Adults

Adults should receive 50 mg./kg./day in divided doses at 6-hour intervals. Patients with infections due to moderately susceptible organisms or with severe infections often require doses up to 100 mg./kg./day.

Children

Dosage of 50 mg./kg./day divided into 4 doses at 6-hour intervals yields blood levels in the range effective against most susceptible organisms. Severe infections (e.g., septicemia or meningitis), especially when adequate cerebrospinal fluid concentrations are desired, may require dosage up to 100 mg./kg./day; however, dosage should be reduced to 50 mg./kg./day as soon as clinical response occurs. When prolonged high dosage is necessary, possible toxic side effects may occur. In this event the dosage should be immediately reduced or discontinued.

Premature and Newborn Infants

An initial dose of 25 mg./kg. may be given to rapidly achieve effective concentrations in blood serum. This should be followed by administration of 25 mg./kg./day in 4 equal doses at 6-hour intervals, which produces and maintains concentrations in blood and tissues adequate to control most infections. Increased dosage in these individuals, demanded by severe infections, should be given only to maintain the blood concentration within a therapeutically effective range. Full term newborn infants ordinarily may receive from 25 to 50 mg./kg./day equally divided into 4 doses at 6-hour intervals.

For comatose or gravely ill patients, chloramphenicol is available in several forms for parenteral administration.

These dosage recommendations are extremely important because blood concentration of chloramphenicol in the premature and newborn infant differs from that of an infant over one month of age. This difference is due to variations in the metabolic disposition of this and other drugs in this age group which in turn depends on the maturity of the metabolic function and status of the liver and the kidneys. When these systems are immature (or seriously impaired in adults) high concentrations of the drug are found which tend to increase with succeeding doses. Toxic reactions and some fatalities have occurred in the premature and newborn age group, these being associated with higher than recommended dosages. The following summarizes the clinical and laboratory studies that have been made:

(1) In most cases therapy with chloramphenicol had been instituted within the first 48 hours of life.

(2) Symptoms first appeared after 3 to 4 days of continued treatment with high doses of chloramphenicol (100 mg./kg. daily or more).

(3) The symptoms appeared in the following order: (a) abdominal distension with or without emesis; (b) progressive pallid cyanosis; (c) vasomotor collapse, frequently accompanied by irregular respiration; and (d) death within a few hours of onset of these symptoms. This has been referred to in some institutions as the "gray syndrome."

(4) The progression of symptoms from onset to exitus was accelerated with higher dose schedules.

(5) Preliminary blood serum level studies revealed unusually high concentrations of chloramphenicol after repeated doses.

(6) No characteristic pathological changes attributable to the use of chloramphenicol were found in any of the organ systems, including the hemopoietic system.

(7) Termination of therapy upon early evidence of the associated symptomatology frequently reversed the process with complete recovery.

Infants and Children with Immature Metabolic Processes

In young infants (those between one month and one year of age) and others in whom immature metabolic processes are suspected, a dose of no more than 50 mg./kg. but not less than 25 mg./kg./day, will produce therapeutic concentrations of the drug in the blood. In this group particularly, the concentration of the drug in the blood should be carefully followed by available microtechniques.

SIDE EFFECTS OF CHLORAMPHENICOL THERAPY

Untoward reactions in man are infrequent with chloramphenicol. Reactions attributed to chloramphenicol may be considered under the following headings:

Blood Dyscrasias

Aplastic anemia, hypoplastic anemia, thrombocytopenia, and granulocytopenia have been associated with the administration of chloramphenicol.

The following statement is quoted from NEW AND NONOFFICIAL DRUGS 1960, evaluated by A.M.A. Council on Drugs, page 82:

"Although serious and even fatal blood dyscrasias are known to occur after the administration of chloramphenicol, current data seem to indicate that these reactions are rare. Blood dyscrasias have occurred with both short-term and prolonged therapy with this drug. Bearing in mind the possibility that such reactions may occur, the physician may use chloramphenicol in the treatment of serious infections caused by organisms which are susceptible to its antibacterial effects. Chloramphenicol should not be used in treating colds, influenza, viral infections of the throat, or as a prophylactic agent to prevent bacterial respiratory disease."

When blood counts show unusual deviations such as leukopenia or thrombocytopenia, chloramphenicol should be discontinued.

Gastro-Intestinal Reactions

After several days of therapy, glossitis may occur. Stomatitis, when it occurs is generally mild and usually consists of congestion and tenderness of the buccal mucosa. This is an indication to stop the drug. On rare occasions, superimposed infection by *Candida albicans* may produce