THE SIGNIFICANCE OF GASTRITIS

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Rapid autolysis, which normally occurs in the stomach after death, prevented satisfactory histological study of the gastric mucosa until Konjetzny in 1923[69] examined specimens of stomach obtained by partial gastrectomy, and Faber[42] began to fill the stomach with formalin immediately after death. To overcome the possibility that agonal changes might alter the appearance of the gastric mucosa, Schindler[96] studied biopsy specimens obtained from the stomach at laparotomy. Historical aspects of gastritis have been discussed by Faber,[42] Schindler,[96] and Moutier and Cornet.[83]

It was hoped that the gastroscope would provide a means of assessing the incidence of gastritis and for classifying its forms. However, the introduction of methods for obtaining gastric mucosal biopsies indicated that the correlation between gastroscopic and histological findings was poor.[1, 98] Correlation is best in atrophic gastritis, but even here it is not above 75% and may be as low as 25%.[57] The gastroscope is of little value in the diagnosis of chronic superficial gastritis.

Gastric Biopsy

Einhorn in 1894[41] was the first to obtain a fragment of gastric mucosa from an intact living patient. It was withdrawn by chance through an aspiration tube. The history of the development of techniques for obtaining biopsy specimens of gastric mucosa from the intact human has been reviewed by Doig and Wood.[34, 35] In spite of the pioneering efforts of Jackson and Jackson[63] and of Swalm and Morrison,[106] using a rigid tube, no material advance was made in this field until Kenamore,[67] Kenamore *et al.*[68] and d'Almeida[19] introduced a type of grab-forceps for attachment to a Wolf-Schindler gastroscope. In 1948 Benedict[6] produced a larger 'operating gastroscope', incorporating forceps similar to those used by Kenamore. With this instrument the biopsy specimen is obtained under direct vision and its main use is for the examination of localized lesions such as polyps, doubtful cancers or the edges of suspect ulcers.[7, 8, 9, 10, 98, 99, 111, 117] With this type of instrument the size of the specimen seems relatively unpredictable and it is doubtful if the full thickness of the mucosa can be regularly obtained.

A different method, using a device for cutting off a knuckle of gastric mucosa sucked through a small hole into a tube, was described independently at about the same time by Wood *et al.*[120] in Australia and Tomenius[108, 109] in Sweden. The latter incorporated the device in a Wolf-Schindler type of gastroscope and similar operating gastroscopes have been designed since then.[51] The Australian instrument is narrow, simple, and flexible throughout. It is easily passed and generally gives little trouble to the patient. The specimen is obtained 'blind', but it is possible to know roughly from which part of the stomach it comes, and it may be placed in fixative within a minute or two of severance. The main use of this instrument is for lesions which are likely to be or are assumed to be diffuse or widespread. Much of the work with it has been done by the Australian group.[31, 32, 33, 36, 46, 65, 82, 122] Results using this type of instrument have also been reported by Palmer,[85, 87, 88, 89, 91] Debray *et al.*,[22, 23, 24, 25, 26] Rubin *et al.*,[94] Badenoch and Richards,[3] Siurala,[101, 102] Goldgraber *et al.*,[48] Badenoch *et al.*,[4] Henning *et al.*,[57] Heinkel *et al.*,[55] Davidson and Markson,[20] and Markson and Davidson.[76]

Personal experience with this instrument led to several modifications,[16, 17] the most important being enlargement of the biopsy hole so that the biopsy could be obtained with relatively low negative pressures, thus reducing haemorrhage into the specimens. There is no reason to believe that this change has increased the risk of bleeding. Over 1,860 biopsy specimens have been obtained from 819 cases. Thirteen patients (1.6%) subsequently bled. Bleeding was of material amount in eight (1%) and only one needed a blood transfusion.

Acute Gastritis

Forms of severe acute gastritis such as phlegmonous gastritis will not be considered, nor will the gastritis sometimes occurring as part of the

syndrome of pseudomembranous enterocolitis, nor that caused by corrosives and heavy metals.

Acute gastritis may be caused by bacterial toxins and other (unknown) agents. Contamination of food with staphylococcal toxin is known to cause a severe gastro-enteritis. Palmer[86] described gastroscopic and histological changes in the gastric mucosa of patients thought to have this condition. Recovery of the gastric mucosa was rapid and complete in those patients who survived. Other agents such as influenza virus and salmonella organisms may cause gastritis, but little is known of the pathological changes, if any, that they induce in the stomach. Alcohol can cause acute mucosal gastritis which soon recovers.[82, 90, 113]

The subject of 'acute erosive gastritis' has been discussed by Faber[42] and Magnus.[73] The condition was described by Nyfeldt and Vimtrup[84] in children dying from acute infections. It may be associated with chronic gastric ulceration and is common in the pyloric antrum. It is a diagnosis sometimes made when acute mucosal erosions are seen through a gastroscope in a patient who has had recent haematemesis or melaena. There are few reports of coincident mucosal biopsy studies.[42, 92] The condition appears to be described as a phenomenon found mainly at autopsy or in specimens removed at operation. To what degree the changes are agonal in the first instance,[112] or due to the operation in the second,[95, 97] has never been fully determined.

