GASTRIC MOTILITY IN DUODENAL ULCER.

by

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INTRODUCTION.

(a) Historical.

Until the latter part of the nineteenth century, physiologists believed that the fasting stomach was in a state of quiescence unless stimulated by the ingestion of food. This belief was dispelled in 1882, when Morat demonstrated the presence of gastric contractions in the fasting unanaesthetised dog. Some years later, he confirmed his findings in the human subject. The first direct proof that hunger in man is associated with gastric contractions was given by Cannon and Washburn in 1912.

In 1916, Carlson published his monograph on the fasting contractions of the stomach in animals and in man. He confirmed the results of Cannon and Washburn and his pioneer work stimulated physiologists to take an increasing interest in gastric motor function. Even to-day, however, gastric motility is still the Cinderella of gastric physiology and continues to take second place to gastric secretory activity, in the regard of both physiologists and clinicians. Important contributions to our knowledge of normal gastric motor activity in man have been made recently by Alvarez (1940) and Wolf and Wolff (1943). There are still, however, few reports relating to the changes in gastric motility in pathological states.

(b) Scope.

The incidence of dyspepsia among the population has risen steadily during the last twenty years and gastric

disorders now rank high in the list of diseases causing severe disability. In particular, duodenal ulcer results in severe and persistent disablement during a working man's most active years and therefore presents a pressing problem demanding investigation from every hopeful viewpoint.

The secretory activity of the stomach has held the interest of most workers in this field without, so far, providing a solution to the ulcer problem. Realising the paucity of our knowledge of gastric motor activity in duodenal ulcer patients, it was thought that a study of this aspect of the disease might be of value.
In the first instance, it was decided to study the presence or absence of any characteristic features in the duodenal ulcer gastrogram (record of gastric motility). It was therefore necessary to standardise a technique for recording motility and to establish the features of gastric motor activity in normal subjects. The thesis opens with an account of this rather monotonous but nevertheless important work.

Subsequent aims have been to study the diagnostic value of the duodenal ulcer gastrogram and to investigate the use of gastric motility recording as an objective method for the assessment of peptic ulcer therapy. The work, which has accomplished these aims, has opened up many other aspects of the duodenal ulcer problem.

The thesis therefore includes an account of gastric motor activity following the operations commonly employed in the surgical treatment of duodenal ulcer, the effects of

smoking on gastric motility and the influence of pyloric stenosis on the duodenal ulcer gastrogram. Further subjects discussed are the pain of ulcer and the effects of olive oil and of glucose on gastric motility in duodenal ulcer patients. The duodenal ulcer gastrogram is compared with those obtained from patients with gastric ulcer, stomal ulcer, gastric carcinoma, and gall bladder disease. The use of gastric motility recording in assessing the efficacy of peptic ulcer therapy is illustrated by a clinical trial of the drug "Benadryl".

PART - I.

GASTRIC MOTILITY - NORMAL SUBJECTS.

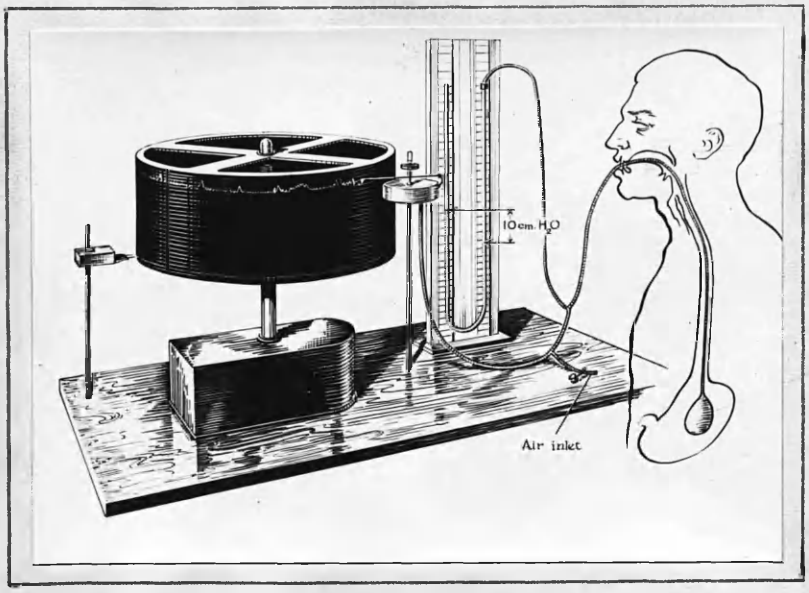
SECTION - 1.

Technique.

Gastric motor activity in man may be studied by observing the barium filled stomach fluoroscopically. The activity of the pyloric antrum and pylorus of the empty stomach may be observed directly by means of the gastroscope. Both methods are extremely valuable but merely provide an impression of motor activity during the brief spell of examination. It is more satisfactory to obtain a tracing of gastric motility over a period of several hours in order that the various phases of activity may be appreciated. This method has not the inherent weakness of all subjective examinations and records may be interpreted by those not present at the original examination. In order to obtain records of gastric motility, most observers have employed a thin-walled rubber balloon introduced into the stomach, changes in intragastric pressure being transmitted to the balloon and so to a suitable recording apparatus. Alvarez (1940) emphasises that the balloon recording device measures only those contractions which alter intragastric pressure and it has been suggested that certain peristaltic waves may course along the stomach without altering intragastric pressure. However, as the balloon conveys not only respiratory movements but also cardiac pulsation (p.14), it is probable that even the minor contractions of the fundus cause a sufficient alteration in intragastric pressure to register through the balloon.

Carlson (1916), Brauch, (1932) and Anderson (1942) used an air filled balloon connected to a water manometer of U-shape incorporating a float recorder. The first few recordings in this investigation were obtained by this method (hereafter referred to as Method B). The majority of the records included in this thesis have been obtained according to Anderson's technique modified by the substitution of a tambour for the float recorder (Method A). This method is now described in detail and its advantages discussed.

(a) Balloon - Tambour System. (Method A - Fig. 1.)



Contact with walls

The patient reports for examination having had neither food nor drink during the preceding 5 - 6 hours. He now swallows a Ryle's duodenal tube around the lower end of which has been attached, by means of fine silk thread, a rubber condom of about 200cc. capacity. The tube is swallowed to a set distance from the teeth. Throughout

Throughout this investigation the last 14cms. of the tube was left protruding from the incisor teeth and strapped by means of adhesive tape to the side of the face. The free end of the Ryle's tube is now connected to the lead from the tambour and air introduced through the air inlet until the pressure within the balloon is equivalent to 10cm. of water - verified by attaching the water manometer to the air inlet. When the exact pressure has been secured, the air inlet is firmly clipped. It has been my custom to delay recording for 20 minutes after inflation of the balloon so that the patient may adjust himself to the experimental conditions. During this interval, the patient's natural fears of the procedure should be allayed and the importance of quiet respiration, silence and the absence of restlessness, yawning, coughing etc., impressed upon him. Opportunity is also taken to describe tests to be applied during the recording. By gaining the patient's confidence in this way, many of the minor difficulties are avoided. X-ray control of the position of the air-filled balloon within the stomach may also be obtained during this interval. With the patient lying comfortably on a couch, facing away from the recording drum and having adjusted the time marker, signal and lever point on the smoked paper, recording is commenced. Few patients object to a two or three hour's session with a short break during which they are reassured and informed that a satisfactory and helpful record is being secured. A level base line in the tracing indicates a stable pressure in the air system but this should be checked

against the water manometer at the end of each tracing and certainly at the end of each experiment. After completion of recording, the air inlet clamp is released and the deflated balloon withdrawn from the stomach.

(b) Balloon - Float Recorder System (Method B. - Fig. 2).

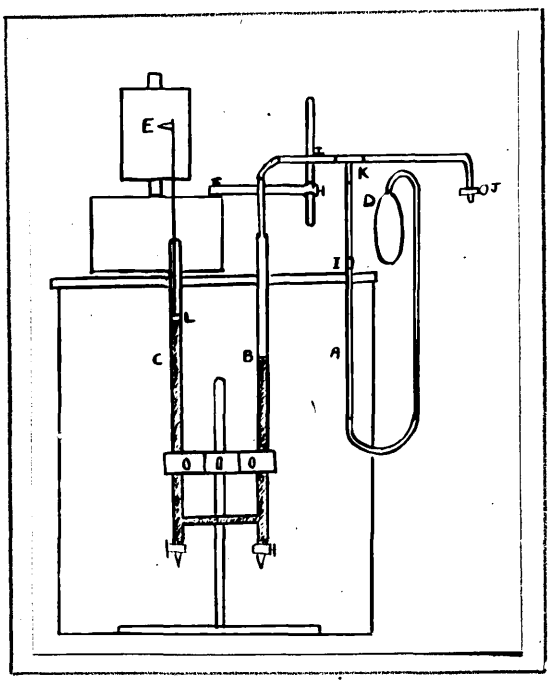


Fig. - 2.

This is also an air system. The recording unit consists of two burettes attached by side pieces at their lower ends to form a U-tube. This U-tube is partly filled with water which assumes the same level in both burettes. The Ryle's tube leading from the balloon is connected to the upper end of one burette; the other limb carries a vulcanite float bearing a recording point (Fig. 2). With this system, sufficient air is introduced through the air-inlet tube to depress the water level in the proximal limb by 5cm. and raise the water in the distal or recording limb by 5cm. Both burettes being of equal diameter, the

pressure in the balloon is equivalent to 10cm. of H_2O. In other respects, the technique was identical with that of Method A.

Disadvantages of the Float-Recorder Unit.

(1) The amplitude of contractions was much greater than in Method A and there was a definite tendency to a "rebound" phenomenon following descent of the float.

(2) Minor oscillations of the recording point were very troublesome. These obscured the essential trend of the tracings and rendered interpretation difficult.

(3) The float was occasionally found to adhere to the side of the burette and, in this way, several tracings were spoiled.

(4) Sudden movements of the float frequently caused it to tilt and for this reason difficulty was encountered in securing constant and efficient contact between the recording point and the smoked drum. A tendency for the float to rotate in the burette, thus swinging the recording point to and from the drum was also troublesome. In both cases, the result was uneven contact with varying definition of the tracing.

Advantages of the Tambour Recording Unit.

(1) Extraneous and minor oscillations can be effectively reduced by this method, particularly if a large diameter tambour is employed. In this investigation, the tambour was fashioned from a tobacco tin of 3" diameter. A circular hole was cut in the lid leaving a $\frac{1}{4}$" margin as a rim. Sheet rubber was introduced between the lid and the tin to form a diaphragm. (Fig. 3).

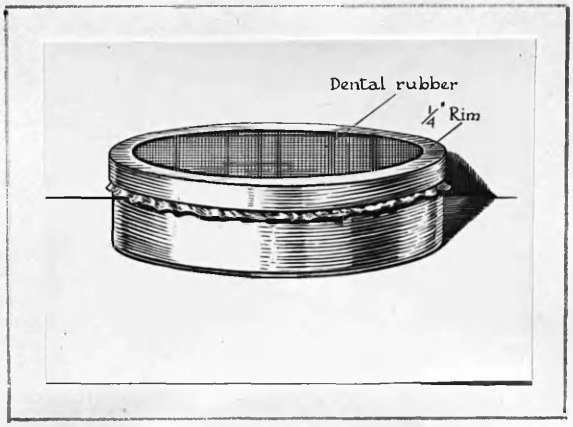


Fig. - 3.

(2) The metal recording point maintained even contact with the smoked strip. Clear and uniformly smooth tracings were constantly obtained in this way.

(3) Since using this method there have been no technical difficulties during recording and the fear of spoiled tracings has been forgotten. Fig. 4 was obtained by Method A: Fig. 5 was obtained by Method B. The marked difference in amplitude of waves, clarity of tracing and the occurrence of minor oscillations is obvious.

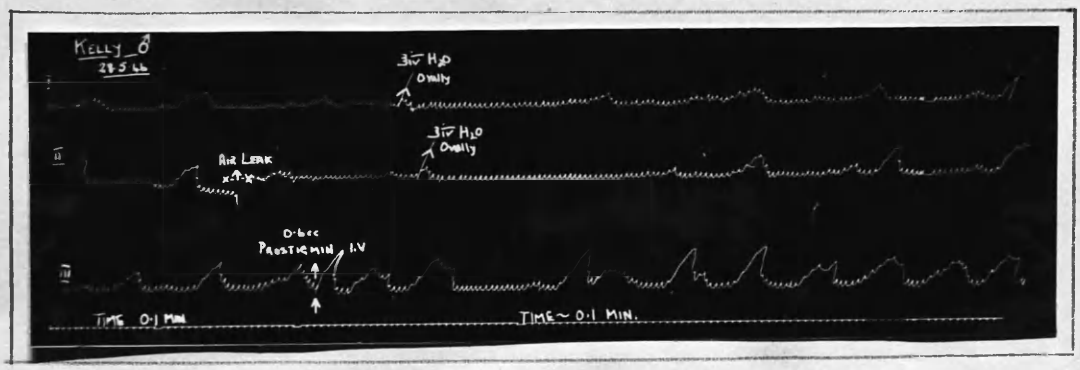


Fig. - 4.

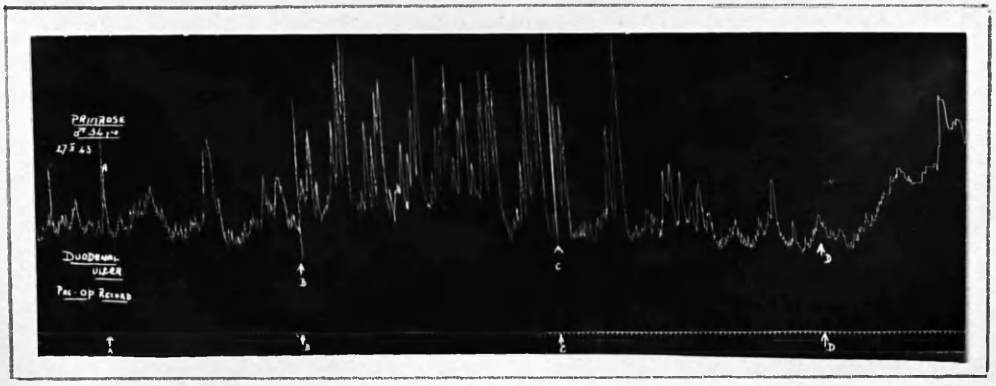


Fig. - 5.

The smoked strips used were 2 - 4 feet in length. The tracings (gastrograms) have been photographed in order to obtain records convenient for inclusion in this thesis.

SECTION - 2.

INTERPRETATION OF THE NORMAL GASTROGRAM.

Description of Gastric Oscillations.

All movements of the recording point result from changes in intragastric pressure; changes in intragastric pressure may result from true gastric waves or from extrinsic movements.

(A) Intrinsic Contractions.

1. True Gastric Contractions.
2. Tonus Waves.
3. Relative Quiescence.

(B) Extrinsic Movements.

1. Respiratory Contractions.
2. The Pulse Tracing.
3. Certain Fallacies.

(A) Intrinsic Contractions.

1. True Gastric Contractions.

The true gastric contractions is represented by a sharp-topped wave lasting 25-30 seconds. (Fig. 6)

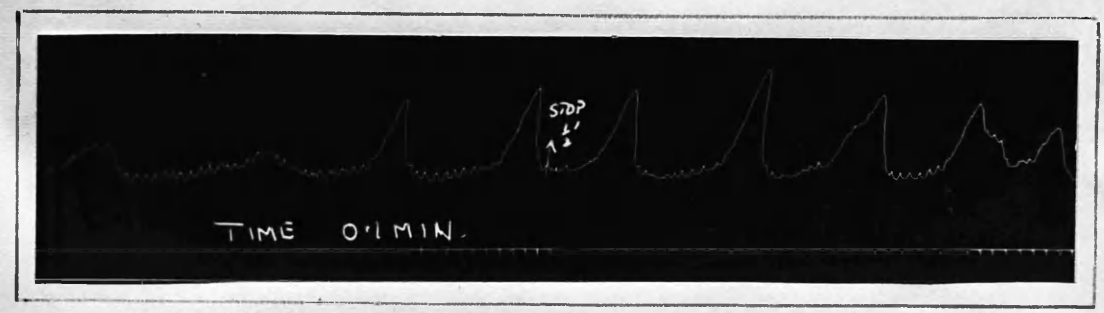


Fig. - 6.

These are powerful rhythmic contractions, alternating with phases of less intense activity and were first described as "hunger contractions" by Cannon and Washburn (1912). In a large series of cases it has been my experience that it is exceptional for the

patient to notice a sensation of hunger immediately before, during, or immediately after a phase of intense activity and the term "fasting contractions" would seem to be more suitable.

(2) Tonus Rhythm.

A regular alteration in gastric tone results in a shallow wave called "the tonus wave". Approximately 75 such waves occur each hour provided this phase is not replaced by fasting contractions or by a quiescent phase. These waves vary in amplitude and it is usual to find low tonus waves giving place to high tonus waves prior to the onset of a phase of true gastric contractions. (Fig. 7).

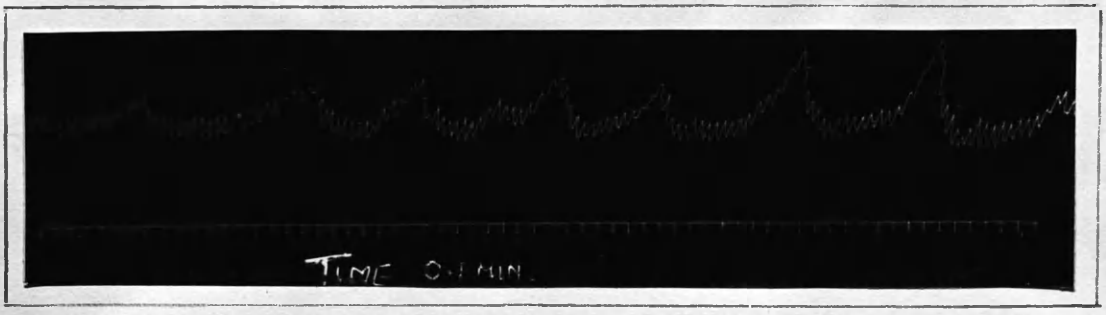


Fig. - 7.

3. Relative Quiescence.

The normal stomach does not show complete quiescence. The closest approximation to complete rest is a series of slight undulations forming the phase of relative quiescence. (Fig. 8). Complete rest may, however, result from drug action (Fig. 9a) or from vagal section (Fig. 9b). It is of great importance to appreciate that the phase of relative quiescence is usually of

about 20 minutes duration but may persist for fully one hour. It is clear that short records are of no value and may in fact lead to quite false impressions. A twenty minute record of quiescence may, for example, be interpreted as indicating an unusually quiescent stomach, when the stomach is in fact quite capable of normal activity.

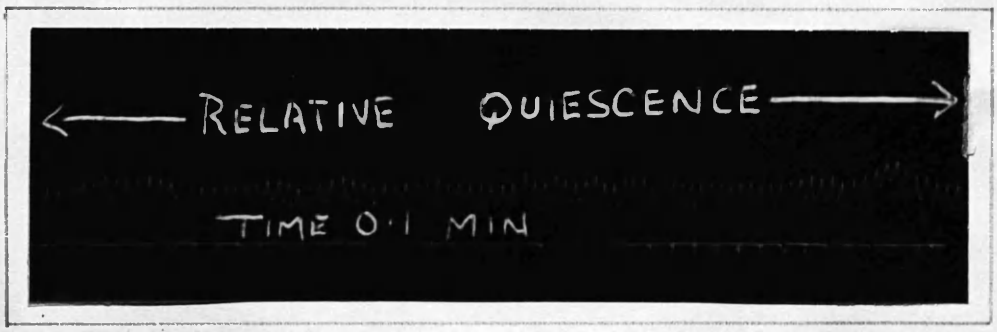


Fig. - 8.

Fig. - 9a.

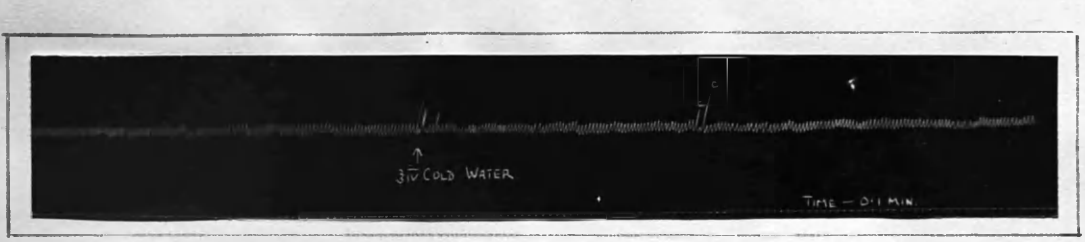


Fig. - 9b.
Inhibition after Vagotomy.

(B) Extrinsic Contractions.

1. Respiratory Contractions.

Small regular contractions are constantly present throughout the gastrogram due to the variation in intra-abdominal pressure - and consequently in intra-gastric pressure - resulting from the diaphragmatic excursions. These waves disappear when the breath is held. (Fig. 10)

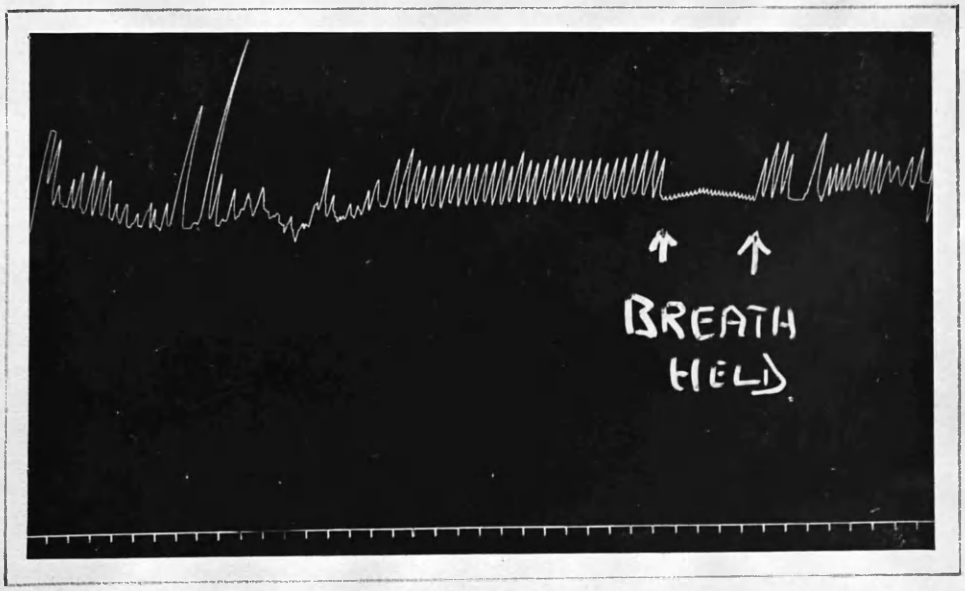


Fig. - 10.

2. The Pulse Tracing.

A small notch is sometimes superimposed on the respiratory wave. This represents transmitted cardiac pulsation and is well demonstrated on cessation of respiration. Each small contraction is then obvious and found to be coincident with the apex beat. (Fig. 10).

5. Sudden Changes in Intra-abdominal Tension.

Sharp-topped waves of brief duration are produced by coughing, sighing and sudden changes of position, all of which alter intra-abdominal tension. (Fig. 11)

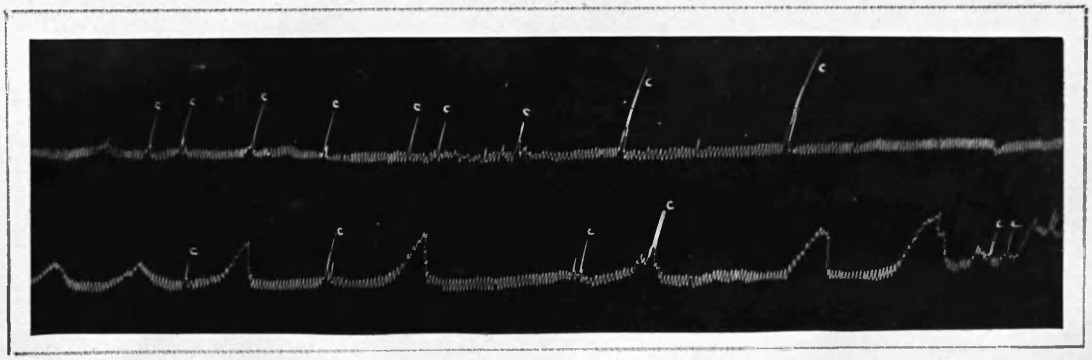


Fig. - 11.

These waves cause difficulties in interpretation and, when the float recorder is in use, the marking point may be thrown off the recording drum. This does not occur with tambour-recording. These fallacies may be excluded by gaining the patient's full co-operation prior to the commencement of the recording. An attempt to record gastric motility in a patient with a troublesome cough is doomed to failure.

Findings in Normal Subjects.

One of the aims of this investigation has been to assess the value of the gastrogram in the diagnosis of gastric disorders. It was therefore essential to use a uniform method of tabulating results. The following scheme has been used throughout:-

(1) Frequency of tonus waves - number of waves per hour.

(2) Features of gastric contractions
(a) Height (cm.)
(b) Duration (secs.)
(c) Frequency (per hour)

(3) Rhythm - regular or irregular, noting in cases of irregular rhythm whether this is of a regular or of a completely irregular type. The presence of fusion of waves is also noted.

(4) Special Tests applied, e.g., drugs etc.

(5) Gastrogram impression, diagnosis and comments.

This is a convenient point at which to establish the normal findings as obtained by the method used in most recordings in this study - Method A.

1. Frequency of Tonus Waves.

The frequency distribution of the number of tonus waves occurring each hour in 30 normal subjects is shown in Figure 12. It should be noted that it would be exceptional

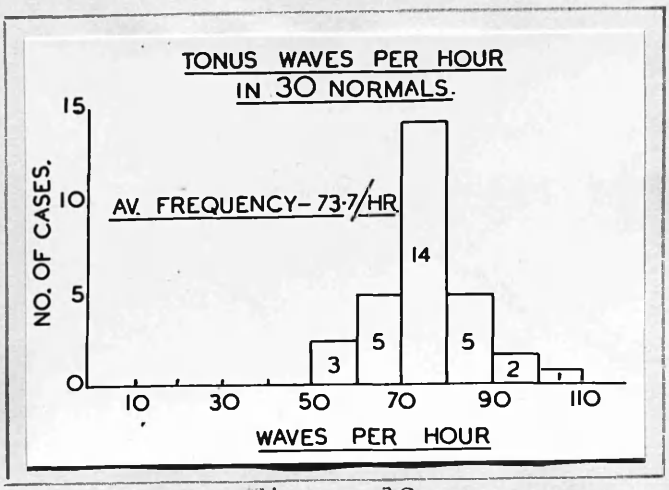


Fig. - 12.

to observe pure tonus rhythm for this length of time but one hour is a suitable unit of time to use as a standard. It will be noted that there is a wide range, viz., from 55 tonus waves per hour to 105 tonus waves per hour. There is however, a marked peak between 70 and 80 and the average value is approximately 74 tonus waves per hour. No attempt has been made to establish an average value for the height of tonus waves as they vary in amplitude throughout an

individual record, e.g., it is usual to find a gradual increase in the amplitude of tonus waves prior to the onset of a phase of gastric contractions.

(2) The Gastric Contractions.

a. Height.

Using the tambour records constantly, together with a constant pressure within the balloon of 10cm. of water in all cases, the height of the wave produced may be of real importance when comparing the records obtained from the normal and from the diseased stomach. The height of the gastric contraction has been measured in centimetres from the base line.

The frequency distribution in 30 normal subjects is shown in Figure 13. In any one record, most gastric

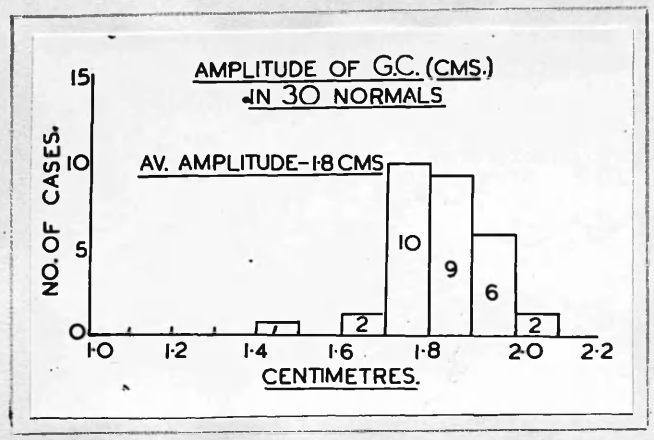


Fig. - 13.

contractions are of approximately the same height although an occasional one may be appreciably smaller as if it had not fully developed. The height of the majority of the waves has been chosen as the value for each individual case. Again, although there appears to be a wide range of normality, 25 of the 30 cases

gave a value between 1·7cm. and 2·0cm. The average height of the gastric contractions in 30 normal subjects was 1·80cm.

(b) Duration.

The duration of a true gastric contraction has been measured from the beginning of the definite up-stroke to the end of the definite downward deflection (Fig. 14)

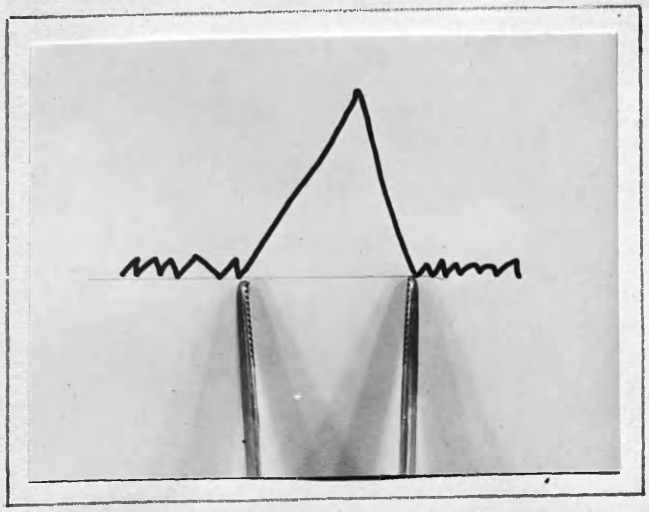


Fig. - 14.
Method of measuring the duration of a gastric contraction.

The frequency distribution of the duration in seconds of gastric contractions in 30 normals is given in Fig. 15.

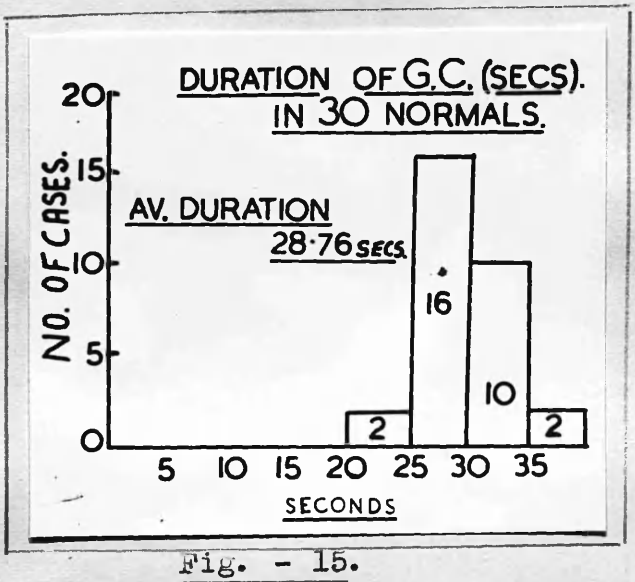


Fig. - 15.

