Gastritis: Etiology and diagnosis

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INTRODUCTION

Gastric inflammatory diseases can be broadly categorized into gastritis and gastropathy based on the presence or absence of associated mucosal inflammation due to gastric injury. Gastritis is predominantly an inflammatory process, while the term gastropathy denotes a gastric mucosal disorder with minimal to no inflammation. Although the term "gastritis" is often used to describe endoscopic or radiologic characteristics of abnormal-appearing gastric mucosa, a diagnosis of gastritis requires histopathologic evidence of inflammation.

This topic will review the etiology, classification, and diagnosis of gastritis. Specific causes of acute and chronic gastritis and gastropathy are presented in detail separately. (See "Acute hemorrhagic erosive gastropathy and reactive gastropathy" and "Acute and chronic gastritis due to Helicobacter pylori" and "Metaplastic (chronic) atrophic gastritis" and "Granulomatous gastritis".)

DEFINITIONS

Gastropathy — Epithelial cell damage and regeneration with minimal or no associated inflammation is termed "gastropathy."

Gastritis — The term "gastritis" is used to denote inflammation associated with gastric mucosal injury.

ETIOLOGY AND CLASSIFICATION

Gastritis is usually caused by infectious agents (eg, *Helicobacter pylori*) or is immune mediated, although in many cases the cause of the gastritis is unknown.

Gastritis has been classified by time course (acute versus chronic), proposed pathophysiology and histologic features, and etiology (table 1) [1]. Although several classifications have been proposed, there is no universally accepted classification of gastritis [1-13]. Classification of gastritis remains controversial because of gaps in knowledge of etiology and pathogenesis, variation in nomenclature, and the frequent coexistence of more than one type in an individual patient. Furthermore, the entities overlap morphologically, and so some conditions are classified by etiology and others by morphologic pattern. Most classification systems distinguish acute, short-term disease from chronic, long-term disease. The terms acute and chronic are also used to describe the type of inflammatory cell infiltrate. Acute inflammation is represented by neutrophilic infiltration, while chronic inflammation is characterized by a mixture of mononuclear cells, chiefly lymphocytes, plasma cells, and macrophages.

The most comprehensive and widely used classification system, the updated Sydney system, classifies gastritis on the basis of the morphology, topography, and possible etiology into acute, chronic, and special (or distinctive) [5]. Special forms of gastritis include those without a clear etiology and gastropathies. Chronic gastritis is categorized as nonatrophic or atrophic. However, the updated Sydney system does not yield actionable prognostic information concerning the risk of gastric cancer in patients with chronic atrophic gastritis and intestinal metaplasia. (See "Metaplastic (chronic) atrophic gastritis".)

In patients with chronic atrophic gastritis and intestinal metaplasia, the Operative Link for Gastritis Assessment (OLGA) and the Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) systems for staging aid in prediction of cancer risk (table 2 and table 3). Some experts suggest using a combination of both to stage chronic atrophic gastritis and intestinal metaplasia. The OLGA/OLGIM staging systems incorporate histologic phenotypes with extent of disease to aid in prediction of cancer risk [8-10]. High-stage disease (OLGA/OLGIM III/IV) are associated with a high risk of gastric cancer. The OLGIM staging system shows less inter-observer variability compared with OLGA but may be less sensitive in identifying high-risk gastritis [8,9,11,12]. (See "Metaplastic (chronic) atrophic gastritis", section on 'Histologic staging of severity'.)

DIAGNOSIS

The diagnosis of gastritis is usually established on biopsy specimens from patients undergoing upper endoscopy for evaluation of often unrelated upper abdominal symptoms.

Endoscopy and gastric mucosal biopsy — Endoscopic information should include a brief narrative and/or endoscopic pictures of focal lesions (eg, thickened folds, polyps, masses, erosions, or ulcers) and abnormal-looking areas. Communication between the endoscopist and pathologist is necessary to optimize the interpretation of the biopsy specimens.

