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 thinking 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 nonexistent. 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
reflux. The close correlation with symptoms of heartburn suggests that the closer proximity of the tips of the papillae to the surface of the epithelium by the lengthening of the papillae and reduction of the squamous layer may bring chemoreceptors or nerve fibres closer to the surface. This might be a possible mechanism for the production of heartburn and the hypersensitivity of the mucosa to acid, heat, and alcohol (see sections 1 and 5).

The correlation between histology and endoscopy using conventional criteria varies widely from one report to another; for example, Siegel and Hendrix (1963) claimed 72% agreement, Schuman and Rinaldo (1966) 32%, and Cocco (1965) and Ward, Wright, and Leigh-Collis (1970) 56% (and see section 6). Ward et al (1970) concluded that oesophageal biopsy is of little value and that the endoscopic appearance is a better guide. This lack of agreement might be because the criteria are confused or because the parameters to be correlated may have been chosen illogically. It seems clear, for example, that it is possible to have symptoms from the mucosa with detectable changes in the epithelium, but without inflammatory 'oesophagitis'. The colour of the squamous mucosa will depend on the thickness of the squamous layer and on the number and the extent of the dilatation of the capillaries of the papillae. The ease with which bleeding occurs with mild trauma might depend very much on the same phenomena. These endoscopic appearances might perhaps more correctly be correlated with the state of the capillaries, papillae, and epithelium than with the number of neutrophils or other evidence of inflammation (see section 6). There is rarely disagreement between visible ulceration or spontaneous bleeding, and marked cellular infiltration of the lamina propria with ulceration, but it is perhaps unreasonable to equate 'reddening' of the mucosa with 'inflammation'.

An alternative cause for disagreement is that at endoscopy a wider field is surveyed and a general impression gained, whereas a biopsy may not be from the most distorted area which is usually at or just proximal to the mucosal junction. There is often difficulty in obtaining a specimen, and especially one of adequate thickness by the biopsy instruments generally used. For a full assessment of the extent of the inflammatory reaction a biopsy deep enough to include the muscularis mucosae is necessary (Palmer, 1955; Ward et al, 1970) and for the minor changes the biopsy must include the full thickness of the epithelium and some underlying lamina propria. The biopsy must also be spread out and fixed flat like a jejunal biopsy, and sections must be cut in a plane vertical to the surface of the epithelium. Two biopsies are desirable for more
accurate interpretation and can be taken with forceps or by suction.

The value of biopsy in the assessment of peptic stricture is debatable. The biopsy is rarely deep enough, and the hazard of trying to obtain an adequately deep one might be unjustifiable. The changes in stricture depend on the criteria for 'stricture' and the pathologist can only indicate the degree of inflammatory change in the piece of tissue given to him, and the degree and type of healing response, which may yield a clue to the elasticity of the tissue and whether the changes are irreversible. Intact mucosa may be present in the biopsy if mucosal regeneration has occurred, yet at the same time there may be considerable fibrosis in the deeper tissues (Sandry, 1962).

The pathological changes associated with stricture have been described by Sandry (1962) who emphasizes the two types of lesion. When mucosal erosion and oesophagitis occur in the squamous epithelium it is usually most extensive at a level just above the junction of columnar and squamous epithelium. The destruction of tissue never extends deeper than the muscularis mucosa but the interstitial fibrosis is always maximal in the submucosa. The muscle layers are very rarely breached and the neural structures of Auerbach's plexus are intact which may explain why a strictured sphincter segment can contract down to obliterate its lumen, yet will not open to more than a few mm bore (see section 3). Fibrosis is often considerable in the periesophageal tissues. This superficial ulceration tends to extend all round the lumen and there is concentric thickening and fibrosis of the wall producing stenosis. This lesion seems to be the main basis of a stricture.

When the ulceration is deeper it is always localized, well defined, and the distal half at least is surrounded by columnar epithelium. The ulcers resemble a chronic peptic ulcer of the stomach and the tissue destruction may extend through the full thickness of the oesophageal wall, cutting through the muscle layers. These deeper ulcers do not seem to be associated with so much fibrosis in the rest of the circumference although local fibrosis may be considerable. A superficial erosion may be adjacent to a deep ulcer at the junction of the two types of epithelium.

In contrast to these fibromuscular strictures the histological changes are minimal in the 'ring' or 'pseudo stricture' of the Schatzki type (Schatzki, 1963). The ring consists of the junction of squamous and columnar epithelium with a few round cells in the lamina propria (fig. 2) (MacMahon, Schatzki, and Gary, 1958) (see sections 1 and 6). It is easy to see why an oesophagoscopy will pass through without much resistance. There is no local muscle hypertrophy, no annular muscle contraction, rarely any fibrosis, and not much inflammatory tissue. The core is composed of connective tissue, and an overgrowth of muscularis mucosa, with no suggestion of an active or healed inflammatory process in some (MacMahon et al, 1958), but in others (Barrett, 1962) there was fibrous tissue and changes of chronic inflammation extending for a short distance above and below the ring itself.

A significant proportion of biopsies apparently obtained from the oesophagus consist of columnar gastric mucosa of the cardiac type with mucin-secreting glands, or of the fundal type with oxyntic and zymogenic glands. In Sandry's specimens the greatest height reached by gastric mucosa was 4 cm but the usual height was 2 cm proximal to the oesophagogastric junction. The mucosa adjacent to ulcerating lesions was columnar without acid- or pepsin-secreting glands. Healing of the ulcerated mucosa seems almost always to be by the extension of columnar epithelium from that distal to the lesion. The squamo-columnar junction most commonly occurs within a few centimetres of the junction of the tube of oesophagus with the bag of stomach, although it may sometimes lie much higher. It is not surprising therefore that gastric mucosa is found in oesophageal biopsies, and they should not be interpreted as necessarily coming from a herniated part of the stomach. If the epithelium is of cardiac type it is almost certainly from the oesophagus; if it contains acid- and pepsin-secreting cells it is most probably from the stomach, but oxyntic cell glands can appear in regenerated mucosa extending into the lower oesophagus.
Symposium on gastrooesophageal reflux and its complications. 2. The spectrum of pathological change.
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Gut 1973 14: 237-239
doi: 10.1136/gut.14.3.237

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