X-rays can cause severe damage to the gastric mucosa with histological appearances of gastritis. They have been used to reduce gastric acid production in the treatment of duodenal ulcers.[14, 30, 93] The gastritis usually takes many months to subside and mucosal atrophy often follows.

There is evidence that the gastric mucosa possesses great powers of recovery and rapid regeneration. Magnus[73] and others have suggested, nevertheless, that repeated assaults on it may result in the changes of chronic gastritis. It is true that in spite of its powers of recovery extensive and seemingly permanent mucosal atrophy is not uncommon in patients without pernicious anaemia, and may even be found in young adults.

Chronic (Idiopathic) Gastritis

This term refers to conditions which involve the mucosa and muscularis mucosae and which are thought to be longstanding and, usually, irreversible. The causes of all forms of this condition are unknown and the group can conveniently be labelled 'chronic idiopathic gastritis'.

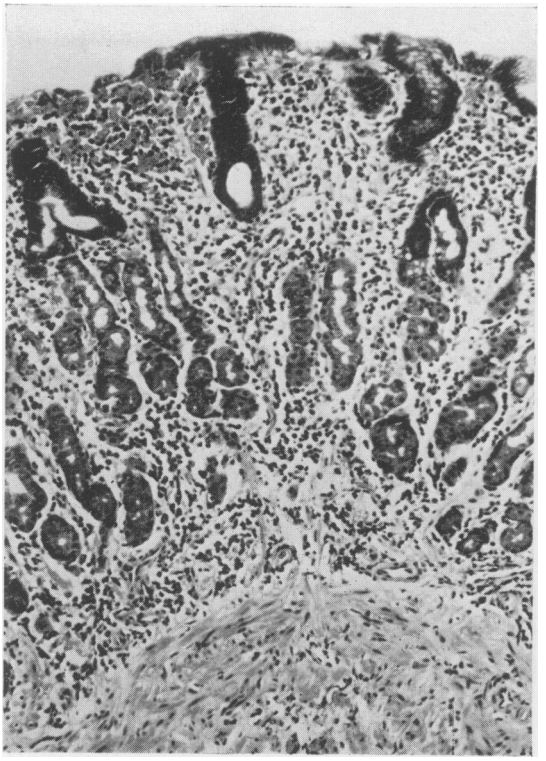

FIG. 1.—Chronic superficial gastritis. H. & E. × 120.

Two rare forms of chronic gastritis must first be mentioned.

Hypertrophic Gastritis. This title has been applied to enlargements of areae gastricae or rugae. The incidence claimed by gastroscopists was far in excess of that encountered by pathologists.[90] Mammillation, seen with the gastroscope in patients with duodenal ulcers, was commonly termed 'hypertrophic gastritis', but histology is normal, or nearly so, in these cases. The classification of Schindler[96] suggested a basic division into hyperplastic and neoplastic groups. Because of the limited size of the mucosal specimen obtained with the flexible biopsy tube, diagnosis may perhaps be difficult with this method.

Fieber[44] was able to collect only 50 histologically authenticated cases of hypertrophic gastritis from the literature, and added two of his own.

Eosinophilic Gastritis. This is a very rare form of gastritis affecting mainly the pyloric antrum. Doniach and McKeown[38] described a case and reviewed the literature. The condition is conceivably allergic in origin and it may be one manifestation of a more widespread disorder affecting other parts of the abdomen and gut.[107]

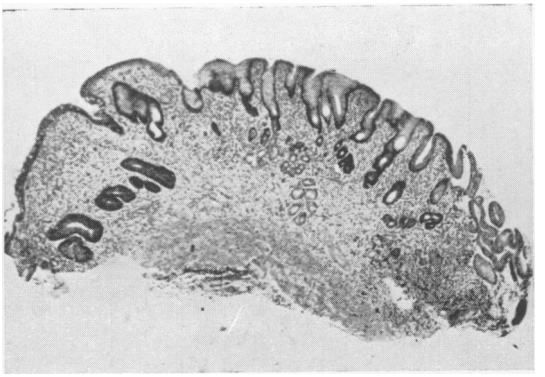

FIG. 2.—Chronic atrophic gastritis. H. & E. ×35.

