Gastric mucosa after partial gastrectomy

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SUMMARY A partial gastrectomy of Billroth I or II type was performed in a series of 146 patients with peptic ulcer. Gastric biopsy was carried out two years later and the histology of the specimens compared with that of the body mucosa at the time of operation. In 138 patients without body atrophic gastritis (AG) before operation this condition was found in 74 (54%) two years after (46% of DU patients and 73% of GU patients). Those with antral or pyloric canal ulcers were particularly liable to develop AG (81%). Apart from site of ulcer various other factors possibly associated with the development of AG were examined: no positive correlations were found with the possible exception of anaemia. Gastric parietal cell antibodies were not found in any patient with AG tested. The cause of gastritis after partial gastrectomy and its possible relationship with gastric carcinoma are discussed.

Some reports of gastritis in the gastric remnant after partial gastrectomy have concerned small numbers and most have included patients examined at variable intervals after operation (Palmer, 1954; Debray *et al.*, 1956; Lees and Grandjean, 1958; Coghill and Williams, 1958; Deller *et al.*, 1962; Valencia-Parparcen *et al.*, 1963; Johnston, 1966; Simon *et al.*, 1973). Different rates of atrophic gastritis have been reported (Kühn, 1963; Stammers and Williams, 1963; Wall *et al.*, 1967). Patients with preoperative gastritis have not been excluded in some cases, and the frequency of postoperative gastritis has been disputed.

It is generally accepted that atrophic gastritis of body mucosa is relatively uncommon in the intact stomach in duodenal ulcer (DU) patients but is more frequent in gastric ulcer (GU). There is some evidence that the incidence of atrophic gastritis increases with time after operation (Gjeruldsen *et al.*, 1968; Aukee and Krohn, 1972).

The object of the present study was to discover what histological changes had taken place in the body mucosa of the gastric remnant of patients with peptic ulcer two years after partial gastrectomy. Postoperative gastric biopsy specimens were compared with the mucosa of the resected stomach.

Methods

PATIENTS

Over a 2½ year period all non-carcinomatous patients

in whom a partial gastrectomy had been performed two years before were considered for gastric biopsy. During this period a partial gastrectomy was performed on 308 non-cancerous patients. At follow-up 22 had died, 20 had left the area, in six the records were not available, 12 were considered unsuitable because they suffered from hypertension, old age, or kyphosis, and 37 did not respond to our request for interview (total 97). The 211 remaining were asked if they would allow biopsy specimens to be obtained from their gastric remnant, the object of the study being explained to them; 39 declined. Nine were excluded because no ulcer was found at operation in stomach or duodenum, or because no body mucosa was available for study from the resected portion of the stomach. One or more biopsy specimens were obtained from the remaining 163 patients. In 17 of these the specimens came from the oesophagus or were otherwise unsatisfactory. This left 146 patients (47.4% of the original group) available for study; 108 of these were men, and 38 women.

Seven patients had a GU as well as a DU and were classified as DU; there were 107 in the DU group (Table 4). There were 10 patients, classified separately, with peptic ulcers in the pyloric canal, two of whom also had GUs. There were 29 patients with GU, in seven of whom the ulcer was in the antrum; two GUs were present in two patients.

OPERATIONS

Mr F. performed 102 operations, Mr S. 40, and Mr B. 4. Mr F. performed a 'no loop' antecolic Polya partial gastrectomy with a Hofmeister valve in

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every case, removing two-thirds to four-fifths of the stomach and making a stoma 2.5 to 4.0 cm in diameter. Mr S. performed similar antecolic Polya partial gastrectomy operations in 30 patients but with a Hofmeister valve in only seven, and a Billroth I operation in 10. Mr B. performed a Polya partial gastrectomy and a Billroth I each in two patients (Table 5). Minimal clamping was used in all cases.

RESECTED PORTIONS OF STOMACHS

The pitfalls in a study of this kind were described by Schindler and Ortmayer (1942) in a discussion of the histopathology of gastritis. The work of Konjetzny (1928) on surgical gastric specimens was vitiated because of erosive gastritis produced by the operative clamps. Gitlitz and Colp (1943) showed that it was possible to obtain gastric tissue in its natural state at the start of the operation.

In the first 44 patients of this study, after passing two sutures through the gastric wall, full thickness biopsy specimens were taken without clamps from the anterior wall of the body of the stomach just distal to the site of subsequent gastrectomy, and fixed at once. The resected portions of the stomachs were fixed as soon as removed and sections made of body mucosa. The close correlation between the pre- and post-resection specimens (Table 1) showed

obtaining several specimens from different levels, it was thought that difficulties arising from biopsying the peristomal area, a part commonly thought to be prone to AG, were avoided. One gastric biopsy specimen was obtained from each of five patients, two from 27, three from 72, four from 37, five from three, and six from two; average 3.1 specimens per patient.

