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THE PSEUDOSTENOTIC SYNDROME

OBSERVATIONS ON INTERMITTENT DYSPEPSIA WITH AND WITHOUT PEPTIC ULCER

BY

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The cyclical pattern of dyspepsia in association with peptic ulcer has long been recognized but never satisfactorily explained, and it is well known that symptoms and radiological demonstration of a crater do not go hand in hand. Fifty-two patients with so-called ulcer symptoms were observed over a period of five to seven years. During this time they had intermittent medical treatment and repeated x-ray examinations. While the majority had the classical clinical and radiological features of peptic ulcer, some had also intermittent signs of duodenal ileus with or without ulcer pain. This led me to study the symptoms and x-ray signs of dyspepsia *per se* rather than as typical or atypical manifestations of an ulcer process.

It at once became obvious that in many patients there were two forms of discomfort: (1) the so-called ulcer pain relieved by eating, and (2) distension pain, sub-sternal and epigastric, the latter aggravated by eating and relieved by vomiting.

A master chart of the 52 patients clearly showed that these two types of symptoms were quite independent of each other, and that the current assumption that all dyspeptic signs in patients with recurrent peptic ulceration are associated with ulcer was probably false.

The pain of an ulcer is readily explained as being due to peritoneal irritation (analogous to pleural pain) or arterial occlusion, or to both. Distension pain has been ascribed, for want of a better explanation, to spasm. The distension symptoms are symptoms of intermittent obstruction, and careful examination of the x-ray findings during attacks of distension invariably reveal abnormalities of the mucosal pattern. These abnormalities consist of thickened or raised mucosa invaginating into the oesophagus at the cardia or across the pylorus into the duodenum. In many instances there were similar abnormal mucosal projections in the second and third

parts of the duodenum, and the appearances on screening corresponded to what has often been described as pendulum peristalsis.

When the x-ray appearances were correlated with the symptoms it was clear that, while ulcer pain was concomitant with a crater and changes characteristic of activity in the adjoining mucosal pattern, distension pain was associated with disordered mucosal pattern at the cardia and/or the pylorus. Both types of pain could occur together, but quite often they occurred independently. For convenience of description I refer to the latter as "pseudostenotic dyspepsia." The symptoms of pseudostenotic dyspepsia have not previously been described as an entity and merit detailed description.

Symptoms

1. Symptoms Attributed to Distension of Lower End of Oesophagus.—These comprise heartburn, acid regurgitation, waterbrash, hiccup, a sense of weight or distension over the xiphoid, substernal pain radiating to the back, towards the right or left scapula, and severe substernal pain radiating to one or both shoulders or mandible and resembling the pain of angina or of gall-bladder colic. Pseudostenotic dyspepsia at the cardia might start at any time: before, after, or even during a meal. But when already hanging fire the attacks would in most cases be evoked by sitting for some time in a hunched-up position—for example, driving a long distance; by a cold and fizzy drink; by eating very fast or having a large meal; or, very typically, by the recumbent position. Eating in a hunched-up position or bending forwards after a meal were found to be particularly apt to bring on the symptoms during the day. Some patients found relief from the pain or discomfort by walking, deep diaphragmatic breathing, taking bicarbonate of soda, or sipping warm water. Some experienced only the less distressing symptoms, but those who suffered from the more severe symptoms knew, without exception, the entire range from slight to severe.

2. Symptoms Attributed to Distension of Pyloric Antrum.—These include epigastric bloating after meals, belching, and nausea in the milder cases; and attacks of epigastric discomfort beginning about an hour after eating and increasing—sometimes accompanied by colic-like pains—until relief was obtained by spontaneous or self-induced vomiting in the severe cases. (It is interesting that the substance of the vomitus was only rarely the undigested meal and that it rarely contained free HCl; more often it was a clear bilious liquid.) In some cases the attacks began with localized pain in the epigastrium, similar to the typical pain experienced in duodenal ulceration. But in one patient with a duodenal ulcer the attacks started with a deep pin-pointed pain almost on swallowing the first bite of food and always before finishing the first course.

In some patients suffering from pseudostenotic dyspepsia one of the above types of symptom would be predominant for a while and then give way in favour of the other.

Unlike ulcer dyspepsia, which is a clearly cyclic disturbance, pseudostenotic dyspepsia does not seem to have any inherent rhythm, but occurs in what may be described as spikes or bursts of spikes on a graph which seems in some patients, who suffer also from recurrent peptic ulceration, to be superimposed on the rhythmic wave-motion of the ulcer activity.

