

Plasma Levels after Repository Injections of Penicillin in Water-in-Oil Emulsions.

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A comparison of the penicillin levels obtained in the same patients after the same intramuscular dose of penicillin given in saline and in a water-in-oil emulsion as advocated by Freund and Thomson¹ was presented in a previous communication.² Some variations were noted in the maximum concentrations obtained and considerably greater differences were noted in the maintenance of levels in the blood after any given dose. Intramuscular doses of 100,000, 200,000 and 300,000 units were given. Higher and better sustained levels followed the larger doses. There was no constant or striking difference between the results obtained in the same subjects after the same dose given in the 2 vehicles. A dose

of 300,000 units in a beeswax-peanut oil mixture gave maximum concentrations which were appreciably lower, but the levels were much better sustained than with the same dose given in saline or in the water-in-oil emulsion. The emulsion base used in the previous study was Pendil, a "cholesterol-derivative and peanut oil" as described by Freund and Thomson.

A second series of observations are reported here with the use of a similar preparation, "Emulgen,"* which is composed of "sesame oil and cholestrin base." Chlorobutanol 3% is added as a preservative and local anesthetic. The methods used were the same as in the previous studies. Each subject was given a single dose of 200,000 or 300,000 units in saline or in the water-in-oil emulsion and

¹ Freund, J., and Thomson, K. J., *Science*, 1945, **101**, 468.

² Ory, E. M., Wilcox, C., and Finland, M., *Proc. Soc. Exp. Biol. and Med.*, 1946, **62**, 86.

* Supplied by Dr. C. O. Miller, Lakeside Laboratories, Inc.

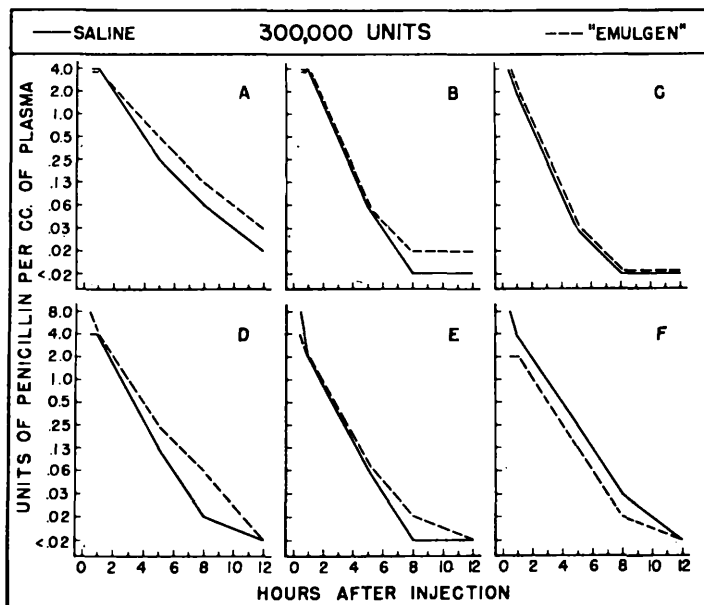


FIG. 1.
Plasma penicillin levels in 6 subjects after intramuscular injections of 300,000 units in saline and in a water-in-oil emulsion.

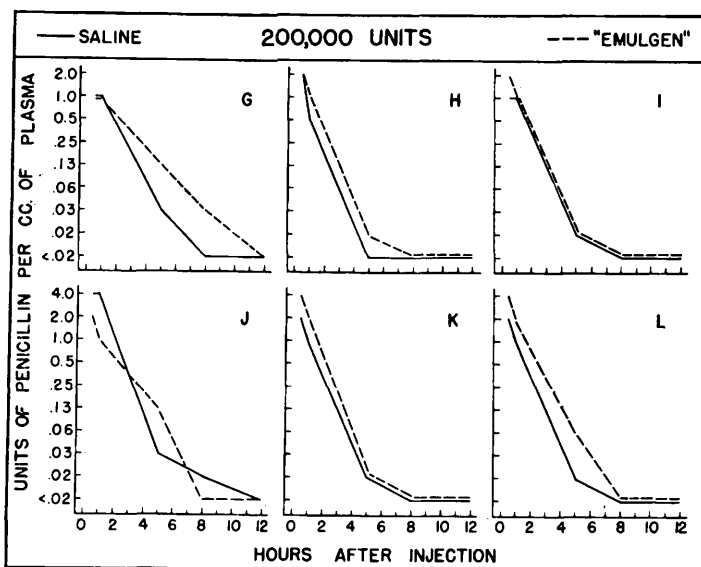


FIG. 2.

Plasma penicillin levels in 6 subjects after intramuscular injections of 200,000 units in saline and in a water-in-oil emulsion.

