morbidity and mortality associated with gross obesity. In addition, we believe that starvation is of value only if it results in permanent weight reduction. Previous experience has shown that almost all obese patients starved for a relatively short time and allowed home while still clinically obese soon regain weight (MacCuish *et al.*, 1968).

This further study was undertaken to determine if more satisfactory results could be obtained by starving obese patients until they have reduced to 25% in excess of their ideal weight. Thirteen failed to lose weight to this extent. These include many of the most grossly obese in whom reduction to less than 25% excess body weight would have required a long stay in hospital. Those who have not defaulted have all regained weight, and though they remain much lighter than before admission, the velocity of their gain is comparable to that observed in the previous study. The long-term prognosis is considered to be poor. Clearly some of them were psychologically unsuitable for this form of treatment, and their admission might have been avoided by the use of formal psychological evaluation. In contrast, 8 of the 12 who did achieve the desired loss of weight have not

regained appreciably though they have required constant supervision. All admit to a radical change in previous eating habits and feel that the main value of starvation has been an improvement in physical and psychological well-being.

These results would appear to confirm our initial impression that starvation of the grossly obese is more likely to be successful in the long term if continued until a weight approaching the ideal is achieved. Whether this can be attributed to increased psychological incentive or to some more fundamental change in eating pattern or body metabolism subsequent to effective weight loss remains to be determined.

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Production of Epigastric Pain in Duodenal Ulcer by Lower Oesophageal Acid Perfusion

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Summary: Thirty-six patients with duodenal ulceration were divided into group 1 (30), who had epigastric pain, and group 2 (6), who had pain in the upper abdomen but not in the epigastrium, and were studied by perfusing the lower oesophagus with dilute acid in an attempt to reproduce epigastric pain. In group 1, 25 suffered epigastric pain, indistinguishable from that which they normally had, after perfusion of 30 ml. of 0·1N HCl in under four minutes (mean values), but none of group 2 had pain.

Introduction

Pain associated with duodenal ulcer may be experienced in the epigastrium, under the right costal margin, around the umbilicus, or between the umbilicus and the xiphisternum in the midline, but there has never been any conclusive evidence as to its origin. Referred pain from the duodenum may be caused by the local action of acid on an ulcer, and inflation of balloons in the duodenum may also cause pain in any of these areas (Bloomfield and Polland, 1931). The stomach is usually insensitive to high levels of acid, though some attempts have succeeded in producing pain (Palmer, 1926; Bonney and Pickering, 1946; Smith, 1955). Because these experiments on the stomach and duodenum have not consistently reproduced epigastric pain it was considered that acid reflux on to a sensitive lower oesophageal mucosa might be a cause. Distension of the lower oesophagus causes lower sternal pain but may also cause epigastric pain (Polland and Bloomfield, 1931), and perfusion of this region with acid in hiatal hernia has been used as a clinical test for the retrosternal pain of oesophagitis with the occasional production of epigastric pain as well (Bernstein and Baker, 1958).

In this study the oesophageal acid perfusion test was modified for the investigation of epigastric pain. The localization of epigastric pain was recorded on a small diagram after

the patient had pointed to the site in question with one finger and after this had been confirmed by the doctor also pressing the area in question. The definition of epigastric pain was "that pain between the rib margin just below the xiphisternum." Since bony landmarks were used as a reference point there was not so much inaccuracy as would have occurred if somewhere in the centre of the abdomen had been pointed out.

Patients and Methods

Thirty-six patients with a duodenal ulcer were divided into two groups on the basis of whether they had epigastric pain or not. Thirty patients in group 1 had epigastric pain in the angle between the rib margins just below the xiphisternum. Six patients in group 2 had other upper abdominal pain—three complained of upper abdominal fullness, two had periumbilical pain, and one had a lower sternal ache. All had had this pain in the previous four weeks, but in the present study no distinction was made because of its severity or last occurrence, so that patients who had been woken by pain during the night before the test were not differentiated from those who had only occasional pain after meals.

