

Primer: histopathology for the clinician—how to interpret biopsy information for gastritis

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SUMMARY

Gastroenterologists can be frustrated, at times, by surgical pathology reports of gastritis that either do not match what was seen endoscopically, or do not indicate the presence of a specific disease. This might be because of one or more factors. First, it has been well established that the correlation between the endoscopic diagnosis of gastritis and histologic gastritis is poor. Second, there are a limited number of well-known histologic gastritides that yield specific diagnoses. Reports that are purely descriptive are, therefore, common, and might require discussion between endoscopist and pathologist.

KEYWORDS atrophic, biopsy, gastritis, gastropathy, *Helicobacter pylori*

REVIEW CRITERIA

This review is based primarily on the authors' clinical experience. PubMed searches were performed as needed to locate appropriate references for the specific points about which the reader might wish to know more.

INTRODUCTION

In an ideal world, an upper endoscopy would be performed for a specific clinical indication, the gastric mucosa would be inspected, and a set of observations made. If indicated, gastric biopsies would be obtained and submitted, along with the relevant clinical and endoscopic information, to a surgical pathologist who is knowledgeable and skilled in interpreting gastric biopsies. A specific clinical question (asked on the requisition) would be addressed in the surgical pathology report received a few days later. This report would include a clearly stated, specific diagnosis that correlated with the patient's symptoms and the endoscopic findings. If the performance of any part of this multistep process is less than ideal, chances are that the outcome will be less than ideal as well.

In the real world, several things can go awry. First, the endoscopic and clinical information might not be communicated to the pathologist. Second, the pathologist might not be an expert in gastrointestinal pathology. Third, the endoscopist might not understand the terminology used by the pathologist. Fourth, the histologic diagnosis might not correlate with the endoscopic appearance of gastritis. So it is that gastroenterologists can, at times, be dissatisfied, annoyed, or confused by the surgical pathology report accompanying a set of gastric biopsies.

It is important to recognize that good endoscopic–histologic correlation for gastric biopsies, satisfying as it would be, should not be expected much of the time. As a matter of fact, each time it has been studied, the correlation between what is interpreted endoscopically as GASTRITIS or EROSION, and histologic confirmation of gastritis or erosion on biopsy, is about 50%, or only as good as a coin toss.^{1–4} In addition, endoscopically normal mucosa will yield biopsies with histologic gastritis in about 25% of cases.^{1,4} When pathologists are unaware of this lack of endoscopic–histologic correlation, they might feel compelled to make diagnoses that explain a report of endoscopic

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Table 1 Summary of gastroenterologist–pathologist interactions, based upon the discussion in the text.

| Pathologist diagnosis ^a | Gastroenterologist assumptions about what the pathologist found | Gastroenterologist response |
|---|--|---|
| Any type of gastritis accompanied by the words <i>H. pylori</i> | There is a chronic gastritis, and the pathologist has found the organism | Accept that the patient has <i>H. pylori</i> gastritis |
| Atrophic gastritis | There is chronic inflammation with loss of glands and probably either intestinal metaplasia or pyloric gland metaplasia, or both | Accept that the patient has one of the atrophic gastritides: if you want to know whether it is autoimmune or multifocal atrophic gastritis, contact the pathologist and ask |
| Chemical or reactive gastropathy | There is foveolar hyperplasia with mucus depletion but with little inflammation | Check whether the patient is an NSAID user or whether bile reflux was found during endoscopy |
| Lymphocytic gastritis | The surface epithelium has many lymphocytes within it | Check whether the patient has an associated condition, such as <i>H. pylori</i> infection or celiac disease. Review the endoscopic findings to see if the patient has a giant-fold disease or a polyp |
| Focally enhanced gastritis | There are one or more foci of lamina propria lymphocytes surrounding and infiltrating a pit, neck or gland | Check whether there is anything to suggest the patient has Crohn's disease or ulcerative colitis |
| Nonspecific gastritis | No assumptions can be made for this diagnosis | Either call the pathologist to ask what was seen and request suggestions as to the cause, or ignore the diagnosis |
| Acute gastritis | The only assumption is that the pathologist saw many neutrophils | Either call the pathologist to ask what was seen, such as chronic <i>H. pylori</i> -type gastritis in the background or an erosion, or decide whether this looks like a diffuse acute bacterial infection |

^aIn all of these, the endoscopic findings can be normal or abnormal. *H. pylori*, *Helicobacter pylori*; NSAID, nonsteroidal anti-inflammatory drug.