Gastric mucosal histopathology

The gastric mucosal appearances were classified by the method of Knudsen (1962) and Croft *et al.* (1966) into five categories: Normal (N), minor miscellaneous changes (M), and atrophic gastritis grades I, II, and III (AG I-III). In 109 patients with multiple biopsy specimens the histology was uniform. In 32 patients (22%) the histological appearances were mixed, showing N or M appearances or varying degrees of AG. In 14 (9.6%) AG was present in some specimens with M changes or normal appearances in others. It is accepted that gastritis may be patchy or uneven. Our present findings indicate less uniformity than that in a previous study (Williams *et al.*, 1957), but were similar to others' reports—for example, Joske *et al.* (1955). The patients were classified according to the most severe gastritis found in any specimen.

Results

The results are summarized in Tables 2-5. Of the whole group of 146 patients 81 (55.5%) had AG two years after partial gastrectomy (Table 2). Atrophic gastritis of varying degree was found in eight of the 146 patients at operation: seven of these had AG two years later of more severe degree, but one with AG I at operation had only M changes postoperatively. Two years after operation AG was found in gastric biopsy specimens from 74 (54%) of the 138 patients whose resected portions of stomach showed no AG (Tables 2 and 3). This difference was highly significant ($P < 0.0005$; χ^2 82.4305). There was a somewhat higher incidence of AG (63.0%) two years after operation in the 27 patients whose resected stomachs showed M changes than that (51.4%) in the 111 patients who had a normal gastric mucosa at operation (Table 3). However, this difference was not significant ($P > 0.05$; χ^2 1.6906).

Of the 111 patients with normal mucosa at operation 31 (28%) developed AG II or III, and of the 27 with M changes at operation 11 (41%) developed AG II or III. This difference was not significant ($P > 0.05$; χ^2 2.3435). In all these groups the incidence of metaplasia corresponded to that of AG (Table 2).

Histology		No.
Before resection	After resection	
Unchanged		31 (70.5%)
Miscellaneous	Normal	7
Normal	Miscellaneous	2
N and miscellaneous	Miscellaneous	1
N and miscellaneous	AG grade I	1
AG grade I	N and miscellaneous	1
AG grade I	Normal	1
		44

Table 1 Comparison of gastric histology before and after resection

that the surgeons' techniques were sufficiently atraumatic to provide unharmed body mucosa at the time of operation suitable for base-line histopathology. The practice of carrying out a biopsy of the stomach at the start of the operation was therefore discontinued.

Gastric biopsy

A suction biopsy tube (Wood *et al.*, 1949) was used, as modified by Coghill and Williams (1955). At the time of the study fluoroscopy was not available but the position of the tube was gauged by measured marks on it. By this means, and by

Resected stomach					Postoperative gastric biopsy								
N	M	AG*			N	M	AG*			Metaplasia†			
		I	II	III			I	II	III	SI P	+P	SI I	+I
111					27	27	26	15	16	31	17	2	3
Totals								57			53		
	27				3	7	6	7	4	14	3	1	1
Totals								17			19		
		5	2	1		1		3	4	2	5		3
Totals			8					7			10		
Totals					30	35	32	25	24	47	25	3	7
								81			82		

Table 2 All histology: resected stomach and postoperative gastric biopsy. All cases: 146

P: pyloric. I: intestinal. SI: slight. +: moderate.

*AG in three grades of severity (as defined).

†Some specimens contained more than one type of metaplasia.

Resected stomach		Gastric biopsy 2 years later			
Patients (no.)	Histology	Histology	Patients		
			(no.)	(%)	
111	N	N	27	24.3	Of 138 patients whose resected stomachs showed no AG: 74 showed AG 2 years later (54%).
		M	27	24.3	
		AG	57	51.4	
		Metaplasia	53	47.8	
27	M	N	3	11.1	
		M	7	25.9	
		AG	17	63.0	
		Metaplasia	19	70.4	
8	AG	M	1		
		AG	7		
		Metaplasia	10		

Table 3 Histology of resected stomach and at gastric biopsy two years later (all cases: 146)

In 146 patients: at gastric biopsy two years after operation AG was found in 81 (55.5%); metaplasia in 82 (56.2%) (nearly always in patients with AG). (Some cases showed more than one form of metaplasia.)

