CLINICAL ASSESSMENT OF GASTRIC FUNCTION

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The methods available for assessing gastric function are crude by comparison with the refined techniques which have been developed for studying renal or cardiopulmonary function in man. One reason for this is that both the secretory and motor functions of the stomach are extremely complex. It is much easier to measure the flow of blood through large arteries than it is to record the 'receptive relaxation' of the stomach as food enters it, or the subtle mechanism of gastric emptying. The gastric glands contain at least three different kinds of cell, the parietal cell, chief cells and the mucous cells of the neck. These are inextricably intermingled and discharge their secretions directly into the lumen of the stomach where they mix with the surface mucus, saliva, food and regurgitated intestinal secretions. Another difficulty is that the secretions and pressures can only be studied by passing tubes into the stomach. Most patients dislike intragastric tubes more than almost any other diagnostic procedure, and there is no doubt that the nausea and distress caused by the presence of a tube has vitiated many studies of gastric function because the patient's emotional state exerts a profound influence on secretion and motility.

One is often asked what is the best clinical test of gastric secretory function. This depends on what kind of information is required, but it is important to realize that these tests will not give much help in diagnosis or in assessing the severity of gastroduodenal diseases. Some clinicians are reluctant to accept this fact, but it is unreasonable to expect as much from these tests as from tests of renal, respiratory, hepatic or pancreatic function. Unlike these organs, the stomach is not indispensable: patients with pernicious anaemia who secrete neither acid nor pepsin are able to digest and absorb food as well as other people, and this is also true of most patients following gastrectomy. Even if we knew all about the mechanism and control of the secretion of acid and pepsin it is by no means certain that this would help in diagnosis,

or in elucidating the etiology of peptic ulcers, or in explaining the mechanism of dyspeptic symptoms. On the other hand, tests of gastric function have done much to clarify the relation between acidity and peptic ulcer; they are also useful for assessing the value of therapeutic measures because acid-pepsin is undoubtedly the factor which permits ulcers to become chronic. In this article it is proposed to discuss the clinical value and limitations of some methods of assessing gastric function and the physiological principles on which they depend.

Assessment of Acid Secretion

The ideal method would be to collect and analyse all the acid secreted throughout the 24 hours while the patient continues to take his meals as usual. Unfortunately this cannot be done because there is no method of measuring the amount of gastric secretion which is produced in response to ordinary meals and it is difficult to imagine how this could be done without constructing a gastric pouch. This is a serious limitation on all tests of gastric function in man,¹³ and it is important to realize that most of our knowledge about gastric secretion has been derived from experiments on animals with gastric pouches. These have shown that secretion is controlled by three successive stimuli and a number of inhibitory mechanisms. In the first or cephalic phase, the anticipation and sight of food and then the act of eating activate a nervous reflex through the vagus. In the second or gastric phase, the presence of food in the stomach stimulates secretion through a humoral agent which is formed in the antrum, partly by mechanical distension and partly by the action of secretagogues in food. In the third or intestinal phase, the presence of food in the intestine activates another humoral mechanism. These secretory stimuli are counterbalanced by mechanisms which tend to inhibit secretion. For example, the accumulation of acid in the stomach tends to prevent further acid secretion; and the presence of fat in

the duodenum, and also of acid and hypertonic solutions has a powerful inhibitory effect which is mediated by a hormone, enterogastrone, and by nervous reflexes acting through the vagus. That similar mechanisms control gastric secretion in man has been shown by means of the Serial Test Meal¹¹ and by observations on patients after certain gastric operations such as vagotomy, and gastrectomy before and after removal of the pyloric antrum.⁶ But even these special methods of investigation can give little or no information about the secretory response to eating in man or about the relative importance of nervous and humoral mechanisms in health and disease.

