Symposium on gastrooesophageal reflux and its complications¹

The symposium aims to present new concepts and provide a plausible working hypothesis as a basis for diagnostic and management decisions.

Section 1 Definitions, the antireflux mechanism, and symptoms

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Definitions

'Hiatal herniation' is a radiological definition or a finding at operation and is not necessarily a permanent anatomical state. Herniation really means the 'capacity to herniate', because in most people found to have a hiatal hernia, most of the time the stomach is not herniated. It herniates only when intraabdominal pressure is increased or in certain positions, which is one reason why herniation may be missed by the radiologist yet seen by the endoscopist or manometrist who examine the supine patient. Herniation in these people is intermittent. Sometimes (see section 3) part of the stomach remains in the chest when the subject stands up. This continuous herniation is rarely missed by the radiologist and the patient is most likely to be sent to the surgeon.

Reflux is the flow of gastric contents into the oesophagus. The capacity to reflux depends on the competency of the antireflux mechanism at a particular moment in time. The antireflux mechanism may be continuously incompetent or intermittently incompetent. If continuously incompetent, it will fail at any time if challenged, and, therefore, during an x-ray examination we can see barium enter the oesophagus. Because continuous incompetency commonly causes reflux symptoms when we lie down or bend over, I have called it the 'recliner's radiological reflux' syndrome.

In other people the antireflux mechanism is intermittently incompetent. Most of the time, when challenged, it prevents reflux but intermittently the

mechanism becomes incompetent for a moment and reflux may then occur. Unless we happen to take radiographs at the precise moment that the antireflux mechanism is incompetent we do not see barium enter the oesophagus. Incompetency must occur because we feel or taste the refluxed material, and we can detect it with a pH electrode in the oesophagus (Tuttle and Grossman, 1958; Patrick, 1970). Most normal people reflux intermittently. The volume which refluxes is difficult to measure, but reflux seems to occur in short spurts, and especially soon after meals (Patrick, 1970). Sometimes reflux is so violent that gastric contents reach the mouth.

Reflux occurs in the standing and sitting positions in the group we are discussing and is not consistently provoked by lying down or bending or increasing intraabdominal pressure, but if we happen to be bending or lying or lifting something when the intermittent incompetency occurs the volume which refluxes seems likely to be greater. Because the symptoms are particularly troublesome after fatty food I have called intermittent incompetency the 'hot fat-heartburn' syndrome to distinguish it from the recliner's reflux syndrome of continuous incompetency.

Intermittent incompetency is a problem because we cannot demonstrate it with barium, but it can produce both unpleasant symptoms and histologically recognizable changes in the oesophageal mucosa. The diagnosis of 'hot fat-heartburn' depends, therefore, on the recognition and reproduction of the symptom pattern and not on radiology; it can be confirmed only by pH electrode or by biopsy and then only if the mucosa is damaged enough (see section 5).

¹This symposium was given at the annual meeting of the British Society of Gastroenterology at Aviemore in September 1972.

The Antireflux Mechanism

THE ABDOMINAL SPHINCTER SEGMENT HYPOTHESIS

What follows is a working hypothesis which is not proven but fits clinical, radiological, and experimental observations at least as well as any other hypothesis. When the stomach is in its normal position the bottom end of the cardiac sphincter is in the abdomen (fig. 1). An increase of abdominal pressure squeezes the stomach but the hypothesis supposes that it also squeezes the sphincter, so that the sphincter is not challenged. If contraction of the stomach wall makes the stomach squeeze harder than the sphincter, the sphincter will be opened and stomach contents can go up the oesophagus. This may be the mechanism of intermittent incompetency. The challenge comes from stomach squeeze and has nothing to do with posture or abdominal squeeze so we would not expect them to induce reflux. If the battle is between sphincter squeeze and stomach squeeze we might find a partial correlation between a manometric estimate of sphincter squeeze and symptoms of reflux.

Anything which increases stomach squeeze or decreases sphincter squeeze, either continuously or intermittently, would increase the possibility of reflux. Endogenous gastrin influences the sphincter squeeze, and a fall in serum gastrin concentration induced by acidification of the antrum is accompanied by a decrease in sphincter squeeze (Castell and Harris, 1970). An increase in serum secretin, produced by the presence of acid or of fat in the duodenum, is also accompanied by a decrease in sphincter squeeze (Cohen and Lipshutz, 1971). These changes might be the mechanism of 'hot fat-heartburn'. Conversely, alkalinization of the antrum increases serum gastrin concentration and is accom-

panied by an increase in sphincter squeeze. This might be part of the mechanism of the relief of heartburn by alkali (Castell and Levine, 1971) (see section 4). We do not know much about changes in stomach squeeze after a meal.

