two in mixture with antisera of appropriate dilutions. In still higher dilutions and with further incubation they show a sharp increase in the number of cells in division as compared to the number of young and mature cells not in division. In some experiments as many as 80 per cent. of all the cells used in the test have been found in division at one time. With continued incubation, running up to 24 hours, many of the pairs of cells which seem unable to complete the process of division have been seen to undergo further abortive attempts at division and develop into chains of three or four parts or into multinucleated giant cells of very irregular shape.

TABLE 1

THE REACTIONS OF TETRAHYMENA, STRAIN H, IN SELECTED ANTISERA

Type	Rabbit Serum Dilution 1–16	1–32	1–64	1–128	1–256	1–512	1–1024	Reaction
homologous immune	++++	++++	++	+	–	–	–	Agglutination
	++++	++++	+++	++	+	–	–	Immobilization
	0	5	15	64	36	10	2	Dividing pairs (1)
	68	55	38	17	12	57	48	Single individuals (2)
	0	0.10	0.40	3.80	3.00	0.20	0.04	Ratio (1) to (2)
heterologous immune	–	–	–	–	–	–	–	Agglutination
	–	–	–	–	–	–	–	Immobilization
	2	8	1	2	7	4	4	Dividing pairs (1)
	38	44	62	39	75	75	52	Single individuals (2)
	0.05	0.20	0.01	0.05	0.10	0.05	0.08	Ratio (1) to (2)
normal	–	–	–	–	–	–	–	Agglutination
	–	–	–	–	–	–	–	Immobilization
	4	4	2	2	3	2	3	Dividing pairs (1)
	52	60	43	48	30	62	50	Single individuals (2)
	0.08	0.06	0.05	0.04	0.10	0.03	0.06	Ratio (1) to (2)

Legend: ++++ to +, strong to weak reaction; – no reaction.

The reaction seems to be an antigen-antibody affair: it has been observed in all combinations of organisms and antisera in which the reactions described by Robertson occur; it has not been observed in combinations with antisera or normal serum in which those reactions do not occur. Table 1 illustrates the specificity of the reaction and the frequence with which it occurs in populations subjected to antibody.

We have been impressed with the ability of these organisms to continue growth in spite of a sharp delay or failure to complete division when under the influence of antibody. The rate of increase of total sedimentable cell volume, as measured in Goetz phosphorous tubes in several experiments, seemed to be about the same in the presence of dilute but effective antibody as in normal control serum. Moreover, the progressive increase in size of many affected cells has been followed microscopically. Thus the principal involvement of the organisms in the reaction seems to be connected with the cell surface.

It is perhaps especially significant that other cultures of this genus have been reported by Chatton and Chatton[4] and Sonneborn[5] to exhibit somewhat similar phenomena when grown in the presence of certain selected strains of bacteria. In both of these studies the occurrence of an increased number of dividing pairs of organisms and the development of monsters was recorded, but there seems to be some difference in the details of events they observed and the reaction recorded here.

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ORAL ADMINISTRATION OF PENICILLIN IN CORN OIL AND LANOLIN

PREPARATIONS for oral administration of penicillin are undoubtedly increasingly in demand. Since Libby's[1] original demonstration that appreciable concentrations of penicillin can be attained in the animal body following the oral administration of penicillin in cottonseed oil, a number of modifications have been offered by other investigators with varying results.

György *et al.*[2] have given penicillin orally with trisodium citrate as a buffer salt to eliminate the destructive action of the hydrochloric acid in the stomach. Chow and McKee[3] delayed the action of penicillin by combining it with human plasma proteins. Little and Lumb[4] report results with a combination of the stabilizing effect of protein and the buffer action of sodium bicarbonate. Their best results were obtained with using raw egg as the protein. The work of Charney,

[3] M. Robertson, *Jour. Path. and Bact.*, 48: 305, 1939.

[4] E. Chatton and Mme. Chatton, *Rev. Suisse de Zool.*, 32: 99, 1925.

[5] T. M. Sonneborn, *Biol. Bull.*, 43: 187, 1932.

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

[2] P. György, H. N. Vandergrift, Wm. Elias, L. G. Colio, F. M. Barry and J. D. Pilcher, *Jour. Am. Med. Asn.*, 127: 639, 1945.

[3] B. F. Chow and C. M. McKee, SCIENCE, 101: 67, 1945.

[4] C. J. Harwood Little and George Lumb, *Lancet*, 1: 203, 1945.

