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SPECIAL ARTICLES

ORAL PENICILLIN[1]

As a result of Libby's demonstration[2] that appreciable concentrations of penicillin in the serum of dogs and man may be attained following the oral administration of suspensions of penicillin in oil, we have investigated the administration of penicillin by the oral route by four methods. On successive days a series of normal subjects ingested (*a*) penicillin in corn oil, (*b*) penicillin in water, (*c*) penicillin in water preceded by a buffer, and (*d*) penicillin in peanut oil and 4 per cent. beeswax. The penicillin was dissolved in 30 cc of water. Magnesium trisilicate was the buffering agent used. A 4-gram dose was administered every hour for 3 hours before the ingestion of the penicillin. It has been shown[3] that the dosage will raise the pH of the gastric content to approximately pH 8. All subjects were kept in a fasting state throughout the period of observation. Three doses of penicillin, 315,000, 100,000 and 50,000 units, were studied. The bioassays of penicillin were performed by the Rammelkamp method.[4]

Serum concentrations of penicillin which were attained following the ingestion of 315,000 units of penicillin by the four methods described above may be seen in Fig. 1. Penicillin concentrations attained following the intramuscular injection of 300,000 units

[1] The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Cornell University Medical College.

[2] R. L. Libby, SCIENCE, 101: 178, 1945.

[3] W. N. Mann, *Guy's Hospital Reports*, 87: 151, 1937.

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

of penicillin in aqueous solution are presented for comparison. Each point on the graph represents (as indicated) an average of three or four experiments. As may be seen in the figure, serum concentrations ranging between 0.312 and 1.25 unit of penicillin per cc were present at 30 or 60 minutes after ingestion. It appears that penicillin concentrations of approximately the same order of magnitude are attained regardless of whether the penicillin is given in oil, in oil and beeswax, in aqueous solution preceded by a buffer or in aqueous solution alone.

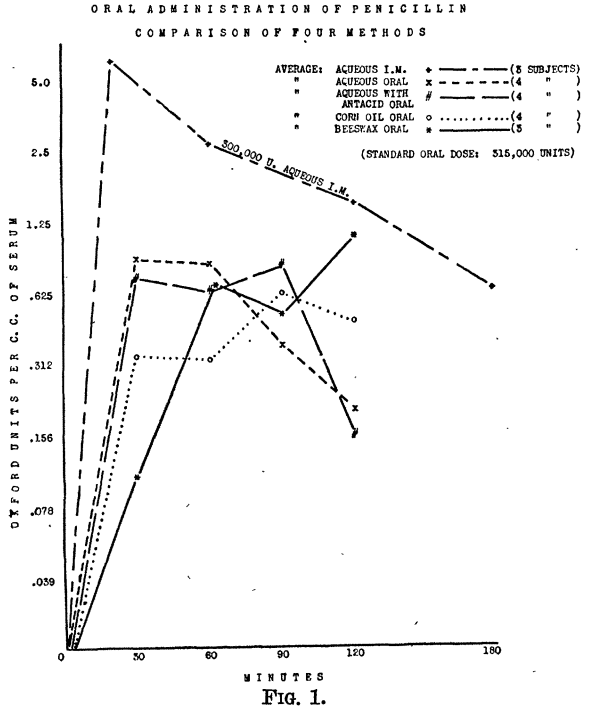

FIG. 1.

The height of the penicillin concentrations at 2 hours after ingestion of the oil and the oil and beeswax preparations suggests that the duration of penicillin action may be prolonged by the use of these vehicles by mouth in a manner similar to the prolongation which Romansky[5] has shown follows the administration of penicillin in oil and beeswax by the intramuscular route.

Only a fraction of the penicillin which was ingested was excreted in the urine during the succeeding 12 hours. The total urinary excretion during this period ranged from 6 to 32 per cent., but in the majority of instances it was approximately 12 per cent. Just as with the penicillin concentrations attained in the blood, there seemed to be no significant difference in the amount of penicillin excreted in the urine after ingestion of the various preparations.

[5] M. J. Romansky and G. E. Rittman, SCIENCE, 100: 196, 1944.

Studies of the serum concentrations and urinary excretion of penicillin following single oral doses of 100,000 and 50,000 units by the four methods described above yielded results which were qualitatively similar to those observed after the 315,000-unit dose.

A clinical investigation of the value of these oral preparations in the treatment of pneumococcus pneumonia is in progress, and thus far 12 patients have been treated. The results are comparable to those observed following the intramuscular administration of penicillin. This study is being continued.

SUMMARY

It is possible to attain serum concentrations of penicillin after oral administration comparable to those attained after intramuscular injection by the use of approximately five times as much penicillin. As the concentrations attained following the ingestion of penicillin by four different methods were all of the same order of magnitude, it would seem that the present problem in oral administration is analogous to that with intramuscular administration, *i.e.*, to find the ideal vehicle whereby the duration of the serum concentration can be prolonged.

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THE ROLE OF FECAL THIAMINE AND COCARBOXYLASE IN HUMAN NUTRITION[1,2]

THE role of the intestinal biosynthesis of thiamine in the nutrition of man and animal has recently been studied by several investigators.[3,4] Considerable amounts of thiamine have been found in human[5,6] and animal feces, but the question of whether this thiamine is readily available for body needs requires clarification.

We believe that the evidence cited in Tables 1 and 2 supports the concept that the thiamine and cocarboxylase in human feces is of no nutritional value to the individual, since it appears to exist largely within

[1] From the Medical Research Laboratories, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School, Boston.

[2] This investigation has been aided by a grant from the Josiah Macy Jr. Foundation.

[3] V. A. Najjar and E. Holt, *Jour. Am. Med. Asn.*, 123: 683, 1943.

[4] C. A. Elvehjem, *Am. Sci.*, December, 1943.

[5] K. Ritsert, *Klin. Wchnschr.*, 17: 1397, 1938.

[6] B. Alexander, *Jour. Biol. Chem.*, 151: 455, 1943.

[7] P. C. Leong, *Biochem. Jour.*, 31: 373, 1937.