ON THE BEHAVIOR OF THE PYLORIC SPHINCTER IN NORMAL MAN*

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Systematic studies of motor phenomena of the normal gastro-intestinal tract have been so largely carried out in the lower animals that but little detailed description of them in man is available. The results obtained from the studies in the lower animals can be applied only in a general way to the physiology of the digestive tract in man. It follows that more intimate knowledge concerning the motor phenomena of the alimentary canal in man would aid in the interpretation of results obtained from experimental studies of various phases of the pathologic physiology of human digestion. For this reason the work, with which the present report deals, was undertaken. It comprises observation on the behavior of the pyloric sphincter of the normal man in relation to various foodstuffs, and also to the presence of acid and alkaline solutions introduced into the stomach and duodenum of persons whose gastro-intestinal tracts were considered normal.

The results obtained from the latter observations bear particularly on the question of the "acid control" of the pyloric sphincter. The theory of the "acid control" of the sphincter was suggested by Pawlow,¹ among others, and was elaborated later by Cannon.² In epitome the theory is that the presence of acid in the antrum of the stomach causes relaxation of the pyloric sphincter, while the presence of acid in the duodenum causes the sphincter to contract. The evidences on which this theory are based were, again, obtained from experiments carried out on the lower animals. There are, however, phenomena occurring in the lower animals which it is admitted that the theory of acid control does not explain, and for this reason other controlling factors are assumed to exist. Whether or not acid or some other factor exerts the principal control of the pyloric sphincter in man has not been demonstrated by previous investigators.

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1. Pawlow: *The Work of the Digestive Glands*, London, 1902, p. 165.

2. Cannon, W. B.: *The Acid Control of the Pylorus*, *Am. J. Physiol.* **20**: 284, 1907.

METHOD OF OBSERVATION

1. The degree of contraction of the pyloric sphincter when food-stuffs partially fill the normal stomach was studied.

The data for this were obtained from fluoroscopic observations of normal human stomachs.

2. The behavior of the sphincter relative to the passage of carbohydrate, protein or fatty foods from the normal stomach into the duodenum was studied.

This was determined by fluoroscopic observations of the stomachs of normal persons after feeding meals composed of thick oat-meal porridge and barium, or 140 gm. of ground lean meat and 40 gm. of barium sulphate baked into a loaf, or 120 gm. of ground fatty bacon, 5 egg yolks and 40 gm. of barium baked into a loaf. The protein and fatty meals were of constant bulk and consistency.

3. Effect of the application of hydrochloric acid and sodium bicarbonate solution to the antral and duodenal ends of the pyloric sphincter on its functioning was studied.

Observations of the functioning of the sphincter were made by means of the fluoroscope.

The duodenal tube was given on an empty stomach and allowed to pass into the antrum in the region of the sphincter, or into the duodenum. Then a meal was fed. This was a meat and barium meal, either rinsed down with 200 c.c. of water or made into a thick mush by grinding in a mortar with water. In certain cases a malted milk, potato starch and barium mixture was also given. After the meal had been ingested fortieth normal, twentieth normal and tenth normal hydrochloric acid and 1 per cent. or 5 per cent. sodium bicarbonate solutions were introduced into the sphincteric region of the antrum or into the various portions of the duodenum, through the duodenal tube.

The subjects used were persons whose physical condition at the time of the observations was considered to be normal. The usual fractional clinical gastric analysis (Ewald test breakfast) showed no abnormalities.

1. The study of the degree of contraction of the normal pyloric sphincter, observed by means of the fluoroscope.

That the pyloric sphincter is closed when fluid food is in the stomach, except during the periods in which it opens to permit the ejection of food into the duodenum, was demonstrated in 1913 by Cole.³ His observations were so readily and easily confirmed by fluoroscopic studies that they are now universally accepted. In this way the authors have confirmed Cole's observations a large number

3. Cole, L. G.: Physiology of the Pylorus, Pilleus Ventriculi and Duodenum as Observed Roentgenographically, J. A. M. A. **61**:762 (Aug. 29) 1913.

of times. Further evidence that the normal quiescent sphincter is in a state of contraction is afforded by the following facts. By the use of considerable pressure on the abdominal wall, barium containing chyme can be forced from the stomach into the duodenum, as observed by means of the fluoroscope. This can be accomplished probably only when the sphincter has opened in relation to the advance of an antral peristaltic wave. When it can be accomplished the filled antrum and first portion of the duodenum are seen to be connected by a narrow isthmus of barium, which represents the sphincter; on cessation of pressure this narrow isthmus disappears.