The range was found to be from 20 seconds to 36 seconds with 26 cases showing values between 25 and 35 seconds. The average duration was 28·76 seconds.

(c) Frequency.

As for frequency of tonus waves, the hour has been taken as the unit of time in estimating the frequency of gastric contractions. Of the 30 normals, 17 records showed a satisfactory sequence of gastric contractions from which frequency of these waves in unit time could be calculated. The frequency varied from 24 to 75 contractions per hour. This wide variation has been observed by most workers in this field. The value given in text books is usually 70 per hour (Macleod, 1941). With such wide variation and with so few available records, it is useless to give an average value. An impression was gained that when the gastric contractions were of high amplitude and short duration the frequency tended to be greater. This impression will be reconsidered in connection with duodenal ulcer records. A sequence of gastric contractions may persist for from 10 to 60 minutes.

3. Rhythm.

The rhythm was found to be regular in all 30 normal subjects. By this, it is meant that the tonus waves followed each other with regularity and that true gastric contractions appeared so regularly that the subsequent wave could be anticipated confidently. Figure 16 shows a typical tracing; occasionally, a true gastric contraction is followed by a high tonus

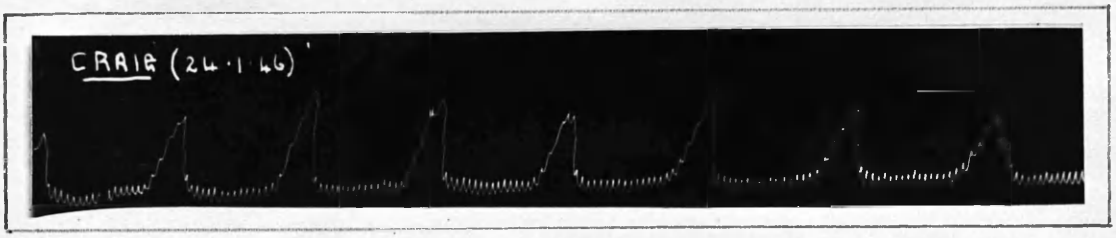


Fig. - 16.

wave, but the rhythm remains unaffected. From these findings, it is clear that regular rhythm is the rule in motility records of the healthy stomach.

4. Special Tests.

The test most frequently applied was the "cold water test". This is described in the next section. When indicated, the action of drugs was tested, e.g., the effect of vagal stimulants after attempted denervation of the stomach.

Summary.

The average findings in 30 normal gastrograms are as follows:-

(a) There is a regular tonus rhythm showing approximately 74 tonus waves per hour. The amplitude of these waves varies considerably and the development of high tonus waves indicates the onset of a phase of true gastric contractions.

(b) From time to time a phase of true gastric contractions is seen. This phase may last for 10 to 30 minutes. The frequency of these waves varies considerably - from 24 to 75 per hour in this series. The average height of these contractions in 30 cases was 1·8cm. and the average duration 28·8 seconds.

(c) In the normal gastrogram, the rhythm is regular, making it possible to predict the occurrence of each contraction.

(d) The reaction of the normal stomach to various stimuli is discussed in subsequent sections.

P A R T - II.

GASTRIC MOTILITY IN DUODENAL ULCER.

SECTION - 1.

COMPARISON WITH NORMAL GASTROGRAM.

The most striking feature on comparing the gastric motility records of normal and duodenal ulcer subjects is the hyperactivity to be observed in the latter. One has the impression of much higher gastric contractions and relatively brief phases of quiescence. Figures 17a and b show typically normal and duodenal ulcer records. The gastrograms of 66 duodenal ulcer subjects have been examined according to the plan set down on page 15. Details of each case are given in Appendix 1. An analysis of these cases is now presented.

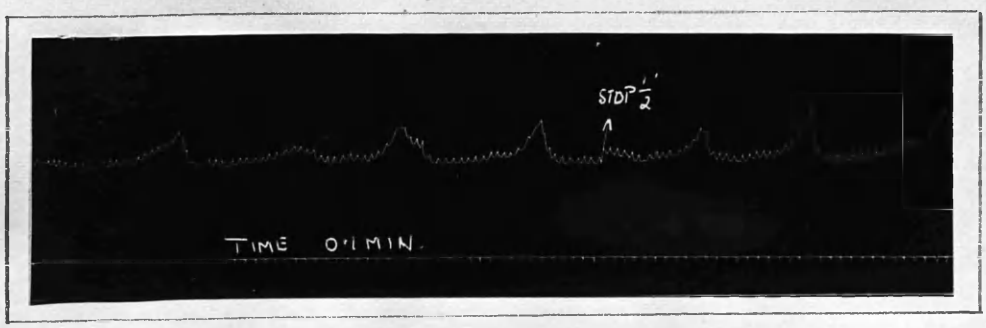


Fig. - 17a.
Normal Gastrogram.

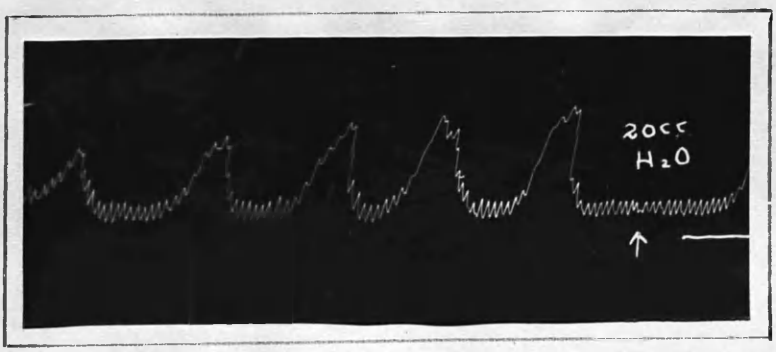


Fig. - 17b.
Gastrogram from Duodenal Ulcer Patient.

(1) Frequency of Tonus Waves.

The frequency distribution of the number of tonus waves occurring each hour in 62 patients with active duodenal ulceration is given in Fig. 18. It will be noted that

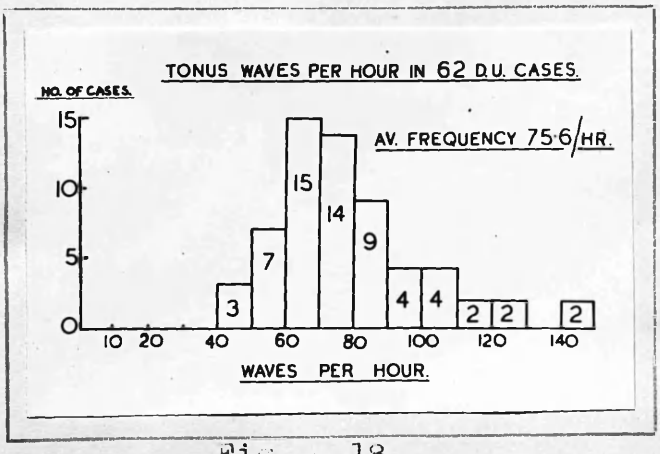


Fig. - 18.

the average value is 75·6 waves per hour. This shows no significant variation from the normal value of 74 waves per hour. There is certainly no indication of hypermotility to be found by estimating the frequency of the tonus waves. As in normals, the range is wide, viz., 45 - 140 tonus waves per hour.

(2) The Fasting Contractions.

(a) Height.

Standard experimental conditions having been observed throughout this investigation, any appreciable and constant variation in the height of the recorded waves can be regarded as significant. In 50 of the 66 cases of duodenal ulcer, a sufficient number of true gastric contractions was observed to determine reliable values for the height of these waves.

Figure 19 shows the frequency distribution in this series.

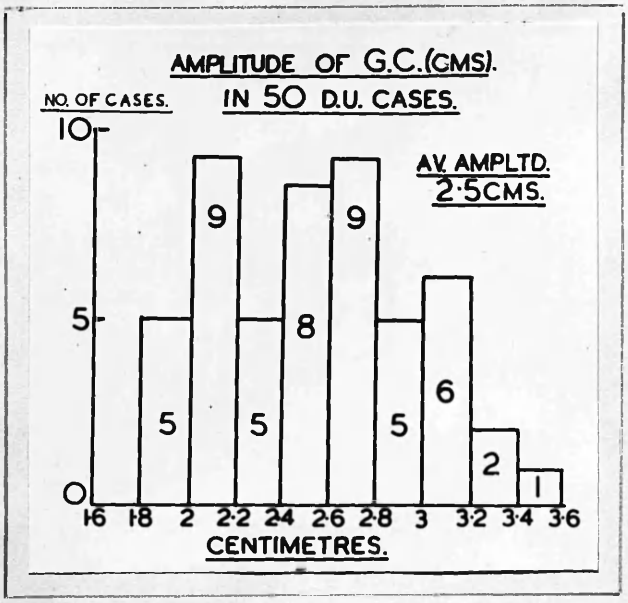


Fig. - 19.

The average height of gastric contractions in these cases of active duodenal ulcer was 2·5cm. as compared with 1·8cm. in normal subjects. Of the 50 normals, only one case presented gastric contractions of over 2·0cm (2·05cm.). Of the 50 duodenal ulcer patients, five showed gastric contractions of less than 2·0cm., but in none of these was the amplitude below 1·80cm. Values of more than 5·0cm. were not uncommon.

(b) Duration of Gastric Contractions.

Duration of gastric contractions has been measured in the manner described on page 18. The frequency distribution in 52 cases is given in Figure 20. The average duration of gastric contractions is 22 seconds as compared with 28·76 seconds in normal subjects. The range of values is 18 - 30 seconds in duodenal ulcer subjects and 20 - 56 seconds in normal subjects.

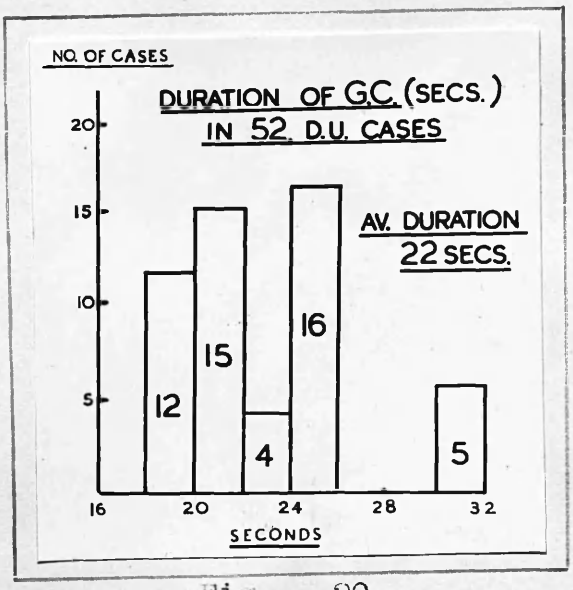


Fig. - 20.

(c) Frequency.

The frequency distribution of the number of gastric contractions occurring per hour in 49 cases is given in Figure 21. The average value is 64·5 occurring with a range of 45 - 100. Macleod (1941) gives the

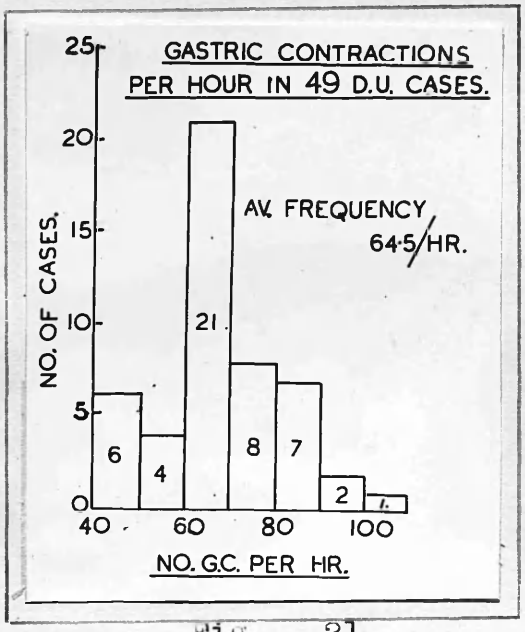


Fig. - 21.

frequency of fasting contractions in the normal stomach as approximately 70 per hour. It would

appear, therefore, that as with tonus waves, the frequency of true gastric contractions in duodenal ulcer subjects varies insignificantly from the frequency in normal subjects.

(3) Rhythm.

Onodera et alii (1931) described two features of the rhythm in duodenal ulcer gastrograms; irregularity was stated to be common and "fusing of gastric contractions" a feature. In 66 cases examined, I found complete regularity in 64 and a regular irregularity in 2. Complete irregularity was not observed. As regards "fusing", my findings in 66 cases are shown in Table I and Figure 22 illustrates fusing of gastric waves. Fusion may occur in both tonus waves and in true gastric contractions. Fusion of gastric waves was not found in normal subjects.

Table I.

Occurrence of "Fusing" in 66 Cases of D.U.

Frequent Fusing	Occasional Fusing	No Fusing.
22	16	28

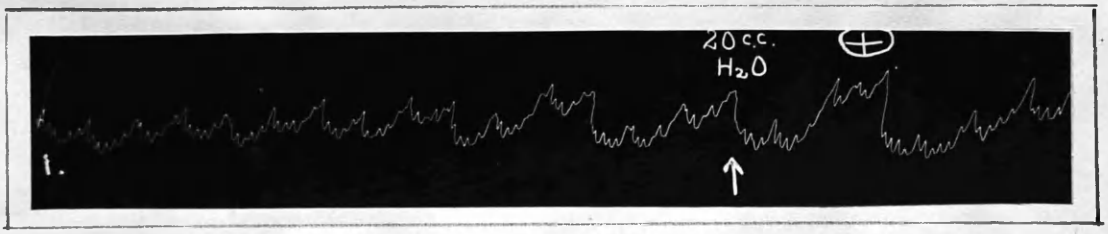


Fig. - 22.

Summary.

Table II shows the average values of the various criteria in both normal and duodenal ulcer cases as determined by gastric motility recording.

Table II.

Feature	Normal	Active Duodenal Ulcer
Frequency of Tonus Waves per hour	73·7	75·6
Amplitude of Gastric Contractions (cms.)	1·8	2·5
Duration of Gastric Contractions (secs.)	28·76	22.0
Frequency of Gastric Contractions per hour	70 Macleod	64·5
Rhythm	Regular	Regular
Fusing of Waves	None	Common

The criteria of diagnostic value in the duodenal ulcer gastrogram are as follows:-

(a) Gastric contractions greater than 2·0cm.
(b) Gastric contractions of less than 25 seconds duration
(c) The presence of fusing of the gastric waves.

The frequency of tonus waves and gastric contractions is of no reliable diagnostic importance. It must be clear that, based on these criteria alone, the gastrographic diagnosis of duodenal ulcer would not be reliable. In subsequent sections a specid test is presented which ensures accurate gastrographic diagnosis of active duodenal ulceration.

SECTION - 2.

THE COLD WATER REVERSAL PHENOMENON.

Carlson (1916) observed that the ingestion of cold water inhibited gastric contractions for about five minutes. Anderson (1945) confirmed this inhibition, lasting 10 - 35 minutes, in normal subjects, but not in patients with duodenal ulceration, in some of whom the ingestion of cold water even stimulated gastric contractions. This abnormal response he called the "water reversal phenomenon".

It was decided to follow up these observations and, if the occurrence of an abnormal response was established in ulcer cases, to investigate the physiological basis of the water response and to explore the possibility of its application to the diagnosis of duodenal ulcer.

The Motor Response of the Normal Stomach to Cold Water.

In order to test the effect of water on gastric motility, normal subjects were given a small draught of tap water or, if a double tube had been swallowed, water was injected through the stomach tube and the test signalled on the tracing. A phase of inhibition of gastric motility lasting 5 - 10 minutes occurred in each of 30 experiments. (Figure 23). It was considered advisable to select a standard water temperature at this stage of the investigation (55° - 65°F). It will be shown later, however, that temperature does not have a prominent role in the production of the water response.

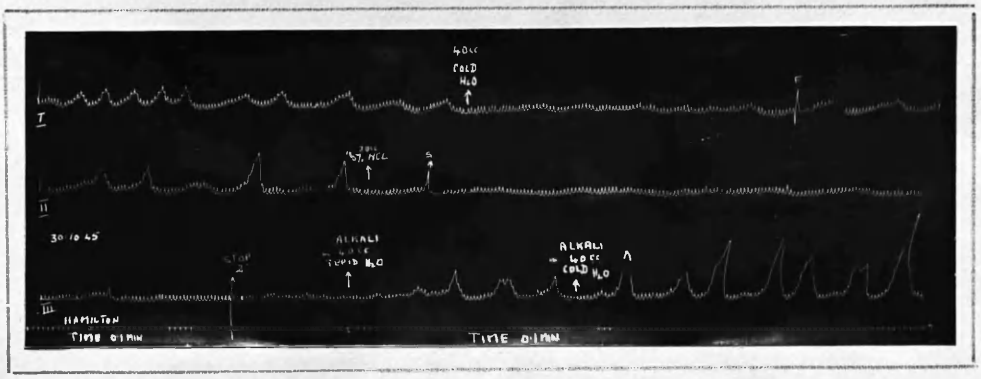


Fig. - 23.

Top tracing shows normal response to water.

The Gastric Motor Response to Cold Water in Patients with Active Duodenal Ulceration.

In 90 patients with symptoms of duodenal ulcer and showing a crater on X-ray examination, the water test excited gastric contractions. Gastric motility was increased in 68 and well-developed activity maintained in 22 patients. The more frequent effect of the water test in patients with duodenal ulcer (increased activity) will from now on be referred to as a Type I reversal response (Fig. 24); the less frequent effect (maintained activity) will be referred to as a Type II reversal response (Fig. 25.)

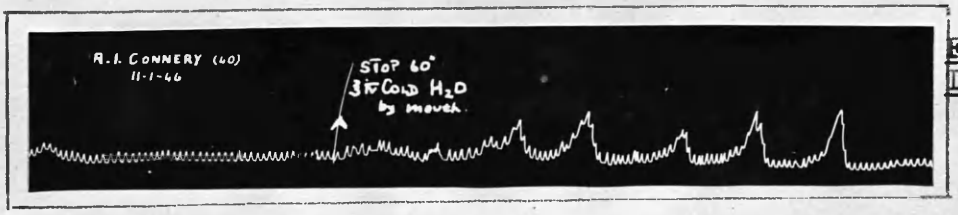


Fig. -24
Type I.

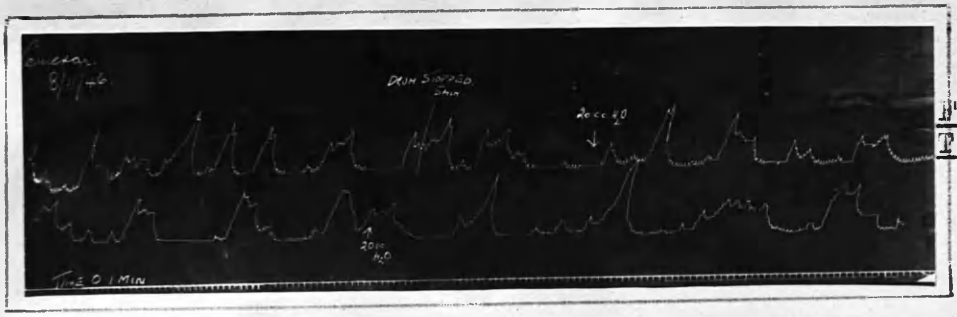
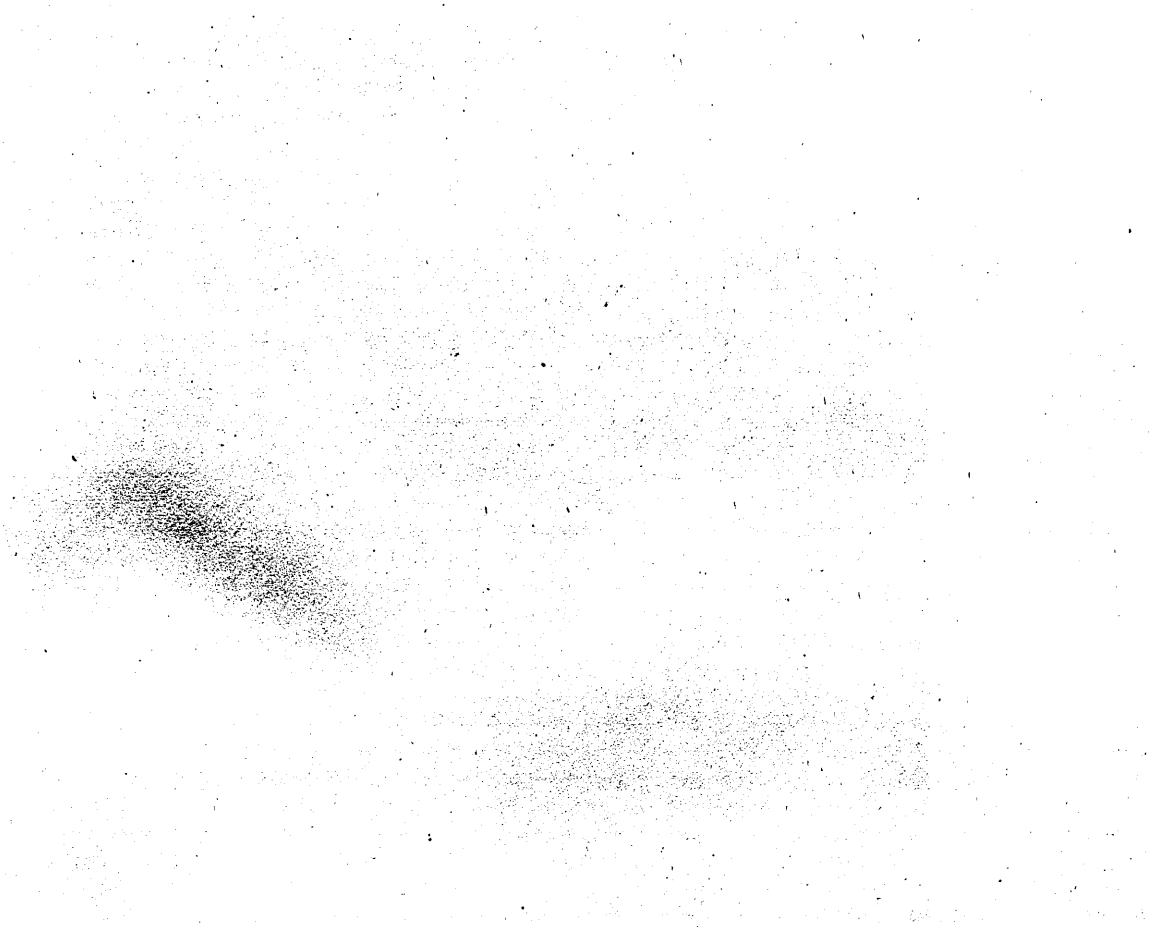


Fig. -25
Type II

This confirmation of the observations of Carlson and Anderson seemed to justify a study of the physiological basis and possible diagnostic application of the gastric motor response to water.



SECTION - 3.

THE PHYSIOLOGICAL BASIS OF THE WATER TEST.

(a) Site of Action.

Carlson believed that the inhibitory effect of cold water on gastric motility was due to afferent stimuli arising in the gastric mucosa. The modification of this response observed in patients with duodenal ulcer has led me to the view that the receptor for this reflex is in the duodenum. The following series of experiments was designed to test this hypothesis.

Experiment A.
Object.

An analysis of the water tests applied to both normal and duodenal subjects revealed that the response had a latent period of 45 - 60 seconds. Does water leave the fasting stomach within 60 seconds of ingestion? If it does not, the duodenum can be excluded as the receptor site.

Method.

A Ryle's tube waspassed into the duodenum of a fasting normal subject and the position of the tube confirmed by X-ray examination. Duodenal aspiration was performed and a draught of coloured water given by mouth. The dye used to colour the water was azorubrum which is itself inert. The experiment was repeated in a patient suffering from active duodenal ulcer.

Result.

A red fluid could be aspirated from the duodenum in both

experiments within 45 seconds of ingestion.

Conclusion.

Since the time taken by water to pass the pylorus corresponds to the delay in the development of the subsequent gastric motor response, it seemed probable that the receptor point is in the duodenum.

Experiment B.

Object.

To determine if the water response can be obtained by introducing water directly into the duodenum, thus excluding the stomach as the site of action.

Method.

In 4 ulcer patients with gastric and duodenal tubes in situ, 20cc. water was introduced first into the duodenum and secondly into the stomach.

Result.

Not only was a reversal response obtained in each patient by the duodenal injection of water, but a reduction in the latent period was observed. After duodenal injection the latent periods of the water response were 18, 15, 20 and 22 seconds; after gastric injection, the corresponding latent periods were 50, 45, 50 and 55 seconds.

Conclusion.

This experiment furnishes strong evidence that a duodenal mechanism is involved in the production of the water response.

Experiment C.
Object.

To determine the water response in patients having active gastric ulceration but no duodenal ulceration.

Method.

Records of gastric motility have been obtained in 12 cases of gastric ulcer. The water test was applied in each case.

Results.

In all cases, a normal response (inhibition) was recorded (Figure 26.)

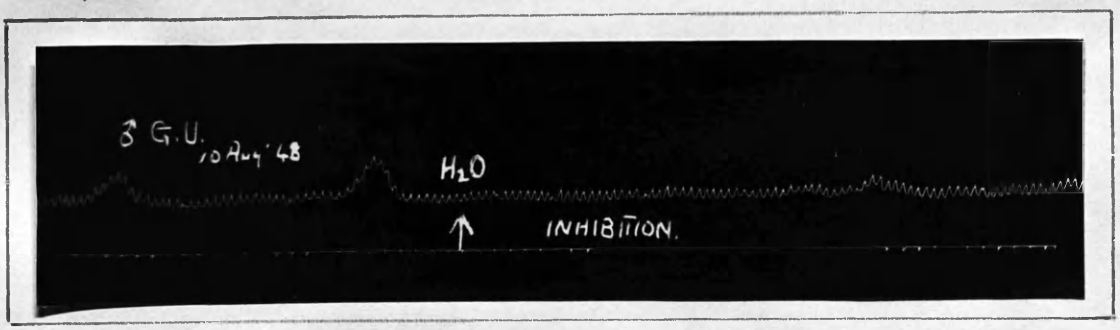


Fig. - 26.

Conclusion.

The fact that water stimulates gastric motility when the ulcer is duodenal but not when it is gastric also suggests that the receptor is in the duodenum.

Experiment D.
Object.

To ascertain the effect of healing of the duodenal ulcer on the gastric response to water.

Method.

The water test was applied to 15 patients who had remained symptom-free for at least one year after perforation of a duodenal ulcer and in whom there was no radiological evidence

of activity. This group was chosen on the assumption that the ulcers had healed completely.

Result.

A normal response (inhibition) was obtained in all cases. Fig. 27 is part of the record taken from a patient who remained symptom-free for two years following perforation of a duodenal ulcer.

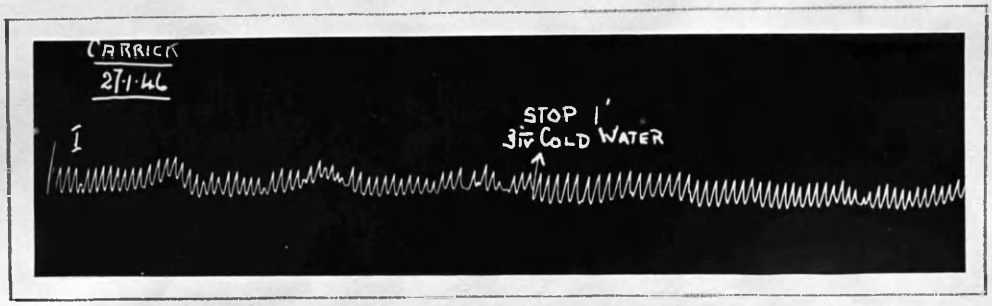


Fig. - 27.

Conclusion.

When a duodenal ulcer has healed completely, the reversed response to water gives way to a normal response. The nature of this physiological response would seem to depend on the state of the duodenum which may be regarded, therefore, as the site of action.

Discussion.

Water inhibits the gastric motility of normal subjects but causes stimulation in patients with active duodenal ulceration. The receptor for this gastric motor response is situated in the duodenum. The evidence for this site of action may be summaried as follows: (1) the time taken for ingested water to leave the stomach has been shown to correspond to the latent period of the water response;

(2) the gastric motor response can be obtained on the duodenal injection of water; (3) when water is introduced directly into the duodenum, the latent period is significantly reduced; (4) the occurrence of an inhibitory response in patients with gastric ulcer indicates that ulceration itself is not the essential cause of a reversed response but that the site of ulceration is the important factor. Stimulation of gastric activity in response to water occurs in the presence of active duodenal ulceration; (5) when a duodenal ulcer has healed, the reversal response to water is replaced by a normal response.

It would seem reasonable to postulate the existence of a duodenal mechanism which normally inhibits gastric motor activity and delays evacuation of gastric contents. The presence of an active ulcer in the duodenum presumably interferes with this mechanism and results in the production of an abnormal response. Though damaged, this mechanism is not destroyed and will function normally with complete healing of the ulcer.

(b) Effect of Solution Tonicity.

The introduction of hypertonic solutions into the stomach is known to cause protracted inhibition of gastric motility in normal subjects. It seemed useful therefore, to investigate the effect of solutions of varying tonicity in cases of duodenal ulcer. In 15 patients with duodenal ulcer, 20cc. each of water, normal saline, 2N saline, 5N saline and 10N saline, again at constant temperature (65°F) was introduced into the stomach and the gastric motor responses were recorded.