- **Endoscopic features** – Endoscopic features of gastritis include erythema, mucosal erosions, the absence of rugal folds, and the presence of visible vessels. However, these features have a low sensitivity and there is significant inter-observer variability for some features [14]. An illustrative study included 488 adults who were randomly selected from the general population and were screened by gastroscopy and biopsy [15]. The authors evaluated the sensitivity of macroscopic features (including erythema, mucosal erosions, the absence of rugal folds, and the presence of visible vessels) compared with histologic findings. None of these endoscopic findings had sensitivity greater than 57 percent for determining the presence of gastritis or *H. pylori* infection.

- **Gastric biopsy protocol and histology** – Histologic findings of gastritis can vary over a wide spectrum, ranging from epithelial hyperplasia with minimal inflammation to extensive epithelial cell damage with infiltration by inflammatory cells. Accurate histologic assessment of gastritis and gastropathy depends upon optimizing the site and number of biopsy specimens. Magnification endoscopy, if available, may improve the identification of areas to biopsy and may reduce the number of biopsies taken. (See "Magnification endoscopy".)

  Biopsy site preferences and number vary in clinical practice based on the incidence and risk factors for gastric cancer. However, there is general consensus among experts on the following biopsy approach [1].

  - Multiple biopsies of both the corpus and the antrum should be obtained when attempting to evaluate gastritis and establish the etiology (eg, *H. pylori* or autoimmune gastritis) (figure 1). For optimal assessment, one to two biopsies from five biopsy sites are taken (greater and lesser curvature of antrum, greater and lesser curvature of the corpus, and the incisura angularis). This approach is endorsed in the updated Sydney Classification [5]. This systematic approach to biopsy sites is recommended, regardless of symptomatology or endoscopic findings, due to the known lack of correlation with histologic features. Although it is preferable to separate the fundic and antral biopsy sites into separate containers, this is rarely done in practice, and the

biopsy sites can usually be differentiated on histology. Of course, if a discrete lesion is seen and biopsied, this must be placed in a separately designated container.

- In first-degree relatives of patients with early onset gastric carcinoma (age <45 years), endoscopic evaluation with at least four biopsies from the gastric antrum and corpus is suggested. Multiple biopsies with adequate sampling are necessary for scoring and staging of premalignant lesions in this subgroup of patients [9].

- Normal-appearing mucosa adjacent to the lesional tissue should also be biopsied.

The pathologist should include a morphologic classification of the gastritis or gastropathy in the biopsy report, including site(s) of involvement, degree of inflammation (mild, moderate, severe), and presence/absence of intestinal metaplasia. In cases of *H. pylori* gastritis, the degree of inflammation often correlates with the number of organisms (picture 1 and picture 2 and picture 3 and table 4) [16].

Determining the etiology — The etiology of gastritis may be clear based on the clinical history and histopathologic examination of the stomach [17]. However, in other cases, additional testing may be required.

History — Key elements of the history include relevant predisposing factors/associated conditions (eg, Crohn disease, sarcoidosis, celiac disease).

Duodenal histology if obtained — Biopsies of the duodenum may also be helpful for diagnosing some forms of chronic gastritis. As examples, duodenal biopsies may show evidence of Crohn disease in patients with granulomatous gastritis or celiac disease in patients with lymphocytic gastritis. (See "Granulomatous gastritis", section on 'Etiology'.)

Additional tests in selected patients

- **Testing for *H. pylori*** – In patients with chronic atrophic gastritis without a clear underlying etiology, hematoxylin and eosin (H&E) plus a second stain should be used for *H. pylori* visualization (nonsilver-based stains, silver-based stains, or immunohistochemical stains). It is frequently possible to identify *H. pylori* in standard H&E preparations. However, the distribution of *H. pylori* in the stomach is variable, and the growth may be attenuated during treatment with proton pump inhibitors. When a low density of *H. pylori* and atrophic mucosal changes are combined, visualization of the organism becomes unreliable on H&E alone. (See "Acute and chronic gastritis due to Helicobacter pylori", section on 'Histopathology'.)

Noninvasive testing for *H. pylori* with urea breath testing and stool antigen testing has high sensitivity and specificity for active *H. pylori* infection. (See "Indications and diagnostic tests for Helicobacter pylori infection in adults", section on 'Diagnostic tests'.)