No tendency to persist was observed, nor was there any predictable minimum spell of immunity as there seems to be in peptic ulcer. In the more severe cases of pyloric (epigastric) distension the symptoms were often very severe for a few days, then entirely absent for the next few days; then they returned. The duration of the symptoms in an attack ranged from seconds to several hours and seemed to be in proportion to their intensity. In many instances pseudostenotic dyspepsia followed closely on situations of strain. Several patients undergoing severe mental and emotional stress suffered from acute pseudostenotic dyspepsia which

was resistant to medical treatment but which disappeared spontaneously as soon as the strain situation was resolved. The association of an obvious stress situation with the onset or termination of ulcer pain was, contrary to widespread current opinion, not observed in the patients of this series.

Radiological Signs

The radiological signs generally thought to be secondary to ulcer can be readily correlated with the symptoms, and are as follows.

1. In patients suffering from the pyloric type of pseudostenotic dyspepsia the barium meal showed the typical hollow mushroom appearance of pyloric mucosa prolapsing (invaginating) into the duodenum. Photographs in two patients showed a transition within a few seconds of the pyloric mucosal pattern from the elongated (Fig. 1), which protrudes into the duodenum, to the compressed or contracted, with close, coarse, circular haustration, and vice versa, in the manner of the opening and closing of a collapsible top-hat.

2. In patients suffering from either of the two types of pseudostenotic dyspepsia the contrast meal showed dilated coils of small intestine with pronounced circular haustration, often described as seesaw or concertina pattern. This was observed in the second and third parts of the duodenum and in the jejunum. On screening, the appearances were of a sequence of intermittent changes: hold-up with ballooning of the proximal segment followed by rush peristalsis when the

FIG. 1.—Mucosal invagination at the pylorus.

invisible block was removed. The appearances on screening could be described as "staggered dumping." Distension of the second and third parts of the duodenum was constantly associated with pyloro-duodenal invagination. When the eye got accustomed to watching the staggered dumping in the jejunal coils the impression was gained that what one would previously have described as pendulum peristalsis of the second part of the duodenum were in fact often syncopated phases of staggered dumping in which the rush emptying of the dilated second part (in a distal direction) was followed within a fraction of a second by a jet from the pyloric antrum filling the duodenal cap. These appearances were observed in some or all segments of the small gut from the second part of the duodenum to the jejuno-ileal junction. Often, the localization of the most marked disturbance was found to be constant in the same patient in several examinations at long intervals during spells of pseudo-stenotic dyspepsia.

3. In some, but not in all, patients who had intermittent symptoms of oesophageal distension (cardia type of pseudostenotic dyspepsia) tenting or invagination of the mucosa at the cardia (Fig. 2) into the phrenic canal was demonstrated. In others, it appeared that cardiac prolapse was occurring, but it was difficult to demonstrate because it was transient

owing to the resistance of the hiatus. In one patient who did not at the time complain of pseudostenotic symptoms there was delicate circular haustration of the first, slightly distended coil of the jejunum (Fig. 3) and coarse circular haustration of the (gastric ? oesophageal ?) mucosa for the length of an inch (2.5 cm.) above the cardia. On the following day this patient had, while sitting in a hunched position over a drawing-board after his midday meal, an attack of very acute substernal pain lasting for about an hour. Pyloro-duodenal invagination was never observed in patients who did not at the time complain of symptoms attributed to distension of the pyloric antrum. Although a tenting or prolapse of cardiac mucosa into the oesophagus could not always be demonstrated in patients suffering from symptoms attributed to distension of the phrenic end of the oesophagus, it was never observed in patients who were free from these symptoms. The alteration of mucosal pattern and motility of the small intestine described as staggered dumping was invariably associated with both types of pseudostenotic dyspepsia. It was not observed in patients who were free from distension symptoms.

Suggested Explanation of Motor Mechanism Involved in Pseudostenotic Dyspepsia

This disturbance of motility is independent of the tone and the emptying time of the stomach. It is seen to be associated with hypertonicity, as well as by hypotonicity of the stomach; nor is the speed of the meal's progression through the small intestine an index of the emptying time of the stomach: the head of the meal may reach the caecum within an hour and gastric evacuation yet be retarded.

The observations suggest that in some individuals the muscularis mucosae of the cardiac region and from the pyloric antrum to the jejuno-ileal junction reacts to "stress" by abandoning its normal manner of functioning in multiple and independent local units, gathered and disbanded ad hoc in response to chemical and mechanical stimuli, to act as an integrated larger unit. It moulds itself into a spiral ridge (the outer mould of an Archimedean screw) to provide a runway for the ingested matter, and, in order to protect its transportation further from the vagaries of the highly nervous and excitable outer muscular tube

FIG. 2.—Mucosal invagination at the cardia.

FIG. 3.—The spiral spring effect—the first loop of the jejunum.

(muscularis propria) in this vital segment of the digestive tract, it also provides a peristaltic mechanism of its own. This it does by segment-wise and alternate contraction and relaxation of its now spirally orientated fibres, so that the systole of one segment coincides with the diastole of the preceding and subsequent segments. It thus acts as a helical spring, or a battery of helical springs pumping the meal in a downward direction.