As the test solution became more hypertonic, an increasing number of patients gave a normal response; in 14 patients 10N saline effected inhibition (Figure 28)

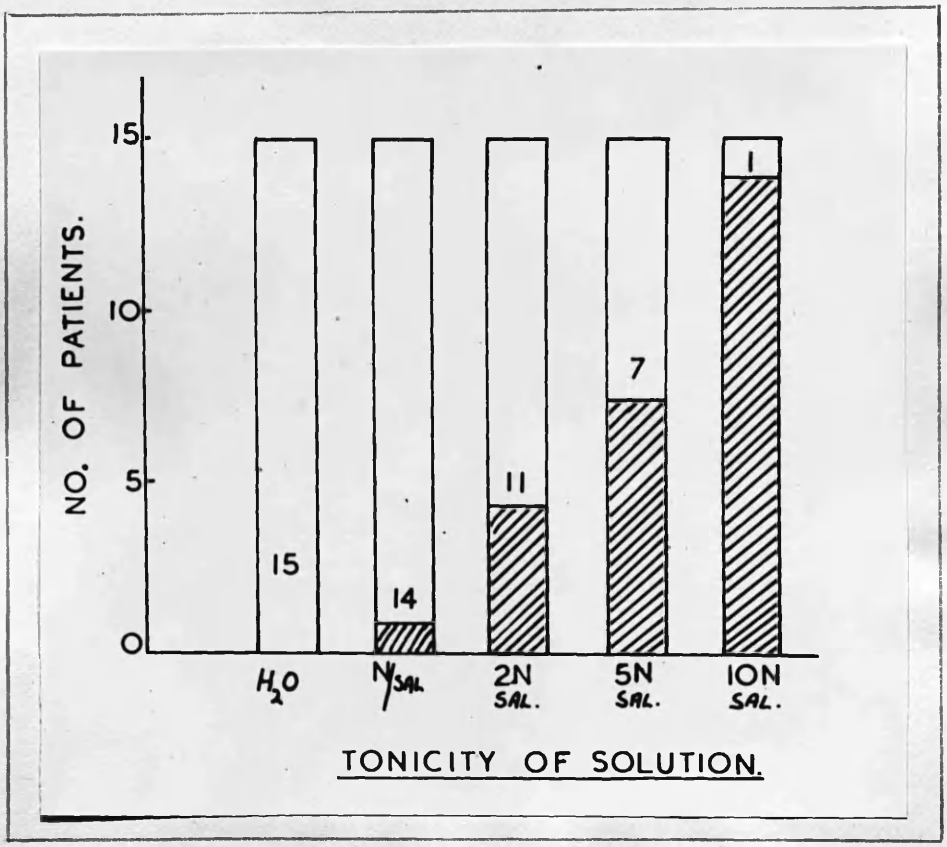


Fig. - 28.
Gastric motor responses in 15 patients with duodenal ulcer, showing return of normal response (inhibition) with increasing tonicity of ingested fluid.

Gastrograms showing a reversal response to water but an inhibitory response to 2N saline, 5N saline and 10N saline respectively, are given in Figures, 29, 30 and 31. Even 10N saline may occasionally fail to effect an inhibitory response in severe cases of duodenal ulcer (Fig. 32).

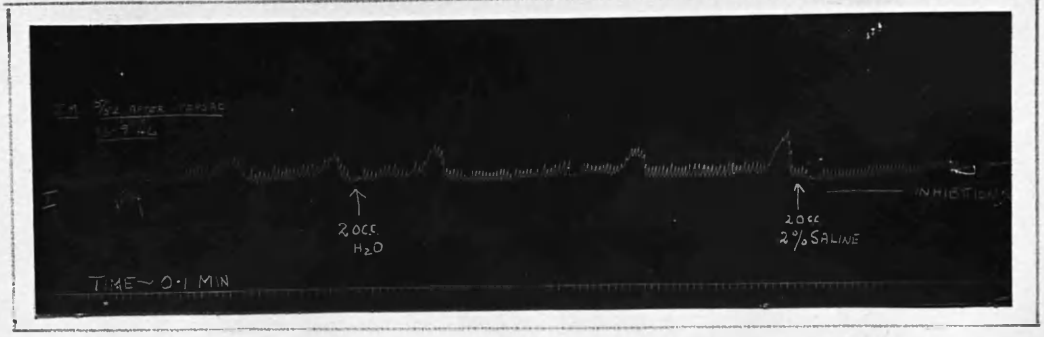


Fig. - 29.

Fig. - 30.

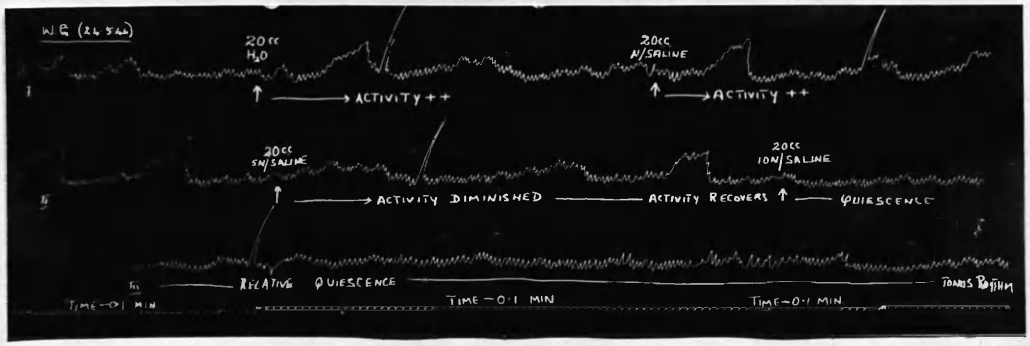


Fig. 31.

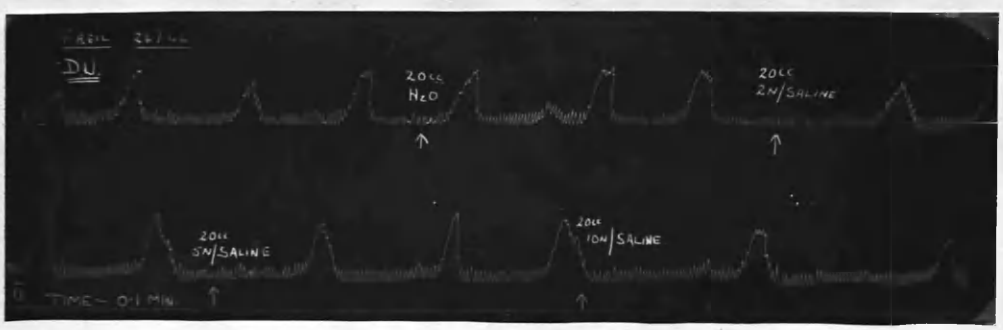


Fig. - 32.
Severe D.U. - 10N/Saline fails to effect inhibition.

(c) Effect of Temperature.

The temperature of the water does not influence the type of gastric motor response but merely alters the duration of that response. In normal subjects, I found that cold water (10°C) had a slightly longer inhibitory effect than warm water (50°C). Similarly, in patients with active duodenal ulcer, cold water had a longer and more pronounced excitatory effect than had hot water (Fig. 33). The type of response

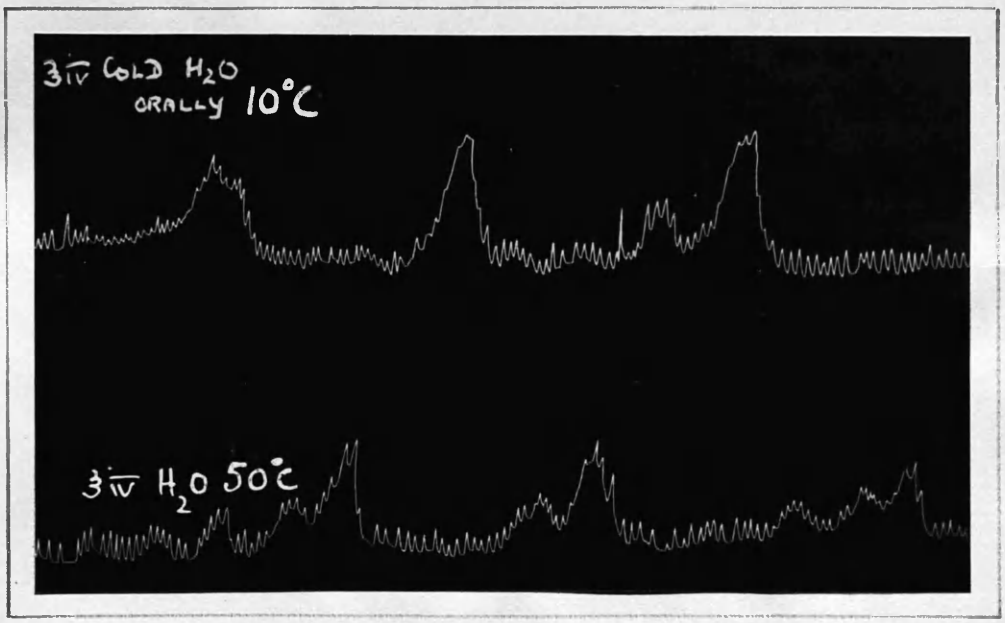


Fig. - 33.

was always recognised without difficulty. On this evidence, the use of the phrase "water reversal phenomenon" is preferable to Anderson's "cold water reversal phenomenon, as the latter suggests that temperature plays a predominant role in the production of the response.

SECTION - 4.

THE CLINICAL APPLICATIONS OF THE WATER TEST.

A. Value in Diagnosis.

To be of value in diagnosis (1) the water reversal response must be given consistently in patients with active duodenal ulcer; (2) it must be replaced by a normal response when the ulcer has healed; (3) it must not be given by other common causes of dyspepsia such as gastric ulcer and gastric carcinoma; and (4) its inherent fallacies must be defined. The extent to which these criteria are fulfilled has been investigated.

(1) In 50 normal subjects, the ingestion of water inhibited gastric contractions. A reversal response was obtained in 90 patients with duodenal ulceration.

(2) A normal response to the water test was obtained in 15 patients in whom there was good reason to assume complete healing of previous duodenal ulceration.

(3) The water test was applied to 14 patients with definite gastric disease (5 ulcer and 9 carcinoma). A normal response was obtained in 13 of these subjects. A reversal response (Type I) was recorded in one patient with carcinoma of the stomach in whom, however, invasion of the duodenum was revealed at laparotomy (Fig. 34). It is of interest to note that this patient, a woman of 44 years, complained of pain two hours after food which was relieved by food. The fractional test meal gave

achlorhydria. The problem of pain and the role of acidity in its production will be considered in a subsequent section.

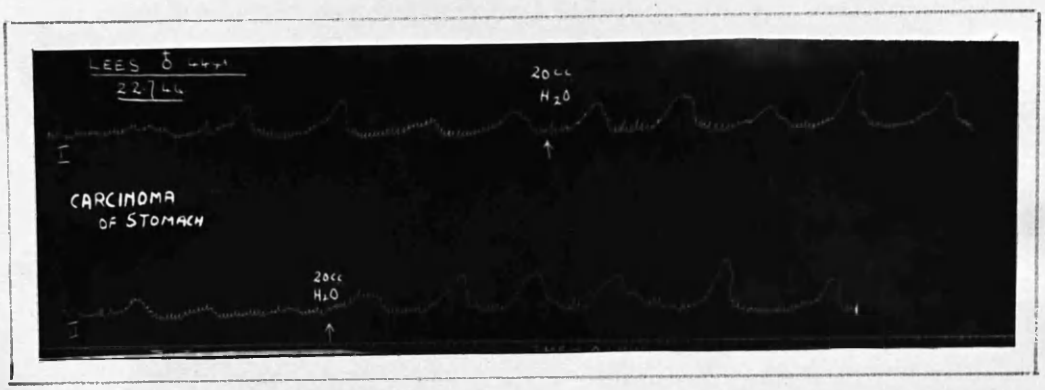


Fig. - 34.

(4) Carcinomatous involvement of the duodenum is so rare that it scarcely merits consideration as a fallacy in the water test. The only common fallacy noted has been in patients with acute inflammation of the gall bladder. Of 5 such patients examined, 2 gave a normal response to the water test, 2 a Type II response and 1 gave a Type I response (Fig. 35). In the last case, laparotomy revealed an empyema of the gall bladder adherent to the duodenum.

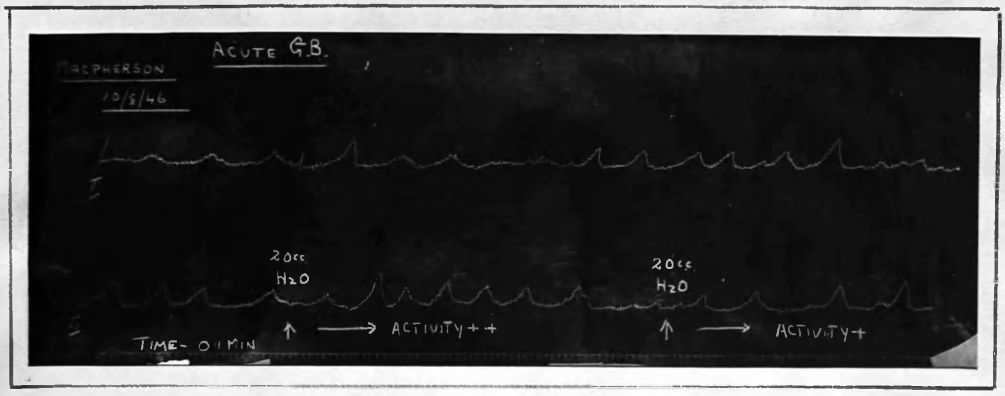


Fig. - 35.

Our four criteria having been fulfilled, has the water test a place in the diagnosis of duodenal ulcer? A gastric ulcer can usually be revealed with certainty with the aid of radiography and gastroscopy. A duodenal ulcer cannot be recognised so readily. Endoscopy of the duodenum is not yet practicable and the radiological demonstration of an ulcer crater in the duodenum is difficult. Thus, Templeton (1944) reported 809 cases of clinically active duodenal ulcer in only 526 (65%) of which a crater could be demonstrated. The gastric motor response to water is proposed as a test of active duodenal ulceration. It is a physiological response and has the advantage of being objective, whereas the personal factor is an inherent weakness of radiological investigation. This test is applied to all cases of "clinical duodenal ulcer" seen at the Peptic Ulcer Clinic, Western Infirmary, in which there is no radiological lesion of the duodenum. In 28 cases of X-ray negative dyspepsia, the water test has confirmed the clinical impression and revealed a duodenal ulcer in 20 patients; the negative X-ray findings were supported in 8 patients (Table III). The case history of one of these patients is provided as an example. (Page 43).

TABLE - III

Results of Water Test in 28 Cases of X-ray Negative Dyspepsia

Case.	Sex.	Age.	Duration (Years)	Clinical Diagnosis	Water Test R= Reversal N= Normal
1	M	41	15	D. U.	RI.
2	M	28	6	D. U.	RI.
3	M	28	10	D. U.	RI.
4	M	37	7	D. U.	RII.
5	M	41	10	D. U.	RI.
6	M	33	9	D. U.	RII.
7	M	26	2	D. U.	RI.
8	M	36	4	D. U.	RII.
9	M	47	4	D. U.	RI.
10	F	16	3	D. U.	RI.
11	F	51	9	D. U.	RI.
12	M	23	4	Not P. U.	N
13	M	35	7	D. U.	N
14	F	25	10	Not P. U.	N
15	M	40	22	D. U.	RI.
16	M	26	$2\frac{1}{2}$	Proved D. U. at op.	RI.
17	M	47	3	Proved D. U. at op.	RI.
18	M	32	5	D. U.	RI.
19	M	49	$\frac{1}{2}$	? Rec. Appendix.	N
20	M	32	4	? Duodenal Ileus.	N
21	M	21	$1\frac{1}{2}$	Migraine	N
22	M	37	1	D. U.	RII.
23	M	30	8	D. U.	RI.
24	M	43	9	Not P. U.	N
25	M	28	2	D. U.	RI.
26	M	26	3	D. U.	RI.
27	M	34	1	? Rec. Appendix.	N
28	M	27	5	D. U.	RI.

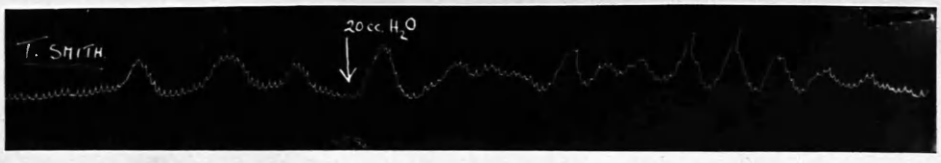


Fig. - 36.
X-ray negative dyspepsia; water test shows Type I reversal response Duodenal Ulcer.

Case History of Thomas Smith, 30 yrs.

Onset of epigastric pain 1½ hours after food, relieved by food, alkalis and rest, occurred while in the Army in 1940. Discharged on this account six months later. X-ray examination in 1941 revealed a normal stomach and duodenum. On the diagnosis of recurrent appendicitis, appendicectomy was performed. He remained symptom-free for almost two years but dyspepsia recurred in 1943. Since then, he has had recurrent attacks every few months. When seen at the Peptic Ulcer Clinic in April 1949, the history was regarded as typical of duodenal ulcer with moderately severe disability. Barium meal on two separate occasions reported / No abnormality seen in oesophagus, stomach and duodenum". Smith was depressed by his continuing symptoms and by our inability to determine a definite cause and began to feel that his complaint would be regarded as functional. Gastric motility was recorded and the gastrogram is given in Fig. 36. A Type I reversal response confirmed the clinical impression of active duodenal ulceration. Gastrectomy was performed in December 1948. At operation, the patient was found to have a chronic active duodenal ulcer.

B. Determination of Healing by Means of the Water Test.

Besides its use in diagnosis, the gastric motor response to water may be used to test the healing of a duodenal ulcer. The gastro-enterologist who tries to assess the relative merits of various "cures" for duodenal ulcer, quickly encounters difficulty in choosing an end-point for the healing of the ulcer. The absence of pain and of occult blood in the stool does not provide satisfactory evidence. The radiological disappearance of the ulcer crater almost certainly preceeds actual healing. The gastroscopists have, in fact, shown that gastric ulcers often become "radiologically negative" for an appreciable time before complete healing is found gastroscopically. I suggest that the return of the normal gastric response to water (inhibition of contractions) is a dependable criterion

of healing. Gastrograms are being recorded in duodenal ulcer patients who become symptom free and cease to show a crater on radiography. So far, I have found that the gastric motor response to water may remain abnormal for as long as four weeks after a barium meal has shown no signs of active ulceration.

Conclusion.

The water test is of value in the diagnosis of active duodenal ulceration and can be used to provide reliable evidence of healing.

SECTION - 5.

GASTRIC MOTILITY IN DUODENAL ULCER COMPLICATED BY STENOSIS.

It has been shown that the normal gastrogram and the gastrogram in uncomplicated duodenal ulcer conformed to definite patterns. The probability that all cases of pyloric stenosis would yield a characteristic tracing was considered to be small; the duration of the stenosis is likely to influence the gastric motor activity; the degree of mechanical obstruction will vary; the ulcer giving rise to stenosis may be healed or may remain active; when gastric motility is recorded, after the standard five hour fasting period, the volume of gastric residue is liable to show considerable case variation.

Gastric motility tracings obtained from 21 cases of clinical pyloric stenosis have supported this view. The frequency of tonus waves and the amplitude, duration and frequency of the true gastric contractions showed considerable variation. As this data is of little value in the absence of an exact knowledge of the local pathology and of the degree of pyloric narrowing, gastrogram values are given in only 16 cases - those subjected to operation. Four cases are described in detail, viz., two cases of active duodenal ulcer with stenosis (one mild and one severe) and two cases of healed ulcer with stenosis (one mild and one severe). This is followed by a table giving the main gastrogram findings in the 16 cases of proven stenosis.

Case 1 - Active Duodenal Ulcer with Mild Stenosis.

Clinical Features — J.D. - Male, 53 years.
Typical history of D.U. for 12 yrs. During past one year has experienced sensation of epigastric fullness relieved by vomiting. Vomiting - unless induced - has occurred infrequently but has contained undigested food. X-ray report "delayed emptying in the presence of active duodenal ulceration".

Operation Note. Active duodenal ulcer, mild degree of organic stenosis with dilatation of the stomach to a moderate degree; sub-total gastrectomy.

Gastrogram. The gastrogram is reproduced in Fig. 37.

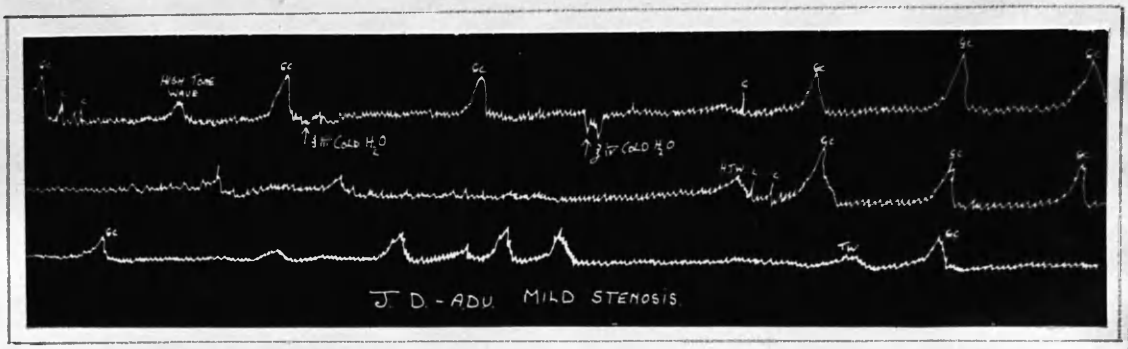


Fig. - 37.

The features to be noted are: (1) the gastric activity, as indicated by gastric contractions, is above normal (Amplitude = 3cms; normal value 1.8cm; duration = 36 secs; normal value = 28 secs.) (2) the water test shows a reversal response indicating an active D.U. (3) the latent period for the development of the water response is almost 3 minutes as compared with 45/60 secs. in the uncomplicated case of duodenal ulcer and (4) the rhythm is regular.

Case 2 - Active Duodenal Ulcer with Severe Stenosis.

Clinical Features. M.K. - Male, 53 yrs.
Infrequent attacks of duodenal dyspepsia for 27 yrs. Attacks more frequent and of longer duration for the past four years. For three years vomiting has been a feature. $2\frac{1}{2}$ stones weight lost in past four months.

Operation Note. Anterior and posterior wall duodenal ulcers with severe and marked dilatation and hypertrophy of the stomach.

Gastrogram. The gastrogram is reproduced in Fig. 38.

Fig. 38.

The features to be noted are; (1) the gastric activity as indicated by gastric contractions is again above normal (amplitude = 3cms; duration = 34 secs.) but the frequency of contractions is diminished. (2) the water test showed a reversal response (3) the latent period of the water response is increased beyond the normal to just over 2 minutes and (4) the rhythm is irregular.

Case 3. – Healed Duodenal Ulcer with Mild Stenosis.

Clinical Features. T.S. - Male, 36 yrs.
6 years history of D.U. Perforation four years ago. Patient is now free from pain but frequently experiences distension in the epigastrium shortly after meals. Occasional vomiting. Admitted to hospital on account of acute small bowel obstruction.

Operation Note. "... the obstruction having been relieved, the stomach and duodenum were examined; there was no evidence of active D.U. but there was a mild degree of pyloric stenosis accompanied by some gastric hypertrophy.

Gastrogram. The gastrogram is reproduced in Fig. 39. The features to be noted are; (1) gastric activity approximates to the normal (amplitude = 1·9cms. and duration = 24 secs., the frequency of the gastric contractions being approximately 45 per hour) (2) the water test gave a normal response; (3) the latent period of this response could not be determined accurately as the application of the test was not followed by any additional contractions and as the preceding ones had been appearing at irregular intervals and (4) the rhythm is irregular.

Fig. - 39.

Case 4. - Healed Duodenal Ulcer with Severe Stenosis.

Clinical Features. J.A. - Male, 46 yrs.
30 years history of typical D.U. symptoms. Pain constant but not severe for the past six months. Vomiting, which had occurred off and on for four years, now frequent and large in amount. X-ray revealed very marked pyloric stenosis.

Operation Note. Greatly dilated stomach; no evidence of active ulcer; an extreme degree of stenosis was present.

Gastrogram. The gastrogram is reproduced in Fig. 40.

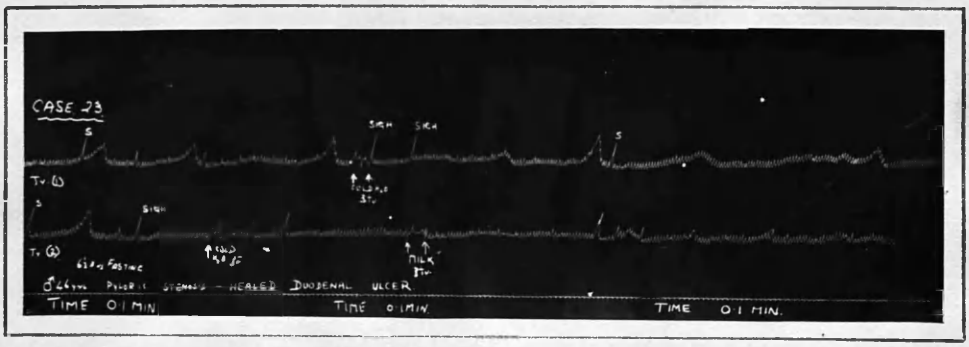


Fig. - 40.

The features to be noted are (1) gastric activity less than normal in that the frequency of waves is only 20 per hour; those waves which are present have an amplitude of 1·8cms. and duration of 24 secs. (2) The water test gave a normal response (3) the latent period of the water test cannot be determined with accuracy and (4) irregular rhythm.

Table IV summarises the main gastrographic findings in 16 cases of proven pyloric stenosis. These cases are classified according to the activity of the ulcer as seen at operation. No attempt has been made to grade the degree of pyloric narrowing.

Table IV.

Analysis of Main Gastrogram Findings in 16 cases of Pyloric Stenosis.

Case.	State of Ulcer at Operation	Rhythm.	Gastric Contrac's Amplt'd (cms.)	Gastric Contrac's Durat'n (secs.)	Water Test	Latent Period of W.T. (mins.)
1	Active	Regular	2·4	30	RI	3·0
2	Active	Regular	2·4	24	RI	2·5
3	Active	Regular	2·4	42	RI	1·5
4	Active	Regular	2·0	30	RI	2·0
5	Active	Irregular	2·2	32	RI	2.0
6	Active	Irregular	3·0	34	RI	2·1
7	Active	Regular	3·0	36	RII	?
8	Active	Regular	3·2	30	RI	2·0
9	Active	Regular	3·0	30	RI	1·5
10	Active	Regular	3·2	27	RII	?
11	Healed	Regular	1·8	30	N	Approx 2
12	Healed	Irregular	1·6	30	N	?
13	Healed	Irregular	1·5	28	N	?
14	Healed	Regular	1·9	24	N	Approx $2\frac{1}{2}$
15	Healed	Irregular	1·8	24	N	?
16	Healed	Irregular	1·9	24	N	Approx 3

Discussion.

Onodera et alii (1931) described three types of gastric motility in duodenal ulcer patients: the acute ulcer reveals an hyperactive stomach; that associated with slight pyloric stenosis shows decreased tone and more quiescence; that complicated by severe stenosis shows greatly diminished tone and feeble gastric contractions. There is no doubt that the gastric hypermotility is the rule in cases of uncomplicated

active duodenal ulcer but these findings in ulcers complicated by stenosis are not in agreement with the observations provided here. The following points emerge from a consideration of our 16 cases.

(1) The Gastric motor activity in pyloric stenosis complicating duodenal ulcer depends mainly on the state of activity of the ulcer.

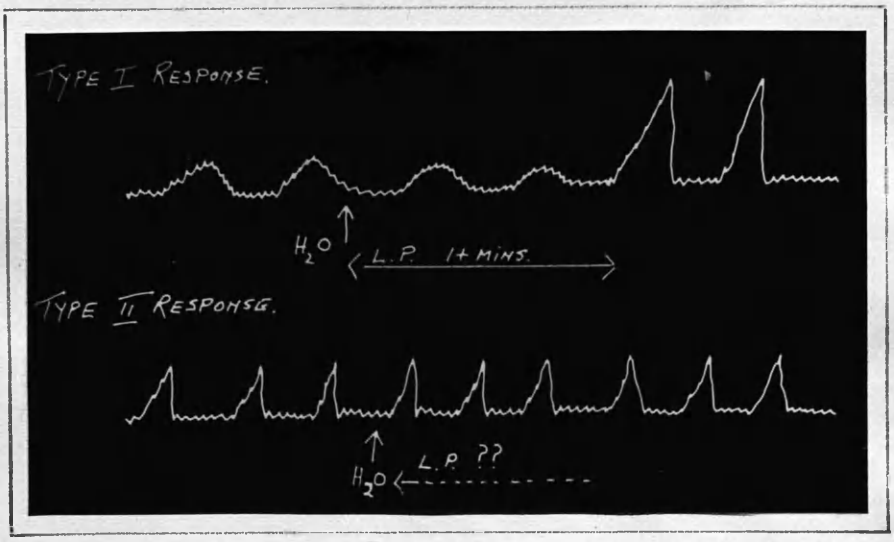
The amplitude of the gastric contractions in healed ulcer stenosis averages 1·75 cms. (normal = 1·8cms.). The average value in active ulcer stenosis was 2·7cms. This latter value is similar to that found in uncomplicated cases of active duodenal ulceration.

The duration of the gastric contractions in healed ulcer stenosis averaged 26·6secs. (normal 28,7secs.) in active ulcer stenosis the value was 32·5 secs. As the average duration of gastric contractions in simple active ulcer is 22·0 secs. it would seem that the onset of stenosis in the presence of an active ulcer tends to prolong each gastric contraction. This does not apply to the healed ulcer.

Thus, gastric motor activity is exaggerated in cases of pyloric stenosis accompanied by an active duodenal ulcer (the gastrogram closely resembles that of uncomplicated duodenal ulcer). In stenosis with healed ulcer, the gastric motor activity is within normal limits (the gastrogram closely resembles the normal gastrogram.) A record of gastric motility unaccompanied by a determination of the water response will therefore fail to give any indication of pyloric stenosis.

(2) <u>In cases of active duodenal ulcer complicated by stenosis the gastrogram reveals a delay in the stomach's response to the water test.</u>

A reversal response was demonstrated in all cases of active ulcer with stenosis and, in every case giving a Type I response, the development of this response was delayed beyond the normal time of 45/60 seconds. In the Type II response, where pre-existing activity remains unchanged, it is clearly impossible to determine the duration of the latent period. Under these circumstances, the test should be repeated when a Type I response will often be obtained from which the duration of the latent period may be measured. Fig. 41.



<u>Fig. 41</u>
Latent period of water test can be estimated only when there is a Type I response.

Thus, in active ulcer cases, a lengthening of the latent period of the water response indicates the presence of stenosis. I have, however, seen a delayed reversal response result from pylorospasm and therefore, the recording should be repeated after an interval of a few days or after a course of belladonna.

The water test was not reliable in revealing the presence of stenosis associated with healed ulcer owing to the nature of the response (inhibition). If one or more contractions follow the application of the test prior to the onset of quiescence then one can say that there is a delay of e.g., approximately two minutes (Fig. 42 upper tracing).

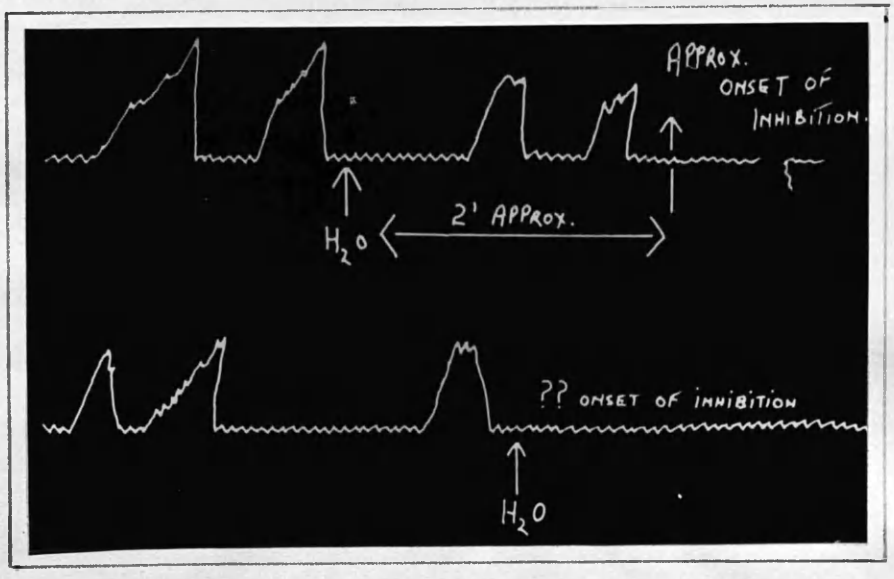


Fig. - 42.