- **Immunologic markers** – In patients with evidence of early/evolving histologic features of autoimmune chronic atrophic gastritis, the presence of antibodies to intrinsic factor or parietal cells, in conjunction with an elevated fasting serum gastrin level, can support the diagnosis. (See "Metaplastic (chronic) atrophic gastritis", section on 'Histologic features of AMAG and EMAG'.)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Gastritis (The Basics)" and "Patient education: Upper endoscopy (The Basics)")
- Beyond the Basics topics (see "Patient education: Upper endoscopy (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Terminology** – Gastric inflammatory disease can be broadly categorized into gastritis and gastropathy. Gastritis is predominantly an inflammatory process while gastropathy denotes gastric mucosal pathology with minimal to no inflammation. (See 'Introduction' above.)

- **Etiology and classification** – Gastritis is usually caused by infectious agents (most commonly, *H. pylori*) or is immune mediated, although in many cases the cause of the gastritis is unknown. There is no universally accepted classification of gastritis/gastropathy, although several classifications of gastritis and gastropathy have been proposed (table 1). (See 'Etiology and classification' above.)

- **Diagnosis** – The diagnosis of gastritis is usually established on biopsy specimens from patients undergoing upper endoscopy for evaluation of often unrelated upper abdominal symptoms. Endoscopic features of gastritis include erythema, mucosal erosions, the absence of rugal folds, and the presence of visible vessels. Histologic findings of gastritis can vary over a wide spectrum, ranging from epithelial hyperplasia with minimal inflammation (gastropathy) to extensive epithelial cell damage with infiltration by inflammatory cells. Accurate histologic assessment of gastritis and gastropathy depends upon optimizing the site and number of biopsy specimens. (See 'Diagnosis' above.)

- **Determining the underlying cause** – The etiology of gastritis may be clear based on the clinical history and histopathologic examination. However, in other cases (often in mild gastritis), additional testing for *H. pylori* and autoimmune gastritis may be required. (See 'Determining the etiology' above.)

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Topic 29 Version 18.0

GRAPHICS

Etiology-based classification of gastropathy and gastritis

Gastropathy	Gastritis
Reactive (chemical) gastropathy ▪ Bile reflux ▪ Alcohol ▪ NSAIDs ▪ Iron salts ▪ Other agents (eg, alendronate, sodium phosphate) **Vascular gastropathy** ▪ Portal hypertensive (congestive) gastropathy ▪ Gastric antral vascular ectasia **Ischemic gastropathy** ▪ Cocaine ▪ Hypovolemia ▪ Sepsis ▪ Burns ▪ Trauma, mucosal prolapse	**Infectious gastritis** ▪ *Helicobacter pylori* ▪ Pyogenic bacteria (phlegmonous gastritis) ▪ Mycobacterial ▪ Syphilitic ▪ Viral ▪ Parasitic ▪ Fungal **Autoimmune gastritis** **Granulomatous disease** ▪ Crohn disease ▪ Sarcoidosis **Uncertain etiology** ▪ Lymphocytic gastritis ▪ Collagenous gastritis ▪ Eosinophilic gastritis

NSAIDs: nonsteroidal anti-inflammatory drugs.

Graphic 91372 Version 5.0

OLGIM staging system for identifying patients with metaplastic (chronic) atrophic gastritis who are at high risk for evolution to gastric cancer

Stage 0	Scores of 0 (no IM) in corpus and antrum
Stage I	Score of 1 (mild IM) in corpus with score of 0 or 1 in antrum, **or** score of 0 in corpus and score of 1 in antrum
Stage II	Score of 2 (moderate IM) or 3 (severe IM) in corpus with score of 0 in antrum; score of 2 in corpus with score of 1 in antrum; **or** score of 0 or 1 in corpus with score of 2 in antrum
Stage III	Score of 3 (severe IM) in corpus with score of 1 or 2 in antrum, **or** score of 0 or 1 in corpus with score of 3 in antrum
Stage IV	Scores of 3 in corpus and antrum, **or** score of 3 in corpus and 2 in antrum or score of 2 in corpus and 3 in antrum

IM: intestinal metaplasia.