The Fractional Test Meal

The traditional test meal is or should be obsolete. In this test gruel is usually used as a stimulus and small samples are aspirated from the stomach at 15-minute intervals for about two hours. The test meal curve cannot be used as a measure of the amount of acid secreted by the stomach, because the acidity of each sample depends not only on the amount of acid but also on the volume of the gastric contents. The latter depends on the rate at which the stomach empties. Therefore, the acidity of each sample is determined by the interplay between the rate of emptying and the rate of secretion, so that an increase of gastric emptying or of secretion will raise the concentration of acid in the gastric contents. Nor can the test meal be used to determine whether the stomach is capable of secreting any acid at all, because gruel has little or no chemical secretagogue activity. It stimulates only by virtue of its bulk which causes mechanical distension of the antrum.

In fairness to the earlier workers who introduced the gruel test meal it should be pointed out that they were well aware that this test did not measure the amount of acid secreted. They used the test as an adjunct in the differential diagnosis of peptic ulceration because they found that patients with duodenal ulcers often reached a higher maximum acidity in a test meal curve than normal subjects, while those with gastric cancer showed a flatter curve. Tests which actually do measure the output of acid also show that patients with duodenal ulcers as a group secrete more acid than normals and that patients with gastric ulcers tend to secrete less. Presumably the interplay between acid secretion and gastric emptying tends to follow a typical pattern in patients with duodenal ulcers and therefore the test meal curve tends to reach a higher level than normal. However, the value of secretory tests in differential diagnosis is very limited because there is such a big overlap between normal subjects and patients with ulcers. The

finding of either hypersecretion or achlorhydria may be useful in the exceptional case where there is a discrepancy between the clinical and radiological findings.

The Serial Test Meal

The serial test meal is an ingenious method of measuring the secretory response to an aqueous test substance given by mouth, but only a physiologist could commit the gastronomic solecism of describing these substances as 'meals'. A liquid 'meal' containing a dye, phenol red, is given to the same subject on successive days for about a week, and the whole of the gastric contents are withdrawn through a tube of large bore after progressively longer periods each day. For example the stomach would be emptied after 15 minutes on the first day and after 30 minutes on the next day, and so on. From the difference between the amount of dye in the recovered gastric contents at two extractions it is possible to calculate the volume of the gastric contents leaving the stomach through the pylorus and also the volume of gastric secretion formed during the interval between the extractions. Thus the amount of acid, chloride and pepsin secreted in response to the meal can be calculated and the rate and pattern of gastric emptying determined.¹¹

It is assumed that the stomach is completely empty when the meal is given, that the gastric contents are homogeneous and uniformly mixed with the dye, and that gastric function is the same on each day. Therefore, the method can only be used with 'meals' consisting of aqueous solutions of sugars or salts which do not react with acid and which stimulate secretion only by virtue of their bulk by distension of the antrum. These limitations may be actually desirable from the physiologist's point of view because they help to standardize the experimental conditions. Hunt has used the method to determine the maximal emptying power of the stomach and the relation between increasing gastric distension and secretory response, and to study the mechanisms which inhibit secretion and emptying in normal subjects and in patients with ulcers. Although it has provided much valuable physiological information it is obviously unsuitable for routine clinical purposes and its reproducibility under such conditions is uncertain. Moreover, it is very unlikely that the stomach empties or secretes in response to ordinary meals as it does to these tasteless solutes.

Basal Gastric Secretion

Gastric juice is secreted more or less continuously in man, even when there is no food in the stomach. The interdigestive, basal or noc-

turnal secretion can be collected by aspirating the stomach continuously throughout the night, but this is a cumbersome method and difficult to supervise. Similar information can be obtained more easily by collecting the basal secretion for an hour or two in the morning after an overnight fast. Great care is required to minimize the loss of secretion through the pylorus and contamination of the gastric juice by other secretions. The saliva is mainly a diluent for it contains only low concentrations of chloride and bicarbonate, and therefore it is sufficient to spit it out because aspiration with a sucker is liable to stimulate further flow; duodenal juices, on the other hand, may contain high concentrations of bicarbonate. Ideally, a double-lumen tube should be used to drain the stomach and duodenum continuously and thus prevent losses of gastric juice through the pylorus and regurgitation of intestinal contents into the stomach; but Ihre¹² compared the results using a double tube with those using a single tube in the stomach in a large series of patients and found surprisingly little difference. The essential point is to position the tip of the tube radiologically, and this applies to all other tests which depend on intragastric tubes. We have found that the tube coils up in the fundus of the stomach in one out of five tests, and this can only be detected radiologically because appreciable amounts of fluid may be aspirated even from a tube in the oesophagus. The tip of the tube should be placed just beyond the angulus, roughly at about the right border of the vertebrae. The stomach is emptied completely and then continuous aspiration is begun, ideally by hand but in practice by mechanical suction.

