Gut, 1977, **18**, 295-300

Symptomatic significance of gastric mucosal changes after surgery for peptic ulcer

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SUMMARY Eighty-four patients who had undergone different types of operation for duodenal ulcer have been studied by endoscopy and gastric biopsy. Half suffered from dyspepsia and vomiting but the other half had no symptoms and acted as controls. Endoscopic and histological abnormalities were found in both groups of patients. However, certain findings occurred more commonly in those with symptoms; severe and extensive hyperaemia, bile staining of the gastric mucus, and bile reflux seen on endoscopy were all significantly more common in those with symptoms than in those without. Active gastritis in the proximal stomach was also more common in those with symptoms. Gastritis of the stoma and antrum was found in 89% of all patients; as it was unconnected with symptoms it can be regarded as a 'normal' finding. The incidences of contact bleeding, erosions, and oedema were not significantly different in the two groups.

An abnormal appearance of the gastric mucosa after partial gastrectomy was observed soon after gastroscopes were introduced (Schindler, 1923). Yet the relevance of this is still controversial. Although Cotton *et al.* (1973) thought that hyperaemia was not significant, others (Keighley *et al.*, 1975; O'Neill *et al.*, 1975) have found it more common in patients with symptoms. There is confusion about the nomenclature of these mucosal changes, some authors have referred to the abnormal endoscopic findings as gastritis (Stempien *et al.*, 1971). We have reserved the term gastritis for atrophy or inflammation seen on histological examination of biopsy specimens. The red mucosa seen endoscopically has been called hyperaemia.

Gastritis is seen in histological specimens taken from both symptomatic and asymptomatic patients after gastric operations (Lees and Grandjean, 1958; Benedict, 1960), but is less common in those with recurrent ulcers (Johnston, 1966). Simon *et al.* (1973) found it was more common after Billroth II than Billroth I resections. It is seen more often after operations for gastric than duodenal ulcer (Wall *et al.*, 1967; Aukee and Krohn, 1972), but this may be due to the higher preoperative incidence of gastritis in those with gastric ulcer.

No studies of gastritis and mucosal changes seen endoscopically have yet been performed comparing patients with symptoms with matched controls. We have therefore performed an endoscopic and histological study of 42 patients with dyspepsia and vomiting after gastric surgery and compared them with a group of matched postoperative patients with no symptoms.

Received for publication 2 February 1977

Methods

PATIENTS

Eighty-four patients, who had undergone one operation for proven duodenal ulcer and who had no recurrent ulcer, have been studied. Forty-two of these had no dyspepsia or vomiting. (Thirty-three patients volunteered for endoscopy and nine were investigated for iron deficiency anaemia and were found to have no gastrointestinal cause of blood loss). All the volunteers had undergone a previous endoscopy and informed consent was obtained before the examination. They have been compared with 42 patients drawn from 150 patients referred because of dyspepsia and vomiting after gastric operations. The patients who most closely resembled the control patients were chosen. The two groups were matched for the type of operation, age (within 10 years) and the interval since operation (within two years if the operation was performed less than 10 years ago, or within five years if greater). Oral cholecystograms had been performed on all patients with symptoms

and only those without biliary disease were included. A total of 32 patients had Billroth II partial gastrectomies performed on average 14 years previously (one to 37 years before), 20 had vagotomy and antrectomy all about one year before, 22 had vagotomy and pyloroplasty on average seven years previously (one to 20 years ago), and 10 had proximal gastric vagotomy, all about one year before. The average age was 52 years and 21 were female.

