

TABLE II.
Passive Immunity After Immunization with Dead
Trypanosomes.

Serum obtained days after active immunization, days	Delay of reinfection, days
0	0
3	0, 0, 3
5	3, 4, 5
10	2, 3, 3
14	5, 5, 5

These results indicate that the trypanocidal power of the serum of infected mice treated with Compound 122 is, apparently, not due to circulating antimony, but to other processes, probably immunologic in nature, and induced by the chemotherapeutic agent. But this action is not characteristic of the antimony compound used, since an experiment in which Neoarsphenamine was used instead of Compound 122 produced the same result. (Table I).

2. The development of anti-trypanocidal activity in the mouse-blood is probably an effect of any successful treatment of dourine with subsequent death of the protozoa. Immunization with killed trypanosomes, with results similar to those obtained in our experiments with Compound 122, has often been obtained, for instance, in mice infected with *Trypanosoma brucei* and treated with

arsacetin.² We had the same results after immunization with *Trypanosoma equiperdum*. Fifteen mice were exsanguinated at the height of the infection, the blood citrated, pooled, and the contained trypanosomes killed by repeated freezing and thawing. This sterile blood, incapable of producing infection, was injected, 0.5 ml doses, into normal mice and groups of 3 inoculated with living trypanosomes immediately and after 3, 5, 10 and 15 days. The results are seen in Table II.

Conclusion. It is confirmed that a single intraperitoneal or subcutaneous injection of a sodium salt derived from melaminyl-phenylstibonic acid (Compound 122) confers a long-lasting protection against numerous consecutive infections of the mouse with *Trypanosoma equiperdum*. This protection is also obtained by oral administration of the compound. In infected mice which have been cured with this product, an immunity to reinfection with *Trypanosoma equiperdum* is achieved. The passive transfer of this immunity has been demonstrated. A similar state is reached if the product is injected first, and subsequently, reinfections with small amounts of trypanosomes are made. It is not established whether this acquired immunity to reinfection plays a role in the prophylaxis conferred by Compound 122.

² Browning, C. H., and Gulbranson, R., *J. Path. and Bact.*, 1936, **43**, 479.

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Pectin Adjuvant for Oral Penicillin.

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Numerous adjuvants have been used individually and in various combinations in attempts to increase the absorption of orally administered penicillin.¹⁻³ For the most part the relative efficacy of these substances has

been determined by comparing the average blood concentrations obtained in small groups of subjects at various intervals following a dose or on the average amount of penicillin recovered from the urine. Individual variations under these conditions, how-

¹ Cutting, W. C., et al., *J. A. M. A.*, 1945, **129**, 425.

² Free, A. H., Parker, R. F., and Biro, B. E.,

Science, 1945, **102**, 666.

³ McDermott, W., et al., *Science*, 1946, **103**, 359.

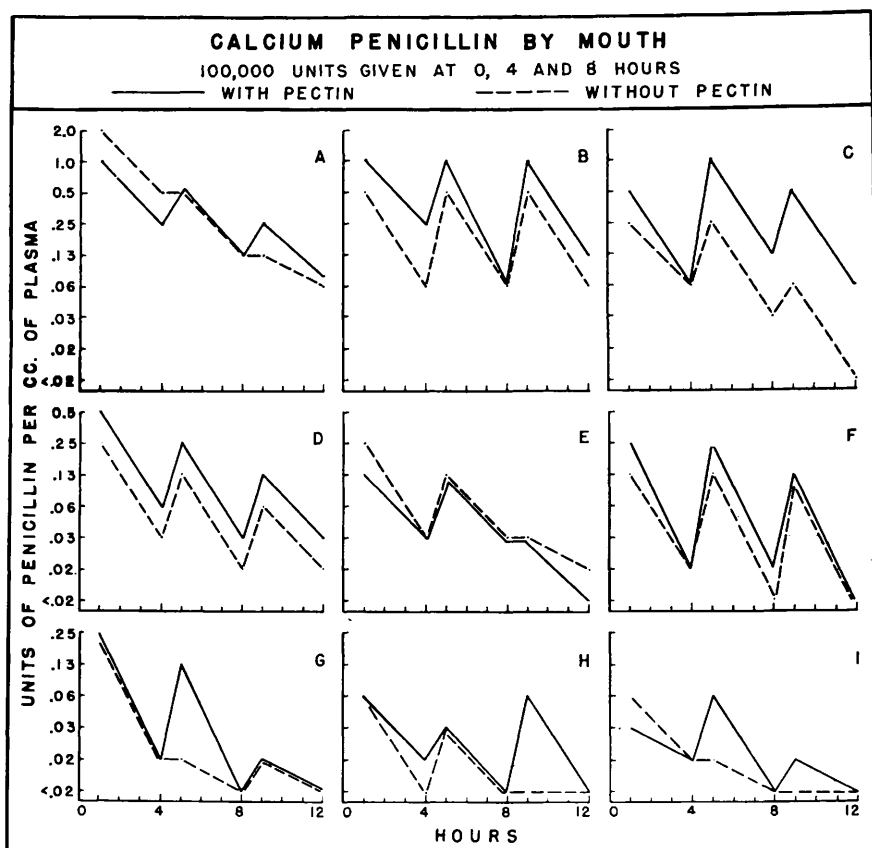


FIG. 1.

