16586

Serum Concentrations of Penicillin Following Administration of Crystalline Procaine Penicillin G in Aqueous Suspension.

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Previous studies have demonstrated prolonged serum penicillin levels following intramuscular administration of procaine penicillin G in vegetable oil.[1] The disadvantages of penicillin preparations in oil and beeswax consist primarily of an increased incidence of cutaneous sensitivity reactions, the danger of oil embolism, and somewhat decreased ease of administration. The importance of an aqueous penicillin preparation which would insure a prolonged serum penicillin concentration is, therefore, apparent. The purpose of this paper is to present pharmacologic data concerning the use in man of procaine penicillin in aqueous suspension.

Materials and Methods. Antibiotic Agents. Crystalline procaine penicillin G in powdered form was suspended in an aqueous diluent with a dispersing agent.* Later preparations consisted of a mixture of crystalline procaine penicillin G and the dispersing agent, necessitating the addition of either water or physiological saline to form a stable suspension. Dilution to provide a concentration of 300,000 units per cc was made shortly prior to injection. A uniform suspension was obtained by vigorous shaking for several minutes.

Method of Administration. The subjects employed in this study were in the main young adults with no known renal, cardiac, or hepatic damage, many of whom were postpartum females or patients convalescing from some acute illness. Dry, sterile syringes and 18-20-gauge needles were used for the intramuscular administration of either 1 or 2 cc containing 300,000 units of crystalline procaine penicillin G per cc.

Method for Determination of Serum Penicillin Concentrations. Serum penicillin concentrations of these samples were determined by the method of Rammelkamp.[2]

Results. Administration of 300,000 *Units Crystalline Procaine Penicillin G in Aqueous Suspension.* Forty-six subjects received a single intramuscular injection of 300,000 units of this suspension with the results shown in Fig. 1 and 2. All subjects within one-half hour showed a level of 0.02 units penicillin per cc or more with 30% attaining levels of at least 0.32 units per cc. The serum penicillin concentrations were uniformly greater 4 hours after administration than at one-half hour with a range of 0.04 to 1.28 units per cc. Twelve hours after administration all subjects had demonstrable levels and 21 (46%) had concentrations of at least 0.08 units per cc serum. Assayable amounts of penicillin were present 24 hours following injection in 36 patients (92%).

Administration of 600,000 *Units Crystalline Procaine Penicillin G in Aqueous Suspension.* The results of a single intramuscular injection of 600,000 units of this suspension in 32 subjects are recorded in Fig. 3 and 4. Serum penicillin concentrations one-half hour after injection varied between 0.08-1.28 units per cc. Maximum serum levels of 0.04-2.5 units per cc appeared 4 hours after injection. Twelve hours after administration levels varied from 0.04-1.28 units per cc. Twenty-four hours after injection assayable concentrations were present in all subjects with 23 (72%) having a level of 0.08 units per cc. Assayable concentrations were present in

* We are indebted to E. R. Squibb & Sons, New Brunswick, N.J., for supplying the penicillin preparations employed in these studies.

1 Hewitt, W. L., Whittlesey, P., and Keefer, C. S., *New Eng. J. Med.*, in press.

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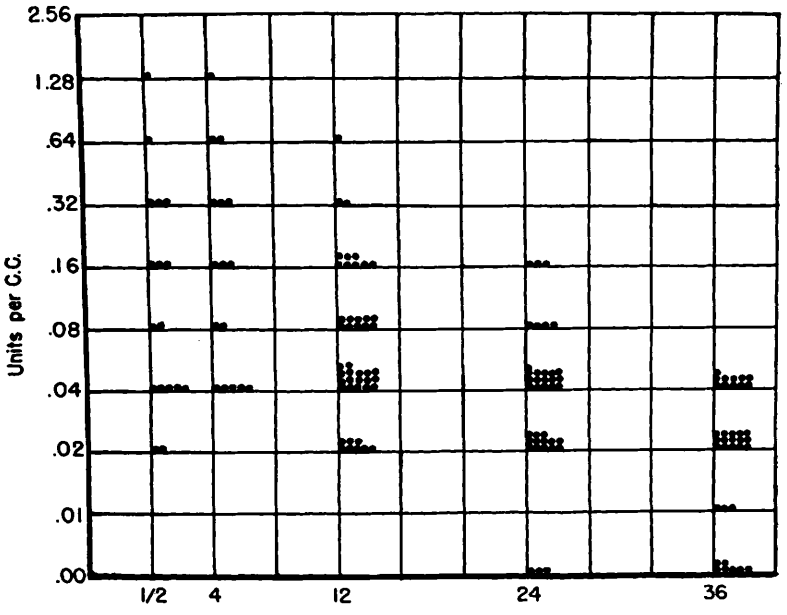