GLOSSARY

GASTRITIS

Histologic inflammation of the mucosa of the stomach, either acute or chronic; often accompanied by epithelial injury and/or metaplasia

EROSION

Loss of integrity of the surface epithelium that results in acute inflammation, with neutrophils and the exudation of fibrin

gastritis or erosion. An endoscopist who sees endoscopic inflammation might not find a pathology report credible if it does not mention inflammation. Or a pathology report of some sort of gastritis might seem at odds with a normal upper endoscopy. The first point to be made in relation to a better understanding of histologic diagnoses of any type of gastritis is, therefore, that endoscopically normal mucosa often has histologic inflammation, and endoscopically inflamed mucosa is often histologically normal.

Once we accept that a pathology report of gastritis will correlate with endoscopy results only about half of the time, these pathology reports can be divided into two broad groups. The first group includes specific diagnoses of gastritis that have names associated with accepted sets of histologic features. The most common of these are *Helicobacter pylori* gastritis, lymphocytic gastritis, chemical gastropathy, the atrophic gastritides, and focally enhanced gastritis. The second group includes those that are descriptive and not specific, and are probably the most confusing.

While we cannot remedy the process problems discussed above, we hope that the explanation of the common pathologic diagnoses of gastric inflammations that follows will be of benefit. The descriptions of the different gastritides can be found in every textbook of gastrointestinal pathology; however, none of these textbooks deal with communication issues between pathologists, who see the biopsies but know little else about the patient or the stomach, and gastroenterologists, who have seen the stomach, know the patient and take the biopsies. We have tried to address these communication deficiencies in this discussion. They are summarized in Table 1.

THE SPECIFIC GASTRITIS DIAGNOSES

***Helicobacter pylori* gastritis**

In the US, in patients with *H. pylori* infection the site most infected and intensely inflamed is the antrum, with variable extension of the infection and inflammation into the body of the stomach. The cardia is also likely to be infected, perhaps because it is histologically similar to the antrum. The body mucosa is

infected by fewer bacteria and, therefore, has less intense inflammation.

Diagnostic biopsies of *H. pylori* gastritis have classic features that include diffuse plasmacytosis of the superficial LAMINA PROPRIA, with or without the presence of a few eosinophils, and can also involve the deeper mucosa. Lymphoid follicles with germinal centers are often present (Figure 1). Neutrophils infiltrate the epithelium at the base of the gastric pits, usually in the same areas where *H. pylori* are visible. *H. pylori* are present in the superficial mucus coat, and can often be seen on hematoxylin and eosin staining as slightly curved rods in the mucus, or attached to the apices of FOVEOLAR CELLS.⁵ Special stains such as Warthin–Starry, Giemsa, or DiffQuik (Dade Behring, Switzerland) can enhance the visibility of *H. pylori* by staining them a different color, but immunostains are the most sensitive and specific. When *H. pylori* are not plentiful they can be difficult or impossible to visualize with any stain, and when there is intense acid suppression, they tend to move from the antrum to the body of the stomach.⁶ It is not uncommon to find patches of GLAND ATROPHY and intestinal METAPLASIA in biopsies of *H. pylori* gastritis.

In patients who are treated for *H. pylori* gastritis, first the organisms and the neutrophils disappear, then the intensity of the plasmacytosis in the lamina propria and the number of lymphoid follicles recede. When we see a case of chronic gastritis with superficial plasma cells, no activity in the form of neutrophils within the epithelium, and no *H. pylori*, we wonder if the patient has *H. pylori* gastritis that has been partly treated. Proton-pump inhibitor (PPI) treatment can lead to the same picture, because an increased antral pH leads to fewer organisms and less inflammation in the antrum, and sometimes intensification of the body gastritis. In most cases, it is not possible to discern the cause of this histologic gastritis.

There is no universally accepted name for *H. pylori* gastritis. It can be called 'chronic nonspecific gastritis' and 'diffuse antral gastritis', both accompanied by mention of *H. pylori*. We refer to it as either '*H. pylori* gastritis' or 'chronic active gastritis with *H. pylori*'. Any diagnosis of gastritis that mentions the presence of *H. pylori* is informative, and should be acceptable to endoscopists. As there are no specific endoscopic findings to suggest *H. pylori* infection, most diagnostic

biopsies are taken from endoscopically normal mucosa, except for the occasional case in which the lymphoid follicles are especially prominent, yielding nodular mucosa.^{7,8}

The chronic atrophic gastritides

The atrophic gastritides are defined by inflammation, gland loss (atrophy) and metaplasia. We recognize two types of atrophic gastritis: autoimmune atrophic gastritis and multifocal atrophic gastritis.