TECHNIQUES

Endoscopy was performed on all patients by one of us (A.M.H.) using an end-viewing Olympus GIF instrument. Assessment was made of the degree of mucosal hyperaemia, bile reflux, bile staining of the mucus on the gastric mucosa, erosions, contact bleeding, oedema, 'granularity' of the mucosa, and veins visible beneath the mucosa. Each factor was graded as absent, mild, moderate, or severe. Bile reflux in this paper refers to reflux seen during endoscopy, or bile seen in the stomach indicating previous reflux. It was considered severe if there was a continuous flow of bile throughout the examination requiring repeated aspiration, and moderate if the stomach was full of bile but only trivial reflux into the stomach occurred after passing the instrument. An endoscopic score has been compiled including the severity and extent of erythema, the presence of a granular mucosa, bile reflux, and bile staining of the mucosa. Each of these factors was graded zero to three and the score was the sum of these grades.

The American Cystoscope Makers spiked forceps were used for taking biopsies. Two were taken from 2·5 and 5 cm from the cardio-oesophageal junction and four from around the stoma or pylorus. In addition, biopsies were obtained 5 and 7·5 cm on the greater curve from the pylorus if partial gastrectomy had not been performed. They were all assessed 'blind' by one of us (E.L.J.) using the criteria of Whitehead *et al.* (1972). The type of mucosa (pyloric, body, or cardiac), grade of gastritis, activity of gastritis, and presence and type of metaplasia (intestinal or pseudo-pyloric) were established. Gastritis was graded as superficial if the inflammatory and reactive changes affected only the superficial epithelium, gastric pit region, and related lamina propria. It was graded as atrophic gastritis when these changes affected the gland layer. Active gastritis was indicated by invasion of polymorphs into epithelial elements of the gastric mucosa associated with degenerative changes.

Except where stated in the text, statistical analysis was performed using the χ^2 test and Fisher's Exact Test when the expected frequencies were less than five.

Results

SYMPTOMS

At the time of endoscopy 39 of the 42 symptomatic patients complained of vomiting, which was bile-stained in 31. Eighteen patients had epigastric pain which was relieved by alkali in six. The pain occurred after meals in 11 patients, and intermittently in the remainder. Twenty-two patients suffered from epigastric discomfort; this occurred after meals in eight and was relieved by alkali in five. The remainder had intermittent discomfort relieved by vomiting in 11. Two patients had symptoms of vomiting without pain or discomfort. Two patients in the 'asymptomatic' group had epigastric fullness after meals, but none complained of epigastric pain, nausea, or vomiting.

ENDOSCOPIC FINDINGS

All of the endoscopic findings (Table 1) were seen in both symptomatic and asymptomatic patients apart from a 'granular mucosa' which was present only in six symptomatic patients. Some findings were significantly more common in those with symptoms than those without them: severe and extensive hyperaemia ($P < 0.01$), severe bile reflux ($P < 0.025$), bile staining ($P < 0.001$), and a granular mucosa ($P < 0.05$). Bile staining and a granular mucosa occurred only in patients with severe bile reflux, and

Table 1 *Endoscopic findings*

	Asymptomatic (42)	*Symptomatic* (42)
Hyperaemia		
None	4	0
Mild	10	10
Moderate	19	14
Severe	9	18
Extent hyperaemia		
Stomal	20	14
Mid-stomach	12	15
Total	6	13
Bile reflux		
None	6	3
Mild	7	7
Moderate	19	11
Severe	10	21
Bile staining		
Absent	39	22
Present	3	20
Granularity		
Absent	42	36
Present	0	6
Contact bleeding		
Absent	26	30
Present	16	12
Oedema		
Absent	31	38
Present	11	4
Erosions		
Absent	33	33
Present	9	9

Number of patients in parentheses.