It has been too readily assumed that basal gastric secretion is entirely dependent on nervous reflexes acting through the vagus, and, therefore, that the high basal secretion which is commonly found in patients with duodenal ulcer is the result of excessive vagal stimulation. It is true that vagotomy depresses basal secretion but it also depresses the secretory response to histamine, which is thought to act directly on the parietal cell. Similarly atropine not only inhibits the psychic or cephalic phase of secretion but also the gastric and intestinal phases which are humoral in nature,¹³ and antrectomy also reduces basal secretion in man.⁶ Moreover, there is some evidence that the level of basal secretion may be related to adrenocortical activity. It is, therefore, clear that the measurement of basal secretion cannot be used simply as a measure of vagal activity.

Like all other methods which involve continuous aspiration of gastric juice, this is a highly artificial and unphysiological test. Yet it has become the standard method for testing the efficacy of anti-secretory drugs. The reproducibility of the

method is also poor but can be improved by using a powerful secretory stimulus.

The Augmented Histamine Test

Histamine is not only the most powerful secretory stimulus but also the most physiological. It used to be customary to inject a dose of 0.01 mg./kg. body weight at the end of a fractional test meal if the patient had failed to secrete 'free acid' during the test. If this failed to produce any free acid the patient was said to have histamine-refractory achlorhydria. It was known, however, that the secretory response to this dose of histamine varied at different times in the same individual, and that some patients who were refractory to histamine could secrete acid in response to ordinary meals. This was shown by measuring the pH of gastric samples aspirated at hourly intervals throughout the day.²⁴ The dose of histamine was limited by its unpleasant side-effects but it was realized that the ideal test would be to inject sufficient histamine to stimulate all the parietal cells to secrete so as to obtain the maximum output of acid. This became possible with the introduction of the antihistamines because they antagonize all the actions of histamine other than its effect on the parietal cell.

Kay¹⁵ carried out a series of tests on normal subjects to whom he gave increasing doses of histamine covered by the appropriate dose of antihistamine, on successive days, and measured the amount of acid secreted in response to each dose. The largest single dose given was 7.1 mg. representing 12 body-weight doses of histamine, but he found that four body-weight doses produced the maximum output of acid and that any further increase in dosage failed to increase the output. This was interpreted to mean that four body-weight doses will stimulate all the parietal cells, and there is evidence that the output of acid is proportional to the number of parietal cells and, therefore, an index of the parietal-cell mass.³ However, even with this maximum histamine stimulus it is necessary to use a meticulous technique to achieve reproducible results. The tube must be of large bore to prevent significant losses of the stimulated juice through the pylorus and it is necessary to ensure that the tube is kept patent throughout the test and that aspiration is continuous. The gastric juice is collected for one hour as in the basal secretion test, then the appropriate dose of mepyramine (i.e. Anthisan) is given, and 30 minutes later a four body-weight dose of histamine acid phosphate is injected. The maximum output of acid is reached about 15 minutes after the histamine injection and it remains maximal for the next 30 minutes; therefore, the output of acid in the 30-minute period

starting 15 minutes after giving the histamine is calculated. The patients are aware only of a sensation of flushing from the histamine and of drowsiness from the antihistamine.