Autoimmune atrophic gastritis

Autoimmune atrophic gastritis can accompany pernicious anemia, but most patients with autoimmune atrophic gastritis do not have this anemia. Autoimmune atrophic gastritis involves the body uniformly, but spares the antrum. When fully developed, it is characterized by the total loss of gastric body glands, some of which are replaced by metaplastic pyloric-type glands. The epithelium in some of the gastric pits and in other glands is replaced by epithelium with intestinal characteristics, mainly goblet cells. The lamina propria contains variable numbers of plasma cells with scattered lymphocytes and even eosinophils (Figure 2).⁵

The evolution of autoimmune atrophic gastritis is not well understood, although it probably begins as diffuse gastric body inflammation with progressive gland loss, followed by the development of metaplasia. It has been suggested that autoimmune atrophic gastritis is an autoimmune reaction, triggered by *H. pylori* infection in childhood.⁹ Complete destruction of the parietal cells leads to achlorhydria, which results in a lack of regulation of the gastrin-producing G CELLS in the antrum, and which, in turn, leads to hypergastrinemia. Gastrin normally stimulates not only parietal cells but also ENTEROCHROMAFFIN-LIKE (ECL) CELLS in the body. The hypergastrinemia of autoimmune atrophic gastritis causes nodular ECL-cell hyperplasia at the base of the mucosa, and sometimes even carcinoid tumors.⁵

Multifocal atrophic gastritis

Multifocal atrophic gastritis is the most common atrophic gastritis, and is ubiquitous in some populations. This type of gastritis can begin as multiple patches of atrophy along the gastric body–antrum junction, and can then extend to involve much of the gastric mucosa, even the whole stomach. How multifocal atrophic gastritis evolves is unclear,

GLOSSARY

LAMINA PROPRIA

The stroma of the mucosa, surrounding the gastric pits and glands; it normally contains only blood vessels and fibroblasts, and very few inflammatory cells

FOVEOLAR CELLS

Mucus cells that cover the gastric mucosal surface and line the gastric pits (foveolae)

GLAND ATROPHY

The loss of glands as a consequence of chronic inflammation

METAPLASIA

The change of one cell type to another, usually in the setting of chronic inflammation and/or injury

G CELLS

Endocrine cells in the antral mucosa that secrete gastrin in response to gastric distention and the presence of certain substances in the gastric lumen

ENTEROCHROMAFFIN-LIKE (ECL) CELLS

Endocrine cells in the fundic mucosa, which produce histamine in response to stimulation by the hormones gastrin and pituitary adenylyl-cyclase-activating peptide

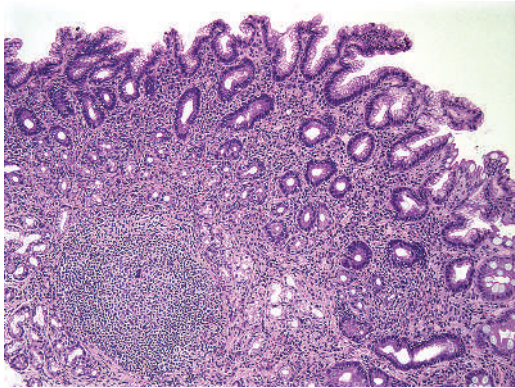


Figure 1 Histologic appearance of *Helicobacter pylori* gastritis. *Helicobacter pylori* gastritis is seen as diffuse expansion of the superficial lamina propria by an inflammatory infiltrate of primarily plasma cells, and frequently includes lymphoid follicles with germinal centers (lower left). The *H. pylori* present in the surface mucus coat cannot be seen at this magnification. (Hematoxylin and eosin staining, $\times 100$).