When herniation occurs the abdominal section of the sphincter is lost and either of two conditions occurs, depending on the size of the hole at the hiatus. If the hole is small (fig. 1b) the walls of the hiatus squeeze and empty the neck of stomach going through it. Abdominal pressure cannot increase unless the diaphragm contracts, which usually means that the neck of stomach going through the hiatus is squeezed more firmly by the hiatal margins. Abdominal pressure squeezes the stomach, but it also squeezes the empty neck of stomach so that scarcely any stomach contents flow into the herniated part and pressure is not transmitted from abdominal to thoracic stomach. I have called this the 'competent hiatus' (Edwards, 1961). It is important in radiology because barium does not flow from abdominal to thoracic stomach and the herniation may be missed (see section 3). The sphincter squeeze only has to withstand the squeeze of the thoracic stomach when these conditions apply, so we should expect that intermittent incompetency would predominate.

On the other hand, if the hiatus is big, the neck of stomach going through the hiatus is unlikely to be squeezed, contents flow, and pressure is transmitted into the herniated stomach (fig. 1c). This is the 'incompetent hiatus' (Edwards, 1961) (see section 3). If the herniation is small the squeeze in the herniated stomach will be nearly as high as the abdominal squeeze. If the herniation is large most of the stomach contents can flow into the thoracic stomach without raising the pressure much and the challenge to the sphincter squeeze will be less than it is with a small herniation (see section 3).

Fig. 1a Stomach in the normal position.

Fig. 1b Herniation through a small hole.

Fig. 1c Herniation through a large hole.

When the hiatus is large, the sphincter squeeze has to withstand a range of pressures. The same battle between sphincter squeeze and stomach squeeze would still cause intermittent incompetency with symptoms predominantly related to type of food and time after food, but, in addition, the sphincter squeeze has to battle with abdominal squeeze. If the yield pressure of the sphincter is about 20 cm water it should withstand pressures up to this but fail when challenged with higher pressures. If abdominal squeeze, caused by lifting or bending, or the sheer weight of abdominal contents when lying down, is greater than sphincter squeeze the sphincter will lose the battle against abdominal squeeze and reflux could occur. We would again expect a partial correlation between symptoms and the strength of sphincter squeeze. This may be the mechanism of continuous incompetency which seems to be related to herniation (see below).

The predictions about treatment from this hypothesis are that when intermittent incompetency is the problem, management should concentrate on increasing sphincter squeeze (see section 4), decreasing stomach squeeze, and decreasing the acidity of what comes up. Postural treatment is unnecessary except at the time when intermittent incompetency occurs.

On the other hand, if continuous incompetency is present, medical treatment can only attempt to reduce the challenge to the sphincter by avoiding an increase in abdominal squeeze, and to reduce the acidity of what comes up (see section 5). Increasing sphincter squeeze may help a little, but it will not help the mechanical problem of free transmission of abdominal squeeze to challenge the herniated sphincter. This mechanical problem could only be solved by returning the lower part of the sphincter to the abdomen and maintaining it there in such a way (a) that the hiatus is small and gently compresses the oesophagus, and (b) that abdominal squeeze acts on the outside of the sphincter (see section 6).

THE SPHINCTER ALONE HYPOTHESIS

Another hypothesis (Lind, Warrian, and Wankling, 1966; Cohen and Harris, 1971) postulates that reflux is prevented solely by the sphincter squeeze, whether the sphincter is herniated or not. The sphincter is supposed to contract in proportion to its basal tone in response to a challenge to open it. If the basal tone is high the sphincter will contract more than the challenge, but if the basal tone is low it will contract less than the challenge, and reflux will follow. A complete correlation between symptoms and basal sphincter squeeze has been claimed by several authors (Winans and Harris, 1967; Pope, 1967) so that this hypothesis predicts that to determine

whether reflux is occurring it is only necessary to measure the sphincter squeeze. A 'good' sphincter would not allow reflux, and a 'bad' one would (see section 4). However, changes in the concentration of circulating gastrointestinal hormones cause changes in the basal tone and, by inference, the response of the sphincter to a challenge (see section 4). Therefore the tone of the sphincter at the time of its measurement by manometry may not be the same as its tone after a meal. At University College Hospital and Central Middlesex Hospital we do not find a complete correlation between sphincter tone and symptoms and I am not convinced that this hypothesis is true.