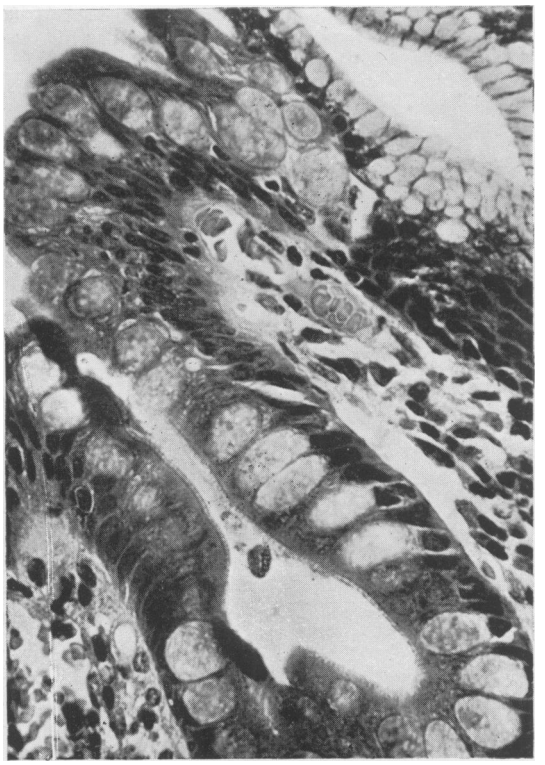

FIG. 3.—Chronic atrophic gastritis with marked intestinal metaplasia. Numerous goblet cells are present and the brush border of the intestinal-type epithelium is well shown. H. & E. ×480.

The Gastric Mucosa

Henceforth we shall be concerned only with body (' fundic ') mucosa. Changes in the pyloric antrum are so diverse and difficult to classify, and the range of normal so little known, that consideration of abnormalities in this part of the gastric mucosa would be fruitless at present.

Uniformity of the Gastric Mucosa. Chronic gastritis may be patchy. Nevertheless, in spite of the small samples of mucosa obtained by the suction tube technique, Joske *et al.*[65] found uniformity among about 75% of specimens, and Williams *et al.*[116] found uniformity of 85-92% in specimens taken at the same time.

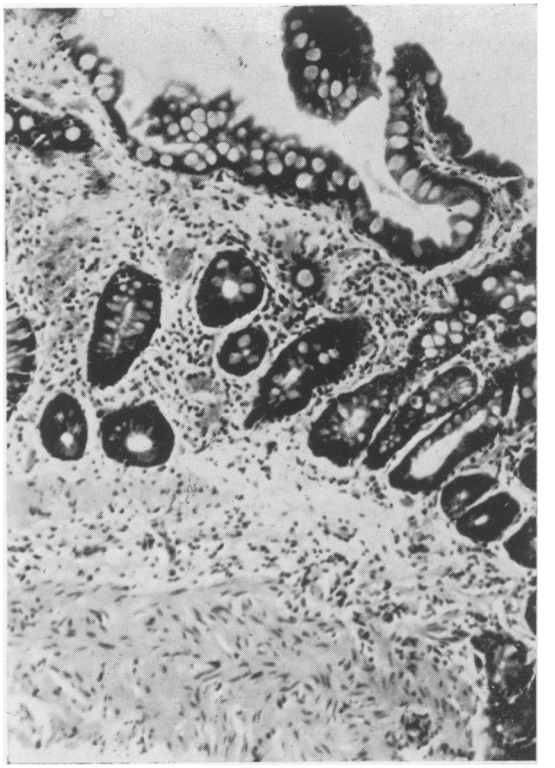

FIG. 4.—Gastric atrophy. H. & E. ×150.

Classification of Gastritis

Everyone working in this field has his own classification. Nevertheless, there is broad agreement as to the main groups of changes. The histopathology of our material has been studied jointly with Dr. A. Wynn Williams and has been classified using the following categories.[116]

Chronic Superficial Gastritis. There is atrophy of the glands, mainly in their superficial part, and infiltration of the stroma with inflammatory cells (Fig. 1).

Chronic Atrophic Gastritis. Glandular atrophy is complete or almost so and there is variable infiltration of the stroma with inflammatory cells. The muscularis mucosae is thickened and fibrotic (Fig. 2). Intestinal metaplasia and pyloric gland heterotopia are of frequent occurrence (Fig. 3).

Gastric Atrophy. The mucosal changes are the same as in atrophic gastritis, but inflammatory cells are inconspicuous (Fig. 4).

In many patients classification is difficult because abnormalities are slight. Such cases have been put in a separate category.

Miscellaneous Minor Mucosal Changes. The glandular pattern is normal, but the surface epithelium or the stroma, or both, are abnormal. Alterations include irregularities in the size, shape, staining properties and numbers of surface epithelial cells; and oedema and an excess of inflammatory cells in the stroma.

