was as a rule somewhat higher in whole blood than in plasma, both before and after the amino acid infusions. Reduction in plasma bicarbonate concentration occurred invariably as an immediate result of the amino acid infusion, both in the patients with liver disease and those not having hepatic impairment.

When the rate of infusion of amino acids was progressively increased, as shown in Table II, the changes in urine and plasma amino acid concentration are found to be similar in the patient with toxic hepatitis and in the patient without liver disease. The amount of amino acid excreted in the urine in the 2 cases increases somewhat, but remains a small percentage of the total nitrogen excreted. At the end of the period of observation, which lasted 9 hr, there was still a large retention of nitrogen in both cases.

Conclusion. The changes in plasma and urine following infusion of an amino acid mixture were found to be comparable in 2 groups of patients, one group having advanced liver disease and the other showing no evidence of hepatic disability. In neither were untoward clinical effects noted.

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A Study of Gastric Secretion as Influenced by Changes in Duodenal Acidity.

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In spite of numerous investigations there remains considerable difference of opinion regarding the effect of injecting HCl into the intestine on the volume output of gastric juice. Some investigators[2,3] have reported that acid in the intestine may stimulate the flow of gastric juice, others have reported inhibition[1,4,5,7] whereas still others[6] have found that injecting acid into the duodenum appeared to have no significant effect on the volume or acidity of gastric juice secreted in response to a standard meal. Similarly discordant results were obtained in experiments carried out in this laboratory some years ago and the results obtained early in this investigation were likewise inconstant.

This communication is a preliminary report of the results obtained up to the present in our efforts to determine why, on one occasion, the addition of a given volume of HCl to the intestinal contents may profoundly inhibit gastric secretion and may, on another occasion, apparently under the same conditions, have little or no effect.

Two dogs were used each of which was provided with a Pavlov pouch and with a gastric and a duodenal fistula as previously described by one of us.[8,9] The volume of the secretion collected from the Pavlov pouch was measured at 15-min intervals for one hr before and for from 4 to 7 hr after a standard meal consisting of 300 g of beef heart free from visible fat. Thirty-two experiments were performed of which 21 were normal

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controls in which only the standard meal was administered. In the remainder, N/10 or N/15 hydrochloric acid was introduced into the first part of the duodenum via the duodenal fistula at a constant rate during various periods after the ingestion of the meal. In 9 of the control experiments and in 8 of the experiments with acid, the pH of the duodenal contents, collected approximately 4 inches distal to the point at which the acid was injected, was determined at 15 or 30 min intervals.

The experiments in which the pH of the intestinal contents was measured during the injection of acid revealed what we believe to be the cause of our own previous discordant results and, perhaps, some of those recorded in the literature. We found that regardless of the volume of acid injected into the duodenum, if the pH of the intestinal contents was thereby lowered to 2.5 or below, some degree of inhibition of secretion of gastric juice by the Pavlov pouch was almost invariably observed. If, on the other hand, in spite of the addition of HCl to the intestinal contents, the pH of the duodenal contents remained above this level, the amount of gastric juice secreted by the pouch in response to the standard meal remained within normal limits.

Fig. 1 shows a typical result. The upper curves show the volume in cc of the secretion collected from the Pavlov pouch in one experiment with acid and in a normal control experiment on the same animal. In the experiment recorded by the broken line HCl was injected into the intestine during the first 2 hr after feeding. The results of the control experiment are indicated by the solid line. The corresponding lines in the lower curves show the variations in duodenal pH during the two experiments. Our results as a whole indicate that when the pH of the intestinal contents is depressed to approximately 2.5 by means of injected HCl, the volume of gastric juice secreted by the pouch in response to a standard meal of raw meat is reduced to about one-half that obtained in the control experiments. When the pH of the duodenal contents falls to 2 or below, due to the injected acid, the volume of secretion is frequently less than during the fasting period.

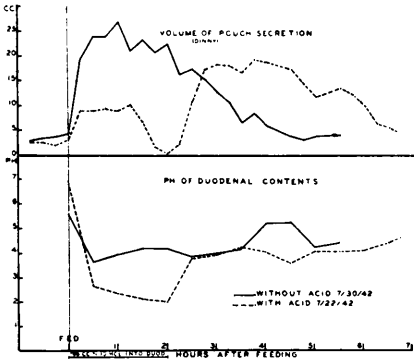

FIG. 1.

Changes in the volume of gastric juice (upper graph—broken line) secreted by a Pavlov pouch in response to a standard meal associated with lowering of the pH of the intestinal contents (lower graph—broken line) to below 2.5 by means of HCl injected into the duodenum. Corresponding data obtained in a normal control experiment (without injecting acid) are also recorded (solid lines).

We wish also to point out the "rebound" or increase in output of pouch secretion following the inhibition produced by acid. In some experiments during this "rebound" phase the volume of pouch secretion reached and maintained levels as high or even higher than were obtained in any control experiments. Considering the large amount of acid that it was necessary to introduce at times in order to depress the duodenal pH sufficiently to cause inhibition of secretion, this "rebound" may have been caused by excess hydration, delayed gastric emptying or other effects of the acid. However, the degree of inhibition preceding the "rebound" appeared to be correlated consistently with the intestinal acidity as measured in pH units and with no other factor that we observed.

Further studies designed to evaluate the effects of hydration, delayed gastric emptying and other incidental effects of the acid injections are at present being carried out and will be reported at a future date.

Conclusions. The introduction of acid into the duodenum inhibits gastric secretion only if a threshold level of duodenal pH (approximately 2.5) is attained. The extent of depression of gastric secretion is dependent upon the level of pH produced.