Pressure measurements of the gastro-oesophageal junction were made with techniques previously described (Fyke *et al.*, 1956). No uniform preparation of the patients was made; some had just eaten and others had fasted overnight. The recording units (Fig. 1) were passed through the mouth into the patient's stomach. Pressure measurements were made with three water-filled polyethylene tubes (external diameter 0·065 in. (1·65 mm.); internal diameter 0·044 in. (1·12 mm.)). The distal tube was covered with a 0·5-cm. balloon, and the two remaining tubes had lateral openings 5 and 10 cm. from the balloon. SE 4-8 Mk 2 transducers converted pressure to electrical activity, which was recorded by an SE 2005 6-channel ultraviolet recorder on 6-in. (15-cm.) paper. A pH stomach electrode (Pye 240 E07) was tied 0·5 cm. proximal

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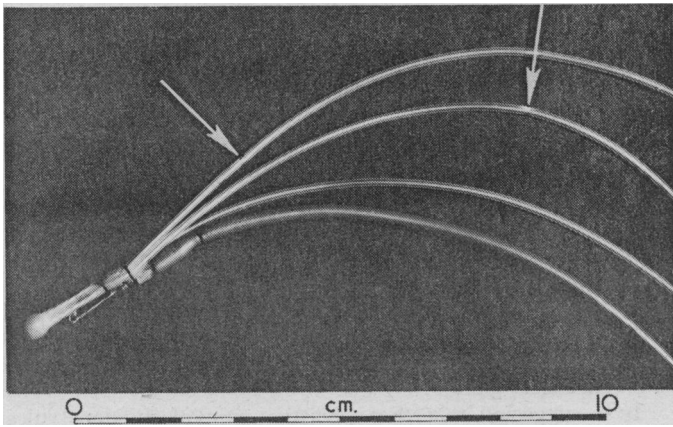* Senior Lecturer in Surgery, the London Hospital, London E.1.

FIG. 1.—Pressure and pH recording units. The tip of the stomach electrode is 0·5 cm. proximal to the balloon; the two lateral openings in the polyethylene tubes, 5 cm. apart, are marked by arrows.

to the balloon, and pH changes, measured by a Pye Model 79 pH meter, were recorded simultaneously with the pressure changes. The units were drawn slowly through the gastro-oesophageal junction at 0·5-cm. intervals to obtain the pressure profile of the sphincter in its resting state.

After two resting studies the balloon was accurately placed at the sphincter (Fig. 2) by noting where sphincteric relaxation and contraction occurred. The pH electrode then also lay in the sphincter with the distal open tip 5 cm. above. The proximal open tip, 10 cm. above the balloon, was used for perfusing solutions of 0·9% NaCl, 0·1N HCl, and 0·1 molar sodium bicarbonate into the oesophagus at a constant rate of 8-10 ml. per minute. If the patient had no pain immediately before this test either NaCl or HCl, chosen at random, was perfused until pain was produced or until 100 ml. had passed through the tube. Then sodium bicarbonate was perfused until the pain disappeared. If the patient already had spontaneous pain, sodium bicarbonate was used first until relief was obtained. The pain-reproduction test was considered positive if pain was produced by 100 ml. or less of 0·1N HCl, and negative if 100 ml. did not cause pain. The amount of sodium bicarbonate perfused before the pain disappeared was also measured. NaCl did not always cause pain, so the quantity perfused was either that which caused pain or the full control amount of 100 ml. During the perfusion of each test solution the pH in the sphincteric zone was recorded.
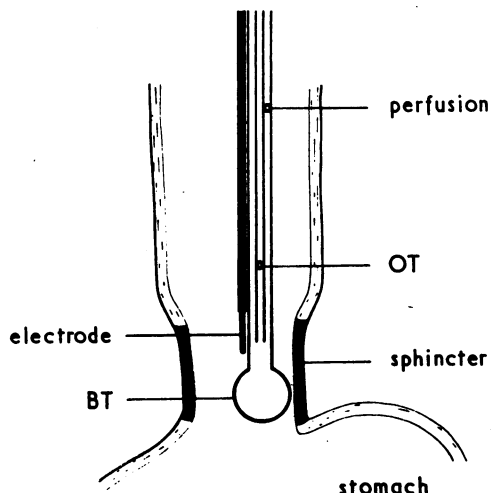

FIG. 2.—Balloon (BT) is placed at the gastro-oesophageal junction so that the distal open tip (OT) is just above the sphincter and the proximal open tip, through which fluid is perfused, lies in the lower oesophagus.