As might be expected, the maximal response is stable from day to day and therefore the Kay test has important theoretical implications and practical applications. Perhaps the most important of these is that it has changed the definition of the word 'achlorhydria' which now implies the virtual absence of parietal cells. On the basis of test meals it had long been accepted that about 4% of healthy young people were achlorhydric and that the percentage increased considerably over the age of 60. The Kay test has shown that the only persons who cannot secrete any acid at all are patients suffering from pernicious anaemia and possibly a very small number of patients with other types of anaemia. This is based on a new criterion for acid secretion, viz. the ability to lower the pH below 6.0 in response to maximal histamine stimulation.⁴ The traditional criterion, viz. the ability to secrete 'free acid' has been under criticism for some time because it means that the acidity exceeds the turning point of Topfer's reagent, which corresponds to about pH 3.5. Since neutrality corresponds approximately to pH 7, and the pH of pure, non-acid gastric secretion is probably higher still, it seems unreasonable to demand a pH as low as 3.5 as evidence that the stomach is capable of secreting acid.

Patients with duodenal ulcers as a group secrete about twice as much acid as normals, but the Kay test is of little more help in the differential diagnosis of dyspepsias than the test-meal. On the other hand, it may be useful in deciding the most appropriate treatment for the individual case because current therapy of ulcer is concerned almost exclusively with reducing acidity. This test measures the secretory capacity of the stomach and is an index of the number of parietal cells, and this varies widely even in patients with duodenal ulcer. However, the problem may not be quite as simple as this because the secretory power of these cells depends on several factors; for example, it has been shown that both vagotomy and antrectomy will reduce the parietal response to histamine.⁶

The Insulin Hypoglycaemia Test

This test has been used to determine the completeness of vagal section. The blood sugar is lowered by an intravenous injection of about 15 units of insulin and samples are aspirated from the stomach for about two hours, and blood-sugar levels are measured at half-hourly intervals. The hypoglycaemia acts centrally to stimulate gastric secretion through the vagus nerves; it stimulates

the secretion of pepsin and mucoprotein as well as acid. The test is often unpleasant for the patient and is not very useful in practice; there is often a fall in secretory rate before the hypoglycaemia begins to stimulate secretion, and this fall may also occur after vagotomy. Moreover, the hypoglycaemia may stimulate further secretion after a delay of several hours and this late phase also occurs after vagotomy but not after adrenalectomy.²⁰ This is part of the evidence that the adrenocortical hormones play some part in controlling gastric secretion in man.

Twenty-four-hour Gastric Analysis

All of these tests are highly artificial procedures, including those which depend on 'physiological' stimuli such as histamine, and particularly when the technique of continuous aspiration is used. The only test which gives some information about gastric acidity under ordinary living conditions is the 24-hour gastric analysis.¹⁴ This is a sampling technique for measuring the pH of the gastric contents without disturbing the normal operation of the three phases of secretion or the inhibitory mechanisms which control gastric secretion. The patient swallows a tube which is left in the stomach for 24 hours. He takes his meals as usual and about 5 ml. of the gastric contents are aspirated every hour throughout the day, and the pH of each sample is measured. Alternatively a glass electrode may be swallowed and the pH of the stomach contents recorded continuously *in situ*. No attempt is made to prevent saliva or regurgitated intestinal juices from entering the stomach, and, therefore, the changes in acidity throughout the day are recorded under normal conditions. The method has proved useful for studying the effect of food and drugs on acidity, the relation between acidity and pain, and the pattern of acidity in patients with gastric and duodenal ulcers. In patients with duodenal ulcers the pH tends to remain low throughout the day and night except for transient neutralization after feeds, whereas in patients with gastric ulcers the pH levels are usually higher and about 50% of them show nocturnal neutralization. This is said to disappear when the gastric ulcer heals. Unfortunately, as with all other tests, there is far too much overlap between normals and patients with ulcers to make the test worthwhile in differential diagnosis, but it may be useful in exceptional cases when the clinical and radiological evidence is conflicting. It may also be useful in establishing the cause of bleeding in the acute stages of haematemesis,⁵ because high nocturnal acidity is usual in bleeding from a duodenal ulcer and nocturnal neutralization with a gastric ulcer, whereas achlorhydria is usually found if the bleeding is due

to acute peptic ulceration. It is necessary to emphasize once again that in this, as in other tests, the positioning of the tube in the stomach is very important, because the degree of mixing of the gastric contents is such that the acidity is far from uniform even after fluid meals.