Clinical and Pathological Significance of Chronic Gastritis

The pathological significance of the changes of chronic gastritis is by no means clear. Furthermore, although symptoms have been ascribed to it,[43, 65] there is as yet no convincing evidence that this type of gastritis has any clinical significance.[54, 89] Ricketts *et al.*[93] noted that none of their patients who developed gastritis after radiotherapy had symptoms referable to the stomach. In my experience patients suffering from dyspepsia with or without hypochromic, or pernicious, anaemia usually lose their symptoms when no physical cause is found on investigation, or the anaemia is cured. Gastritis is present in only a proportion of patients with non-ulcer dyspepsia and hypochromic anaemia, but in all these patients it probably remains unchanged after treatment, and certainly does so in pernicious anaemia.

Gastritis is a common condition and its incidence in different disorders and groups of patients is becoming known. This is a pre-requisite to elucidation of its significance.

Possible Clinico-Pathological Associations

1. *Age.* The changes of chronic gastritis are almost certainly absent in the newborn and are very rare before the age of 10 years. As age advances gastritis appears with increasing frequency in different groups of patients and, probably, in the general population.[50, 53, 105, 112] Nevertheless, Palmer[87, 90] was unable to find gastritis in any biopsies from a large number of normal persons, including 30 over 60 years of age. The problem was discussed by Williams *et al.*[116] in relation to non-ulcer dyspepsia. In this condition most of the patients with gastritis were over 40 years of age. In 'idiopathic' hypochromic anaemia on the other hand nearly as many patients under, as over, 40 had gastritis[18] (Fig. 5). An increasing incidence of chronic gastritis with mucosal atrophy as age advances could explain the fact that the ability of the stomach to secrete HCl appears to decline with age.[62]

2. *Dyspepsia.* In most cases of duodenal ulcer gastritis is mild or absent. Gastritis of varying degree has been described in association with

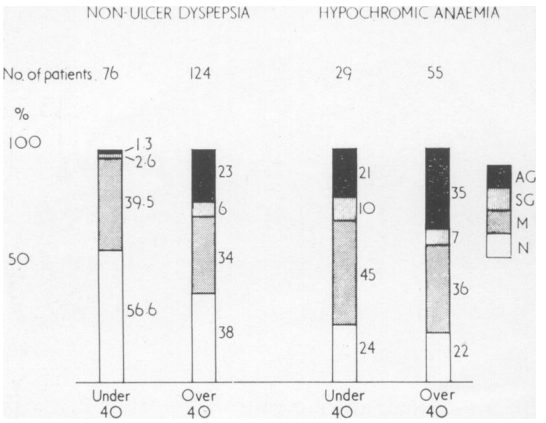

FIG. 5.—Percentage distribution of mucosal changes in 200 patients with non-ulcer dyspepsia and 84 patients with hypochromic anaemia under and over 40 years of age.
AG = Chronic atrophic gastritis.
SG = Chronic superficial gastritis.
M = Miscellaneous minor mucosal changes.
N = Normal mucosa.

gastric ulcers. There is a large group of patients suffering from dyspepsia in whom investigation fails to reveal organic disease,[37, 40, 45, 64] but there have been few studies of the gastric mucosa in patients with non-ulcer dyspepsia (N.U.D.). Williams *et al.*[116] found that in a series of 200 patients the mucosa was normal in 45%. There were minor miscellaneous changes in 36%. Chronic superficial gastritis was present in 4.5% and chronic atrophic gastritis in 14.5% (Table 1).

TABLE 1
ABNORMALITIES OF THE GASTRIC MUCOSA IN NON-ULCER DYSPEPSIA AND HYPOCHROMIC ANAEMIA
(Williams *et al.*, 1957; Coghill and Williams, 1958)

Mucosa	Non-ulcer Dyspepsia (200 patients)		Hypochromic Anaemia (84 patients)	
	No.	%	No.	%
Normal	90	45	19	21
Minor lesions ..	72	36	33	39
Chronic superficial gastritis	9	4.5	7	8
Chronic atrophic gastritis	29	14.5	25	30
	38	19	32	38

In a somewhat similar series of 150 patients Motteram[82] found a higher incidence of atrophic gastritis but the results were not strictly comparable. The findings in the series of 50 patients with N.U.D. reported by Shiner and Doniach[100] agreed more closely with ours.

