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Inhibition of Gastric Peristalsis Due to a Substance Found in Commercial Peptones.

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In previous communications one of us^{1,2} called attention to the importance of gastric inhibition due to stimuli acting in the duodenum, in the regulation of gastric emptying. In the case of acid and certain other chemical stimuli the inhibition was found to be due to an "enterogastric" reflex over the vagus nerves. Later the present authors with Dr. Mogan³ reported additional experimental evidence leading to the same conclusions and added proof that the normal duodenal contents following a meal of raw lean beef act as adequate stimuli to cause gastric inhibition. Experiments were reported which indicate that the inhibitory effect is in part due to chemical stimuli, the nature of which was not determined. The present study is an effort to identify the inhibitory agent.

The type of animal preparation and the methods used are described in the previous reports.

Brunemeier and Carlson⁴ observed that 10% Witte's peptone in 0.2% HCl, when injected into the duodenum, stopped gastric hunger contractions. In experiments performed in July, 1935, we attempted to use Witte's peptone as a buffering agent for HCl solutions to be used in a further study of gastric inhibition from the duodenum. We found that the peptone, even in neutral solution, caused inhibition of gastric peristalsis.

In those experiments, after a meal of raw lean beef, the duodenum (of dogs) was perfused through its lumen with various solutions, using normal saline as a control. Fig. 1 (Exp. of July 24, 1935,) shows the effect on antral peristalsis of changing the perfusion fluid from normal saline to 0.5% Witte's peptone in neutral solution.

A further study of this phenomenon has been made by injecting 10 cc. quantities of distilled water solutions of various commercial

¹ Thomas, J. Earl, *J. A. M. A.*, 1931, **97**, 1663.

² Thomas, J. Earl, and Mogan, C. J., *Proc. Soc. Exp. Biol. and Med.*, 1931, **28**, 968.

³ Thomas, J. Earl, Crider, J. O., and Mogan, C. J., *Am. J. Physiol.*, 1934, **108**, 683.

⁴ Brunemeier, E. H., and Carlson, A. J., *Am. J. Physiol.*, 1915, **36**, 191.

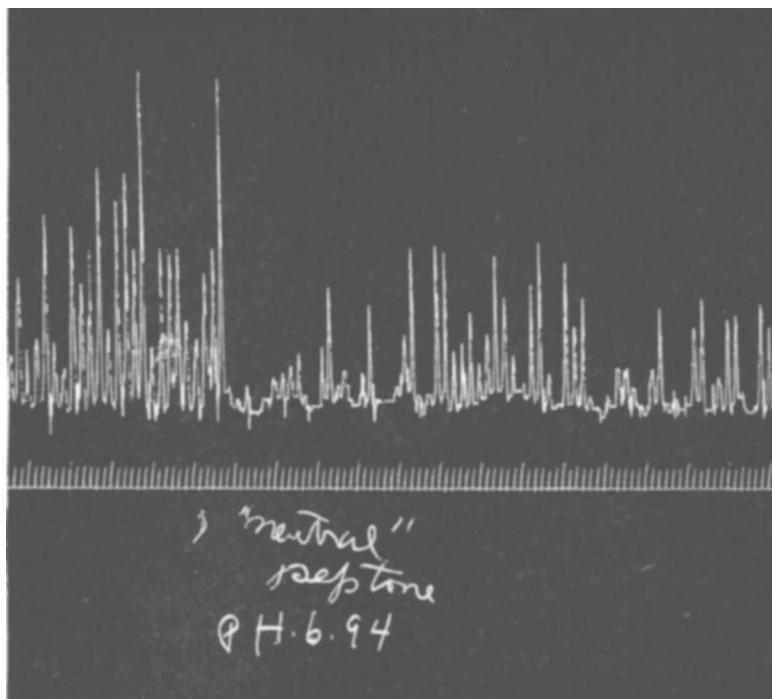


FIG. 1.

Balloon record of antral peristalsis during perfusion of the duodenum. Perfusion fluid was changed at the point indicated from normal saline to 0.5% Witte's peptone in neutral solution in normal saline. Time in 10-second intervals. Bromoform manometer.

peptones into the first part of the duodenum of dogs with the stomach empty or shortly after feeding a meal of dog biscuit. Witte's peptone, "Proteose" peptone, "Bacto" peptone and a granular peptone produced by a French manufacturer have been investigated.

Witte's peptone caused gastric inhibition from the duodenum in 2% solution, "Proteose" peptone in 5%, and "Bacto" peptone in 10% solution. "Proteose" peptone in 2% and "Bacto" peptone in 5% solution gave questionable reactions. In 2% solution "Bacto" peptone and the French peptone were without effect. The French peptone was not investigated further.

Solutions of Witte's peptone and of "Bacto" peptone were saturated with ammonium sulphate and the redissolved precipitate investigated. The precipitate is assumed to consist mainly of proteoses. The proteose solutions were approximately as effective as the corresponding solutions of the whole peptone mixture from which they were obtained, making some allowance for loss in the

manipulations necessary to free the preparations from adherent ammonium sulphate. We conclude that the active substance is mainly proteose or is precipitated with it.

Further evidence that the inhibitory substance is one of the higher derivatives of protein digestion appears when our results are compared with chemical data kindly loaned us by Dr. Carl J. Bucher. This comprises an analysis of various commercial peptones for protein nitrogen, non-protein nitrogen, polypeptid nitrogen, amino acids, salt and sugar. The inhibitory effect of the various preparations varies directly with the amount of "protein" nitrogen, inversely with the amount of non-protein nitrogen and polypeptid nitrogen, and is in no way related to the total nitrogen. The analysis shows an insignificant amount of salt and amino acid in the most effective preparations and no sugar (a possible source of error) in Witte's peptone.

We conclude that certain products of protein hydrolysis, probably proteoses, act in the intestine to inhibit gastric peristalsis. The observation has a bearing on the regulation of gastric emptying during protein digestion and completes the list of major foodstuffs, each of which has now been shown to be capable of inhibiting gastric activity when present in the intestine in adequate concentration and in certain stages of digestion.

Further work is contemplated directed toward the isolation of similarly active material from the products of normal digestion in the animal and to learn whether the inhibitory effect is reflex, humoral, or both. Present indications point to a reflex effect inasmuch as the latent period for inhibition is often less than 30 seconds.

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Creatine Content of Human Hearts.

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Even before the important rôle of phosphocreatine in muscular contraction was recognized, Constabel¹ noted that there was a decreased total creatine content in those human hearts that showed either clinical or post-mortem evidence of damage. Recently

¹ Constabel, Fr., *Biochem. Z.*, 1921, **122**, 152.