This auxiliary and compensatory peristaltic mechanism is efficient up to a point, but it also carries the risks of its imperfection. As had been demonstrated already by Gösta Forssell, the mucosa of the stomach may move, actively, almost as independently from the muscular coat proper as can, passively, the unattached lining of a glove.

Without this freedom of the mucosa to move as if semi-detached from its base it could not act as an auxiliary or compensatory organ of peristalsis. Because of this there are two major flaws in the otherwise ingenious device: (1) The systole of a given segment pulls the adjacent part of the neighbouring proximal and distal segments, which are in diastole, towards and into itself. (This too might appear, on screening, as antiperistalsis.) (2) In the same way, the systole at one of the two anatomical straits (cardia and pylorus) tends to pull the mucosa of the neighbouring and wider diastolic segment into itself; the gastric mucosa being pulled, in the case of the cardia, towards the oesophagus, and in the case of the pyloric canal towards the duodenum. This is like trying to pull a paper filter in a funnel into its narrow tubular section, and is likely to cause a—temporary—obstruction. If the stomach reacts with increased secretion and peristalsis, this only worsens the position by forcing its contents under pressure in the direction of the prolapse.

In addition, the circular contraction of the pyloric muscle and the clamplike action of the crura of the diaphragm may interfere with the blood supply of the prolapsed mucosa, causing congestion and pain and hindering its return to normal position.

This hypothesis would also explain, in severe degrees of pseudostenotic dyspepsia, the failure of treatment with drugs which inhibit parasympathetic ganglionic transmission or the parasympathetic nerve-endings.

The integrated action of normally autonomous units suggests, however, some kind of central control directing spiral-spring peristalsis. Harvey Cushing's (1932) experiments and observations on the effect of intraventricular injections of pituitrin and pilocarpine in man—he describes hyperperistalsis followed by antiperistalsis and vomiting—may possibly indicate where and what type of control one should be looking for.

Further support for this theory comes also from the work of Bergmann (1932), Ritvo (1936), and Farah and Pinkston (1940) on mucosal prolapse and on the effect of large doses of amphetamine on duodeno-jejunal hyperperistalsis, which was not inhibited by atropine and allied drugs.

Conclusion

Apart from sharing some of the playground, peptic ulceration and mucosal dyskinesia seem to have little in common. Peptic ulceration and ulcer dyspepsia tend to occur periodically and in discrete attacks of regular duration. The incidence of these attacks is perhaps as much determined by the time of the year as by anything else, and the morbid anatomy is consistent with the occlusion of a small end-artery. Pseudostenotic dyspepsia, on the other hand, shows all shades and degrees of periodic but irregular incidence and duration; it affects the entire muscularis mucosae and seems far more clearly related to emotional, dietary, and postural factors.

If this hypothesis be correct, it calls for a new approach in treatment. Because of the psychological

effects of any new treatment in dyspeptics this cannot be done within the limited resources of a private practice, but its value could readily and quickly be assessed by a large-scale hospital survey.

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BENETHAMINE PENICILLIN

A STUDY OF ITS USE IN A CLINIC FOR SEPTIC HANDS

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The use of penicillin has revolutionized the treatment of hand sepsis, and there is little doubt that it is the antibiotic of choice in infections with penicillin-sensitive organisms. We agree with Lowden (1953) that the clinical results justify its retention generally in spite of the increased incidence of penicillin-resistant staphylococci reported from several clinics. A recent analysis of our cases of septic hands has shown that 95.9% are due to *Staphylococcus pyogenes* and that 23% of these are showing an *in vitro* resistance to penicillin (Williams *et al.*, 1955). The tendency of general practitioners to give the broad-range antibiotics for septic hands without laboratory facilities should be discouraged. Apart from increasing the population of resistant organisms and the consequent loss of valuable therapeutic agents for more dangerous conditions, their indiscriminate use has already produced a number of reports of superinfection, fatal gastro-enteritis, and bone-marrow depression. It is our policy to limit the administration of the broad-range antibiotics to cases making unsatisfactory progress and where the sensitivity pattern is known.

The Investigation

Having accepted the view that penicillin is the first line of defence in hand sepsis, we made an investigation to discover the most satisfactory method of administration in a clinic dealing with 400 new cases a month. The following preparations have been tried: crystalline penicillin, oral penicillin, procaine penicillin, and benethamine penicillin.

Crystalline Penicillin.—This is the most effective preparation where serious infection is present. In such cases injections are given at frequent intervals—a regime that is not practicable for out patient therapy. Less than 0.5% of all cases attending this clinic have septic hands severe enough to warrant admission to hospital.

Oral Penicillin—Self-administered.—Despite its obvious advantages, not all patients can be relied upon to take it. Minor gastro-intestinal upsets are not infrequent. A trial in conjunction with serum assay levels was carried out in this department, and our results, which were similar to those