3. *Hypochromic Anaemia.* There have been a number of reports about the gastric mucosa in

hypochromic anemia. aAtrophic gastritis was found by Badenoch and Richards[3] and by Coghill and Williams.[16] Davidson and Markson[20] described their findings in 42 patients and 31 controls, and Badenoch *et al.*[5] in 50 patients and eight controls (Table 2). Both sets of authors

TABLE 2

HISTOLOGY OF GASTRIC MUCOSA IN IRON DEFICIENCY ANAEMIA AND CONTROLS

Mucosa	Anaemia		Controls	
	Davidson and Markson (1955) (42 cases)	Badenoch *et al.* (1957) (50 cases)	Davidson and Markson (1955) (31 cases)	Badenoch *et al.* (1957) (8 cases)
	%	%	%	%
Normal ..	26	14	71	100
Chronic superficial gastritis	31	46	6	—
Chronic atrophic gastritis	33 } 43	} 40	10 } 23	—
Gastric atrophy	10		13	

have included instances of what we would term minor changes in their superficial gastritis group and some cases we would term superficial gastritis in their atrophic group. This explains, in part at least, the much higher incidence of gastritis found in hypochromic anaemia by these authors, and may also explain the curious findings in the control group reported by Davidson and Markson.[20]

Coghill and Williams[18] reported their findings in a series of 84 patients with 'idiopathic' hypochromic anaemia. In most of the patients the anaemia was not directly due to ascertainable physical disease. The mucosa was normal in 21%. For the rest, 39% had minor mucosal changes, 8% were classed as superficial gastritis, and 30% as atrophic gastritis. These results are shown in Table 1 where they are contrasted with our findings in N.U.D. In hypochromic anaemia there was a level incidence of severe gastritis of about 30% in each 10-year age group up to the age of 60 after which the incidence doubled (Fig. 6).

If gastritis is causally related to hypochromic anaemia it might be expected more often in patients in whom other possible causes were less prominent, and the reverse should hold. We therefore searched for causes for the anaemia in our cases. A dietetic history was obtained from every patient by a qualified dietitian. The intake of iron, protein and vitamin C was recorded for the five years before the anaemia was first diagnosed. The intake of iron and other dietary factors was expressed as a percentage of the allowances suggested as normal in the Report of

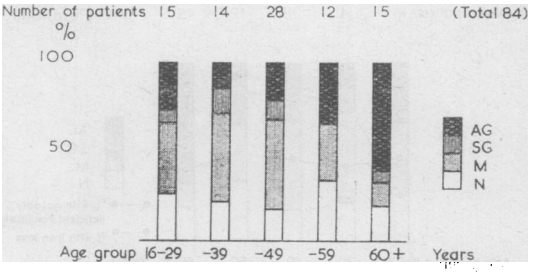

FIG. 6.—Incidence of gastritis, by age, in 84 patients with hypochromic anaemia.

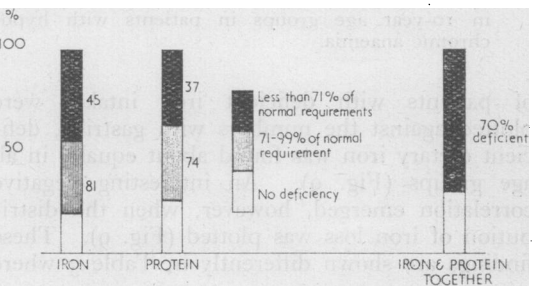

FIG. 7.—Percentage distribution of dietary deficiencies in 84 patients with hypochromic anaemia.

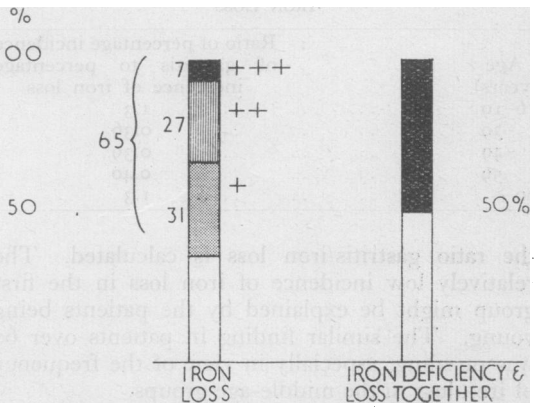

FIG. 8.—Percentage distribution of different degrees of iron loss alone, and of iron loss and deficient iron intake together, in 84 patients suffering from hypochromic anaemia.

the Committee on Nutrition of the B.M.A.[13] The result (Fig. 7) indicated that in a majority of the patients dietary iron and protein had been deficient. Of the patients 70% were taking a diet poor in both iron and protein. Intake of vitamin C was low in 10% of patients, though none had scurvy. Iron loss over the whole of the patient's life was estimated and the patients were graded by its degree (Fig. 8). In all but three of the patients there was clear evidence of deficient iron intake or excessive iron loss, and in half of them there was both. When the numbers

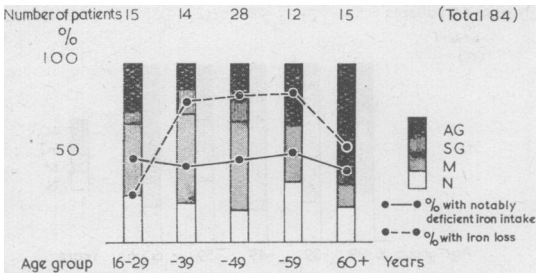

FIG. 9.—The percentage distributions of deficient diet (iron intake <71% of normal) and of iron loss (2 or 3+), plotted against the incidence of gastritis in 10-year age groups in patients with hypochromic anaemia.