When a fluid barium meal first enters the antrum of the stomach it frequently passes directly into the duodenum. Careful observation has shown that the barium does not fall through an open sphincter by means of gravity, but that from one to four small peristaltic waves are present in the antral region and that the pyloric sphincter opens in relation to the advance of a peristaltic wave; which latter seemingly ejects the barium into the duodenum.

2. The study of the behavior of the pyloric sphincter, observed by means of the fluoroscope, relative to the passage of carbohydrate, protein and fatty foods from the stomach into the duodenum.

By means of the fluoroscope a fluid carbohydrate meal, consisting of 500 c.c. of malted milk in which 90 gm. of barium sulphate are held in suspension by the aid of potato starch, is seen to start through the normal pyloric sphincter from at once to within a few minutes after it has been ingested. The normal sphincter opens regularly as each antral peristaltic wave approaches and permits the passage of barium containing chyme into the duodenum over a period of about ten seconds. In two normal young men the same phenomena occurred after the ingestion of thick oatmeal porridge mixed with barium. Except in pathologic conditions accompanied by pylorospasm, opening of the pyloric sphincter at irregular intervals, as described by Cannon in cats, was not observed. The regular opening and closing of the pyloric sphincter, except in the presence of pylorospasm, is so well known after the ingestion of fluid carbohydrate meals that no further observations on them were attempted in the present investigation.

Observations on the behavior of the pyloric sphincter after the ingestion of protein food were made in young men, ten normal, one with a quiescent duodenal ulcer, and one woman whose physical condition was normal. Similar observations were made after the ingestion of fatty food in eight normal young men. The duration of each experiment varied from one-half hour to six hours.

Since the results obtained in the various subjects were consistently uniform, only three of the experiments will be given in the following illustrative protocol.

REPORTS OF OBSERVATIONS

PROTOCOL I.—*Observation 1.*—Male, aged 25.

MEAT MEAL

Meat and barium meal with 100 c.c. of water to drink.

5:25 p. m.: Began eating meal.

5:35 p. m.: Finished eating the meal.

Fluoroscopic observations; subject in reclining position.

5:35-5:38 p. m.: Gastric peristalsis active. As each wave approached the pyloric sphincter barium passed into the duodenum over a period of about 10 seconds.

5:45-5:47 p. m.: Ditto.

5:53-5:55 p. m.: Ditto.

6:00-6:05 p. m.: Ditto.

FATTY MEAL

Fatty and barium meal with 100 c.c. of water to drink.

6:07 p. m.: Began eating the meal.

6:14 p. m.: Finished eating the meal. The meal was nauseating to patient since he did not like fat; no nausea present after having eaten the meal.

Fluoroscopic observation; subject in erect posture.

6:14-6:16 p. m.: Gastric peristalsis active. As each wave approached the pyloric sphincter barium passed into the duodenum over a period of about 10 seconds.

6:21-6:24 p. m.: Ditto.

6:29 p. m.: Ditto.

Observation 2.—Male, aged 22.

FATTY MEAL

Bacon, egg and barium meal eaten as a dry loaf and without water to drink.

9:21 a. m.: Began eating the meal.

9:29 a. m.: Finished eating the meal.

Fluoroscopic observations; subject in erect position.

9:29-9:40 a. m.: Gastric peristalsis active. As each wave approached the pyloric sphincter barium passed through into the duodenum.

10:02-10:04 a. m.: Ditto.

10:28 a. m.: Ditto.

11:02 a. m.: Ditto.

Observation 3.—Male, aged 24. Meat and barium meal eaten as a dry meat loaf and without water to drink.

9:47 a. m.: Began eating the meal.

9:57 a. m.: Finished eating the meal.

Fluoroscopic observations; subject in erect position.

9:57 a. m.: Gastric peristalsis active. As each wave approached the pyloric sphincter barium passed through into the duodenum.

10:17-10:23 a. m.: Ditto.

11:09-11:12 a. m.: Ditto.

11:40-11:42 a. m.: Ditto.

12:35-12:37 a. m.: Ditto.