If on the other hand, the waves are appearing irregularly, inhibition may appear to follow at once and no conclusion can be reached (Fig. 42 lower tracing).

Thus, the water test will reveal stenosis complicating active duodenal ulcer and may do so in cases of healed ulcer stenosis. These facts have no important clinical application since the patient is not concerned about a symptomless pyloric stenosis. When symptoms are present, fractional test meal and barium meal examinations will reveal a delay in gastric emptying time. It is, however, of some practical importance to appreciate that the water

test applied to a patient with pyloric stenosis will give reliable evidence relating to the activity of the duodenal ulcer - a point which is by no means always decided with certainty on X-ray examination. The certain knowledge that an active ulcer is present is of assistance in planning gastrectomy as opposed to gastrojejunostomy for the surgical treatment of pyloric stenosis.

(3) <u>The degree of pyloric stenosis cannot be deduced from a gastrogram.</u>

A comparison of the tracings from cases 1 and 2 and of these from cases 3 and 4 gives no indication that the degree of stenosis was slight and in 1 and 3 and severe in 2 and 4. Hamilton and Curtis (1942) described motility changes in two cases of pyloric stenosis. In one case, the stomach was active but in the other chronic pyloric obstruction had produced gastric dilatation and "decompensation" with resultant gastric motor quiescence. Active gastric motility was constantly present in this series of 21 cases. As decompensation must be an extremely rare event, I feel that it is justifiable to affirm that gastric motility recording cannot be relied upon to reveal the degree of pyloric obstruction. It is obvious, however, that the completely atonic stomach of an unusually severe case will provide a gastrogram showing complete quiescence.

(4) <u>In the majority of cases of active ulcer stenosis, the rhythm of gastric motility is regular. It tends to be irregular in healed ulcer stenosis.</u>

In 10 cases of active duodenal ulcer with stenosis the rhythm was observed to be regular in 8 . In 6 cases of

healed ulcer with stenosis, the rhythm was irregular in 4. I have found no reference to this question in the literature on gastric motility but a definite statement should not be made from a consideration of this small number of cases.

Summary.

(1) A recording of gastric motility, unacompanied by a determination of the water response, will fail to reveal with certainty the presence of pyloric stenosis.

(2) The gastrographic diagnosis of pyloric stenosis depends on the demonstration of an increased latent period between the application of the water test and the subsequent response. A confident diagnosis of stenosis can therefore be made,

(a) in cases of active ulcer with a Type I reversal response
(b) in these cases of healed ulcer where an approximate measurement of the latent period gives a value sufficiently above the normal figure of 45/60 seconds to demonstrate undoubted delay.

(3) In pyloric stenosis, the water test will provide reliable information about the activity of the original duodenal ulcer. Activity is recognised by the development of a reversal response to water. The knowledge that an active ulcer is present may be of assistance in making a pre-operative decision between gastrectomy and gastrojejunostomy for the treatment of the stenosis.

(4) The extent of pyloric stenosis cannot be deduced from a gastrogram. The rare case of extreme stenosis with gastric atony will be confirmed by complete quiescence of gastric motility.

(5) The gastrogram from normal subjects and from patients with uncomplicated duodenal ulcer shows a regular rhythm. Arrhythmia may occur when duodenal ulcer is complicated by stenosis. If the causative ulcer is active, the rhythm tends to be regular; if the ulcer is healed the rhythm is frequently irregular. Arrhythmia occurring in an otherwise normal tracing should suggest the possibility of pyloric stenosis.

SECTION - 6.

THE EFFECT OF TOBACCO SMOKING ON GASTRIC MOTILITY IN PATIENTS WITH DUODENAL ULCER.

I have observed that most ulcer patients expect the advice "stop smoking!". This common reaction on the part of the ulcer patients reflects the opinion of the great majority of medical practitioners. A search through the literature on the effect of smoking on gastric function has not brought to light any convincing evidence in support of this popular belief. It may have arisen as a "clinical impression" - a not altogether reliable form of evidence. Again, the ill-repute of smoking may have followed a consideration of the effects of toxic doses of nicotine in animals or of the acute toxic manifestations experienced as a result of the "first cigarette". This reasoning should not be accepted lightly.

Several facts about the effect of smoking on the digestive system can be accepted: toxic doses of tobacco may provoke vomiting or diarrhoea; the degree of tolerance to tobacco varies considerably from person to person. The habitual smoker experiences a certain pleasurable restfulness which, if smoking is kept within bounds of tolerance, favours digestive activities.

The literature relating to the effect of tobacco smoking on gastric motility is not extensive. Carlson (1916) and Danielopolu (1925) reported that hunger contractions in man cease shortly after starting to smoke and may not recover for 15 - 60 minutes after cessation of smoking. Gray and Irving (1929) showed that most of the radiographic and clinical signs

of duodenal ulcer could be initiated by the tobacco habit. However, Schnedorf and Ivy (1939) noted that smoking, although stimulating salivary secretion, rarely increased the gastric acidity and tended to retard gastric emptying by depressing gastric motility. Wolf and Wolff (1943) in their studies on "Tom", observed that smoking a pipe or cigarettes was not accompanied by any alteration in the pattern of gastric contractions, provided smoking was pleasurable. When Tom found smoking distasteful, he experienced nausea which was accompanied by a phase of gastric quiescence. The gastric inhibition gave way to activity as the nausea diminished.

When recording gastric motility of duodenal ulcer patients, opportunity has been taken to observe the effect of smoking.

Procedure:- The effect on gastric motility of smoking one cigarette has been observed in 20 patients with active duodenal ulceration. All of these patients were habitual smokers; this excluded the possibility of producing acute toxic manifestations. Gastric motility was recorded in the usual way. In 10 cases, the recording was continued during the period of smoking but the irregular respiration caused by smoking, while not masking the general trend of the gastric waves, resulted in extraneous spiked respiratory oscillations. In another 10 cases, recording was stopped while the subject was smoking (8 - 12 minutes). Nausea was not experienced by any of these subjects and can therefore be excluded as a cause of diminished gastric activity.

Results:- In 8 patients, existing gastric motor activity remained unaltered after smoking (Fig. 43); in 1,

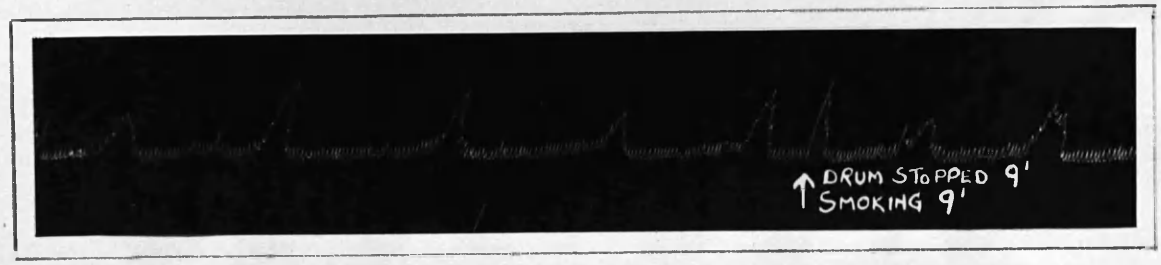


Fig. 43.

the activity was increased (Fig. 44), in 7, activity gave way to a brief phase of inhibition (Fig. 45) and in 4, existing quiescence persisted (Fig. 46).

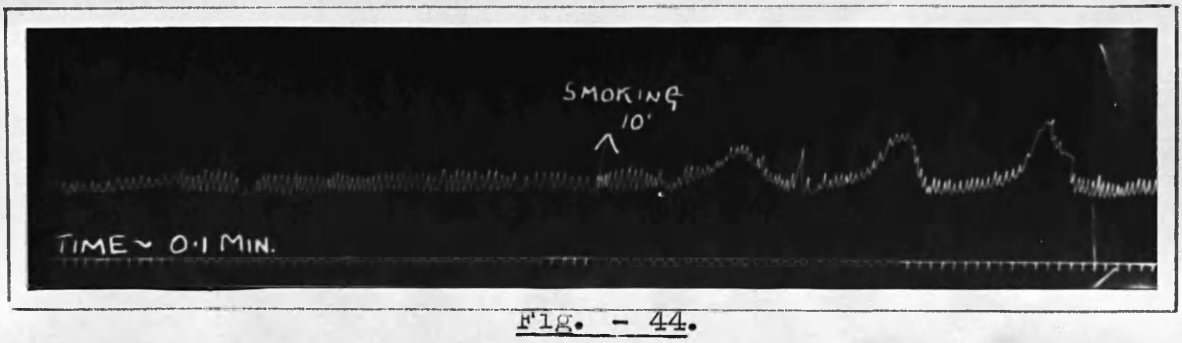


Fig. - 44.

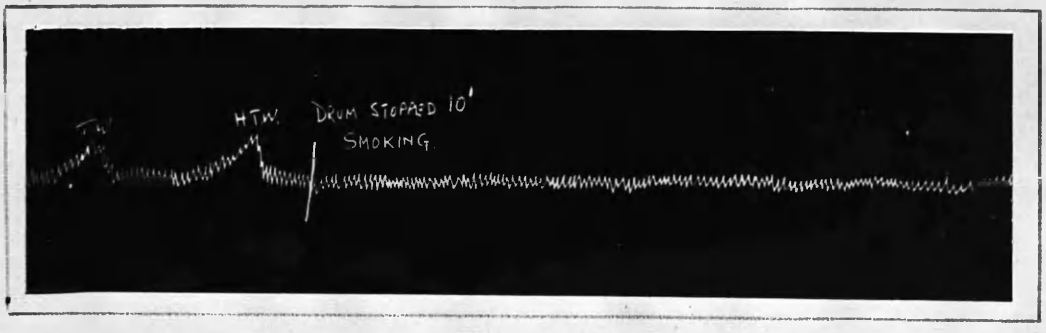


Fig. - 45.

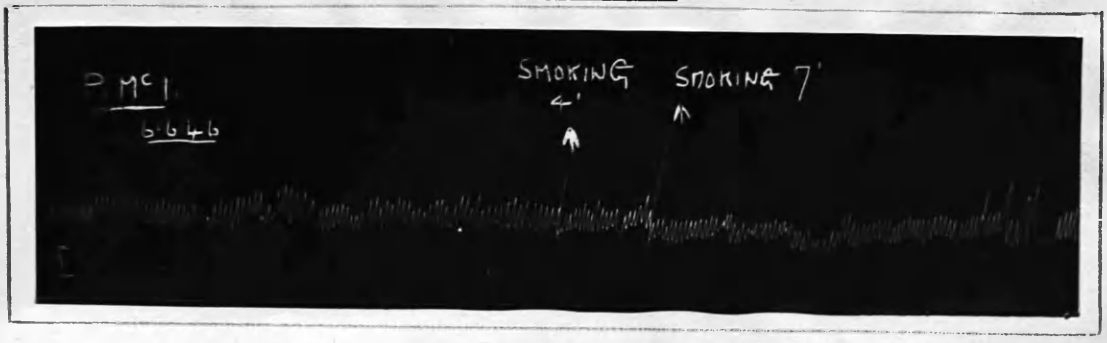


Fig. - 46.

It is of interest that the patient demonstrating increased gastric motility after smoking voluntarily gave up smoking during his relapses because he realised that it caused an aggravation of pain. At operation his ulcer was found to be almost on the pyloric ring. This situation of the crater probably explains why smoking, by increasing motility, resulted in an increase of pain.

Discussion:- We have found that, in 19 of 20 duodenal ulcer patients, gastric motility was either unaffected or diminished by smoking a cigarette. Ivy, (1959) found that in patients with ulcer, smoking had no significant effect on the rate of gastric emptying of a test meal nor on the level of gastric acidity. This is in accordance with my results, as the longest period of quiescence following smoking was 20 minutes. Thus, smoking has no constant effect on gastric motility in patients with duodenal ulcer; when any change of activity is observed, it tends to be in the direction of inhibition. The fact that inhibition is not the rule (as Carlson found in normal smokers) is not surprising when one considers that the hyperactive stomach of the ulcer subject is less easily depressed than is the normal stomach.

Although we believe that patients with peptic ulcer should be cautioned not to strain their tolerance to tobacco, these results do not indicate that smoking

need be prohibited. There is no evidence that moderate smoking produces undesirable effects on gastric function. I feel that the position of smoking in regard to ulcer may be stated thus: in most cases, smoking within tolerance will not be harmful; certain people may be allergic and should not smoke; those, like one of my patients, who discover that symptoms are aggravated by smoking should not require medical advice on the question of abstaining from tobacco.

Conclusion:- Gastric motility in ulcer patients is not significantly affected by smoking an occasional cigarette. Ivy has shown that the level of gastric acidity is unaffected by smoking. Moderate smoking is probably not harmful to the ulcer patient.

SECTION - 7.

THE PAIN OF ULCER.

In the course of this investigation of gastric motility in duodenal ulcer, opportunity has been taken to make some observations on spontaneous ulcer pain. While no attempt has been made to embark on a lengthy experimental assault on the controversial problem of peptic ulcer pain, a consideration of the observations presented here has stimulated a review of the literature. This has been found to be weighty and to present a variety of conflicting evidence.

In this section, I present some personal observations on the pain of peptic ulcer. This is followed by a review of the literature on the subject. The section is completed by a discussion of the various theories of causation of ulcer pain.

Observations on Ulcer Pain.

Case I. J.M., a male patient of 55 years had suffered ulcer symptoms for 11 years. The pain occurred 2 hours after food and was relieved by food and, to a lesser extent, by alkalis. The patient described the character of his pain as "gripping" and insisted that he rarely experienced the continuous type of pain which is usual in duodenal ulcer. Vomiting, which occurred on rare occasions, relieved his pain. At a subsequent operation, the ulcer giving rise to this patient's symptoms was found to be almost on the pyloric ring - "$\frac{1}{8}$ inch on the duodenal side of the pyloric ring."

A gastrogram was obtained before operation and again

two weeks after vagotomy. Fractional test meals are also available.

Observations on Pain.

(1) During the recording of the pre-operative gastrogram the patient experienced spontaneous pain and, on request, raised his hand with each spasm. Each gripping pain was found to coincide with a gastric contraction. (Fig. 47 upper tracing).

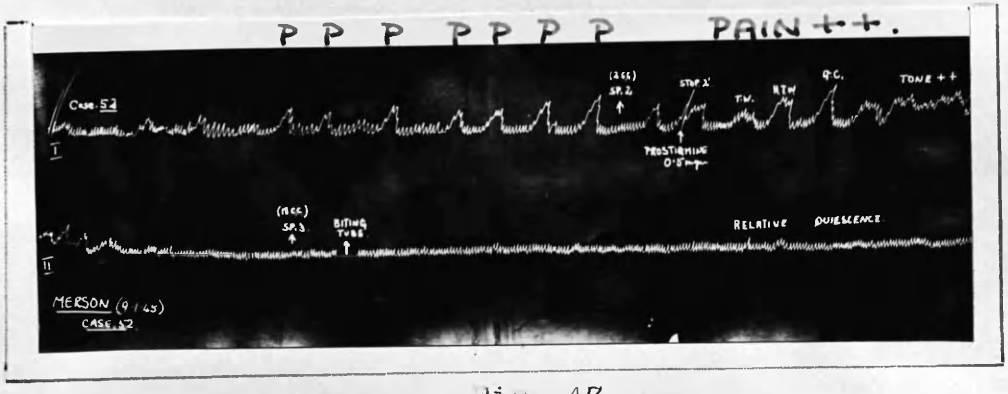


Fig. 47.

(2) The increased amplitude of gastric contractions following the intravenous injection of 0·5mg. Prostigmin was accompanied by an appreciable increase in the intensity of each painful spasm. (Fig. 47 upper tracing).

(3) Pain was absent during the phase of quiescence recorded in the lower tracing.

(4) Vagal section was immediately followed by complete freedom from pain. The gastrogram made two weeks after

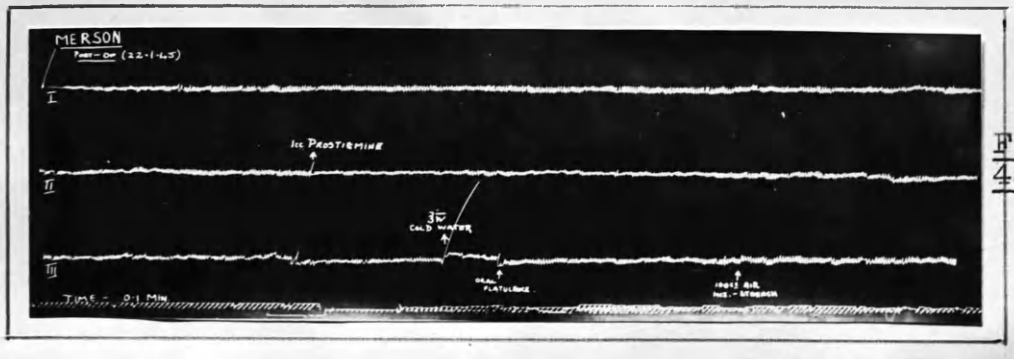


Fig. 48.

operation revealed complete gastric inhibition. The intravenous injection of Prostigmin failed to produce either pain or an increase in gastric activity (Fig. 48).

(5) The gastric secretory response to a fractional test meal was not notably altered by vagotomy (Fig. 49 is the pre-operative and Fig. 50 is the post-operative record).

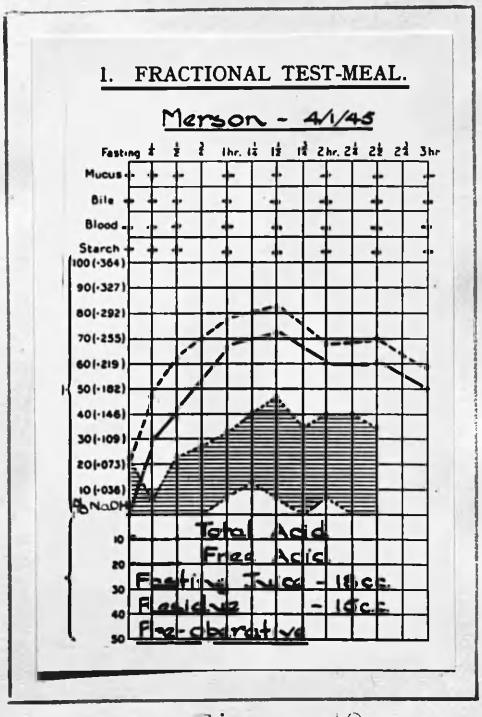


Fig. - 49.

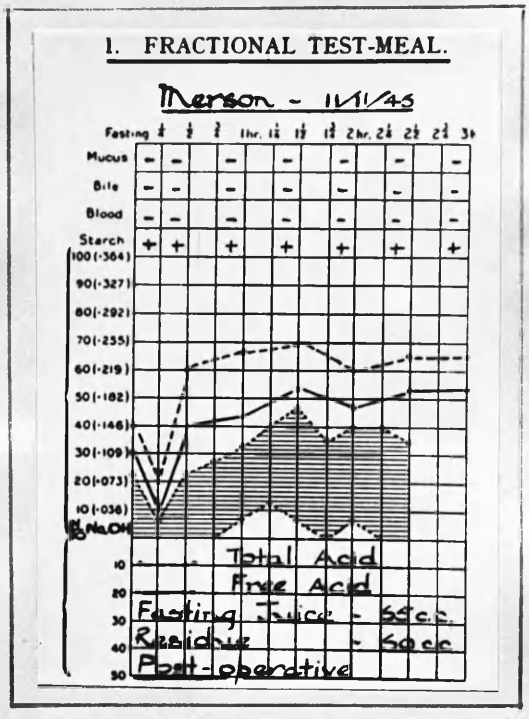


Fig. - 50.

It is difficult to believe that the ulcer crater healed within a few days of operation and, when the patient was completely free from pain, it must still have been bathed by acid gastric juice. It may be argued that, with section of the vagi, the pathway for afferent pain impulses has been severed. The recent work of Wolf and Andrus (1947), who made observations on gastric pain in a patient who had both a gastrostomy and a recent vagotomy, has shown that the vagal pathway

cannot be the sole route for painful sensations originating in the stomach and duodenum.

Conclusion.

In this patient, pain has been shown to be related to gastric contractions and to have no clear relation to gastric acidity. It should be noted, however, that this man's ulcer pain was of a spasmodic character whereas the pain of ulcer is usually steady and continuous. Furthermore, at operation, the ulcer was found to be juxta-pyloric in site and not, as is more common, clearly beyond the pyloric ring.

Case II. R. Mc A., a male subject aged 41 had a seven years history of epigastric pain occurring 3 hours after meals and relieved by food and alkalis. He described his pain as a "gripping pain which makes me want to double up". He was admitted to hospital with a severe relapse which had persisted for two months. During this period, vomiting had been a frequent symptom and always resulted in temporary but complete relief of pain. At operation he was found to have an active duodenal ulcer on the anterior wall of the duodenum very close to the pyloric sphincter. Gastrographic records and fractional test meal charts were obtained before and after section of the vagus nerves.

Observations on Pain.

(1) With each gripping pain the patient raised his hand and the drum was marked directly above the recording point. The tracing shows that each spasm of pain

coincided with a gastric contraction (Fig. 51).

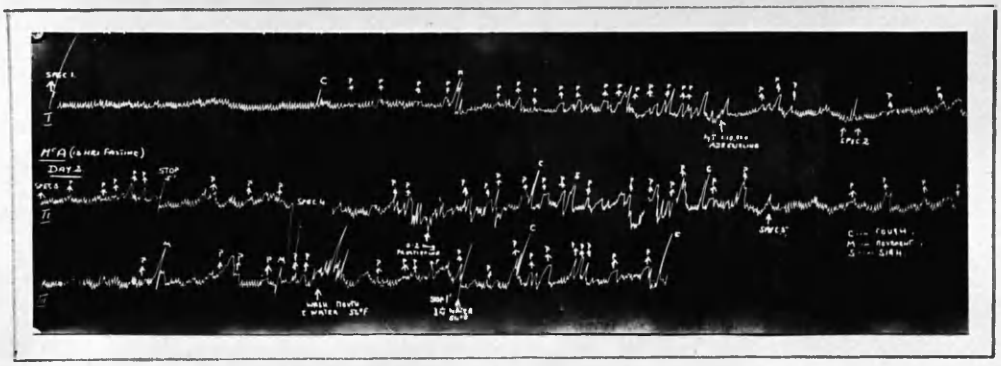


Fig. - 51.

(2) The intravenous injection of 1 minim of 1:10,000 adrenaline solution reduced the frequency of gastric contractions; the frequency of painful spasms was also reduced (Fig.51, recordI).

(3) The patient did not experience pain during the phase of gastric quiescence occurring at the beginning of the gastrogram. Pain occurred with the onset of gastric contractions (Fig. 51, record I).

(4) Following the intravenous administration of 0·2 mgm. Prostigmin there was a return of frequent gastric contractions and a corresponding increase in pain (Fig.51, record II).

(5) Throughout this recording, five samples of gastric juice were aspirated at the points indicated on the tracing (Fig.51). The stomach was emptied at each aspiration. The levels of gastric acidity (Free HCl estimated in cc. of N /10NaoH) were as follows:-

specimen 1 = 60cc.	specimen 2 = 65cc.
specimen 3 = 60cc.	specimen 4 = 70cc.
specimen 5 = 70cc.	

There is, therefore, no significant variation in the

level of free hydrochloric acid in the stomach throughout the experiment.

Thus, although a simple relationship exists between pain and gastric contractions, no relationship has been demonstrated between pain and gastric acidity.

(6) Shortly after the completion of the tracings shown in Figure 51, there was a phase of gastric quiescence during which the patient was free from pain. Gastric contractions were stimulated by increasing the tension within the balloon from 10cms. to 30cms. of water. Pain recurred with the return of gastric contractions.

(7) The pain resulting from distension of the balloon was promptly relieved by the introduction of 200cc. of 0·5% hydrochloric acid into the stomach through a Ryle's tube. (This quantity and strength of HCl is that recommended by Palmer for the production of pain in gastric and duodenal ulcer - 1927). The introduction of acid was followed by complete gastric motor inhibition for thirty minutes; during this period the patient did not experience pain.

(8) As in Case I, section of the vagi was followed by immediate and complete relief of pain. Gastric motility was recorded eighteen days after operation (Fig. 52). It will be noted that gastric quiescence persists even after the intravenous injection of 0·2mgm. Prostigmin. In contrast to the striking effects on pain and on motor activity following vagotomy, the gastric secretory response to a test meal was not diminished (Figs. 53 and 54)

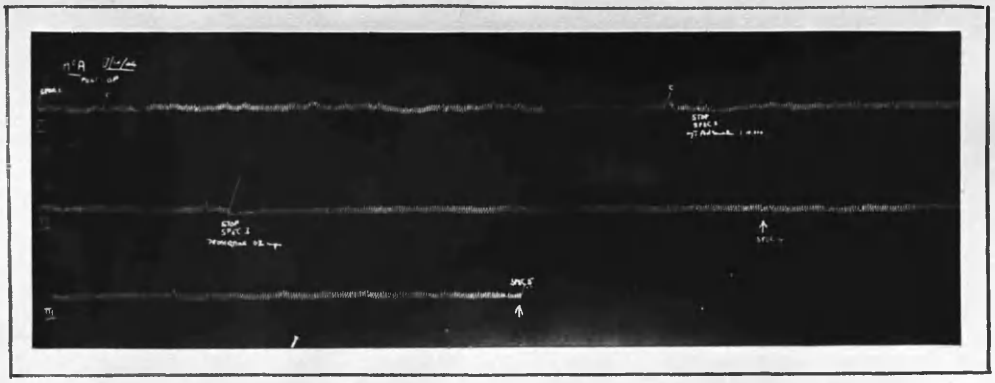


Fig. - 52.

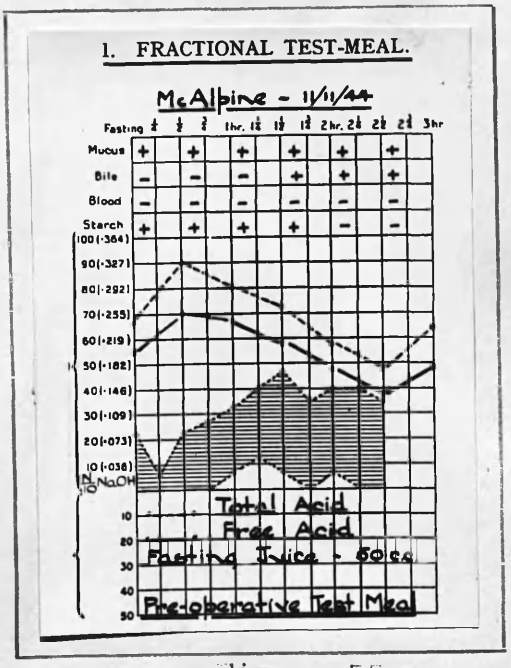


Fig. - 55.

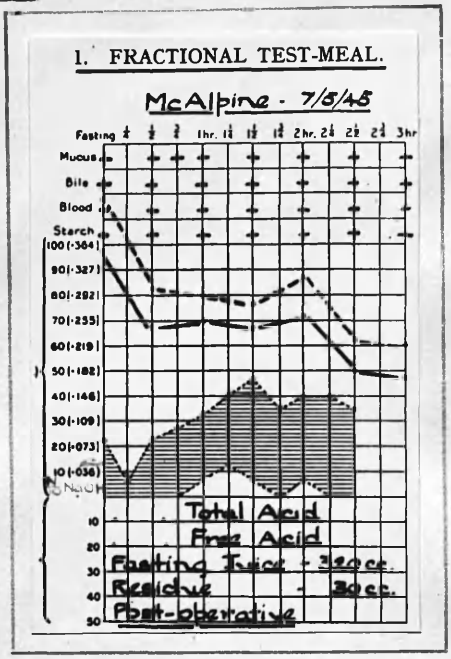


Fig. - 54.

Conclusion.

The investigation of this patient has shown that his pain was associated with gastric contractions. Thus, with quiescence, pain was absent; with spontaneous contractions pain was present; the abolition of gastric activity by means of adrenaline or of hydrochloric acid resulted in relief of pain; stimulation of gastric motility by means of Prostigmin or by distension of the indwelling balloon provoked a series of painful spasms.

Pain was not related to the level of gastric acidity.

Once again it must be stressed that this patient experienced pain of a spasmodic character - which is not typical of ulcer pain - and that the ulcer, though situated on the anterior wall of the duodenum, was found to be unusually close to the pyloric sphincter.

Case III.

H.M., a male patient aged 58 had a twelve years history of pain in the epigastrium two hours after food, relieved by food, alkalis and vomiting. During the eight months preceding his admission to hospital, the patient had experienced almost constant pain. He described his pain as a "continuous gnawing pain". He had never been aware of spasmodic pain. At operation he was found to have an active anterior wall duodenal ulcer and a posterior wall gastric ulcer.

Observations on Pain.

Gastric motility was recorded for two hours. During this time, the patient was experiencing spontaneous pain of a continuous nature which did not vary in severity. The following observations were made:-

(1) Pain was constant in intensity and was not influenced in any way by the occurrence of well developed gastric waves.

(2) The frequency of gastric contractions was diminished by the intravenous injection of 1 minim of 1:10,000 adrenaline; the nature and severity of pain was unchanged (Fig. 55).

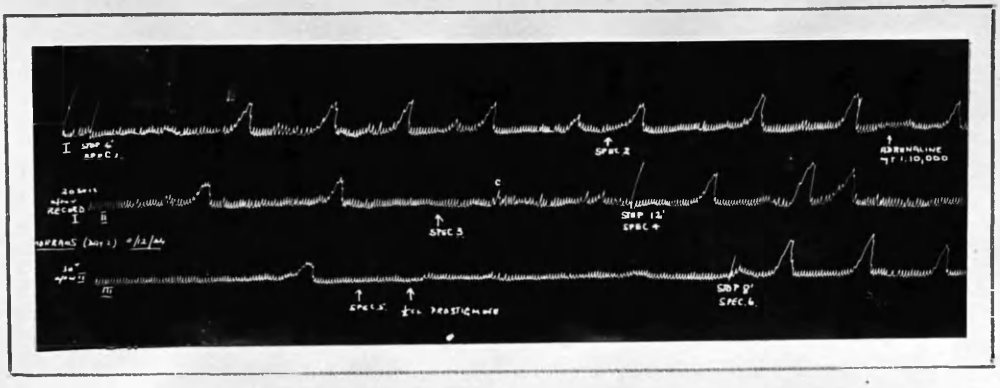


Fig. - 55.

