fibrin. Penicillin diffuses almost as well into fibrin as into agar. It is suggested that the diffusibility of penicillin into fibrin is an important factor in the efficacy of this substance in the treatment of subacute bacterial endocarditis.

We are indebted to Dr. Gordon Alles for helpful suggestions.

15381

Serum Levels After Repository Injections of Penicillin.

EDWIN M. ORY, CLARE WILCOX, AND MAXWELL FINLAND.

From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston, Mass.

There is considerable interest in the development of methods for administering penicillin which are both simple and efficient. Oral administration would be the obvious solution were it not for the marked irregularity of absorption as well as the low efficiency of this method with the materials thus far available.[1-4] Various attempts have been made to maintain and prolong the effective concentrations of penicillin after parenteral administration with the hope of reducing the number of injections necessary. Most promising at the present time is the use of a repository injection of a relatively large dose in a medium from which absorption takes place slowly. Among the various combinations proposed, the mixtures of beeswax in peanut oil have been studied most extensively.[5-9] With this method effective serum levels can be maintained quite regularly over a 12-hour period and in most instances for 18 to 24 hours, but the concentrations after more than 12 hours following a dose of 300,000 units or less may be quite irregular or not measurable. While the beeswax-peanut oil mixtures have been used successfully in several clinics, their high melting point and the marked viscosity of the preparations make the injections of these materials technically difficult for most inexperienced persons. Substances which are more easily manipulated at ordinary room temperatures would be much more desirable.

Freund and Thomson[10] proposed the use of a simple, rapid technic of preparing water-in-oil emulsions of penicillin. The penicillin is put into solution in a small volume of saline and added to a mixture of a lanolin-like substance (Falba) and peanut oil and thoroughly emulsified before the injection. This method has been used by Cohn *et al.*[11] in the treatment of 52 cases of acute gonorrhea by the single injection of the emulsion containing 150,000 units of penicillin, with only 2 failures. The serum levels obtained in 3 subjects given the penicillin in this manner were somewhat better sustained than in 2 others in which the same amount of penicillin was given in saline. Similar or identical materials have been prepared commercially (Solvecillin, Pendil, Emulgen, etc.) and have the advantage that they flow readily at or

1 Free, A. H., Parker, R. F., and Biro, B. E., *Science*, 1945, **102**, 666.

2 Cutting, W. C., *et al.*, *J. A. M. A.*, 1945, **129**, 425.

3 Finland, M., Meads, M., and Ory, E. M., *J. A. M. A.*, 1945, **129**, 315.

4 McDermott, W., *et al.*, *Science*, 1946, **103**, 359.

5 Romansky, M. J., and Rittman, G. E., *Science*, 1944, **100**, 196.

6 Romansky, M. J., and Murphy, R. J., *J. A. M. A.*, 1945, **128**, 404.

7 Romansky, M. J., and Rittman, G. E., *New England J. Med.*, 1945, **233**, 577.

8 Leifer, W., Martin, S. P., and Kirby, W. M. M., *New England J. Med.*, 1945, **233**, 583.

9 Kirby, W. M. M., *et al.*, *J. A. M. A.*, 1945, **129**, 940.

10 Freund, J., and Thomson, K. J., *Science*, 1945, **101**, 468.

11 Cohn, A., PROC. SOC. EXP. BIOL. AND MED., 1945, **59**, 145.

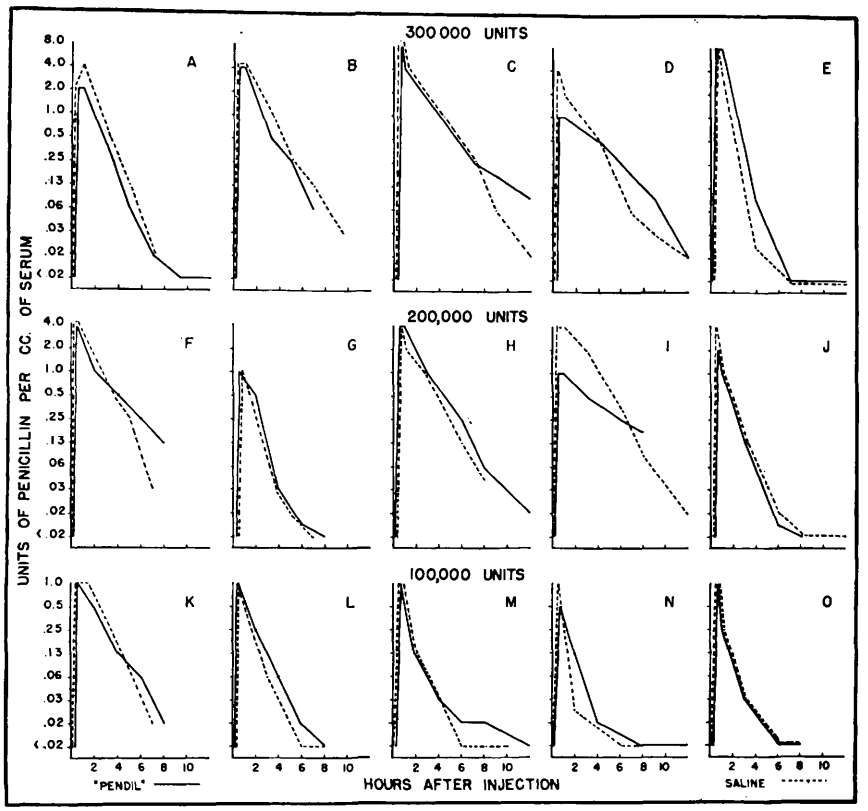

FIG. 1.
Serum penicillin concentrations in the same subjects after intramuscular injections of various doses in saline and in a water-in-oil emulsion.

slightly above room temperature and can therefore be easily manipulated. From that point of view, this type of mixture would be much preferable to the thicker beeswax mixtures, which readily solidify at the same temperatures.