An important prediction of the 'sphincter alone' hypothesis is that herniation has nothing to do with reflux, and therefore there is no point in repairing a hernia because if the sphincter is a poor one it will not work any better when returned to the stomach than it does when it is in the chest. There are two pieces of circumstantial evidence which suggest that this prediction of the hypothesis is incorrect. First, I am sure that most of us feel that there is some connexion between herniation and reflux. Peptic stricture is the manifestation of the most vicious reflux and in my personal experience of 170 patients with a peptic stricture, every one of them had radiological evidence of the capacity to herniate and to reflux. My own experience of screening several thousands of patients with symptoms of reflux is that it is most unusual to see barium reflux without demonstrating the capacity to herniate, and I suspect that continuous incompetency nearly always needs the capacity to herniate. Secondly, surgeons do sometimes succeed in stopping continuous incompetency by repairing a hernia and creating an intraabdominal segment of oesophagus (see section 6). Perhaps they are creating an additional antireflux mechanism.

Symptoms

HERNIATION

The movement of stomach in and out of the chest does not produce symptoms and even large herniations rarely cause any respiratory or cardiac embarrassment. We do not feel the sudden herniation that occurs as we bend over, and we do not feel barium flowing into the oesophagus if we reflux during an x-ray examination. When the amount of stomach in the chest is very large, torsion of the stomach may occur and if severe there may be bouts of lower chest or upper abdominal pain which characteristically switch on and off with dramatic suddenness (see section 3).

REFLUX

Symptoms from gastrooesophageal reflux are of two kinds: (1) regurgitation and rumination and (2) heartburn and paraesthesiae. Regurgitation, which is the flow of something from oesophagus to mouth, and rumination, which is the projection of stomach contents into the mouth without vomiting, are most commonly called 'vomiting' by the patient and frequently misinterpreted as such by the doctor. Since their mechanism and implications are so different it is particularly important to establish which occurs, and whether regurgitation is so nauseating that it is followed by vomiting (see section 5).

Heartburn and the paraesthesiae of a lump in the throat, or that food is sitting like a lump in the chest, seem to arise where there is a combination of two events. First, the mucosa must be hypersensitive, perhaps because the epithelial layer is thinner or more pervious (see section 2) or the stimulus is applied for an unusually long time. Almost certainly a normal mucosa does not give rise to symptoms unless the stimulus is applied for a long time (see section 2).

Secondly, the stimulus must be sufficiently vicious. Hypersensitivity is greatest to hydrogen ions, so the acidity of the refluxing gastric contents must be above a critical level. Hypersensitivity to heat and to alcohol causes the patients to let their tea or their coffee get cold and to give up gin; otherwise it burns as it goes down (see section 5). A mucosa which is hypersensitive to heat or alcohol will also be hypersensitive to acid. The effect of hot tea or alcohol is a good, simple, cheap test. The acid infusion test (Bernstein and Baker, 1958; Bennett and Atkinson, 1966b) also tells us whether the mucosa is hypersensitive (see section 5) and the duration of infusion gives some indication of the degree of sensitivity.

Reflux does not produce symptoms, therefore, unless the mucosa is abnormal and the refluxing material is sufficiently obnoxious; so it is possible to have reflux from either intermittent or continuous incompetency and yet not have any symptoms; and it is also possible to have symptoms and no radiologically visible reflux (see section 3). It is possible, too, to have an abnormal mucosa and not have any symptoms because what comes up or goes down does not stimulate the nerve endings.

Heartburn and hypersensitivity to acid, heat, and alcohol are not synonymous with oesophagitis, and unpleasant symptoms are common in people with minimal histological change in the mucosa (see section 2).

STRICTURES

Many radiologists and many endoscopists miss early

strictures, but they have a characteristic symptom pattern by which they can be diagnosed with accuracy and confidence. We should be able to tell the radiologist that bolus obstruction occurs so that he knows what to look for (see section 3).

A stricture is a zone of increased resistance to stretch that obstructs the passage of food, but is still an open channel which allows liquid to flow easily. The patient can drink normally but if food sticks it does so within a few seconds of swallowing, and provokes pain or discomfort or a choking sensation which persists until the food either passes through or is regurgitated. The patient often calls it a 'spasm' or complains that he 'vomits' when he eats.