ASSOCIATION OF VARIOUS FACTORS WITH INCIDENCE OF POSTOPERATIVE AG

Site of ulcer (Table 4)

In the DU group 49 of the 106 patients (46%) who were free of AG at operation subsequently developed it. Among the 29 patients with GU seven (24%) had AG at operation; AG developed in 16 of 22 GU patients (73%) previously free of it. The difference in the postoperative rates of AG in DU and GU was significant ($P < 0.025$; χ^2 6.2344). Of 22 patients with ulcers exclusively in the body of the stomach six (25%) had AG at operation; of the 16 patients in this group with no AG 12 (75%) developed it after operation. The difference in the postoperative rates of AG in DU patients and those with body gastric ulcers was significant ($P < 0.025$; χ^2 5.8267). In a group of six patients with antral GUs (included in the GU group) and 10 with pyloric canal ulcers all of whom had no AG before operation, four and nine respectively developed AG

postoperatively, an 81% incidence in this combined group of 16 patients. The difference in the postoperative AG rates in DU, and pyloric and antral GU was highly significant ($P < 0.005$; χ^2 8.2961). Pyloric canal ulcers should probably be classed with DUs and here they behaved more like DUs in having no preoperative AG; nevertheless, postoperatively they had the highest rate of AG. However, they were a small group. Placing them with the DUs produced an only marginally higher postoperative AG incidence of 58 in 116 patients (50%). In all these groups metaplasia was found in similar extent to AG.

Surgeon and type of operation

There was no significant difference in postoperative AG incidence between surgeons F (52.0%) and S (58.5%). Analysis by type of operation (Table 5) revealed that there was a marginally lower incidence of AG after ordinary Polya partial gastrectomy when a Hofmeister valve was incorporated ($P > 0.5$;

Diagnosis and number of patients		Resected stomach: histology		Postoperative gastric biopsy in patients without preoperative AG								
				N	M	AG			Metaplasia*			
		N or M	AG					I	II	III	SI	P
GU body of stomach only	22	16	6		4	1	7 12	4	9	5 16		2
Total	29	22	7	2	4	3	7 16	6	11	7 20		2
Pyloric canal ulcer	10	10			1	4	1 9	4	5	1 6		
DU	107	106	1	28	29	25	14 49	10	32	13 50	3	2
DU + pyloric canal ulcer	117	116	1	28	30	29	15 58	14	37	14 56	3	2

Table 4 Primary diagnosis, and preoperative and postoperative mucosal histology

*Some patients had more than one form of metaplasia.

Operation	No.	No. of patients without AG at operation	AG found at gastric biopsy postoperatively		Patients with GUs who had no AG at operation	
			No.	%	No.	%
Polya partial gastrectomy	25	24	14	58.5	—	—
Polya partial gastrectomy with Hofmeister valve	109	105	53	50.5	18	17
Billroth I	12	9	7		4	

Table 5 Distribution of postoperative AG according to operation performed

χ^2 0.2196). The Billroth I group was too small for analysis; there was a high rate of postoperative AG but two-thirds of the patients had pyloric canal ulcers or GUs who appeared to be more likely to develop AG than those with DU.

Sex

In DUs there was a higher incidence of AG two years after operation in men (51%) than in women (33%) ($P > 0.05$; χ^2 3.3727). A similar ratio was found for metaplasia in DUs (46% and 37% respectively). Eight of the 10 patients with pyloric canal ulcers were men and all developed AG.

Age

It is well known that the prevalence of AG increases with age. However, when the resected gastric specimens were analysed by age at the time of operation it was found that 5% of the 79 patients under 50 years, and 6% of the 67 over 50 years showed AG. In respect of age at biopsy there was little difference between the 70 patients under 50 years who developed AG (53%) and metaplasia (40%) and the 76 over 50 years whose respective figures were 58% and 57%.

Duration of preoperative symptoms

There was no evidence that the length of dyspeptic

history was related to the finding of AG two years after operation, whether the patients who had AG before operation were included or not.

Anaemia

The haemoglobin (Hb) level was estimated in all patients two years after operation. Of 22 whose Hb was 12.0 g/dl or less 11 had AG at biopsy and of nine with a Hb of 10.0 g/dl or less five had AG. On the other hand, 70 of 81 patients with AG had a Hb of more than 12.0 g/dl. Thus, while there was an even chance of hypochromic anaemia being associated with AG, 88% of patients with AG at the time of biopsy were not anaemic. Anaemia did not predominate in any operative group. Four of nine postoperative female GU patients were anaemic (Hb 12.0 g/dl or less) and, of these, three had AG, compared with two male anaemic GU patients out of 20, one of whom had AG. Twelve of 27 female DU postoperative patients were anaemic and five of these had AG, compared with four anaemic male DU patients, two of whom had AG. Thus 16 of 38 females (42%) were anaemic and six of 108 males (5.5%).