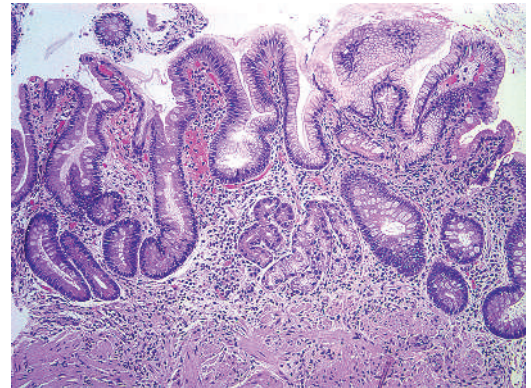


Figure 2 Histologic appearance of autoimmune atrophic gastritis. Autoimmune atrophic gastritis is characterized by nearly complete loss of fundic glands, the presence of metaplastic mucus glands resembling pyloric glands (lower center of field), and intestinal metaplasia of surface and gastric pits (on the left and right sides). (Hematoxylin and eosin staining, $\times 100$).

although it probably starts with inflammation, followed by gland atrophy and intestinal metaplasia.⁵ Worldwide, most multifocal atrophic gastritis is a sequela of *H. pylori* infection, and we often find patches of multifocal atrophic gastritis in biopsies that also contain *H. pylori* gastritis.

Diagnosing autoimmune versus multifocal atrophic gastritis

It is difficult for pathologists to tell which type of atrophic gastritis is present, unless they know the site of the biopsy. Any atrophic gastritis in the antrum is multifocal atrophic gastritis, while both types can involve the body mucosa. Deep ECL-cell nodules are characteristic of autoimmune atrophic gastritis, but they are often small and easily missed. When biopsying a stomach for the possibility of gastritis, therefore, it is important that the pathologist knows which site the biopsies were taken from. A pathologist's diagnosis of atrophic gastritis is usually multifocal atrophic gastritis, since it is far more common than autoimmune atrophic gastritis, but if the specific type is felt to be clinically important, then the pathologist must be asked for clarification.

Chemical gastropathy

Chemical gastropathy, reactive gastropathy, bile-reflux gastropathy, and type C gastritis are all synonyms for a characteristic pattern of gastric-

surface mucosal injury. This has been traditionally included among the gastritides, although it is not really an inflammation so much as a reaction to surface injury. This injury pattern was first recognized in patients who had undergone surgical gastroenterostomy resulting in the reflux of bile into the stomach, and was, therefore, called bile-reflux gastropathy. Later, this pattern was seen in intact stomachs, and was found to have a number of clinical associations. As this injury can be seen both in operated and intact stomachs, the diagnostic terms of chemical gastropathy and reactive gastropathy were introduced.

Whatever the name used or the clinical setting, the histologic features of this pattern of injury are the same: elongation and tortuosity of the gastric pits and foveolae; regenerative changes of surface epithelium, which usually has decreased mucus content; and variable superficial mucosal capillary dilatation, edema, and smooth-muscle fibers. There is little, if any, inflammation (Figure 3). In some cases, the surface injury results in erosions. Presumably an agent, such as bile or a drug, injures the mucosal surface, resulting in the loss of surface epithelial cells and increased proliferation of cells at the regenerative zone (which is in the foveolar neck region).^{10,11}

In addition to bile reflux, chemical gastropathy has been associated with the ingestion of a number of pharmaceutical agents, most notably nonsteroidal anti-inflammatory drugs

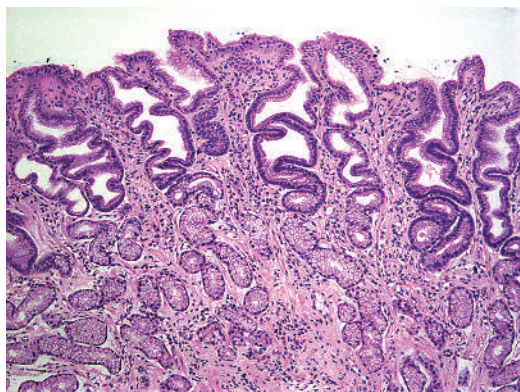


Figure 3 Histologic appearance of chemical gastropathy. In chemical gastropathy, the gastric pits are elongated and tortuous, and lined by regenerative epithelium. There are small groups of smooth-muscle cells between the pits, and scant inflammation. (Hematoxylin and eosin staining, $\times 200$).