Original table modified for this publication. From: Capelle LG, de Vries AC, Haringsma J, et al. The staging of gastritis with the OLGA system by using intestinal metaplasia as an accurate alternative for atrophic gastritis. Gastrointestinal Endoscopy 2010; 1150. Table used with the permission of Elsevier Inc. All rights reserved.

Graphic 116254 Version 1.0

OLGA staging system for identifying patients with metaplastic (chronic) atrophic gastritis who are at high risk for evolution to gastric cancer

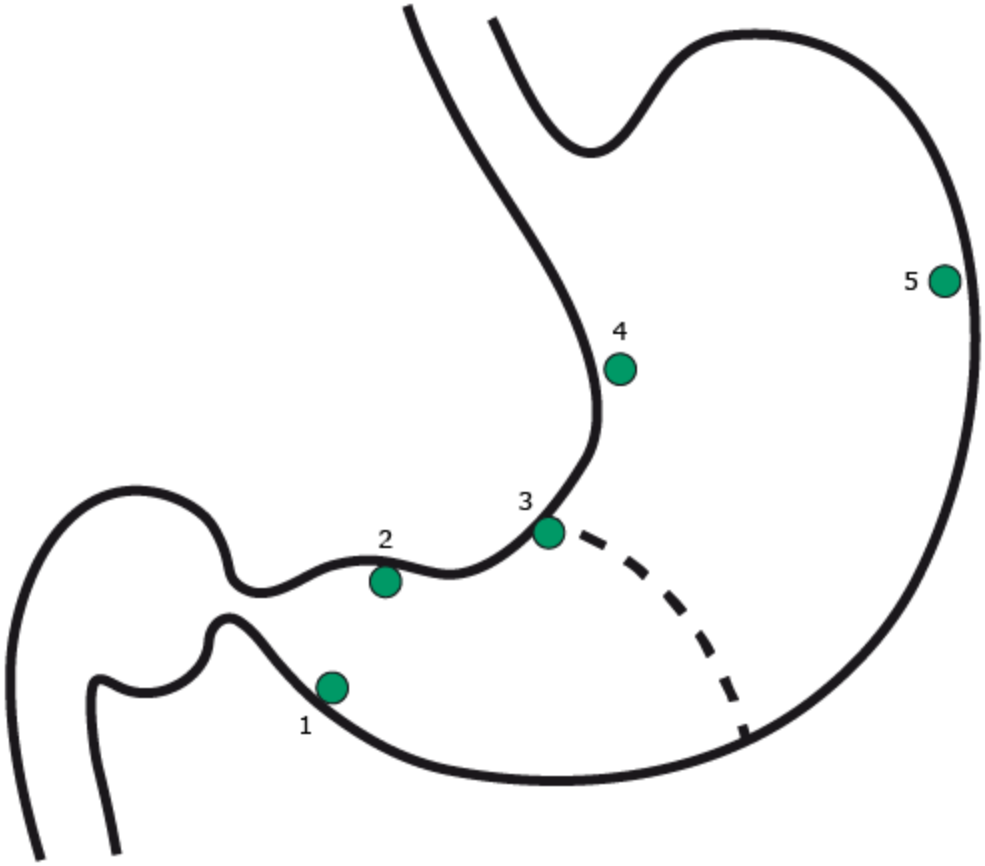
Stage 0	Scores of 0 (no atrophy) in corpus and antrum
Stage I	Score of 1 (mild atrophy) in corpus with score of 0 or 1 in antrum, **or** score of 0 in corpus and score of 1 in antrum
Stage II	Score of 2 (moderate atrophy) or 3 (severe atrophy) in corpus with score of 0 in antrum, **or** score of 2 in corpus with score of 1 in antrum, **or** score of 0 or 1 in corpus with score of 2 in antrum
Stage III	Score of 3 in corpus with score of 1 in antrum, **or** score of 2 in corpus and 2 in antrum, **or** score of 0 or 1 in corpus with score of 3 in antrum
Stage IV	Scores of 3 in corpus and antrum, **or** score of 3 in corpus and 2 in antrum or score of 2 in corpus and 3 in antrum

OLGA: Operative Link for Gastritis Assessment.