FIG. 1.

Serum penicillin concentrations following administration of 1 cc aqueous suspension containing 300,000 units of crystalline procaine penicillin G.

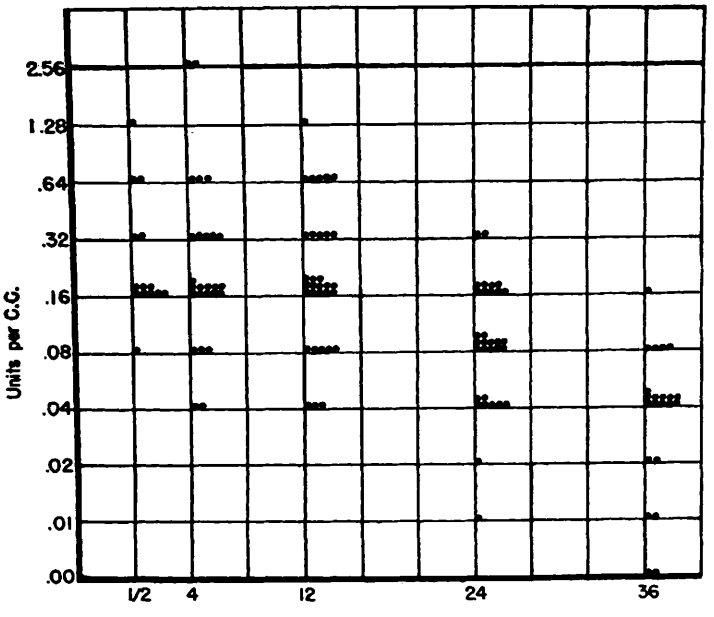

FIG. 2.

Serum penicillin concentrations following administration of 1 cc aqueous suspension containing 600,000 units of crystalline procaine penicillin G.

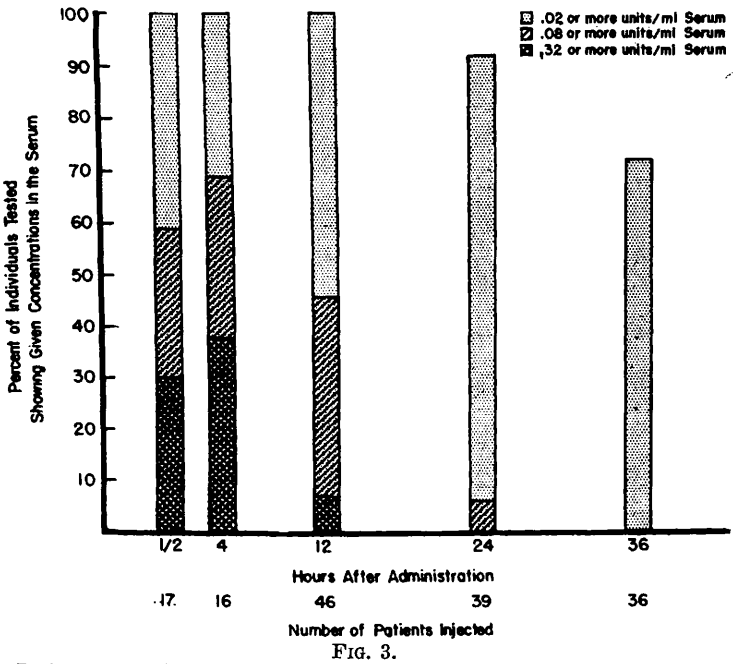

FIG. 3.

