with emulsion of stool for 24 hours. No inactivation was demonstrable in one experiment which was conducted for only four hours. In general, the rate of inactivation varied, but considerable destruction had

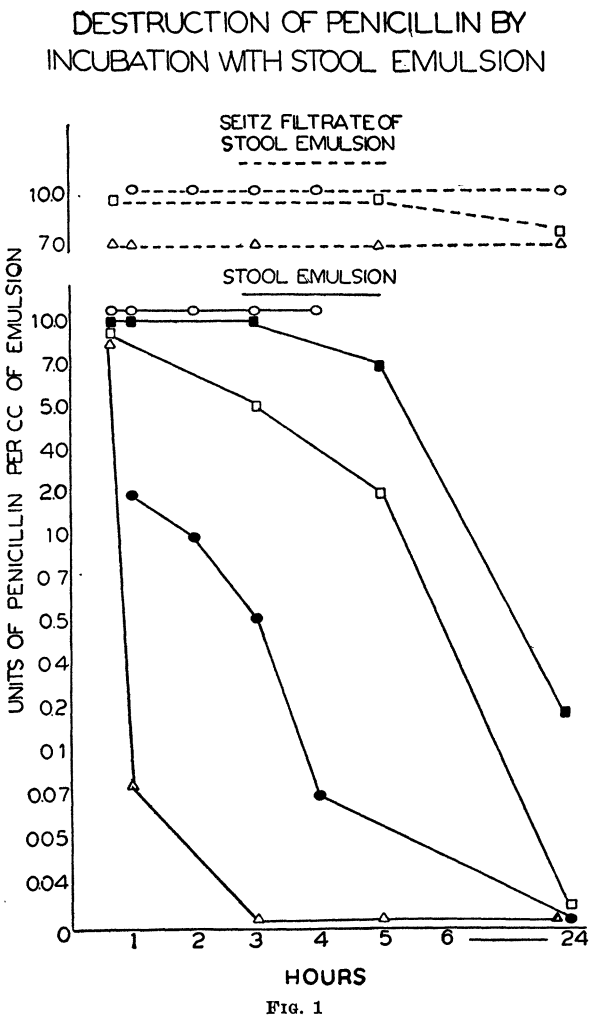

FIG. 1

usually occurred by the end of the third hour of incubation. When emulsions of stool were passed through a Seitz filter prior to incubation with penicillin, little or no destruction of the penicillin occurred, although unfiltered specimens from the same emulsion destroyed penicillin.

Thus, there are two mechanisms for the destruction of penicillin in the alimentary tract: the secretion of acid in the stomach and some agent, presumably bacterial, in the intestine. It is impossible to determine in an individual case the relative proportions of an ingested dose of penicillin which are destroyed by these respective mechanisms. One operates before, the other after, the penicillin has reached the site of greatest absorption, the duodenum (*8*). Of greater importance, however, is the fact that even if destruction by acid does not occur at all, because of achlorhydria, successful neutralization, or the normal fluctuations of gastric acidity, the greatest absorption which has been noted is only 34 per cent of the ingested dose. The penicillin which is not absorbed is eventually destroyed by the action of the second mechanism or is excreted in the feces.

It appears, therefore, that the maximal benefit which is attainable from protecting the penicillin against acid destruction is limited to the difference between the amount of absorption which occurs in the absence of such protection and the maximal absorption which has been noted when acid destruction is not a factor. As the theoretical advantage of protection of all of the material against acid is so largely counterbalanced by the fact that no more than a third of the ingested dose is absorbed in any event, it would seem that no penicillin preparation for oral use which is based solely on the principle of protection against acid will prove to be significantly superior to penicillin alone.

Furthermore, in the presence of maximum absorption approximately three times as much penicillin is required by the oral as by the intramuscular route to produce comparable penicillin concentrations in the blood. Since maximum absorption does not generally occur, the usual ratio of oral to intramuscular dosage will be in the neighborhood of 5:1.

References

1. ABRAHAM, E. P., and CHAIN, E. *Nature, Lond.*, 1940, **146**, 837.
2. ABRAHAM, E. P., CHAIN, E., FLETCHER, C. M., GARDNER, A. D., HEATLEY, N. G., JENNINGS, M. A., and FLOREY, H. W. *Lancet*, 1941, **2**, 177.
3. CHARNEY, J., ALBURN, H. E., and BERNHART, F. W. *Science*, 1945, **101**, 251.
4. FREE, A. H., LEONARDS, J. R., MCCULLAGH, D. R., and BIRO, B. E. *Science*, 1944, **100**, 431.
5. HEATLEY, N. G. *Lancet*, 1945, **1**, 590.
6. LITTLE, C. J. H., and LUMB, G. *Lancet*, 1945, **1**, 203.
7. MCDERMOTT, W., BUNN, P. A., BENOIT, M., DUBOIS, R., and HAYNES, W. *Science*, 1945, **101**, 228.
8. MCDERMOTT, W., BUNN, P. A., BENOIT, M., DUBOIS, R., and REYNOLDS, M. E. *J. clin. Invest.*, in press.
9. MARTIN, S. P., and KIRBY, W. M. M. (To be published.)
10. RAMMELKAMP, C. H. *Proc. Soc. exp. Biol. Med.*, 1942, **51**, 95.
11. RAMMELKAMP, C. H., and HELM, J. D., JR. *Proc. Soc. exp. Biol. Med.*, 1943, **54**, 824.
12. RAMMELKAMP, C. H., and KEEFER, C. S. *J. clin. Invest.*, 1943, **22**, 425.
13. WELCH, H., PRICE, C. W., and CHANDLER, V. L. *J. Amer. med. Ass.*, 1945, **128**, 845.