This is also a valuable method for assessing the usefulness of drugs in controlling acidity in the treatment of peptic ulcer.¹⁸ It is a simple matter to demonstrate the action of pharmacological agents such as histamine, insulin or acetazolamide on gastric secretion, but difficulties arise in assessing the likely clinical effect and duration of action of drugs when given by mouth for therapeutic purposes. This is why the therapeutic claims which have been made for innumerable antisecretory drugs in recent years have not been fulfilled in clinical practice, although the pharmacological tests in man have been very encouraging. One of the problems is to establish criteria as to what constitutes a significant effect on secretion. Variations in gastric secretion between individuals are so large that each must act as his own control, but even in the same person the output of acid may vary by a factor of 5 on different occasions, and by a factor of 2.5 from hour to hour during a single test lasting five hours, even in trained subjects who are accustomed to repeated intubations.^{21, 22} One method of overcoming this variation in the basal, interdigestive secretion is to test the action of the drug on histamine- and insulin-stimulated secretion. Valuable information may be obtained in this way, but it is difficult to interpret the results in terms of the likely effect of the drug under ordinary clinical conditions. For this purpose, the best method for testing a drug will depend on whether it is expected to stimulate or to inhibit secretion. If the object is to determine whether a drug is likely to be useful in controlling the hypersecretion of acid in patients with duodenal ulcer, it is essential to test it in patients who are secreting continuously and at a high rate, and several tests will be necessary on each patient.¹⁸ Not only is it difficult to measure the effect of an antisecretory drug in normal subjects, the results will give little or no indication of its effect in patients with hypersecretion.

Let us suppose that the maximum dose of an antisecretory drug reduces the output of acid by 50%, for example, from about 100 mN to 50 mN. This would commonly be described as a 'marked inhibitory effect' and likely to be valuable in controlling acidity in patients with duodenal ulcer. However, the common practice of expressing acidity in terms of normality may be misleading when the object of the test is to assess the clinical effect of a drug. For this purpose, the significant measurement is its effect on pH, for it is this which

determines peptic activity, and the object of using antisecretory drugs in clinical practice is to inactivate pepsin by maintaining the pH at about 3.5 or 4.0. A reduction of acidity by 50% seems impressive, but a fall from 100 mN to 50 mN represents a rise of only about 0.4 pH units from about pH 1.1 to 1.4; the pH would still be less than 2.0 even if acidity were reduced by 80%, from 100 mN to 20 mN. A further difficulty arises in interpreting the results in clinical terms because a test which involves the continuous aspiration of gastric juice will mask any effect a drug may have on the rate of gastric emptying. The majority of antisecretory drugs are anticholinergic and therefore prolong the emptying time, so that food and secretion remain in the stomach for longer periods and continue to stimulate further secretion in the gastric phase. There is no way of measuring this but it is likely to be significantly greater than the rate of interdigestive secretion; no account is taken of it in these tests, nor of any possible inhibitory effect of the drug on the alkaline pancreatic and duodenal juices. It follows that an antisecretory drug must have a very profound inhibitory effect on the output of acid as tested by this method, in order to inactivate peptic activity in patients with hypersecretion.¹⁷

This problem has been discussed at some length to show how a method may provide important quantitative data about the pharmacological action of a drug and yet give a misleading impression of its clinical usefulness. It is essential to obtain all possible information before embarking on laborious clinical trials, and probably the best final test of an antisecretory drug is to measure its effect on the pH of small samples of gastric juice, aspirated at frequent intervals over 24 or 48 hours under normal conditions. Such a method is about as far removed from the controlled techniques of experimental physiology as can well be imagined, but it tests the drug under the actual conditions of clinical use. It also allows for the wide variations in secretion in different patients, because a drug which can be shown to maintain the pH above 3.0 is a very powerful inhibitor indeed. Since the tube is placed in the stomach it may be objected that this method does not provide information about the pH of the milieu of a duodenal ulcer. It is possible to place the tube in the first part of the duodenum but this is a tedious process,² and the pH levels correspond so closely to those in the antrum that the additional information does not justify the additional distress suffered by the patient.