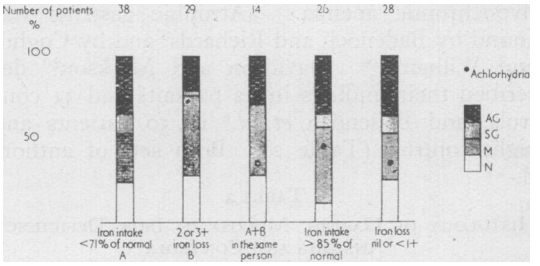

FIG. 10.—The relationship between deficient iron intake, iron loss, achlorhydria and gastric mucosal histology.

of patients with deficient iron intakes were plotted against the numbers with gastritis, deficient dietary iron was found about equally in all age groups (Fig. 9). An interesting negative correlation emerged, however, when the distribution of iron loss was plotted (Fig. 9). These findings are shown differently in Table 3 where

TABLE 3

RELATIONSHIP BETWEEN GASTRITIS AND A HISTORY OF IRON LOSS

Age (years)	Ratio of percentage incidence of gastritis to percentage incidence of iron loss
16–19	1.3
–39	0.36
–49	0.39
–59	0.40
60+	1.3

the ratio gastritis/iron loss is calculated. The relatively low incidence of iron loss in the first group might be explained by the patients being young. The similar finding in patients over 60 was puzzling, especially in view of the frequency of iron loss in the middle-age groups.

In Fig. 10 the patients are shown divided into those with some reason for their anaemia (either notably deficient iron intake or notable iron loss, or both) and those without. Gastritis appeared to be a little less common in patients whose anaemia could have been attributed to the factors mentioned. These results are compatible with the suggestion that gastritis might be an aetiological factor in hypochromic anaemia. However, if the incidence of achlorhydria in each group is also plotted, being associated with atrophic gastritis it, too, tended to be commoner among patients with more truly idiopathic anaemia (Fig. 10).

Another group of 24 patients suffering from chronic intestinal disorders presumed to be causing their hypochromic anaemia had a low incidence—12%—of severe gastritis (Table 4).

TABLE 4

CASES OF ULCERATIVE COLITIS, STEATORRHOEA OR CROHN'S DISEASE, WITH HYPOCHROMIC ANAEMIA

(24 patients)

Mucosa	No.	%
Normal	16	67
Minor lesions	5	21
Chronic superficial gastritis	0	—
Chronic atrophic gastritis	3	12

Nineteen of these patients were aged 40 or over; five were aged 60 or over. The ages of the cases with atrophic gastritis were 59, 59, 81 years.

This is further evidence of a negative correlation between gastritis and overt causes of hypochromic anaemia.

Lees and Rosenthal[71] examined biopsy specimens from 19 patients with hypochromic anaemia before, and one year after, correction of the anaemia. If anything the gastritis progressed.

It has not so far proved possible to correlate the state of the gastric mucosa with the duration of the anaemia. However, much of the evidence does not support the suggestion that gastritis is a result of chronic iron deficiency;[118] rather the reverse.

4. *Addisonian Pernicious Anaemia.* There are a number of reports on the gastric mucosa in this condition. Magnus and Ungley[75] and Magnus[73, 74] did all their work on material obtained at autopsy, taking care to ensure proper tissue fixation. Biopsy studies in this condition have been carried out principally by Doig and Wood,[34] Siurala,[101] Debray *et al.*[25, 26] and Williams *et al.*[115] The last authors, summarizing their own and others' experience, found that in 'adult' Addisonian pernicious anaemia atrophy of the mucosal body glands was always present and was usually complete. A moderate degree of infiltration of the stroma with inflammatory cells was common. However, scattered parietal cells survived in 32% of their patients. It is evident that the histological appearances of the gastric mucosa in pernicious anaemia are frequently indistinguishable from

those seen in other patients without this disorder and that there are no lesions pathognomonic of pernicious anaemia.