(3) Frequent gastric contractions of high amplitude returned twenty minutes after the intravenous injection of 0·2mgm. Prostigmin. Pain was unaffected by this change in gastric motor activity.

(4) Six samples of gastric juice were withdrawn during the period of investigation (see arrows on tracing). The values of free hydrochloric acid (estimated in terms of cc. N/10NaoH required for neutralisation) were as follows:-

specimen 1 = 70cc.	specimen 2 = 95cc.
specimen 3 = 97cc.	specimen 4 = 85cc.
specimen 5 =100cc.	specimen 6 = 70cc.

Thus, there was always a high level of free hydrochloric acid within the stomach. It seemed probable that acid was the essential factor in producing this man's continuous pain.

(5) After completion of the gastrogram and before removing the indwelling tube, 200cc. of 0·5% hydrochloric acid was introduced into the stomach. Within a few minutes, the patient was acutely aware of a severe aggravation of his usual ulcer pain.

Conclusion.

This patient's ulcer pain was of the classical type - a steady gnawing pain. Variations in gastric motility were unaccompanied by any alteration in the severity or character of the pain. During the observed period of spontaneous pain, there was a high level of free hydrochloric acid within the stomach. The introduction of 200cc. of 0·5% hydrochloric acid resulted in an increase in the severity of pain.

Case IV.

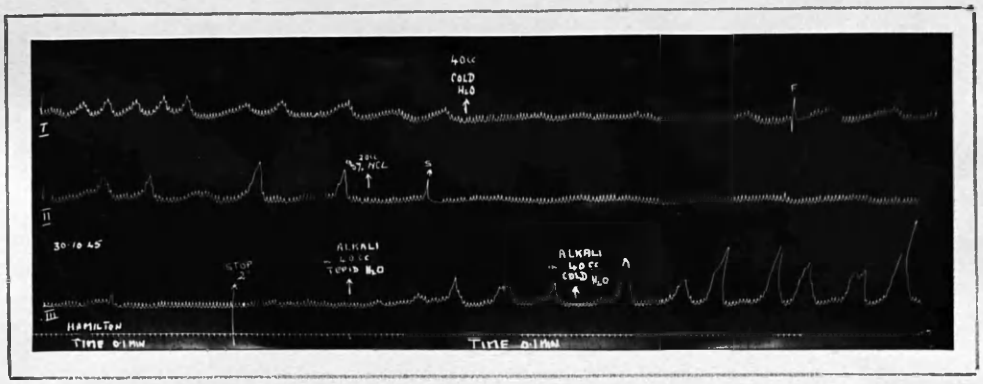


Fig. - 56.

Fig. 56 is the gastrogram obtained from a normal subject. In the first record, water gives a normal (inhibitory) response, proving that there is no duodenal lesion. 20cc. of 5·0% hydrochloric acid was injected into the stomach during the course of the second record. This was followed by a lengthy period of inhibition but did not produce any painful sensation. Gastric contractions of high amplitude followed the administration of alkali but, once again, there were no subjective symptoms.

Thus, despite the administration of a hydrochloric acid solution which was at least ten times more concentrated

than occurs in normal gastric juice, pain was not produced. It seems probable that acid can provoke pain only when there is a break in the continuity of the mucous membrane.

Case V.

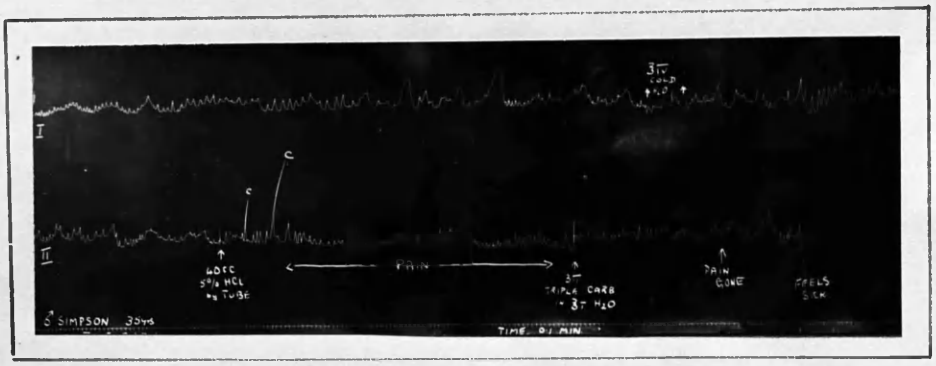


Fig. - 57.

J.S., a male patient aged 35 was seen on account of vague epigastric discomfort, loss of appetite and loss of weight of 3 months duration. Fractional test meal showed an achlorhydria. X-ray report: "Large filling defect in distal portion of stomach ". The presence of an ulcerating gastric carcinoma was confirmed by gastroscopy.

Observations on Pain.

(1) During gastrography, 40cc. of a 5% solution of hydrochloric acid was introduced into the stomach. This was followed by a phase of quiescence of motor activity and by a severe burning pain in the epigastrium (Fig. 57)

(2) Alkali administration relieved this painful sensation and restored gastric motility (Fig. 57).

Case VI.

In a patient with active duodenal ulceration, not experiencing spontaneous pain, the intragastric injection of a small amount of a dilute solution of hydrochloric acid (20cc. 0.5% HCl) caused gastric motor inhibition and

resulted in a brief spell of typical ulcer pain. (Fig. 58).

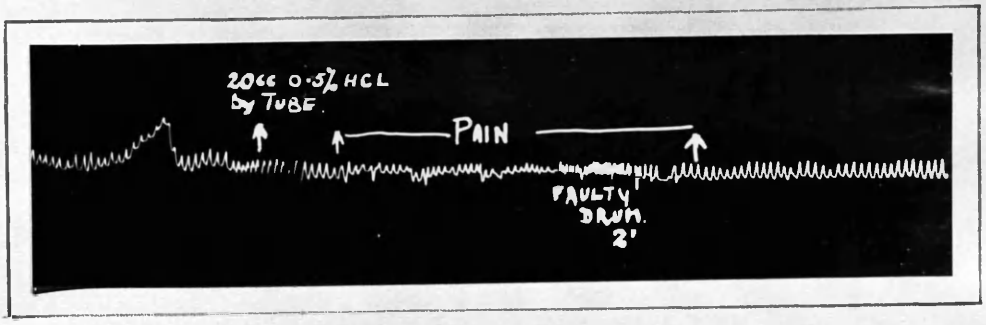


Fig. - 58.

Conclusion.

In cases V and VI, pain was produced by the intragastric injection of hydrochloric acid. In both cases, pain was accompanied by inhibition of gastric motility. This suggests that hydrochloric acid is frequently responsible for ulcer pain. It is noted that even a high concentration of hydrochloric acid did not produce pain in the patient with an intact gastric and duodenal mucosa.

Summary.

In two cases of juxta-pyloric duodenal ulcer, pain has been shown to be related to gastric motor activity. In a further two cases of duodenal ulcer, pain has been produced by hydrochloric acid and has been shown to bear no relation to gastric contractions. The introduction of hydrochloric acid into the normal stomach has not produced pain. It seems probable that the pain resulting from the action of acid occurs only if there is a breach in continuity of the mucous membrane.

Stimulated by these apparently conflicting observations, I have reviewed the literature relating to the pain of peptic ulcer.

Review of Literature.

Four theories which have been proposed in an endeavour to explain the pain of ulcer, merit consideration.

(1) Pain is due to the chemical action of the hydrochloric acid of the gastric juice on a defective gut wall.

In 1927, Palmer showed that the intragastric injection of 200cc. of 0.5% hydrochloric acid would produce pain in most patients with chronic peptic ulceration during a relapse. The acid stimulus was not effective in normal subjects nor in ulcer patients during a remission of symptoms. In addition, Palmer reported that in 198 of 217 patients, pain was not related to gastric motor activity.

Mann and Ballman (1932) demonstrated that, if dilute hydrochloric acid is allowed to trickle over the mucosa of the dog's stomach for a lengthy period, the mucous membrane will become red and congested and may eventually ulcerate. The animals show signs of discomfort prior to the development of obvious ulceration.

Palmer and Heinz (1954) again reviewed the evidence in favour of the acid theory of ulcer pain. They laid stress on the fact that any neutraliser of the gastric acid is likely to relieve pain and they were impressed by the relief of pain following complete gastric aspiration and by the return of pain on re-introduction of the gastric contents.

More recently, Bonney and Pickering (1946) have investigated the relationship between the development and subsidence of pain and changes in intragastric acidity. These observations were

made on patients suffering from peptic ulceration and in a small number of patients with gastric carcinoma. The gastric samples were obtained by aspiration through a Ryle's tube, the pH being determined electrometrically with the double quinhydrone electrode. The results of their experiments may be summarised as follows:-

(a) Naturally occurring pain is relieved by aspiration of the gastric contents and returns if the original contents are re-injected. Pain does not return if the acidity of the gastric contents is neutralised prior to reinjection.

(b) Naturally occurring pain is closely related to changes in gastric acidity. It was found that pain tended to occur if the hydrogen ion concentration remained at a certain level for some time and disappeared as the acidity fell. The threshold of acidity producing pain varies from one patient to another and may vary in any one patient according to the state of the causative lesion.

(c) When an ulcer patient is having symptoms, the introduction of 200cc. to 300cc. of N /20 to N/30 hydrochloric acid induces pain after a latent period of about ten minutes; withdrawal of the acid relieves the pain which does not recur after injection of 200cc. to 300cc. of the same molecular concentration of sodium chloride.

(d) During a remission of ulcer symptoms, and in normal subjects, injection of acid does not induce pain.

(e) A close relationship obtains between the levels of gastric acidity associated with naturally occurring pain and those associated with pain resulting from injecting hydrochloric acid into the stomach.

(f) Finally, Bonney and Pickering believe that nerve endings, the stimulation of which gives rise to the pain of ulcer, are situated in the ulcer crater.

(2) Hurst (1911) believed that tension within the stomach was the only stimulus to which the gastric pain receptors were sensitive.

In developing his hypothesis, Hurst supposed that an abnormally high intragastric tension in the pyloric vestibule results from a combination of a reflex closure of the pylorus and strong contraction rings bearing down towards the closed pylorus. The well-recognised relief of pain following the administration of sodium bicarbonate has been attributed not so much to its properties as an antacid as to its ability to make the patient belch and so relieve intragastric tension.

(3) Pain in peptic ulceration may be related to gastric contractions.

In 1916, Ginsburg and others stated that ulcer pains are analogous to those of hunger contractions and are the result of contractions of the stomach and duodenum.

Carlson, (1917) supported this theory and provided evidence from studies on a medical student with ulcer. He presented kymographic records, obtained by means of a balloon in the stomach, in which the patient's appreciation of pain was synchronous with the gastric contractions. He noted that the waves producing pain were not unusually deep and powerful and suggested that the change from normal hunger discomfort to ulcer pain may be due to an increase in the sensitivity of the nerve endings.

Christensen (1931) has been one of the most enthusiastic supporters of the gastric contraction theory. He has presented

many cases of peptic ulcer in which there was an obvious correlation between pain and hunger contractions. He observed that the relief of pain following a milk feed or alkalis corresponded with a period of inhibition of vigorous gastric contractions.

In their delightful monograph "Human Gastric Function", Wolf and Wolff (1945) record some observations on pain provided by studies on their laboratory assistant "Tom " who had a permanent gastrostomy. They found that unusually vigorous gastric contractions induced pain and that sensitivity to pain was increased in the presence of hyperaemia and engorgement of the mucosa; the more engorged the mucosa, the less powerful was the contraction required to produce pain. It is a short step to relate gastric contractions with the pain of an ulcer which, in an active phase, is usually surrounded by congested and oedematous mucosa.

(4) Ulcer pain is due to an increase in tissue tension around the ulcer.

This theory was first proposed by Kinsella (1928) and has received much support in recent years from the work of Ivy (1939). Ivy points out that oedema, vascular engorgement and muscle spasm will effect an increase in tissue tension and that hydrochloric acid increases oedema and vascular engorgement. The rising tension in and around the ulcer stimulates the nerve endings responsible for pain.

Discussion on the Pain of Ulcer.

To be acceptable, any hypothesis explaining the pain of ulcer must explain (a) the classical food-pain relationship, (b) the almost constant relief afforded by alkalis, (c) the relief which follows vomiting, particularly in gastric ulcer, (d) the periodicity of ulcer pain and (e) the fact that ulcer pain is usually steady and continuous.

The Acid Hypothesis.

In most respects, the acid theory is acceptable. The three main methods of relieving ulcer distress, viz., ingestion of food, ingestion of alkali and vomiting, have one common factor - the removal of hydrogen ions from the stomach. In fact, the simplest explanation of pain in peptic ulcer is that it depends on the degree of acidity of the gastric content. There are, however, several valid objections to the acid theory:

(1) Reynolds and McClure (1922) studying both normal and ulcer subjects, found that they were able to administer 0.5 - 2.0% hydrochloric acid without producing pain. Similar observations have been recorded by Carlson and Braafladt (1915) Baird, Campbell and Hern (1924) and by Cobet and Gutzeit (1926).

(2) In cases I and II reported at the beginning of this section, a phase of gastric motor quiescence was noted to be pain-free despite the presence of free hydrochloric acid in the stomach. In case II pain was actually relieved by the administration of 200cc. of 0.5% hydrochloric acid. Hardt (1918) noted that ulcer pain

may be relieved by giving 0·3% hydrochloric acid.

(3) When secondary malignant change occurs in a gastric ulcer, the concentration of acid generally drops at a time when the pain is growing worse and becoming more constant.

(4) Alvarez quotes a case of typical pain occurring in a patient with persistent absence of free hydrochloric acid.

Hurst's Hypothesis.

One of the most serious objections to this hypothesis lies in the failure of many radiological observations to demonstrate a closed pylorus and exaggerated peristalsis of the distal half of the stomach in association with pain. Furthermore, in cases V and VI we have seen that hydrochloric acid injected into the stomach produced pain, but in addition, resulted in a phase of complete inhibition of gastric motor activity.

This theory does not satisfy the first of our criteria, viz., the food-pain relationship. Following the ingestion of food, the pylorus closes in the early phase of digestion and gastric contractions continue. Despite this, pain is relieved.

The Gastric Contraction Hypothesis.

When considering the claims of this hypothesis, it must at once be conceded that the usual continuous character of ulcer pain is not in keeping with the regular rhythm of gastric waves. In juxta-pyloric ulceration, however, a clear relationship is present between the spasmodic pain experienced by the patient and the gastric contractions recorded on the kymograph (Cases I and II)

Homans (1919) studied the relationship between the pain of gastro-duodenal ulcer and the motor activity of the stomach. He could find little evidence in support of the mechanical theory; sometimes he observed severe pain occurring at the height of gastric waves and at other times he recorded deep contractions in the absence of pain.

Marie Ortmayer (1925), using the methods employed in this investigation, recorded gastric motility in peptic ulcer patients. In her published tracings, the subjects were quite unaware of exacerbations of pain at the height of gastric contractions. She found that alkali relieved pain but observed that there was no constant change in motility following its administration; in 10 of her 25 cases, relief of pain was accompanied by a definite increase in the motor activity of the stomach.

Thus, the mechanical theory fails to satisfy at least one of our criteria, viz., the almost constant relief afforded by alkalis.

In my case III, who was experiencing spontaneous pain of classical type, variations in gastric motility were not accompanied by any alteration in the severity of the pain. In case V, the administration of alkali relieved pain and increased gastric motility. In case VI, the administration of hydrochloric acid induced pain but inhibited gastric motility.

It must therefore be concluded that, save in patients with juxta-pyloric ulceration, gastric contractions do not cause the pain of ulcer.

The Tissue Tension Theory.

From my brief research into this complex problem, I have found evidence that ulcer pain may be produced by hydrochloric acid or by gastric contractions. During the past twenty-five years, Palmer has been the champion of the acid hypothesis and Christensen has carried the banner of the mechanical hypothesis. I believe that these two theories, which seem so widely divorced from one another, can be reconciled in the view first suggested by Kinsella and later supported by Ivy, viz., that the pain of ulcer is due to an increase in tissue tension around the ulcer. Oedema and vascular engorgement are therefore the proximate causes of pain as they will effect an increase in tissue tension; hydrochloric acid has been shown to increase vascular engorgement (Wolf and Wolff, 1945); muscular contractions can also effect an increase in tissue tension (Ivy, 1939).

Let us now examine this hypothesis in the light of the criteria laid down at the beginning of this discussion and in the light of certain irrefutable clinical facts:-

The food-pain relationship, alkali-relief, relief following vomiting and the fact that the ulcer pain is typically continuous in character can all be explained on the acid hypothesis and will, therefore, be satisfied by this hypothesis. The well-recognised periodicity of relapse and of remission of symptoms cannot be explained by the action of acid on exposed nerve endings. Thus, a patient's symptoms may have a periodicity of 2/52: 2/52; it is difficult to believe that the ulcer crater heals completely and then breaks down with this frequency - it almost certainly

remains unhealed during the fortnight of remission from symptoms. It is conceivable, however, that the inflammatory mass and the oedema around the ulcer may vary from time to time and, by altering the tissue tension, cause a fluctuation in the severity of symptoms.

Thus, Kinsella's view is acceptable in that it explains the classical features of ulcer pain. Can we, on this basis, explain certain irrefutable facts concerning ulcer pain? Why is it that a perforation or a haematemesis may be the first indication of chronic peptic ulceration? Why does ulcer pain vanish on the first day of the summer vacation? Why is a haematemesis frequently followed by sudden and complete relief of pain?

A medical colleague, without any previous indigestion, suffered a severe haematemesis. He was persuaded to undergo a radiological investigation which revealed a chronic posterior wall duodenal ulcer. He was also shown to have hyperchlorhydria and hypersecretion. It is ridiculous to suggest that he was achlorhydric before his haematemesis and so his lack of pain cannot be explained on lack of hydrochloric acid. From my knowledge of the patient, I do not believe that his pain- threshold is higher than that of most peptic ulcer patients. It seems probeble that an absence of an inflammatory mass, oedema and of an increased tension in the tissues around the ulcer might reasonably explain the symptomless character of his ulcer. The other views discussed here cannot explain the occurrence of such cases of haematemesis or perforation in patients with hitherto

symptomless chronic peptic ulceration.

It is not uncommon to find that the ulcer patient becomes free from pain as soon as he goes on holiday. His ulcer surely does not heal overnight and so exposed nerve endings remain to be stimulated by HCl. It may be that vascular engorgement and hypersecretion diminish as he leaves his cares and worries behind him. If so, Kinsella's view is once more acceptable. In addition, the explanation of this interesting anomaly may depend, in part at least, on an altered threshold for pain.

The relief of pain following haematemesis is probably due to the recognised fall in the level of free hydrochloric acid. Thus, the simple acid hypothesis or Kinsella's hypothesis would provide a satisfactory explanation.

Conclusion.

There remains much to be done to clarify beyond any reasonable doubt the exact cause of ulcer pain. Obviously, several stimuli can produce pain and the most usual one is hydrochloric acid. The view that these various stimuli act by increasing tension within the tissues around the ulcer has much to commend it. It explains the classical features of peptic ulcer pain and provides a reasonable answer to the apparent anomalies mentioned in the course of this discussion.

SECTION - 8.

OBSERVATIONS ON THE EFFECT OF GLUCOSE ON GASTRIC MOTILITY IN DUODENAL ULCER.

In 1889, Oppenheimer stated that the opening of the pylorus and the evacuation of the stomach are probably functions of the small intestine rather than of the stomach itself. It is a striking fact, noted by several workers including Hirsch (1893), that the stomach will empty rapidly if the material which comes through the pylorus is immediately diverted to the exterior by means of a fistula. If the diverted material is collected and returned to the upper small intestine, the stomach will empty itself normally. Hypertonic solutions of sodium chloride have been shown to depress gastric motor activity and evidence has been presented indicating that the site of action is in the duodenum or upper small intestine (Section 3). This is in line with the work of McSwiney and Spurrell (1933) who showed that hypertonic meals produce a delay in gastric emptying varying with the degree of hypertonicity. They came to the conclusion that the osmotic pressure of a liquid suspension of a foodstuff is of more importance in determining the rate of gastric emptying than is the nature of the food. Glucose has for long been recognised as a depressant of gastric function.

As long ago as 1900, Leconte demonstrated that the introduction of strong solutions of glucose into the duodenum would inhibit gastric secretion. Since then, the inhibitory effect of sugar on gastric secretion has been shown in man by Kalk and Meyer (1932). Shay et al. (1942) found that strong solutions of glucose would

not only depress gastric secretion but would also delay the evacuation of an Ewald test meal. Preventing hyperglycaemia by the use of insulin, they concluded that the inhibitory effect of glucose was mainly an osmotic one acting on the upper small intestine. This conclusion is supported by the work of Day and Komarov (1939) who found that a larger amount of glucose was necessary by the intravenous route than by the intra-duodenal route in order to produce the same degree of inhibition of gastric secretion in dogs.

These observations have been made on animals and on normal human subjects. A substance which will inhibit normal gastric motility will not necessarily be effective in the duodenal ulcer patient. We have already seen that water, which inhibits gastric motor activity in the normal human subject will actually stimulate contractions in patients with active duodenal ulcer. Similarly, even 10/N saline may fail to inhibit gastric motility in ulcer subjects. A few experiments have been designed to determine the effect of glucose on gastric motility in patients with duodenal ulcer.

Experiment 1.

Object: Does the oral administration of glucose inhibit gastric motility in patients with duodenal ulcer?

Method: In three patients with duodenal ulcer, 50G. of glucose was given by stomach tube during a phase of active gastric contractions.

Result: In each patient, complete inhibition of motility followed the administration of the glucose solution and persisted for approximately one hour (Fig. 59)

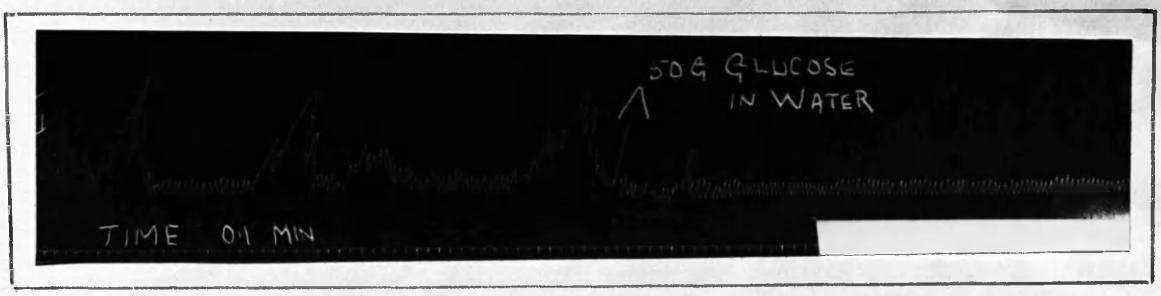


Fig. - 59.

Conclusion: The oral administration of a strong solution of glucose in water will inhibit gastric activity in duodenal ulcer subjects. The immediate onset of inhibition favours a local action rather than a mechanism depending on absorption of sugar with subsequent hyperglycaemia.

Experiment 2.

Object: Can insulin-induced hypermotility be inhibited by raising the blood sugar level?

Method: Insulin hypermotility was produced by the intravenous injection of XIV units of soluble insulin. When active gastric contractions had developed, 20cc of 50% glucose was administered intravenously.

Results: Hypermotility developed 26 minutes after the administration of insulin. This hyperactivity was allowed to continue for 12 minutes, when the blood sugar level was found to be 40mgm.% The patient began to complain of an empty sensation in the epigastrium and of cold perspiration but did not experience "hunger pains" as described by Carlson. The intravenous injection of glucose was followed by dramatic

symptomatic relief and complete inhibition of gastric contractions within two minutes (Fig. 60). Blood sugar level rose to 120mgm.%

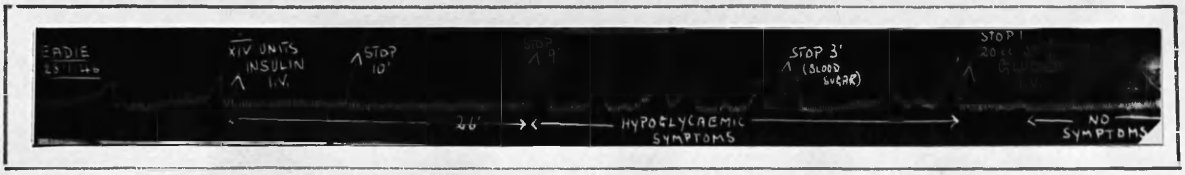


Fig. - 60.

Conclusion: Gastric motility can be increased by inducing a hypoglycaemic state. Adequate elevation of the blood sugar level will inhibit the hypermotility.

Experiment 3.

Object: Can spontaneous gastric motor activity be inhibited by the intravenous administration of glucose?

Method: 20cc. of 50% glucose was given intravenously to each of three duodenal ulcer subjects during a phase of active gastric contractions.

Results: In each patient, inhibition followed the injection of glucose (Fig. 61). The inhibition persisted for

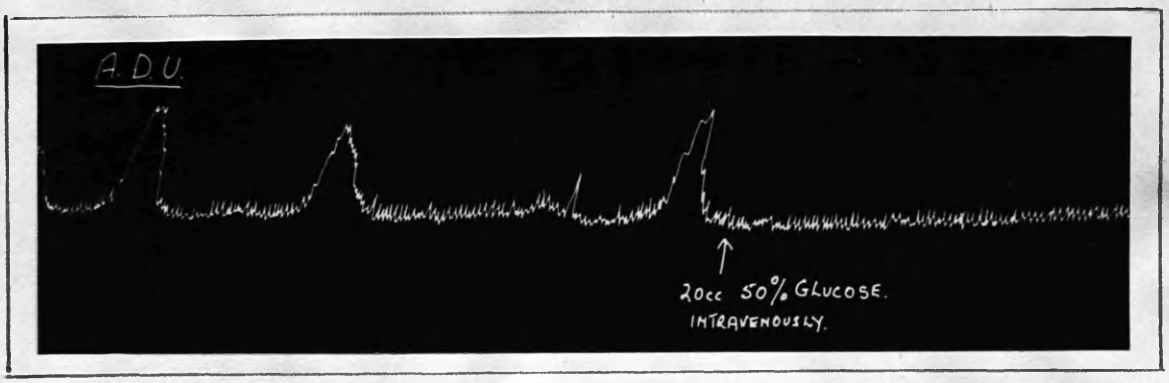


Fig. - 61.

approximately 30 minutes, i.e., it was of shorter duration than that following 50G of glucose by mouth.

Conclusion: Spontaneous gastric motor activity can be inhibited by raising the blood sugar level. It would appear therefore, that glucose has a more complicated action in inhibiting gastric motility than has hypertonic saline. Hypertonic saline has a purely local site of action; the action of glucose has two components - a local effect (probably osmotic) on the duodenum and a depressant effect on vagal activity by virtue of a rise in blood sugar level.

Because of its depressant effect on gastric activity, glucose has been considered as a therapeutic measure for the treatment of peptic ulcer. It is therefore of interest to endeavour to assess the relative merits of the two ways in which it depresses gastric motility.

Experiment 4.

Object: To compare the effect of the same dose of oral glucose and of intravenous glucose on gastric motor activity.

Method: Hypermotility was induced in a male duodenal ulcer patient by a subcutaneous injection of 20 units of soluble insulin. The effect of 20cc. 10% glucose solution intravenously was then tested and, after a reasonable interval, 20cc. 10% glucose solution was given by a Ryle's tube into the stomach.

Results: Hypermotility was well defined 80 minutes after the administration of insulin. A blood sugar estimation gave a value of 55.6mgm.% 20cc. 10% glucose

intravenously failed to depress the existing motor activity within ten minutes. (Blood sugar = 62·0mgm%) As the inhibitory effect of intravenous glucose has already been shown to develop almost immediately after administration, it was now thought reasonable to apply the second test viz., the intragastric injection of 20cc. 10% glucose. This was immediately followed by an inhibitory phase lasting 15 minutes (Fig. 62)

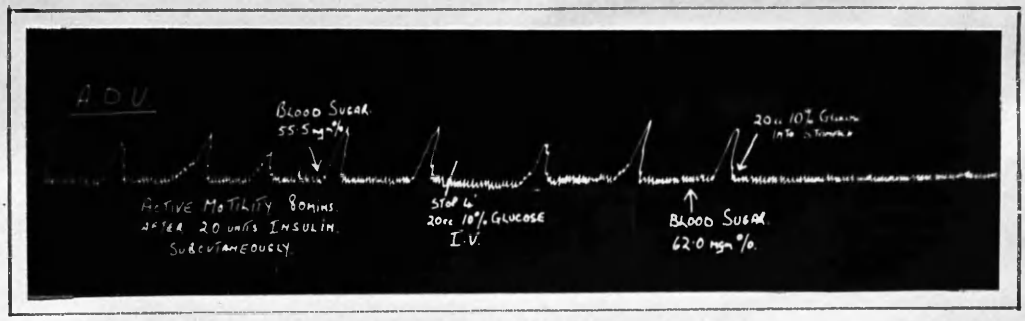


Fig. - 62.

Conclusion: A small dose of glucose intravenously (20cc. 10%) was not effective in reducing insulin hypermotility in a duodenal ulcer subject. The same dose by the oral route was immediately effective. The rapid development of this inhibitory response indicates that it does not result from a further rise in blood sugar due to absorption. This result emphasises the importance of the role played by the duodenal component of the action of glucose on gastric motility and demonstrates that larger amounts of glucose must be given to effect inhibition if the intravenous route is employed.

Discussion.

These observations support the conclusion of Shay et al. (1942) that glucose is capable of inhibiting gastric motility in man and show that it is also effective in patients with active duodenal ulceration. Glucose causes inhibition of gastric motility in two ways: it may act locally on the upper small intestine and it may act by raising the blood sugar level. The work of Shay et al. (man) and that of Day and Komarov (dog) stresses the importance of the duodenal component of the action of glucose and indicates that the oral administration of glucose is more effective than is its intravenous administration. The results of the experiments presented here support this view.

With the knowledge that oral glucose will depress gastric hypermotility of the duodenal ulcer patient, the use of a continuous intraduodenal or intragastric glucose drip is worthy of trial in the treatment of resistant cases of peptic ulcer.

SECTION - 9.

OBSERVATIONS ON THE EFFECT OF OLIVE OIL ON GASTRIC MOTILITY IN DUODENAL ULCER.

Though not in common use to-day, *olive oil was formerly regarded as a valuable item in the therapeutic regime for peptic ulcer. The physiological basis for the use of olive oil in the treatment of peptic ulcer is somewhat obscure. It was probably developed as a result of experimental work on animals which showed that the introduction of fat into the duodenum would delay the emptying time of the stomach (Edelmann, 1906; Best,1911).

In 1941, Card reported that olive oil injected into the duodenum of normal human beings would inhibit gastric contractions. As we have already seen, it does not follow that the hyperactive motility of the duodenal ulcer patient will necessarily be inhibited by the ingestion of olive oil. Observations on the effect of olive oil on the gastric motility of male duodenal ulcer patients are reported in this section. The course of this investigation is best illustrated by reporting the experiments in the order in which they have been performed.