In view of the fact that there may be considerable individual variations in the absorption of penicillin even after intramuscular injections of the same dose, it seemed essential to compare serum levels obtained from any given dose in the repository injection with those obtained with saline solutions in the same individuals.

Intramuscular doses of 100,000, 200,000 and 300,000 units, each in a volume of 4.5 cc were used. The subjects were ward patients who had not recently received any chemo- or antibiotic therapy. About one-half of the subjects were given a single dose of penicillin in saline and 3 or more days later the same amount of penicillin was given in water-in-oil emulsion* as advocated by Freund and Thomson.[10] The other subjects received the doses in the reverse order. Blood was drawn at intervals after the injection and the concentration of penicillin in the serum determined by a slight modification of the serial dilution method of Rammelkamp.[12] The minimum concentration detectable by this method was 0.0156 unit per cc of serum.

The results are shown in Fig. 1. There were slight variations in the maximum concentrations obtained and somewhat greater individual variations in the maintenance of serum levels after the same dose. The larger doses gave higher and more prolonged levels in either menstruum. There was no constant

* "Pendil," generously supplied by Endo Products, Inc., through the courtesy of Dr. Samuel M. Gordon.

12 Rammelkamp, C. H., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 95.

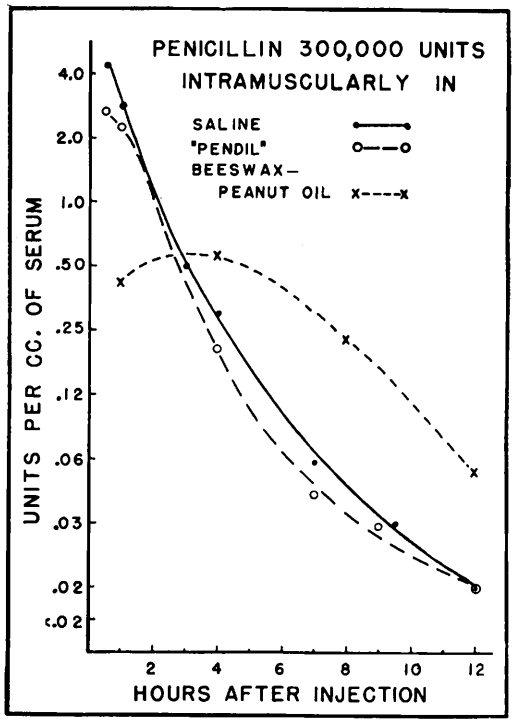

FIG. 2.
Serum penicillin concentrations after intramuscular injections of 300,000 units of penicillin in 3 vehicles.

or striking difference between the results obtained in the same subject after the same dose given in the 2 vehicles.

In Fig. 2 are shown the mean concentrations obtained over a 12-hour period after intramuscular injections of 300,000 units of penicillin given in saline, in Pendil, and in 4.8% beeswax in peanut oil (Delacillin, Squibb), the latter being contained in a volume of 1 cc. Each curve is based upon the results obtained in 6 subjects. It is seen that the maximum concentration obtained with the beeswax-peanut oil mixture was appreciably lower, but the levels were much better sustained than with the same dose in saline or in Pendil.

Conclusions. When tested in the same subject, the serum concentrations obtained after a single injection of penicillin in a water-in-oil emulsion were not superior to those obtained with the same dose given in the same volume of saline, and the levels were not better sustained. A dose of 300,000 units in 1 cc of 4.8% beeswax in peanut oil gave lower maximum concentrations, but the serum levels were better sustained over a 12-hour period.

15382 P

Suppression of Circulating Antibodies in Pyridoxin Deficiency.

HERBERT C. STOERK AND HERMAN N. EISEN.
From the Department of Pathology, College of Physicians and Surgeons, Columbia University, New York City.

There has recently accumulated evidence to indicate that there may be an important relationship between lymphocytes and antibodies.[1,2,3] Data suggesting that pyridoxin may be a factor essential for the maintenance of lymphoid tissue have been reported previously.[4,5,6] It therefore seemed of interest to study the effect of pyridoxin deficiency on circulating antibodies.

Methods. Twenty-four male albino rats of the Sherman strain, close to 4 weeks of age, were divided into 3 groups of litter mates.

The animals in the first group were weaned

[1] Ehrich, W. F., and Harris, T. N., *Science*, 1945, **101**, 28.

[2] Daugherty, T. F., Chase, J. H., and White, A., PROC. SOC. EXP. BIOL. AND MED., 1944, **57**, 295.

[3] Daugherty, T. F., Chase, J. H., and White, A., PROC. SOC. EXP. BIOL. AND MED., 1945, **58**, 135.

[4] Stoerk, H. C., and Zucker, T. F., PROC. SOC. EXP. BIOL. AND MED., 1944, **56**, 151.

[5] Stoerk, H. C., *Fed. Proc.*, 1946, **5**, 227.

[6] Stoerk, H. C., PROC. SOC. EXP. BIOL. AND MED., in press.