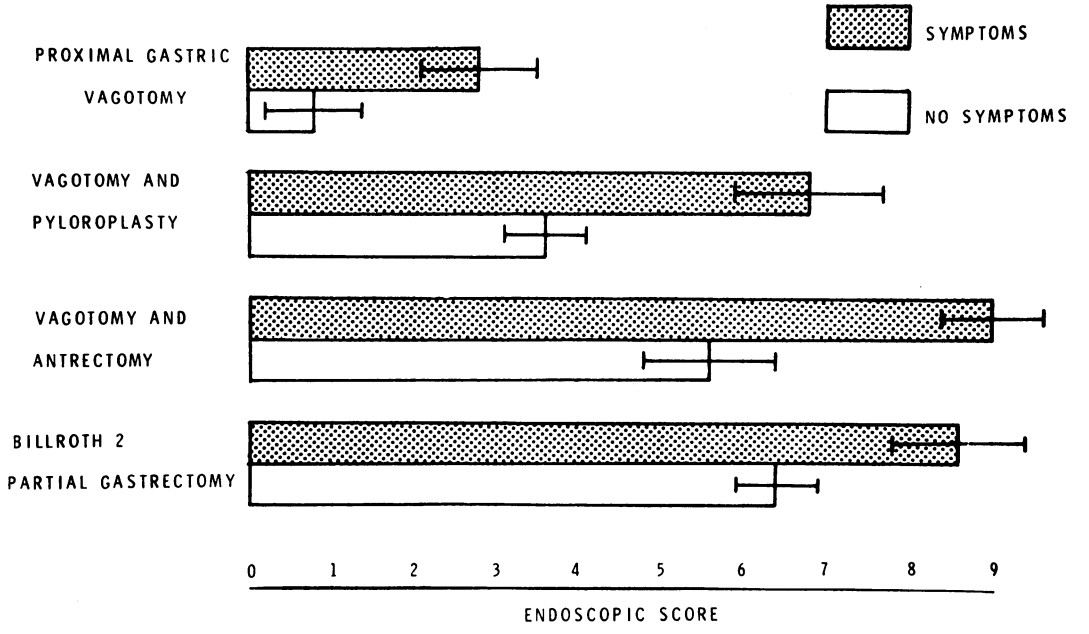

Fig. 1 *'Endoscopic score' in patients with and without symptoms after four gastric operations*

the severity and extent of hyperaemia correlated with bile reflux ($P < 0.002$ using Spearman's rank correlation coefficient).

The average endoscopic scores of symptomatic patients are higher than those of the patients without symptoms (Fig. 1). Using the Sign test the differences are significant for patients after Billroth II partial gastrectomy ($P < 0.05$), vagotomy and antrectomy ($P < 0.02$), and vagotomy and pyloroplasty ($P < 0.05$), and for all patients ($P < 0.0001$).

HISTOLOGICAL APPEARANCE

Atrophic gastritis was recognised in biopsies from the antrum or stoma in 45 patients (54%). In all patients with atrophic gastritis the intervening lamina propria showed a heavy infiltrate of plasma cells and frequently contained large lymphoid follicles (Fig. 2). In 27 patients atrophic gastritis was seen in biopsies from the antrum or around the stoma but not in those from the proximal stomach.

The appearances of biopsies from the antrum or stoma are shown in Table 2. There was no correlation between symptoms and the presence of atrophic gastritis or chronic superficial gastritis. 'Active' gastritis with focal collections of polymorphs within the gland lumen and invasion of the gland epithelium (Fig. 3) was seen in 26 patients. Polymorphs in the gastric pits, mimicking the appearance of crypt abscesses in ulcerative colitis, were also seen in these patients (Fig. 4). Active gastritis in the distal stomach was more common in patients with symptoms than those without, but the differences were not statistically significant. Intestinal metaplasia was seen in at least one biopsy in 10 patients with dyspepsia and vomiting and six without such symptoms. The surface mucosa was covered by projecting pseudovilli lined by small intestinal absorptive cells and frequent globlet cells (Fig. 5).

The results of histological examination of biopsies taken high on the lesser curve are shown in Table 3. After Billroth II partial gastrectomy and vagotomy and antrectomy atrophic gastritis was commoner in symptomatic patients than in those without symptoms. The differences between the symptomatic and asymptomatic patients are significant when Billroth II partial gastrectomy and vagotomy and antrectomy are considered together ($P < 0.05$). They are not significant for all operations or any individual operation. Active gastritis in the proximal stomach was found significantly more frequently in those with symptoms than those without ($P < 0.01$).