Observations on the various subjects, similar to the ones illustrated in the foregoing protocol, demonstrated that either the protein or the fatty meals began to leave the stomach within from three to ten minutes after the first mouthful of food was ingested; that is, as soon as the subject could ingest the meal and be prepared for fluoroscopic observation. The consistency of the food did not modify its initial leaving-

time. Furthermore, the food passed through the pyloric sphincter into the duodenum as each and every antral peristaltic wave approached that orifice, and during a period of about ten seconds. In the same subject no difference in the amounts, either of the same food or of the different foods, which passed through the sphincter at different times, was observed.

3. Effect of hydrochloric acid and sodium bicarbonate solutions on the opening and closure of the pyloric sphincter, as observed through the fluoroscope.

In observations on two subjects from 10 to 20 c.c. portions of twentieth-normal hydrochloric acid were repeatedly poured into the stomach almost on the antral end of the pyloric sphincter. No effect on the opening or closure of the latter could be observed. In a third subject a loop of the duodenal tube entered the duodenum in such a manner as to pull the metal tip up against the antral end of the sphincter. The pouring of 20 c.c. of this acid on the antral end of the sphincter resulted in almost complete cessation of gastric peristalsis on one occasion and, on another, complete pylorospasm developed without demonstrable disturbance in peristalsis. The introduction of 20 c.c. of 1 per cent. sodium bicarbonate solution was immediately followed by acceleration of gastric peristalsis; i. e., the duration of a wave decreased to thirteen seconds from twenty-two seconds. The action of the pyloric sphincter, as judged by its regularity of opening and the amount of barium which passed through it, was not affected. In an observation on another subject, 5 per cent. sodium bicarbonate solution was poured into the sphincteric region of the antral end of the stomach. The result obtained is outlined in Observation 3 of Protocol II.

The effect of the introduction of acid and alkaline solutions into the duodenum is outlined in Protocol II.

PROTOCOL II.—*Observation 1.*—Male, aged 26.

The patient complained of belching, occasional vomiting, pains in various regions of the abdomen associated with bowel movements, constipation, shooting pains in the chest, back and legs, and insomnia. Diagnostic studies were all negative. After an Ewald test breakfast free hydrochloric acid was 15 and total acidity was 25. The patient was observed for two months and no evidence of organic disease was elicited during this period.

1:00 p. m.: Light lunch of toast, cereal and coffee. Duodenal tube swallowed.

4:00 p. m.: Subject was given 500 c.c. of barium, malted milk, potato starch mixture.

Fluoroscopic observations; subject in erect posture.

4:05 p. m.: Metal tip of duodenal tube in third portion of duodenum. It was pulled back into the first portion to a point just beyond the sphincter. Active peristalsis. Barium passed over in normal amount as each peristaltic wave approached the pyloric sphincter; 5 c.c. twentieth normal hydrochloric acid was quickly introduced through the tube as a gastric peristaltic wave

approached the sphincter and before the proper time for the sphincter to open. The sphincter opened and a normal amount of barium passed through into the duodenum.

Second observation twenty-four hours later.

Subject was not given food or drink for fourteen hours prior to introducing the duodenal tube.

8:25 a. m.: Duodenal tube swallowed; 85 c.c. of fasting gastric contents aspirated containing free hydrochloric acid 20.

11:25 a. m.: Meat and barium meal eaten. Metal tip of duodenal tube found in third portion of duodenum. Gastric peristalsis active. Barium passed over in normal amount as each peristaltic wave approached the sphincter. Five c.c. twentieth normal hydrochloric acid was introduced through the tube a short period before the proper time for the sphincter to open and when the duodenum was empty. Gastric peristalsis, the opening of the sphincter and the amount of barium which passed over were unaffected.

11:30 a. m.: Six c.c. twentieth normal hydrochloric acid were again introduced into duodenum a short period before the proper time for the sphincter to open and when the duodenum was empty. The same result occurred as in the preceding observation.

11:35 a. m.: The metal tip was pulled back into the first portion of the duodenum to a point just beyond the opening of the sphincter. Six c.c. twentieth normal hydrochloric acid were quickly introduced a short period prior to the time that the pyloric sphincter should open and when the duodenum was empty. The time of opening of the sphincter, the amount of barium passing through it, and gastric peristalsis were unaffected.

Observation 2.—Male, aged 28.

