Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Gastritis

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What is gastritis? There are many and varied answers. To the layman it is epigastric discomfort and vomiting, particularly related to heavy alcohol consumption. Clinicians find gastritis a convenient term when dealing with virtually any upper abdominal symptom, for it provides a quasi-scientific label with which to satisfy the patient. The gastroscopist's definition of gastritis depends on a visual appearance which has been shown to correlate poorly with the histological state of the mucosa, except when there are acute haemorrhagic erosions. The pathologist diagnoses gastritis by criteria such as the presence of inflammatory cells and the degree of atrophy, but these histological changes may bear little relation to the patient's symptoms. To the haematologist gastritis implies the total gastric atrophy characteristic of pernicious anaemia.

In context the term is reasonable when used by any of these individuals, but because it embraces such a variety of situations gastritis has come to be almost meaningless as a concept of disease. In relation to clinical medicine the term gastritis is best considered as embracing two distinct and probably unrelated entities: *acute gastritis*, which is the transient reaction of the gastric mucosa to irritants, and *atrophic gastritis*, in which the mucosa is permanently altered and its normal function impaired. In both conditions the lesion is diffuse and inflammatory cells are present to a greater or lesser degree, but these two features are the only similarities between acute and atrophic gastritis. In this article the clinical aspects of acute and atrophic gastritis will be considered in relation to recent work on the histology and physiology of the gastric mucosa.

Gastric Cells and Gastric Function

Before considering these diffuse lesions of the stomach it is worth recalling the normal architecture of the gastric mucosa. Our knowledge of the mucosal structure in man has increased greatly in recent years through the use of blind suction gastric biopsy.¹ By this technique samples of human gastric mucosa may be simply and safely obtained, and fixed before autolysis of the cells occurs.

The surface of the gastric mucosa facing the gastric lumen is covered with mucus-producing columnar (surface epithelial) cells. These cells are formed by mitoses in the base of the gastric pits and they migrate up the walls of the pits to the surface, where they are extruded into the lumen of the stomach (Figure). In man the life span (or turnover) of these cells is two to four days, and it has been estimated that there is a continuous loss into the gastric lumen of half a million cells per minute.² This active turnover of epithelial cells functions to protect the mucosa from damage.

Below the gastric pits is the glandular or secreting part of the mucosa, where the cells are of a very different type. The two important cells in this part of the mucosa are the large

parietal or acid secreting cells, and the smaller zymogenic or pepsin secreting cells. In terms of turnover these cells are static cells and mitoses are not seen in them. Intrinsic factor, which is required for vitamin B₁₂ absorption, is also produced in this part of the mucosa, possibly from the parietal cells themselves. At the two ends of the stomach, the cardia and the antrum, the normal histological picture is different, for acid and pepsin secreting cells are missing and the mucosa is mainly

Diagram of a histological section through normal gastric mucosa. The epithelial compartment is a dynamic structure composed of columnar cells which are continuously produced by mitoses at the base of the gastric pits. This high turnover of cells probably functions to protect the mucosa from external insults. The cells of the glandular or secretory portion of the mucosa are static; the large circular ones represent parietal or acid secreting cells, and the smaller ones the zymogenic or pepsin secreting cells.

composed of mucus secreting surface epithelial cells arranged as a glandular structure. Gastrin, the hormone which stimulates gastric acid secretion, is produced in the antrum, but from which cell is not known.

Thus the mucosa is composed of two main compartments, a dynamically active surface epithelium which serves to protect the mucosa, and a glandular portion containing static cells which secrete hydrochloric acid, pepsin, and intrinsic factor. Acute gastritis is a transient lesion which affects predominantly the surface epithelium, leaving the gland cells intact. In atrophic gastritis there is permanent destruction of the glandular portion and also important changes in the surface epithelium.

Acute Gastritis

The physiological response of the gastric mucosa to irritants is to exfoliate surface epithelial cells. This was demonstrated in the dog³ in response to 5% ether and 5% clove oil, and in a patient with a gastrostomy in response to 95% alcohol, copper sulphate, hydrochloric acid, and a 1 in 30 suspension of mustard in water.⁴ More recently a similar effect has been shown when three soluble aspirin tablets suspended in 50 ml. saline were

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left in contact with the human stomach for five to ten minutes.⁵ It seems likely that many other substances may have a similar irritative effect on the gastric mucosa; but mild acute gastritis, even to the extent of epithelial cell exfoliation, produces no pain or gastric symptoms. Under these circumstances it is a physiological effect and no clinically significant blood loss or gastric lesion occurs, presumably because of the regenerative capacity of the surface epithelium. Some patients, however, develop epigastric pain and discomfort when they ingest particular irritants, such as aspirin, but this pain is more likely to be due to the presence of a peptic ulcer.

Nevertheless, acute gastritis following the ingestion of irritants can have clinical significance. The patients may present with epigastric pain, nausea, and vomiting as the main features, or with overt or occult gastrointestinal bleeding.