Active gastritis was found only in those patients with severe bile reflux and an endoscopic 'score' greater than 7. All those with a granular mucosa on endoscopy had active gastritis. After Billroth II partial gastrectomy and vagotomy and antrectomy atrophic gastritis was more often found in those with severe bile reflux, but the correlation is not

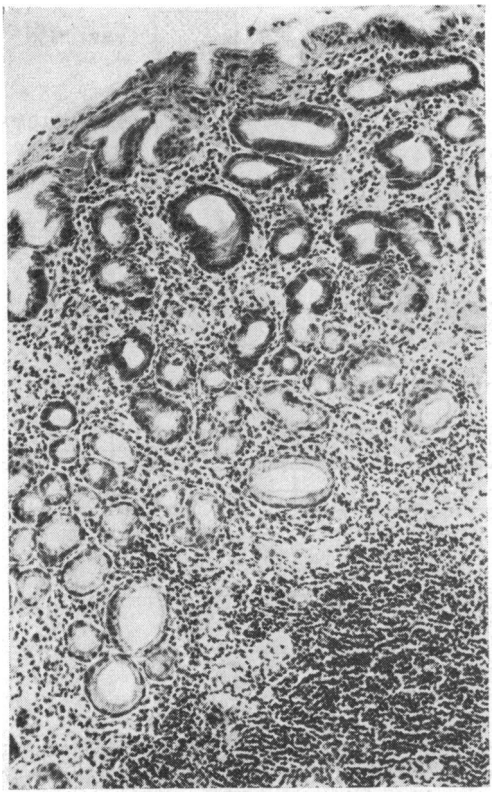

Fig. 2 *Gastric stoma. Atrophic gastritis showing loss of tubules, degeneration, and atrophy of others associated with a diffuse chronic inflammatory cell infiltrate and lymphoid follicle. H and E, × 120*

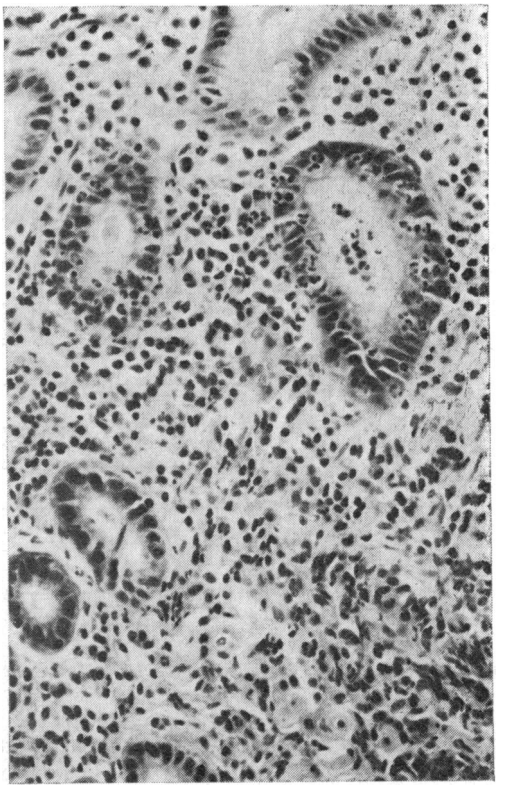

Fig. 3 *Pyloric mucosal glands. Polymorph infiltrate of lamina propria and glands. H and E, × 300*

