of life. None of the infants tested after 7 days of age showed accumulation of nitro compounds in the blood. The majority of these older infants failed to maintain levels in the therapeutic range on 25 mg/kg/day, whereas doses of 50 mg/kg/day produced therapeutic levels without toxic symptoms. Premature infants over 1 week of age can be treated with 1 daily dose of 50 mg/kg of chloramphenicol with reasonable safety.

The young infants also showed greater variability of levels on a given dosage than did prematures over 7 days of age. This is well demonstrated in Figure 1, representing 1-4-day-old infants given microcrystalline chloramphenicol, 10 mg/kg every 12 hours. On this dose, one infant accumulated nitro compounds to toxic levels, while another failed to reach therapeutic levels.

The young infants tested on low doses of microcrystalline chloramphenicol given twice daily accumulated nitro compounds more rapidly than when a larger dose was given once a day. Since adequate levels are maintained for 24 hours after a single injection of both types of chloramphenicol tested, the total dose should be given once daily.

The symptoms of chloramphenicol toxicity in the premature infant have been reported by several authors. (3–6) The time necessary for symptoms to appear depends on the dose used. When 125–165 mg/kg/day were given intramuscularly, the earliest symptoms appeared from 48 to 96 hours after the start of treatment and involved the gastrointestinal tract. (3) The infants refused to nurse, began to regurgitate formula, their abdomens became distended, and they developed loose green stools. Within 24 hours after the appearance of toxic symptoms, they became ashen gray, lethargic, and developed rapid, shallow respirations. Death, when it occurred, followed within an additional 24 hours. The infants who recovered had no demonstrable sequelae on discharge from the nursery.

Of the 126 infants tested during this study, 6 developed symptoms similar to those described. One infant was receiving intravenous medication, and the correlation between symptoms and blood levels seems clear cut. Lethargy and grayish pallor appeared within an hour of starting the intravenous medication, when the blood level was 72μg/cc. and the symptoms disappeared rapidly coincident with a fall in level to 53μg/cc. The accumulation of nitro compounds in this baby was caused by too rapid an intravenous infusion, and the symptoms could have been prevented by slower administration. This is a precaution that must be carefully observed when giving chloramphenicol intravenously.

Two infants, both under 4 days of age, developed symptoms of chloramphenicol toxicity on intramuscular medication, but recovered. In both of these infants the symptoms appeared on the third day of treatment, when their blood levels were over 50μg/cc. and the symptoms disappeared as the levels fell. In the 3 surviving infants, toxic symptoms seemed to be correlated directly with elevation in blood levels of nitro compounds. The blood levels varied from 53μg/cc to 73μg/cc at the time symptoms appeared.

Three infants died while receiving chloramphenicol, with symptoms similar to those described above. The symptomatology of septicemia is very similar to that of chloramphenicol toxicity. One case had abnormal blood chemistries at the start of treatment, and a chloramphenicol-resistant organism was grown from blood culture taken before death. Symptoms appeared after 5 days of treatment, when the infant was 9 days old. This death was probably due to infection, but may represent a toxic reaction to chloramphenicol. Autopsies were not performed on the remaining 2 infants, and blood cultures taken at the time of death were sterile. The levels of chloramphenicol in these infants were never over 54μg/cc. A definite cause of death could not be determined on the basis of the clinical findings. Unexplained deaths, particularly without autopsy, are too common on a premature service to definitely assign these deaths to chloramphenicol toxicity; however, it is possible that these 3 infants represent a toxic reaction at relatively low blood levels. It is perhaps important that these babies were under one week of age at the start of treatment.

If chloramphenicol is used for young premature infants, it should be given in a dosage of 25 mg/kg once daily. If toxic symptoms appear, the drug should be discontinued immediately and blood levels determined where possible. Blood levels can be determined by following the method of Glazko et al. (11).§ The determination requires 0.2 cc. of whole blood, which can be obtained from a heel puncture. The method is a relatively simple colorimetric comparison, which could be performed by the average hospital laboratory.

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§Detailed procedure available from Parke, Davis & Company.