Tubeless Gastric Analysis

These methods depend on the use of cation exchange resins which are dissociated in the

presence of free hydrogen ions in the stomach, so that the cation is absorbed and excreted in the urine.^{8,19} Two compounds are available, both marketed under the trade name 'Diagnex'; in one of these quininium is used as the exchange cation and in the other the dye Azure A. If this was a quantitative method not only would it have the advantage of being tubeless, but it would also be a measure of the total gastric secretion including that which is normally lost through the pylorus. Unfortunately the amount of the cation which is displaced from the resin and absorbed from the intestine and then excreted in the urine is not directly proportional to the amount of acid secreted by the stomach. The method can, therefore, only be used to determine whether or not the stomach is capable of secreting any acid, and even for this purpose neither the quininium nor the Azure A resin gives complete correspondence with the ordinary histamine test. False negative results may arise from defective absorption of the cation in such conditions as pyloroduodenal obstruction, malabsorption syndromes, and severe diarrhoea, or from delayed excretion in diseases of the urinary tract. Since the test can at best be only a screening procedure for achlorhydria, a few false negative results are unimportant, but false positives are very misleading. These may arise because the cation can be displaced by substances other than hydrogen ions, such as magnesium, iron, aluminium, calcium and kaolin, and, therefore, these should not be taken by mouth for two days before the test; but a few false positives will still occur. Nevertheless, this test is useful as a screening procedure for picking out patients with defective gastric secretion for further study.

Non-acid Gastric Secretion **Chloride**

The estimation of chloride is not very useful in routine clinical tests but it is crucial in physiological studies; the experimental evidence for the different hypotheses about the composition of gastric secretion depend very largely on the relation between chloride concentration and acidity. For example, the Hollander two-component hypothesis is based on the fact that there is a linear relationship between the concentration of acid and chloride over a fairly wide range of acidities. According to this theory, which is fairly widely held, gastric secretion is made up of two hypothetical components, each of which is assumed to have a fixed composition in respect to acid, chloride and bicarbonate, the concentration of acid in the parietal component being 155 mN. The hypothetical non-parietal component is neutral or alkaline and consists of mucus, chlorides and some bicarbonate. Hyperacidity cannot occur, but

hypersecretion of acid implies a high rate of formation of the parietal component because variations in the acidity of gastric secretion result from the presence of different proportions of the two components. Neither this nor any of the other hypotheses will account for all the facts. The application of this hypothesis to clinical problems has not been very fruitful, but it is a relatively simple matter to calculate the volumes of the two components by estimating chloride as well as acid.

Mucus

The analysis of gastric mucus is still a research procedure because both chemical and electrophoretic techniques are difficult and technically unsatisfactory. It has been shown that albumin is present in gastric secretion and also that there are a number of mucoproteins but the normal electrophoretic pattern has not yet been established. However, the analytical techniques are being improved rapidly and there are many reasons for thinking that the study of gastric mucus will be more rewarding than that of acid-pepsin in relation to the pathogenesis of ulcer. Research was undoubtedly stimulated by the discovery that the incidence of peptic ulcers and gastric carcinoma was related to the patient's ABO blood group and to the presence or absence in his saliva and gastric juice of the ABH blood group substances which are mucopolysaccharides.

