobacteria. They have no activity against anaerobes.

**PHARMACOLOGY:**

Aminoglycosides are primarily used for parenteral therapy. There is reasonable distribution into tissues because of its low protein binding and water solubility. Penetration across the blood brain barrier is poor as is penetration into bronchial secretions. Aminoglycosides are excreted virtually unchanged in the urine.

**TOXICITY:**

These drugs have significant toxicity. This includes nephrotoxicity in 5-25% of patients, ototoxicity including both cochlear and vestibular damage, and, infrequently, neuromuscular blockade. To reduce the risks of these complications drug levels are generally monitored in subjects with renal disease.

**INDICATIONS FOR USE:**

Empiric combination therapy for life-threatening infections. Used as combination therapy for resistant bacterial infections, and combination (synergy) therapy for enterococcal infections that require bactericidal activity.

**ADVERSE EFFECTS:**

Aminoglycosides are known to cause ototoxic damage, vestibulo-toxic impairments, nephrotoxicity (kidney damage), and encephalopathy.