Examination of the gastric mucosa may help with the diagnosis in patients presenting with neurological signs suggestive of subacute combined degeneration of the cord but without anaemia and with a normal bone marrow.[33] However, vitamin B_{12} should be given in such cases whatever the results of the gastric biopsy, because this complication can occasionally arise in vitamin B_{12} deficiency arising in vegans,[2] or from disease of the small intestine.[12]

In the very rare instances of ' juvenile ' Addisonian pernicious anaemia[52, 77] the gastric mucosa looks normal on biopsy. In these patients ability to secrete intrinsic factor has been lost independently of any histological change in the mucosa, and ability to secrete HCl is retained.

5. *Other Megaloblastic Anaemias.* When there is deficiency of vitamin B_{12} or folic acid due to inadequate diet or disease of the small intestine with resulting megaloblastic anaemia the gastric mucosa may be normal. However, some patients with tapeworm infestation of the small intestine have been thought to develop atrophic gastritis along with their vitamin B_{12} deficiency. It is claimed that the gastric mucosa may become normal when the patient has been freed of worms.[101, 102]

Gastric Mucosal Changes after Operations on the Stomach. Palmer[88] examined the gastric mucosa of 45 patients, all with normal histology pre-operatively, at various intervals after different kinds of gastric operation. Twenty-two patients developed gastritis mostly of a minor kind, but in eight glandular atrophy and intestinal metaplasia were found. Debray *at al.*[27] found intestinal metaplasia in 25% of 111 post-operative stomachs biopsied, but atrophy was reported as uncommon. Lees and Grandjean[70] examined 41 symptomless non-anaemic patients after partial gastrectomy. Severe gastritis (with atrophy) was found in half of them. Coghill and Williams[18] found severe gastritis in 52% of 21 patients with hypochromic anaemia after gastric operations and in 44% of 16 such patients who were not anaemic. Knowledge of what happens to the gastric mucosa after gastric operations is still regrettably scanty.

Ability to Secrete Hydrochloric Acid in the Stomach. There have been several reports of a direct relationship between decreasing HCl production and atrophic gastritis.[5, 20, 116, 121] Lees and Rosenthal[71] found that in two patients in whom the second of two gastric biopsies done after an interval showed an increase in atrophy, the presence of HCl was no longer detectable.

Gastric Secretion of Pepsin. Wood *et al.*[121] showed that patients with atrophic gastritis (not all suffering from pernicious anaemia) secreted much less pepsin in the gastric juice than patients without atrophy of the gastric mucosa. Badenoch *et al.*[5] measured the secretion of pepsin and the excretion of uropepsin in patients with hypochromic anaemia. The values for both substances fell progressively to low levels, as the degree of gastric mucosal atrophy increased.

Secretion of Intrinsic Factor. As chronic atrophic gastritis may occur in patients without Addisonian pernicious anaemia and as the gastric mucosal lesion in this condition is usually no different from that in these other patients, the question arises as to the relationship between the state of the gastric mucosa and the ability to secrete intrinsic factor. Some studies have suggested that atrophic gastritis may, in some patients, be associated with diminished secretion of intrinsic factor.[2, 15, 49, 77, 103] A study of 124 patients with gastritis associated with some degree of mucosal atrophy, but with no clinical or haematological signs of pernicious anaemia by Whiteside *et al.*[110] (to be published) showed that the serum vitamin B_{12} levels were lower, and the ability to absorb radioactive B_{12} less, the more severe the atrophic gastritis. However, in spite of these related trends, in a minority of patients HCl or intrinsic factor production were, together or separately, greater or less than the degree of atrophic gastritis would have suggested from the average findings. The authors suggest that this may indicate that for clinical pernicious anaemia to develop gastric mucosal atrophy alone is not enough, and that an additional factor must be present, such as loss of part of the stomach (partial gastrectomy) or a hereditary trait.

Better understanding of the function of different gastric mucosal cells and of the results of their loss in atrophic gastritis must await the perfection of promising new techniques. Improved fractionation of gastric juice seems possible by paper electrophoresis[47] and, perhaps more hopefully, by ion-exchange chromatography[119] or starch zone electrophoresis.[66] A method for isolating intestinal epithelial cells from supporting elements has been developed by Dale[21] for the purpose of studying their enzyme activities.

Gastric Carcinoma. It is generally agreed that gastritis is common in stomachs harbouring carcinoma and it has long been thought that it is a precursor of cancer.[58, 59, 60] However, the relationship is not yet clear and stomachs removed for carcinoma have sometimes been reported to be free of atrophic gastritis.[105] The subject has been reviewed by Ivy.[61]

The relatively high incidence of carcinoma of the stomach in patients with Addisonian per-

nicious anaemia is well known. However, it has been suggested that this incidence is not as high as was once thought.[11] Curiously enough, the carcinoma is often in the pyloric antrum,[81] which is unaffected in pernicious anaemia, and not in the body where the atrophic gastritis is found.