Proteolytic Enzymes

The estimation of pepsin is not worthwhile as a routine procedure because the amount secreted usually corresponds to the amount of acid secreted, and there is no evidence, for example, that patients with peptic ulcer secrete more pepsin per unit of acid than normal persons. However, there has recently been a revival of interest in the estimation of blood and urinary pepsinogen as a diagnostic test.¹⁰ Pepsin is synthesized in the chief cells of the gastric glands and about 1% of it enters the blood stream and is excreted in the urine. There is undoubtedly some correlation between the pepsinogen secreted in gastric juice and both the blood and urinary pepsinogen, but the latter can only be used as an approximate index of gastric secretory activity. There are many instances where gastric pepsin is increased by secretory stimuli without any change in the excretion of uropepsin, and vice versa, and there is no doubt that many conclusions that have been drawn about gastric pepsin from measurement of uropepsin are invalid. We need to know much more about how the pepsinogen enters the blood and how it is excreted by the kidney. The available evidence suggests that the blood and urinary pepsinogen parallel the

mass of chief cells in the gastric glands rather than the rate of gastric secretion. Although the blood and urinary pepsinogen levels are higher in patients with duodenal ulcer as a group than in normal persons or patients with gastric ulcer, the overlap is so great that the test is rarely helpful in differential diagnosis. In this respect it resembles tests of acid secretion but with the important advantage that the patient is not obliged to swallow a tube, and the chemical estimation is a simple one. In iron-deficiency anaemia the blood and urinary pepsinogen levels are usually low if the patients are achlorhydric to the ordinary histamine test. In pernicious anaemia the levels are always very low: this is about the only statement about uropepsin which has not been contradicted by someone or other in the vast literature on the subject. Because it is always low or absent in pernicious anaemia, estimation of the blood or urinary pepsinogen is useful as a screening test for picking out patients for further study, and also in the investigation of suspected but unproven cases of pernicious anaemia who have already been treated and in whom the diagnosis is still in doubt.

There has also been a revival of interest in another proteolytic enzyme which is present in the gastric juice of normal people and has an optimal pH of about 4.0, in contrast to pepsin which is most active between 1.6 and 2.4; in the past this enzyme has been regarded as a cathepsin. Taylor²³ has recently produced evidence that proteolytic activity occurs at three pH maxima in patients with peptic ulcers.

Assessment of Gastric Motility

There is a great deal of evidence that dyspeptic symptoms are more closely related to subtle disturbances of motility than to changes in gastric secretion. The techniques available for studying motility are not sufficiently refined to make it possible to record precisely how the stomach relaxes to accommodate a meal, or how it discharges the food in a controlled manner into the intestine, or what part the pyloric sphincter plays in the process of gastric emptying. Many of the symptoms of the dyspepsias almost certainly result from disturbances of some of these mechanical functions of the stomach and duodenum. The methods available for studying motility in man are: the serial test meal, radiological methods and manometric techniques.

The Serial Test Meal

This method is very useful for investigating the rate and pattern of gastric emptying and the factors which control it. Hunt has shown that liquid 'meals' leave the stomach in an exponential manner so that a constant fraction of the gastric

contents passes into the duodenum every minute until the stomach is empty. Unfortunately this elegant method cannot be used with ordinary meals.

Radiological Methods

It is possible to mix sufficient barium with an ordinary meal so as to outline the stomach, and the recent development of image intensifiers has reduced the radiation hazards so that cineradiography can be used for more prolonged studies. The simultaneous use of cineradiography and manometric techniques is an important advance and is now being exploited in several centres.

Manometry

Some useful information has been obtained about the function of the pylorus by measuring intraluminal pressure by means of open-ended tubes or very small balloons.¹ Unfortunately, manometric methods do not provide all the data necessary for analysing gastric motility, because the intraluminal pressures recorded are not directly related to movements of the gastric contents nor to the tension in the muscular wall of the stomach and duodenum.⁹ The diameter of the lumen varies from place to place and is constantly changing. There can be considerable muscular activity and rapid transport of contents with variations of only 1 to 2 cm. water pressure in the lumen, whilst pressure-waves of large amplitude may be recorded without any movement of the gastric contents. What is needed is a simple method for measuring the tension developed in the wall of the gut and the movements of the gastric contents. The recent development of methods of telemetering data from the alimentary tract by means of 'radio pills' may make it possible to study both secretion and motility under natural conditions without the patient being aware that he is being studied at all.⁷

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