The subject complained of more or less constant mild headache. Diagnostic studies were negative. Fasting gastric contents: amount, 30 c.c.; free hydrochloric acid, 40; total acidity, 50. The patient had had a lumbar puncture several days prior to the observation. As a result he had a headache when in the erect posture, which disappeared completely on reclining. On the morning of the observation patient was given neither food nor drink.

9:00 a. m.: Duodenal tube swallowed.

10:10 a. m.: Began eating the meat and barium meal, which was ground up with water into a very thick mush.

10:17 a. m.: Finished eating the meat meal.

Fluoroscopic observations; subject in erect posture.

10:17 a. m.: Metal tip of duodenal tube in duodenum. Antral peristaltic waves very shallow.

10:25 a. m.: Antral peristalsis very weak, but a small amount of barium passed into the duodenum as each antral peristaltic wave approached the sphincter. Metal tip pulled back into third portion of duodenum.

10:40 a. m.: Subject nauseated, with moderately severe headache. Gastric peristaltic waves very shallow, and no barium passed through the sphincter. The metal tip was now found in the first portion of the duodenum just beyond the end of the sphincter.

The subject was now placed in reclining position on horizontal fluoroscopic table. His nausea and headache disappeared and about 15 minutes later antral peristalsis was active, and barium passed into the duodenum in easily demonstrable amount as each antral peristaltic wave approached the pyloric sphincter.

Fluoroscopic observations; subject in reclining position.

Metal tip in first portion of duodenum. Ten c.c. fortieth normal hydrochloric acid introduced beginning about five seconds before, and continued up to the time of opening of the sphincter. The sphincter opened normally, and also at the approach of the next two antral peristaltic waves.

Fifteen c.c. fortieth normal hydrochloric acid were now introduced under the same conditions as before. Sphincter opened normally and also at the

approach of the next four antral peristaltic waves. This procedure was now repeated twice with 20 c.c. of twentieth normal hydrochloric acid and with same result as noted before.

Twenty c.c. of 5 per cent. sodium carbonate solution were now introduced the latter part of the time the sphincter was open and up to the time of its complete closure. The sphincter closed normally and reopened normally. This procedure was repeated with 10 c.c. and then 15 c.c. of 5 per cent. sodium bicarbonate solution. The opening and closure of the sphincter were unaffected.

The duodenal tube was now washed with 60 c.c. of water (in 20 c.c. portions). For a few minutes following this, antral peristaltic waves became very shallow.

11:45 a. m.: Antral peristalsis active. Barium passing through sphincter in considerable amount with each antral peristaltic wave. During the periods barium was passing through the sphincter into the duodenum on three successive times the contents of the first portion of the duodenum were aspirated. Eight c.c. were obtained. This material was liquid, containing a small amount of barium and of meat fibers. Its acidity was: free hydrochloric acid, none (Töpfer's reagent); 5 c.c. neutralized 1 c.c. of tenth normal sodium hydrate. Hydrogen ion concentration = 5.60 (determined by potentiometer).

Observation 3.—Male, aged 47.

Subject had a mild type of chronic arthritis. At the time of the following observation the subject was in good health.

7:00 a. m.: A light breakfast was eaten.

1:00 p. m.: Duodenal tube swallowed, followed by a glass of water.

5:35-5:40 p. m.: Subject given one half of meat and barium meal and 450 c.c. of malted milk, potato starch and barium mixture.

5:48 p. m.: Antral peristalsis weak and but small quantities of barium pass into the duodenum as each peristaltic wave approaches the sphincter. Metal tip of duodenal tube in third portion of duodenum.

6:00 p. m.: Metal tip of duodenal tube pulled back into first portion of duodenum. This act resulted in almost complete cessation of gastric peristalsis for several minutes. After peristalsis again became active barium passed into the duodenum as each antral peristaltic wave approached the sphincter. On one occasion 5 c.c. and on three occasions 10 c.c. of fortieth normal hydrochloric acid and on one occasion 12 c.c. of twentieth normal hydrochloric acid (all warmed to 38 C.) were introduced into the first portion of the duodenum through the duodenal tube. Each portion of acid was introduced before and up to the time of opening of the sphincter in relation to the advance of an antral peristaltic wave. The introduction of the acid was not followed by a demonstrable effect on the opening of the pyloric sphincter, the amount of barium passing through it into the duodenum or on gastric peristalsis.