In a ring stricture the inelastic zone may seem to be no more than the junction of oesophageal squamous and gastric columnar epithelium which in some people can be responsible for very distressing symptoms (see section 2). On the radiograph it looks as though someone has tied a piece of string loosely around the gullet at the junction of columnar and squamous epithelium (fig. 2) (see section 3). The mucosa is usually not hypersensitive and the ring stretches in front of the endoscope which passes through it without any appreciable resistance, so that the endoscopist reports that the gullet is normal, and when the endoscope is withdrawn it leaves the ring as unyielding to food as before. These rings are often attributed to spasm but have nothing to do with muscle contraction. They have many names including 'Schatzki' ring (Schatzki, 1963) 'A' ring (Wolf, 1967), and 'contractile' ring. They raise the question of what is a stricture—is it something that we cannot get the oesophagoscope through or is it anything that holds up food but not liquid. I think we should base our nomenclature on what the patient suffers and not on pathology or endoscopy. The magnitude and direction of the forces acting on a bolus of food are very different from those at the end of an oesophagoscope or bougie.

Fig. 2 Diagram of the inelastic zone at the junction of squamous and columnar epithelium in a ring stricture.

If the oesophageal wall is stiffened by oedema and early inflammatory changes a bolus of food or liquid that stretches the wall may provoke discomfort or pain for a few seconds as it passes by, but it always goes through. If the food is held up for more than a few seconds and sometimes will not go through, and there is a hypersensitive mucosa, then I suspect that irreversible damage to the wall has occurred. One of the questions we ought to be think-

ing about is, 'What is reversible, and what is irreversible histological change?' Irreversible change means a degree of stiffening of the oesophageal wall that produces dysphagia and, even if a surgical repair succeeds in stopping reflux, the dysphagia usually remains (see section 6). If we could define the stage before this point of no return we could say that surgery is now urgently indicated, at least to stop stricturing.

Section 2 The spectrum of pathological change

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Normal oesophageal mucosa consists of three layers: (1) squamous epithelium, (2) lamina propria, and (3) muscularis mucosae. The epithelium has a thin basal zone of several layers of basophilic cells with dark nuclei; beyond this are the stratified squamous cells. The basal zone normally occupies 10% of the total thickness of the epithelium (Ismail-Beigi, Horton, and Pope, 1970). The papillae of lamina propria extend less than 66% of the distance to the surface of the epithelium (fig. 3). The measurements are made using a micrometer eyepiece or by visual estimation. Small numbers of lymphocytes and plasma cells are present in the lamina propria together with occasional lymphoid aggregates.

Until recently the histological criteria for 'oesophagitis' were what the pathologist means by inflammation, namely, hyperaemia, oedema, infiltration with neutrophils, lymphocytes, and plasma cells, and fibrosis. Erosion of the epithelium, baring of the tops of the papillae with their extensive capillary bed, leading to haemorrhage and to ulceration, are characteristic. The inflammatory reaction may be limited to the outer part of the lamina propria or may extend into its deeper layers or even into the muscularis mucosae (Palmer, 1955, 1968; Peters, 1955; Lodge, 1955; Sandry, 1962).

Recently Ismail-Beigi *et al* (1970) have described new histological criteria for the assessment of earlier changes which take place predominantly in the epithelial layers. There is hyperplasia of the basal cell layer which constitutes 15 to 80% or more of the total thickness (fig. 4). More nuclei are present and the impression is of proliferation and a

faster turnover of the basal cells. The squamous layer is correspondingly thinned and may be non-existent. The papillae of the lamina propria are elongated towards the epithelial surface, extending beyond the normal 66%, and may show increased vascularity. There may be a few neutrophils in the lamina propria or in the epithelium in some of these mildly abnormal biopsies but the characteristic feature of this stage of damage is the absence of the classical signs of an inflammatory process: the changes are limited to the proportions of basal and squamous cells, and to the relative length of the papillae.

Ismail-Beigi *et al* (1970) found that three observers were in complete agreement in 80% of their biopsies using these criteria and when histological assessment was without knowledge of the clinical picture or the endoscopic appearance. They consider that blind assessment is essential. They found these changes in 85% of biopsies from patients with symptoms from reflux, a very much better correlation of histology with symptoms than that obtained by most authors who have used the 'inflammatory response' criteria for a diagnosis of 'oesophagitis'; nevertheless it must be remembered that two of 21 control subjects without symptoms had these abnormal changes.

These new criteria provide a much more sensitive index of an early or mild pathological change which seems likely to be reversible and scarcely merits the term 'oesophagitis'. Ismail-Beigi *et al* (1970) consider that the histological features suggest the possibility of an increased rate of loss and replacement of squamous epithelium in the presence of