Histological appearances of the gastric mucosa 15-27 years after partial gastrectomy

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SUMMARY Sixty-three patients, who had had a partial gastrectomy 15-27 years previously, were examined by endoscopy and multiple mucosal biopsies. No patient had a completely normal gastric mucosa; they showed varying degrees of gastritis, intestinal metaplasia, and dysplasia; 21% had significant dysplasia, and these are regarded as an 'at-risk' group requiring frequent follow-up examinations. One patient had severe dysplasia (carcinoma-in-situ), but no case of infiltrating carcinoma was found.

Carcinoma of the gastric stump as a late complication of resection for benign disease is a well-recognised clinical entity (Saegesser and Jämes, 1972; Morgenstern et al., 1973). There have been a number of reports of an increased incidence of stump carcinoma compared with carcinoma in the normal population (Krause, 1958; Schrumpf et al., 1977), although some authors have drawn the opposite conclusion (Liavaag, 1962). Opinions also vary over whether the nature of the original disease or the type of operation performed is significant (Helsingan and Hillestad, 1956; Stalsberg and Taksdal, 1971; Domellöf et al., 1976). Some authors (Domellöf et al., 1977b; Schrumpf et al., 1977) have recommended endoscopic follow-up on all patients 20 years after gastric surgery. We have examined by endoscopy and gastric biopsy a group of patients who had undergone partial gastrectomy 15-27 years previously. Our aims were to determine the incidence of carcinoma of the stump, to identify, if possible, a high-risk group among the patients, and to study the histological appearances of the mucosa of the stomach remnant.

Patients and methods

During the years 1951-63 (15-27 years previously) 224 patients under the care of one surgeon had had a gastric resection for benign ulcer performed at Southmead Hospital; 115 (51%) who were still alive and living in the area were traced and offered gastroscopy, and 65 (29%) accepted (Table 1). None had symptoms sufficiently severe to present to their doctors and most were asymptomatic. All the patients were endoscoped by one examiner (SJ) and four to five biopsy specimens were taken from around the stoma and a further four to five from elsewhere in the stomach, usually the lesser curve. Further specimens were taken from any visible lesion. Two patients reacted adversely to endoscopy and no specimens were obtained. All the specimens were fixed in formol saline and embedded in paraffin. Five-micron sections at three levels were cut from each block and stained with haematoxylin and eosin. An extra section at the second level was stained with a combined periodic acid-Schiff/alcian blue method. All the histological material was examined by one of us (AS) without knowledge of the endoscopic appearances, and later reviewed without knowledge of the previous report, to arrive at a final diagnosis. The histological appearances were classified according to the following criteria:

ACUTE GASTRITIS
A significant infiltration of neutrophil leucocytes in
the mucosa was regarded as acute gastritis. A crypt abscess or similar collection of neutrophils was considered significant. Usually the acute inflammation was associated with a considerable chronic inflammatory cell infiltrate.

**CHRONIC GASTRITIS**

Our classification is based on that of Lambert (1972).

**Chronic superficial gastritis** (mild gastritis)
The gastric mucosa is of normal depth with no atrophy of specialised cells. There is increased chronic inflammatory cell infiltration, usually confined to the luminal third of the mucosa but occasionally found more deeply (Fig. 1).

**Chronic atrophic gastritis** (moderate gastritis)
There is infiltration of chronic inflammatory cells throughout the lamina propria of varying degree. The mucosa is reduced in depth due to partial atrophy of specialised cells, which are partly replaced by undifferentiated cells. The lesion may be diffuse or focal (Fig. 2).

**Gastric atrophy** (severe gastritis)
There is complete atrophy of specialised cells with partial replacement by undifferentiated cells. The mucosal depth is markedly diminished. Inflammatory cell infiltration is commonly slight, but the lesion is frequently focal and mixed with atrophic gastritis; in that case the inflammation is more pronounced (Fig. 3).

**INTESTINAL METAPLASIA**

The presence of goblet cells containing mucin staining positively with alcian blue was the pathognomonic feature of intestinal metaplasia. Paneth cell metaplasia was frequently present in addition.

**CYSTIC DILATATION OF GLANDS**

A gland distended to twice or more its normal diameter was scored as cystic (Fig. 4). There was rarely any difficulty with borderline lesions.

**DYSPLASIA**

Definition was based on the work of Nagayo (1971).

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*Fig. 1  Mild gastritis. Chronic inflammatory cell infiltrate is mainly in the luminal third of the mucosa. (Haematoxylin and eosin × 170)*
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Fig. 2 Moderate gastritis. There is inflammation throughout the lamina propria with partial loss of specialised cells. Intestinal metaplasia is present near the bottom of the photograph. (H and E x 500)

Fig. 3 Severe gastritis. There is inflammation with complete atrophy of specialised cells. Many areas show mild dysplasia of epithelial cells. (H and E x 500)
Mild dysplasia
The epithelial cells lining a tubule are tall and hyperchromatic with elongated, pointed nuclei. Nucleo-cytoplasmic ratio is increased; nuclei are fairly uniform and arranged basally.