7:00 p. m.: Metal tip of duodenal tube pulled back into stomach and lay at the pyloric orifice of the sphincter. Forty c.c. of 5 per cent. sodium bicarbonate solution were introduced through the duodenal tube. The pyloric sphincter continued to open at the approach of antral peristaltic waves and barium was ejected into the duodenum in normal amount. Then the duodenal tube was washed by injecting 10 c.c. of water through it. Then 10 c.c. of gastric contents were aspirated and a few minutes later 2 c.c. more were withdrawn. Both these specimens were faintly alkaline to phenolphthalein.

Observation 4.—Male, aged 21.

Six years ago temporary jaundice had occurred following an attack of malaria. Beginning two years ago and lasting until one year ago there had been attacks characterized by nausea, vomiting and diarrhea. These attacks occurred at intervals of from two to three months and persisted for from one to seven days. There had been no hematemesis, and no bloody, tarry or clay-colored stools. Six months ago jaundice again recurred. During this time there had been constipation.

Physical examination was negative, except for slight icterus of the sclerae. The laboratory examinations were negative. The urine contained no bile pigments. After an Ewald test breakfast the gastric contents showed free hydrochloric acid 14 and total acidity 70.

At the time of the present observation jaundice of the sclerae had disappeared and the patient was free from symptoms.

On the morning of the observation the subject was given neither food nor drink.

8:00 a. m.: Duodenal tube swallowed, followed by a glass of water.

10:15-10:20 a. m.: Meat and barium meal eaten with 200 c.c. of water to drink.

Fluoroscopic observations; subject in erect posture.

10:30-10:40 a. m.: Metal tip of duodenal tube is in the third portion of the duodenum.

Gastric peristalsis regular and active. Pylorospasm was present and no barium passed through into the duodenum.

10:47-11:00 a. m.: Peristalsis active. A very slight amount of barium passed through the sphincter as each peristaltic wave approached that orifice. Subject placed on right side in the reclining position.

11:02-11:20 a. m.: Subject in the reclining position. Fluoroscopic findings during this period remain the same as in the preceding observation.

11:35 a. m.: Subject in the reclining position usual for fluoroscopic gastric examination. Metal tip of duodenal tube was at the junction of the second and third portions of the duodenum. Five c.c. of twentieth normal hydrochloric acid were slowly introduced beginning at the time of the starting of a peristaltic wave in the antrum and continued until a second similar wave had reached the pylorus. Both waves pushed barium through the sphincter in normal amount. The metal tip of the duodenal tube was now pulled back until it lay in the first portion of the duodenum, just beyond the end of the pyloric sphincter. Following this procedure gastric peristalsis ceased, except for some very shallow, feeble waves, which sent but a very small amount of barium through the sphincter into the duodenum.

After the lapse of a period of thirty minutes peristalsis again became active and barium in normal amount passed through the pyloric sphincter into the duodenum. Then 20 c.c. of twentieth normal hydrochloric acid were introduced slowly and continuously from the beginning of one antral wave until the end of the third. All three waves, as they approached the sphincter, were followed by the passage of a normal amount of barium into the duodenum. The same procedure was immediately repeated with a second 20 c.c. amount of twentieth normal hydrochloric acid and with the same result as noted before. A few minutes later peristaltic waves became weak and feeble and sent but a very small amount of barium through the sphincter.

After a period of about five minutes peristalsis again became active and barium passed through the sphincter in normal amount. The same procedure was repeated with 20 c.c. tenth normal hydrochloric acid and with the same results as before. After a few minutes peristaltic waves again became shallow and feeble and sent but small amounts of barium through the sphincter.

After about five minutes peristalsis again became active and barium passed through the sphincter in normal amount as each peristaltic wave approached that orifice. The same procedure was repeated with 20 c.c. of 1 per cent. sodium bicarbonate solution. No effect was noted on gastric peristalsis, the time or manner of the opening or closure of the sphincter or on the amount of barium which passed through it into the duodenum.

Observation 5.—Male, aged 35.

The subject had suffered with acute articular rheumatism, from which he had promptly recovered. At the time of the observation he was in normal health.

The subject was given neither food nor drink on the morning of the observation.

9:10 a. m.: Duodenal tube swallowed.

Fasting contents—amount 100 c.c., free hydrochloric acid, 50; total acidity, 60.

11:00 a. m.: Began eating one half of a meat and barium meal ground up with water into a thick mush.

11:07 a. m.: Finished eating half of the meal.

