

12. Glazko, A. J., Wolf, L. M. Dill, W. A. and Brattan A. C. Jr. Biochemical studies on chloramphenicol (Chloromycetin): tissue distribution and excretion studies *J. Pharmacol. & Exper. Therap.* 96:445-459 1949.
13. Smith, R. M., Joslyn, D. A., and Gruhzit, O. M. Chloromycetin: biological studies. *J. Bact.* 55:425-448 1948.
14. Stephens, P. R. Unsuccessful treatment of typhoid fever with chloramphenicol *Lancet* 1:731, 1950.
15. Patel, J. C., Banker, D. D., and Modi, C. J. Chloramphenicol in typhoid fever; preliminary report of clinical trial in 6 cases. *Brit. M. J.* 2:908, 1949.
16. Farinaud, M. E., and Portes, L. La chloromycetine a doses progressive dans le traitement des fievers typhoides a forme hypertoxique. *Presse med.* 59:3, 1951.
17. Izar, G. Collasso acuto di circolo da cloroamfenicolo. *Riforma med.* 64:1237-1240, 1950.
18. Chatterjee, P. K., and Roy, B. B. Vasomotor collapse after chloramphenicol. *Brit. M. J.* 2:1334, 1950.
19. Sutherland, J. M. Fatal cardiovascular collapse in infants receiving large amounts of chloramphenicol. *J. Dis. Child.* 97:761-767, 1959.
20. Sutherland, J. M., et al. Toxicity of chloramphenicol for newborn infant. Presented at twenty-ninth annual meeting of Society for Pediatric Research, Buck Hill Falls, Pennsylvania, May 8 and 9, 1959.
21. Dorn, A., and Smith, M. Blood levels of palmitate ester of chloramphenicol in infants and children. Presented at twenty-ninth annual meeting, Society for Pediatric Research, Buck Hill Falls, Pennsylvania, May 8 and 9, 1959.

APPENDIX V

[From American Journal of Diseases of Children, vol. 101, February 1961, pp. 140-148]

SAFE AND EFFECTIVE CHLORAMPHENICOL DOSAGES FOR PREMATURE INFANTS

(By Joan E. Hodgman, M.D. and Lafayette E. Burns, M.D., Los Angeles)

Infections are a significant cause of death in premature infants. Arey and Dent(1) reported, in 1953, a survey of 102 neonatal deaths of which 84 were premature. They listed infection as the major cause of death in 13 (15.4%) of the prematures. Six years later Branton,(2) in a report of 176 consecutive newborn deaths, of which 136 were prematures, attributed death to infection in 20 (14.7%) of the prematures. He reported gram-negative coliform bacilli in 5 of 6 positive blood cultures. Infection also plays a significant role in the mortality at the Premature Center of Los Angeles County Hospital, which cares for over 1,200 premature infants yearly. The main organisms cultured from infections have been gram-negative coliform bacilli, particularly *E. coli* and *Klebsiella aerogenes* group. Studies have indicated that these organisms are most consistently sensitive to chloramphenicol. The toxicity of chloramphenicol to premature infants in doses over 100 mg/kg is well documented (3-6). Reported studies have correlated this toxicity with high blood levels of chloramphenicol. Prophylaxis with chloramphenicol as well as other antibiotics has been discontinued at the Premature Center, since in a controlled study they did not lower the mortality rate(3). Chloramphenicol would still be useful for the treatment of infected prematures if a safe dosage schedule were established.

This paper is a report of studies of blood-level responses to intramuscular and intravenous chloramphenicol made to determine whether lower doses would give therapeutic blood levels without toxicity.

METHOD

Premature infants of varying weights and ages were given microcrystalline or the succinate ester of chloramphenicol intramuscularly and intravenously, according to planned dosage schedules. Blood levels of total nitro compounds were

Accepted for publication Oct. 27, 1960.

1200 N. State St. (33).

Supported by a grant from Parke, Davis & Company, Detroit.

From the Premature Center of the Los Angeles County Hospital and the Department of Pediatrics, University of Southern California School of Medicine, Assistant Professor of Pediatrics (Dr. Hodgman) and Instructor in Pediatrics (Dr. Burns).

NOTE.—Numbered references at end of article.