* The "olive oil" dispensed at present is usually peanut oil. Pure olive oil has been used throughout this investigation.

Experiment 1.

Object; Does olive oil depress the motility of the fasting stomach?

Method: Gastric motility was recorded after a 12 hour fast. A control period of spontaneous gastric motor activity was secured prior to the intragastric

injection of 20cc. of pure olive oil through a Ryle's tube which had been secured to the side of the tube bearing the indwelling balloon. Three patients were examined in this way.

Results: In the three cases examined, olive oil effected a period of inhibition lasting 2 hours or more. The latent period preceding the onset of inhibition was approximately 5 minutes (Fig. 63).

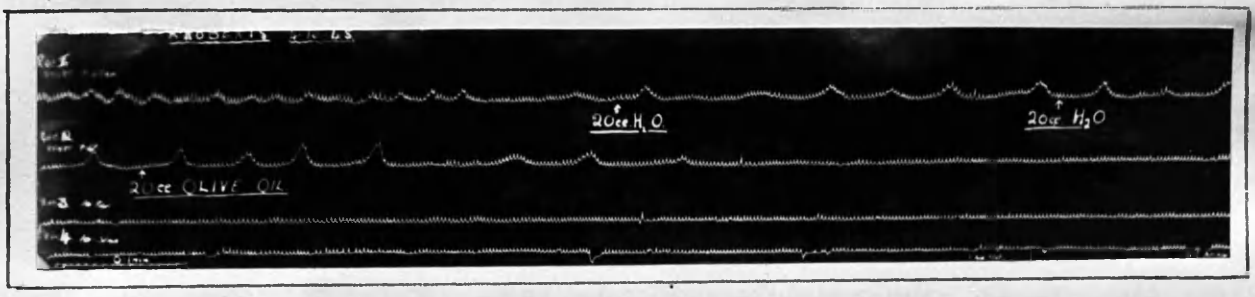


Fig. - 63.

The individual results were:

	Latent Period	Duration of Inhibition.
Case 1	7·8 mins.	140mins.
Case 2	4·0 mins.	125mins.
Case 3	3·0 mins.	120mins.

Fasting periods of 12 hours should not occur in any scheme of medical treatment for peptic ulcer! It seemed useful, therefore, to investigate the effect of olive oil firstly, when given shortly before a meal (as has been the custom when using it therapeutically) and secondly, shortly after a meal.

Experiment 2.

Object: Does olive oil depress gastric motility when given ¼ hour before meals?

Method: Following a control period of spontaneous gastric activity, 20cc. olive oil was given through an

indwelling Ryle's stomach tube. Recording was continued for a further 15 minutes. The kymograph was now stopped and the patient given an ordinary hospital lunch consisting of soup, meat and pudding. It was not found necessary to remove the stomach tubes. The drum was restarted when the patient had finished eating. Three patients were examined by this method.

Results: In the three patients, olive oil resulted in prolonged inhibition. The total period of quiescence following the administration of olive oil averaged 129 minutes; the duration of quiescence following the completion of the meal averaged 90 minutes (Fig. 64)

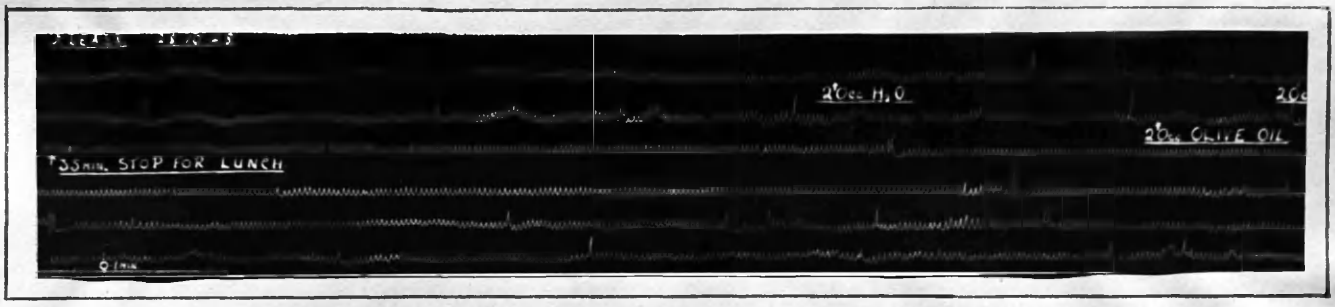


Fig. - 64.

The individual results were:

	Total Inhibition	Inhibition p.c.
Case 1	105 mins.	80 mins.
Case 2	163 mins	132 mins.
Case 3	120 mins.	70 mins.

Experiment 3.

Object: Does olive oil depress gastric motility when given ¼ hour after meals?

Method: The method of the preceding experiment was repeated, save that 20cc. of olive oil was given ¼ hour after completion of the meal. Three subjects were used for this experiment.

Results: The administration of the oil was again followed by a period of inhibition of gastric contractions. On this occasion, however, the quiescence lasted for approximately 30 minutes, i.e., there was considerable reduction of inhibition as compared with that following olive oil given before food (Fig. 65).

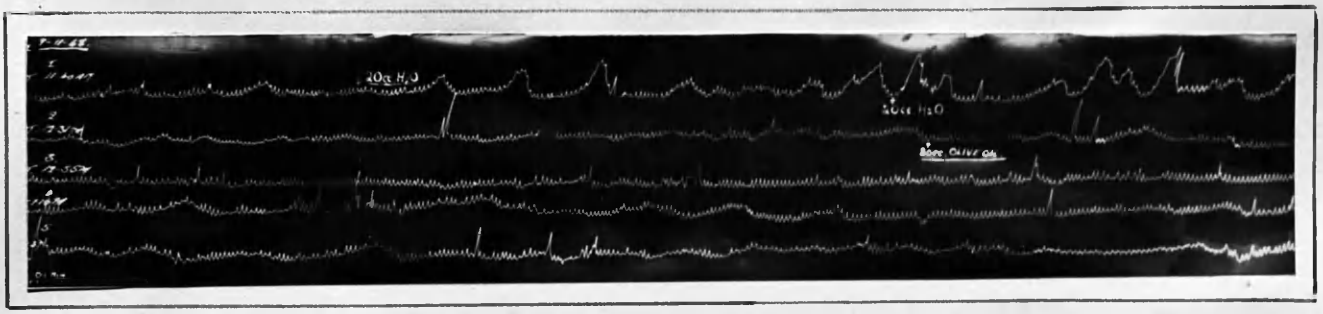


Fig. - 65.
Meal taken between end of Record I and start of Record II. Complete inhibition begins at end of Record II and ends at start of Record IV.

The individual results were:-

	Latent Period	Duration of Inhibition
Case 1.....	3·5 mins.	30 mins.
Case 2	5·0 mins	35 mins.
Case 3	4·0 mins.	27 mins.

Having demonstrated that olive oil will depress gastric motor activity, it seemed valuable to determine whether this response resulted from its physical or from its chemical properties.

Experiment 4.

Object: To determine the effect on gastric motility of an oil which does not undergo any chemical change in the alimentary tract and which is not absorbed from the alimentary tract.

Method: Liquid paraffin was chosen as a suitable substance with which to investigate the possibility that the oily nature of olive oil was responsible for the depression of gastric motility. 20cc. of liquid paraffin was injected into the stomach through an indwelling gastric tube after a control phase of gastric activity had been recorded in a fasting subject. Three duodenal ulcer patients were used for this experiment.

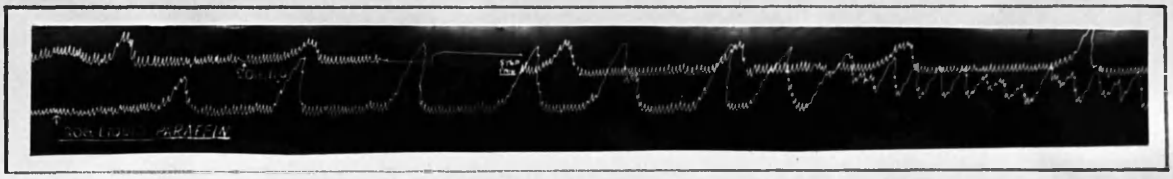


Fig. - 66.

Results: In two experiments, the activity of gastric contractions was definitely increased (Fig. 66): in one experiment the existing activity remained unchanged.

It therefore seemed unlikely that the physical nature of olive oil was responsible for its inhibitory effect on gastric motility. When olive oil is hydrolysed, it is split into glycerine and oleic acid. The next experiment was designed to determine the effect of glycerine and oleic acid on gastric motility.

Experiment 5.

Object: To determine the effect of glycerine and oleic acid on gastric motility.

Method: Since 20cc. of olive oil had been the standard dose given in previous experiments, it was considered

necessary to administer that amount of glycerine and oleic acid which would be obtained by the hydrolysis of 20cc. of olive oil. The chemical reaction is as follows:-

$C_{57}H_{104}O_6$ (Olive Oil) $\longrightarrow$ $C_3H_8O_3$ (glycerine) + $3C_{18}H_{34}O_6$ (oleic acid)

Substituting molecular weights:-

884 G olive oil $\longrightarrow$ 92 G glycerine + 846 G oleic acid.

Converting to volumes by use of the formula $V = \frac{W}{D}$

960cc. olive oil $\longrightarrow$ 73cc. glycerine + 940cc. oleic acid

Thus, 20cc. olive oil $\longrightarrow$ 1·5cc. glycerine + 19cc. oleic acid

After recording a control period of gastric motility in a fasting subject, 1·5cc. of glycerine was given by stomach tube. Having determined the effect of glycerine, 19cc. of oleic acid was then administered by the same route and its effect recorded. Three patients were used for this investigation.

Results: In three experiments, glycerine failed to inhibit gastric motility and slight stimulation of contractions was observed in two cases. In all, oleic acid effected a period of complete inhibition (average = 150mins.) and in each experiment the latent period was approximately 1 minute (Fig. 67). The individual results are as follows:-

	Glycerine	Oleic Acid. Latent Period	Inhibition.
Case 1.	Activity+	1·0 mins.	150 mins.
Case 2.	Activity+	1·0 mins.	140 mins.
Case 3.	Activity isq.	1·5 mins.	160 mins.

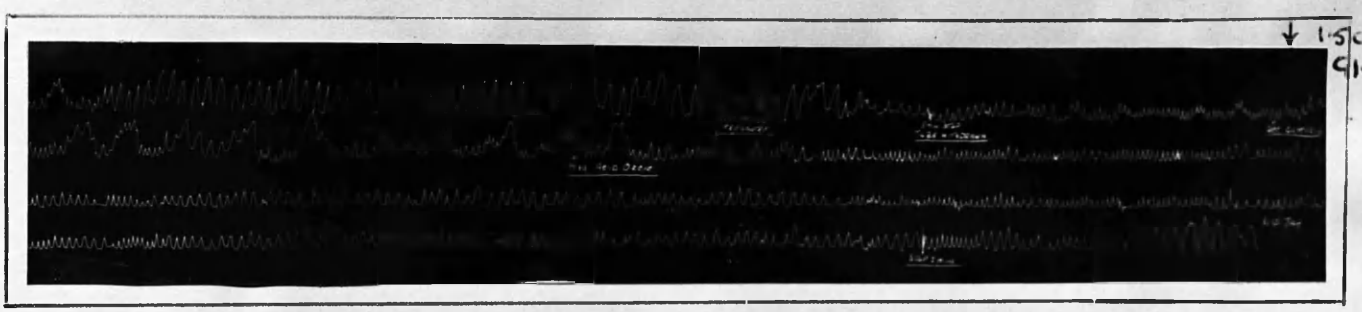


Fig. - 67.

This series of experiments permits the following conclusions to be made:-

(1) Olive oil is capable of inhibiting the motility of the fasting stomach in patients with active duodenal ulcer. An inhibition of approximately 2 hours may be expected after the oral administration of 20cc. of olive oil.

(2) The inhibitory effect of olive oil is not appreciably affected by food provided the oil is administered before the meal.

(3) The inhibitory effect of olive oil is considerably reduced if it is given after food. Under these conditions a half-hour period of inhibition is likely to follow the ingestion of 20cc. of olive oil.

(4) Evidence is presented which suggests that the physical properties of olive oil are unimportant in the production of gastric quiescence.

(5) The chemical properties are of great importance. Olive oil is hydrolysed into glycerine and oleic acid. Glycerine does not depress gastric motor activity and may actually cause stimulation. The fatty acid is the effective agent in producing inhibition.

(6) As would be expected, the latent period for the inhibitory

response is less following oleic acid than after olive oil. The difference is probably to be explained by the time required for hydrolysis of the parent oil in the acid medium of the stomach.

Discussion.

The results of this investigation provide a sound physiological basis for the use of olive oil in the treatment of peptic ulceration. They have led to its use in certain cases attending the Peptic Ulcer Clinic at the Western Infirmary. While the clinical trial is far from complete, my impression is that olive oil is a useful adjunct to the dietetic treatment of duodenal ulcer in patients who can tolerate the taking of one tablespoonful of olive oil thrice daily before meals.

The realisation that the active principle in olive oil is the fatty acid has directed attention to other non-toxic members of the fatty acid series. An investigation has been started in which an attempt is being made to test the relative inhibitory effects of various fatty acids. The degree of saturation of the fatty acid or the carbon atom linkage may be revealed as a significant factor in the production of the inhibitory response.

The inhibition of gastric motor activity - a beneficial effect in peptic ulcer - resulting from the ingestion of olive oil is extremely interesting when we consider that the great majority of ulcer patients volunteer a distaste for fatty foods and particularly for fried foods. This apparent anomaly requires explanation. Preliminary investigations have shown that chip fat rarely inhibits gastric motility and usually results in

striking augmentation of the existing contractions. (Fig. 68)

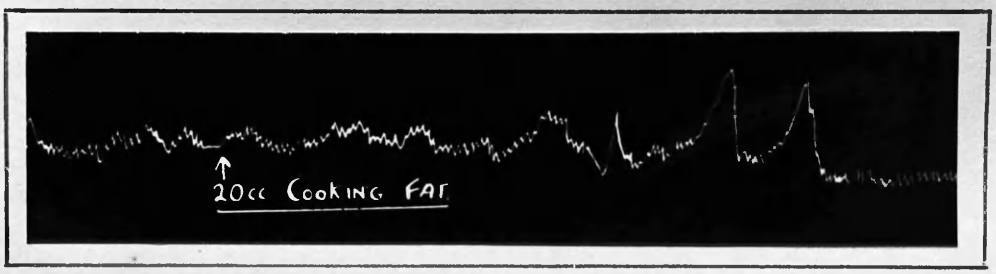


Fig. - 68.

Further experiments, which will include the chemical analysis of fats repeatedly used for cooking purposes, are required to clarify these interesting results.

The exact mechanism of the olive oil response is not certain. Robins and Boyd (1923) were able to inhibit the movements of a Heidenhaim pouch, in which all possible connections with the stomach had been destroyed, by introducing fat into the main stomach. This work has been repeated by Farrell and Ivy (1926). These observations indicate that the effect is mainly transmitted through some humoral agency. In 1930, Kosaka and Lim found that they could extract from the mucosa of the small bowel, previously in contact with fat, a substance now known as "enterogastrone" which would delay gastric evacuation and depress gastric secretion. Enterogastrone has been greatly purified by Ivy and his associates and they have found the purified extract to be effective in preventing ulceration in Mann-Williamson dogs (Grossman, Dutton and Ivy, 1946). It seems probable that the inhibitory effect of olive oil and of its fatty acid component depends on the production of enterogastrone from the mucosa of the upper intestine i.e., on a humoral mechanism.

SECTION - 10.

THE EFFECTS OF SURGICAL TREATMENT OF DUODENAL ULCER ON GASTRIC MOTILITY.

Many operations have been devised in the search for a cure for duodenal ulcer. Although meeting with considerable success, surgery has produced a new clinical entity which is becoming of considerable importance and which itself demands careful investigation - the so-called "post-operative stomach". It is not uncommon to find patients who, following gastrectomy and even gastroenterostomy, complain of troublesome post-prandial distress in the absence of recurrent ulceration. The most common symptoms are epigastric discomfort, abdominal distension, weakness, perspiration, bilious vomiting and even syncope. This syndrome has been attributed to a "dumping stoma", hypoglycaemia, gastrojejunitis, faulty placing of the stoma, etc. The explanation of this troublesome symptom complex is not yet fully understood. No attempt is made in this thesis to investigate this problem, but since the explanation must clearly lie in disturbed physiology following gastric surgery, opportunity has been taken to note the effects on gastric motor activity of the more common operations performed for duodenal ulcer.

At the outset, it was essential to define the effect of anaesthesia and laparotomy on gastric motility. As the unit's gastric surgery is performed with gas-oxygen-ether anaesthesia, motility studies were performed on three patients before and ten days after cholecystectomy and similarly on three routine appendicectomies. All six operations were performed under gas-oxygen-ether anaesthesia. A ten day interval was chosen for

several reasons: - morphine and other sedatives - known to influence gastric motility - have been discontinued; the convalescent patient is more co-operative; post-operative cough, which interferes with satisfactory recording, is minimal or absent; our interest is not in the symptoms encountered in the first few days after gastric surgery but in the ultimate effects of operation. In the six cases examined, gastric motor activity recorded post-operatively was comparable with the pre-operative motility. Figure 69 is a record obtained from a patient prior to routine appendicectomy and Figure 70 is the post-operative tracing.

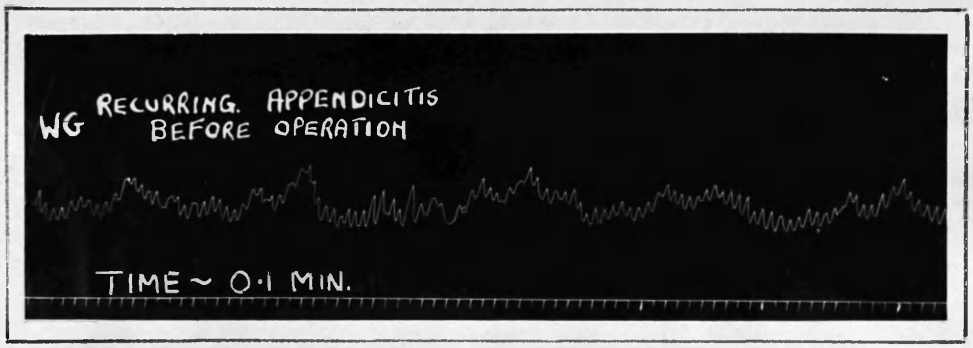


Fig. 69.

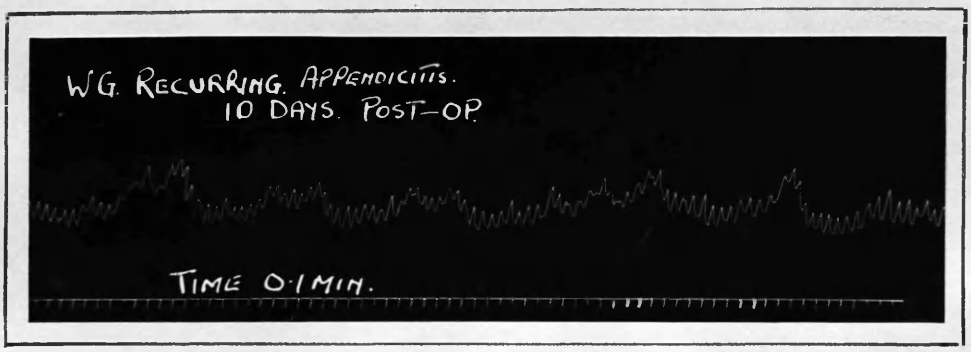


Fig. 70.

Barron and Curtis (1957) examined the gastric motility of patients before and after cholecystectomy and herniorraphy.

The gallbladder operations were performed under spinal anaesthesia. Inhibition or hypomotility was always noted during the 72 hours immediately after operation but, thereafter, normal motility returned.

Before considering disturbed gastric motor function after gastric surgery, we are therefore in a position to state that gastric motility returns to normal within ten days of laparotomy performed under gas-oxygen-ether anaesthesia, even when the gastro-intestinal tract has been interfered with as in cholecystectomy and appendicectomy.

Observations have been made on the three common surgical procedures used in the treatment of duodenal ulcer, viz., simple closure of perforation, gastroenterostomy and partial gastrectomy. Motility changes following simple closure of perforation and gastroenterostomy are considered briefly; motility changes following partial gastrectomy are considered in more detail. In addition, opportunity has been taken to study the motility changes in six cases of subdiaphragmatic vagotomy performed for duodenal ulceration.

(1) Simple Closure of Perforated Duodenal Ulcer.

(a) Early Post-operative.

Gastrograms were recorded from three patients at the end of the second week following simple closure of a perforated duodenal ulcer. It was not possible to obtain pre-operative recordings. The main gastrogram findings are given in Table V and Figure 71 is the tracing obtained from case 2.

Table V.

Gastric Motility Findings 2 Weeks after Simple Closure of Perforated Duodenal Ulcer.

Case	Rhythm.	Gastric Contractions. Amplitd. (cms.)	Gastric Contractions. Duration (secs.)	Response to Water Test R = Reversal	L. P. of W. T. (mins)	Conclusion.
1	Regular	2·4	30	R	1·2	Hyperactive stomach. Delay in Water Response.
2	Regular	2·0	30	R	1·5	Hyperactive stomach. Delay in Water Response.
3	Irregular	1·8	28	R	1·0	Normal but Irregular Activity.

Fig. - 71.

In the three cases, gastric activity is well developed and in the first two patients the hyperactivity typical of duodenal ulcer was present. The water response indicates that complete healing of the ulcer has not occurred despite the fact that these patients were free from symptoms. The delay in the development of the water response, indicating some stenosis, may be the result of actual narrowing due to the operative closure or to residual oedema around the site of closure.

(b) Late Post-operative.

Records were obtained from six patients with a history of perforated duodenal ulcer occurring at least $1\frac{1}{2}$ years previously. Three patients had remained symptom free from the time of the simple closure operation; three had suffered recurrence of symptoms. Table VI gives the main gastrogram findings (Fig. 72 is the record of Case 3 and Fig. 73 the record of Case 4).

Table VI.

Gastrogram Features in D.U. Patients with Previous Perforation.

Case	Time since Oper'n in Months.	Symptoms.	Rythm.	Gastric Contract'ns		Water Res'se	L.P. of W.T. (secs)	Conclusion.
				Ampt. (cms)	Dur'n (secs)			
1.	18	None	Reg.	2·0	24	N	-	Healed D.U.
2.	29	None	Reg.	2·9	34	N	-	Healed D.U
3.	19	None	Reg.	1·5	20	N	-	Healed D U
4.	19	Sev'r	Reg.	3·0	30	R	36	Active D U
5.	48	Mod.	Reg.	3·0	30	R	42	Active D U
6.	36	Sev'r	Reg.	2·6	24	R	50	Active D U

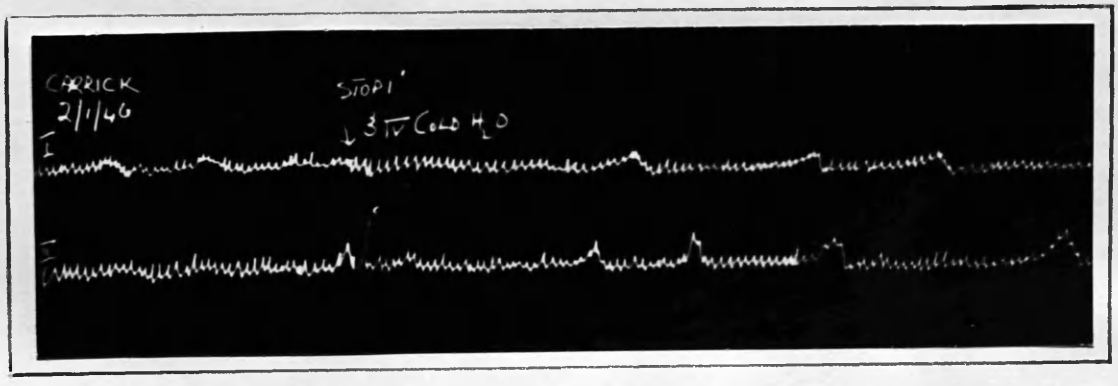


Fig. - 72.

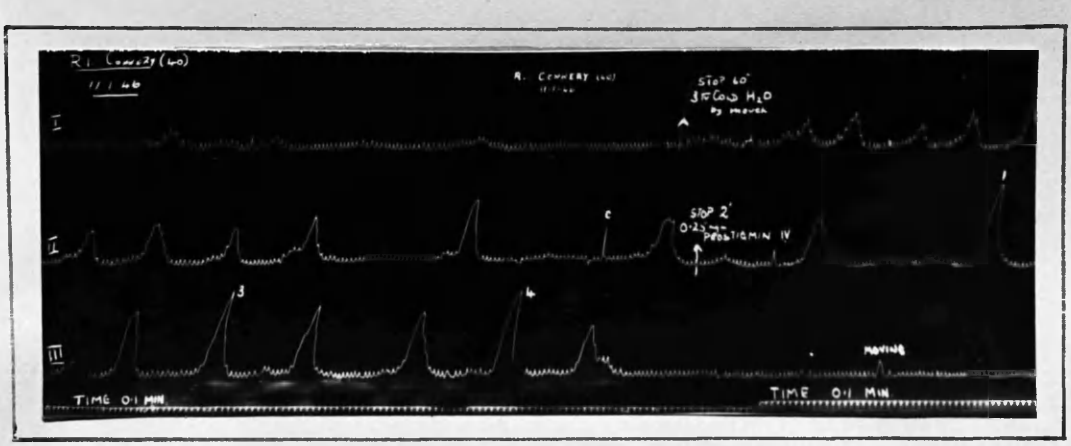


Fig. - 73.

As expected, the gastrograms of Cases 1, 2 and 3 were typical of healed duodenal ulcer and Cases 4, 5 and 6 typical of active duodenal ulcer. Hypermotility persisted in two of the healed-ulcer patients but the record in Case 3 might have come from a normal patient; the water response was the normal one of inhibition. In the active-ulcer patients, hypermotility was present, the water response was reversal in type and there was no delay in its development. An increase in the latent period of the water response would occur with the onset of pyloric stenosis (Section 5).

There was no indication that the previous operation for perforation had influenced gastric motility save in so far as it may have influenced the course, and hence the state of activity, of the ulcer.

Conclusions.

(1) Gastrograms taken two weeks after simple closure of a perforated duodenal ulcer are typical of active duodenal ulceration.

(2) A delay in the response to the water test is commonly

found in the immediate post-operative phase. This may result from the presence of oedema around the sutured area. A study of late post-perforation records reveals that this delay is temporary.

(3) It is of interest to note that, although the patients were completely symptom free two weeks after operation the water response was reversal in type indicating that the ulcer had not healed.

(4) Simple closure of a perforated duodenal ulcer affects gastric motor function only in so far as it affects the state of activity of the ulcer.

(2) Gastroenterostomy.

Alvarez,(1940)and Anderson (1942) state that gastric activity remains unaltered following gastroenterostomy. We have been able to confirm this. Two observations, however, seem worthy of note:

(a) The gastrogram recorded two weeks after gastroenterostomy shows normal gastric motor activity (Fig. 74).

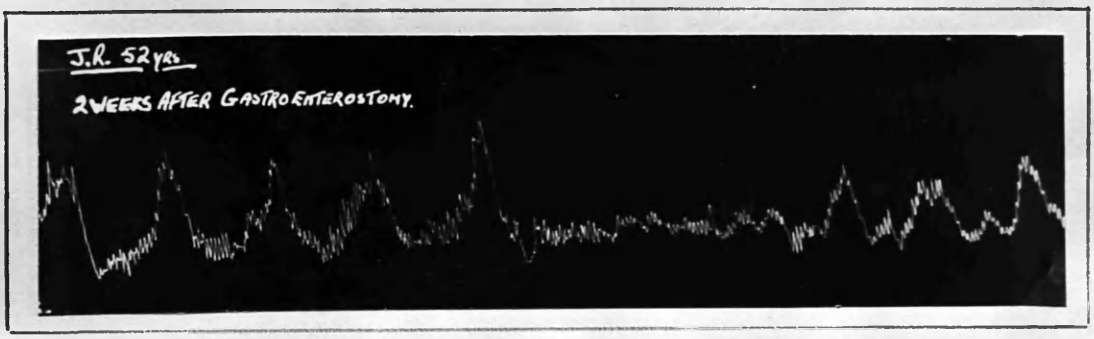


Fig. - 74.
(Method - B)

(b) Two of my patients, though showing no evidence of duodenal or anastomatic ulcer, complained of troublesome fullness, discomfort and lassitude after meals. In both

of these patients, the gastric motor activity as recorded by the balloon technique, was normal.

It seems unlikely that symptoms (not due to recurrent ulceration) following gastroenterostomy can be attributed to alteration in gastric motility. Case (1925), in a series of fluoroscopic studies, pointed out that the stomach behaved as if there was no new opening present and that gastric waves will always be found running towards the pylorus and endeavouring to effect emptying through the natural channel. Case also showed that, despite normal gastric activity, the emptying time is usually shorter than that of the normal stomach. Even so, the average emptying time after gastroenterostomy for sixty patients with good clinical results was 3 hours and 40 minutes. He has confirmed the work of Cannon and Blake (1905) which showed that, after gastroenterostomy, gastric emptying is delayed by rhythmic contractions and rings of contriction in the jejunum which alternatively let down and hold back the gastric contents. Since we know that gastric motor activity remains unchanged, it may be that a failure of this mechanism is responsible for a poor clinical result in certain cases of gastroenterostomy where symptoms cannot be attributed to anastomatic ulcer or gastrojejunal inflammation.

Conclusion.

Gastroenterostomy does not influence the motor activity of the stomach and normal motility is present within two weeks of operation.

(3) Partial Gastrectomy.

Many observations have been made on the emptying time of the stomach after subtotal gastrectomy. Feldman (1938) states that the gastric remnant empties in from 15 to 60 minutes. It would appear that kymographic balloon studies have been neglected in favour of barium X-ray examinations.

In this unit, the surgical treatment of the severe duodenal ulcer has been subtotal gastrectomy of the Polya type with antecolic anastomosis. The observations recorded here relate to the gastric motility changes following this operation.

Before proceeding to the consideration of gastric motility following gastric resection, attention is drawn to one important fallacy in the interpretation of the gastrogram in these cases. If the tube carrying the balloon is swallowed to within its last 2 or 3 inches or if it is not fixed to the side of the cheek, the balloon may readily pass through the stoma. The tracing may then show combined gastric and jejunal motility (Fig. 75) or pure jejunal motility (Fig. 76). Jejunal contractions can be recognised as sharp spikes occurring at the rate of 17 - 31 per minute. When the tracing shows the appearance

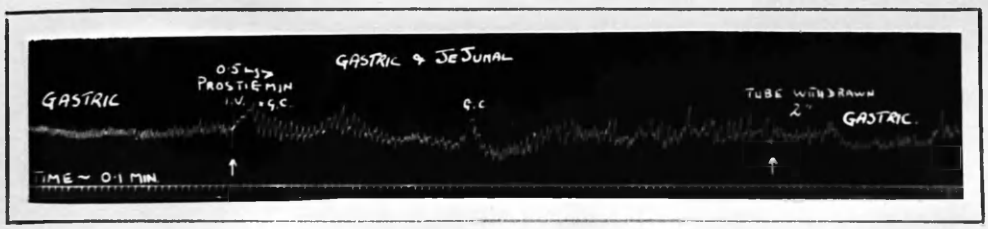


Fig. - 75.

of any abnormal deflections, the balloon's position may

be checked by X-ray examination or it may be withdrawn until jejunal activity disappears. (Fig. 75).