Fluoroscopic observations; subject in erect posture.

11:07 a. m.: Metal tip at first was in the third portion of the duodenum, and then slowly receded to the first portion. The movement of the metal tip was accompanied by pylorospasm which continued for ten minutes after its movement ceased. Antral peristalsis then became active and barium passed from the stomach into the duodenum as each peristaltic wave approached the pyloric sphincter.

Ten c.c. fortieth normal hydrochloric acid were introduced into the first portion of the duodenum before each opening of the sphincter in relation to the advance of two consecutive antral peristaltic waves (the acid was introduced before and up to the time of opening of the sphincter). No effect was observed on the opening or closure of the sphincter immediately following the introduction of the acid or its opening in relation to the advance of the three succeeding waves. Following the latter antral peristaltic waves became shallower and less barium passed through the sphincter. After peristalsis again normal 12 c.c. fortieth normal hydrochloric acid introduced under the same conditions. No effect on the opening of the sphincter in relation to the next four waves was observed. The patient now coughed and the next two waves were very shallow; but the next waves were again normal. Then 20 c.c. fortieth normal hydrochloric acid were introduced, and no effect on the opening of the sphincter in relation to the next six waves was observed.

12:10 p. m.: Duodenal tube washed with 5 c.c. of water and then emptied with air. Chyme flowing into the first portion of the duodenum on two consecutive openings of the sphincter was aspirated, about 8 c.c. were obtained. Subject was now given 300 c.c. of malted milk, starch and barium mixture. Then 20 c.c. of fortieth normal hydrochloric acid were introduced into the duodenum prior and up to the time of opening of the sphincter. No effect on the behavior of the sphincter was observed. Twelve c.c. of twentieth normal hydrochloric acid were now introduced as before, without effect on the opening of the sphincter. Ten c.c. 5 per cent. sodium bicarbonate solution were introduced into the first portion of the duodenum just before and during the opening of the sphincter and continued up until it closed completely. The sphincter closed normally. Twenty c.c. 5 per cent. sodium bicarbonate solution were introduced during the period the sphincter was open and up until it had closed. The sphincter closed normally.

In terms of normal acid the aspirated duodenal contents contained five hundredth normal free hydrochloric acid; the total amount of sodium hydrate neutralized was equivalent to an acidity of twenty-fifth normal, titrated to phenolphthalein.

DISCUSSION

In the observations outlined in the above protocol twenty-two observations were made on the effect of introducing acid solutions into the first, second or third portions of the duodenum. The time of the introduction of the acid in relation to the normal opening time of the pyloric sphincter varied. Acid was introduced: (1) a short period prior to the normal opening time of the pyloric sphincter in relation

to the advance of an antral peristaltic wave; or (2) at the time just mentioned and continued until after the sphincter had opened for a second or third successive time.

In all the observations of the above protocol, the introduction of acid into the duodenum had no demonstrable effect on either the opening or the closure of the pyloric sphincter, on the amount of barium containing chyme ejected into the duodenum, or on gastric peristalsis. In Observations 4 and 5 the introduction of acid into the duodenum had no initial effect, but a late effect was noted. The latter consisted of partial cessation of gastric peristalsis. Moving the duodenal tube produced the same effect in these two observations and also in Observation 3, while in Observation 5 it produced pylorospasm on one occasion. These phenomena were interpreted as the result of abdominal irritation of the mucosa of the sphincter and duodenum due to movements of the tube. On this basis the partial cessation of gastric peristalsis, in Observations 4 and 5, may be explained; movements of the tube may have been produced by gastric and duodenal peristalsis. In this connection possible irritation of the duodenal mucosa incident to the introduction of fluid, its temperature, or its acid character must be considered. Irritation incident to the presence of the tube in the sphincter and duodenum can explain the pylorospasm present on the first observation in Observation 4. In two duodenal observations, on two subjects not outlined in the above protocol, the introduction of 20 c.c. amounts of twentieth normal hydrochloric acid into the first portion of the duodenum resulted in duodenal antiperistalsis associated with either prolonged pylorospasm or almost complete cessation of antral peristalsis. These phenomena were considered as the result of abnormal irritation of the duodenal mucosa resulting from the introduction of the acid. It will be remembered that mention has already been made of the development of pylorospasm and of partial cessation in gastric peristalsis after pouring twentieth normal hydrochloric acid onto the antral end of the pyloric sphincter.