Results

Group 1.—Of the 30 patients, 25 experienced pain during the test that could not be distinguished by them from the pain of which they were complaining, except in severity. Pain was caused by 30 ml. of 0·1N HCl in under four minutes and was relieved by 26 ml. of 0·1 molar sodium bicarbonate in a similar time (mean values); 30 ml. of 0·9% NaCl (mean value) produced pain in 13, but in the remainder 100 ml. did not cause pain. Sodium bicarbonate never caused pain. The five who did not have a positive pain reproduction test had mild symptoms, not having been woken at night by pain in the previous four weeks.

Group 2.—None of these six patients experienced pain during perfusion of the lower oesophagus with 100 ml. of 0·1N HCl, 0·9% NaCl, or 0·1 molar sodium bicarbonate.

pH recording.—Perfusion with 0·1N HCl caused the pH to fall below 2 within one minute, though pain did not occur until later. With 0·9% NaCl the pH recorded was 6·5 whether pain occurred later or not. The pH during perfusion with 0·1 molar sodium bicarbonate, which never caused pain, was usually 8·5. The pH measured in this way did not closely correlate with pain, though solutions of greater acidity were more likely to be associated with pain; so it is suggested that the electrode measured the pH of the perfusing solutions rather than that of the lower oesophageal mucosa, where the pain arises.

Discussion

Most of the previous theories concerning the aetiology of pain in duodenal ulcer have agreed that it is referred pain from a viscus but disagreed as to its origin. The subject is discussed in great detail by Spira (1956) and Bockus (1963). Principally, support has been given to three main theories suggesting that the pain arises (1) from the duodenal ulcer itself, (2) from increased acidity in the stomach, and (3) from increased or abnormal gastric motility.

Pain from Duodenal Ulcer Itself.—It is obvious clinically that an ulcer and upper abdominal pain are associated, and the discrepancy between the anatomical site of the ulcer and the pain experienced is explained by the phenomenon of referred pain from the autonomic nervous system. Experimental proof that pain could be referred from the duodenum to the upper abdomen was given by balloon distension (Bloomfield and Polland, 1931) and instillation of dilute HCl into the duodenum (Meyer et al., 1932; Smith, 1955). Though there is a close relationship between gastric antral pH and duodenal pH (Atkinson and Henley, 1955; Archambault et al., 1967) there is no connexion between the actual amount of acid and the occurrence of pain.

Pain from Increased Gastric Acidity.—The recognition that duodenal ulceration is associated with high levels of gastric secretion, both of acid and of pepsin, led to a series of experiments altering gastric acidity to produce pain. Clinically vomiting may relieve ulcer pain, and aspiration of gastric contents also causes relief (Smith, 1955). Three different groups have demonstrated that adding dilute HCl to the stomach can cause pain (Palmer, 1926; Bonney and Pickering, 1946; Smith, 1955). The quantity of acid needed was at least 200 ml. though amounts up to 600 ml. occasionally had to be used. Pain occurred in seven minutes (Smith, 1955) to 30 minutes (Palmer, 1926). These experiments may be interpreted as showing either that the gastric mucosa is sensitive to HCl or that the acid passes through the pylorus and then irritates the duodenal ulcer, having penetrated its covering slough (Bonney and Pickering, 1946). But one experiment with a mixture of barium and acid demonstrated pain reproduction without any barium leaving the stomach (Ruffin et al., 1953). It must be emphasized that most workers have found that the normal gastric mucosa is insensitive to HCl

and that no pain is produced when acid is instilled into the stomach (Spira, 1956).