Acute Gastritis Without Bleeding.—This occurs when the stomach is subjected to a large dose of a gastric irritant and may be a feature of ingestion of certain poisons such as lysol. In clinical practice the two most common substances involved are alcohol and staphylococcal endotoxin.

The symptoms of alcoholic gastritis may occur within hours of ingestion but are commonly notable the following morning, when the subject experiences nausea, epigastric discomfort, and vomiting. Gastric biopsy performed during this phase demonstrates damage and denudation of the surface epithelium, with the glandular epithelium left intact.⁶ These histological alterations are transient and the mucosa returns completely to normal in a few days. One or two teaspoonfuls of sodium bicarbonate dissolved in half a glass of warm water and taken immediately on waking offers some relief for alcoholic gastritis.

Staphylococcal gastroenteritis presents with vomiting and diarrhoea. The onset is abrupt and occurs four to six hours after eating contaminated food. Similar alterations in the gastric mucosa to those of acute alcoholic gastritis have been noted, with return of the mucosa to normal within 96 hours.⁶ Staphylococcal gastroenteritis is a self-limiting condition, and though the patient may be acutely uncomfortable for some hours the symptoms subside spontaneously within 12 to 24 hours. Dehydration can occur during the acute phase and may require treatment with intravenous fluids.

Acute Gastritis With Bleeding.—There is now overwhelming evidence that there is an association between haematemesis and melaena and recent consumption of aspirin.⁷ The lesions responsible for this bleeding are haemorrhagic erosions which are probably initiated by the exfoliative effect of aspirin on gastric surface epithelial cells. Haemorrhage occurs with both soluble aspirin and plain aspirin tablets, but as there is evidence that undissolved aspirin particles can "burn" larger holes in the gastric mucosa, it is sensible to advise all patients to take soluble aspirin dispersed in half a glass of water. Alcohol has a similar effect, for it is not uncommon to find diffuse haemorrhagic erosive gastritis when patients are gastroscoped during the acute bleeding induced by an alcoholic bout.

Haematemesis or melaena or both caused by alcohol or aspirin consumption may require urgent blood transfusion, but most of these acute bleeds stop spontaneously within 36 hours, with complete healing of the erosions within a few days. Because of this it is important to establish in a patient with a haematemesis and melaena whether alcohol or aspirin in any form has been taken during the previous few days. If this history is forthcoming and there is no clinical evidence of a chronic peptic ulcer it should incline the physician towards conservative, non-surgical management. A few of these patients, however, will continue to bleed, and under these circumstances an emergency operation will be needed, but the surgical management of these patients can be extremely difficult, particularly if there is bleeding from multiple gastric erosions.

Occult oozing of blood from the stomach occurs in 70% of subjects who ingest two to three aspirin tablets four times per day, usually for rheumatoid arthritis.⁸ This bleeding occurs

whether or not the aspirin is in the soluble form. In most subjects it is of no clinical significance, but in a minority the blood loss may be more than 10 ml. per day, and these individuals are prone to develop chronic iron deficiency anaemia. The bleeding can be substantially reduced by giving enteric-coated aspirin, which can be used in these subjects as long as it controls their rheumatic symptoms. It does not always do so, probably because of erratic absorption. Patients taking aspirin habitually should have regular haemoglobin estimations performed and may require oral or parenteral iron.

Atrophic Gastritis

Unlike acute gastritis, in which the gastric mucosa suffers a transient episode from which it makes a complete recovery, the histological changes of atrophic gastritis are permanent. Atrophic gastritis occurs in association with pernicious anaemia, and also without pernicious anaemia, in which case it is called simple atrophic gastritis. It may involve the whole mucosa or only parts of it. Three main alterations in the histological picture are present.

Atrophy occurs primarily in the glandular portion of the mucosa and may be partial or complete. In pernicious anaemia it is invariably complete with total absence of parietal cells, resulting in histamine-fast achlorhydria.

Inflammatory cell infiltration occurs both in the epithelial compartment and beneath it. Many of the cells are lymphocytes, but polymorphs may be seen infiltrating between surface epithelial cells.

The surface epithelial cells are commonly stunted and abnormal. In severe forms of atrophy the mucosa may alter in such a way as to look like intestinal epithelium with finger-like projections similar to intestinal villi, a condition termed intestinal metaplasia. The turnover of epithelial cells is increased in atrophic gastritis, for there are more mitoses in epithelial cells and a higher loss of these cells into the gastric lumen.²

Cause of Atrophic Gastritis

There is no one cause of atrophic gastritis, but a number of factors are known to be associated with its presence. Age is clearly one of the most important of these, for simple atrophic gastritis is uncommon under the age of 40 and becomes progressively more frequent with advancing age.⁹ Constitutional factors also play a part. The well-known tendency for the gastric atrophy of pernicious anaemia to run in families is one indication of these, and another is the higher incidence of simple atrophic gastritis in subjects with blue eyes.

Gastric autoantibodies occur in the blood of patients with pernicious anaemia and simple atrophic gastritis, which suggests that these conditions are caused by an autoimmune process. However, it may be that the gastric autoantibodies may be merely a secondary phenomenon related to the presence of an abnormal mucosa.

