with chloramphenicol were report as cases of aplastic anemia with pancytopenia; other forms noted include erythroid hypoplasia without pnacytopenia, thrombocytopenia with no change in red or white blood cells, leukopenia, and agranulocytosis. Aplastic anemia has occured after the administration of small doses for short periods, as well as after prolonged therapy; the other forms of blood dyscrasias appear more likely to be associated with large doses or prolonged therapy and also are more likely to be reversible if the administration of chloramphenicol is discontinued.

Skin rash and gastrointestinal and neurologic reactions, including optic and peripheral neuritides, also have been reported. Sensitization may occur when the drug is applied topically. As with other antibiotics, an overgrowth of nonsusceptible organisms may occur when chloramphenicol is used.

In premature and newborn full-term infants, chloramphenicol has produced toxic reactions referred to as the "gray syndrome," which is characterized by abdominal distension, progressive pallid cyanosis, and peripheral vascular collapse; in a number of cases, death has resulted.

PRECAUTIONS

It is essential that adequate blood studies be made during treatment with this drug. However, although blood studies may reveal early peripheral blood changes such as leukopenia or granulocytopenia before they become irreversible, the studies cannot be relied upon to detect bone marrow depression prior to the development of aplastic anemia.

Because of the possibility that serious and even fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, granulocytopenia) may occur after both short-term and prolonged therapy with chloramphenicol [chloromycetin], the drug should be used only for serious infections caused by organisms that are susceptible to its antibacterial effect. Chloramphenicol should not be used when other less potentially dangerous agents will be effective; or in the treatment of trivial infections such as colds, influenza, or infections of the throat; or as a prophylactic agent to prevent bacterial infections of the respiratory tract.

The dosage recommendations for premature and newborn infants should not be exceeded: moreover, the levels of the drug in the blood should be carefully followed, since the concentration in premature infants and in those under two weeks of age differs from that in older infants. This difference is due to the immaturity of metabolic mechanisms for the disposition of chloramphenicol, as well as of many other drugs; thus, high blood concentrations result and tend to increase with succeeding doses.

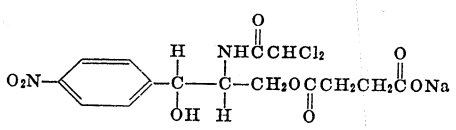
Since patients with impaired hepatic or renal function may retain an excessive amount of chloramphenicol because of decreased metabolism and excretion, the dosage should be adjusted accordingly or, preferably, the blood concentration should be determined at appropriate intervals.

PHARMACOLOGY

Chloramphenicol [chloromycetin] is absorbed rapidly from the gastrointestinal tract and, after a single oral dose, the maximal blood concentration is reached within two hours. It appears to be well distributed, although not uniformly, in the body tissues. The drug passes readily into the cerebrospinal and pleural fluids, and appreciable quantities are found in the bile. It passes into the aqueous and vitreous humor of the eye and crosses the placental barrier. Chloramphenicol is rapidly conjugated by the liver to a monoglucuronide which has no antibacterial activity. It is excreted mainly in the urine. The rate of excretion is proportional to the blood level, and 5% to 10% of the total amount excreted is in the active form.

Chloramphenicol Sodium Succinate, U.S.P.

[Chloromycetin sodium succinate]



D-(—)-*threo*-2,2-dichloro-N[β-hydroxy-α(hydroxymethyl)-ρ-nitrophenethyl] acetamide, α-sodium succinate