Postoperative appetite

The state of the appetite was assessed in 134 patients at the time of gastric biopsy. Twelve of 19 patients

whose appetite was poor had AG (63%) (68% had intestinal metaplasia), 29 of 49 with a moderate appetite had AG (59%) (57% had metaplasia), and 34 of 66 who had a good appetite had AG (52%) (49% had metaplasia). There was a trend therefore to less AG and metaplasia in those with a better appetite but these differences were not statistically significant. There was no particular relationship between the type of operation and the appetite at follow-up.

Body weight

This was measured in each patient at gastric biopsy. There was a higher incidence of AG and metaplasia (about 60% in each case) among the 52 patients whose weight had increased postoperatively, than among the 14 who had lost weight (43% in each case) but these differences were not significant. There was virtually no difference in the follow-up weights in the different operative groups, about 90% of patients maintaining or increasing their weight in each.

Dumping

This was divided into mild, moderate, and severe forms. To be included in the last group patients had to feel faint or lose consciousness. Twenty-one patients (14.4%) in the whole series had dumping symptoms, seven severe. They were present in three patients with GU (severe in two), in one with pyloric canal ulcer (mild), and in 17 with DU (severe in four). The incidence of AG two years after operation was lower (68 in 125; 54%) in those patients without dumping symptoms than in those (13 in 21, 62%) with them. This difference was not significant. The numbers in some of the groups were small but the findings suggested that dumping was less likely after a Polya partial gastrectomy when a Hofmeister valve was constructed (11%) than with simple Polya (24%) or Billroth I (three out of 12) operations.

Diarrhoea

Five patients had diarrhoea postoperatively, not always associated with dumping. It was mild in all, and occurred only after a Polya partial gastrectomy with a Hofmeister valve. In three AG was present at biopsy.

Recurrence of symptoms

In seven patients symptoms present before operation recurred (haemorrhage in one, pain in six). AG was present at biopsy in only one of these.

Autoantibodies

Sera from 44 patients were tested by immuno-

fluorescence for gastric parietal cell (PCA), thyroid and other tissue antibodies. Parietal cell fluorescence was positive in two of 27 male DU patients and negative in 12 female DU, four male GU, and one male patient with a pyloric canal ulcer. Of the 44 patients AG was present in 24 on gastric biopsy two years after partial gastrectomy; in none of the 24 was PCA present.

In six male patients (four DU, one GU, and one pyloric canal ulcer) in whom the histology of the resected stomach was unknown and in one operated on for stomal ulcer after a previous gastroenterostomy (all excluded from the main analysis) there was none with PCA. AG was present in two of these patients after operation.

Thus in a total of 51 patients after partial gastrectomy only two had doubtfully present PCA. In 26 of these patients AG was present postoperatively and none of these had PCA.

Discussion

In those patients in this series without preoperative AG highly significant numbers developed AG of the body mucosa: 46% of DU patients and 73% of GU patients. The figures for metaplasia were similar. Patients with antral and pyloric canal ulcers seemed particularly liable to postoperative AG (81%). Although there was a higher incidence of AG after operation in the patients with preoperative minor gastritis (M changes), the difference was not significant.

There have been a few previous studies in which mucosal histology has been compared with that found at or just before operation. Excluding patients with preoperative AG Wall *et al.* (1967) found AG in 74% of DU patients and 51% of GU, the reverse of our findings. Gjeruldsen *et al.* (1968) found a preoperative AG rate of 8.7% in 46 patients with DU and a one-year postoperative rate of 74% in 54 patients (mostly the same ones). Aukee and Krohn (1972) reported AG before operation in 42.8% of 14 GU patients and 23.5% of 17 with DU. Twelve months postoperatively the incidence of AG in these groups was 78.6% and 53.0% respectively, increases of 35.8% and 29.5%. Seifert *et al.* (1966) and Simon *et al.* (1973) each reported an incidence of 46% in series respectively of 114 and 105 DU patients at variable times postoperatively.

RELEVANT FACTORS

Sex and age

More men than women developed AG and metaplasia but the difference was not significant, and this is not a usual finding in AG (Edwards and Coghill,

1966). In this series the incidence of AG before and after operation had no relation to age. In other conditions the presence of AG is related to increasing age (Joske *et al.*, 1955; Coghill, 1960; Edwards and Coghill, 1966).