Alburn and Bernhart,[5] using the gastric antacid trisodium citrate, demonstrates that such neutralization of the gastric acidity permits the absorption of a significant quantity of penicillin by the oral route of administration.

In order to protect the penicillin from the gastric acidity and thus make it available for absorption from the small intestines, where most of the fat digestion occurs, we combined a light oil with a heavier greasy substance (lanolin) and found that in this way the absorption period could be materially extended. The lanolin is also instrumental in providing a uniform and stable suspension.

PREPARATION OF PENICILLIN SUSPENSION

Ingredients:

Anhydrous Lanolin U.S.P.	50 per cent.
Corn Oil (Edible grade)	50 " "
Penicillin calcium	q.d.

Weigh the lanolin and corn oil in a suitable container and heat gently to 55–60° C. Mix well in a Micro-mincer[6] until homogeneous. Allow to cool to about 40° C, at which point incorporate the penicillin. Mix thoroughly and dispense in No. 1 gelatin capsules (55,000 Oxford units per capsule).

EXPERIMENTAL

One capsule was taken by each subject at 7:00 A.M., following an overnight fast. No food or liquid was allowed for a minimum of two hours after the dose was taken. Each urinary excretion was collected during a period of 48 hours, the volume recorded and an aliquot placed in a bottle containing ether and phosphate buffer for preservation until assayed. The assay of penicillin was performed by the Rammelkamp method.[7]

RESULTS

Urine concentrations of penicillin which were attained at the various time intervals are recorded in Fig. 1. The penicillin levels in the control subjects who received their dose of penicillin in normal saline solution are presented for comparison.

The average total recovery of penicillin in human urine in the vehicle described was 14 to 16 per cent. in the 24-hour period. The average total recovery of penicillin in the control subjects taking the penicillin saline combination was 2 to 3 per cent. under the same test conditions.

Previous investigations disclose measurable urinary excretions of penicillin following oral administration up to 6 to 12 hours.[1, 4, 5]

[5] J. Charney, H. E. Alburn and F. W. Bernhart, SCIENCE, 101: 251, 1945.

[6] W. C. Alford and E. D. Palmes, *Jour. Lab. Clin. Med.*, 29: 1104, 1944.

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

In a group (I) of individuals (predominately males) as shown in Fig. 1 (A) the highest level of penicillin appears in the urine in approximately 2 hours; whereas in another group (II) of individuals

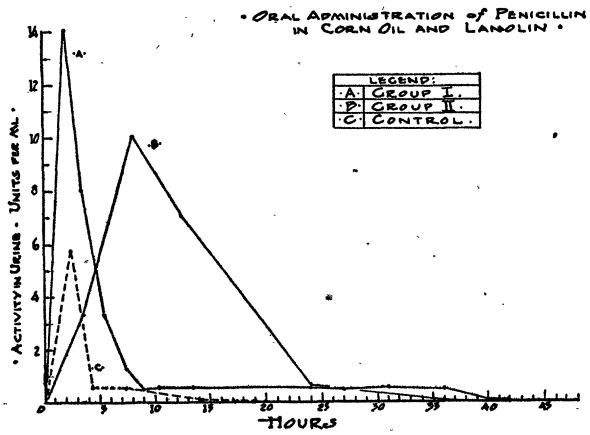

FIG. 1

(predominately females) as shown in Fig. 1 (B) the highest level of penicillin does not appear in the urine until after approximately 8 hours. No explanation for this difference is advanced.

The combination of penicillin in corn oil and lanolin here reported was found in human urine in measurable quantities for 24 hours and in some individuals for more than 42 hours. The prolonged absorption of the penicillin may be attributed to the additive value of both ingredients. The degradation of the corn oil undoubtedly does not occur under the acidic condition of the stomach but rather in the small intestines.[1] The lanolin is chiefly composed of the esters of higher alcohols (cholesterol and isocholesterol) which are by their nature very difficult to decompose. This has the distinct advantage of further delaying the absorption.

SUMMARY

Oral administration of penicillin suspended in equal parts of corn oil and lanolin extends the maintenance of the penicillin level in the system (as determined by urine bio-assay). Measurable quantities were found 24 to 42 hours after ingestion.

Recovery of the penicillin is about five times higher than under administration in saline solution.

We wish to express our sincere appreciation to the various members of our staff who volunteered as subjects for these experiments.

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