TABLE I.
Average Concentrations of Penicillin in Plasma Following Intramuscular Injections in Two Vehicles.

Hours after injection	Units per cc of plasma			
	After 200,000 units in		After 300,000 units in	
	Saline	"Emulgen"	Saline	"Emulgen"
½	2.00	2.50	5.33	4.33
1	1.42	1.33	3.33	3.00
5	0.016	0.06	0.13	0.17
8	0.003	0.005	0.02	0.04
12	0	0	0.003	0.008

the same dose was given to the same subjects 2 or 3 days later in the same final volume of the alternate vehicle. A single batch of penicillin was used in this study. This was a purified product which consisted almost entirely of crystalline penicillin G.[†] Special care was taken to obtain a smooth, creamy emulsion as advocated by Freund and Thomson. There was no local irritation from any of the injections. Blood for penicillin levels was drawn at ½, 1, 5, 8 and 12 hours after the injections. The results are shown graphically for each subject in Fig. 1 and 2 and the average levels for each dose level are given in Table I. Comparable, but not

the same subjects were used for the 2 dosages.

As in the previous report, the maximum concentrations varied somewhat in different subjects, but there were greater variations in the rate of decline in the plasma levels. After a dose of 300,000 units, demonstrable levels were no longer present at 12 hours except in one subject. After 200,000 units, there was no demonstrable penicillin in the plasma after 8 hours in almost every instance. In about one-half of the subjects receiving each dose, the penicillin levels were slightly better sustained when given in water-in-oil emulsion. The average blood levels after 5 and 8 hours were also somewhat higher in subjects receiving the emulsion. Much more striking, however, is the fact that the plasma levels obtained after 300,000 units in saline

[†] Supplied by the Commercial Solvents Corporation.

were considerably higher and much better sustained than those observed after 200,000 units given in the same volume of the water-in-oil emulsion.

Conclusion. The previous observation that only a slight and inconstant prolongation of penicillin blood levels is obtained by the use of a water-in-oil emulsion is confirmed. The

present findings suggest further that a substantial increase in the intramuscular dose of penicillin in the same volume of saline will give considerably higher and better sustained plasma levels than the smaller dose given in a water-in-oil emulsion and the disadvantages of the latter method are thus avoided.

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A Constant Current Square Wave Stimulator.

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In the study of neuromuscular excitability, both experimental and clinical, a source of stimulating electric current is required. As the tests employed have been refined, there has been simultaneous refinement and complication of the apparatus required to perform them, with the development of a multiplicity of stimulators, each designed for one specific test. It is the purpose of this paper to de-

scribe the construction of a stimulator which may be used both for the older and the more recent tests, yet which is not unduly complex, and which may be constructed from standard radio components.

This stimulator is capable of producing waves of essentially square form as seen in Fig. 1, with constant current at full output of 20 milliamperes so long as the output re-

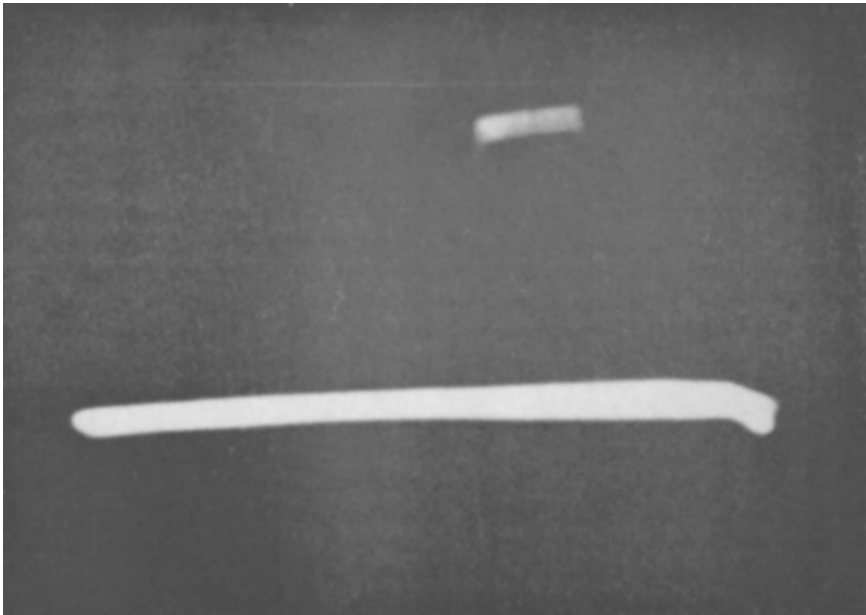


Fig. 1.

Cathode ray oscillographic tracing of stimulus of 5 milliseconds duration, showing square wave form.