Moderate dysplasia
The nuclei are rounded and the nucleo-cytoplasmic ratio is further increased; some nuclei reach the luminal border of the cell. There may be some pleomorphism and mild architectural abnormalities of the tubules (Fig. 5).

Severe dysplasia
The features of moderate dysplasia are more frequent or more pronounced, with greater pleomorphism and, in particular, increased architectural abnormality (Fig. 6). Some pathologists would regard this lesion as carcinoma-in-situ. We considered that the presence of lesions in this group would be an indication for excision.

POLYPS
These were defined endoscopically and divided histologically into two groups:

Adenomatous
These are similar to adenomatous polyps in the large bowel.

Regenerative (hyperplastic)
Glands are mingled with collagen and smooth muscle cells. The glands are frequently cystic and lined by hyperplastic cells, which are large, but with small basal nuclei. There is a variable inflammatory cell infiltrate.

Results
The results of the first endoscopy are shown in Table 2. Patients with moderate dysplasia in the initial biopsy specimen were requested to attend for repeat endoscopy within three to six months, and of the 14 patients 13 accepted. Ten or more specimens were taken from the suspicious area and further specimens from any lesion seen. The results of these repeat endoscopies are shown in Table 3. Most patients had lesions similar to or more severe than at the initial biopsy, but in only one was the lesion significantly worse. This patient had severe dysplasia
H. stomachological appearances of the gastric mucosa 15-27 years after partial gastrectomy

Fig. 5  Moderate dysplasia, mainly in the glands to the right of the photograph. (H and E x 500)

Fig. 6  Severe dysplasia. The changes are more severe and more extensive than in Fig. 5. (H and E x 500)
Table 2  Results of first endoscopy (63 patients)

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Stoma No.</th>
<th>Stoma %</th>
<th>Lesser curve No.</th>
<th>Lesser curve %</th>
</tr>
</thead>
<tbody>
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<td>Normal</td>
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<td>7</td>
<td>11</td>
<td></td>
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<tr>
<td>Acute gastritis</td>
<td>46</td>
<td>73</td>
<td>38</td>
<td>60</td>
</tr>
<tr>
<td>Chronic gastritis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>7</td>
<td>11</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Moderate</td>
<td>34</td>
<td>53</td>
<td>34</td>
<td>53</td>
</tr>
<tr>
<td>Severe</td>
<td>26</td>
<td>41</td>
<td>11</td>
<td>17</td>
</tr>
<tr>
<td>Intestinal metaplasia</td>
<td>22</td>
<td>34</td>
<td>21</td>
<td>33</td>
</tr>
<tr>
<td>Cystic dilatation of glands</td>
<td>35</td>
<td>55</td>
<td>25</td>
<td>39</td>
</tr>
<tr>
<td>Dysplasia</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>22</td>
<td>34</td>
<td>28</td>
<td>44</td>
</tr>
<tr>
<td>Moderate*</td>
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<td>3</td>
<td>4</td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
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<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regenerative</td>
<td>8</td>
<td>12</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>'Lipid island'</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

*One patient had moderate dysplasia at the stoma and on the lesser curve.

Table 3  Results of repeat endoscopy (13 patients)

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Stoma No.</th>
<th>Stoma %</th>
<th>Lesser curve No.</th>
<th>Lesser curve %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute gastritis</td>
<td>11</td>
<td>85</td>
<td>9</td>
<td>69</td>
</tr>
<tr>
<td>Chronic gastritis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>9</td>
<td>69</td>
<td>10</td>
<td>77</td>
</tr>
<tr>
<td>Severe</td>
<td>4</td>
<td>31</td>
<td>3</td>
<td>23</td>
</tr>
<tr>
<td>Intestinal metaplasia</td>
<td>8</td>
<td>62</td>
<td>5</td>
<td>38</td>
</tr>
<tr>
<td>Cystic dilatation of glands</td>
<td>10</td>
<td>77</td>
<td>6</td>
<td>46</td>
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<tr>
<td>Dysplasia</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>0</td>
<td>2</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>11</td>
<td>85</td>
<td>9</td>
<td>69</td>
</tr>
<tr>
<td>Severe</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

in one of the repeat biopsy specimens, and excision of most of the stomach remnant was carried out.

The stomach was received fresh and fixed after opening. Blocks were made of the entire stomach (Fig. 7), and sections were examined from the areas

Fig. 7  Gastrectomy specimen showing plan of blocks taken. Blocks 1-22, 32-38, and 45-46 were sectioned. The polyps indicated were regenerative in type. (Approx. natural size)
indicated. An extensive area of severe dysplasia was found and, in addition, a wide range of appearances, including varying degrees of chronic gastritis, intestinal metaplasia, and dysplasia. No infiltrating carcinoma was found.