Table 2 *Gastritis of stoma or antrum*

			Gastritis		
	Number	*Normal*	*Superficial*	*Atrophic*	*Active*
Billroth II					
Asymptomatic	16	1	10	5	4
Symptomatic	16	5	4	7	8
Vagotomy and antrectomy					
Asymptomatic	10	1	3	6	4
Symptomatic	10		3	7	4
Vagotomy and pyloroplasty					
Asymptomatic	11		5	6	1
Symptomatic	11	1	5	5	2
Proximal gastric vagotomy					
Asymptomatic	5			5	1
Symptomatic	5		1	4	2
Total					
Asymptomatic	42	2	18	22	10
Symptomatic	42	6	13	23	16

significant. After proximal gastric vagotomy nine patients had a patchy red appearance of the antrum (described as scarlatina by Taor *et al.*, 1975) and all had atrophic gastritis in the antrum. Apart from this, there is no relationship between endoscopic and histology findings. Eleven patients had veins visible in the mucosa but only one of these had atrophic gastritis histologically. Neither endoscopic 'score' nor gastritis was related to the patient's age, sex, smoking habits, or alcohol intake. The severity of the endoscopic change and degree of gastritis did not increase with time after the operation.

Discussion

Assessment of endoscopic changes is subjective, but all gastroscopies in this study were performed by one person. All those who had undergone a vagotomy and antrectomy or proximal vagotomy were assessed without knowledge of the symptoms. This was not so with all the remaining patients but the results for these were the same as for those assessed blind. The high incidence of endoscopic abnormalities was similar to other series after gastric surgery (Hirschowitz and Luketic, 1971; Cotton *et al.*, 1973). The extent of changes varied with the operation per-

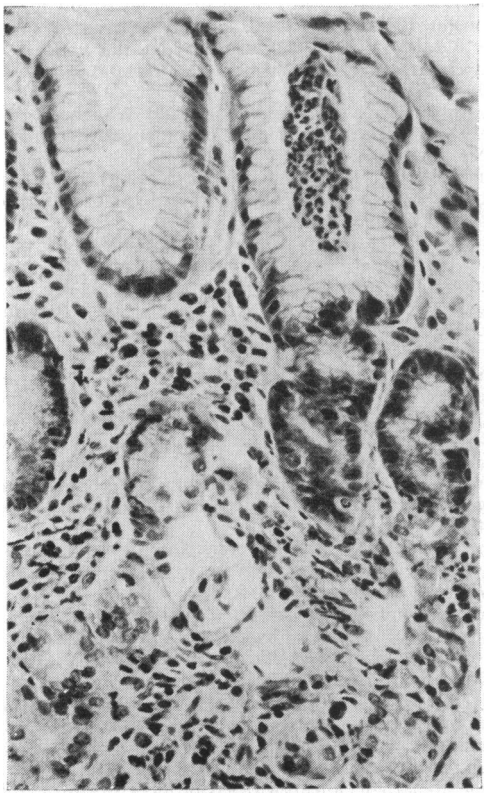

Fig. 4 *Gastric pits. Polymorph aggregates in lumen resembling crypt abscesses. H and E, × 300*

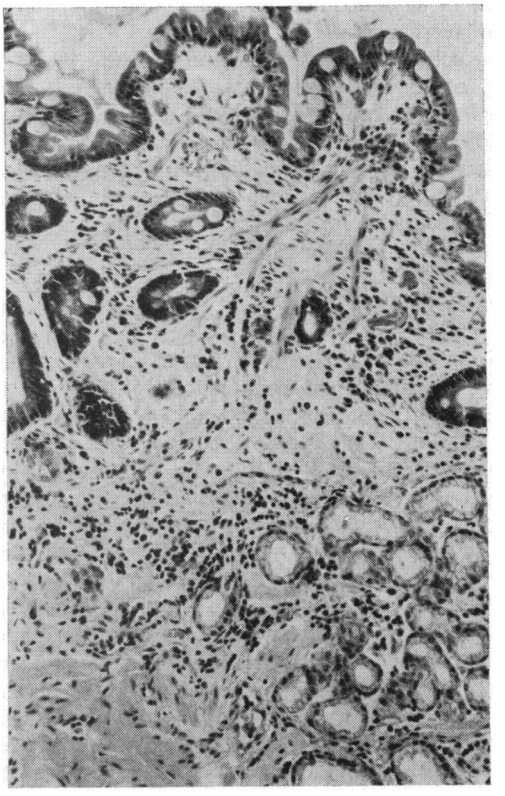

Fig. 5 *Pyloric mucosa. Intestinal metaplasia and pseudo-villi. H and E, × 150*

formed, the most frequent and severe being after Billroth II partial gastrectomy and the least after proximal gastric vagotomy.

