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 obtained 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.

[4] Rammelkamp, C. H., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 95.

† These determinations were done by Clare Wilcox.

[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] Brockelbank, M. C., *J. Exp. Zool.*, 1925, **42**, 293.

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

series of organs was allowed to regenerate normally. In the 36 experimental cases the lateral line nerve was transected anterior to the level of tail-tip amputation and was resectioned sufficiently often to prevent reinnervation of the posterior portion of the stump and the regenerating series of organs. In 10 of these the lateral line nerve was severed after regeneration of sense organs had begun; in 19, it was severed at the same time as tail-tip amputation; and in 7, it was cut 7-10 days previous to tail-tip amputation. In these 3 experimental series, as well as in the controls, placodal material developed from the most posterior organ on the stump or from one of the organs of the most posterior cluster. These cells rapidly proliferated and usually within 10 days formed a long chain of interconnected clumps of cells extending posteriorly on the regenerating tail tip. No contributing placodal material ever developed from the more anterior organs. The clumps of cells, possessing at first no hair cells, differentiated into typical, though small, lateral line-sense organs with sensory cells possessing hairs. The organs eventually attained the same size as those removed by amputation. The progress of differentiation was directed posteriorly, *i.e.*, the regenerate organs which were first fully differentiated were those nearest the original site of amputation, and a wave of differentiation proceeded posteriorly. There never was the slightest indication that denervation before, after, or simultaneously with tail-tip amputation had any effect upon the time or mode of regeneration of lateral line sense organs,* and it is, therefore, concluded that any trophic or inductive influence on the part of the lateral line nerve is unnecessary for normal regeneration of the sense organs.

Further evidence that there is considerable independence of the sense organs of their nervous connections is demonstrated by a third type of experiment. Living, denervated, lateral line sense organs of the dorsal tail fin were observed and compared with normally innervated organs on the opposite side over extended periods of time. Sixty-seven experiments, involving repeated observations on a total of 2,313 lateral line sense organs were followed for 6-142 days. These included 37 experiments on hypophysectomized Rana species and 30 on normal *Rana clamitans* tadpoles. The normally occurring degeneration of lateral line sense organs and nerves due to metamorphosis is circumvented by hypophysectomy. In no instance was there any immediate apparent effect of denervation on the sense organs, but only after prolonged denervation was the removal of the trophic action of the nerve on the sense organs made visible by the degeneration of some sense organs.* However, there was great variation in the ability of these organs to withstand degeneration. Some still appeared normal after 142 days of denervation, while others degenerated as early as 39 days after denervation. Degeneration of the denervated organs could not be correlated with any lack of proper blood circulation and must be attributed rather to the lack of specific nervous connections. A far greater dependence of the lateral line sense organs on the trophic influence of the lateral line nerve of some of the fishes has been reported.[1,2]

In 2 cases where some lateral line organs had degenerated the nerve was allowed to regenerate. There was no reappearance of organs in the position of the degenerated organs. Again, this indicates an apparent lack of inductive influence of the lateral line nerve in the formation of sense organs.

* This is in agreement with the observations reported in abstract by Speidel, C. C., *Anat. Rec.*, 1944, **68**, 458.