Environmental factors also play a part, for simple atrophic gastritis is commoner in those of low social class. Other environmental factors include heavy alcohol consumption, smoking, hot tea drinking, and possibly habitual aspirin consumption.⁹ An individual over the age of 60 who smokes and drinks heavily has a 60% chance of having simple atrophic gastritis.

Clinical Significance

The most important association between atrophic gastritis and clinical disease is in the case of pernicious anaemia. In this condition there is total gastric atrophy, histamine-fast

achlorhydria, and failure of the stomach to secrete adequate amounts of intrinsic factor. Without intrinsic factor vitamin B₁₂ cannot be absorbed in the terminal ileum; the body runs out of vitamin B₁₂ in the course of four to five years and megaloblastic anaemia ensues.

Most patients with atrophic gastritis do not have gastric symptoms. Some clinicians believe that epigastric pain or discomfort, nausea, and anorexia can be ascribed to this histological change, but there is no real evidence that this is the case. A higher incidence of atrophic gastritis has been found in patients with non-ulcer dyspepsia—indigestion and negative barium meal and/or negative gastroscopy. However, as atrophic gastritis is commonly associated with gastric ulcer it is possible that these subjects have a gastric ulcer which was missed by barium meal or gastroscopy. In our present state of knowledge it is better to regard atrophic gastritis as predisposing to gastric ulcer.

Rarely, patients with simple atrophic gastritis suffer from recurrent bleeding from gastric ulceration.¹⁰ This is certainly not the case in most patients with this condition; in fact there is some evidence that subjects with atrophic gastritis may be protected against aspirin-induced occult gastrointestinal bleeding.⁸ On the other hand, haematemesis and melaena induced by aspirin do appear to occur from acute erosions which have developed in areas of atrophic gastritis.¹¹ This suggests that under certain circumstances aspirin initiates acute bleeding from susceptible, atrophic areas of the gastric mucosa.

For many years it has been known that patients with recurrent iron deficiency anaemia may be achlorhydric, and more recently they have been found to have a higher than expected incidence of atrophic gastritis. Iron deficiency associated with atrophic gastritis cannot be adequately explained by chronic bleeding or failure of iron absorption. Other possible mechanisms involved include the production by gastric mucosa of an iron binding protein, or an excessive rate of loss of iron into the gastric lumen in exfoliated gastric epithelial cells. With regard to the latter it is interesting to note that patients with simple atrophic gastritis associated with iron deficiency anaemia have higher than normal cell loss from the gastric mucosa as measured by gastric D.N.A. (deoxyribonucleic acid) rates.²

Some 5–10% of subjects with pernicious anaemia develop carcinoma of the stomach. Even in patients without pernicious anaemia carcinoma of the stomach arises in atrophic gastric mucosa. A factor predisposing to cancer in atrophic gastritis is probably the higher than normal turnover of epithelial cells in this condition. The turnover of epithelial cells is particularly high in areas of intestinal metaplasia² which are the sites of atrophic mucosa that are most premalignant.¹²

Atrophic gastritis, even when diagnosed by gastric biopsy, does not merit treatment. Its finding should alert one to the possibility of associated conditions such as gastric ulcer, carcinoma of the stomach, pernicious anaemia, or recurrent iron deficiency anaemia, which require their own specific treatment. The recent finding that administration of corticosteroids will improve the secretory capacity and histological appearance of the atrophic mucosa of pernicious anaemia in no way implies that these drugs should be used to treat patients with atrophic gastritis.

Rare Forms of Gastritis

Menetrier's disease is a diffuse disorder of the stomach in which the mucosa becomes thickened and hyperplastic. Radiologically giant rugal folds are seen. An important feature of this condition is that patients may present with oedema due to

hypoproteinaemia. The hypoproteinaemia has been shown to be due to excessive loss of protein from the abnormal gastric mucosa. The disease is very rare, but is notable as it was the first condition in which protein-losing gastroenteropathy was described.

True infective gastritides have been described due to bacteria, syphilis, and tuberculosis. These are extremely rare and can only be regarded as medical curios.

Conclusion

To the clinician the term gastritis embraces two distinct and probably unrelated entities.

(1) Acute gastritis is a transient response of the gastric mucosa to the ingestion of irritating substances such as alcohol, staphylococcal endotoxin, and aspirin. The symptoms of excessive intake of these substances include epigastric discomfort, nausea, and vomiting. Haematemesis and melaena may occur from gastric erosions, and in Britain it is particularly associated with aspirin consumption.

(2) Atrophic gastritis is a permanent atrophy which affects part or all of the gastric mucosa. Total atrophy is a feature of pernicious anaemia. The cause of simple atrophic gastritis is not known, but in susceptible individuals it occurs particularly over the age of 50 and appears to be related to heavy alcohol consumption and smoking. It is commonly associated with other clinically important conditions; in particular with gastric ulceration, recurrent iron deficiency anaemia, and gastric carcinoma. The alteration in the gastric mucosa may be involved in the pathogenesis of these conditions, but only research will determine their exact relationship one to another.

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