Glazko et al., (1, 2) which includes both the active and the inactive metabolites of chloramphenicol. Figure 2 shows the levels in the babies. Both infants died within four hours of the last blood level indicated. Autopsy showed intraventricular hemorrhage in baby E. No autopsy was done on baby J.

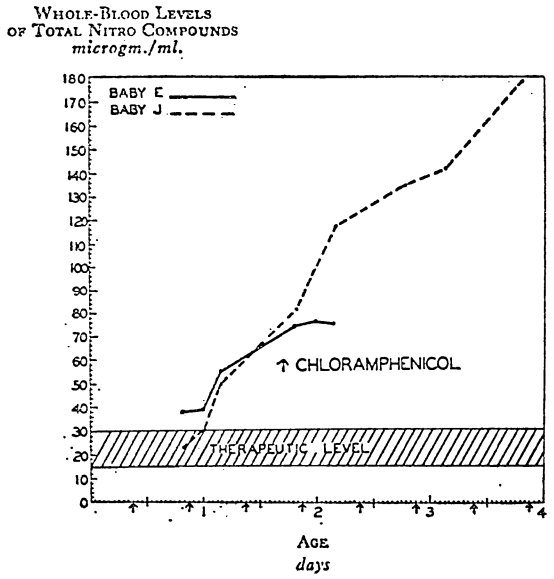

FIGURE 2.—Chloramphenicol Blood Levels.

Although the groups were small, there was no increase in mortality in infants who received 140 to 165 mg. of chloramphenicol per kilogram of body weight as compared to those given 110 to 140 mg. per kilogram per day.

DISCUSSION

Physiologic studies have shown that liver and kidney functions are poor in the premature infant as compared to the adult. Potter and Thierstein (3) found histologically immature kidneys in almost all premature infants weighing 2000 mg. or less. The volume of urine excreted is small, and the ability to concentrate it is poor. Glomerular filtration, as measured by urea and inulin clearance, and tubular excretion, as measured by iodopyracet compound and para-amino-hippurate excretion, are markedly reduced. (4–6) Deficiency in the glucuronide conjugation of bilirubin in the premature liver has been well established. (7–9) This deficiency is thought to be due to a lack of conjugating enzyme. (10) In adults, Glazko and his associates (11) demonstrated that chloramphenicol is detoxified in the liver and excreted by the kidney. They found that detoxification is mainly by glucuronide conjugation. They were able to recover 90 per cent of a given dose from the urine of adults. (12) The bulk of the excreted drug was in the form of an inactive glucuronide conjugate. Less than 10 per cent was excreted unchanged. Renal plasma-clearance studies in adults suggest that the active form is filtered by the glomerulus, and the inactive form is excreted by the tubules.

The toxicity of chloramphenicol has been extensively studied in animals. Smith et al. (13) found that the LD_{50} for chloramphenicol given by mouth to adult mice was 245 mg. per kilogram of body weight. Smaller doses caused tremors and prostration followed by recovery. They also found that dogs given chloramphenicol intravenously responded with a fall in blood pressure. With the use of high doses, the bloodpressure fall was followed by respiratory failure and death.

Several reports in the European literature describe fatal circulatory collapse in patients with typhoid fever treated with chloramphenicol, the shocklike state appearing three to five days after the start of medication. (14–18)

NOTE.—Numbered references at end of article.