Anaemia

AG has been reported in about 40% of patients with iron deficiency anaemia (Davidson and Markson, 1955; Badenoch *et al.*, 1957; Coghill, 1960). In this series only 21 patients (14%) had a haemoglobin of less than 12 g/dl after operation. Half of these had AG. One in 10 patients with post-operative AG was anaemic. Hobbs (1961) found iron deficiency anaemia in half his male and nearly all his female patients after partial gastrectomy. In our patients the overall incidence of anaemia was much less but most of the cases were females. In a series of 265 patients after partial gastrectomy Deller and Witts (1962) found anaemia in 20%; there was vitamin B₁₂ deficiency in 14% and low serum iron levels in 34%. Nielsen *et al.* (1972) found that 10 of 15 iron deficient DU patients had AG after partial gastrectomy. Postoperative iron deficiency may be a result of several factors. There is evidence not only of diminished iron absorption after the operation (Baird and Wilson, 1959), but also of bleeding from the gastric remnant in some patients (Holt *et al.*, 1970) and of increased non-haem iron loss into the gut both after partial gastrectomy, and in AG (Sutton *et al.*, 1970).

Appetite and body weight

It is not uncommon for patients after partial gastrectomy to be underweight (Glober *et al.*, 1974). However, 90% of our patients maintained their normal weights in each operative group, and those underweight had less AG and metaplasia. Seifert *et al.* (1966) found the contrary: AG was most frequent in patients who were 20% or more below their normal weight.

Autoantibodies

No patient with postoperative AG who was tested had parietal cell antibodies in the blood. This is in agreement with others' findings (Fisher *et al.*, 1967; Kravetz *et al.*, 1967; Ashurst, 1968), and contrasts with the frequent appearance of these antibodies in patients with Addisonian pernicious anaemia and simple idiopathic AG (Coghill *et al.*, 1965).

There was no evidence that the following factors had a bearing on the postoperative development of AG; the surgeon, the type of operation, the duration of preoperative symptoms, the postoperative presence of diarrhoea or recurrence of symptoms.

CAUSE OF THE GASTRITIS

There has been speculation about possible factors in the pathogenesis of gastritis after partial gastrectomy. Whatever part gastric autoantibodies and age play in the causation of other forms of gastritis it seems unlikely that they are implicated here.

Effect of duodenal contents on gastric mucosa

It is known that in GU in which AG is common (Rhodes *et al.*, 1969) and in other patients with AG (Siurala and Tawast, 1956) bilious reflux into the stomach is frequent. However, the evidence that bile itself causes gastritis, though suggestive (Menguy and Max, 1970), is not conclusive (Byers and Jordan, 1962). There is conflicting evidence as to whether bile alone or mixed duodenal contents is most likely to cause gastritis in dogs (Lawson, 1964; 1965; Nakajima *et al.*, 1967). It has been suggested that pyloric reflux may account for the higher incidence of AG sometimes reported after Billroth I procedures. Simon *et al.* (1973) found significant differences in the frequency of reflux between Billroth I and II operations and even more so between postoperative patients with and without AG. However, Wall *et al.* (1967) reported a higher incidence of AG after Billroth II operations. The present findings suggest that a Hofmeister valve may have a protective effect.

Effect of vagotomy and antrectomy

Crean *et al.* (1969) and Capoferro and Nygaard (1973) found that vagotomy and antrectomy in rats were followed by a significant reduction in the parietal cell population. This was not found in dogs, however, by Ritchie and Delaney (1972) unless the procedure were accompanied by a Billroth II type reconstruction of the stomach. Capoferro and Nygaard (1973) found evidence that in rats lack of gastrin might be a factor in the pathogenesis of gastric atrophy after partial gastrectomy.

SIGNIFICANCE OF GASTRITIS

Studies of the histopathology of gastrectomy specimens removed for carcinoma (Morson, 1955 a, b), and follow-up studies of patients with AG (Siurala *et al.*, 1966; Walker *et al.*, 1971; Cheli *et al.*, 1973) suggest the possibility of a causal connection between simple AG and gastric carcinoma. There may be an increased risk of cancer in the gastric remnant after partial gastrectomy for GU, but not for DU (Nicholls, 1974). This might be related to the higher pre- and postoperative incidence of atrophic gastritis in GU. The risk of cancer appears to increase with postoperative time (Seifert *et al.*, 1966; Stalsberg and Taksdal, 1971).

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