Penicillin levels in plasma after oral administration of calcium penicillin in gelatin capsules with and without a pectin adjuvant. Meals were given at $1\frac{1}{4}$, $5\frac{1}{4}$, and $9\frac{1}{4}$ hours.

ever, may be very great³ and may profoundly affect the averages in small groups. For that reason it seems more appropriate to compare any given substances at different times in the same individuals under as nearly identical conditions as possible. A comparison of this sort was made with 2 oral preparations of calcium penicillin one of which contained a pectin derivative as an adjuvant.

Materials and Methods. The calcium penicillin used for the 2 preparations was predominantly penicillin G. In one of them the penicillin was conjugated with a pectin hydrolysate, pH 6.0-7.0, made from a high grade pectin which conformed to the standards prescribed therefor by the N.F. Both the control and the pectin preparation were contained in simple gelatin capsules without formalin, hardening or other preservatives

added. Each capsule contained 25,000 units of penicillin.* The subjects were convalescent patients who had not recently received antibiotics or sulfonamide drugs. After an overnight fast, each subject was given a dose of 100,000 units of penicillin (4 capsules) at 6 a.m. and again at 10 a.m. and at 2 p.m. Blood for plasma penicillin levels was drawn 1 and 4 hours after each dose, the third and fifth samples being taken just before the second and third doses. Meals were served about 15 minutes after each of the one-hour bloods. Half of the subjects used each day received one of the preparations and the rest were given the other.

* These materials and the data concerning them were obtained through the kindness of Commercial Solvents Corporation.

TABLE I.

Average Plasma Penicillin Levels After Oral Administration of 2 Preparations of Calcium Penicillin* in the Same 9 Subjects.

Hour	Plasma level, units per cc	
	With Pectin	Without Pectin
1	.41	.42
4	.08	.08
5	.34	.18
8	.04	.03
9	.24	.11
12	.03	.02

* 100,000 units given at 0, 4, and 8 hours. Meals at 1¼, 5¼, and 9¼ hours.

Several days later the test was repeated in the same subjects, each receiving the alternate preparation. Plasma penicillin levels were done by a slight modification of the serial dilution method of Rammelkamp,⁴ using the same strain of hemolytic streptococcus (No. 98).† The smallest amount of penicillin measured was 0.0156 unit per cc (shown as .02 unit in Fig. 1).

Results. The plasma penicillin levels ob-

⁴ Rammelkamp, C. H., *Proc. Soc. Exp. Biol. and Med.*, 1942, **51**, 95.

† These determinations were done by Clare Wilcox.

tained in 9 subjects are shown in Fig. 1. It is at once apparent that there are wide differences in the plasma levels obtained in individual subjects with either preparation. These differences are much greater than those obtained in the same subjects with the 2 substances. In addition, there was a general downward trend in the plasma levels of all of the subjects after the second and third doses. This may have been the cumulative influence of the meals.⁵ While the differences between the plasma levels obtained with the 2 preparations in the same subjects were not striking, those obtained with the pectin-containing preparation were either the same or higher, and they were more often higher after the second and third doses. This is also evident from the higher average plasma levels obtained in the 9 subjects as shown in Table I.

Conclusion. Pectin hydrolysate used as an adjuvant for oral calcium penicillin resulted in somewhat better sustained plasma penicillin levels as compared with the same materials without the pectin.

⁵ Finland, M., Meads, M., and Ory, E. M., *J. A. M. A.*, 1945, **129**, 315.

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Experiments on the Lateral Line System of Anurans.

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It has been claimed that in fishes^{1,2} ordinary epithelial cells are transformed into lateral line sense organs under the influence of the regenerating lateral line nerve. However, in 19 *Rana clamitans* tadpoles observed frequently under the compound microscope for as long as 200 days, no new sense organs developed in association with the regenerating lateral line nerve fibers growing under

skin not originally containing these organs.

In another series of experiments living lateral line sense organs were observed during the regeneration of tail tips following tail-tip amputation in 53 *Rana* tadpoles. Thirty-two were hypophysectomized animals, which, due to the reduction of skin pigmentation, are of great value in making observations upon the sense organs, peripheral nerves and blood vessels. Twenty-one were normal tadpoles. In 17 control cases the lateral line nerve supplying the regenerating

¹ Broekelbank, M. C., *J. Exp. Zool.*, 1925, **42**, 293.

² Bailey, S. W., *J. Exp. Zool.*, 1937, **76**, 187.