The introduction of 5 per cent. sodium bicarbonate solution into the first portion of the duodenum in Observations 2 and 5, and 1 per cent. solution in Observation 4, produced no effect on the opening or closure of the pyloric sphincter, on the amount of barium passing into the duodenum, or on gastric peristalsis.

SUMMARY

Observations illustrated in Protocol I demonstrate that finely divided foodstuffs, either of carbohydrate, protein or fat, do not differ in the initial time at which they begin to leave the stomach and pass into the duodenum. This initial leaving time was not affected by variations in the consistency (viscosity) of the various foodstuffs. The food

was passing through the sphincter by the time the subjects could ingest the meals and be prepared for fluoroscopic observation; i. e., in from three to twelve minutes.

The barium containing chyme passed through the pyloric sphincter as each and every peristaltic wave approached that orifice. It continued to pour through the sphincter for a period of about ten seconds and then closed completely. The opening of the pylorus at irregular intervals, as described by Cannon⁴ in cats, was not observed. The regular opening of the sphincter in man was observed by Cole,⁵ but unfortunately his publication gives no experimental details.

In the five duodenal observations outlined in Protocol II the introduction of acid into the duodenum did not prevent the opening of the sphincter, or produce its closure. The amount of free acid present in the first portion of the duodenum is slight; in two subjects it was present in the concentration of eighty-fifth normal and five hundredths normal, and in another (Observation 2) no free hydrochloric acid was present. The acidity as titrated to phenolphthalein is low; expressed in terms of normal acidity, twenty-fifth normal, fiftieth normal and twentieth normal were found. These findings confirm those of McClendon and Myers.⁶ The latter observers determined the hydrogen ion concentration of the duodenal contents. Their findings showed that a low degree of acidity was usually present. From this discussion it is obvious that the amount of acid introduced in these observations was always much in excess of the amounts of free hydrochloric acid present normally in the duodenum and its titration value varied from a lesser amount to an excess in relation to the total acidity, titratable to phenolphthalein, normally present. Furthermore, as shown in Observation 2 of Protocol II the titration value of the total acidity of the duodenal contents is no index to its hydrogen ion concentration. It may, therefore, be stated that the amount of acid introduced was always of a hydrogen ion concentration much in excess of that normally present in the duodenum. These observations do not support the theory that acid in the duodenum is the principal factor causing contraction of the pyloric sphincter.

In Observations 2 and 5 chyme was collected as it entered the first portion of the duodenum. The concentrations of hydrochloric acid in the chyme in the two observations were none and five hundredth normal, and total acidities titratable to phenolphthalein were equivalent to fiftieth normal and twenty-fifth normal. In these observations sodium

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5. Cole, L. G.: Am. J. Physiol. **43**: 618, 1917.

6. Myers, F. J., and McClendon, J. F.: Note on the Hydrogen Ion Concentration of the Human Duodenum, J. Biol. Chem. **41**: 187, 1920.

bicarbonate solution was poured into the duodenum after the pyloric sphincter had opened and up until the time of its complete closure. The amounts of sodium bicarbonate solution introduced were sufficient to neutralize, in the concentrations in which it was found to be present, a quantity of acid several times greater than the cubic contents of the first portion of the duodenum. For this reason, it is safe to assume that the contents of the duodenum were alkaline in reaction. Then, according to the "acid control" theory, the sphincter should have remained patent as long as the duodenal contents were alkaline. This it did not do, but was observed to close completely. Similar results were obtained in Observation 4. However, absolute evidence that the amount of carbonate solution introduced in the observation neutralized all the acid in the duodenum was not obtained, although but little doubt can reasonably exist but that neutralization was effected. In Observation 3, in which the gastric contents in the region of the sphincter were alkaline, the contents of the duodenum are known positively to have been alkaline. Nevertheless, there was no demonstrable effect on the opening or closure of the pyloric sphincter.

Since the sphincter opens in relation to the advance of each antral peristaltic wave the contents of the antrum are not undergoing a mixing process between the times of opening of the sphincter, as was described by Cannon⁴ in cats. For this reason the degree of acidity of the antral contents must be constant during the interval in which the sphincter is closed. That the contents are acid is known. This statement is based on the following facts:

1. The authors, among others, have found the food when first ejected from the stomach into the duodenum to be slightly acid.
2. The contents aspirated from the stomach, after feeding various kinds of meats⁷ and after the Riegal test meal⁸ of meat and potatoes, are acid and contain free hydrochloric acid.
3. Free hydrochloric acid is constantly present in the stomach after feeding the Ewald test breakfast of bread and water.