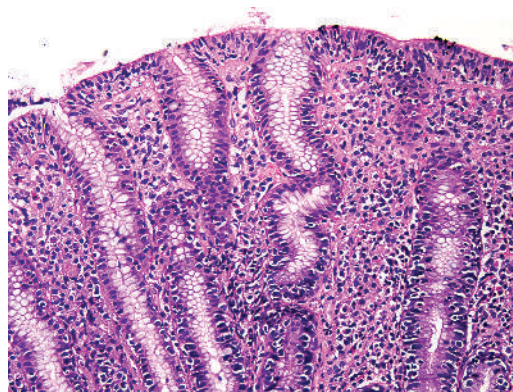


Figure 4 Histologic appearance of lymphocytic gastritis. In this example of lymphocytic gastritis, innumerable lymphocytes are present in the mucosal surface and gastric pit epithelium, and the lamina propria contains plasma cells and lymphocytes. (Hematoxylin and eosin staining, $\times 200$).

(NSAIDs). In the nonoperated patient, not all patients with chemical gastropathy are taking NSAIDs or another drug, and not all patients taking NSAIDs have chemical gastropathy.^{12,13} In our experience, biopsies of endoscopic antral gastritis, erythema or erosions are likely to be histologically described as chemical gastropathy.

What, then, does a diagnosis of chemical gastropathy mean? This diagnosis indicates mucosal surface injury, possibly due to NSAIDs, another drug, or bile reflux. It correlates well with the antral erythema, erosion, or gastritis seen endoscopically.

Lymphocytic gastritis

Lymphocytic gastritis is not one specific entity, but rather a pattern of gastritis associated with various clinical conditions. Lymphocytic gastritis is characterized by a striking increase in the number of lymphocytes in gastric and foveolar epithelium, with chronic inflammation of the lamina propria (Figure 4). Occasionally, there are foci of neutrophilic infiltrates in the gastric pits or necks.

Three clinical situations are associated with lymphocytic gastritis. Between a third and half of patients with celiac disease have lymphocytic gastritis,^{14,15} and this is usually most prominent in the antrum.¹⁶ Lymphocytic gastritis can also be found in patients with *H. pylori* gastritis,¹⁷ in which case it is more prominent in the gastric body and subsides with *H. pylori* eradication therapy. In patients with lymphocytic gastritis

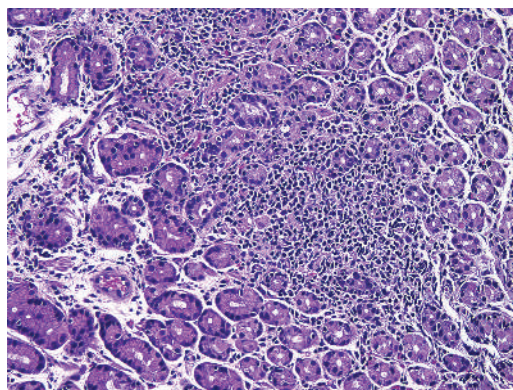


Figure 5 Histologic appearance of focally enhanced gastritis. Focally enhanced gastritis is the term applied to intense, but circumscribed, foci of lymphocytic inflammation that infiltrate gastric pit or gland epithelium, such as this example in gastric fundic glands. (Hematoxylin and eosin staining, $\times 200$).

and *H. pylori* gastritis, the *H. pylori* might be histologically undetectable. With both celiac disease and *H. pylori* gastritis, lymphocytic gastritis is thought to indicate that there has been an immune response to luminal antigens. In the occasional case of lymphocytic gastritis, there is a characteristic endoscopic appearance called varioliform gastritis, in which there are large folds in the fundus and mucosal nodules, which might be eroded;¹⁸ however, most cases do not have this appearance. Some patients with the large-fold form of lymphocytic gastritis have a MENETRIER'S-DISEASE-like syndrome with

GLOSSARY

MENETRIER'S DISEASE

Giant folds in most or all of the gastric body covered by an expanded mucosa; accompanied by hypochlorhydria and hypoproteinemia due to protein loss

hypoalbuminemia. Not all cases of lymphocytic gastritis fit into one of the above three categories—some have no underlying clinical or endoscopic disease.¹⁶ By contrast, some endoscopically detected polyps might be nothing more than lymphocytic gastritis, histologically.

A diagnosis of lymphocytic gastritis suggests that a patient has one of the known clinical associations, such as *H. pylori* gastritis, in which the organisms are not identifiable even with the use of special stains. A patient might have gluten sensitivity, but this can be addressed if a duodenal biopsy is also performed. If not, and if the clinical presentation warrants it, further evaluations for celiac disease might be appropriate. If large folds or mucosal nodularity are seen, a diagnosis of lymphocytic gastritis correlates with the endoscopy, but does not point to a specific etiology.