Original table modified for this publication. From: Rugge M, Correa P, DiMario F, et al. OLGA staging for gastritis: A tutorial. Dig Liver Dis 2008; 40:650. Table used with the permission of Elsevier Inc. All rights reserved.

Graphic 121370 Version 2.0

Gastric biopsy mapping protocol



Gastric biopsies should be obtained from the following sites:

(1) Antrum, greater curvature, within 3 to 5 cm of pylorus

(2) Antrum, lesser curvature, within 3 to 5 cm of pylorus

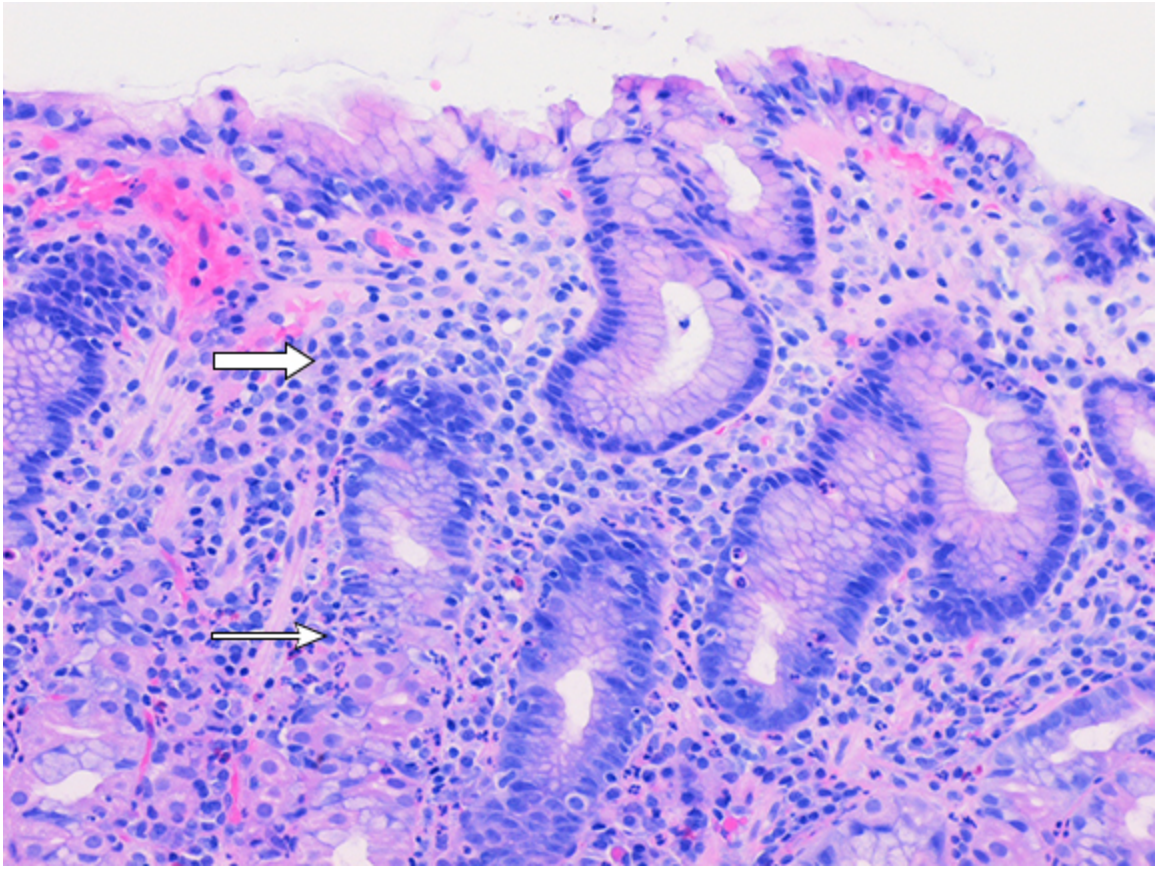
(3) Incisura angularis

(4) Corpus, lesser curvature

(5) Corpus, greater curvature

Graphic 90132 Version 2.0

H. pylori related chronic active gastritis

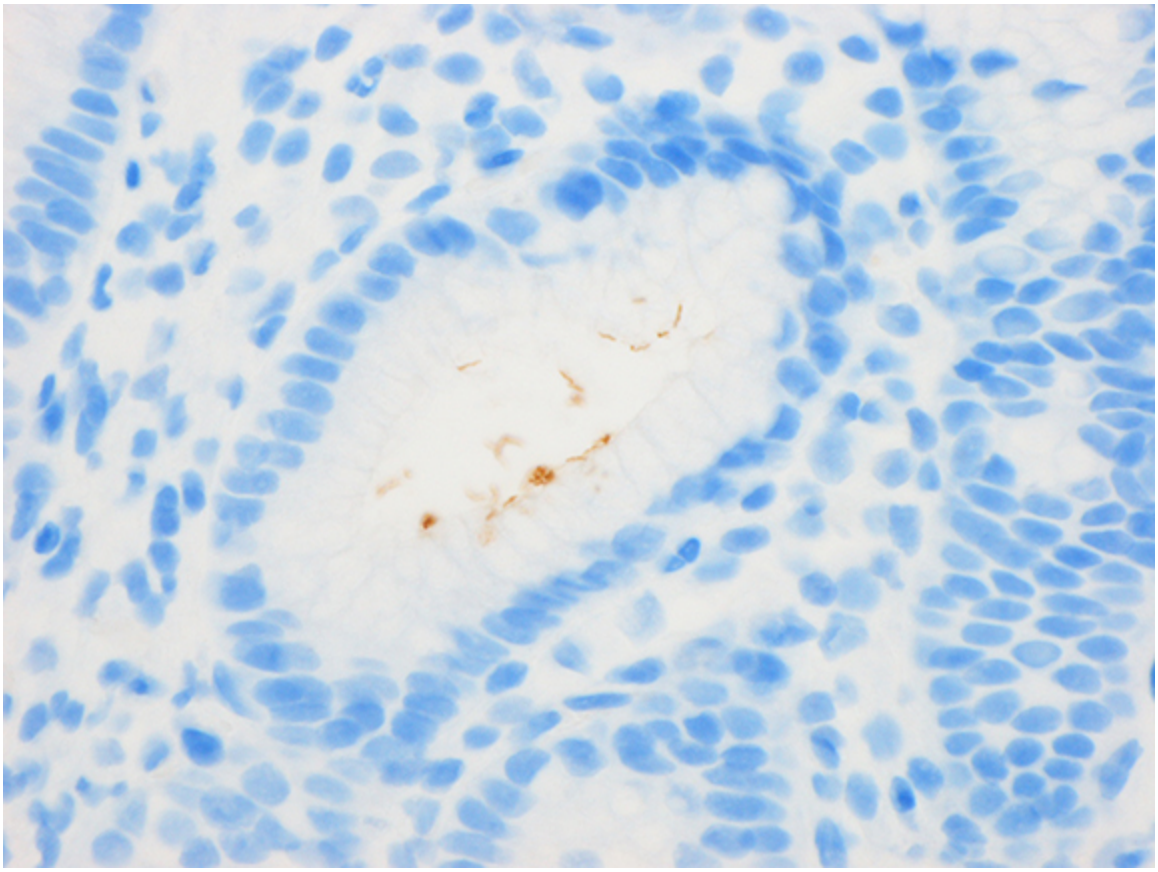


The lamina propria is expanded by mononuclear cells (thick arrow), and neutrophils infiltrate the gastric pits (arrow) within the mucous neck region (H&E, 200×).

H&E: hematoxylin and eosin.