Pain from Abnormal Gastric Motility.—Increased frequency or amplitude of gastric contractions has been recorded during attacks of pain (Ruffin *et al.*, 1953). If the stomach has previously been filled with acid then gastric contractions are more likely to cause pain. These contractions do not necessarily cause emptying of the stomach contents into the duodenum, because pain may occur with the pylorus still closed (Ruffin *et al.*, 1953). Inhibition of the contractions by nitrites (Beams, 1932) or Banthine (Hightower and Gambill, 1953) can cause the pain to disappear. Again, most workers have shown that there is no good correlation between pain and a local or generalized contraction of the stomach (Palmer, 1926; Bonney and Pickering, 1946; Smith, 1955).

The main criticism of these experiments, which may or may not produce duodenal ulcer pain, is that the localization of the pain was not accurately described. Clinically the commonest duodenal ulcer pain is epigastric, with epigastric tenderness on pressure, but many have pain in the right subchondral region with tenderness on deep palpation in this area, and some have vague waves of pain in the upper abdomen which the patient himself associates with contractions. There is unlikely to be agreement over one cause for all these different types of pain, so the previous experiments must be regarded as showing possible mechanisms rather than the only mechanism responsible for a specific type of pain.

The present study was designed to investigate the cause of the commonest type of pain in duodenal ulcer—namely, epigastric pain. The classical teaching is that epigastric pain and tenderness arise from a duodenal ulcer whereas retrosternal pain is caused by reflux oesophagitis; but this is not completely true. Epigastric pain can also be produced by balloon distension of the lower oesophagus in most normal people (Polland and Bloomfield, 1931), and acid perfusion of the lower oesophagus in the original Bernstein test for oesophagitis caused in many instances epigastric pain (Bernstein and Baker, 1958). Those two studies and the present one have shown that epigastric pain can arise from the lower oesophagus. The gastro-oesophageal junction in the present series of patients was situated in its normal position and was not displaced to form a hiatal hernia as in the original Bernstein test. This suggests that if the lower end of the oesophagus is displaced upwards, as in a hiatal hernia, stimulation of the susceptible mucosa will produce retrosternal pain, but if it is situated normally at the diaphragm stimulation may cause epigastric pain.

In this study no oesophagoscopy or histological investigations were made to establish whether reflux oesophagitis was present. The accurate localization of the perfusion was considered sufficient evidence that the pain arose from the oesophagus and not from the stomach. In addition, when this test was performed on patients with a full stomach after a meal the same results were obtained, which would not have been possible if the pH of all the contents had to be changed as well. In contrast with those experiments in which 200-600 ml. of acid was instilled into the stomach pain was reproduced by 30 ml. of O.1N HCl in this study, and the time taken for pain to occur was also far less—under four minutes with oesophageal acid compared with up to 30 minutes with gastric acid. It would therefore seem that gastric acidity is not so important as oesophageal acidity in the production of epigastric pain. Those experiments where pain was reproduced by instillation of acid into the duodenum may have produced pain in a site other than the epigastrium. Similarly those experiments in which pain was associated with gastric motility can be explained by different sites of pain, so the present theory does not necessarily exclude other causes of duodenal ulcer pain.

It is suggested that the epigastric pain of duodenal ulcer may be best explained by the reflux of acid gastric contents on to the lower oesophagus. If pain arises from the lower oesophageal mucosa it would explain why pain may disappear even though an ulcer is seen to be active radiologically and would clarify why small doses of antacid quickly produce relief of pain without altering the pH of all the gastric contents. If the actual pain came from the oesophagus and not the duodenum it would also explain why there is epigastric tenderness on deep palpation in many patients who have no tenderness over the site of the duodenal ulcer itself. Finally, the close clinical relationship between retrosternal and epigastric pain would be more explicable if they were both associated with acid regurgitation into the oesophagus.

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