PRODUCTS FOR PARENTERAL USE AND DOSAGE RECOMMENDATIONS

CHLOROMYCETIN SUCCINATE (Steri-Vial No. 57)

This is the preferred and the only suitable parenteral product form for intramuscular, intravenous, and subcutaneous use.

The powder in the Steri-Vial is prepared for injection by the addition of an aqueous diluent such as Water for Injection or 5% Dextrose Injection. Although Chloromycetin Succinate is highly soluble, the rate of solution is somewhat slower in the more highly concentrated solutions. Gentle shaking of the vial hastens solution. The following dilution table may be used as a guide for preparing solutions for injection.

DILUTION TABLE

Strength of Solution		Volume of Diluent Required
%	mg. per cc.	
40	400	2 cc.
25	250	3.8 cc.
10	100	11 cc.

Adults—dose recommendations: For most infections due to susceptible organisms, adults should receive 50 mg./kg./day. Patients with infections due to less susceptible organisms often require 100 mg./kg./day. Severe infections may require even higher doses. In either case, this should be divided into 4 doses at 6-hour intervals. Note carefully the dosage table below.

DOSAGE TABLE

Dose	Volume to be Injected		
	40% Solution	25% Solution	10% Solution
1 Gram	2.5 cc.	4 cc.	10 cc.
500 mg.	1.25 cc.	2 cc.	5 cc.
100 mg.	0.25 cc.	0.4 cc.	1 cc.

The following methods of administration are recommended on the basis of tolerance, ease of handling and safety:

1. *Intramuscularly*, as a 25 to 40 per cent solution injected deep into the muscle at one of the common sites of intramuscular injection.
2. *Intravenously*, as a 10 per cent solution to be injected over a one-minute interval. If desired, the solution can be added to a larger volume of parenteral fluid for intravenous infusion.
3. *Subcutaneously*, as a 10 per cent solution injected through a short, small gauge needle. As with the intravenous route, the concentrated solution can be added to fluids for subcutaneous clysis.

Children—dose recommendations: Chloromycetin Succinate is the preferred parenteral dosage form for pediatric use. Dosage of 50 mg./kg./day is adequate for infections caused by 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 dosage should be immediately reduced or discontinued. Chloromycetin Succinate may be administered intramuscularly, intravenously, or subcutaneously, as above and should be divided into doses at 6-hour intervals.

Premature and Newborn Infants—dose recommendations: Chloromycetin Succinate may be used in an initial dose of 25 mg./kg. followed by 25 mg./kg./day in 3 equal doses at 8-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, as best determined by available microtechniques. Full term newborn infants ordinarily may receive from 25 to 50 mg./kg./day equally divided into 3 doses at 8-hour intervals. The same routes of administration as noted above may be employed; generally intramuscular administration is preferred.

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 depends upon 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./day or more).

3. The symptoms appeared in the following order: (a) abdominal distention 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 hematopoietic 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—dose recommendations: In young infants (those between one month and one year of age) and others in whom immature metabolic