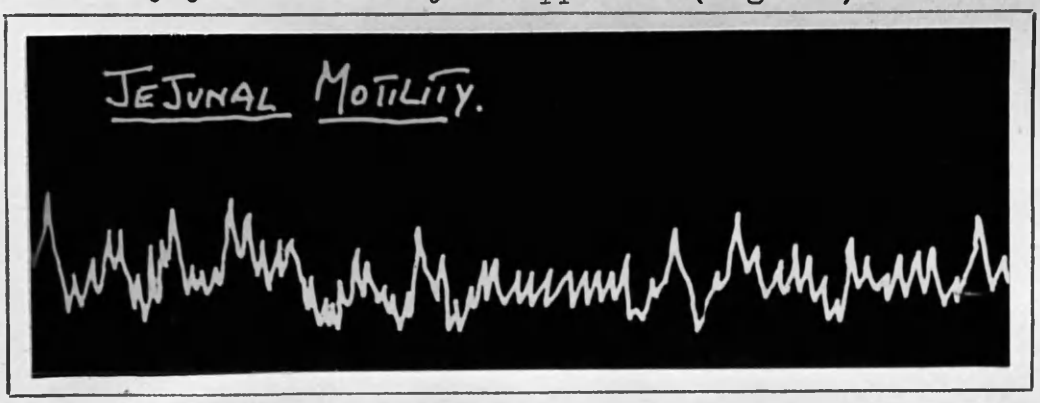


Fig. - 76.

(a) The Gastric Motility Two Weeks after Subtotal Gastrectomy for Duodenal Ulcer.

Gastrograms were recorded from five patients before and at the end of the second week following a Polya gastrectomy. Each patient had active duodenal ulceration with disabling symptoms and in every case the pre-operative record revealed hyperactive gastric motility.

Two weeks after operation, the gastrogram showed a complete absence of true gastric contractions. Tonus rhythm was always present but the amplitude of the waves was lower than in the pre-operative tracing and their frequency was increased (Table VII). Furthermore, the tonus waves after gastrectomy showed little tendency to vary in amplitude whereas prior to operation low tonus waves were followed by waves of increasing amplitude prior to the onset of gastric contractions. The amplitude of the tonus waves could be increased following administration of prostigmine but gastric

contractions were not induced. Figure 77 and Figure 78 are respectively the pre-operative and post-operative tracings from one of these cases.

Table VII.

Features of Gastric Tonus Waves Before and 2 weeks after Polya Gastrectomy for Duodenal Ulcer.

Case	Amplitude of Tonus Waves (cms)		Frequency of Tonus Waves (No. per Hour)	
	Before Gastrectomy	After Gastrectomy	Before Gastrectomy	After Gastrectomy
1	0.5-1.7	0.8	75	110
2	0.4-2.0	1.0	80	130
3	0.6-1.9	0.7	90	150
4	0.7-2.2	1.0	70	160
5	0.5-2.5	0.9	65	155

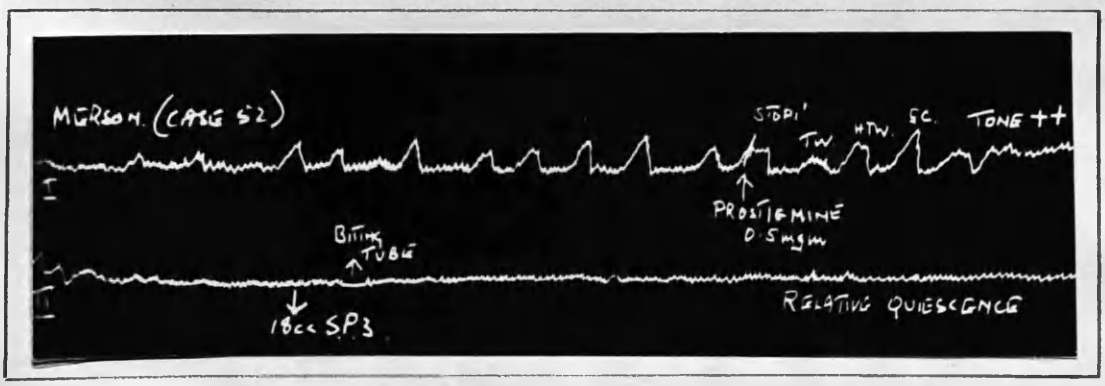


Fig. - 77.

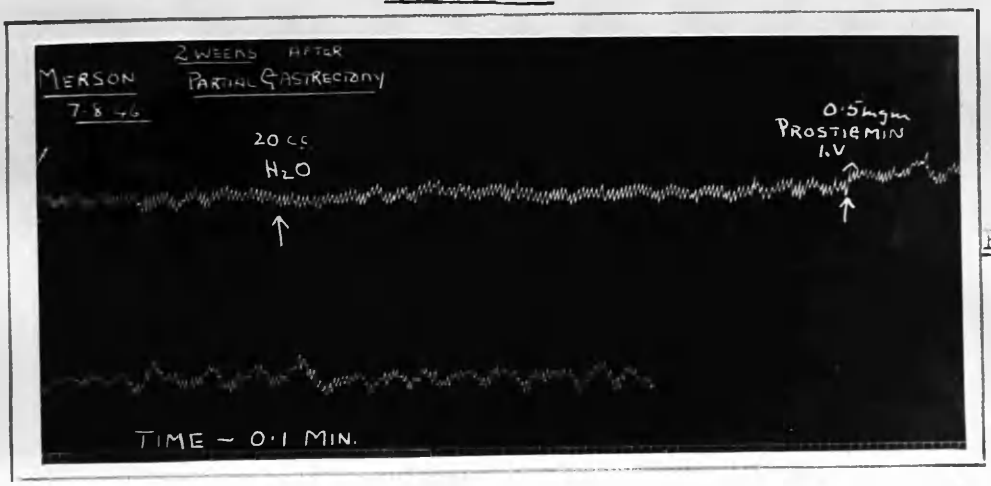


Fig. 78.

(b) Gastric Motor Activity at Intervals Varying from 8 days to 16 months after Subtotal Gastrectomy.

12 patients who had undergone gastrectomy for duodenal ulcer were carefully questioned concerning residual symptoms and records taken of gastric motility after a four hour fasting period. The results of these observations are set down in Table VIII. It will be seen that the presence of symptoms in Cases 10 and 12 is not reflected in the gastrogram.

Features of Gastric Tonus Rhythm following Polya Gastrectomy for Duodenal Ulcer.

Case	Time Since Oper'n	Tonus waves		Symptoms.
		Amplitude (cms.)	Frequency (No/hour)	
1.	8 days	0·8	110	-
2.	10 days	0·6	130	-
3.	2 wks.	0·7	150	-
4.	2 wks.	1·0	130	-
5.	2 wks.	1·0	165	-
6.	2 wks.	0·7	170	-
7.	18 days	0·5	165	-
8.	2 mnths.	0·9	150	-
9.	4 mnths.	1·0	160	-
10.	7 mnths.	0·6	140	Fullness p.c.: nausea
11.	12 mnths.	0·9	155	-
12.	16 mnths.	1·0	170	Fullness, weakness p.c

Table - VIII.

Conclusion.

The gastric motility changes following polya gastrectomy for duodenal ulcer are as follows:-

(a) True gastric contractions are not seen after gastrectomy.

(b) The tonus waves in the gastric remnant are shallow, show very little variation in amplitude in any one case, are capable of increase on stimulation with

prostigmine and their frequency is constantly much greater than in the intact stomach. The greatest amplitude noted in 12 patients was 1·0cms. and the average frequency following gastrectomy was 150 per hour (Normal = 73·7 per hour: Active D.U. = 75·6 per hour).

Discussion:

(1) The absence of gastric contractions and the presence of tonus rhythm alone is perhaps not surprising. Barium examination of the normal stomach shows that the upper half of the stomach maintains a state of tone while active contractions are seen only in the lower part of the body and pyloric antrum. Of greater interest is the study of muscle strips removed from the cardiac and pyloric ends of the stomach. Alvarez, (1917) noted that muscle fibres in the pyloric region are bulkier and more separate than are the fibres of the cardiac portion of the stomach and that in the frog, the former showed contractions of high amplitude whereas the latter presented tonus rhythm. He suggested that the muscle of the pyloric region is fitted to do the active work of the stomach, while the muscle of the fundus is designed to exert a steady pressure.

In association with Mr. R.A. Jamieson, I obtained kymographic records from muscle strips taken from the human stomach immediately after gastrectomy. Pyloric strip revealed systolic contractions whereas

the cardiac strips revealed small and frequent waves. It is not then surprising that the portion of the stomach remaining after gastrectomy shows only tonus waves.

From the practical standpoint it is important to realise that, despite the absence of high gastric contractions following gastrectomy, the emptying time of the stomach is reduced and the majority of patients are completely free from post-prandial discomfort. It is of further interest to note that those patients experience the sensation of hunger in the absence of hunger contractions.

(2) The marked increase in frequency of tonus waves in the gastric remnant suggests the removal of a pacemaker when gastrectomy is performed. Alvarez (1916) found highly rhythmic muscle in the lesser curvature in the region of the incisura angularis which may serve to originate and control gastric motor activity. This question might be clarified by a study of gastric movements in animals following a series of sleeve resections.

The fact that the tonus waves have a low fixed amplitude following partial gastrectomy also points to the removal of a controlling influence. An alternative explanation is that the remaining muscle fibres are less powerful than those of the adjacent, resected part of the body of the stomach which may

well be responsible for the production of the higher tonus waves. This last hypothesis is compatible with the law of the intestine.

(3) The increase in amplitude of the tonus waves in the gastric remnant following the administration of prostigmine indicates intact vagal innervation.

(4) Although Cases 10 and 12 had some post-prandial distress following gastrectomy, the gastrograms from these patients showed no apparent variation from those of the symptomless patients. No attempt has been made to investigate duodenal or jejunal activity, but it might be profitable to do so in a full investigation of the post-gastrectomy syndrome. The large incision requiring to be made in the jejunum when performing a Polya anastomosis divides completely an appreciable extent of circular muscle which might readily interfere with function.

Although there are obvious changes in gastric motor activity following partial gastrectomy, the majority of patients do not have any permanent discomfort and it therefore seems unlikely that these changes are responsible for the occasional occurrence of the dumping syndrome.

(4) <u>Vagotomy in the Treatment of Duodenal Ulcer with Special Reference to Gastric Motility Changes.</u>

In the treatment of peptic ulcer, whether by medical measures or by conservative surgery, there are two main objectives - to reduce the acidity of the gastric juice

and to put the ulcerated part at rest. Since vagus stimulation is known (Pavlov, 1910) to cause the secretion of the "appetite juice" and (Cannon and Washburn, 1912) to influence the motor activity of the stomach, it seemed reasonable to suppose that these objectives might be attained by division of the vagal nerves. The operation of vagotomy was introduced by Exner in 1914 for the relief of pain in the gastric crises of tabes dorsalis. Attempts to treat peptic ulcer in man were reviewed by Hartzell (1929) but it was with the work and writing of Dragstedt and Owens (1943) that vagotomy became a recognised operation for peptic ulcer.

Since then, many reports have been published in America but follow-up studies of the resulting changes in gastric motility have not been reported. Orr and Johnson (1947) studied gastric motility before and shortly after vagotomy but they have not provided observations on the late effects of operation.

In late 1944 and early 1945, Professor C.F.W. Illingworth performed six vagotomies by the subdiaphragmatic operation. Opportunity was taken to follow them for a long period after operation and to reinforce the clinical assessment by full laboratory investigations. The results of these observations are presented in this thesis with particular reference to the effects of vagotomy on gastric motility.

Methods.

Gastric motility was recorded prior to operation and at

regular intervals thereafter. Gastric secretory response to a gruel test was obtained before and after operation. In addition, a critical assessment of symptoms was made by repeated examination both before and after operation.

Operative Technique.

The vagi may be divided as they lie on the thoracic oesophagus by a trans-thoracic approach or on the terminal part of the oesophagus by an abdominal approach. Since the operations were being primarily performed as an experimental observation, the latter approach was chosen because it permitted an accurate inspection of the lesion and the exclusion of other intra-abdominal disease. In our first case, no difficulty was found in securing the anterior vagal trunk but isolation of the posterior nerve was troublesome and the danger of puncturing the thin-walled oesophagus was readily appreciated. On this account, and also because it is known that some parasympathetic fibres reach the stomach via the sympathetic leashes surrounding the left and right gastric arteries, it was decided to perform denervation at a lower level in the remaining five patients and to include both sympathetic and parasympathetic fibres. This operation has been described by Latarjet (1922).

At the cardia, the left gastric artery is divided along with the accompanying nerve fibres and the division is carried down to the mucosa on the lesser curvature and for an inch or more over both surfaces of the stomach in order to include all vagal fibres. At the pylorus, all nerve

fibres accompanying the right gastric and right gastro-epiploic arteries are cut across.

This operation is less formidable than a subtotal gastrectomy and in five of our patients the convalescence was uneventful. In one, acute dilatation of the stomach developed 36 hours after operation but this responded to gastric drainage and the administration of an acetylcholine preparation, the value of which has since been stressed by Machella and others (1947) for use in cases of troublesome gastric atony following vagotomy.

Clinical Cases.

Since the observations were of an experimental character, it seemed proper to restrict them to a small series of 6 cases. The patients were selected carefully. All had duodenal ulcer; in one there was also a gastric ulcer. All were men of similar ages, all gave a long history of severe indigestion which had resisted or relapsed after one or more periods of careful medical treatment in hospital. All were suffering, at the time of operation, from a severe and prolonged attack. (See Table IX).

Vagotomy for Peptic Ulcer

Case.	Site of Ulcer.	Age.	Duration of Symptoms (Years).	Duration of Last Pre-operative Relapse (Months).
1	Duodenum	34	14	48
2	,,	34	16	9
3	,,	41	7	2
4	Stomach and duodenum	38	12	8
5	Duodenum	34	12	2
6	,,	33	11	5

Table IX.

Results.
Observations on Gastric Motility.

In all six cases the pre-operative gastrogram revealed hyperactive gastric motor activity with frequent high gastric contractions. Without exception, the records obtained two weeks after operation were characterised by almost complete quiescence; tonus waves of low amplitude were occasionally seen but true gastric contractions were not observed (Figs. 79a and b). It was notable that the quiescence observed two weeks after vagotomy was much more complete than that following partial gastrectomy where tonus rhythm was always present.

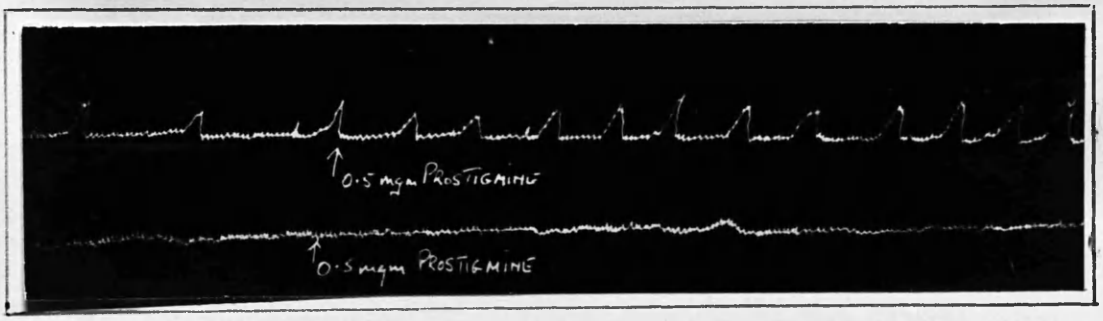


Fig. - 79.

In four cases, the opportunity was taken to observe the effect of a drug acting by parasympathetic stimulation. Before operation, 0·5mgm. prostigmine intravenously brought about a well-marked increase in gastric motility. After operation, the excitatory effect of prostigmine was abolished.

Unfortunately, this state of gastric rest has not been permanent. In four subjects, well developed gastric

contractions were present within the first year; in one, Case V, quiescence has persisted for at least eighteen months; Case II left the neighbourhood, and although I have been able to secure information regarding his clinical progress, gastrograms could not be obtained. The excitatory effect of prostigmine returned in all but Case V. The progress of gastric motor recovery is given in Table X which also shows symptomatic progress.

Vagotomy for Peptic Ulcer
Effect on Symptoms and Motility

Case.	Pre-operative.	Post-operative.				
		Two Weeks.	Six months.	One Year.	Eighteen Months.	Two Years.
1. Symptoms	++	–	–	–	–	++*
Motility	++	–	–	+	++	++
2. Symptoms	++	–	–	–	–	–
Motility	++	–	...	...	...	...
3. Symptoms	++	–	–	–	+	+
Motility	++	–	–	+	++	...
4. Symptoms	++	–	++*	...	...	...
Motility	++	–	+	...	...	...
5. Symptoms	++	–	–	–	–	–
Motility	++	–	–	–	–	...
6. Symptoms	++	–	–	–	++*	...
Motility	++	–	–	–	+	...

Table X.
* Gastrectomy performed.

Observations on Gastric Acidity.

Fractional test meal curves were secured before operation and 2 - 3 weeks after operation. (Fig. 80). It will be seen that an appreciable reduction in acidity occurred in only three cases. The reduction was never striking and certainly insufficient to influence peptic activity.

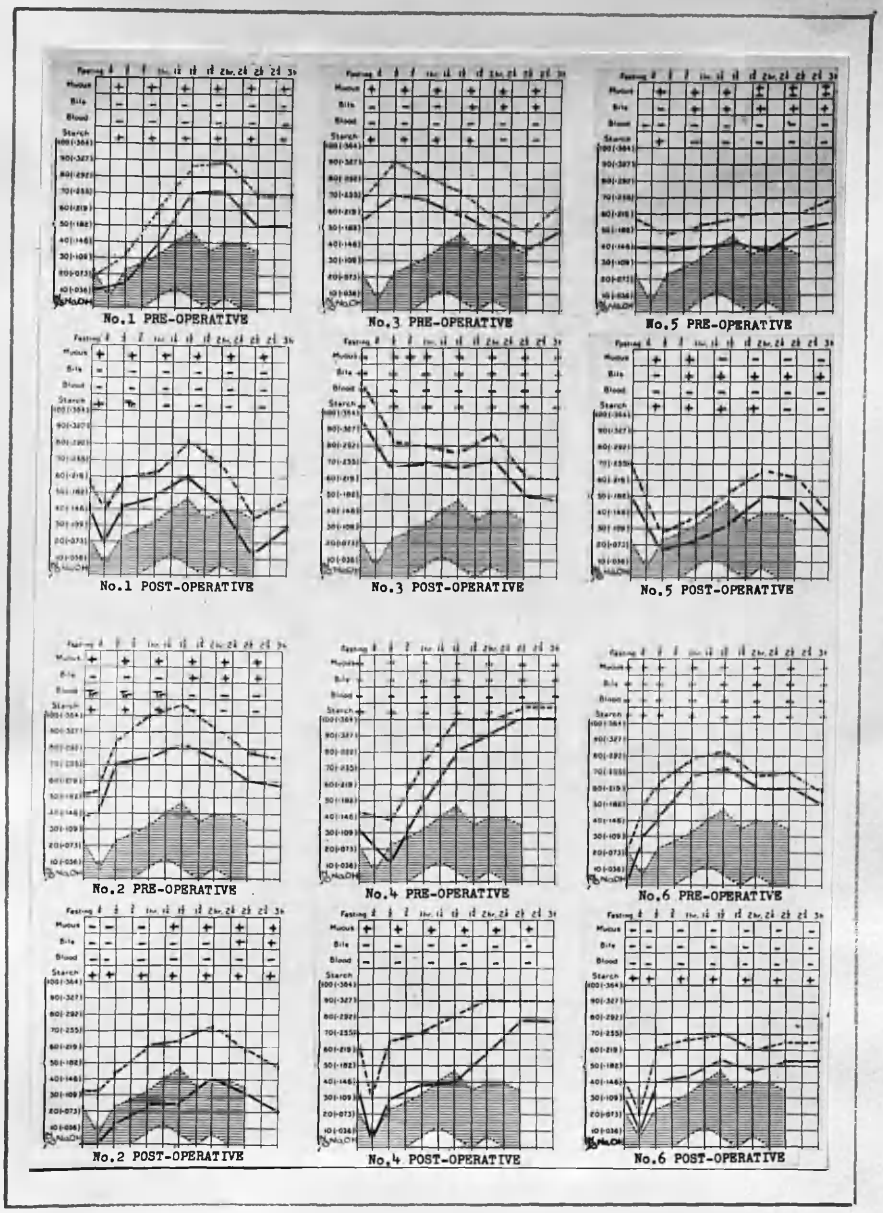


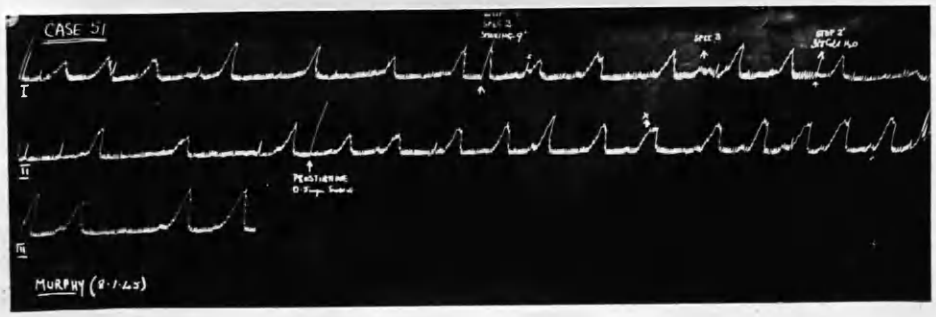
Fig. - 80.

Observations on Symptomatic Progress.

As indicated in Table IX, each patient suffered a continuous spell of severe pain prior to operation. In each instance the relief of pain following operation was immediate and appeared to us to be more complete than the relief encountered after any other surgical procedure for peptic ulcer. Our optimism and the patients' delight

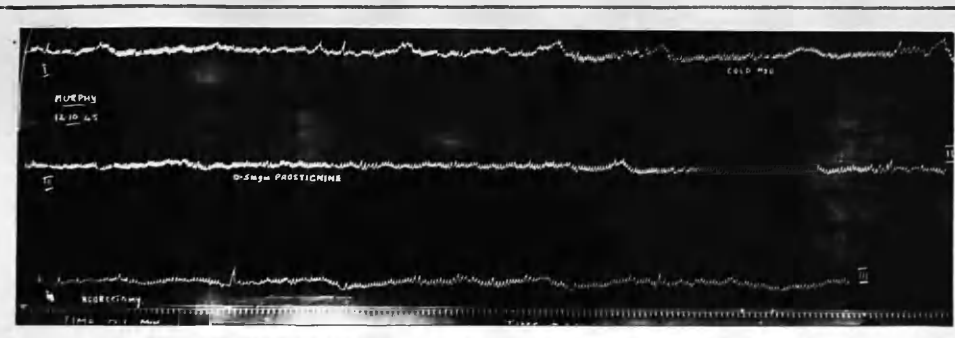
have been short-lived. Recovery of gastric motor activity was followed by a return of symptoms. Three patients have since required gastrectomy on account of severe and disabling symptoms at 3 months, 18 months and 27 months after the denervation operation. One patient had a recurrence of symptoms 18 months after vagotomy but although these have continued intermittently, he has been able to do full work. Two patients remain symptom free 24 and 27 months after operation (Cases II and V). Symptomatic progress is given in Table X.

An assessment of these results shows that two patients remain well after 2 years and the remaining four cases must be regarded as failures. Gastrograms of a successful case (V) and of a failure (IV) are given in Figures 81a, b and 82a,b.



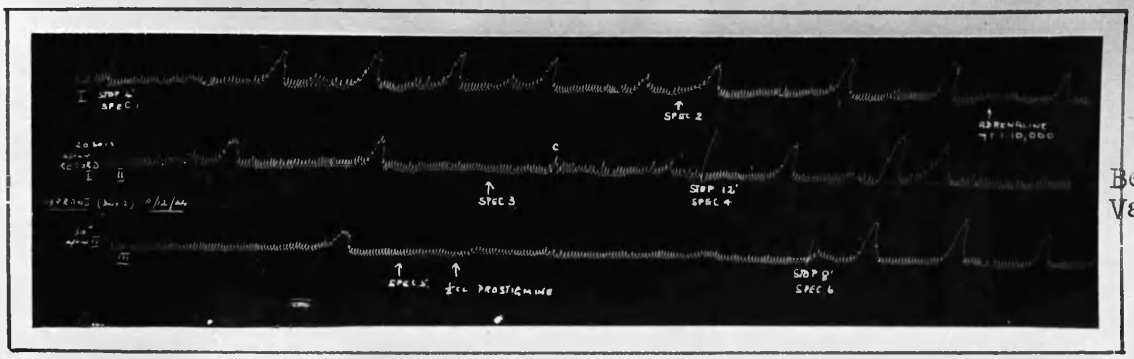
Before Vagotomy

Fig. - 81a.



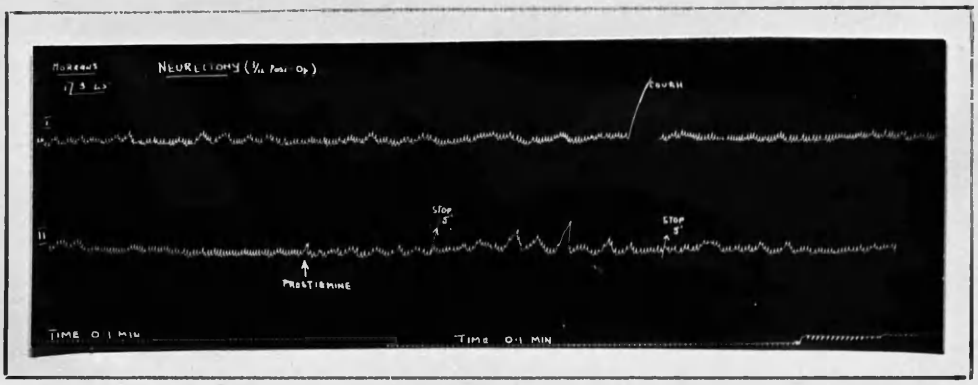
9/12 after Vagotomy

Fig. - 81b.



Before Vagotomy.

Fig. 82a.



3/12 after Vagotomy.

Fig. - 82b.

Discussion.

Latarjet's operation of gastric denervation has been performed in six cases of duodenal ulcer. It has been shown to result in almost complete immobility of the fasting stomach, a slight reduction in the gastric acid secretory response to a gruel test meal and complete symptomatic relief during the early post-operative phase. Follow-up for over two years has revealed that these beneficial effects have not been permanent in four of the six cases treated. The total supression of gastric motor activity immediately after operation and for several months thereafter suggests that the para-

sympathetic denervation was complete. Significant recovery of active gastric contractions was demonstrated in three cases within the first year and within eighteen months in a fourth. That recovery is presumably due to nerve regeneration is supported by the return of the excitatory gastric motor response to prostigmine. In two cases, this was confirmed by microscopic examinations after gastrectomy. I believe that gastric motility studies provide an ideal objective method of estimating adequate denervation and evidence of regeneration.

The unimpressive effect of vagotomy on the gastric secretory response to a fractional test meal was in accord with expectation since the hormonal stimulation of acid remains unaffected. Dragstedt and Schafer (1945) made a particular study of night secretion after interruption of the vagal innervation of the stomach by transthoracic vagotomy. They found that the excessive night secretion was markedly reduced after vagal section. As expected, however, gastric secretion in response to histamine was unaffected. Vagotomy does not provide a means for the abolition of acid secretion; the answer to that lies in the finding of some innocuous method of blocking the parietal cell.

The results of Latarjet's operation of vagotomy in our six cases of gastroduodenal ulceration make it clear that the operation cannot be recommended for the prevention of peptic ulcer recurrence. This statement may not apply

to supradiaphragmatic vagal section with excision of 3 - 4 cm. lengths of the nerve trunks. Under these circumstances, and particularly where the upper end of the nerve is encapsulated in an impermeable cylinder as recommended by Allen (1947), regeneration may not occur. The series published by Dragstedt (1947), Crile (1947) and Moore (1947) provide encouraging reading, although some of their results are invalidated by the performance of gastroenterostomy in addition to vagotomy. It should be remembered, moreover, that the anatomy of the vagi is variable and Mitchell (1938) pointed out that they may give off filaments, high in the thorax, which penetrate the wall of the oesophagus and run down in it to the stomach. These fibres will clearly be untouched by section just above the diaphragm.

Finally, the complete quiescence of gastric motor activity following vagotomy may be of serious import if it brings to light a mild pyloric stenosis. A stomach which could contend with some narrowing at its exit before vagal section may afterwards be unable to empty itself.

Summary.

In six cases of peptic ulcer treated by vagotomy by the abdominal route, the immediate effect was to relieve all symptoms. Pain recurred in one case within 3 months, in two cases after 18 months, and in a fourth after 27 months. Recurrence is attributed to regeneration of the cut nerves.

Vagotomy had a pronounced effect in reducing gastric motility. It had no effect on the acid concentration of the gastric juice.

SECTION - 11.

THE GASTROGRAM IN DYSPEPSIA NOT DUE TO DUODENAL ULCERATION.

It is important to know whether the gastrogram of a patient suffering from dyspepsia other than that due to duodenal ulcer can be differentiated from the typical duodenal ulcer gastrogram. There is practically no literature on the subject of differential diagnosis of the dyspepsias by a study of gastric motility. The results of a study of 20 cases of dyspepsia (excluding duodenal ulcer) are presented in this section.

Procedure.

Gastrograms have been recorded from 20 cases of dyspepsia resulting from the following conditions:-

Gallbladder disease - 5
Gastric ulcer - 4
Stomal ulcer - 2
Gastric carcinoma - 9

The pathology in each case has been adequately demonstrated in that the biliary and carcinoma cases all came to operation as did two of the gastric ulcers and one of the stomal ulcers. The other stomal ulcer and the remaining two gastric ulcers were radiologically and gastroscopically confirmed. The water reversal test has been applied in all cases.

Results.

The gastrographic findings in each of the four groups are shown by means of tables. The following average values should be remembered when studying the tables:-

Normal Gastrogram: Amplitude of G.C. = 1·8cms.
Duration " " = 28·76 secs.
Frequency " " = 70 per hour

D. U. Gastrogram: Amplitude of G.C. = 2·5cms.
Duration " " = 22·0 secs.
Frequency " " = 64·5 per hour.

1. Gallbladder Dyspepsia.

The main gastric motility findings in 5 cases of gallbladder disease are given in Table XI.

Table XI
Features of Gastrograms in 5 Cases of Biliary Dyspepsia.

