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QUESTION: Write on a named bacterial protein synthesis, stating its mechanism of action, indication for use, toxicity and adverse effect.

ANSWERS

CHLORAMPHENICOL

Chloramphenicol is a bacteriostatic broad spectrum antibiotic that is active against both aerobic and anaerobic gram positive and gram-negative organism. It is bacteriostatic because of its capability to inhibit protein synthesis. It hinders protein chain elongation by peptidyl transferase inhibition of bacterial ribosome.

MECHANISM OF ACTION

* Chloramphenicol blocks proper binding of 50S site which stop protein synthesis.
* It does inhibit mitochondrial ribosomal protein synthesis because these ribosomes are 70S, the same as those in bacteria
* It hinders the transfer of the elongating peptide chain to the newly attached amino acyl Trna at the ribosome Mrna complex
* It specifically attaches to the 50S ribosome and therefore hinder the access of aminoacyl-Trna to the acceptor for amino acid incorporation
* It prevents formation of peptide bond
* This may be responsible for the dose related anemia caused by chloramphenicol

INDICATION FOR USE

* Following oral administration, chloramphenicol is rapidly and completely absorbed
* It is widely distributed to virtually all tissues and body fluids. The drug penetrated cell membranes readily
* Excretions of active chloramphenicol and of inactive degradation products occurs by way of the urine. A small amount of active drug is excreted into bile or feces
* Newborns less than a week old and premature infants clear chloramphenicol inadequately
* Because of potential toxicity, bacterial resistance and the availability of other effective drugs, chloramphenicol may be considered mainly for treatment of serious rickettsial infections, bacterial meningitis caused by a markedly penicillin-resistant strain of pneumococcus or meningcoccus, and typhoid fever

ADVERSE EFFECTS

* Gastrointestinal disturbances: Adults occasionally develop nausea, vomiting and diarrhea.
* Oral or vaginal candidiasis may occur as a result of alteration of normal microbial flora
* Bone marrow disturbances: Chloramphenicol commonly caused a dose-related reversible suppression of red cell production at dosages exceeding 50mg/kg/d after 1-2 weeks.
* Aplastic anemia is a rare consequence of chloramphenicol administration by any route. It is an idiosyncratic reaction unrelated to dose, though it occurs more frequently with prolonged use.
* It tends to be irreversible and can be fatal

TOXICITY

* Newborn infants lack an effective glucoronic acid conjugation
* Mechanism for the degradation and detoxification of chloramphenicol
* Consequently, when infants are given dosages above 50mg/kg/d, the drug may accumulate, resulting in the gray baby syndrome , with vomiting, flaccidity, hypothermia, gray color, shock, and collapse
* Interaction with other drugs
* Chloramphenicol inhibits hepatic microsomal enzymes that metabolize other drugs
* Like other bacteriostatic inhibitors of microbial protein synthesis, chloramphenicol can antagonize bacteriocidal drugs such as penicillin or aminoglycosides