Severe erythema, which occurred even if the gastric mucosa was normal histologically, was associated with bile reflux and possibly due to it. Other changes related to bile reflux were bile staining of the mucus, a granular mucosa, and active gastritis in the proximal stomach. Although objective methods of measurement of bile reflux have been devised (Capper *et al.*, 1966; Rhodes *et al.*, 1969; Black *et al.*, 1971), none has been assessed in patients who have had gastric surgery. A simple reliable test of bile reflux is needed. Our patients with bile reflux and associated endoscopic changes suffered from symptoms more commonly than those without these findings. There was no statistically significant relationship between the incidence of gastritis and bile reflux, though gastritis was rare in the proximal stomach after proximal gastric vagotomy, which produces little reflux. The failure to correlate bile reflux and gastritis may be due to the crude method of assessing bile reflux endoscopically. Experimental work in animals has shown that reflux of duodenal contants into the stomach causes gastritis (Du Plessis, 1962; Lawson, 1964, 1972) and this finding has led to bile diversion operations performed in man for dyspepsia and bile vomiting. Results have been classified as universally good in some series (Joseph *et al.*, 1973; Herrington

Table 3 *High lesser curve gastritis*

			Gastritis		
	Number	*Normal*	*Superficial*	*Atrophic*	*Active*
Billroth II					
Asymptomatic	16	7	8	1	0
Symptomatic	16	5	6	5	7
Vagotomy and antrectomy					
Asymptomatic	10	5	4	1	0
Symptomatic	10	0	6	4	4
Vagotomy and pyloroplasty					
Asymptomatic	11	2	6	3	2
Symptomatic	11	4	4	3	2
Proximal gastric vagotomy					
Asymptomatic	5	1	3	1	0
Symptomatic	5	3	2	0	0
Total					
Asymptomatic	42	15	21	6	2
Symptomatic	42	12	18	12	13

et al., 1974), but others have had some poor results (Van Heerden *et al.*, 1975).

Gastritis of the stoma or antrum was found in 89% of all patients and was unconnected with symptoms, so can be regarded as a 'normal finding'. Endoscopic changes of gastritis may be obscured by erythema. There is little erythema after proximal gastric vagotomy and then a patchy red or 'scarlatina' appearance in the antrum, described by Taor *et al.* (1975) indicates atrophic gastritis as it does before an operation.

Other mucosal lesions were not associated with the symptoms of dyspepsia or vomiting, but they may be significant for other reasons. Erosions may cause gastrointestinal bleeding, though none of the asymptomatic patients with iron deficiency anaemia had erosions. Oedema can be mistaken for a carcinoma radiologically or even endoscopically; indeed, one of the symptomatic patients with mucosal oedema was originally thought to have a neoplasm. The high incidence of oedema after vagotomy and antrectomy is unexplained.

There are no specific endoscopic changes associated with dyspepsia after gastric surgery, but endoscopy and gastric biopsy can be helpful in assessing a patient, who has symptoms after gastric surgery but no recurrent ulcer. Mucosal hyperaemia, granular mucosa, bile-stained mucus, bile reflux seen endoscopically, and active gastritis in biopsies of the proximal stomach are associated with dyspepsia and vomiting, but not inactive gastritis, oedema, contact bleeding, or erosions.

We thank the consultants who referred their patients and allowed us to study their asymptomatic patients, and the patients who willingly agreed to endoscopy. We are grateful to Mr K. Matthews and Dr Cross of the Department of Hospital Statistics for their help with the statistics.

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