Effect of Penicillin on Growth of *Alcaligenes fecalis*

MACDONALD FULTON, CHARLES E. LANKFORD, and MARTHA CHILTON

University of Texas School of Medicine, Galveston

The literature contained no information on the effect of penicillin on *Alcaligenes fecalis* previous to a recent paper by Altemeier (*1*), who reported the marked susceptibility of five strains to penicillin. In

view of the well-known fact that gram-negative bacilli are in general relatively resistant to this antibiotic, it seemed advisable to test a larger number of strains of this species.

Nine strains of *Alcaligenes* were available in stock, six having been collected from human feces and three from human urine. The tests were carried out on Bacto Proteose No. 3 hemoglobin agar plates containing various concentrations of penicillin, as used routinely for tests of penicillin resistance in our laboratory. The plates were inoculated from young tryptose phosphate broth cultures by making a radial streak with the tip of an absorbent cotton swab dipped in the broth culture. They were examined after overnight incubation at 37.5° C.

In repeated tests no inhibition was observed at penicillin concentrations less than 10 units/ml. of agar. In a typical experiment, only one of the nine strains was inhibited by 10 units/ml. Fifty units inhibited another strain and almost completely inhibited a third. At 100 units, five of nine strains were still able to grow, although somewhat inhibited as compared with controls.

We have thus been unable to confirm the findings of Altemeier. Despite the fact that the genus *Alcaligenes* is now separated from the *Enterobacteriaceae* and grouped with other genera in the family *Rhizobiaceae*, it occurs with, and resembles physiologically, the members of the former family. The resemblances include insensitivity to penicillin.

Reference

1. Altemeier, W. A. *Surg. Gynec. Obstet.*, 1945, **81**, 379.

Intravenous Utilization of Partial Acid Hydrolysates of Proteins

William C. Risser, Jay R. Schenck, and Douglas V. Frost[1]

Abbott Laboratories, North Chicago, Illinois

Complete hydrolysates of casein fortified with tryptophane and cysteine monohydrochloride monohydrate were given intravenously to female dogs. The hydrolysates were given daily in one injection over a period of 80 minutes in some experiments and two hours in others. The minimum intake of nitrogen which maintained nitrogen balance was approximately 120 mg./N/kg./day. By the method of White and Elman (*1*) we have prepared partial acid hydrolysates in which approximately one-third of the amino acids exist in the free state. When these hydrolysates were fortified to the same content of tryptophane and cysteine as employed in the complete hydrolysates, nitrogen balance was produced at an intake of 120 mg./N/kg./day. Thus, the peptide nitrogen of a partial acid hydrolysate appears to be available for the purpose of maintaining nitrogen balance in the adult dog when the hydrolysate is given intravenously.

TABLE 1

Summary of Nitrogen Balance Experiments

Hydrolysate	Total N* Wt. of tryptophane present†	Total N* Wt. of cysteine HCl · H_2O added	Dog No.	Injection time (minutes)	Intake of hydrolysate in mg./N/kg./day	Balance in grams/N/week
Casein, complete	12.0 (dl-tryptophane added)	4.90	1	80	100	−0.94
					80	−0.99
					120	−0.49
Casein, complete	12.0 (dl-tryptophane added)	3.31	2	80	100	−1.33
					80	−0.99
					120	+0.26
Casein, partial	11.0 (l-tryptophane added)	4.83	1	80	120	+0.33
					100	−0.38
					80	−0.62
			2		120	−0.14
					140	+0.54
Casein, partial	25.0 (no tryptophane added)	4.83	3	80	140	+0.78
				"	140	+0.20‡
				100	120	+0.14
				90	100	−0.05
Fibrin, partial	9.0 (no tryptophane added)	14.06	4	120	100	+1.02
					100	−0.13‡

* In this ratio, Total N represents nitrogen (in grams) of the hydrolysate before any additions of amino acids were made.

† The amount of tryptophane in the partial hydrolysates was determined. "Tryptophane present" represents the amount (in grams) of the tryptophane retained in the partial hydrolysate plus the quantity added; for the complete hydrolysates, it represents the amount added.

‡ Five-day periods.

The nonprotein diet consisted of 73 grams sucrose, 20 grams lard, 3 grams corn oil, 0.5 gram fish-liver oil containing 65,000 U.S.P. units of vitamin A and 13,000 U.S.P. units of vitamin D per gram, 4.0 grams U.S.P. salt mixture I, 0.2 gram choline chloride, 1.0 gram agar, 0.6 mg. thiamine hydrochloride, 0.6 mg. riboflavin, 12.0 mg. nicotinamide, 0.4 mg. pyridoxine, 1.2 mg. calcium pantothenate, and a liver concentrate low in nitrogen but rich in vitamin B_c. The amount of this diet consumed usually supplied considerably less than 5 per cent of the total nitrogen intake.

Reference

1. White, A., and Elman, Robert. *J. biol. Chem.*, 1942, **143**, 797.

[1] With the collaboration of Robert T. Olsen, Oscar H. Walther, and Everett W. Doede.

The authors wish to thank Dr. E. H. Volwiler, Mr. Carl Nielsen, and Dr. D. W. MacCorquodale for encouragement and counsel in the course of this work, and to acknowledge the cooperation of Mr. H. C. Spruth in various phases of the problem.