Incidence of given serum penicillin concentrations following administration of 1 cc aqueous suspension containing 300,000 units of crystalline procaine penicillin G.

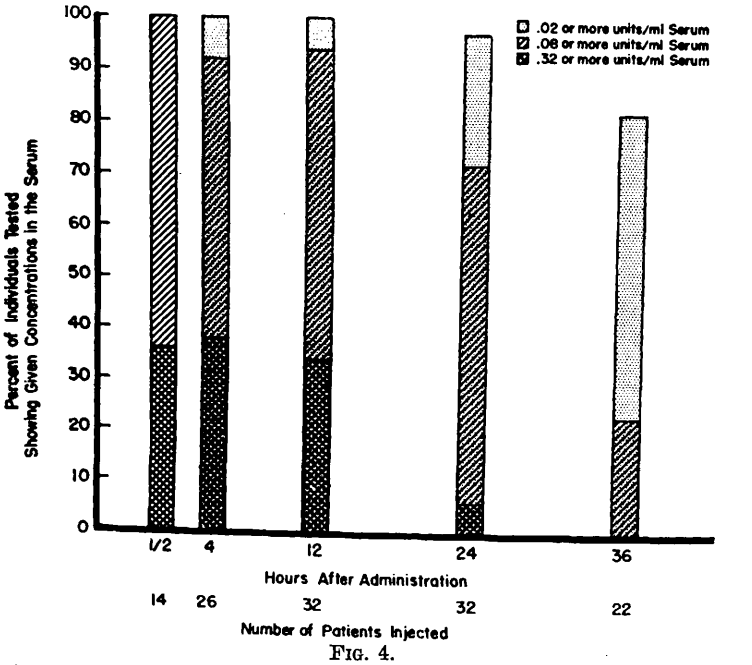

FIG. 4.

Incidence of given serum penicillin concentrations following administration of 1 cc aqueous suspension containing 600,000 units of crystalline procaine penicillin G.

94% of subjects 36 hours after injection.

Comment. Ease of administration characterized the injections of procaine penicillin in aqueous suspension. Clogging of needles occurred occasionally due to aggregation of procaine penicillin crystals. The frequency of this may be minimized by thorough shaking of the preparation prior to withdrawal into the syringe, immediate injection, and use of 18 or 19 gauge needles for administration. Pain, inflammatory reaction or subcutaneous nodules were not observed at the site of injections. No systemic reactions occurred.

The serum penicillin concentrations following similar doses of vegetable oil suspension and aqueous suspension of procaine penicillin G manifested the same general pattern differing from peanut oil-beeswax preparations by the absence of a high initial peak shortly after injection and the presence of a more uniform serum level during the 24 hours after administration.[1] However, it was noted that with 300,000 units a slightly higher percentage of patients maintained a level of 0.02 units per cc or more but a lower percentage maintained 0.08 units per cc with the aqueous suspension. In using 600,000 units the aqueous suspension group showed a lower percentage throughout of comparable serum levels.

Summary. 1. Administration of 300,000 units of crystalline procaine penicillin G in aqueous suspension produced demonstrable serum penicillin concentrations at 12 hours after administration in all subjects and at 24 hours after injection in 92% of subjects studied.

2. Administration of 600,000 units of this material produced demonstrable serum penicillin concentrations 24 hours after injection in all subjects.

3. Similar patterns of serum penicillin concentrations were obtained for both the oil and the aqueous suspensions of procaine penicillin G although slightly lower values were generally observed with the aqueous suspension.

4. Ease of administration and absence of untoward local or systemic reaction were uniformly observed with the administration of procaine penicillin G in aqueous suspension.

We are indebted to Miss Doris McCarthy for technical assistance.

16587 P

The Effect of Streptomycin on Well-Established Experimental Tuberculosis of Mice.*

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Previous studies have shown streptomycin to be effective for the suppression of experimental tuberculosis in mice when treatment was started at the time the animals were infected.[1,2,3] Although well-established tuberculosis of guinea pigs is known[4,5,6,7] to be favorably affected by streptomycin therapy, there is no information available as to the degree of effectiveness of this agent on well-established tuberculous infections of mice.

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