Case	Biliary Lesion.	Rhythm.	Gastric Contractions. Ampl'd (cms.)	Freq. (no/hr.)	Response to Water Test
1	Empyema of Gallbladder	Regular	1·5	80	Reversal I
2	Chronic Cholecystitis	Regular	2·0	55	Reversal II
3	"	Regular	1·4	85	Reversal II
4	"	Regular	1·8	70	Normal
5	"	Regular	1·7	65	Normal.

It will be seen that a study of rhythm, amplitude and frequency of gastric contractions would fail to differentiate the gastrogram of the choleycystitis patient from that of a normal patient. The amplitude of these contractions is significantly less than is usual in duodenal ulcer.

The occurrence of a reversal response to the water test in 3 cases is of interest. In one of these, empyema of gallbladder (Fig.85), the duodenum was helping to wall-off

the infection; in the other two cases, Hartman's pouch was adherent to the duodenum. It is thus reasonable to assume that this extrinsic involvement of the duodenum was responsible for the production of the duodenal type of response

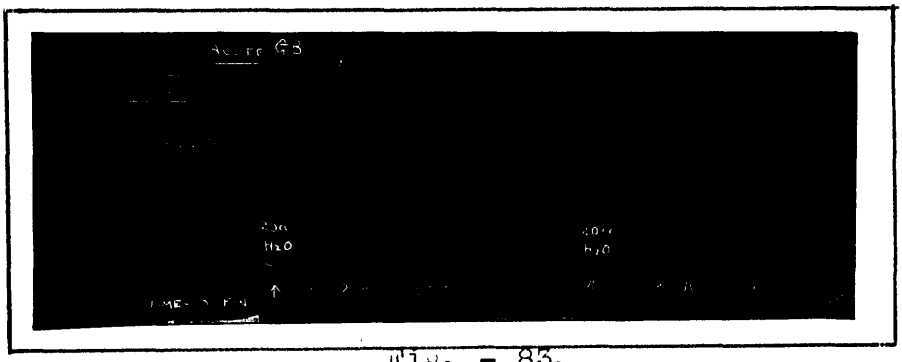


Fig. - 85.

Thus, certain cases of gallbladder disease giving a reversal water response will provide a gastric motility tracing differing from that of duodenal ulcer only in the amplitude of gastric contractions. In these cases, a confident gastrogram diagnosis cannot be made. When there is a normal water response, however, duodenal ulceration can be excluded as the cause of dyspepsia.

2. Gastric Ulcer Dyspepsia.

The gastrographic features of the four cases of gastric ulcer are presented in Table XII.

Features of Gastric Ulcer Gastrogram.

Case	Site of Ulcer	Rhythm.	Gastric Contractions.		Response to Water Test.
			Ampl't'd (cms.)	Freq. (no/hr)	
1.	Prepyloric	Irregular	1·7	60	Normal
2.	Lesser curve near angulus	Regular	1·9	50	Normal
3.	" "	Regular	1·8	70	Normal
4.	Prepyloric	Irregular	1·6	68	Normal

Table XII.

The four gastric motility tracings might have been taken from normal subjects save that in two the rhythm was irregular. The water response was normal (Fig. 84)

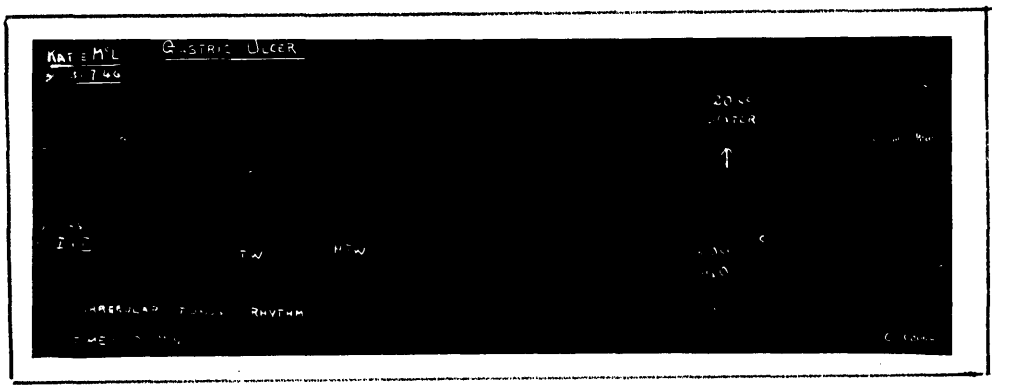


Fig. - 84.

There is, therefore, no difficulty in differentiating gastric ulcer dyspepsia from duodenal ulcer dyspepsia gastrographically. A positive diagnosis of gastric ulcer cannot be made from a study of gastric motility.

(3) Stomal Ulcer.

The features of two gastrograms recorded from patients with stomal ulcer following gastroenterostomy are given in Table XIII.

Features of Stomal Ulcer Gastrogram.

Case.	Rhythm.	Gastric Contractions.		Response to Water Test.
		Ampl'd (cms.)	Freq. (no/hr.)	
1.	Regular	2.0	60	Normal
2.	Regular	3.0	66	Normal

Table XIII.

It has been shown in Section 10 that gastric motility following gastroenterostomy is indistinguishable from

normal motility once the convalescent period has passed. In my two cases of stomal ulcer, the only additional feature is that the motility shows a return to hyperactivity of duodenal type as indicated by the amplitude of the gastric contractions (Fig. 85)

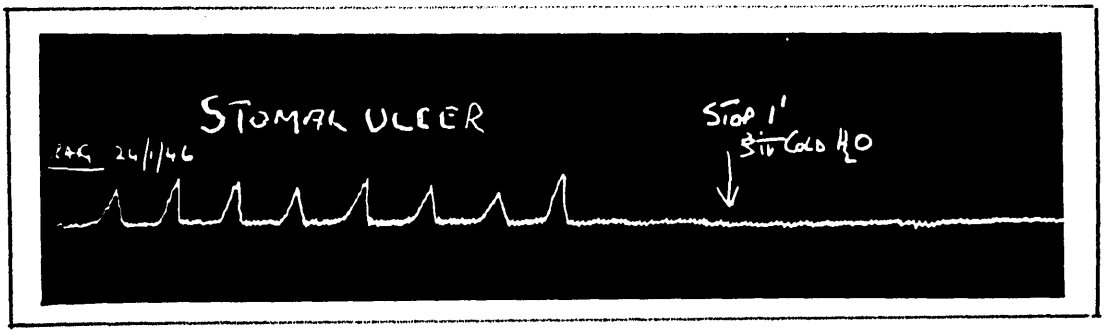


Fig. - 85.

It is of interest to contemplate the disposition of the "cart" and the "horse". Does the hyperactivity produce the ulcer or does the development of the secondary ulcer result in a return of hyperactivity similar to that found in cases of simple duodenal ulcer.

The water test yields a normal response. This does not, of course, necessarily rule out the simultaneous occurrence of active duodenal ulceration as the water may leave the stomach by the stoma and so fail to stimulate the duodenal cap.

(4) Gastric Carcinoma

The gastrogram features and the location of the neoplasm in 9 cases of gastric carcinoma are presented in Table XIV. In all nine cases of gastric carcinoma, the gastrograms were abnormal.

Gastrogram Features in Gastric Carcinoma.

Case	Lesion	Rhythm	Respir'y Waves.	Gastric Contractions		Response to Water Test
				Amp'd (cms.)	Freq. (no/hr)	
1.	Antrum & Body	Irreg'r	Absent	1·4	21	RII
2.	Extensive	Irreg'r	Absent	1·5	30	RII
3.	Extensive	Irreg'r	Absent	-	-	Normal
4	Extensive	Irreg'r	Present	-	-	RII
5.	Pyloric Canal	Regular	Present	3·0	24	Normal
6.	Antrum	Irreg'r	Present	2·5	20	Normal
7.	Antrum	Regular	Present	2·5	40	RI
8.	Cardiac end	Irreg'r	Present	1·0	18	Normal
9	Lesser curve Ulcer	Irreg'r	Present	-	-	Normal.

Table XIV.

The variations from normality were:-

1. Rhythm irregular in 7 cases.

   In the two cases with regular rhythm, the neoplasm was confined to the pyloric antrum.

2. Gastric contractions absent or of low amplitude, in 6 cases. In the 3 cases showing well developed gastric contractions, the neoplasm was confined to the pyloric antrum (Cases 5, 6 and 7).

3. Infrequent gastric contractions in all cases.

   The values varied between 18 - 40 gastric contractions per hour in contrast to the normal value of 70 per hour.

4. Respiratory oscillations were absent in the gastrogram from three of the four cases in which extensive malignant infiltration of the stomach was found at operation.

5. A Type II Reversal Response to the water test was found in 3 patients with extensive carcinoma in whom

operation failed to reveal any evidence of duodenal involvement. Case 7 gave a Type I Reversal Response but this was readily explained by invasion of the duodenum from subpyloric glands as discovered at operation.

Discussion.

The gastrogram in gastric carcinoma is always abnormal. The departures from the normal depend on (a) the site of the lesion and (b) the extent of stomach infiltrated by the tumour. The only way in which the gastric motility differs constantly from that of normal subjects is in the reduced frequency of gastric contractions.

(a) Site.

The site has obviously an important bearing on the resulting gastrogram.

Where the lesion is confined to the pyloric antrum and is producing a degree of obstruction, one can expect gastric contractions of higher amplitude than normal - the result of a fully compensated pyloric obstruction. (Fig. 86 - Case 5)

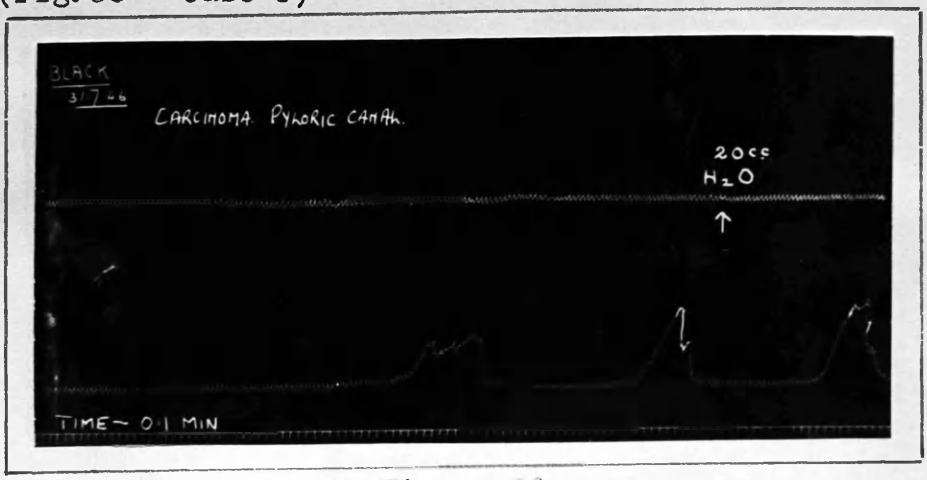


Fig. - 86.

When the antral lesion spreads to infiltrate the body of the stomach, those well developed waves disappear (Case 1).

In addition, the rhythm of gastric motor activity, which is frequently irregular in carcinoma of the stomach, may be regular in lesions confined to the antrum.

(b) Extent.

Cases 1 - 4 were shown at operation to have extensive carcinomatous infiltration of the body of the stomach. In three of these, respiratory oscillations were not present in the motility tracing (Fig. 87).

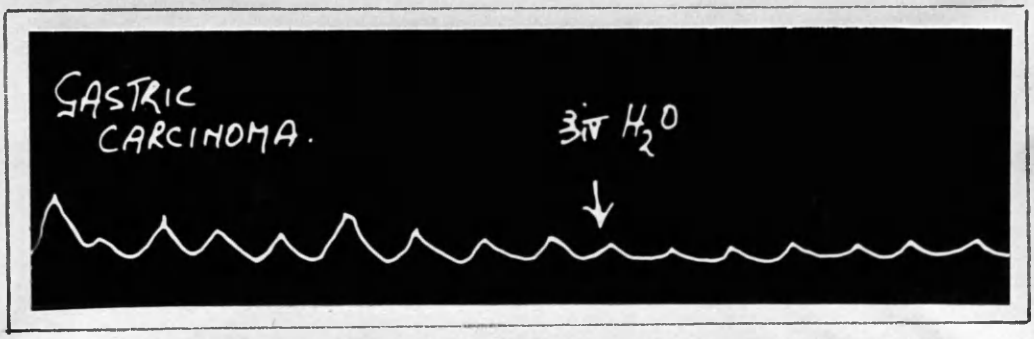


Fig. - 87.

This is probably due to the fact that respiratory movements could not be conveyed to the balloon on account of the rigid gastric wall.

In 5 of these patients with extensive gastric carcinoma, the application of the water test had no effect on existing activity - the feature of our Type II reversal response (Fig. 87). This may be due to delayed emptying or to the fact that the gastric side

of the duodeno-gastric mechanism is destroyed by the infiltrating neoplasm.

It has been shown that involvement of the duodenum by extrinsic carcinoma can produce a typical Type I reversal response (Fig. 88)

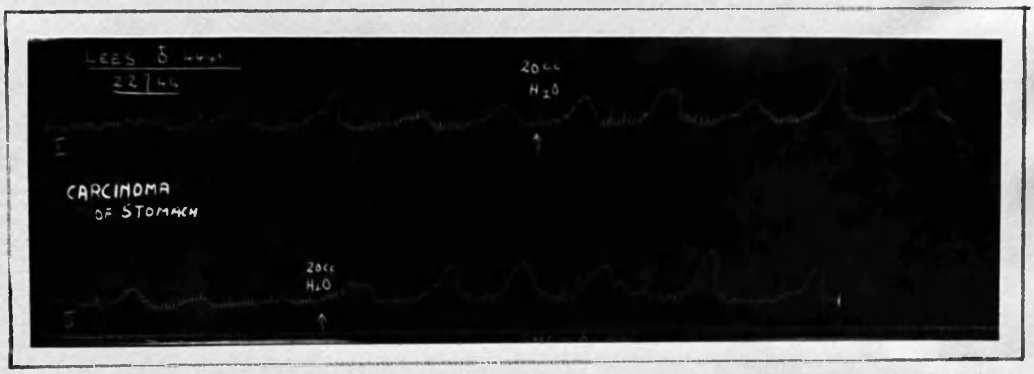


Fig. - 88.

The infrequent gastric contractions will distinguish this from the duodenal ulcer gastrogram.

Summary.

The main points on which one can attempt to differentiate the common organic dyspepsias gastrographically are given in Table XV.

Our aim, from the viewpoint of this thesis, was to find if any other common form of dyspepsia provided a gastric motility record indistinguishable from that of duodenal ulcer. The only condition liable to cause difficulty is cholecystitis. In this condition, a reversal response to the water test is not uncommon, but the duodenal ulcer gastrogram is further characterised by a striking hyperactivity of gastric contractions not observed in gallbladder disorders.

The Value of the Gastrogram in the Differential Diagnosis of Dyspepsia.

Condition	Rhythm.	Resp'y Oscl's	Gastric Contractions		Response to Water Test
			Ampl'd (cms.)	Freq. (no/hr)	
Normal	Regular	Present	1·8	70	Normal
Active D.U.	Regular	Present	> N	N	Reversal
G.B. Lesion	Regular	Present	N	N	Normal or Reversal
Gastric Ulcer	Regular or Irreg'r	Present	N	N	Normal
Stomal Ulcer	Regular	Present	> N	N	Normal
Gastric Carcinoma					
1. Pyloric Antrum	Regular	Present	> N	< N	Normal
2. Massive	Irreg'r	Absent	< N	< N	Normal or Reversal.

Table XV.

SECTION - 12.

OBSERVATIONS ON THE USE OF BENADRYL IN DUODENAL ULCER.

It is accepted that hypersecretion and hypermotility are characteristic of duodenal ulceration although it is by no means certain whether these conditions are causal or secondary. It is, however, reasonable to employ any drug which is thought capable of diminishing secretion and depressing motility. Benadryl (dimethylaminoethylbenzhydryl ether hydrochloride) has been shown to have an antihistaminic and antispasmodic effect (Loew, Kaiser and Moore, 1945; Loew and Kaiser, 1945) and since histamine is of importance in stimulating the secretion of hydrochloric acid, its use has been suggested in peptic ulceration. (McGavack, Elias and Boyd, 1946).

Observations have been made in the Peptic Ulcer Clinic, Western Infirmary, on the use of Benadryl in duodenal Ulcer. Although observations were also made on both the clinical effects of the drug and on gastric secretion, the recording of gastric motility was chosen as the main objective method of assessing the drug's action.

Procedure.

The patients selected were males having clinical and radiographic evidence of duodenal ulcer. They were all experiencing severe symptoms and were untreated apart from taking alkali when pain was troublesome. After 24 hours detention in hospital for the purpose of examination, the patients attended as out-patients.

In the first group of patients, the effect of a single dose of Benadryl was observed. The drug (57 to 200mgm.) was administered through a Ryle's tube during gastrography and recording was continued for at least 1 hour thereafter. With the larger doses, drowsiness appeared early (10 to 15 minutes), showing that the absence of a positive result could not be attributed to delay in absorption.

In the second group, Benadryl was given three or four times daily for periods of from one to four weeks. In this way, it was hoped to demonstrate the possibility of a maintained sedative effect on gastric motility.

Results.

Although the trial was primarily designed to assess the action of Benadryl on gastric motility, opportunity was taken to estimate its influence on gastric acidity and a record was also made of the patient's clinical progress. The results will be considered under these headings:-

The Effect of a Single Dose of Benadryl on Gastric Motility.

Six patients, during the recording of a gastrogram, were given a single dose of Benadryl (dose varied from 57mgm. - 200mgm.). In no case was there any change in gastric motor activity (Fig.89). By comparison, 1·3mgm. of atropine sulphate taken orally abolished gastric motor activity (Fig.90).

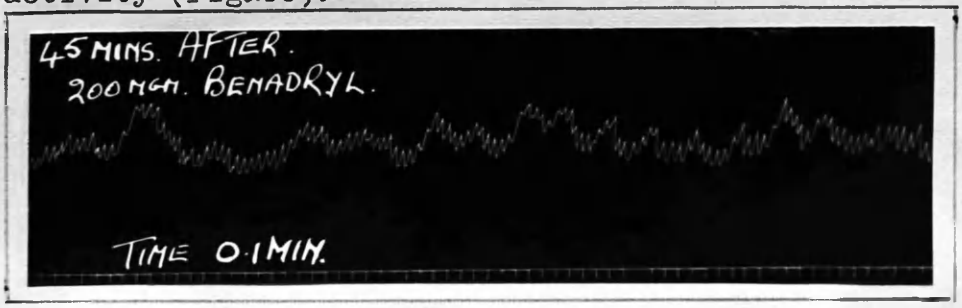


Fig. - 89

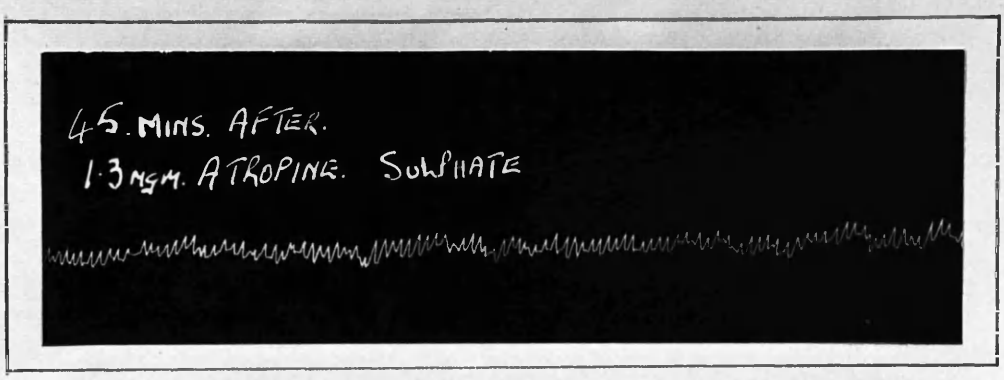


Fig. - 90.

The Effect of Continued Use of Benadryl on Gastric Motility.

In six cases, gastrograms were recorded before and at intervals during treatment with Benadryl. The drug was administered in doses of from 150 - 300mgm. daily for varying periods.

In four patients, no change in the motor activity of the stomach was observed, the dosage in these cases being 200mgm. for 16 days; 200mgm. for 21 days; 300mgm. for 8 days and 300mgm. for 21 days. In the fifth patient, relative quiescence of motility followed treatment with 200mgm. daily for 17 days. The remaining patient showed a striking motor inhibition after taking 150mgm. Benadryl for 7 days but this was not maintained after two subsequent courses of 200mgm. a day for 5 days and 300mgm. a day for 14 days.

The Effect of Benadryl on Gastric Acidity.

In six patients taking Benadryl over a period of time, alcohol test meals were performed before and after completion of the course. In 5 patients, a fall in the maximum level of free hydrochloric acid was observed amounting to 10, 16 and 25 clinical units, the dosage of

Benadryl being respectively 200mgm./21 days, 150mgm./3 days, and 300mgm./21 days. In the other 3 cases, a rise of 6, 10 and 24 clinical units was noted, the dosage of Benadryl being 200mgm./17 days, 200mgm./16 days and 300mgm./8 days.

The Effect of Benadryl on Dyspepsia.

Three patients were completely symptom free after a course of Benadryl. Two patients appreciated diminished frequency and severity of their pain and the remaining case was not aware of any improvement. Troublesome drowsiness (three patients) was the only side-effect of Benadryl treatment.

Discussion.

Benadryl has no demonstrable effect on gastric motor activity even when administered in dosage sufficient to cause troublesome drowsiness. The inhibition achieved in one case cannot be regarded as significant since it was not maintained on continuing treatment with an increased dosage of the drug. By comparison, atropine effects complete inhibition but it's side effects preclude continued use in the treatment of duodenal ulcer.

A constant lowering of gastric acidity has not been demonstrated.

However, only one case can be classed as a definite clinical failure. The treatment of peptic ulceration with its characteristic remissions, cannot be assessed readily on a purely clinical basis. Objective measurement is desirable

and, as a means of controlling hypermotility, Benadryl can be accounted inadequate.

GENERAL SUMMARY.

1. The pressing problem of peptic ulcer merits investigation from any hopeful viewpoint. The physiological upset which occurs in peptic ulceration is by no means fully understood and, in particular, our knowledge of the gastric motor activity is small. This thesis reports the results of a study of gastric motility in duodenal ulceration.

2. The technique of recording gastric motility is first described. With the patient fasting, a swallowed balloon is inflated to a standard pressure of 10cm. of water and connected to a tambour-kymograph unit for recording. The advantages of this method of gastrography over other reported methods are discussed.

The interpretation of the waves obtained is provided and certain difficulties and fallacies are defined.

3. The pattern of gastric motility in 30 normal subjects has been ascertained before investigating patients with duodenal ulcer. It was noted that the fasting stomach is never completely at rest and that, even in its most quiescent state, minor changes in tone are occurring constantly.

4. A detailed study has been made of the gastrograms obtained from 66 patients with active duodenal ulceration. Gastric contractions were found to be of greater amplitude and of shorter duration than in normal subjects and fusing of waves, not seen in controls, was common.

Based on these criteria alone, the gastrographic diagnosis of duodenal ulcer would not be reliable.

5. The fact that inhibition of gastric motility follows the ingestion of cold water has been confirmed in 30 normal subjects. In addition, it is shown that the temperature of the water does not influence the type of gastric motor response but merely alters the duration of the response.

In the presence of active duodenal ulceration, gastric activity was found to be either unaltered (Type II Reversal Response) or even stimulated (Type I Reversal Response) by the ingestion of water. This reversed response to water has been demonstrated consistently in 90 patients with active duodenal ulcer and it has been shown that a normal response returns with healing of the ulcer. Thus, the water test is of value in the diagnosis of active duodenal ulceration. This test has been used as an aid to the diagnosis of the "X-ray negative dyspepsias" and examples are provided which demonstrate its usefulness.

6. Evidence is presented which suggests that the receptor point for the gastric motor response to water is in the duodenum. This duodenal mechanism, which normally inhibits gastric motility, is damaged by active ulceration but functions normally when the lesion has healed. The water test can therefore be used to provide reliable evidence of healing.

7. The gastrographic diagnosis of pyloric stenosis depends on the demonstration of an increased latent period for the water test. This test also gives accurate information concerning the activity of the causal ulcer, provided it is duodenal.

Save in extreme cases of stenosis accompanied by gastric atony, the gastrogram gives no accurate indication of the degree of pyloric obstruction.

Gastric arrhythmia may be present in patients with pyloric stenosis resulting from duodenal ulceration. It is especially common when the original ulcer is no longer in a state of activity.

8. It is a common practice to advise the patients suffering from peptic ulcer to smoke less tobacco. A study has been made of the effect of tobacco smoking on gastric motility in patients with duodenal ulcer. Smoking was not found to produce any constant change in gastric motor function. This result, taken in conjunction with similar reported observations on gastric acidity and on symptomatology, indicates that moderate smoking is probably not harmful to the ulcer patient.

9. Opportunity has been taken to make observations on spontaneous ulcer pain. In two patients, pain was definitely related to the occurrence of true gastric contractions; in other cases, the level of gastric

acidity appeared to play the predominant role.

The literature on ulcer pain is reviewed and the merits of the various theories of its causation are discussed. It seems certain that a variety of stimuli can produce pain and the most usual one is probably hydrochloric acid. The view that these various stimuli all act by increasing the tissue tension around the ulcer has much to commend it.

10. It has long been known that the introduction of strong solutions of glucose into the duodenum would inhibit gastric function in normal subjects. This fact has been shown to apply even to duodenal ulcer subjects in whom gastric motor activity is exaggerated beyond the normal.

The mode of action of glucose has two components: gastric motility can be inhibited by raising the blood sugar level; inhibition can also be effected through a local osmotic effect on the upper small intestine. Evidence is presented which indicates that the latter component plays the major part in producing gastric quiescence.

11. Olive oil is regarded as a useful drug in the treatment of peptic ulceration. A study has been made of the effect of olive oil on gastric motility in patients with duodenal ulcer.

Olive oil effectively inhibits the motility of the fasting stomach and a 2 hour period of quiescence may

be expected after the ingestion of 20cc. of oil. A similar phase of inhibition will follow the administration of olive oil before food. Olive oil taken shortly after food is much less effective in causing gastric motor quiescence.

The physical properties of olive oil are unimportant in regard to its inhibitory effect on motility which depends on the liberation of oleic acid following hydrolysis of the parent fat. Glycerine, the other product of hydrolysis, does not cause inhibition of gastric motor function.

Of special interest is the observation that fat, repeatedly used for cooking purposes, does not inhibit and may even stimulate gastric motility. This result provides ground for much speculation when we consider that most ulcer patients volunteer a distaste for fried foods.

12. It has been stated that the surgical treatment of peptic ulcer may lead to the development of fresh clinical syndromes. Though not subscribing to this view, I think it is fair to say that symptoms, not due to recurrent ulceration, may occasionally follow gastroenterostomy or partial gastrectomy. As it seemed probable that some of these symptoms might result from disturbances of gastric motor function, gastrograms have been recorded from patients subjected to simple closure of perforated duodenal ulcer, gastroenterostomy, partial

gastrectomy and vagotomy.

The changes found in gastric motor activity following gastroenterostomy and partial gastrectomy do not explain the occurrence of symptoms after operation. Vagotomy had a pronounced effect in reducing gastric motility.

13. Gastrograms have been recorded from patients having cholecystitis, gastric ulceration, anastomotic ulcer, or gastric carcinoma. While not suggesting that gastrography deserves recognition in the diagnosis of these conditions, this study has shown that they can be distinguished readily from duodenal ulceration. Thus, the claim is upheld that active duodenal ulcer can be diagnosed accurately by a study of gastric motor activity incorporating the application of the water test.

14. The recording of gastric motility is well suited for assessing the action of drugs. This has been illustrated by observations on the use of Benadryl in the treatment for duodenal ulcer.

APPENDIX.

Gastrogram Findings in 66 Cases of Duodenal Ulcer.

Tonus Waves Freq. (no/hr)	Gastric Contractions. Ampl'd (cms.)	Gastric Contractions. Duration (secs.)	Gastric Contractions. Freq. (no/hr)	Rhythm.	Fusing of Waves.
54	-	-	-	Reg.	Occ.
85	2·7	24	75	Reg.	Occ.
72	2·5	18	72	Reg.	-
120	-	-	-	Reg.	-
60	2·5	18	45	Reg.	Occ.
100	-	-	-	Reg.	-
80	-	-	-	Reg.	Occ.
65	2.0	25	45	Reg.	-
60	3·0	25	45	Reg.	-
60	3·2	24	65	Reg.	+
58	2·7	21	60	Reg.	Occ.
60	3·0	24	68	Reg.	-
77	3·0	19	45	Reg.	Occ.
45	2·7	30	51	Reg.	-
65	-	-	-	Reg.	-
60	3·0	24	60	Reg.	+
45	-	-	-	Reg.	-
90	-	-	-	Reg.	-
70	2·0	20	80	Reg.	+
100	2·0	20	75	Reg.	Occ.
140	1·8	19	60	Reg.	+
115	2·0	20	75	Reg.	-
80	2·5	18	60	Reg.	Occ.
-	2·7	30	45	Reg.	-
75	2·0	25	68	Reg.	-
140	2·8	22	60	R. Irreg.	+
80	-	-	-	Reg.	+
70	2·0	20	60	Reg.	+
120	2·8	22	60	Reg.	-
60	1·9	24	55	Reg.	Occ.
80	-	-	-	Reg.	-
-	2·8	30	60	Reg.	-
60	2·5	24	60	Reg.	-
-	3·1	30	65	Reg.	Occ.
80	2·0	20	60	Reg.	-
80	2.2	18	55	Reg.	-
60	2·5	30	60	Reg.	Occ.
90	2·4	20	100	Reg.	+

(continued.)

Tonus Waves Freq. (no/hr)	Gastric Contractions. Ampl'd (cms.)	Gastric Contractions. Duration (secs.)	Gastric Contractions. Freq. (no/hr).	Rhythm.	Fusing of Waves.
90	1·8	18	80	Reg.	-
80	2·5	18	75	Reg.	+
55	2·8	24	70	Reg.	+
100	1·8	24	80	Reg.	-
65	1·8	25	80	Reg.	-
50	2·8	18	72	Reg.	+
75	-	-	-	Reg.	+
70	3·2	19	62	Reg.	-
70	2·7	20	80	Reg.	Occ.
50	-	-	-	Reg.	-
45	3·0	20	50	Reg.	+
90	-	-	-	Reg.	+
55	2·1	20	70	Reg.	Occ.
60	2·7	24	-	Reg.	+
76	Meth B	24	60	Reg.	+
-	2·5	22	-	R. Irreg.	-
75	2·5	20	90	Reg.	+
80	Meth B	24	87	Reg.	+
75	2·0	20	90	Reg.	+
110	2·5	24	89	Reg.	+
72	-	-	-	Reg.	+
78	3·4	24	60	Reg.	Occ.
60	2·5	20	68	Reg.	-
105	2·2	18	-	Reg.	-
50	2·6	18	48	Reg.	Occ.
60	-	-	-	Reg.	Occ.
70	2·6	20	60	Reg.	-
65	2·6	20	60	Reg.	+

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