It has frequently been observed that intestinal metaplasia is common in patients with gastritis,[56, 72, 112] and studies by Stout[105] and Morson[79] showed how often this condition was present in stomachs the seat of carcinoma. Morson found that intestinal metaplasia was commonest in pyloric mucosa, and was next most frequently found on the lesser curve (a fact which, by itself, raises doubts about its relationship with cancer). He and Stout[105] both found it most frequently (92-94%) in stomachs removed for carcinoma, less frequently in gastric ulcer, and least in duodenal ulcer. Guiss and Stewart[50] were unable to show that gastric cancer depended on the presence of gastric atrophy alone. If there is a relationship with gastritis it is more likely to involve the epithelial changes that so commonly occur in atrophic gastritis, and Morson[80] has brought forward impressive evidence that intestinal metaplasia can be one precursor of carcinoma. If this is so, factors in the causation of gastritis and its attendant changes will in turn be of interest in the study of the prevention of such a therapeutically unrewarding condition as gastric cancer.

Gastric Haemorrhage. Nothing is known as to whether gastric mucosa affected by chronic gastritis is more or less likely to bleed than normal mucosa. It has been suggested that the atrophic gastritis commonly found after operations on the stomach may result in mucosal bleeding and that this accounts for the hypochromic anaemia so frequently found after these operations. There is little evidence for this. However, seven of our 13 patients who bled after gastric biopsy had severe atrophic gastritis and it may be that patients with this condition bleed on biopsy more readily than others.

Aetiology

To deal with causal factors at the end rather than the beginning merely reflects our ignorance about aetiology in chronic gastritis. I have mentioned the suggestion of Magnus[73] that it may result from repeated minor traumata to the mucosa. The effect of alcohol on the gastric mucosa was studied by Joske *et al.*[65] who found atrophic gastritis in 12 out of 95 patients with chronic alcoholism—not a very high proportion. Debray *et al.*[28] found a higher incidence of atrophic gastritis in heavy wine drinkers. Palmer[90] and Williams[113] concluded that the relationship of alcoholism to chronic gastritis was uncertain.

The general question of the effect of external agents, of a minor kind, on the gastric mucosa was reviewed by Edwards and Edwards.[39] They investigated the temperature at which 155 dyspeptic patients, from whom gastric biopsies had been obtained, liked to drink their tea. There was good evidence that gastritis and mucosal atrophy increased with the temperature at which the patient commonly drank tea. This association was not explicable on grounds of sex or age. It seems possible that heat may be a common source of injury to the gastric mucosa as suggested by Hurst[59] many years ago. This would be important should gastritis prove to be a precursor of carcinoma.

The suggestion was made by Williams *et al.*[116] that after the onset of chronic gastritis the development of atrophy of the body glands might be a continuous one. The increase of chronic gastritis with age may be merely a reflection of this process, producing an increasing population with atrophic gastritis; or it might imply the appearance of involutional factors.

The possible role of iron deficiency as a cause of gastritis has been mentioned.[118]

Siurala and Tawast[104] investigated the presence of surface-active agents, as evidence of regurgitation of bile, in the stomachs of different patients. They found such agents more frequently in patients with mucosal atrophy than in subjects with a normal mucosa.

Some of the appearances of the gastric mucosa in gastritis suggest similarities with the state of other organs in conditions where auto-antibodies are present (e.g. Hashimoto's disease). This consideration led my colleague, Dr. Wynn Williams[114] to try and induce the changes of chronic gastritis in guinea pigs and rabbits by sensitizing them to injections of extracts of homologous gastric mucosa. Although antibodies were produced to the antigenic material, no gross gastric mucosal changes resulted.

Treatment

It seems relatively unimportant to attempt the treatment of a condition of which we know neither the cause nor the clinico-pathological significance. Perhaps the most important thing to be done is to fix the relationship of chronic gastritis to cancer of the stomach (as Ivy[61] has emphasized) and to residual gastric function. Then, if these relationships are positive, an attempt could be made to determine the preventable causes of chronic gastritis.

Summary and Conclusions

The history and technique of gastric biopsy have been reviewed. It is so far of only limited

usefulness in clinical practice, but it remains a valuable research tool. As a result of its use the incidence of gastritis in particular conditions is becoming known.

It seems that in general the secretory powers of the stomach in respect of HCl, pepsin and intrinsic factor decline as the degree of mucosal atrophy increases. However, these secretory functions sometimes fail at different rates.

Further work is needed to elucidate the causes of gastritis and to determine its significance in relation to gastric cancer and anaemia.

The clinical significance of gastritis awaits clarification.

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