From the above it follows that in order for the stimulation of acid in the stomach to open, and in the duodenum to close, the sphincter, there must be assumed the existence of a very delicate balance between the antral and duodenal reflexes in relation to the presence of acid, the duodenal reflex being much the more sensitive.

McClendon and Myers⁶ and the authors have found the contents of the first portion of the human duodenum to be either neutral or of low acidity. After emptying itself of food just ejected from the

7. Fishback, H. R.; Smith, C. A.; Bergheim, O.; Lichtenthaeler, R. A.; Reh fuss, M. E., and Hawk, P. B.: Gastric Response to Foods, *Am. J. Physiol.* **49**:174, 204, 222 and 254, 1919.

8. Riegal, F.: *Die Erkrankungen des Magens*, Wien. **1**:123, 1903.

stomach the duodenum will, therefore, be practically neutral in reaction, and in the presence of pancreatic juice possibly alkaline. Then, if acid in the stomach causes the sphincter to relax, the sphincter should become patent when the duodenum empties itself of food. That the sphincter does not relax is demonstrated by the difficulty experienced in pushing barium through the sphincter into the duodenum by palpation of the abdominal wall. In fact, as has already been stated, it is probable that barium can be forced into the duodenum by this means only when the sphincter opens in relation to the advance of an antral peristaltic wave. From this it follows that, if the pyloric sphincter is under "acid control," then the fact that it opens at regular intervals and normally only in a definite relation to the advance of an antral peristaltic wave makes it necessary to assume: (1) either that there is a finely adjusted acid regulatory mechanism in the antral region of the sphincter which produces the proper degree of acidity to relax the sphincter at a fairly exact time in relation to the approach of a peristaltic wave toward the sphincter; or (2) that a comparable mechanism for properly neutralizing the contents of the duodenum must exist. If either or both such mechanisms exist they must be so adjusted as to permit of changes in the rhythm of the time of opening of the sphincter as occurred in one of our observations after pouring alkali onto the antral end of the pyloric sphincter. Furthermore, while the sphincter closes suddenly it remains open an appreciable length of time. Barium flows through the sphincter as an antral peristaltic wave approaches and continues to do so until the wave has spent itself. The sphincter, therefore, does not close as soon as acid enters the duodenum, and the presence of acid we have demonstrated. If acid in the duodenum causes closure of the sphincter then: (1) either the proper degree of acidity must be developed always at a time when an antral wave has spent itself; or (2) a secondary mechanism in some way regulating the reflex must be assumed.

The existence of the various factors outlined are necessary to explain the theory of "acid control" of the sphincter and their existence has not been proved. The assumption of the existence of these factors renders the mechanism of the control of the sphincter exceedingly complex. It is possible that some other less complicated mechanism may exist in man. The latter has been suggested, but not proved, by Luckhardt, Phillips and Carlson.⁹ These investigators found a relation existed between the muscular activity of the antrum and the opening of the sphincter.

9. Luckhardt, A. B.; Phillips, H. T., and Carlson, A. J.: Contributions to the Physiology of the Stomach; The Control of the Pylorus, *Am. J. Physiol.* **50**:57, 1919.

CONCLUSIONS

The conclusions which may be drawn from the observations here presented are as follows:

1. Finely divided carbohydrate, protein or fatty foodstuffs begin to leave the normal human stomach within a comparatively few minutes after their initial ingestion.

2. Under normal conditions the human pyloric sphincter opens regularly at the approach of each antral peristaltic wave, allows chyme to pass through into the duodenum during an appreciable length of time, and closes when the antral peristaltic wave has spent itself.

3. The introduction of fortieth normal, twentieth normal or tenth normal hydrochloric acid solutions into the first, second or third portions of the normal human duodenum either produced no effect on the opening of the pyloric sphincter as observed by means of the fluoroscope, or produced effects which were interpreted as the result of abnormal irritation of the duodenal mucosa.

4. Neutralization of the contents of the first portion of the duodenum did not prevent the closing of the pyloric sphincter.

5. The results obtained indicate that acid is not the principal factor controlling the opening and closure of the pyloric sphincter in man.