Focally enhanced gastritis

The term 'focally enhanced gastritis' was introduced by Oberhuber in 1997 to describe small foci of inflammation that are commonly encountered in biopsies of endoscopically normal gastric mucosa in patients with Crohn's disease.¹⁹ Focal collections of inflammatory cells, predominantly lymphocytes, surround and infiltrate gastric foveolar or glandular epithelium (Figure 5). There can be single or multiple foci of inflammation, and they are generally separated by intervening normal mucosa.¹⁹ This focal inflammation was first identified in 30–76% of patients with Crohn's disease, so it was originally considered to have significant specificity for that diagnosis.^{20,21} Later, it was also found to be common in endoscopically normal stomachs of ulcerative colitis patients, so it was thought to be a marker for inflammatory bowel disease.²² More recently, it has been shown that such inflammatory foci are so common that most cases occur in patients who do not have chronic inflammatory bowel disease.²³ Unless there are multiple intense foci, or other clinical features that suggest inflammatory bowel disease, this diagnosis does not tell you anything specific about your patient. Usually these focal inflammations are seen in patients with normal endoscopy.

Acute gastritis

Our concept of an 'acute gastritis' is a neutrophil-rich edematous mucosa with lysis of pits and glands, and no chronic inflammation

in the background. This is so rare that we have yet to see it. It has been suggested that it occurs in patients who were acutely infected by *H. pylori*, but the histologic details of such infections are not known. We have seen the diagnosis of acute gastritis made by pathologists in several settings, such as in chronic *H. pylori* gastritis, in which there is a lot of neutrophil activity in the gland necks, and in the acute erosive chemical gastropathy, with some neutrophils around the necrotic superficial mucosa and in the overlying tiny exudates. Any pathologist's diagnosis of acute gastritis must, therefore, be viewed with suspicion, and probably warrants communication with the pathologist to find out exactly what was seen.

DESCRIPTIVE DIAGNOSES WITHOUT SPECIFICITY

Pathologists often issue diagnoses of gastritis that do not match any of the described gastritides, either one of those discussed above, or other, less common gastritides described in the literature. Typical examples include diagnoses such as 'chronic nonspecific gastritis' and 'mild chronic gastritis'. These diagnoses are issued for a variety of reasons.

Although a normal gastric lamina propria is not supposed to contain a single inflammatory cell, in fact, many or even most biopsied stomachs have a few such cells—usually plasma cells in the superficial lamina propria. Some pathologists feel that it is necessary to diagnose these few plasma cells as some kind of chronic gastritis, resulting in one of these uninformative, nonspecific gastritis diagnoses. Other pathologists, recognizing how common the cells are, ignore them.

As discussed above, treated *H. pylori* gastritis can result in biopsies with diffuse plasmacytosis but few of the other features of *H. pylori* gastritis, and no identifiable *H. pylori*.²⁴ This is perhaps another reason for a diagnosis of something like 'chronic nonspecific gastritis'.

Many pathologists have a tendency to try to fit any gastritis into the well-known categories, which prevents them from identifying unusual gastric inflammations. Some diagnoses of nonspecific gastritis might actually be unique inflammations, distinct from the recognized forms. Unfortunately, there is no way for the clinician to recognize from such a pathology report that the patient has something unique that has not previously been described.

How should a clinician deal with a pathology report of this type? When a clinician is given a diagnosis of 'chronic nonspecific gastritis' or something similar, it could be time to contact the pathologist for an explanation.

CONCLUSIONS

Endoscopists might better understand pathology reports if they are familiar with the findings and clinical correlates of the most common diagnoses, as discussed above, and understand that endoscopic–histologic correlation is imperfect. In addition, specific diagnoses are more likely to be forthcoming from the pathologist when relevant clinical and endoscopic information and clinical questions are transmitted, with the biopsy, to the pathology laboratory.