Graphic 139284 Version 1.0

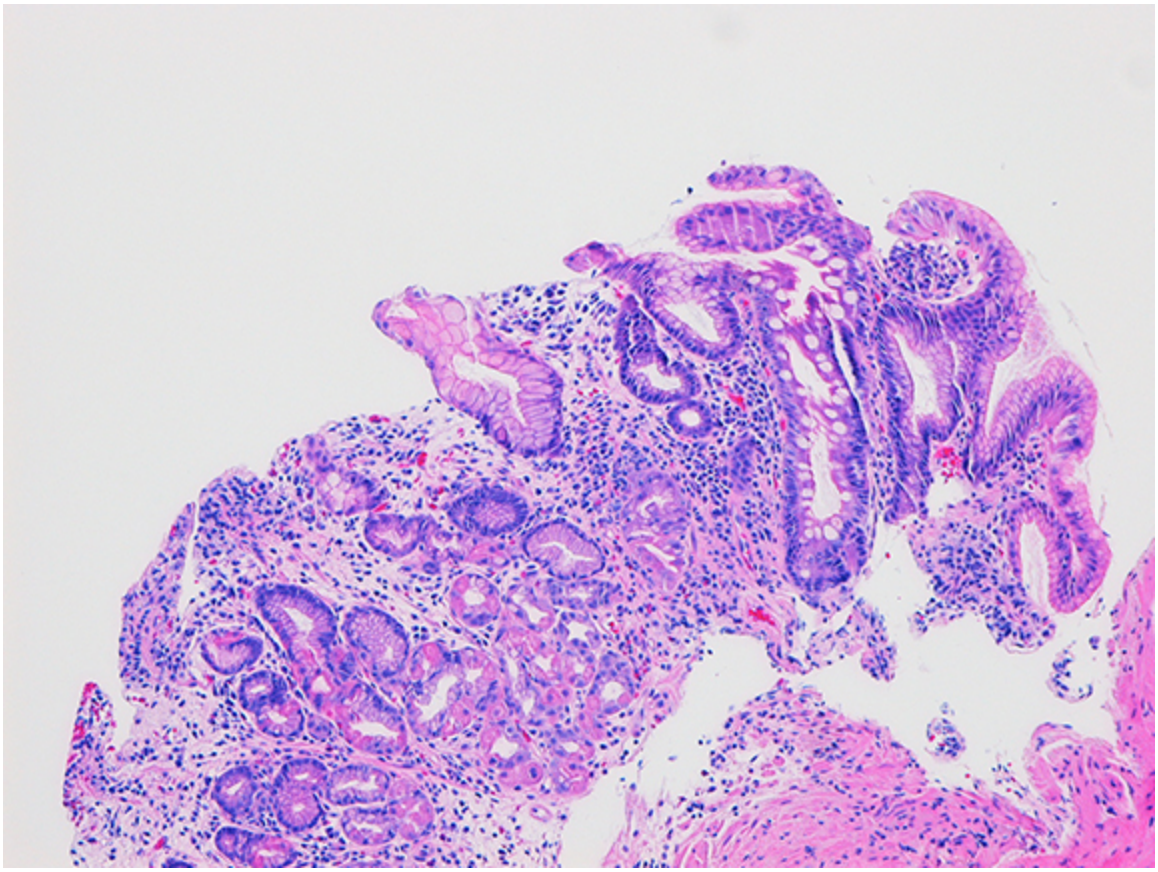
Helicobacter pylori immunohistochemical stain



H. pylori immunohistochemical stain with glandular luminal organisms, shown in brown, as curved slender rods (600×).

Graphic 139285 Version 1.0

Chronic atrophic gastritis



Chronic atrophic gastritis with glandular loss, chronic inflammation, and intestinal metaplasia (H&E, 100×).

H&E: hematoxylin and eosin.

Graphic 139286 Version 1.0

Morphologic classification of gastritis or gastropathy

Location of process:	Antral predominant, corpus predominant, or pangastritis
Type of inflammation:	Acute, chronic, mixed, eosinophilic, lymphocytic, or granulomatous
Topography of inflammation:	Diffuse or focal Gastric site
Atrophy:	Present or absent, graded*
Intestinal metaplasia:	Present or absent, graded*

Infectious agent:	Helicobacter pylori, Helicobacter heilmannii, virus (eg, cytomegalovirus), other

* Mild, moderate, or marked.

Graphic 80329 Version 3.0

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