Discussion

Among our 63 mainly asymptomatic patients who accepted screening, no case of infiltrating carcinoma and only one of severe dysplasia was found. This was unexpected, as Schrumpf et al. (1977) had found four cases of infiltrating carcinoma and three of severe dysplasia among their 108 patients who had had a previous Billroth II gastrectomy. Domellöf et al. (1977b), in their large series of 214 post-gastrectomy patients (Billroth II type), reported that four had infiltrating carcinoma, one had 'pre-cancerous' changes, and one had an adenomatous polyp, if their symptomatic and necropsy cases are excluded. Of their 74 post-Billroth I patients, four had carcinoma and one an adenomatous polyp (Domellöf et al., 1976). It is possible that the incidence of stump carcinoma is less in British than in Scandinavian patients. Although only about half of our original group of patients were traced, it is unlikely that many had died of carcinoma of the stomach before follow-up. Stalsberg and Taksdal (1971) have shown that the risk of stump carcinoma less than 15 years postoperatively is less than that of unoperated stomachs, and the risk increases gradually with time thereafter. No firm conclusions can be drawn about the incidence of stump carcinoma from our results.

The biopsies revealed a wide range of pathological changes, and no stomach was completely normal, although two had only mild gastritis at the stoma. It is important to consider whether the lesions found are premalignant. Siurala et al. (1974), in a prospective survey of 116 patients with atrophic gastritis, found 10 cases of carcinoma that had developed during a follow-up period of 19-23 years, whereas none had developed in similar groups of patients with normal stomachs or with superficial gastritis. In an earlier survey of a rural population in Finland, Siurala et al. (1968) found atrophic gastritis in 28% of those between 16 and 65 years, and, if those over 50 years only are considered, the prevalence was 54%. However, he found that the patient group had more severe gastritis with an increased frequency of atypia and metaplasia, compared with his randomly selected group, and thus he could not conclude that atrophic gastritis itself was necessarily premalignant.

Intestinal metaplasia was present in 29 (46%) of our patients in association with either moderate or severe gastritis. Morson (1955a) has shown that intestinal metaplasia is more common in stomachs with carcinoma than in those removed for benign lesions and has demonstrated (Morson, 1955b) transitions from metaplastic mucosa to carcinoma. Reynolds et al. (1975) consider intestinal metaplasia to be premalignant and suggest that all patients with this lesion should have regular endoscopic biopsies; they wonder if there is a place for prophylactic surgery in long-standing cases. However, Siurala et al. (1968) found that 24% of their randomly selected rural population over 50 years had intestinal metaplasia. While one must be cautious in relating Finnish data to a British population, it seems that intestinal metaplasia is not in itself sufficient indication for radical measures.

No adenomatous polyps were found in our series. Although polypoid lesions were fairly common these were of a regenerative type. Neoplastic transformation is not seen in these polyps (Ming and Goldman, 1965), although they are sometimes found in association with gastric cancer. Cystic dilatation of the gastric glands was a common finding in our series, as in others (Domellöf et al., 1977b), and has been described in the mucosa adjacent to early carcinomas (Nagayo, 1974). There is little evidence, however, that it has any premalignant significance.

'Lipid islands' in the gastric mucosa after gastrectomy were described by Domellöf et al. (1977a), who found them in 60% of patients 23 years after a Billroth II resection. We found only two in our 42 patients who had had a Billroth II gastrectomy (5%) despite a careful search. The reason for this difference is not clear.

Dysplasia was always associated with acute or chronic inflammation in our cases, and it seems likely that mild dysplasia is a reactive change which can safely be left alone. While it is generally accepted that significant dysplasia (moderate or severe dysplasia) is premalignant, the degree of risk is unknown. This makes management of individual cases difficult. We decided to follow Japanese practice (Nagayo, 1971) and to keep all moderate dysplasia lesions under review, probably bi-annually. However, patient cooperation may be a limiting factor here. Our case with severe dysplasia was subjected to total gastrectomy, and the lesion found was much more extensive than had been suspected from biopsy. However, no infiltrating carcinoma was found. If operation is undertaken nothing less than a total gastrectomy can be recommended, since significant dysplasia was found at the gastro-esophageal junction. At present each of these patients must be managed in the light of individual circumstances.

Our results do not confirm the high incidence of stump carcinoma found by others (Domellöf et al., 1976).
1976; Domellöf et al., 1977b; Schrumpf et al., 1977) but do reveal the presence of an ‘at risk’ group (21% of those submitted to biopsy) requiring close follow-up. A prospective study of this group of patients with significant dysplasia may shed further light on the problem.

We thank Mr A. G. McPherson, who kindly allowed us to study patients under his care, and Mrs Elizabeth Scott and Mr Brian Glover, who provided invaluable help in the endoscopy clinic. In addition, we are most grateful to Mr Vernon Perry and the technical staff of the Pathology Department, without whose help this study could not have been undertaken. We also thank Mr Brian Amer for the photomicrographs and Miss Carol Jenkins and Mrs Betty Curtis for secretarial assistance.

References


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