KEY POINTS

- Good endoscopic–histologic correlation for gastric biopsies is to be expected only ~50% of the time
- Endoscopically normal mucosa often has histologic inflammation, and endoscopically inflamed mucosa is often histologically normal
- Pathology reports of gastritis can be divided into two broad groups: specific gastritis diagnoses and descriptive nonspecific diagnoses
- Specific diagnoses are more likely when clinical and endoscopic information and clinical questions are sent with the biopsy to the pathology laboratory
- Clinicians should ask the pathologist for an explanation when they receive a histologic diagnosis of gastritis that does not match any of the described gastritides

References

- 1 Fung WP *et al.* (1979) Endoscopic, histological and ultrastructural correlations in chronic gastritis. *Am J Gastroenterol* **71**: 269–279
- 2 Toukan AU *et al.* (1985) Gastroduodenal inflammation in patients with nonulcer dyspepsia. A controlled endoscopic and morphometric study. *Dig Dis Sci* **30**: 313–320
- 3 Gad A (1986) Erosion: a correlative endoscopic histopathologic multicenter study. *Endoscopy* **18**: 76–79
- 4 Elta GH *et al.* (1987) A study of the correlation between endoscopic and histological diagnoses in gastroduodenitis. *Am J Gastroenterol* **82**: 749–753
- 5 Fenoglio-Preiser CM (1999) *Gastrointestinal Pathology: An Atlas and Text*, edn 2. Philadelphia: Lippincott Williams & Wilkins,
- 6 Moayyedi P *et al.* (2000) Changing patterns of *Helicobacter pylori* gastritis in long-standing acid suppression. *Helicobacter* **5**: 206–214
- 7 Redeen S *et al.* (2003) Relationship of gastroscopic features to histological findings in gastritis and *Helicobacter pylori* infection in a general population sample. *Endoscopy* **35**: 946–950
- 8 Miyamoto M *et al.* (2003) Nodular gastritis in adults is caused by *Helicobacter pylori* infection. *Dig Dis Sci* **48**: 968–975
- 9 Presotto F *et al.* (2003) *Helicobacter pylori* infection and gastric autoimmune diseases: is there a link? *Helicobacter* **8**: 578–584
- 10 Pashankar DS *et al.* (2002) Chemical gastropathy: a distinct histopathologic entity in children. *J Pediatr Gastroenterol Nutr* **35**: 653–657
- 11 Sobala GM *et al.* (1990) Reflux gastritis in the intact stomach. *J Clin Pathol* **42**: 303–306
- 12 Frezza M *et al.* (2001) The histopathology of non-steroidal anti-inflammatory drug induced gastroduodenal damage: correlation with *Helicobacter pylori*, ulcers, and haemorrhagic events. *J Clin Pathol* **54**: 521–525
- 13 El-Zimaity HM *et al.* (1996) Histological features do not define NSAID-induced gastritis. *Hum Pathol* **27**: 1348–1354
- 14 De Giacomo C *et al.* (1994) Lymphocytic gastritis: a positive relationship with celiac disease. *J Pediatr* **124**: 57–62
- 15 Wolber R *et al.* (1990) Lymphocytic gastritis in patients with celiac sprue or spruelike intestinal disease. *Gastroenterology* **98**: 310–315
- 16 Wu T-T and Hamilton SR (1999) Lymphocytic gastritis: association with etiology and topology. *Am J Surg Pathol* **23**: 153–158
- 17 Dixon MF *et al.* (1988) Lymphocytic gastritis—relationship to *Campylobacter pylori* infection. *J Pathol* **154**: 125–132
- 18 Hayat M *et al.* (1999) Effects of *Helicobacter pylori* eradication on the natural history of lymphocytic gastritis. *Gut* **45**: 495–498
- 19 Oberhuber G *et al.* (1997) Focally enhanced gastritis: a frequent type of gastritis in patients with Crohn's disease. *Gastroenterology* **112**: 698–706
- 20 Wright CL and Riddell RH (1998) Histology of the stomach and duodenum in Crohn's disease. *Am J Surg Pathol* **22**: 383–390
- 21 Parente *et al.* (2000) Focal gastric inflammatory infiltrates in inflammatory bowel diseases: prevalence, immunohistochemical characteristics, and diagnostic role. *Am J Gastroenterol* **95**: 705–711
- 22 Sharif F *et al.* (2002) Focally enhanced gastritis in children with Crohn's disease and ulcerative colitis. *Am J Gastroenterol* **97**: 1415–1420
- 23 Xin W and Greenson JK. (2004) The clinical significance of focally enhanced gastritis. *Am J Surg Pathol* **28**: 1347–1351
- 24 Genta RM *et al.* (1993) Changes in the gastric mucosa following eradication of *Helicobacter pylori*. *Mod Pathol* **6**: 281–289

Competing interests

The authors declare they have no competing interests.