ACTIONS AND PHARMACOLOGY

In vitro chloramphenicol exerts mainly a bacteriostatic effect on a wide range of gram-negative and gram-positive bacteria and is active *in vitro* against rickettsias, the lymphogranuloma-psittacosis group and *Vibrio cholerae.* It is particularly active against *Salmonella typhi* and *Hemophilus influenzae.* The mode of action is through interference or inhibition of protein synthesis in intact cells and in cell-free systems.

Chloramphenicol administered orally is absorbed rapidly from the intestinal tract. In controlled studies in adult volunteers using the recommended dosage of 50 mg./kg./day, a dosage of 1 gm. every 6 hours for 8 doses was given. Using the microbiological assay method, the average peak serum level was 11.2 mcg./ml. one hour after the first dose. A cumulative effect gave a peak rise to 18.4 mcg./ml. after the fifth dose of 1 gm. Mean serum levels ranged from 8-14 mcg./ml. over the 48-hour period. Total urinary excretion of chloramphenicol in these studies ranged from a low of 68% to a high of 99% over a three-day period. From 8 to 12% of the antibiotic excreted is in the form of free chloramphenicol; the remainder consists of microbiologically inactive metabolites, principally the conjugate with glucuronic acid. Since the glucuronide is excreted rapidly, most chloramphenicol detected in the blood is in the microbiologically active free form. Despite the small proportion of unchanged drug excreted in the urine, the concentration of free chloramphenicol is relatively high, amounting to several hundred mcg./ml. in patients receiving divided doses of 50 mg./kg./day. Small amounts of active drug are found in bile and feces. Chloramphenicol diffuses rapidly, but its distribution is not uniform. Highest concentrations are found in liver and kidney, and lowest concentrations are found in brain and cerebrospinal fluid. Chloramphenicol enters cerebrospinal fluid even in the absence of meningeal inflammation, appearing in concentrations about half of those found in the blood. Measurable levels are also detected in pleural and in ascitic fluids, saliva, milk and in the aqueous and vitreous humors. Transport across the placental barrier occurs with somewhat lower concentration in cord blood of newborn infants than in maternal blood.

INDICATIONS

IN ACCORD WITH THE CONCEPTS IN THE "WARNING BOX" AND THIS INDICATIONS SECTION, CHLORAMPHENICOL MUST BE USED ONLY IN THOSE SERIOUS INFECTIONS FOR WHICH LESS POTENTIALLY DANGEROUS DRUGS ARE INEFFECTIVE OR CONTRAINDICATED. HOWEVER, CHLORAMPHENICOL MAY BE CHOSEN TO INITIATE ANTIBIOTIC THERAPY ON THE CLINICAL IMPRESSION THAT ONE OF THE CONDITIONS BELOW IS BELIEVED TO BE PRESENT; *IN VITRO* SENSITIVITY TESTS SHOULD BE PERFORMED CONCURRENTLY SO THAT THE DRUG MAY BE DISCONTINUED AS SOON AS POSSIBLE IF LESS POTENTIALLY DANGEROUS AGENTS ARE INDICATED BY SUCH TESTS. THE DECISION TO CONTINUE USE OF CHLORAMPHENICOL RATHER THAN ANOTHER ANTIBIOTIC WHEN BOTH ARE SUGGESTED BY *IN VITRO* STUDIES TO BE EFFECTIVE AGAINST A SPECIFIC PATHOGEN SHOULD BE BASED UPON SEVERITY OF THE INFECTION, SUSCEPTIBILITY OF THE PATHOGEN TO THE VARIOUS ANTIMICROBIAL DRUGS, EFFICACY OF THE VARIOUS DRUGS IN THE INFECTION, AND THE IMPORTANT ADDITIONAL CONCEPTS CONTAINED IN THE "WARNING BOX" ABOVE: