
VÅRMÖTE I PATOLOGI
NPM 2025
19–21 MAY
NORDIC PATHOLOGY MEETING

Distinguished Speaker

Dr. Yantiss is an internationally respected educator, prolific author with over 150 scientific publications, and recipient of numerous prestigious awards for excellence in pathology and education.

- With great admiration, we honor Dr. Yantiss for her enduring impact on the global pathology community.

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Gastric Mucosal Biopsy Interpretation: Things that Matter, Things that Don't, and Cases that Keep You Up at Night

Nordic Pathology Meeting 2025
Stockholm, Sweden
May 19-21, 2025

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Rhonda Yantiss has no relevant financial relationships to disclose

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PATTERNS OF GASTRIC INJURY

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Patterns of Gastric Injury

- Gastropathy: epithelial injury without much/any inflammation
  - Final common pathway for disorders that alter mucosal barrier
    - Chemical gastropathy (acid or bile-related injury)
    - Chemical gastropathy with an etiology for mucosal damage (e.g., drug)
    - Vascular alterations cause mucosal damage (e.g. portal hypertension)
    - Apoptosis resulting from a variety of etiologies diminishes barrier
- Gastritis: epithelial injury with inflammation
  - Acute: mostly neutrophilic inflammation
    - Uncommonly seen in biopsy material and usually due to drug or infection
  - Chronic: mononuclear cell-rich inflammation

Chemical Gastropathy

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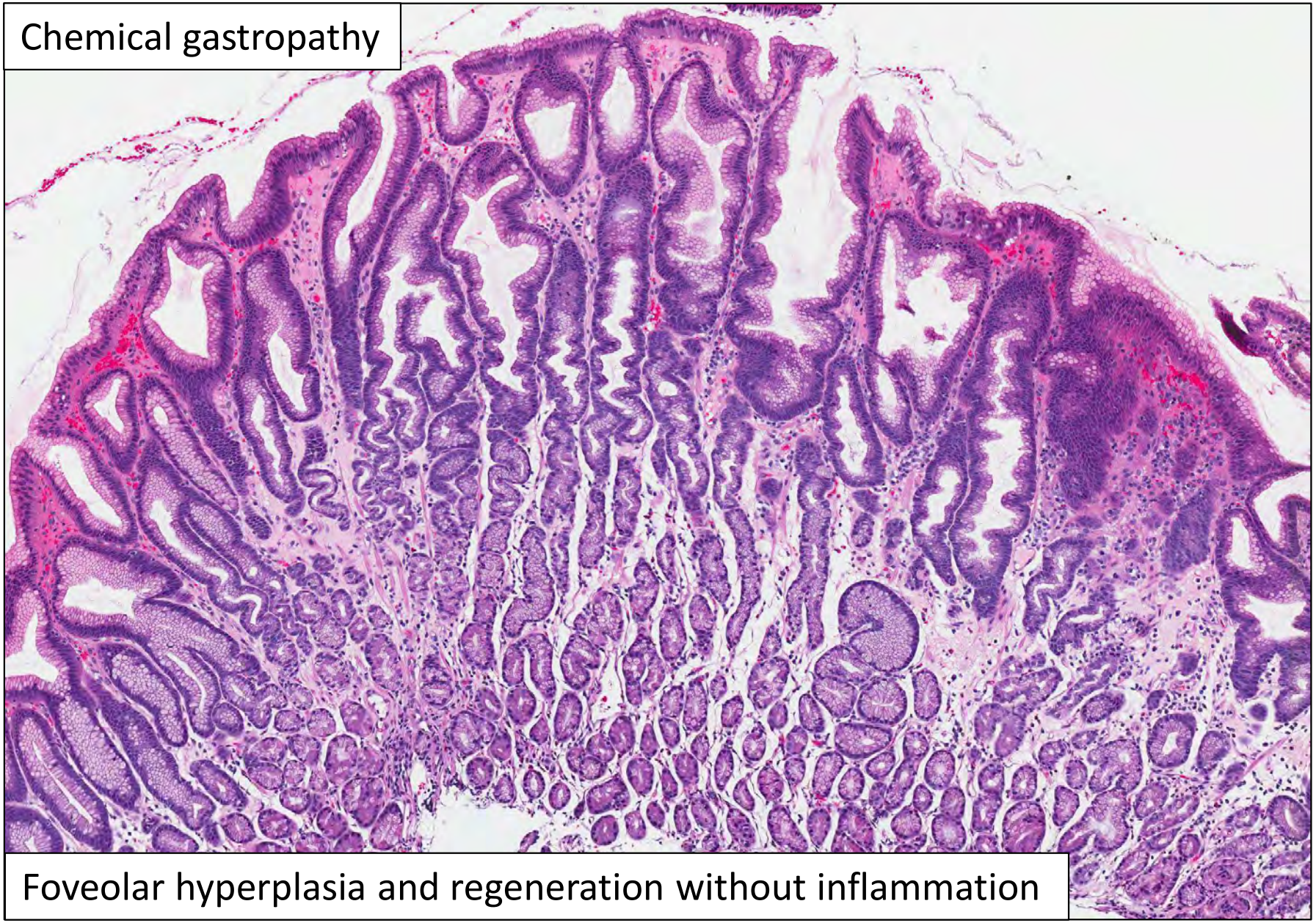
Gastric Injury without Inflammation

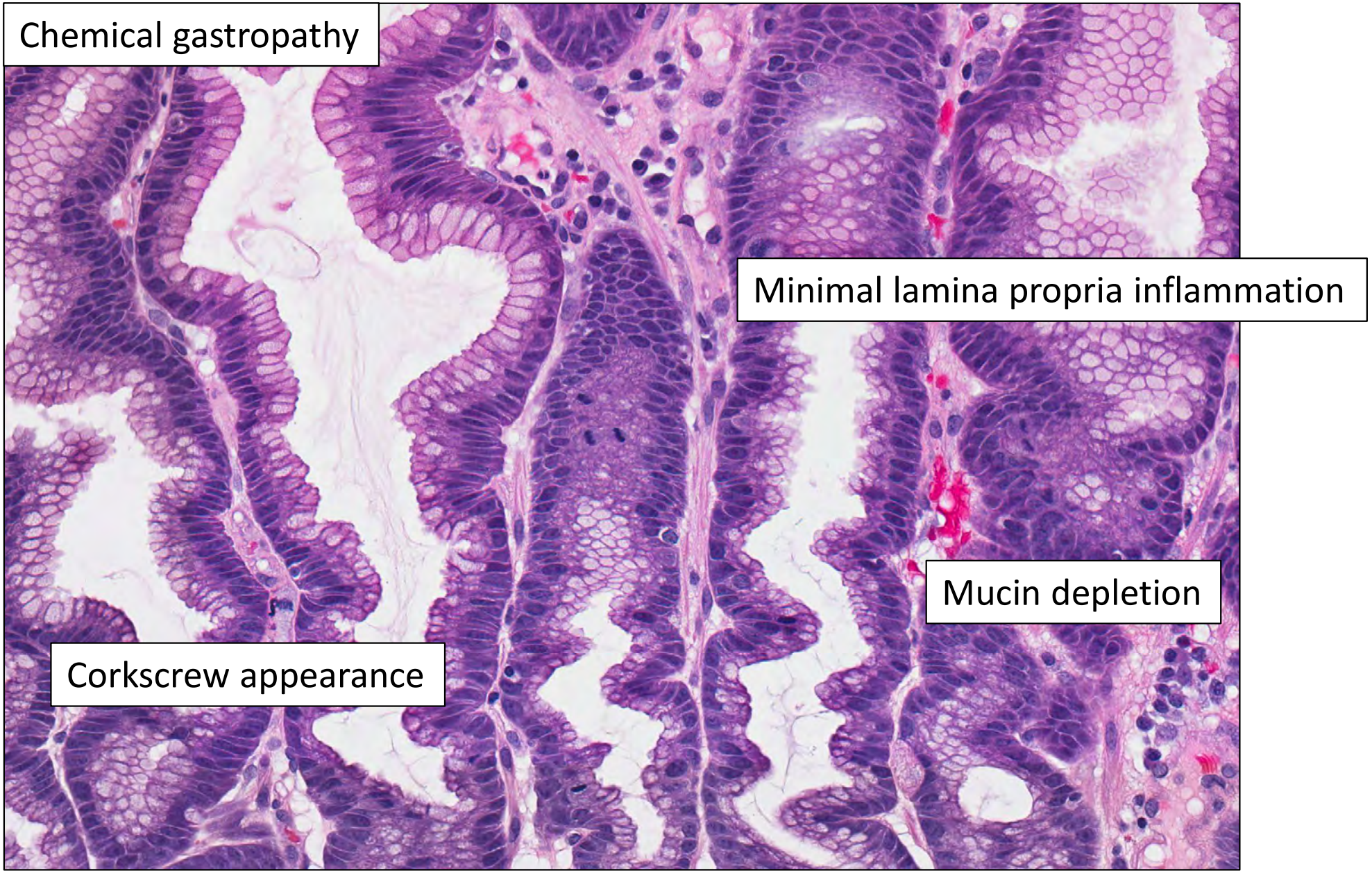
Chemical Gastropathy

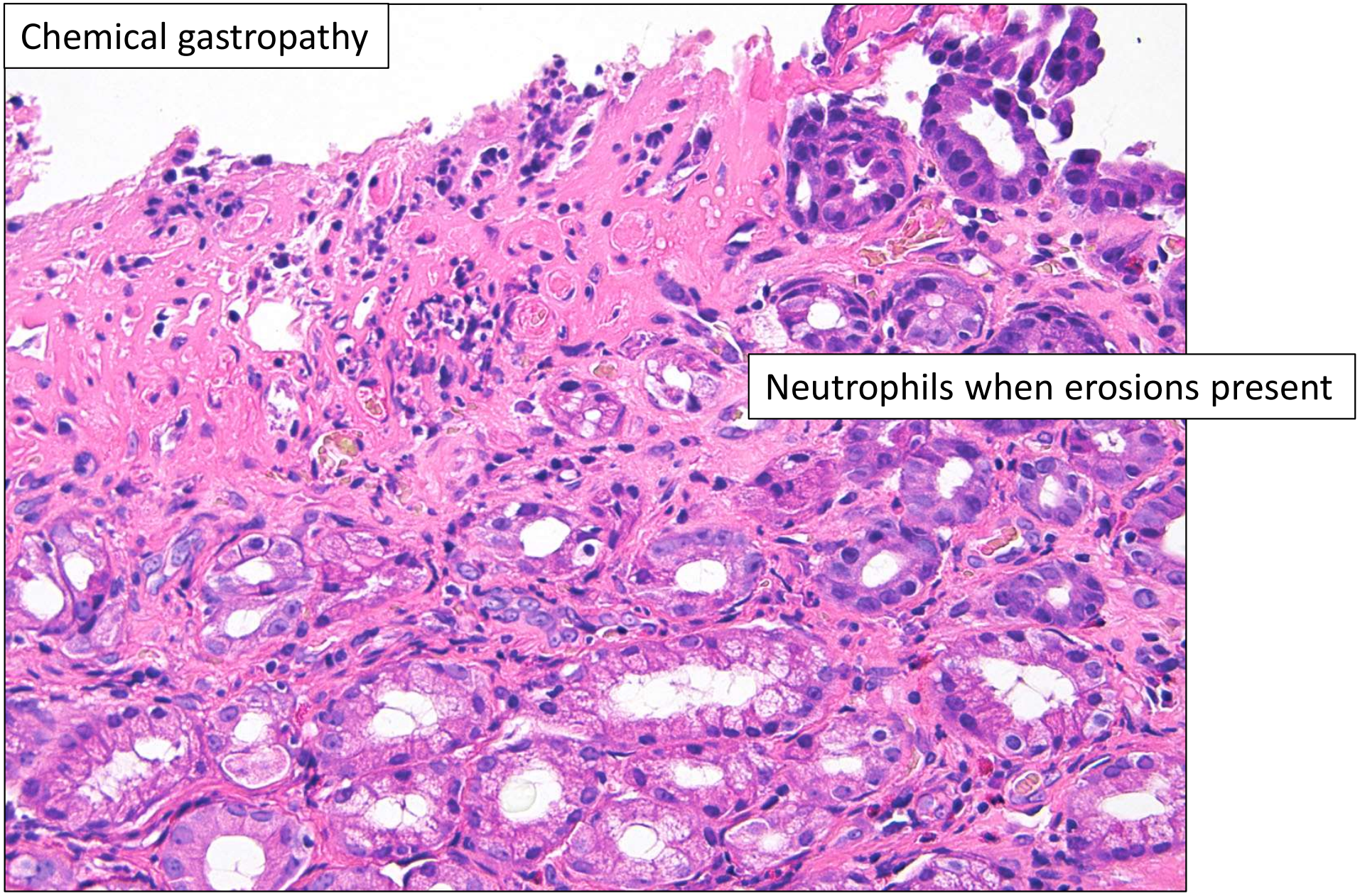
- Most common type of gastric injury
- Surface irritation
  - Acid, bile, alcohol, medications that promote acid-related injury
- Usually affects the antrum

Chemical gastropathy

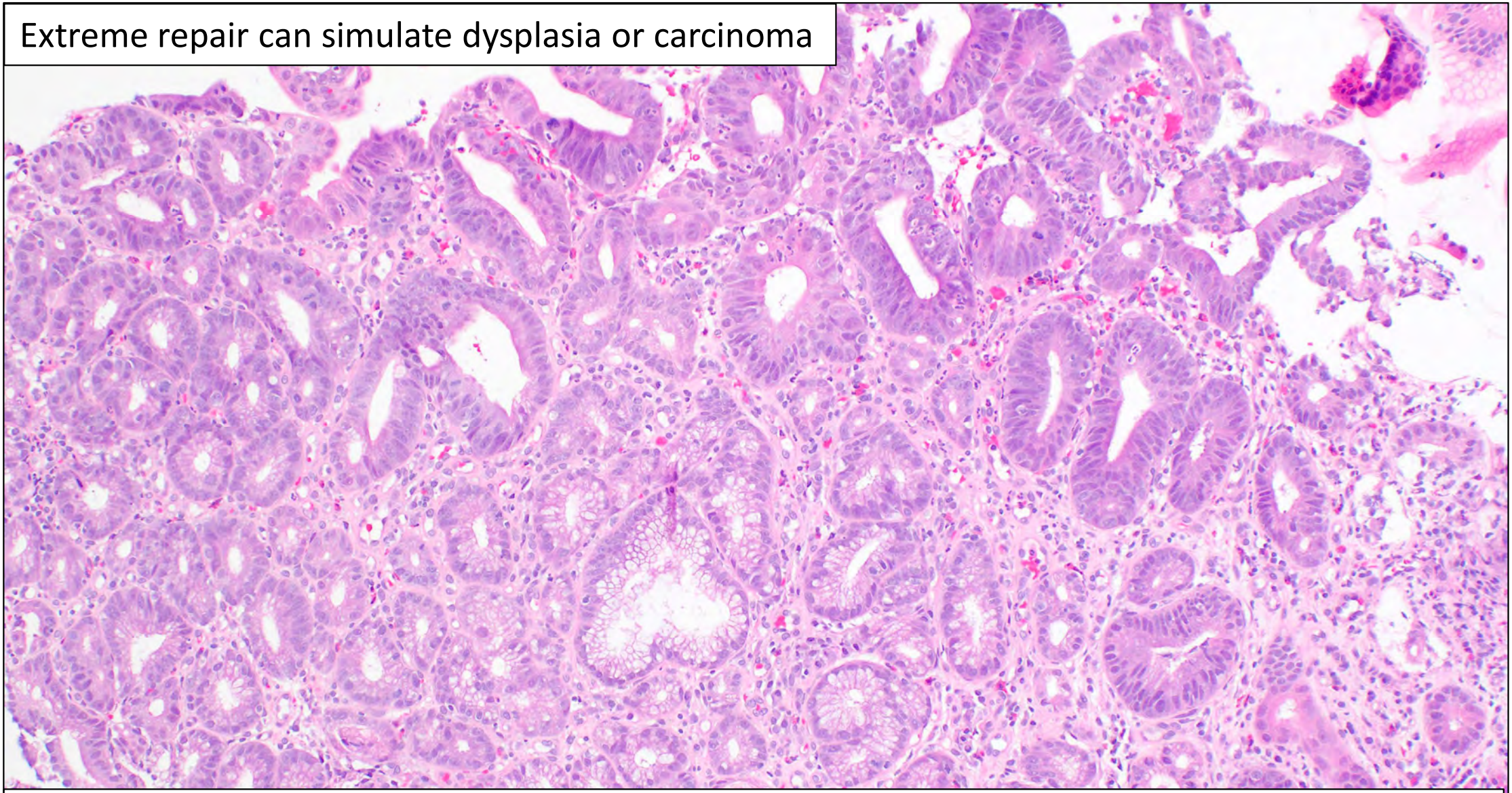


Foveolar hyperplasia and regeneration without inflammation

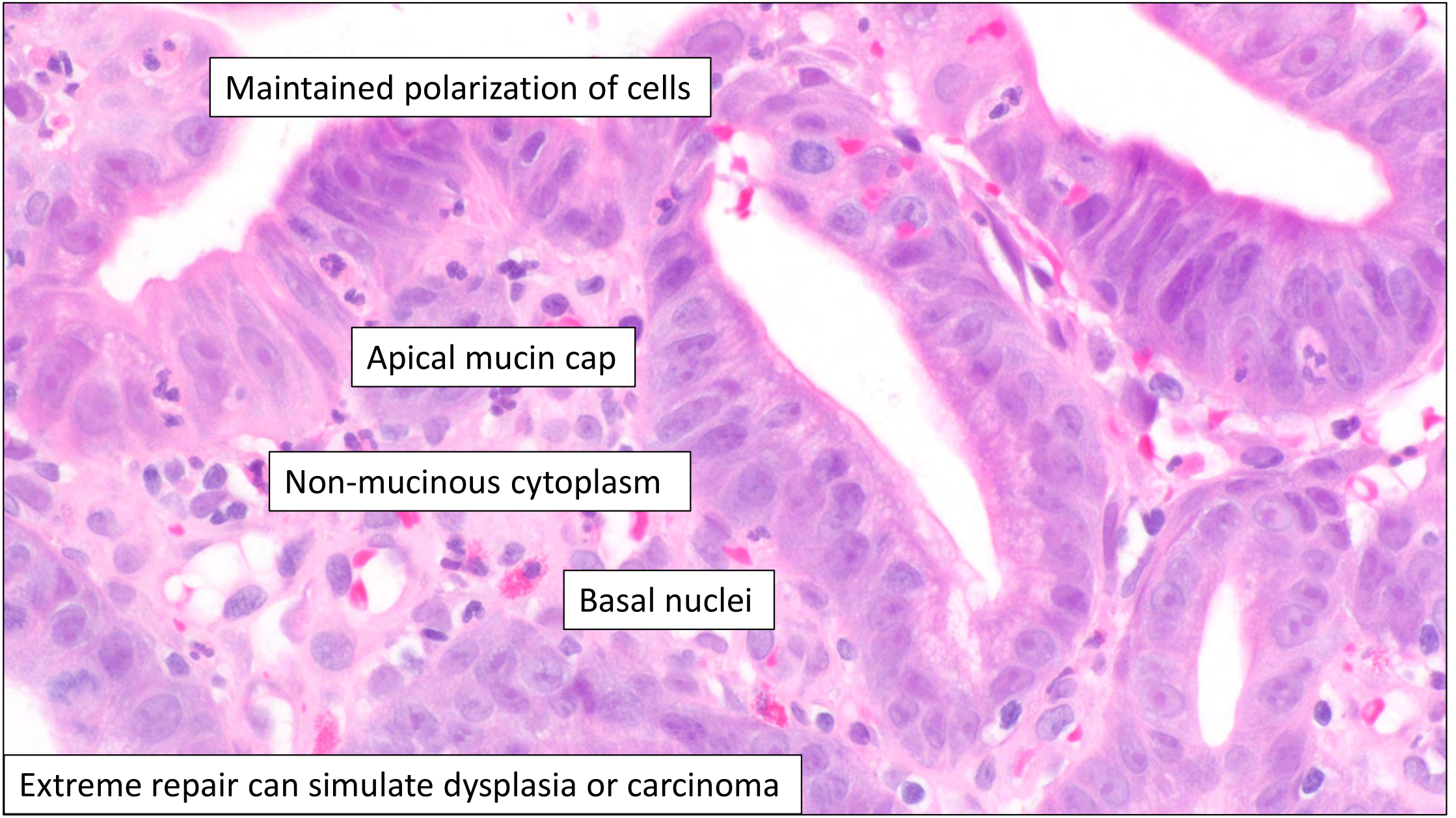

Chemical gastropathy
Minimal lamina propria inflammation
Mucin depletion
Corkscrew appearance


Chemical gastropathy
Neutrophils when erosions present

Extreme repair can simulate dysplasia or carcinoma



Density of glands similar to that of the background (not carcinoma and probably not dysplasia)


Maintained polarization of cells
Apical mucin cap
Non-mucinous cytoplasm
Basal nuclei
Extreme repair can simulate dysplasia or carcinoma

Chemical Gastropathy
Practical Issues

- Poor correlation with endoscopy, especially when changes are mild
- High interobserver variability
- Frequently no treatment
  - Patients generally acid-suppressed already
- Identify treatable conditions that may cause a pattern of chemical gastropathy or avoid confusing changes with dysplasia or carcinoma

Chemical Gastropathy with an Etiology

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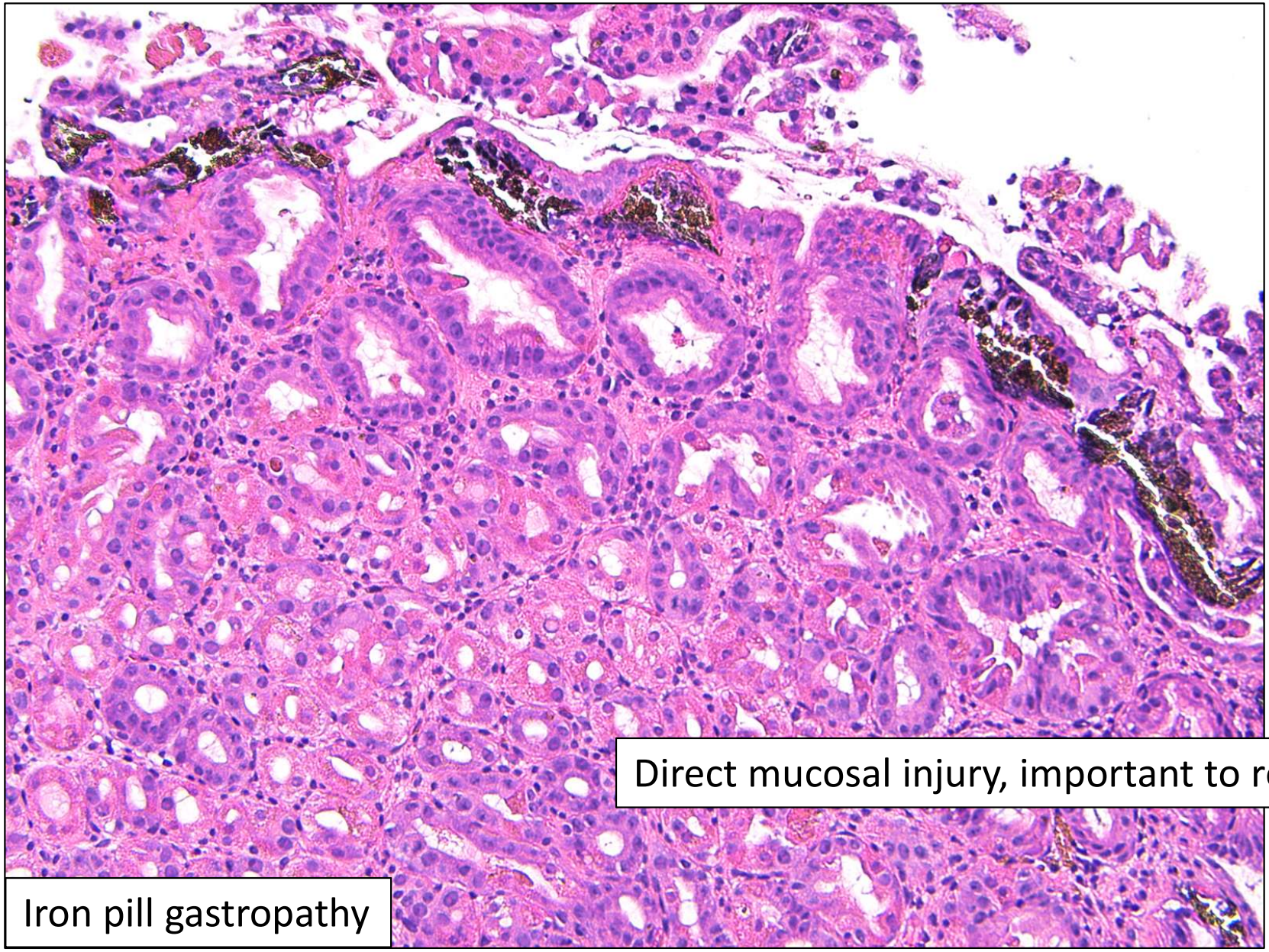
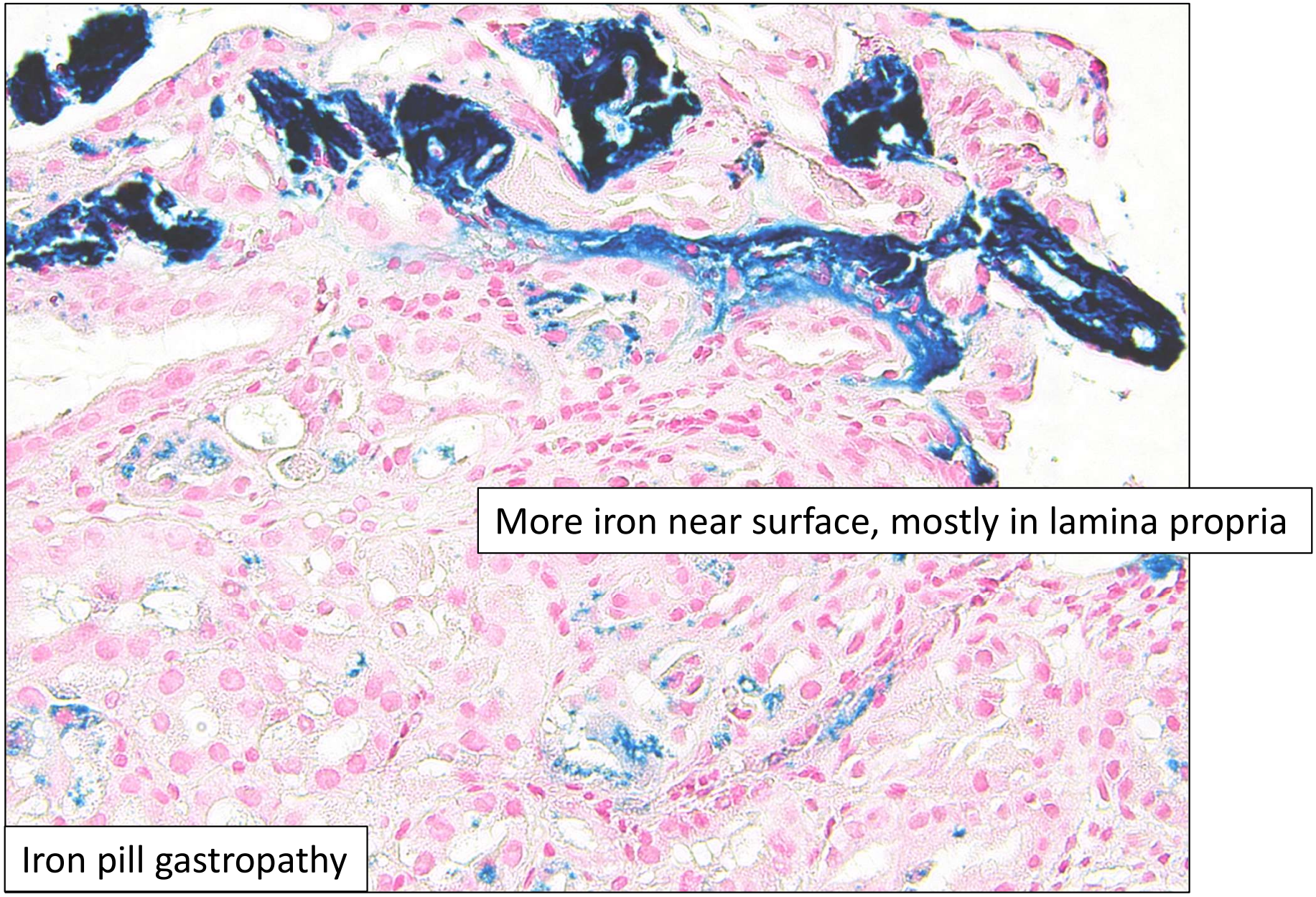
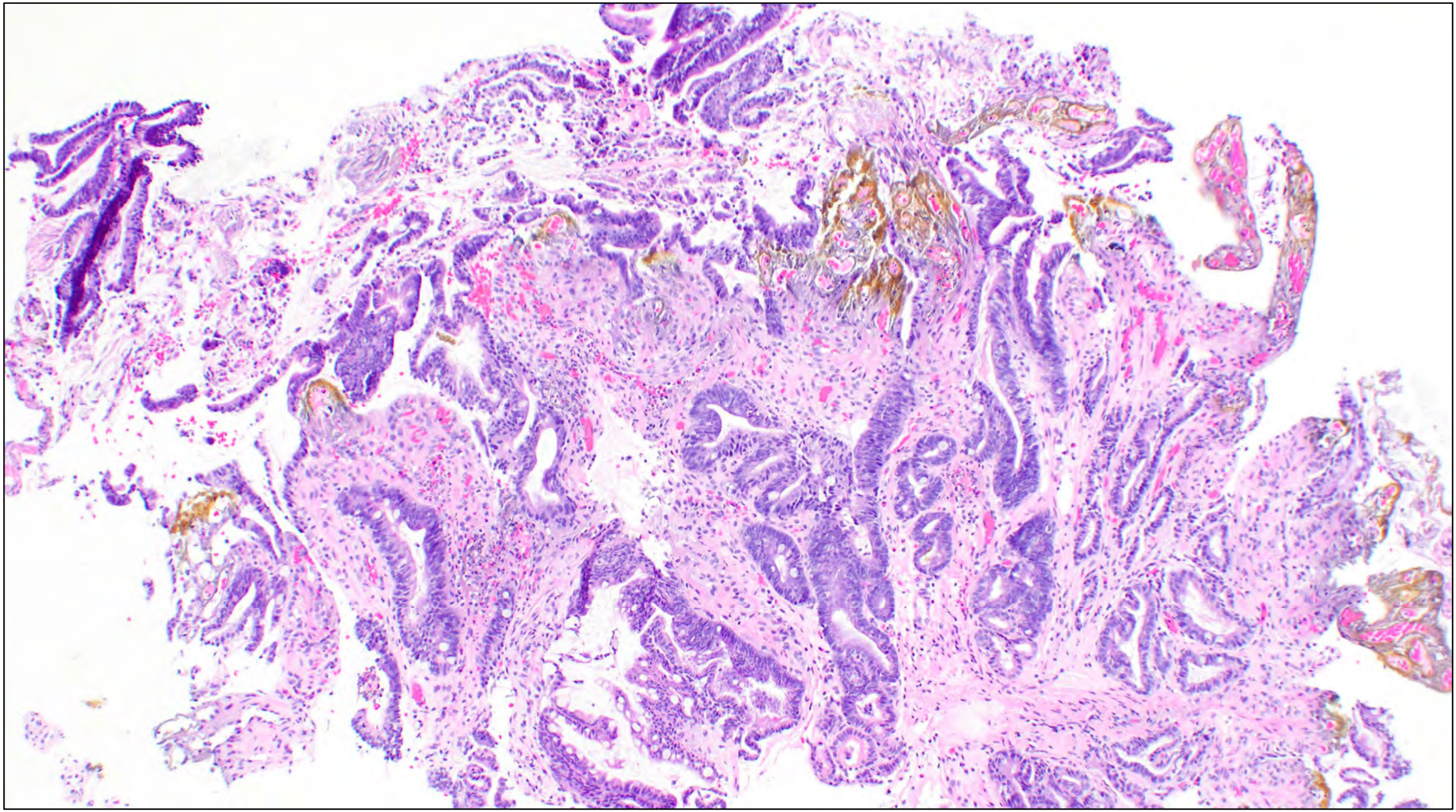
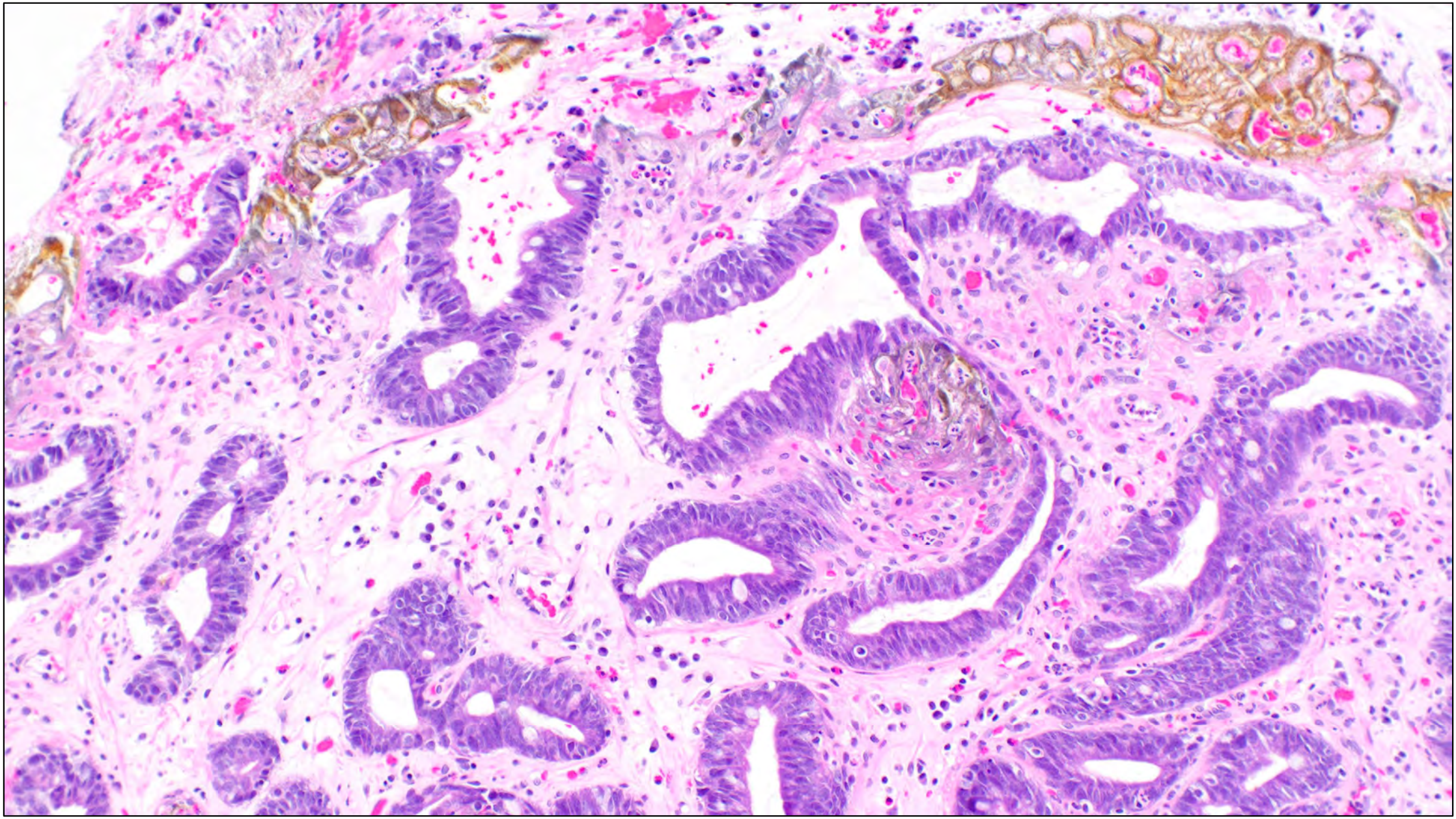


Direct mucosal injury, important to recognize

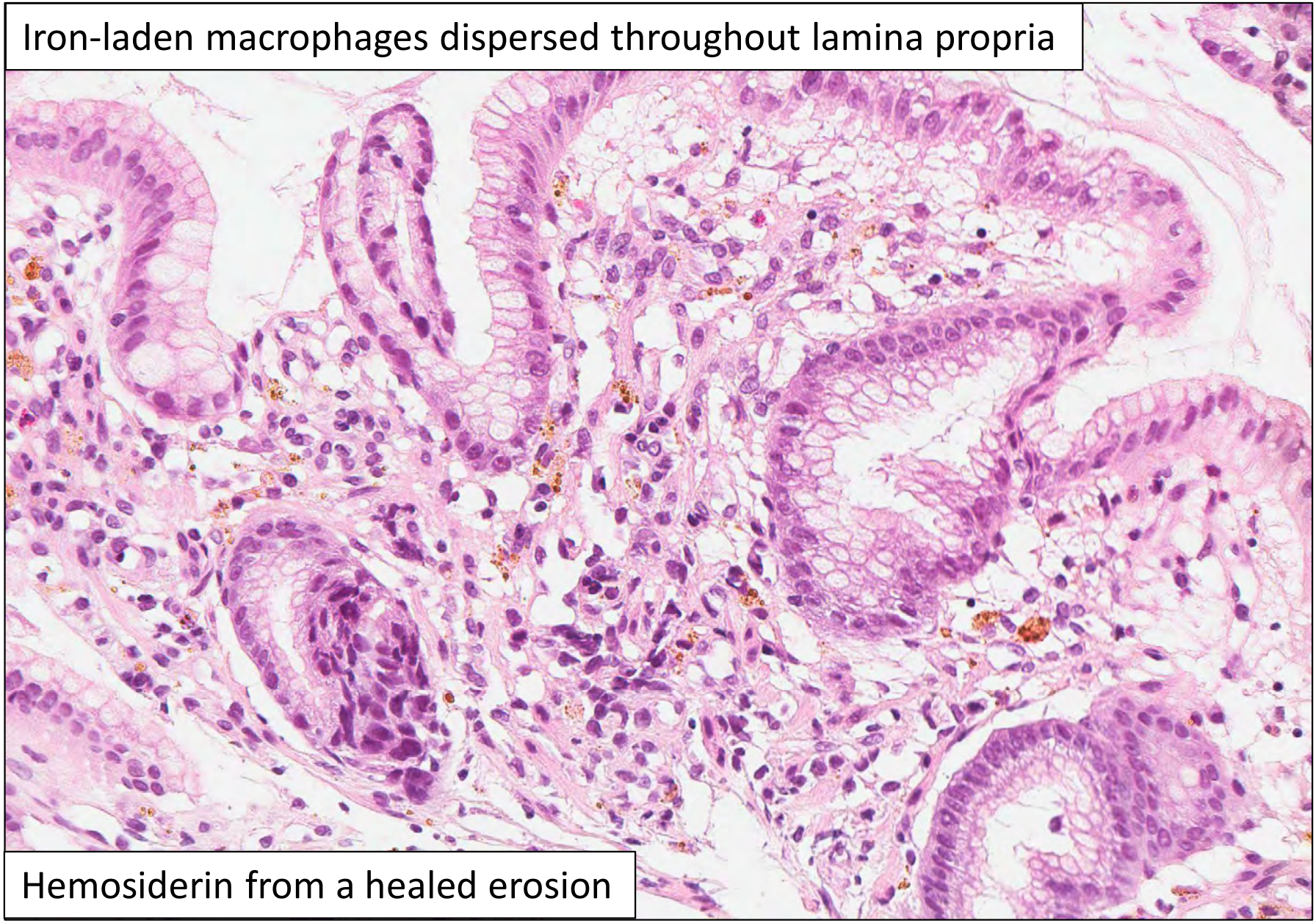
Iron pill gastropathy


More iron near surface, mostly in lamina propria
Iron pill gastropathy



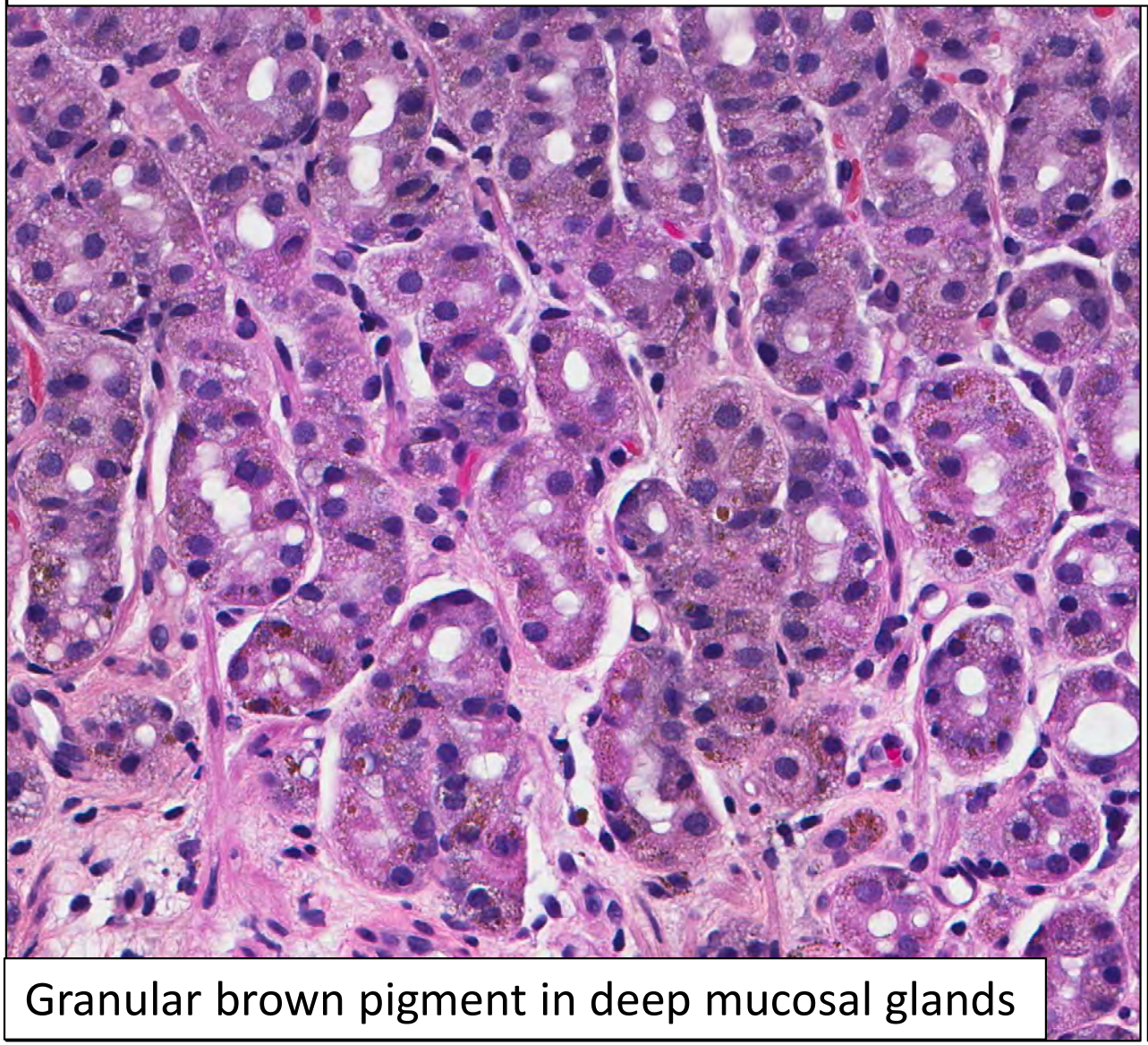


Iron-laden macrophages dispersed throughout lamina propria

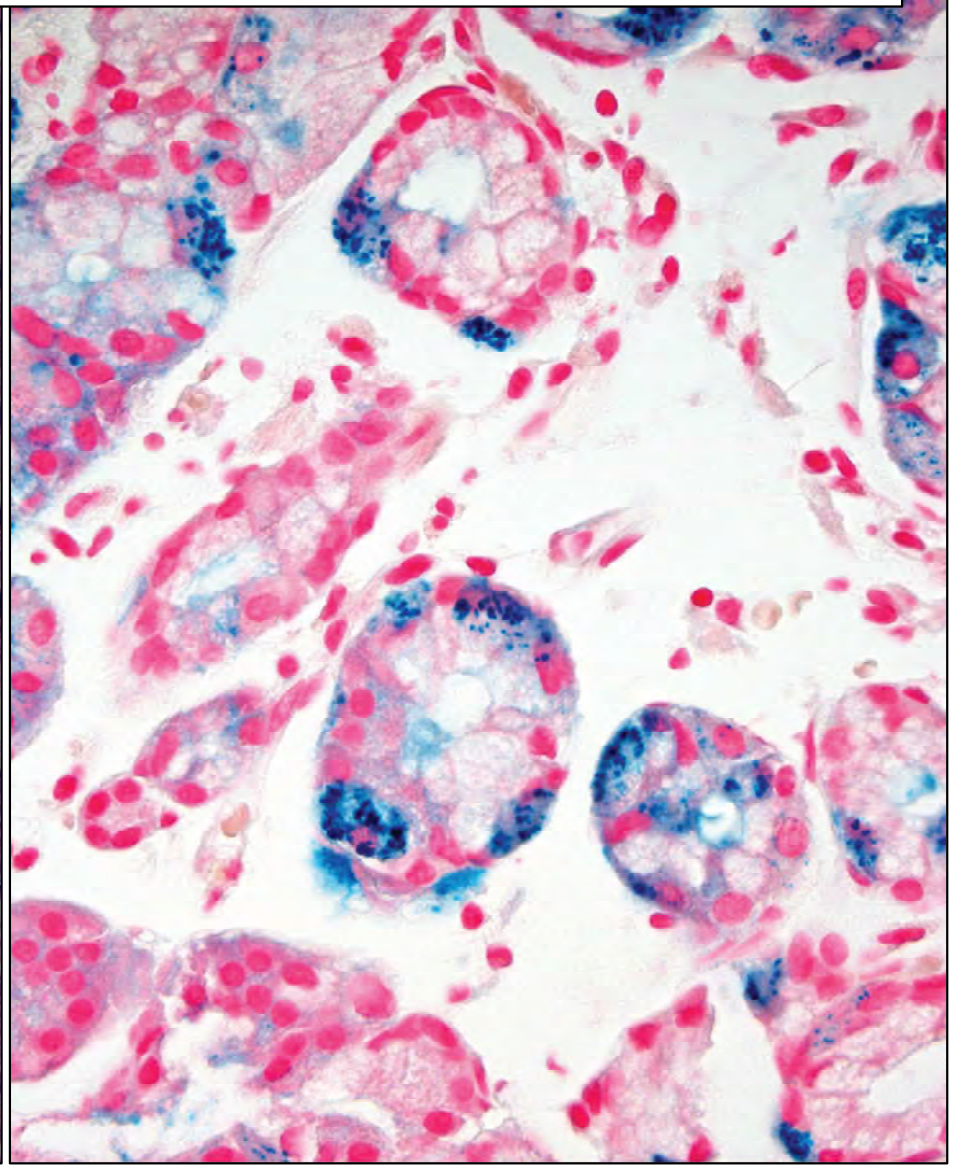


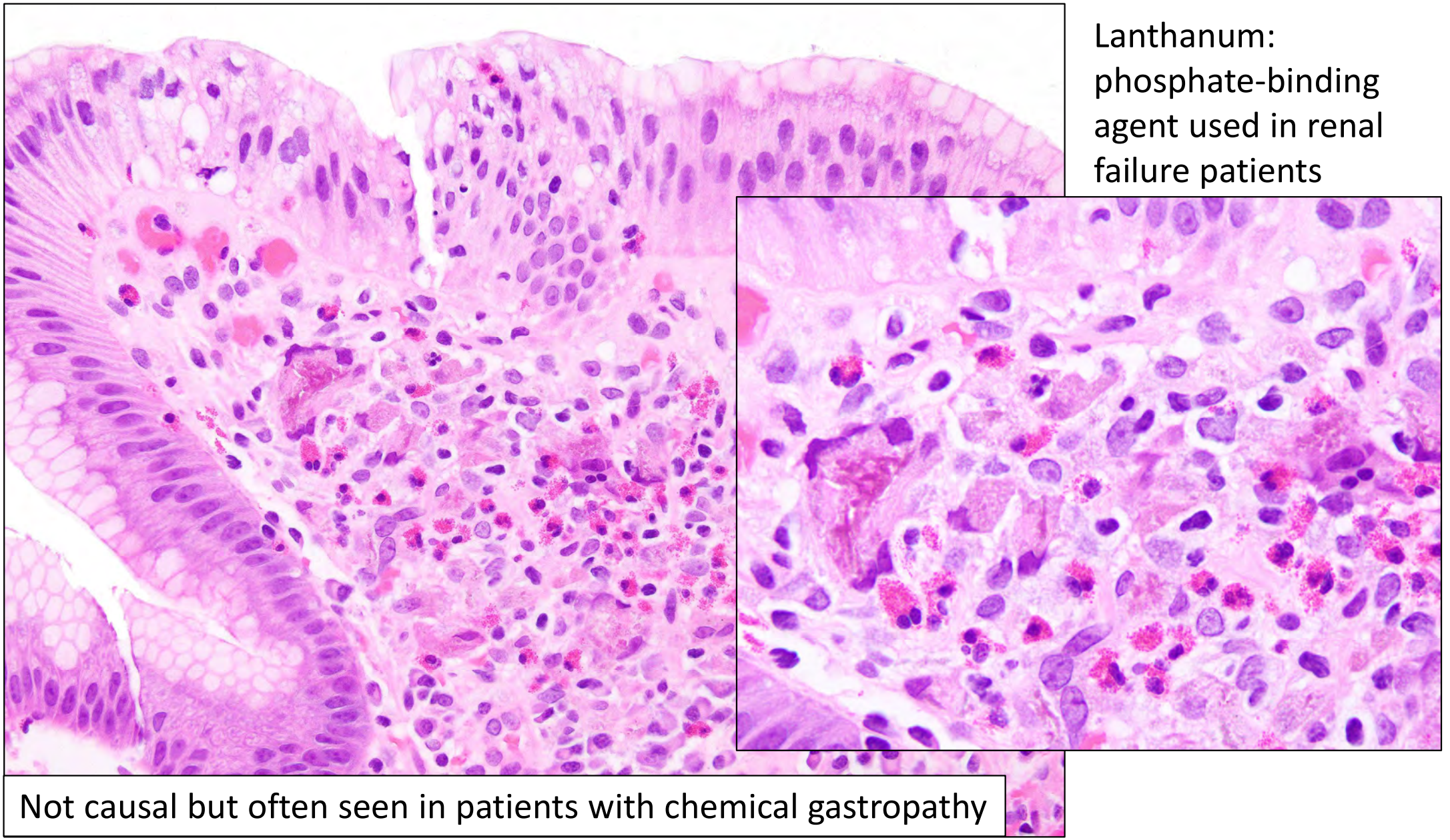
Hemosiderin from a healed erosion

Gastric siderosis due to elevated circulating iron (hemochromatosis or multiple transfusions)



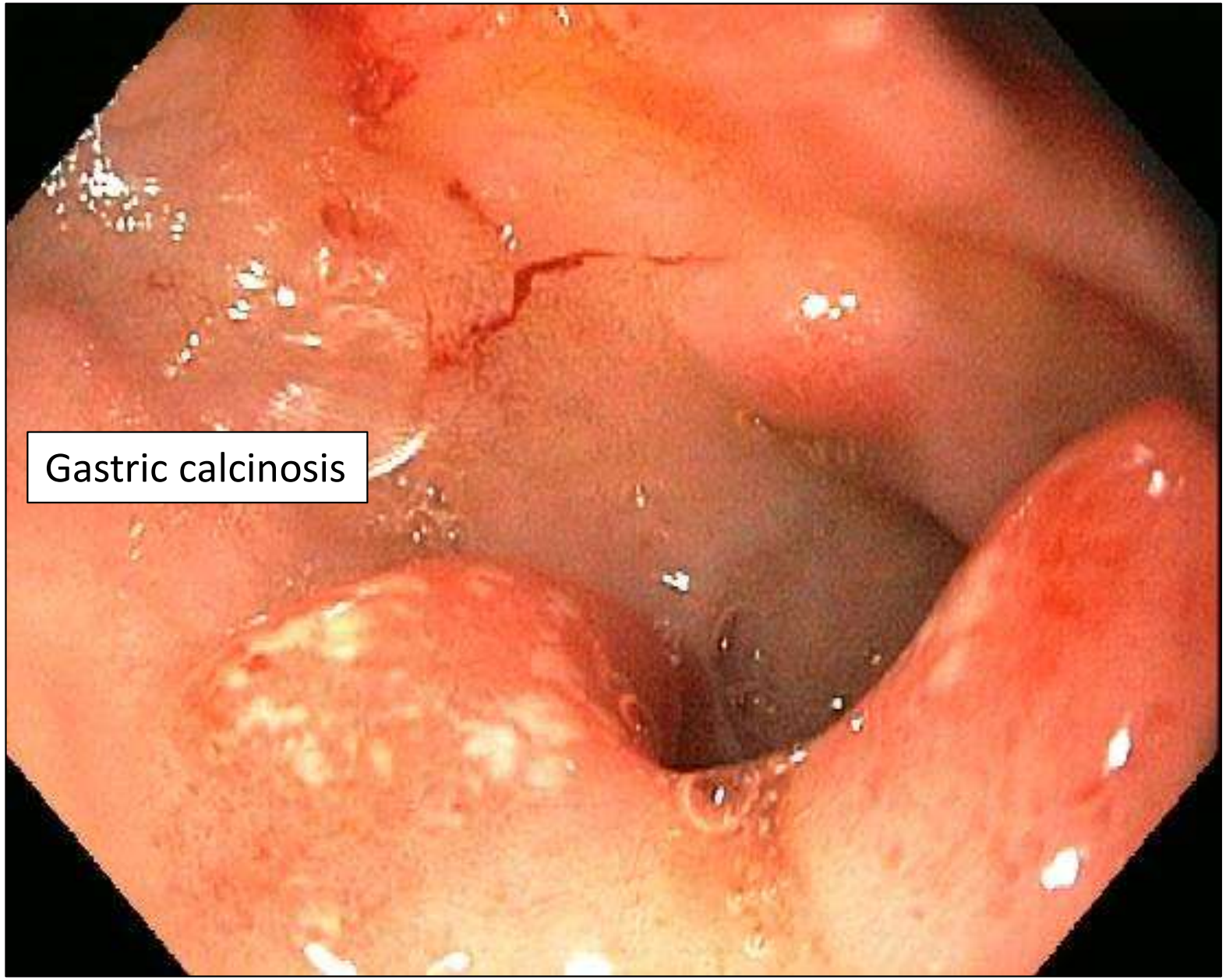
Granular brown pigment in deep mucosal glands



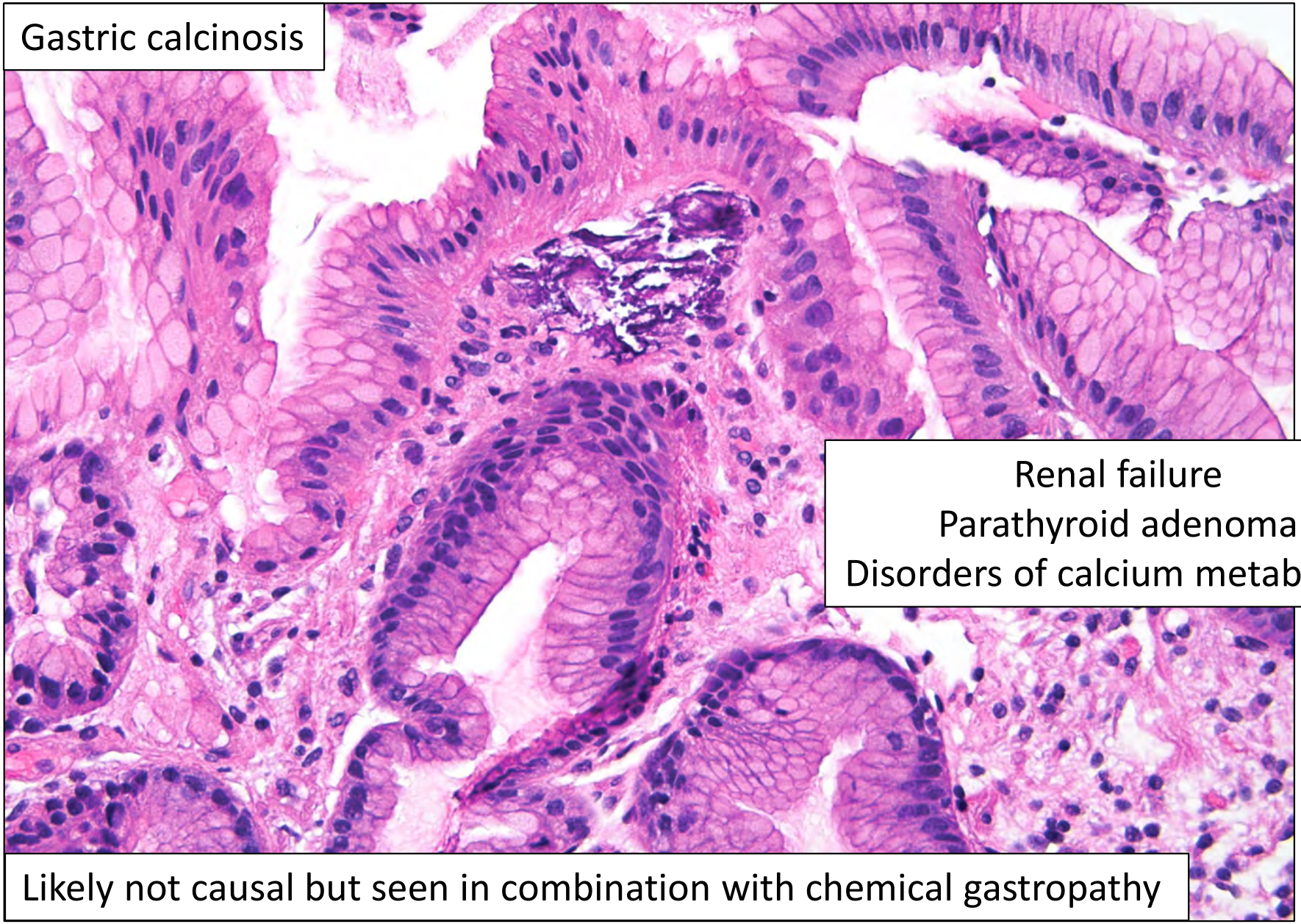


Lanthanum: phosphate-binding agent used in renal failure patients

Not causal but often seen in patients with chemical gastropathy


Gastric calcinosis

Gastric calcinosis

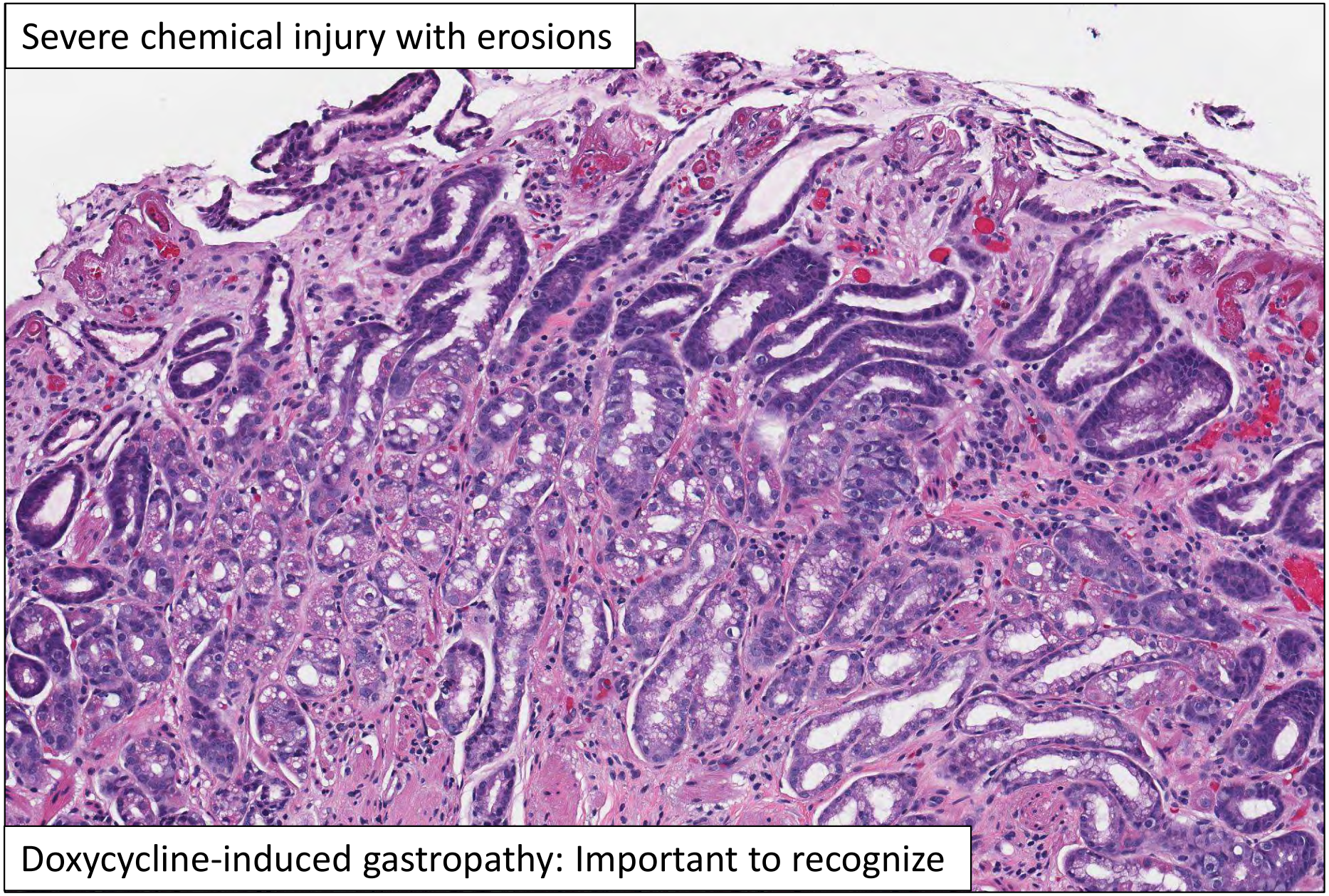


Renal failure
Parathyroid adenoma
Disorders of calcium metabolism

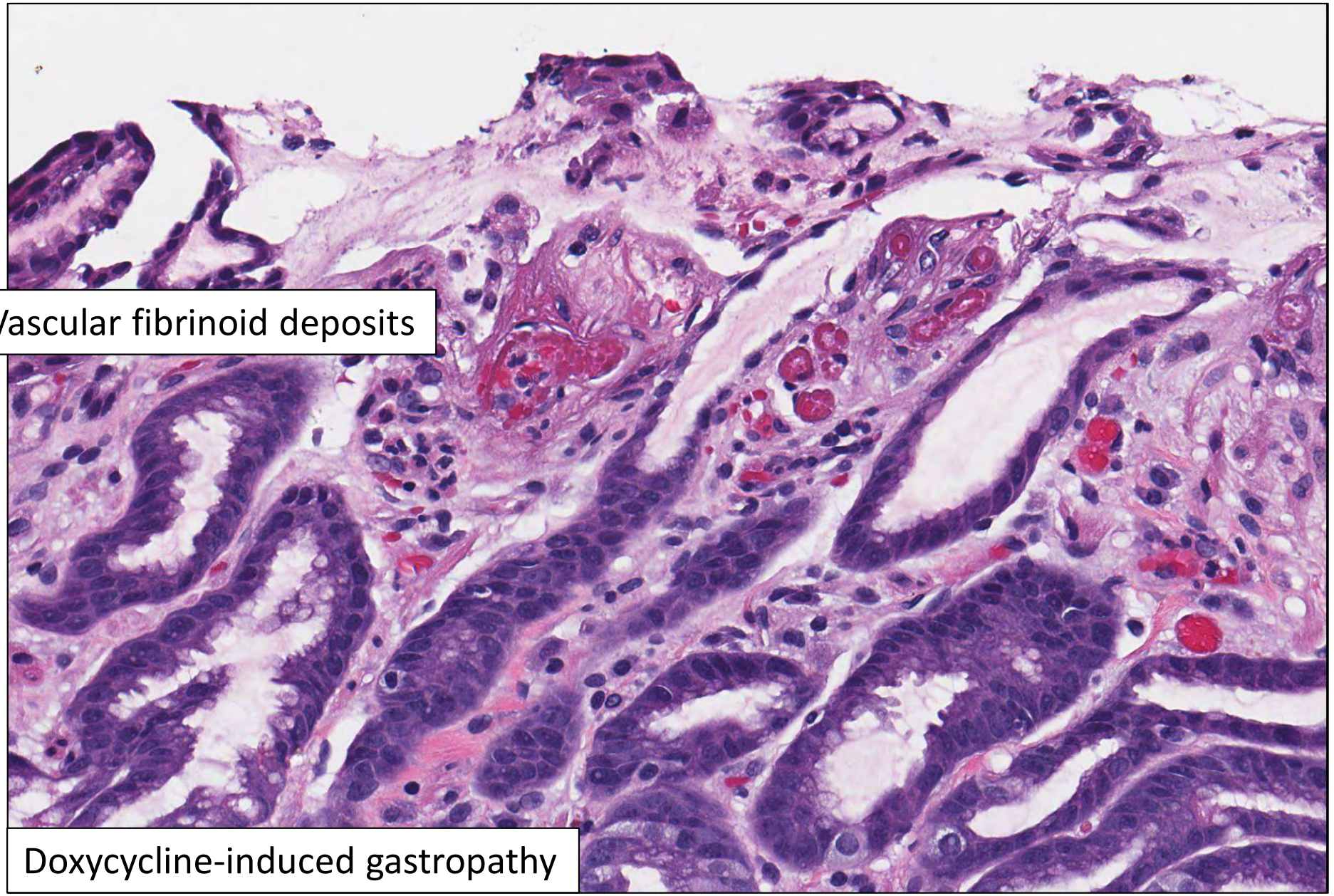
Likely not causal but seen in combination with chemical gastropathy


Von Kossa stain
Gastric calcinosis

Severe chemical injury with erosions



Doxycycline-induced gastropathy: Important to recognize


Vascular fibrinoid deposits
Doxycycline-induced gastropathy

Vascular Alterations with or without Chemical Gastropathy

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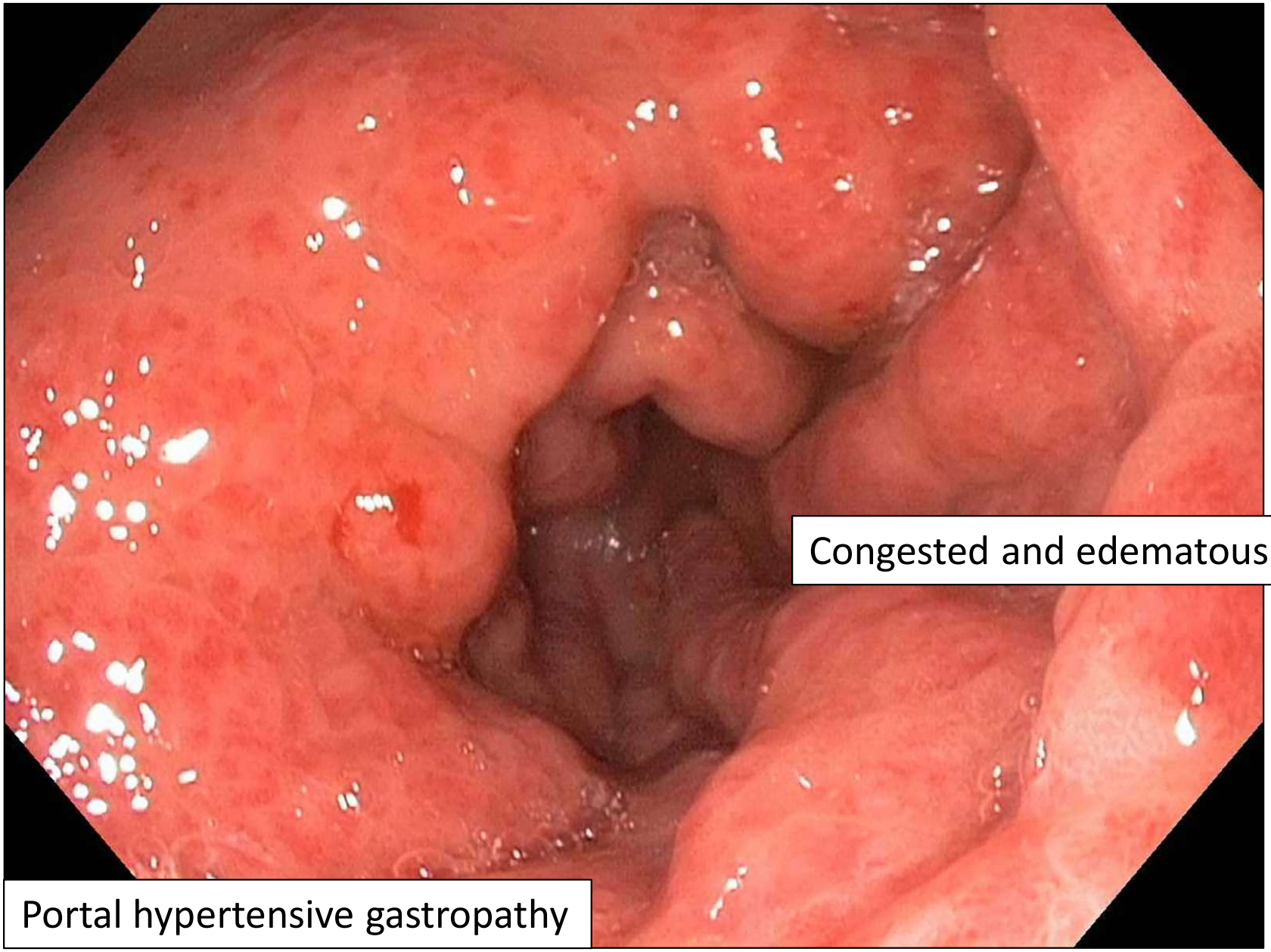
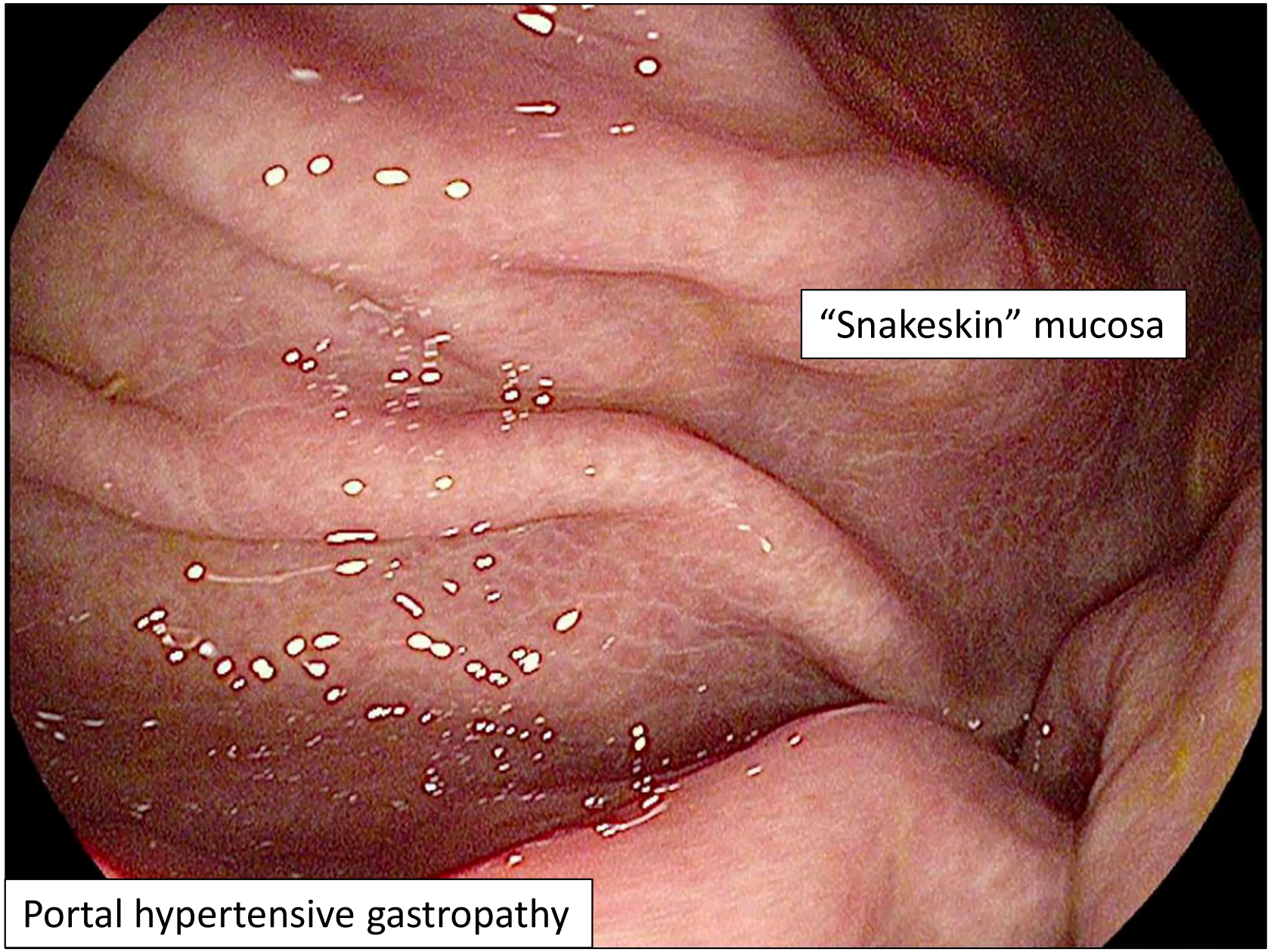
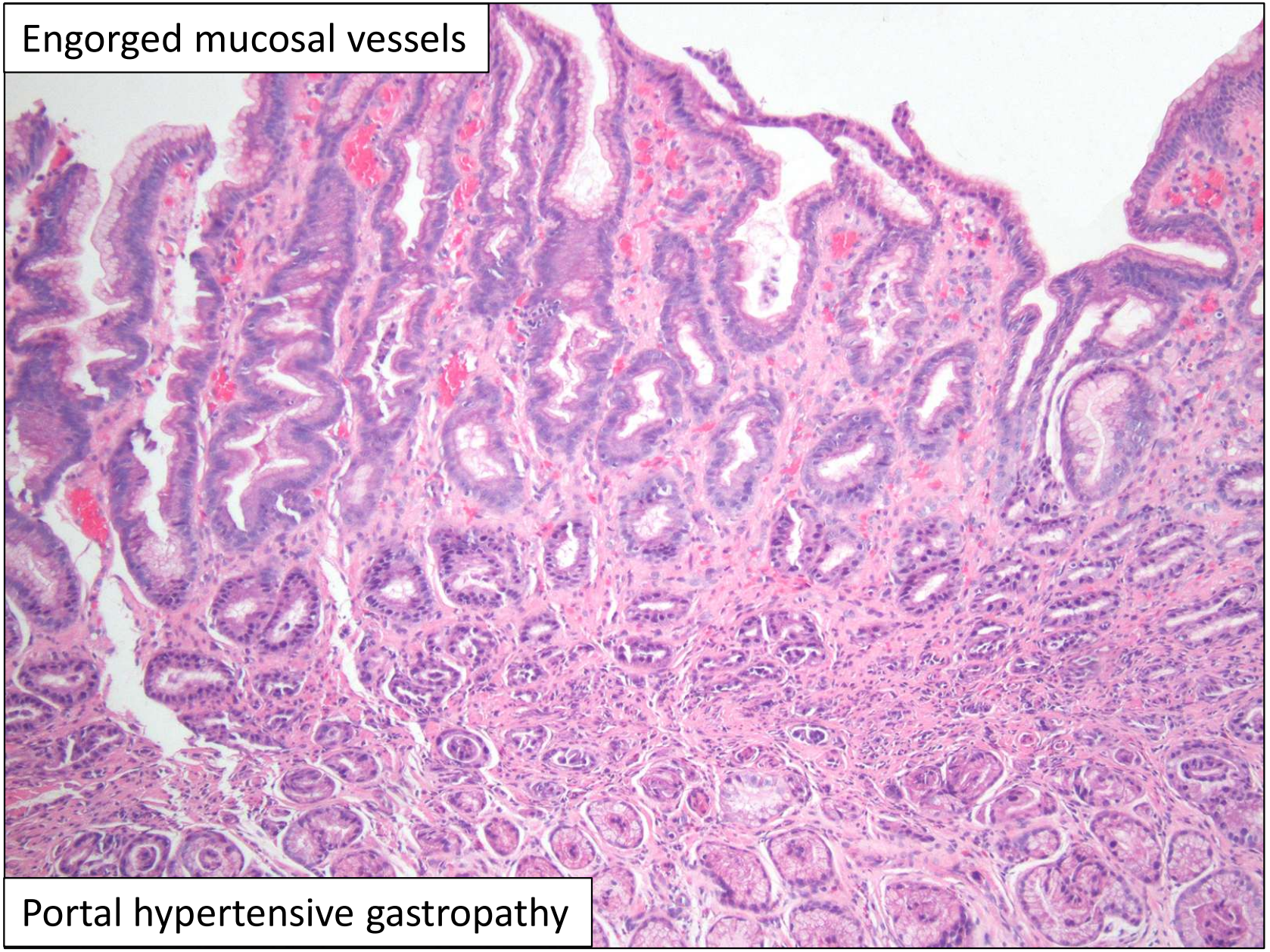
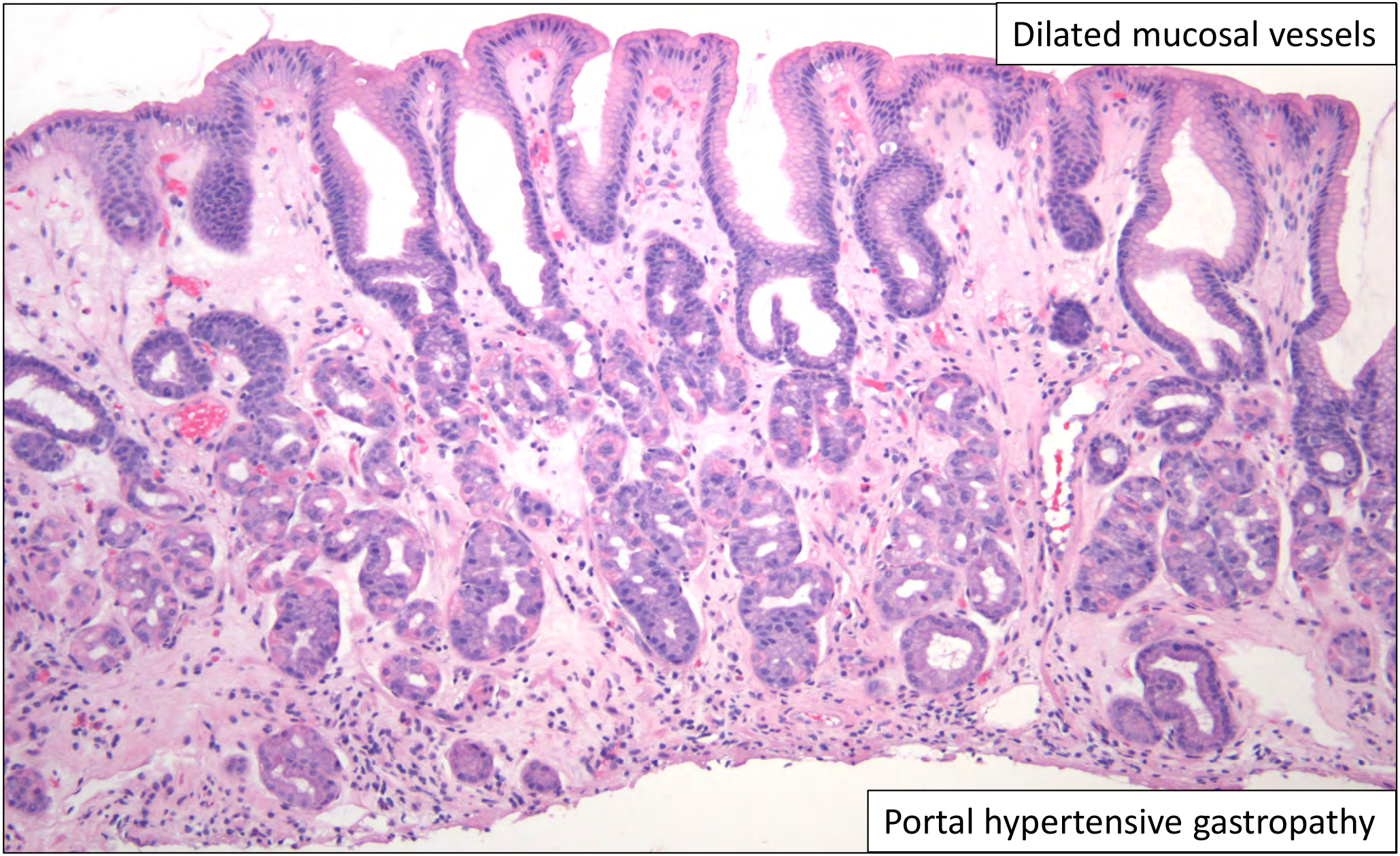

Congested and edematous mucosa
Portal hypertensive gastropathy

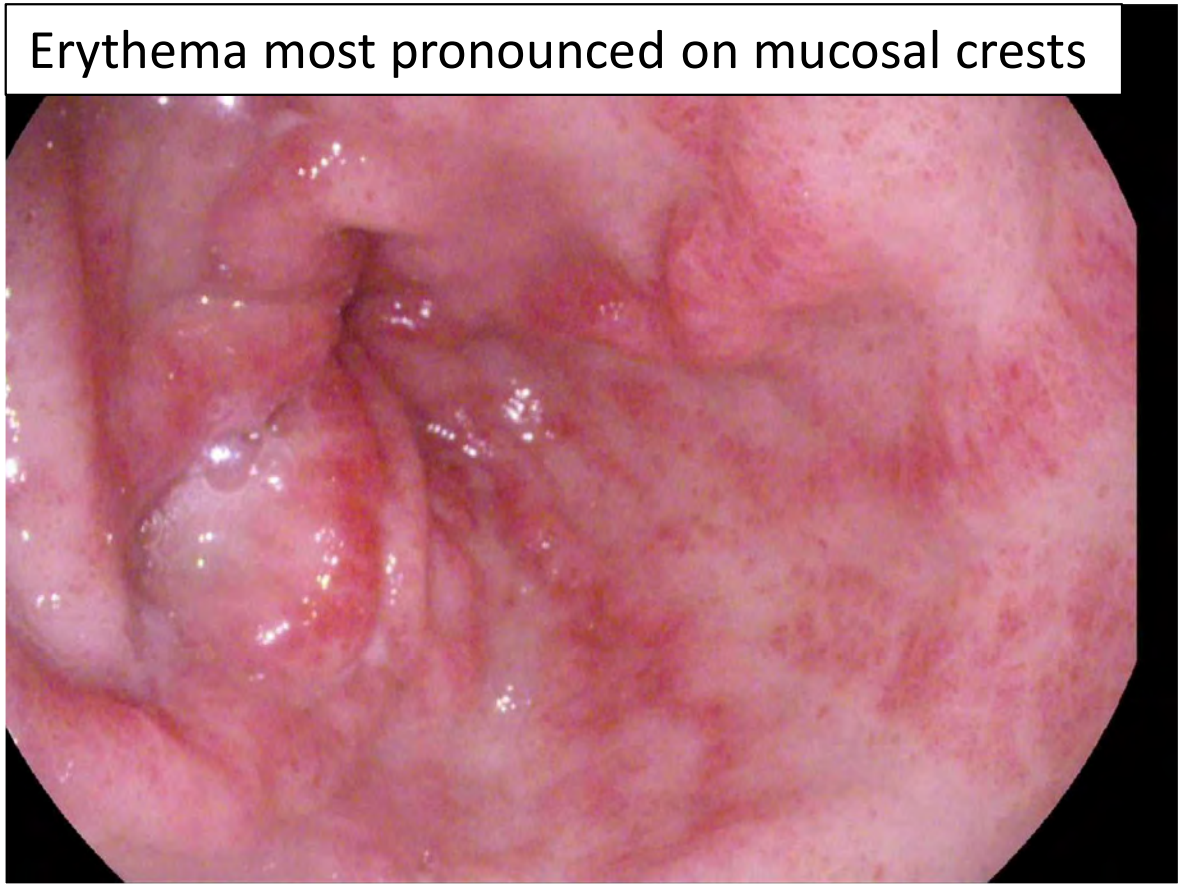

“Snakeskin” mucosa
Portal hypertensive gastropathy


Engorged mucosal vessels
Portal hypertensive gastropathy

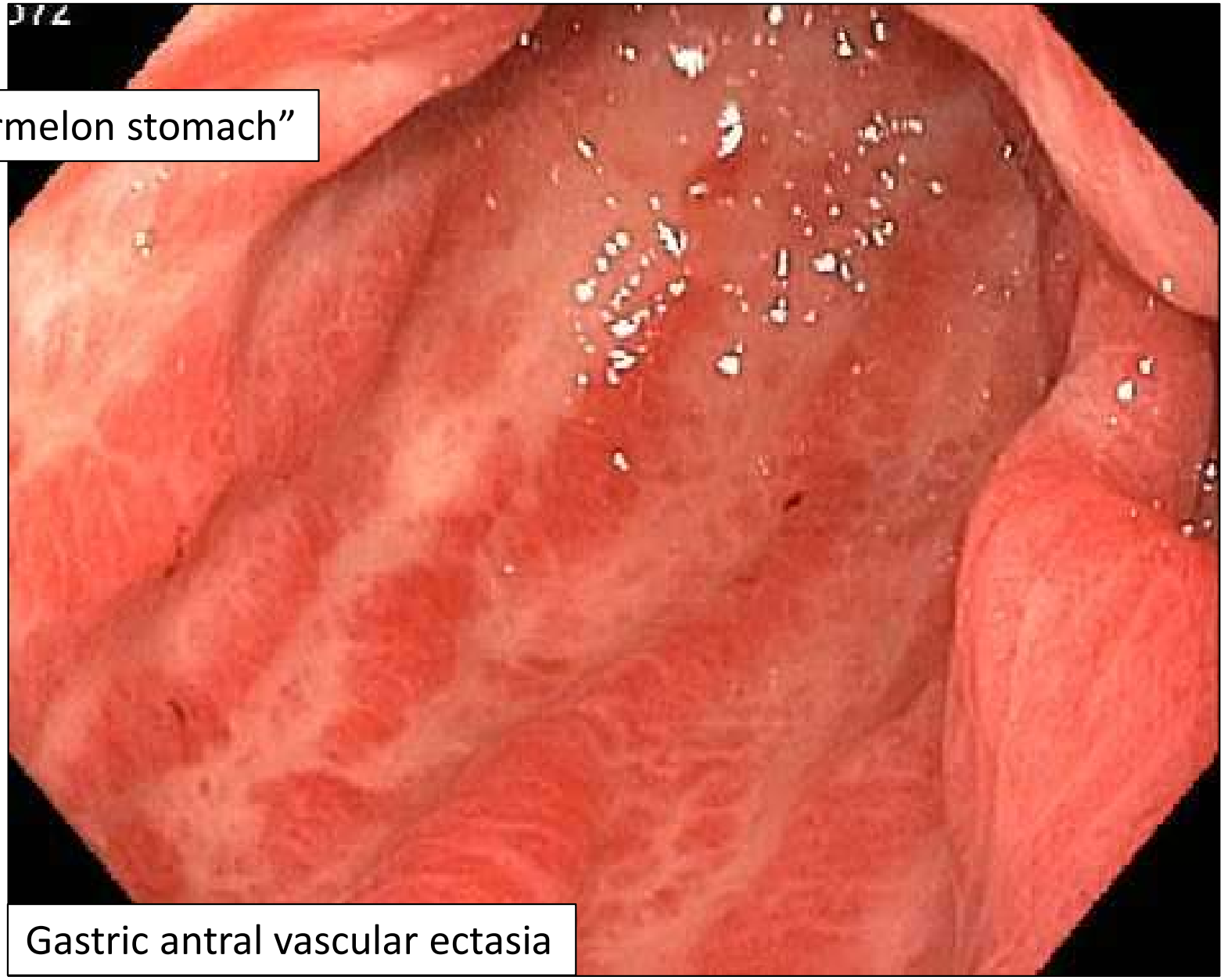

Dilated mucosal vessels
Portal hypertensive gastropathy

Gastric Antral Vascular Ectasia

- Women>men
- Connective tissue disorders
- Autoimmune conditions
- Gastrointestinal bleeding



“Watermelon stomach”



Gastric antral vascular ectasia


Gastric antral vascular ectasia
Dilated, thin-walled vessels
Fibrin thrombi
Looks a lot like chemical gastropathy

Gastric Injury with Prominent Apoptosis

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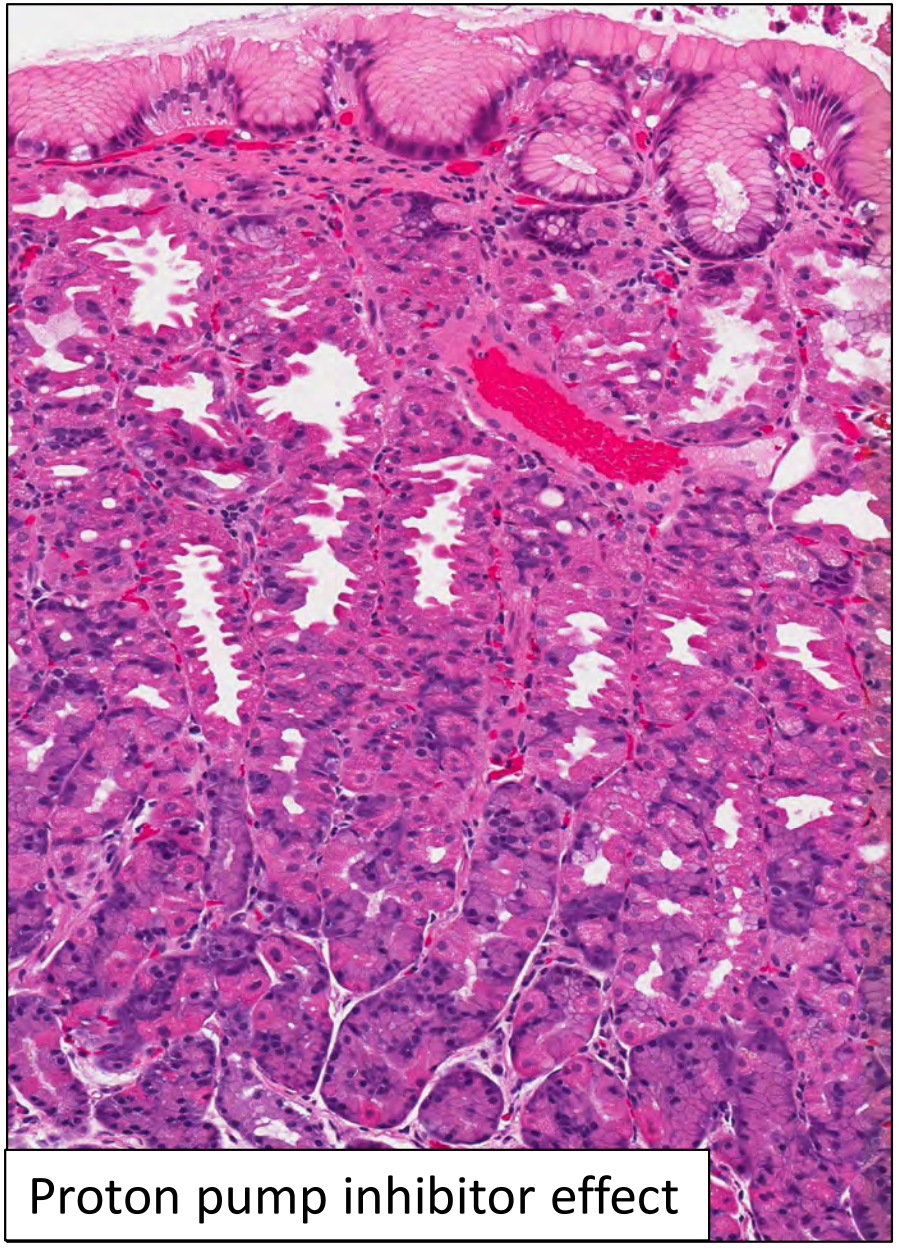
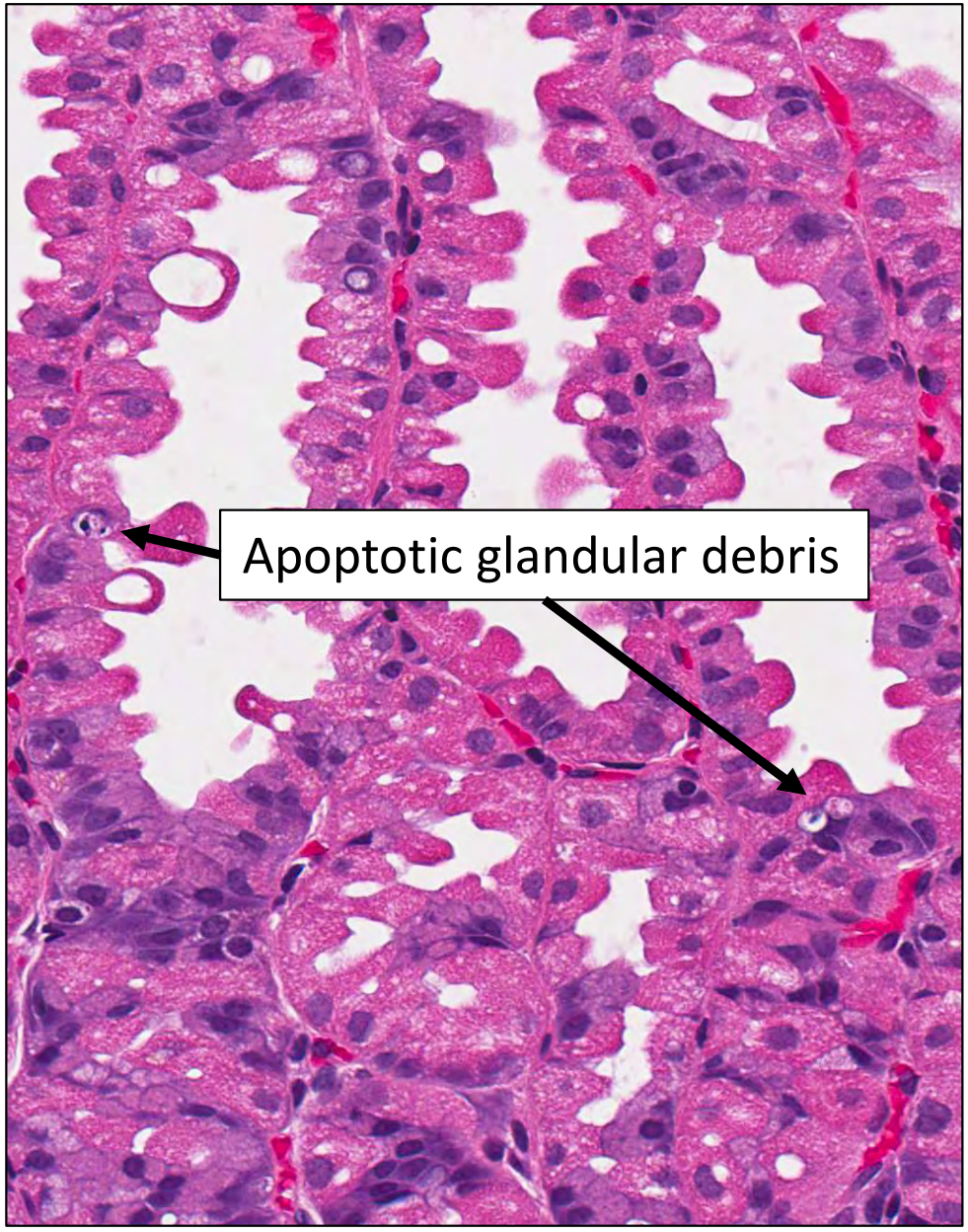
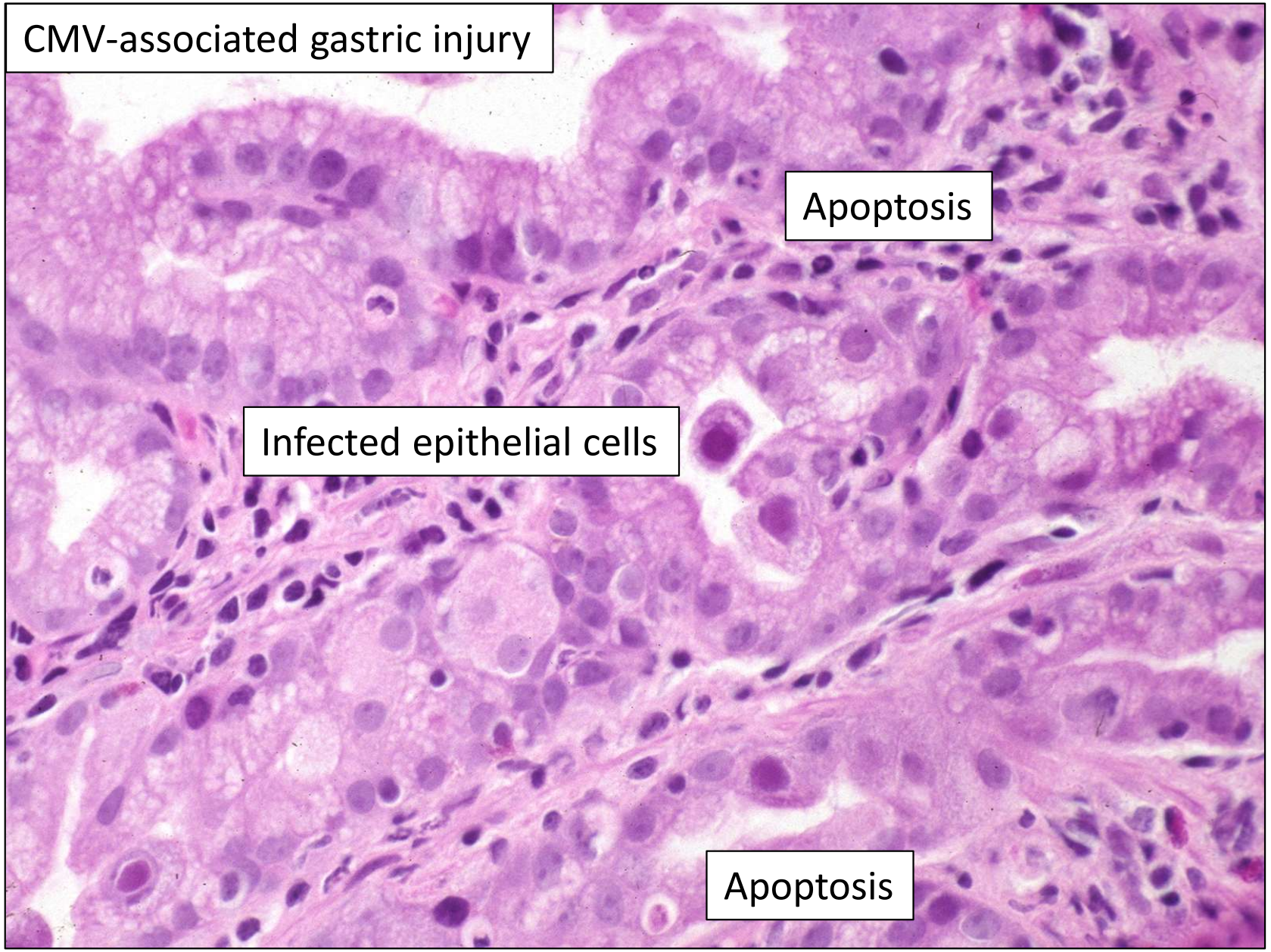
Differential Diagnosis of Apoptosis

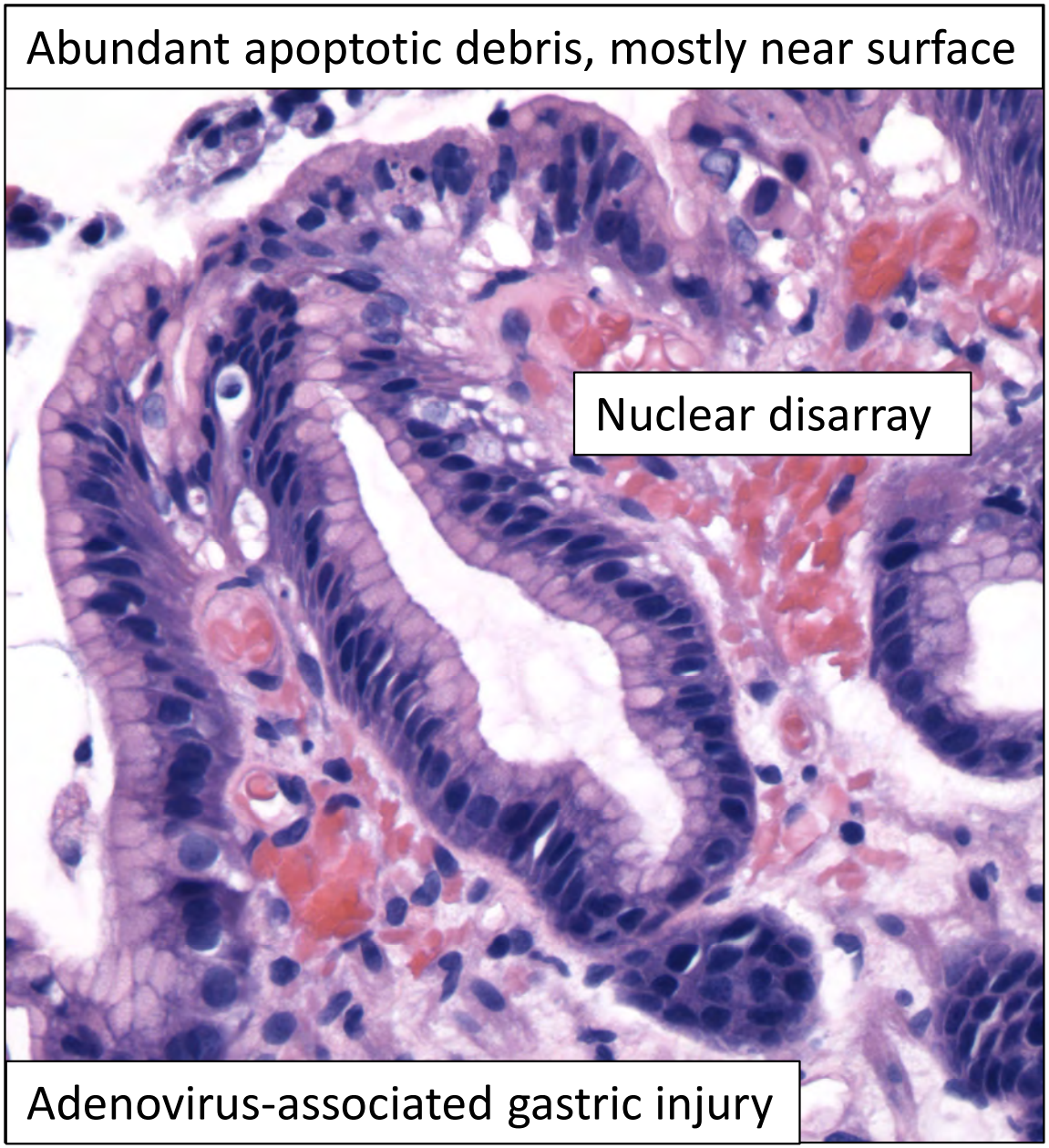
- Immunocompetent
  - Medications, most notably proton pump inhibitors
- Immunodeficient
  - Viral infection
  - Graft *versus* host disease
- Iatrogenic injury
  - Medications
  - Radiation
  - Immunotherapy

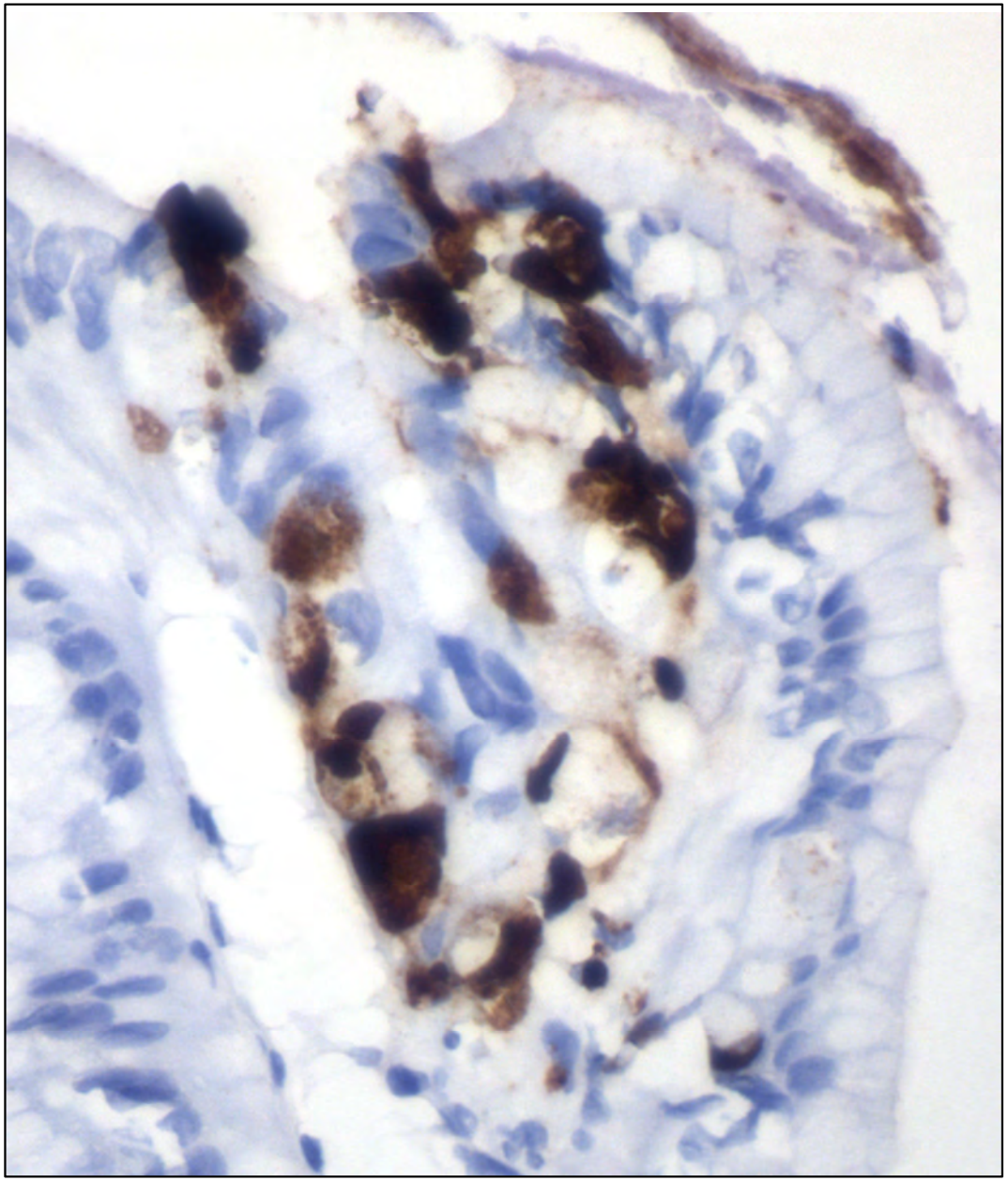


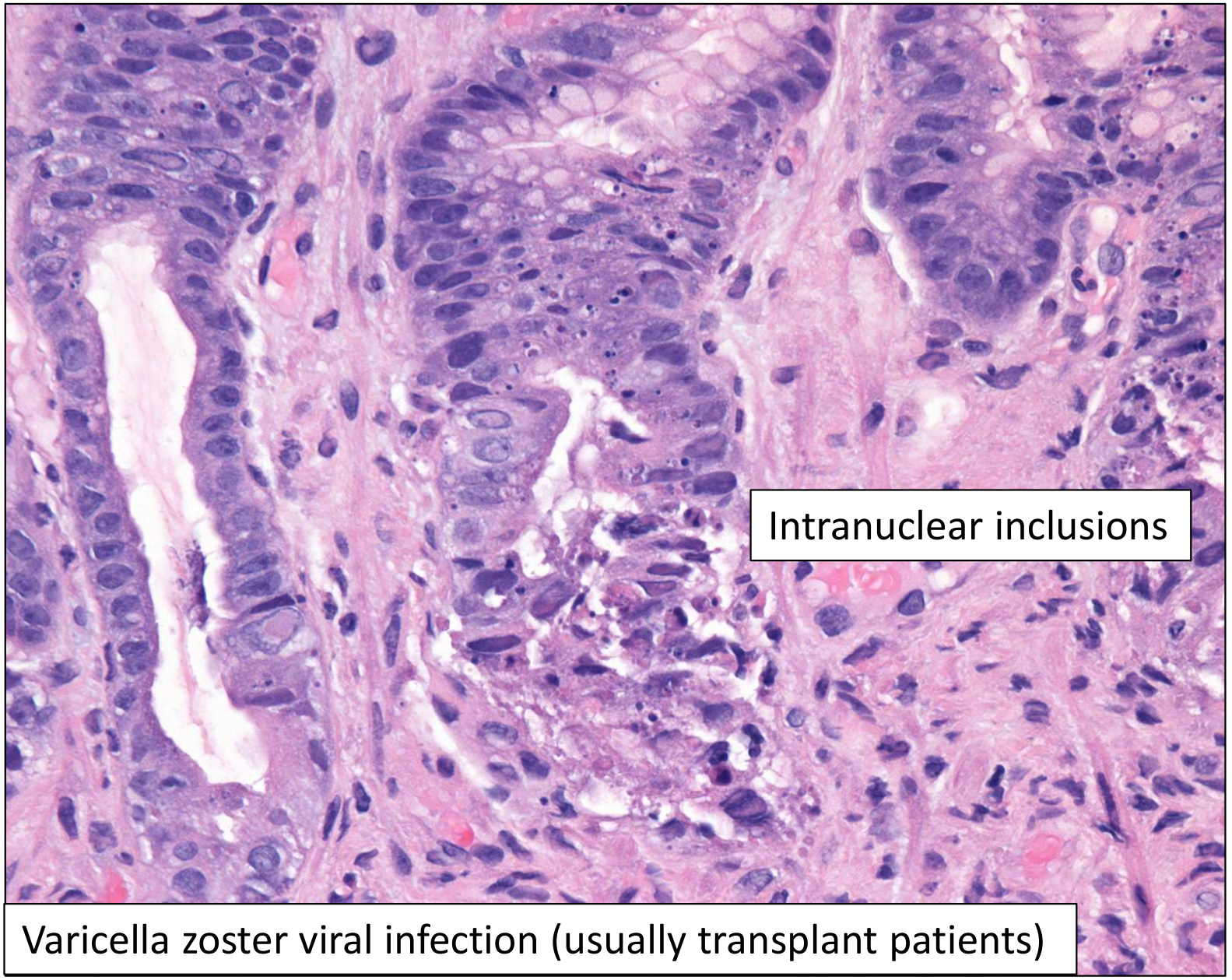
Proton pump inhibitor effect



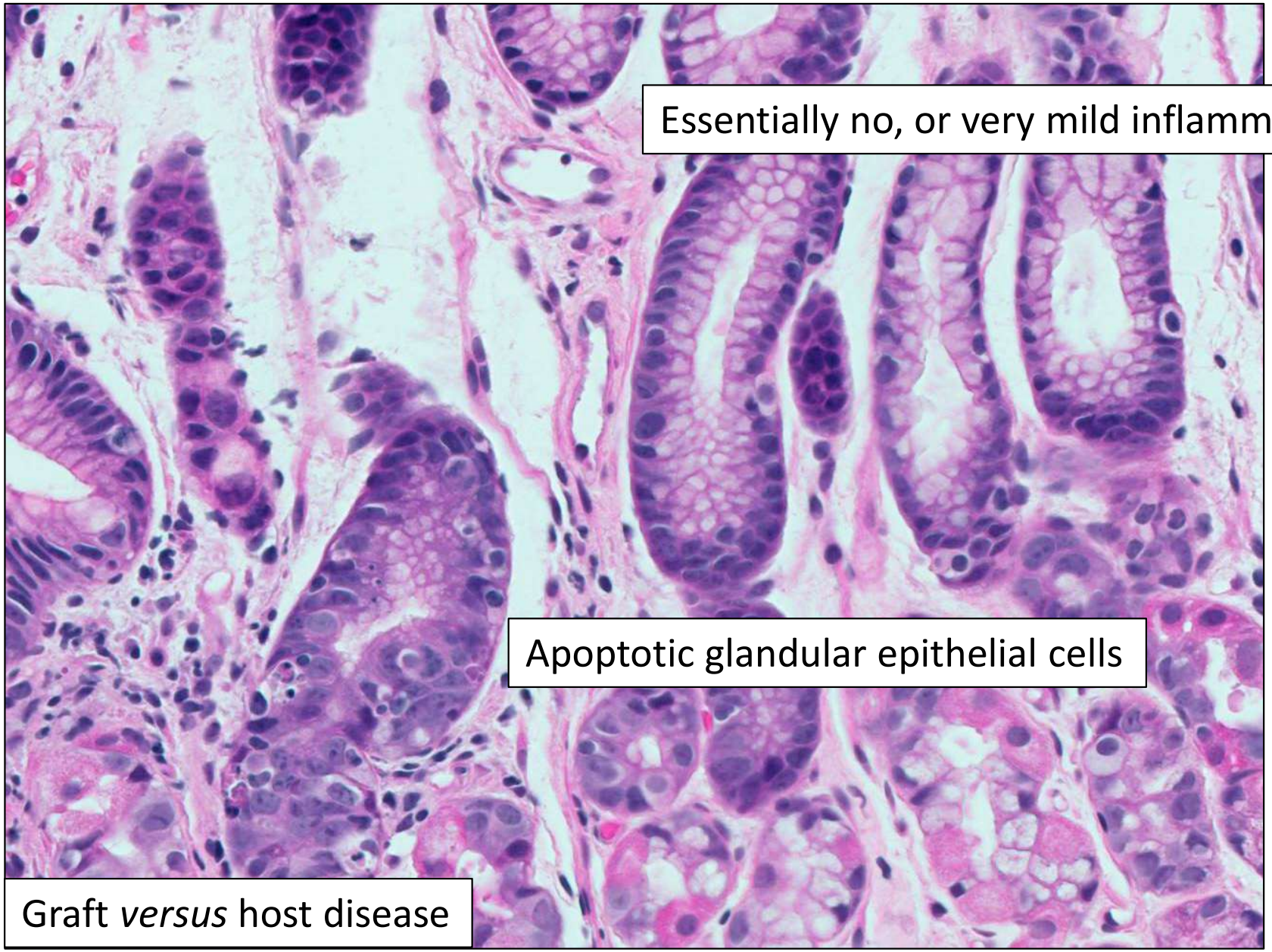

CMV-associated gastric injury
Apoptosis
Infected epithelial cells
Apoptosis

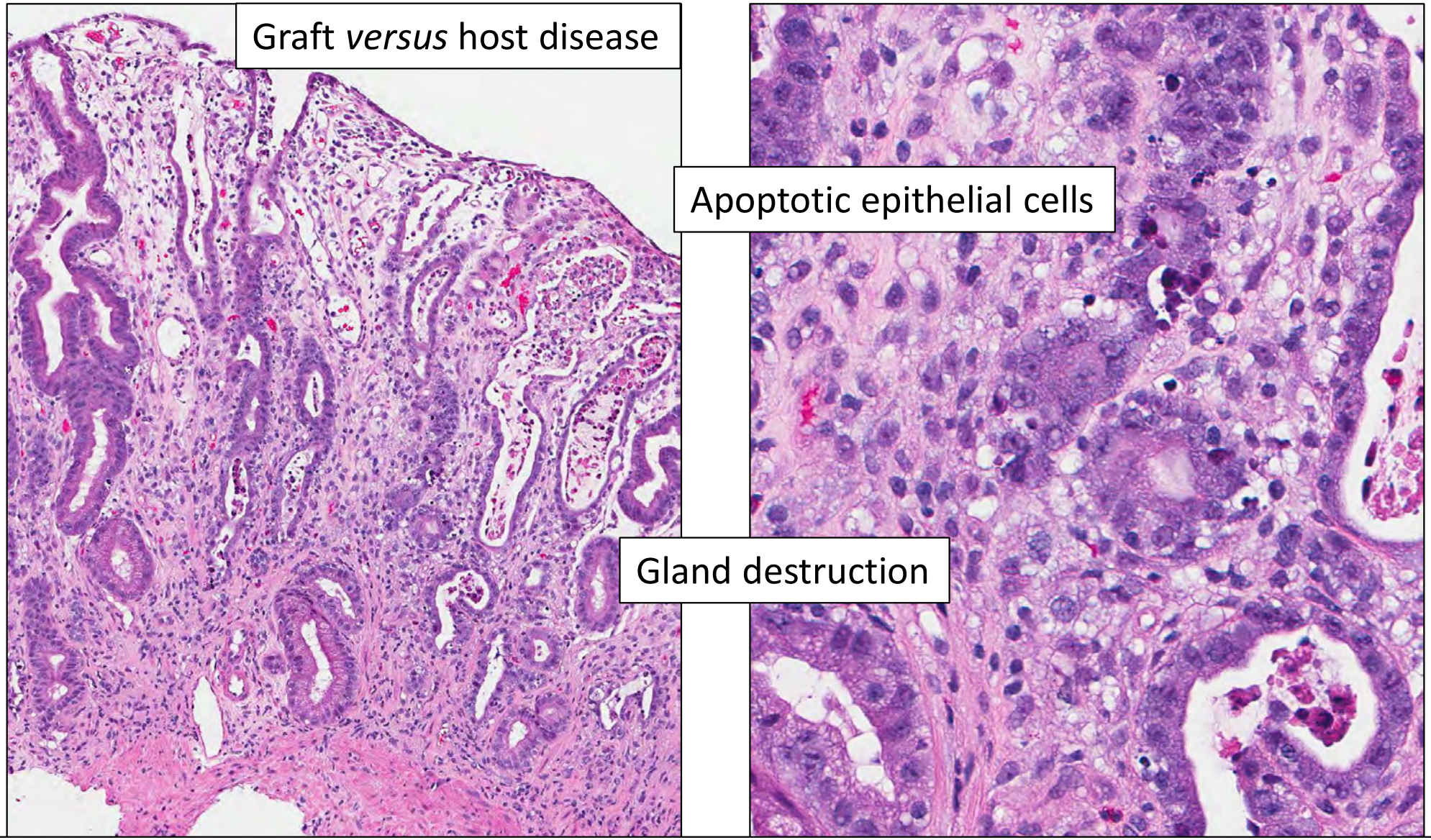

Abundant apoptotic debris, mostly near surface
Nuclear disarray
Adenovirus-associated gastric injury





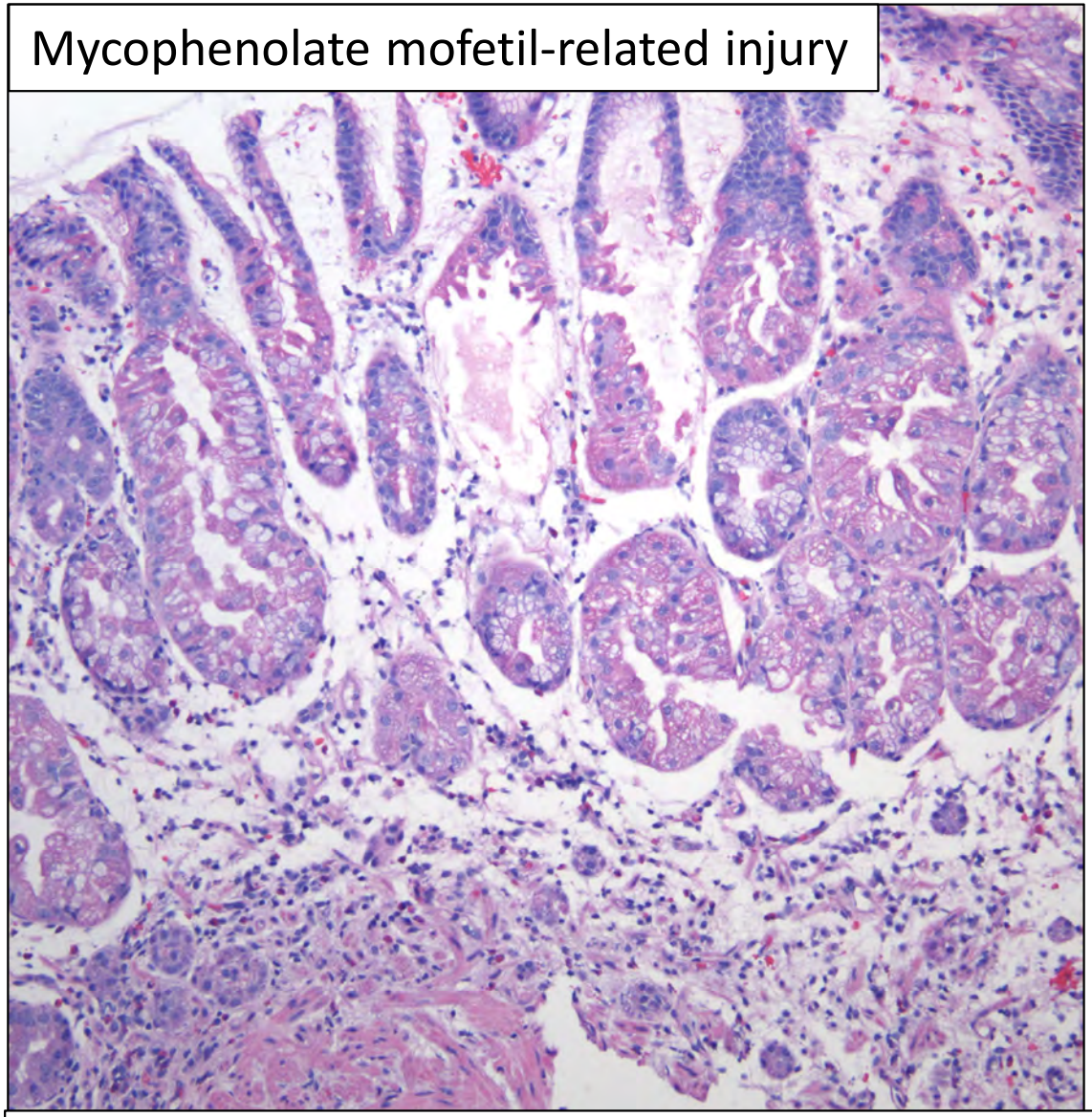
Varicella zoster viral infection (usually transplant patients)

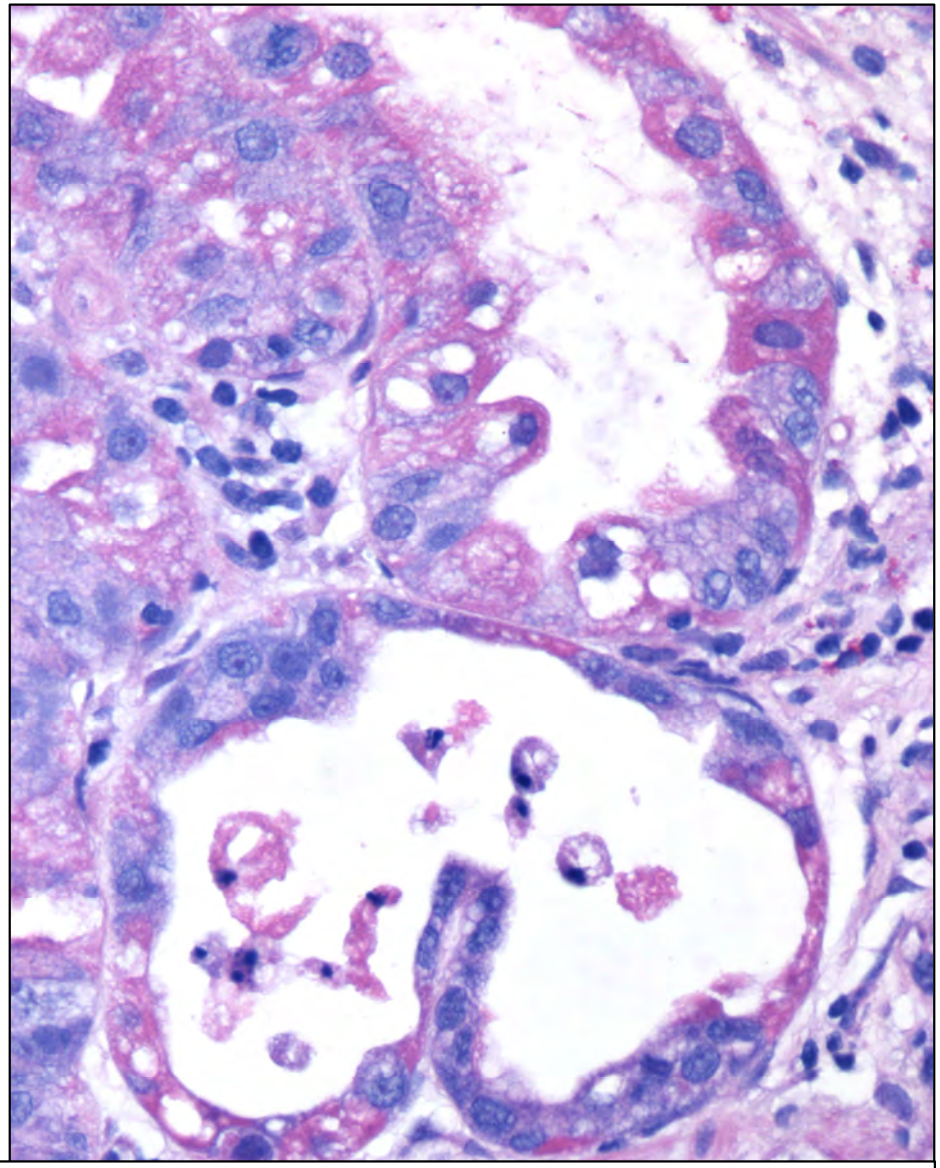

Essentially no, or very mild inflammation
Apoptotic glandular epithelial cells
Graft *versus* host disease



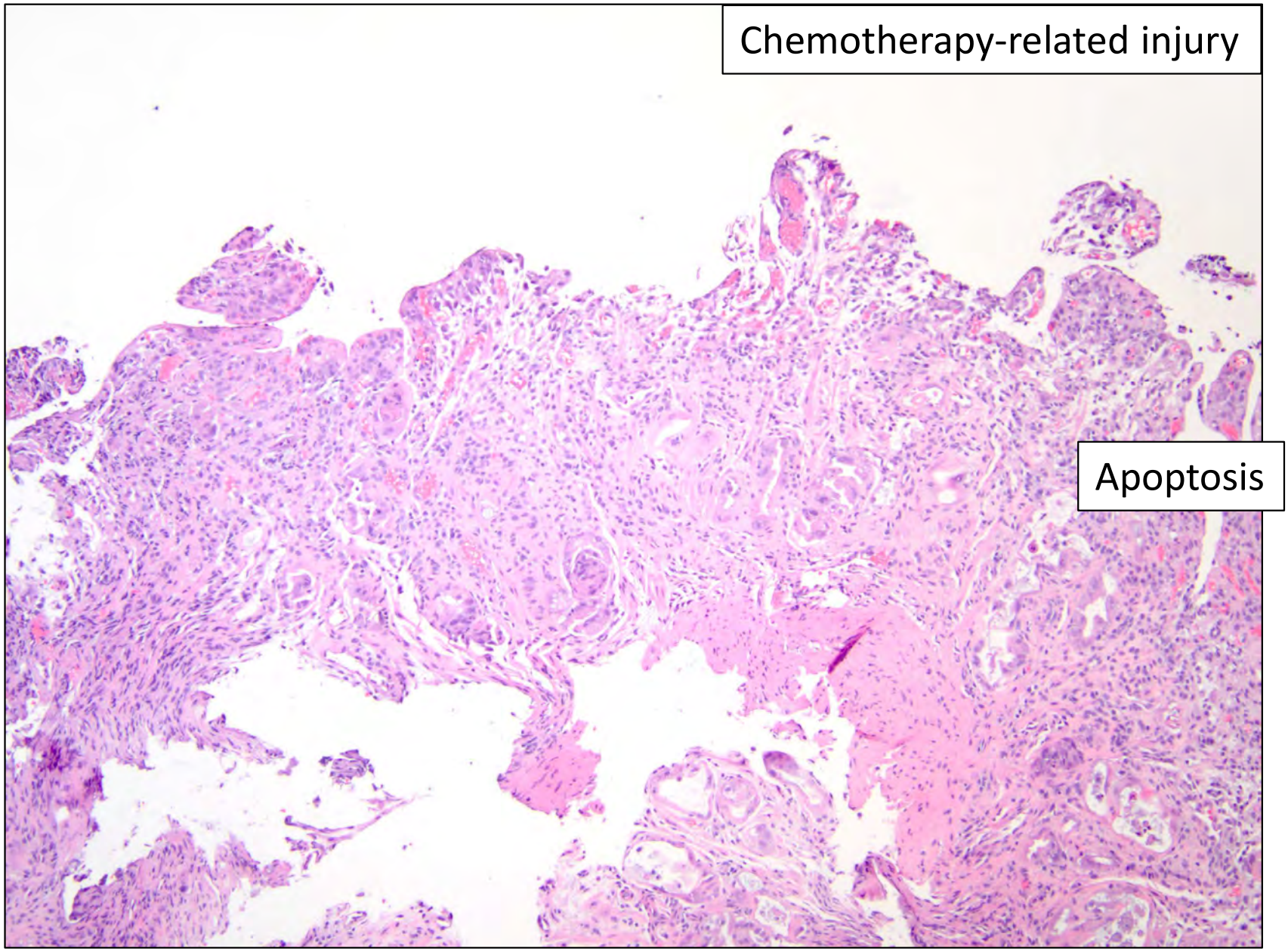
Disproportionate gland injury given the amount of lamina propria inflammation present

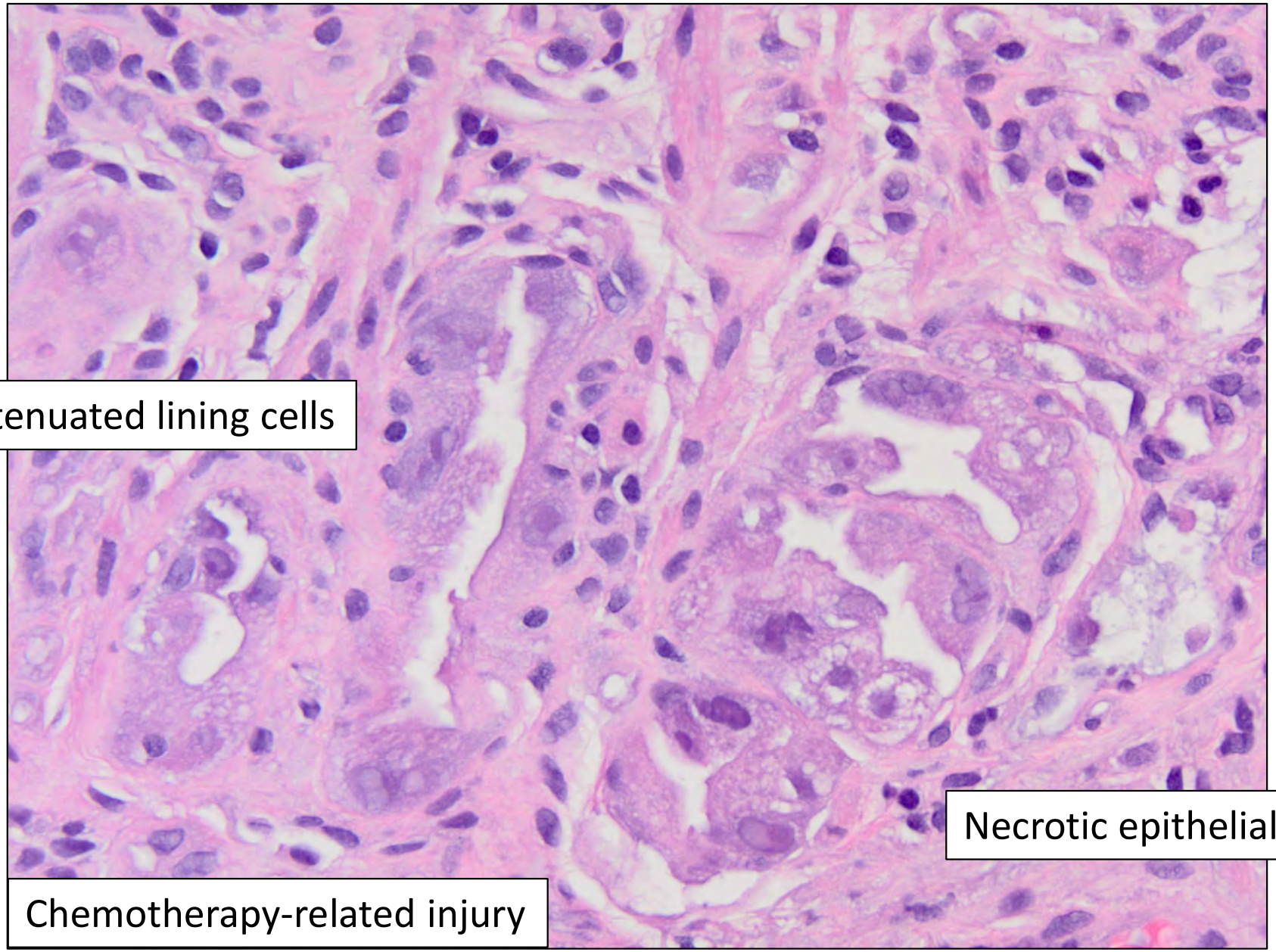
Mycophenolate mofetil-related injury

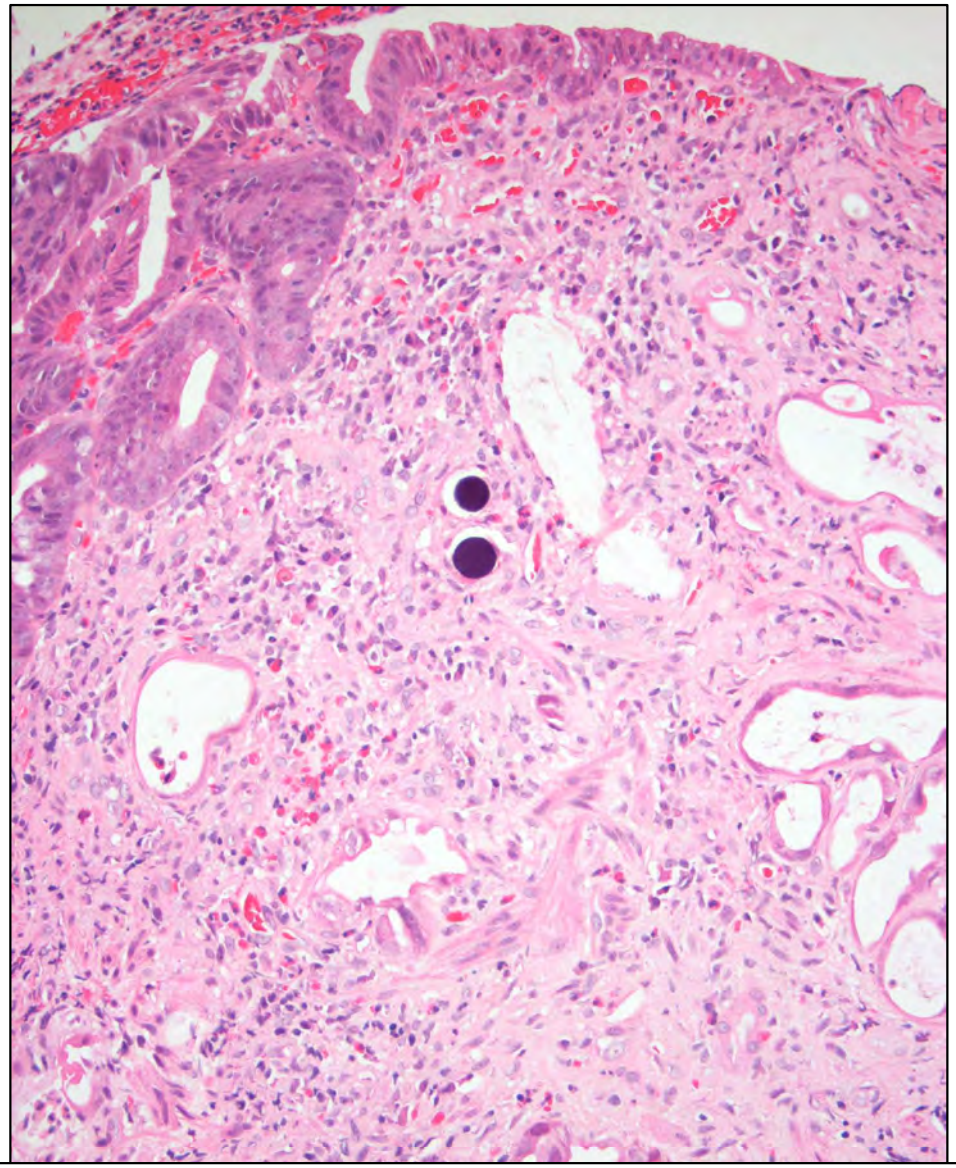


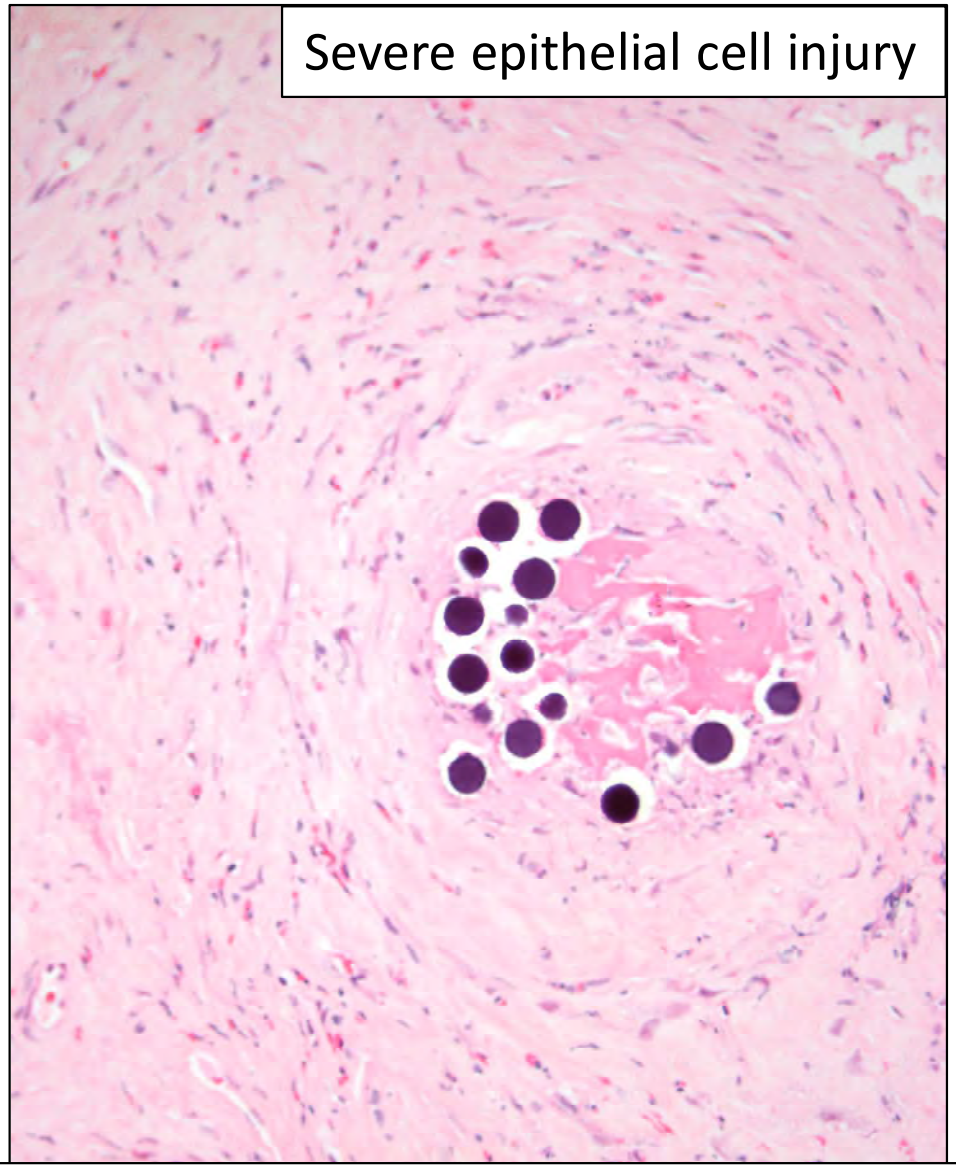


Disproportionately mild inflammation with eosinophil-rich inflammation in lamina propria

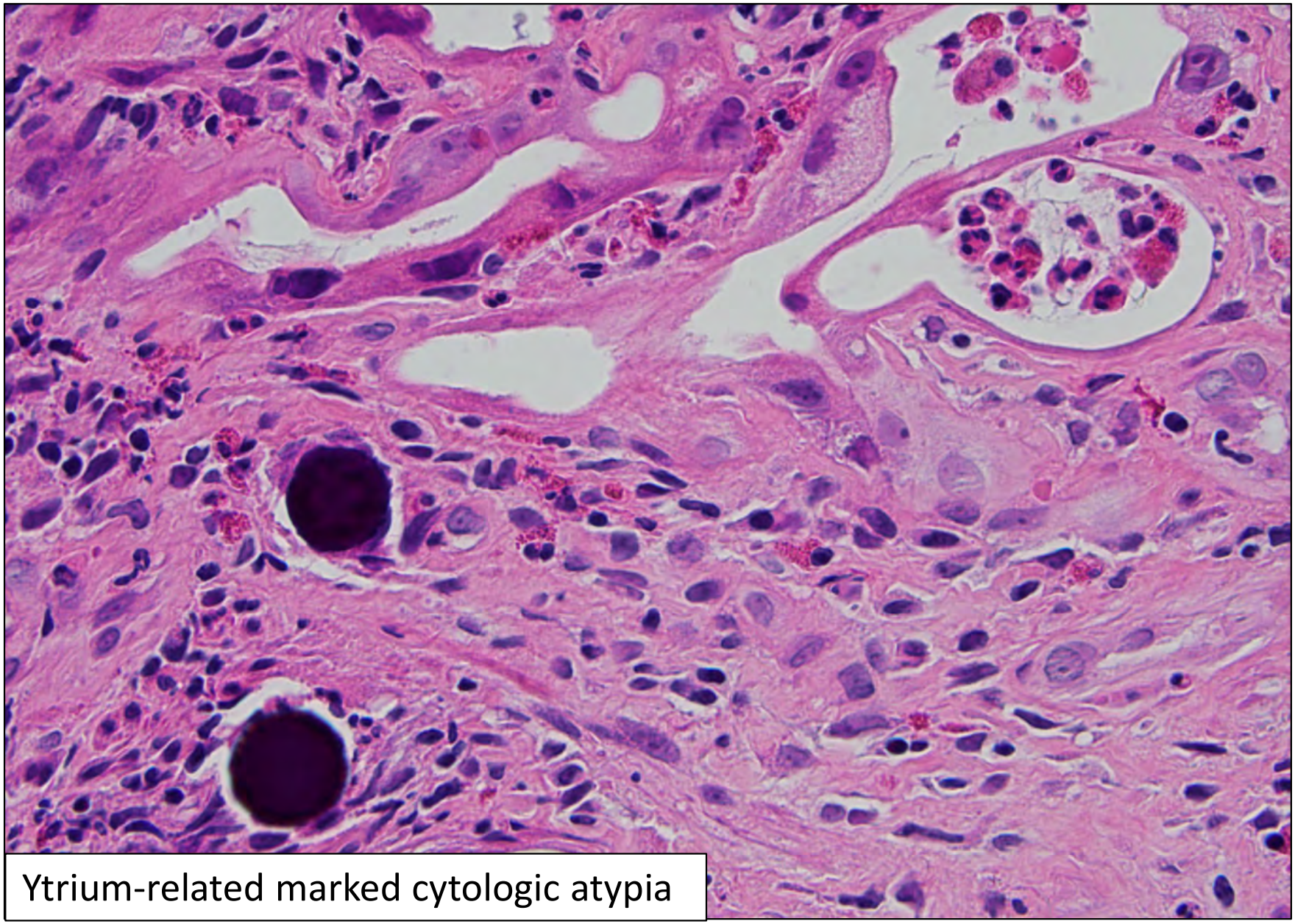

Chemotherapy-related injury
Apoptosis


Attenuated lining cells
Necrotic epithelial cells
Chemotherapy-related injury

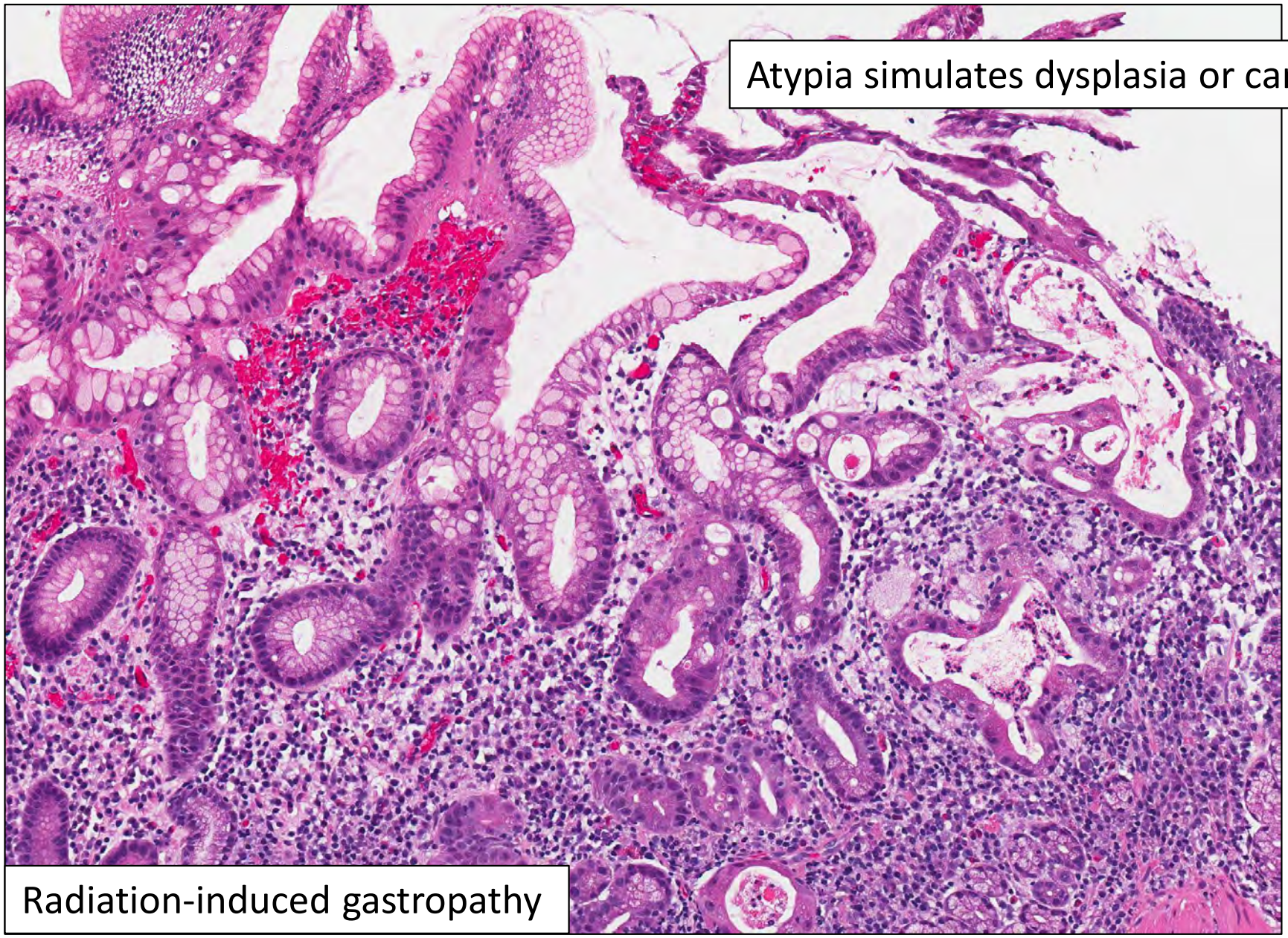


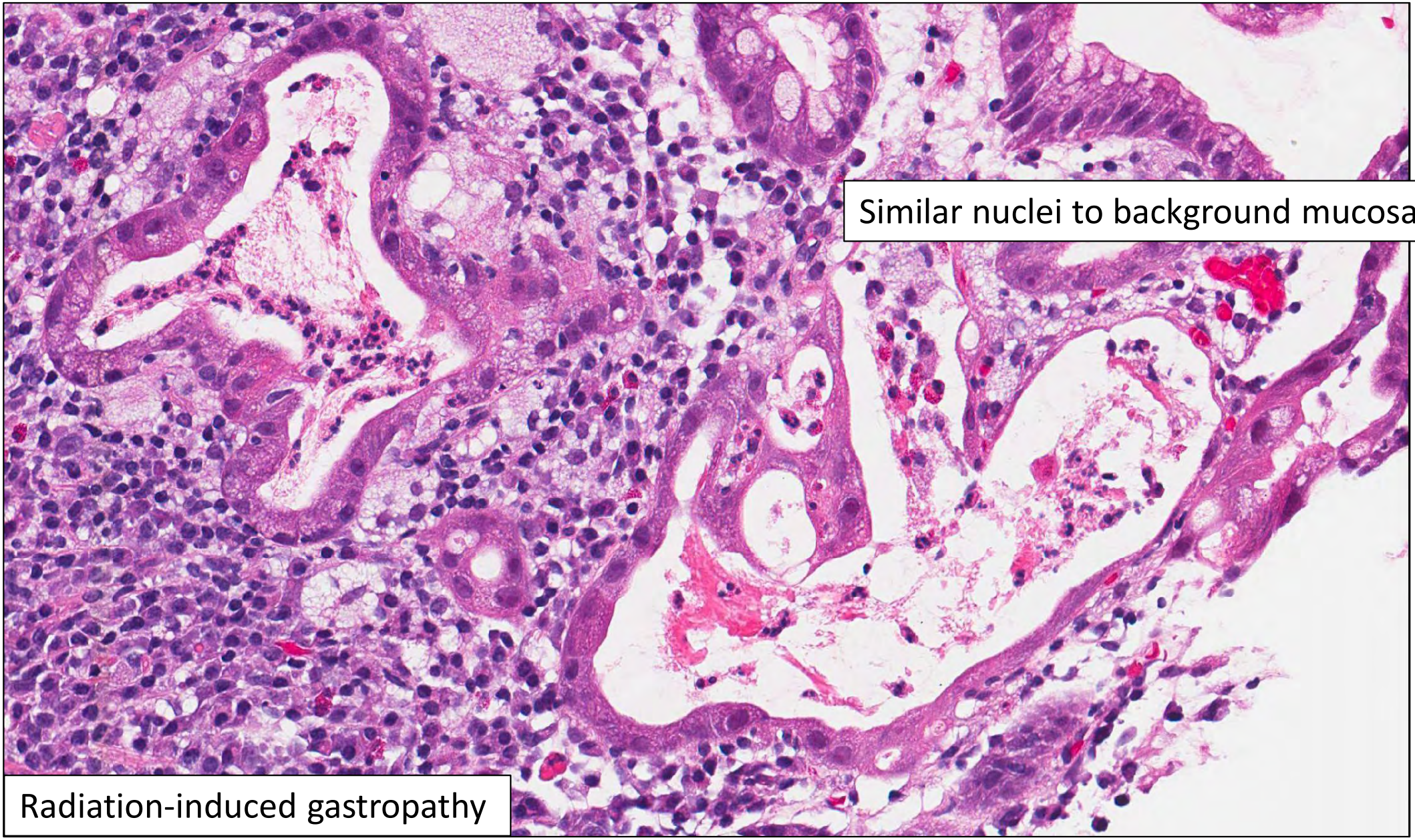


Ytrium-induced radiation (Y^{90} beads from Selective Internal Radiation Therapy gone awry)



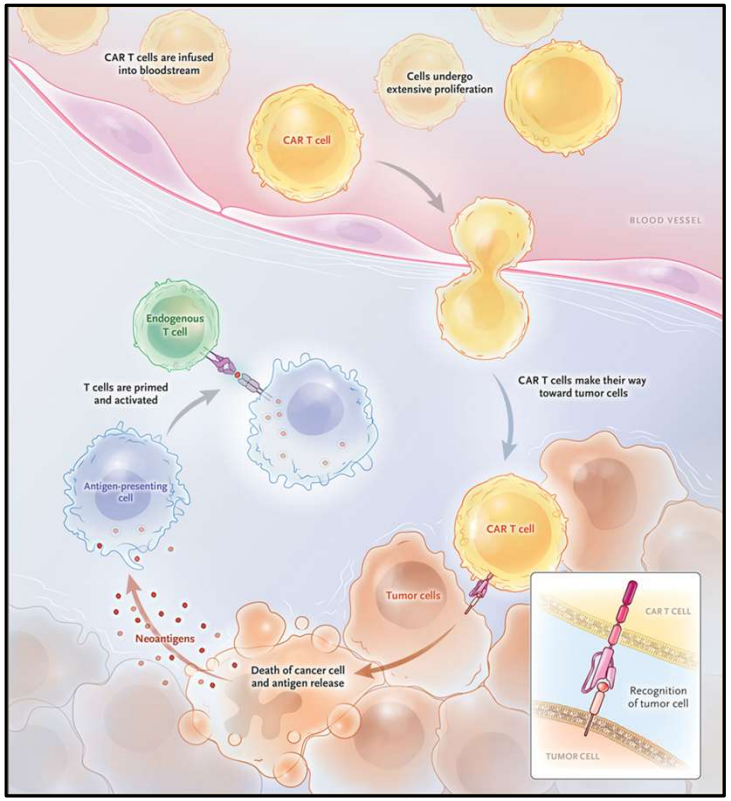
Ytrium-related marked cytologic atypia


Atypia simulates dysplasia or carcinoma
Radiation-induced gastropathy

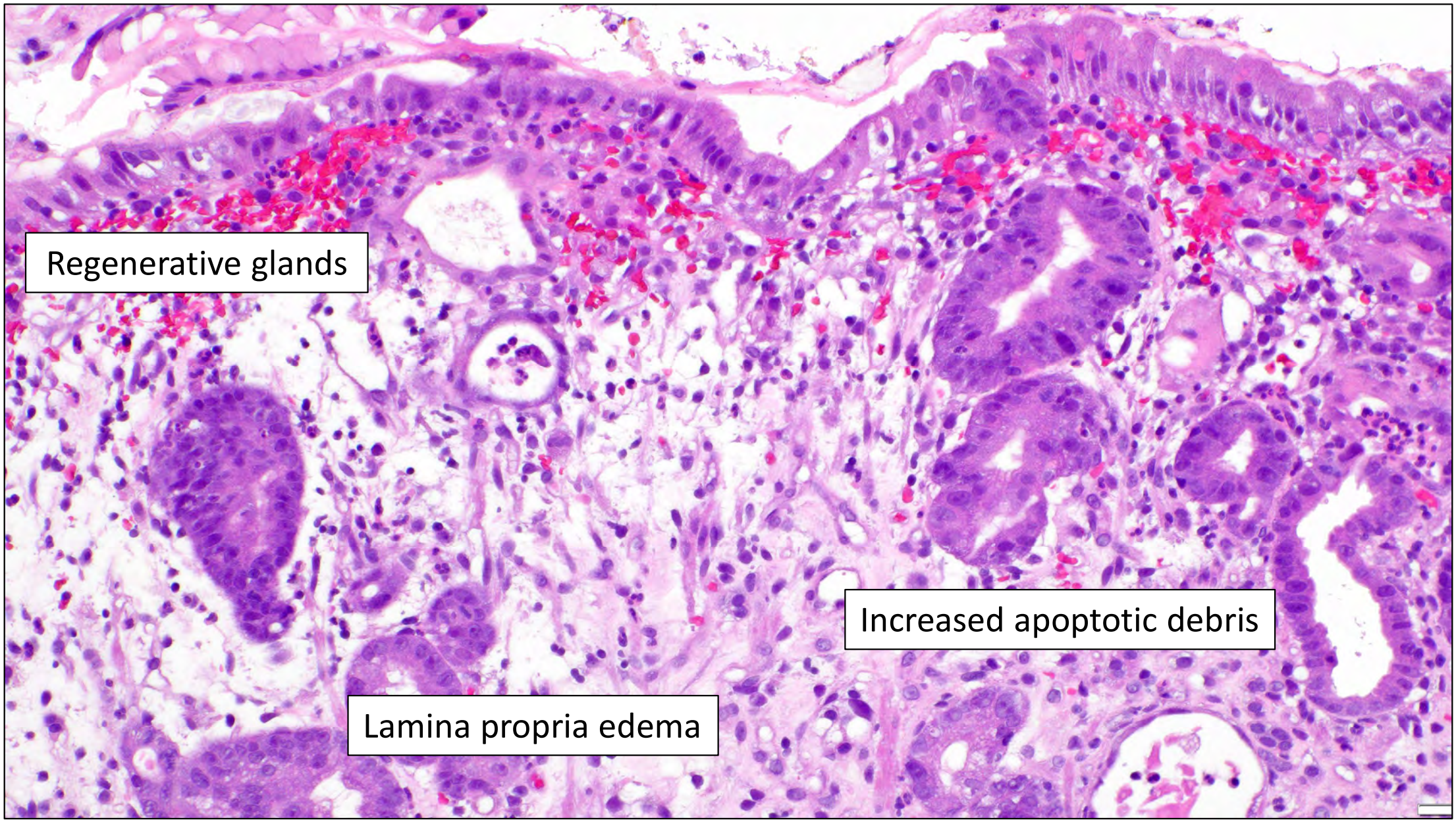

Similar nuclei to background mucosa
Radiation-induced gastropathy

CAR-T Therapy

- Chimeric antigen receptor T-cell (CAR-T) therapy is a type of immune effector cell (IEC) therapy targeting
  - B-cell maturation antigen (BCMA) of multiple myeloma
  - CD19 expressed by various lymphoid malignancies



June, *et al.* Chimeric Antigen Receptor Therapy. *N Engl J Med*. 2018 Jul 5;379(1):64-73.


Regenerative glands
Increased apoptotic debris
Lamina propria edema

Chronic Gastritis

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The Differential Diagnosis of Chronic Gastritis

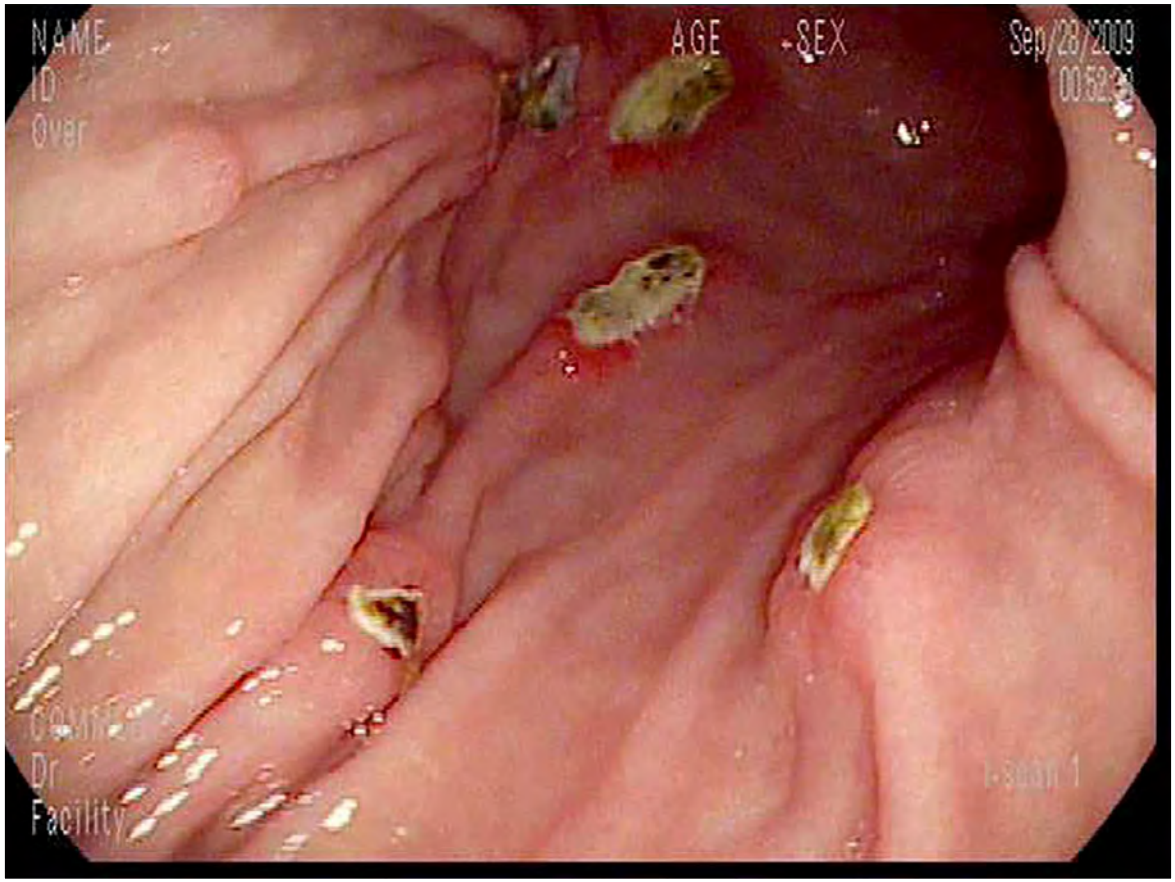
- *Helicobacter pylori* and related organisms
- Autoimmune gastritis, pernicious anemia type
- Medications, particularly olmesartan
- Other immune-mediated injury
- Some non-*Helicobacter* infections

Classifying Chronic Gastritis

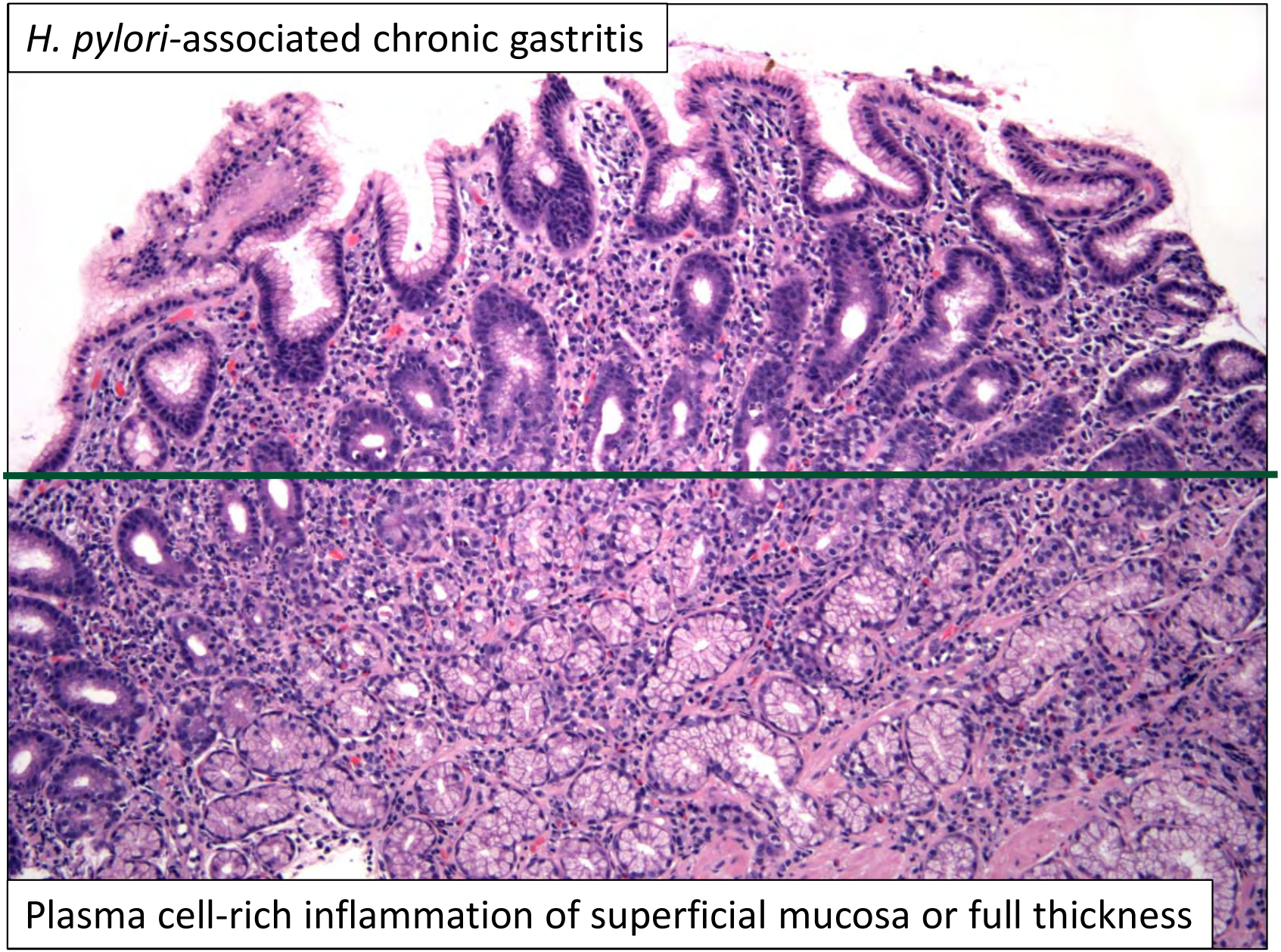
- Location of infiltrate (antrum, body, or both)
- Distribution of inflammation in mucosa
- Components of inflammatory infiltrate
- Alterations of glands and architecture
  - Severe epithelial destruction should make one consider unusual infections, drug injury, or hematopoietic neoplasia

H. pylori-Associated Gastritis

- Gram-negative, curved flagellated rod
- Chronic gastritis, duodenal and gastric ulcers, MALT lymphoma, adenocarcinoma

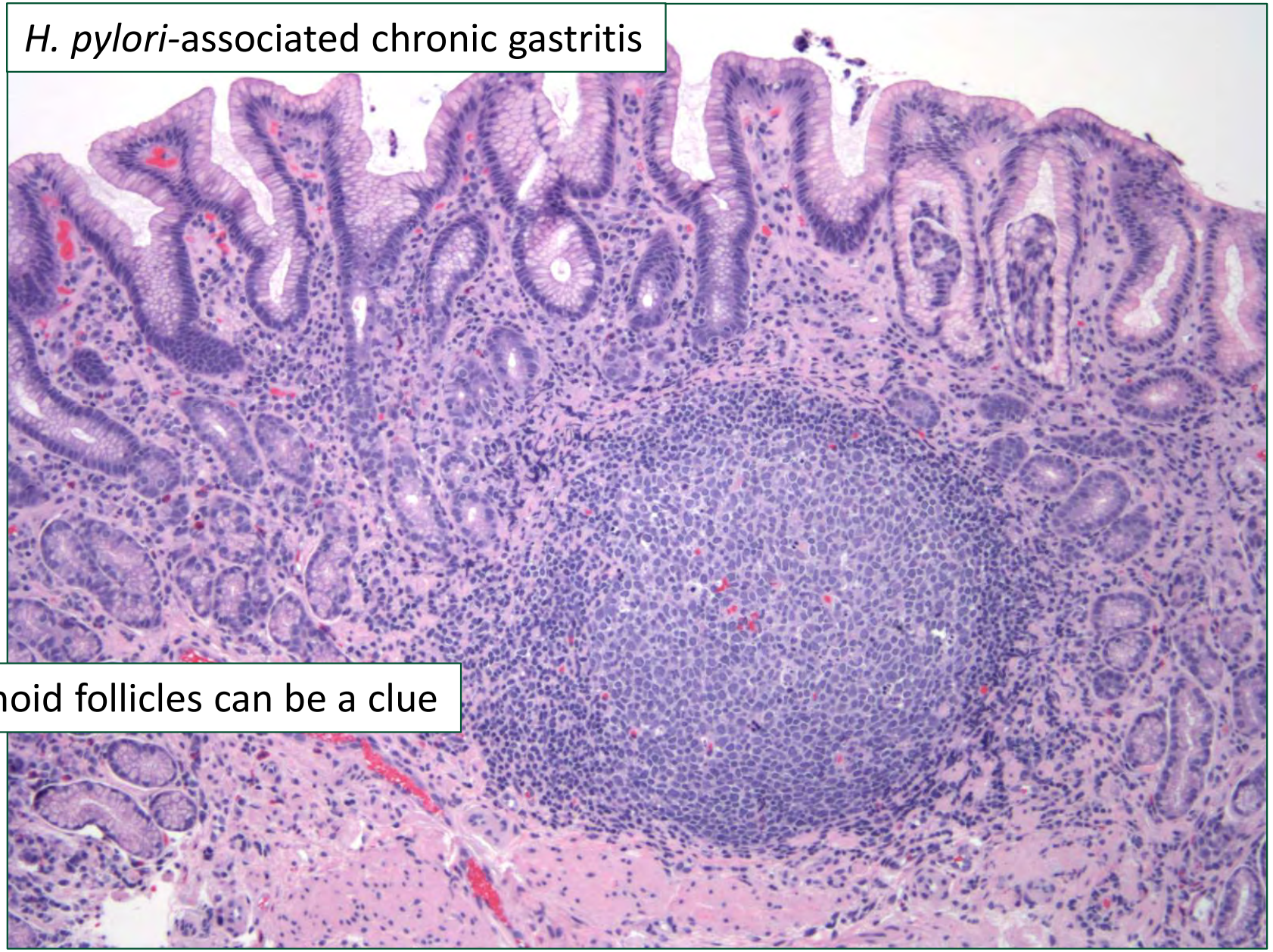


H. pylori-associated chronic gastritis



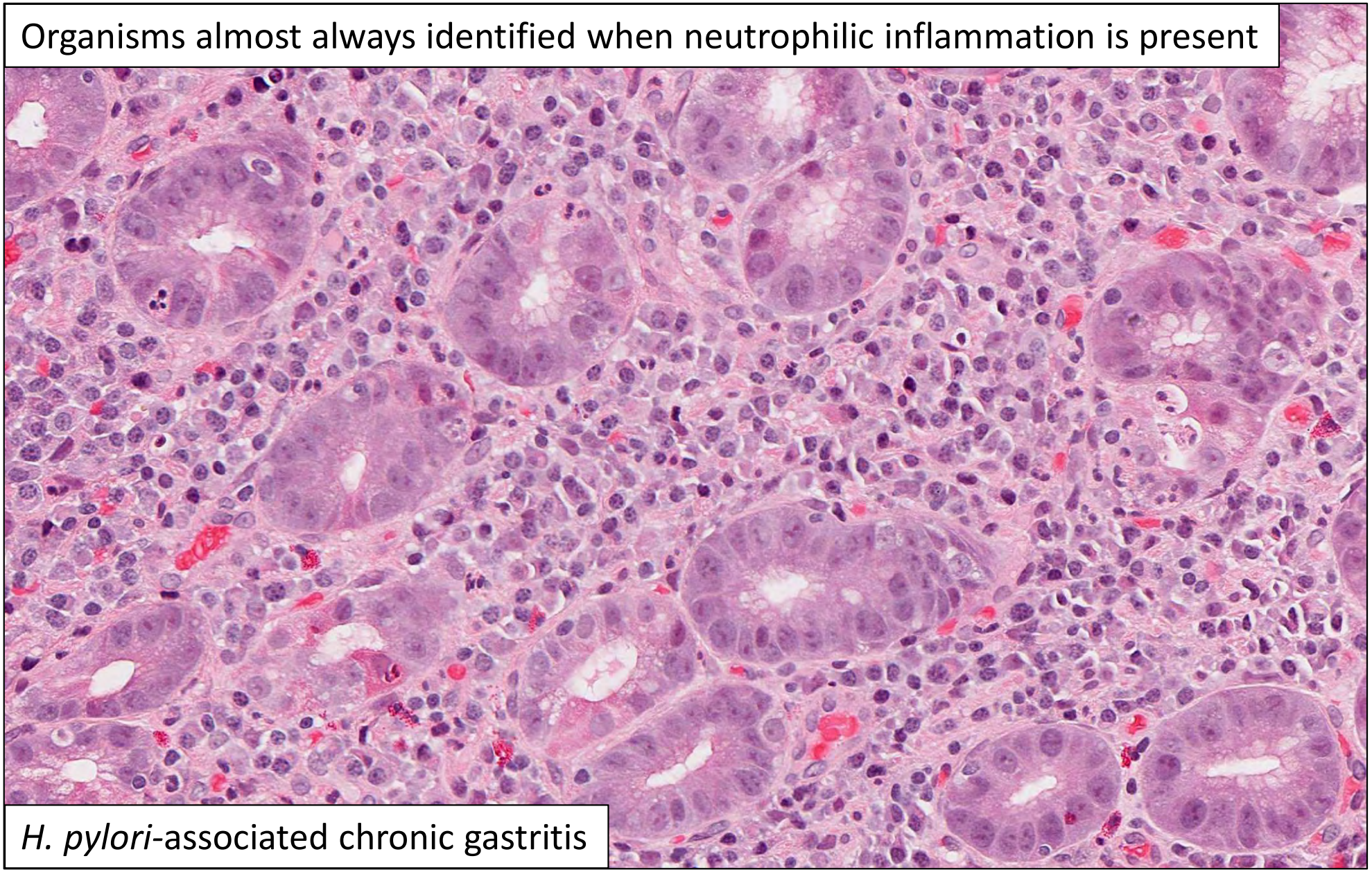
Plasma cell-rich inflammation of superficial mucosa or full thickness

H. pylori-associated chronic gastritis

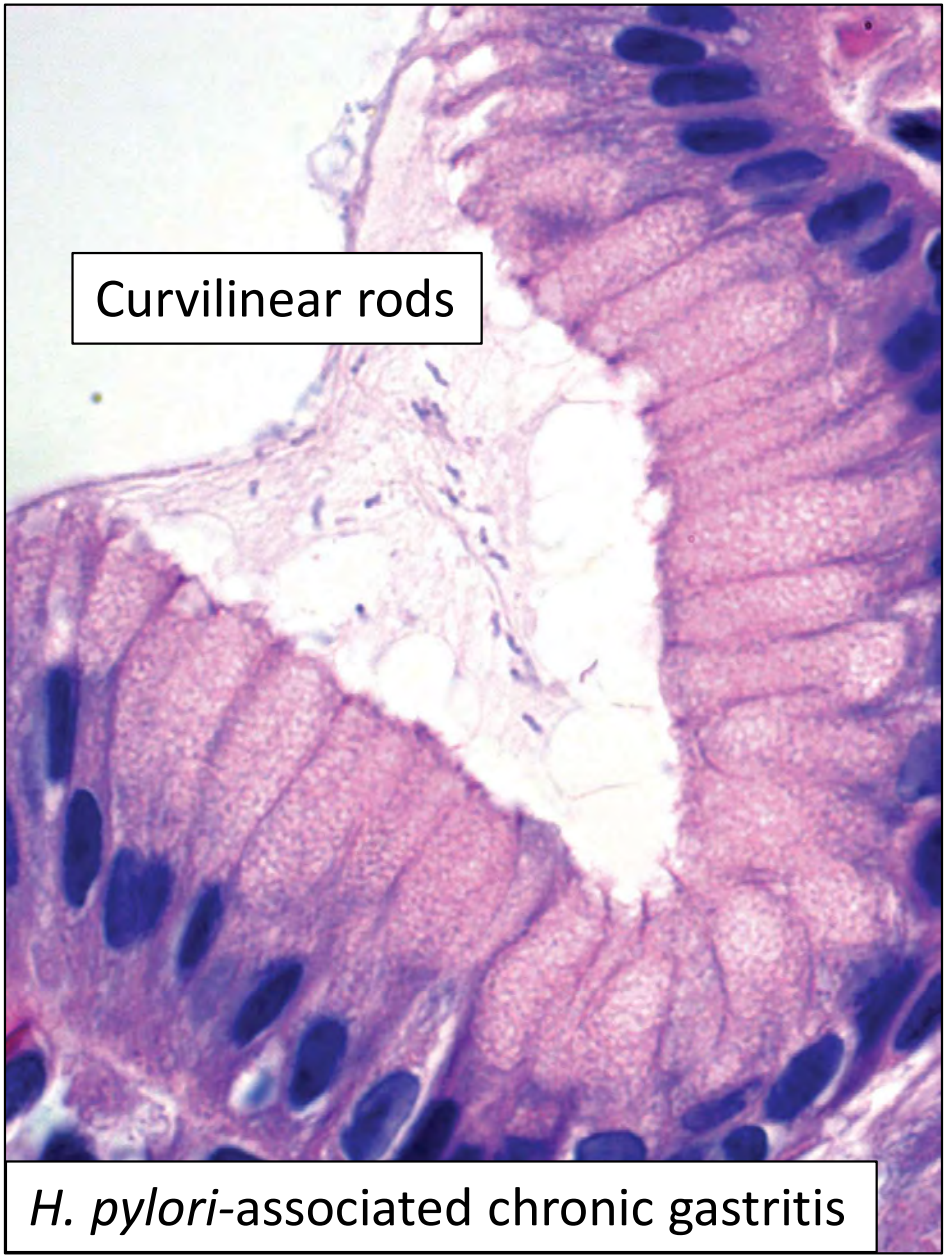


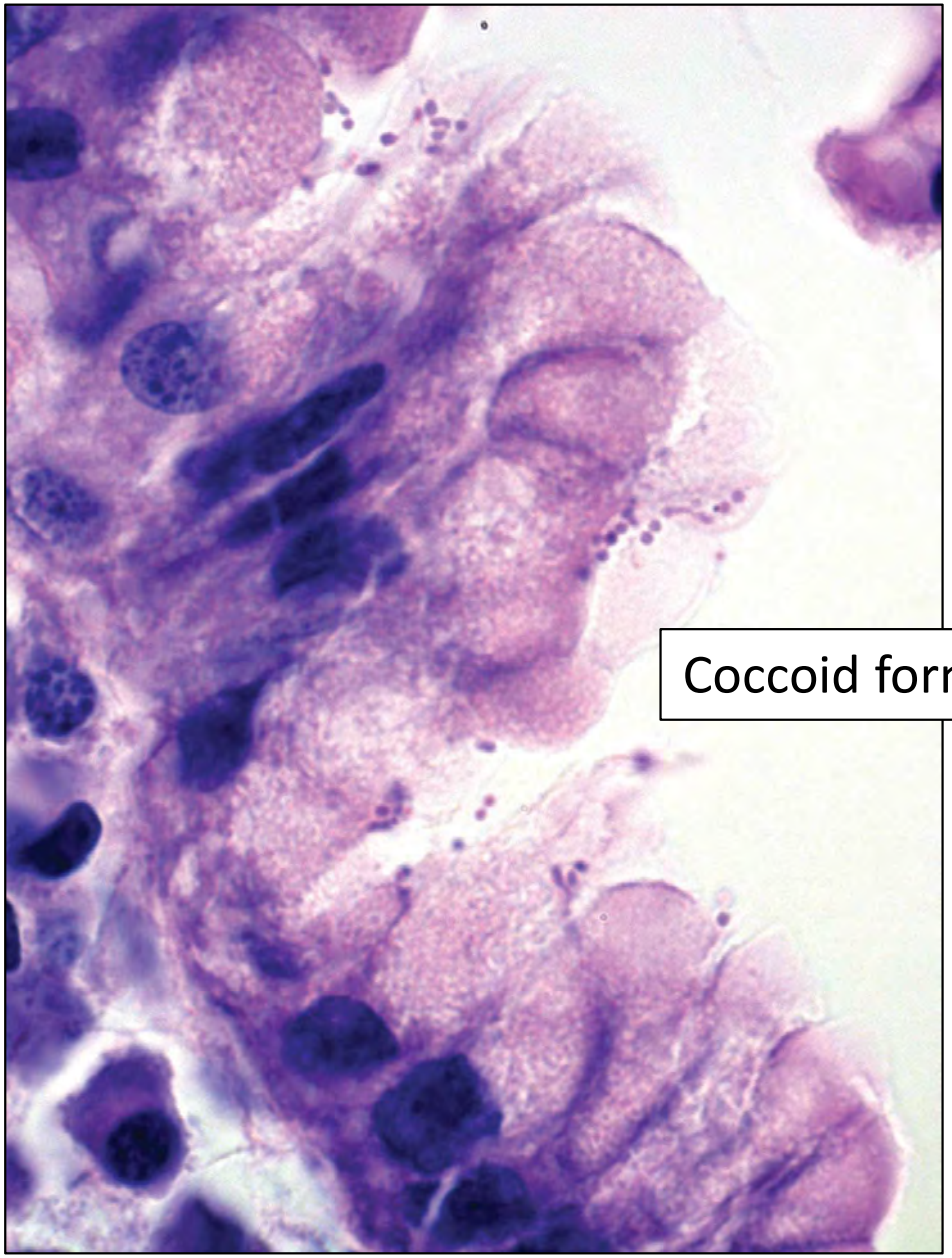
Lymphoid follicles can be a clue

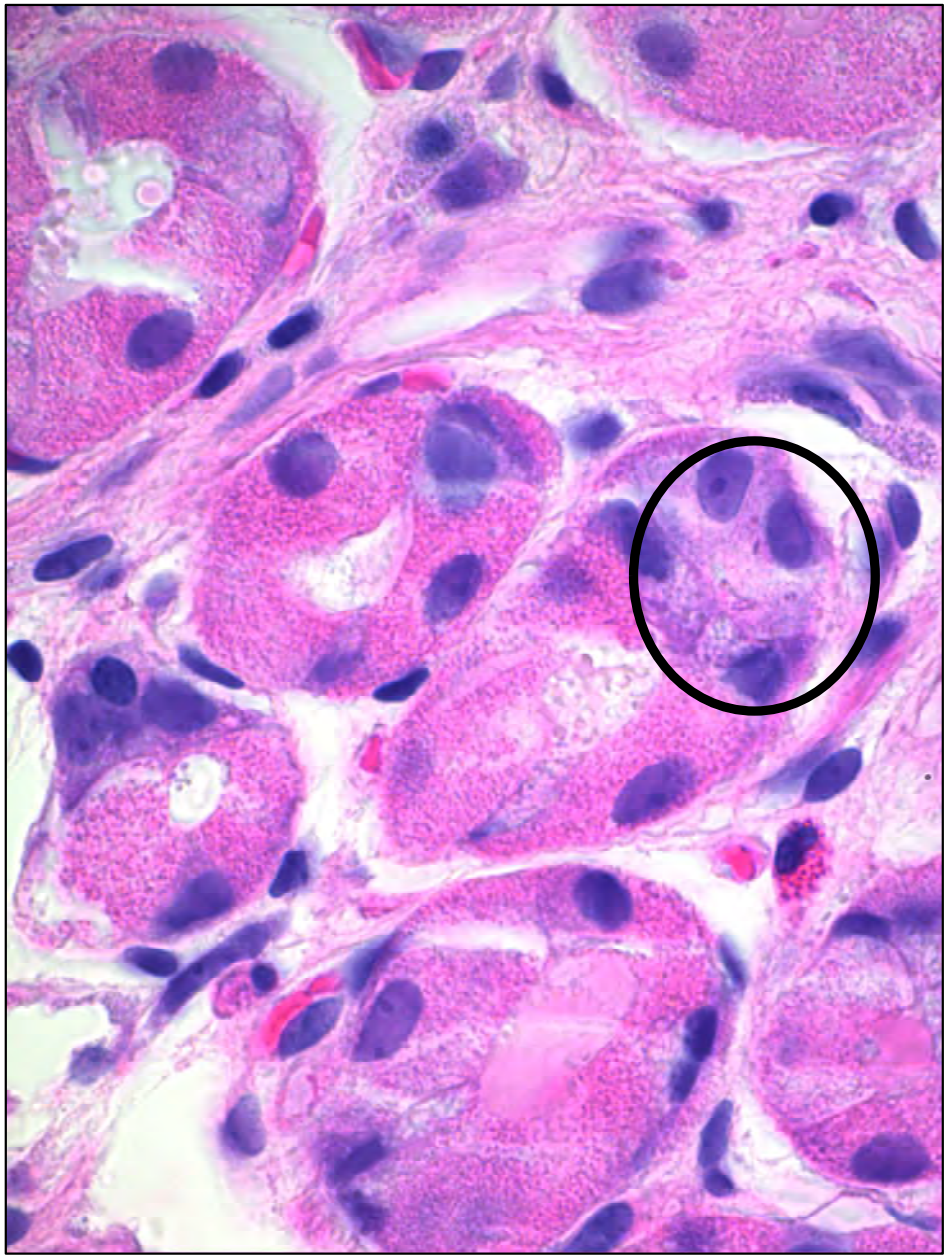
Organisms almost always identified when neutrophilic inflammation is present

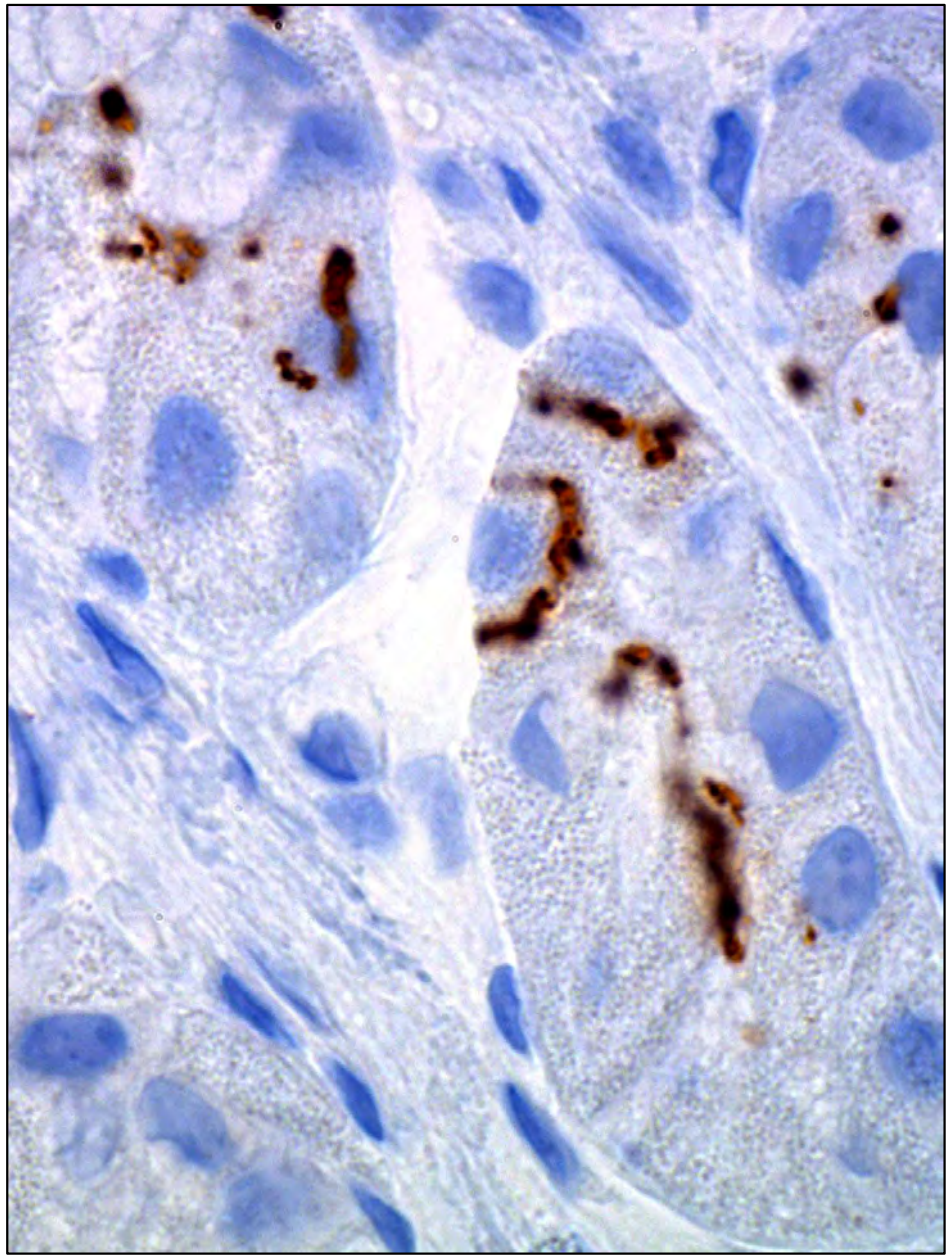


H. pylori-associated chronic gastritis


Curvilinear rods
H. pylori-associated chronic gastritis

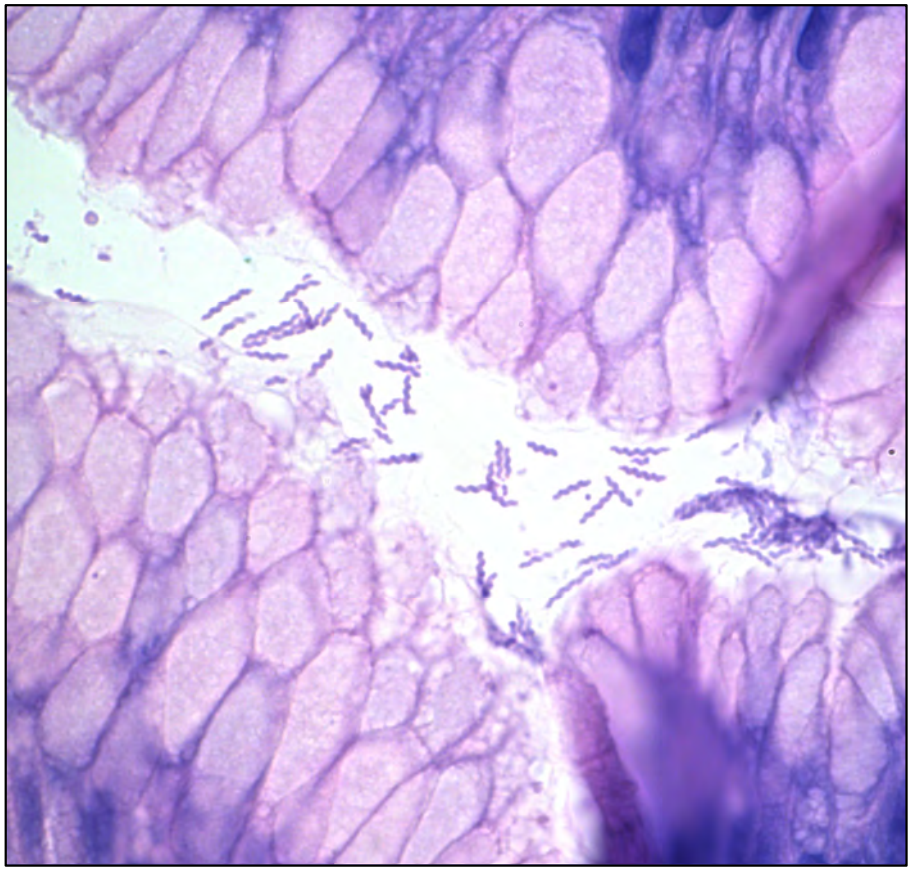

Coccoid forms





H. heilmannii-Related Chronic Gastritis

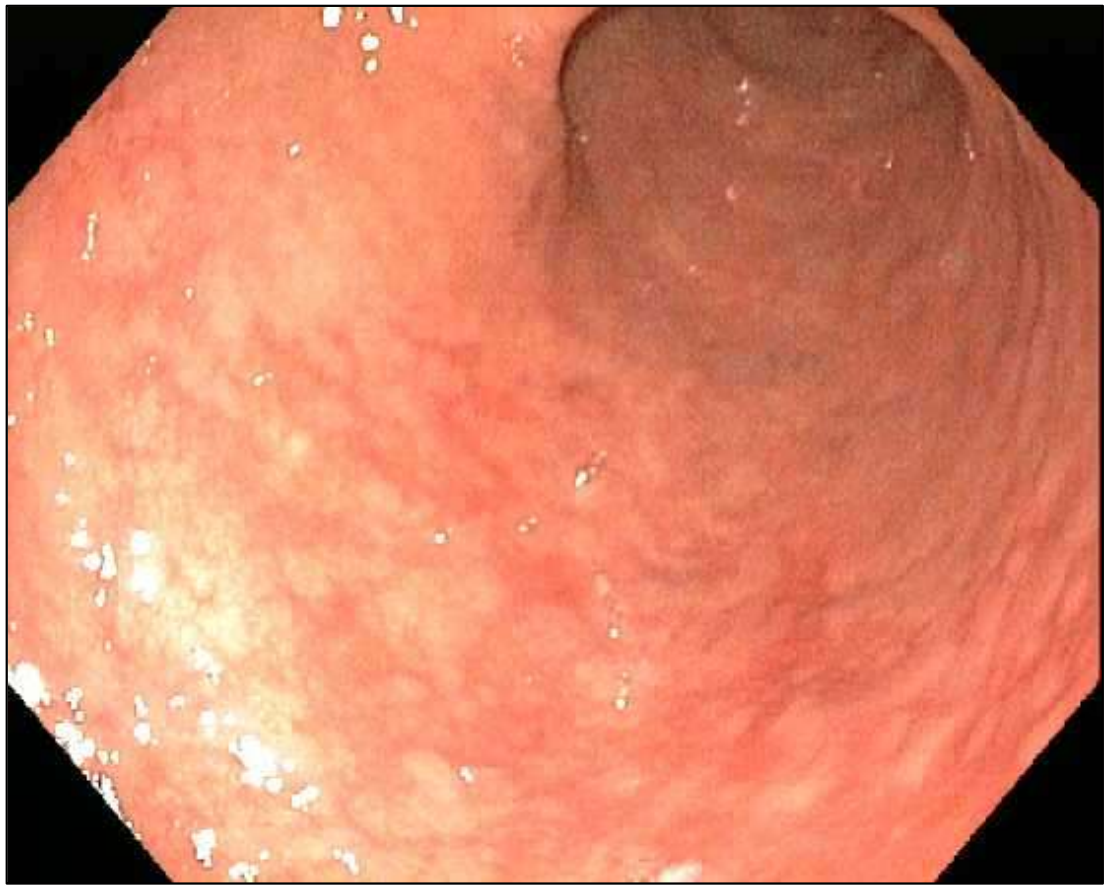
- Long, tightly coiled rods
- Usually mild gastritis
- Low risk of lymphoma and carcinoma
- Cross reacts with *H. pylori* antibody
- Similarly treated compared with *H. pylori*

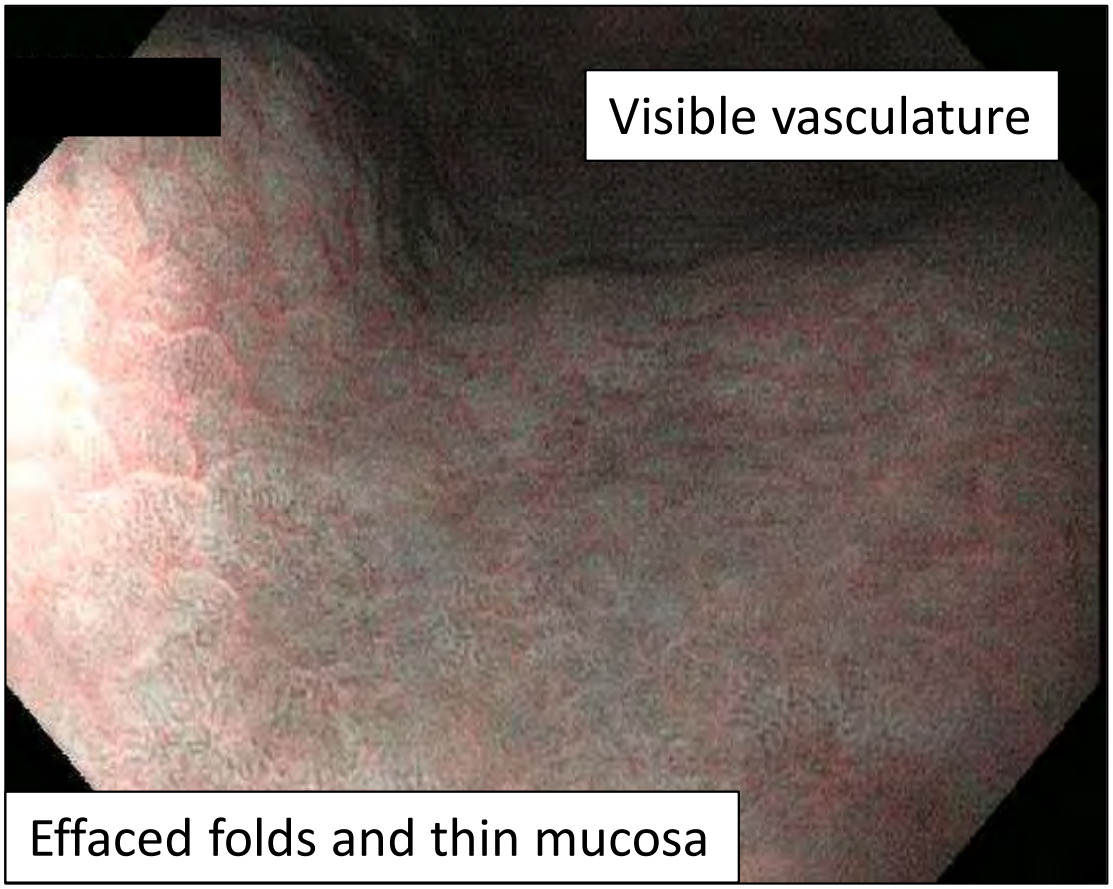


Autoimmune Gastritis
Corpus-Predominant Chronic Gastritis

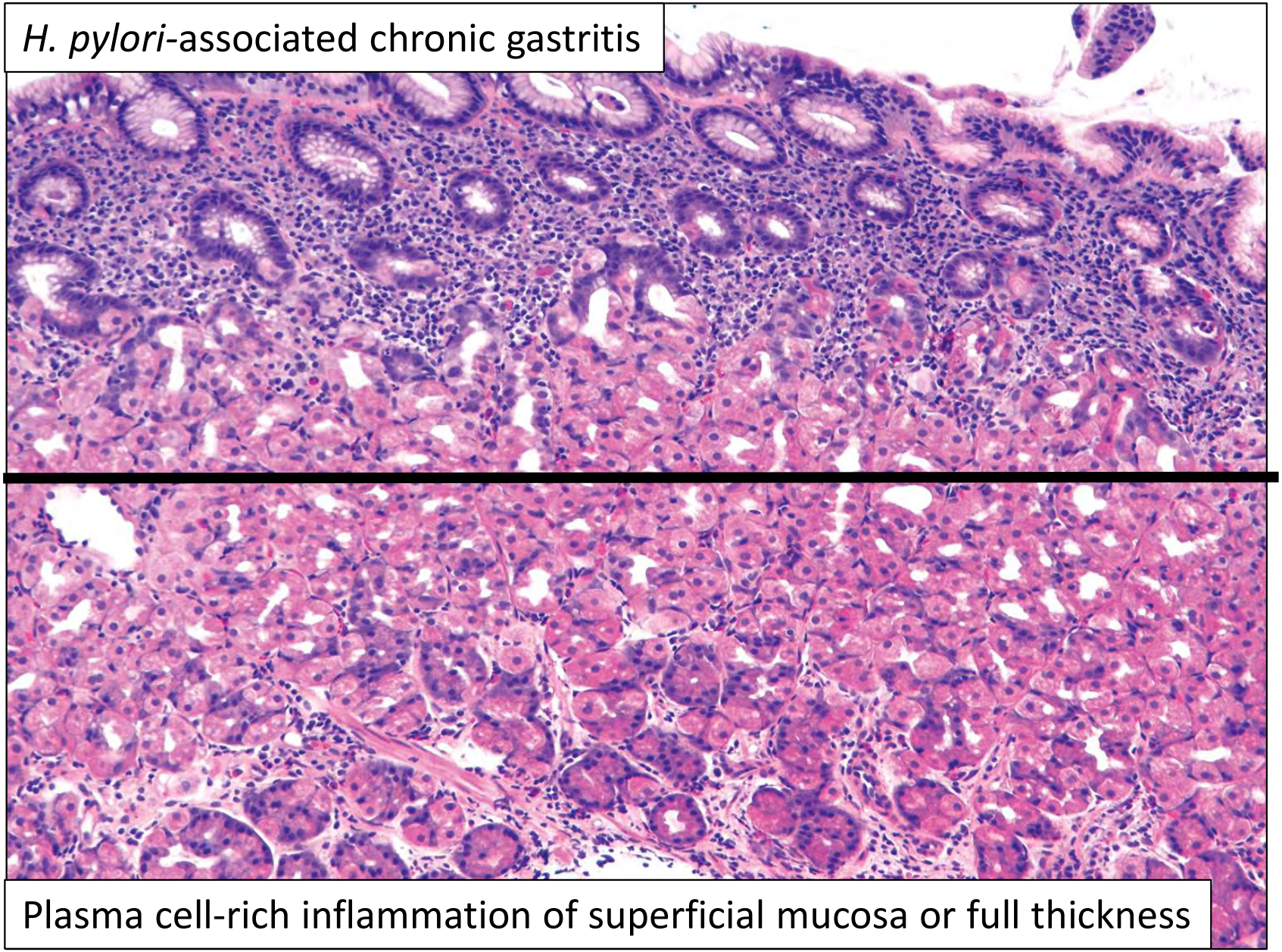
- Reportedly <5% of gastritis cases, but underrecognized
- Middle-aged and older adult women
- Associated with other immune-mediated conditions
- Probable link to *H. pylori* trigger
- Asymptomatic, iron deficiency anemia, or pernicious anemia
- Adenocarcinoma risk 3-5x general population

Autoimmune Gastritis



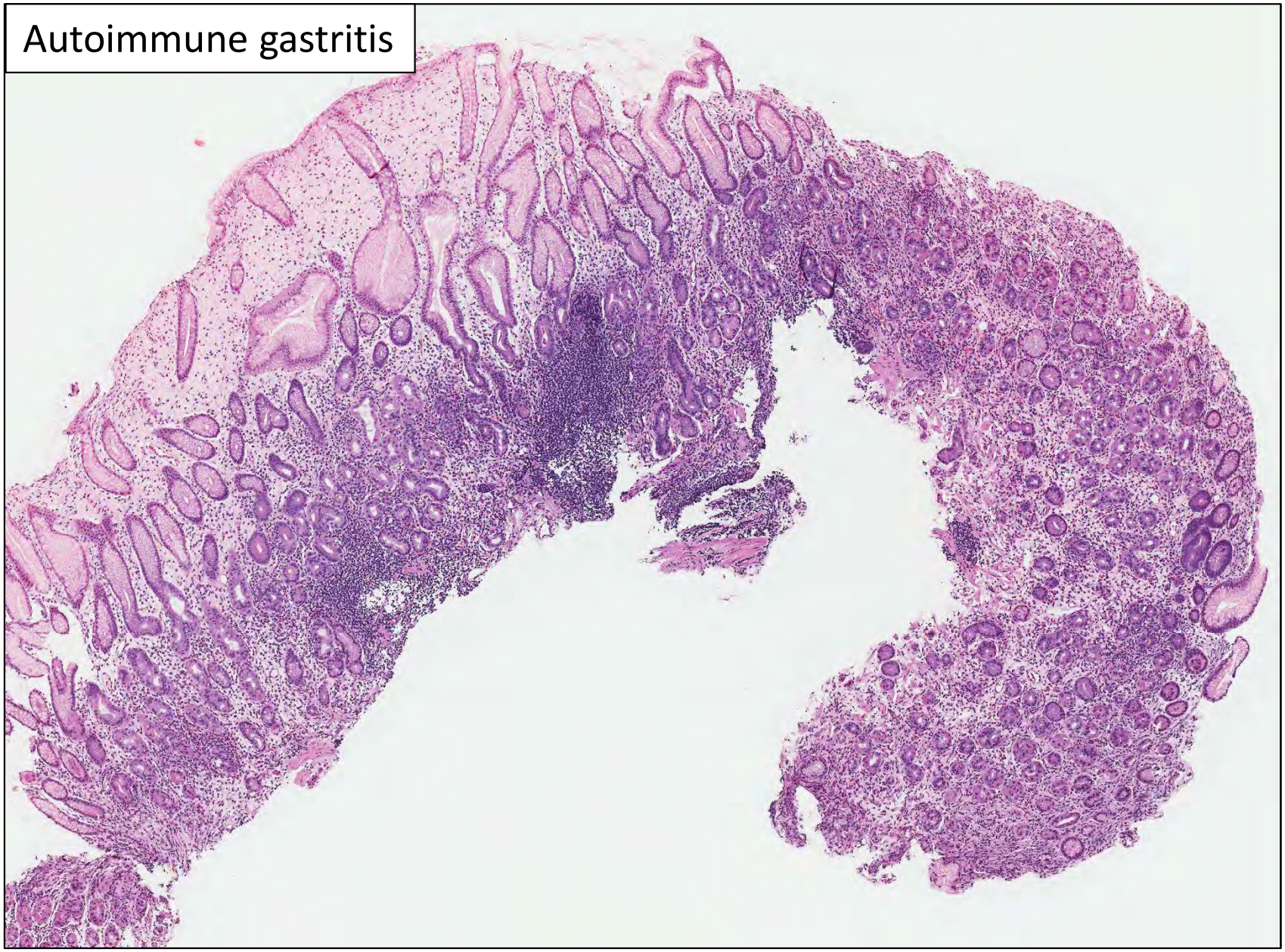


H. pylori-associated chronic gastritis

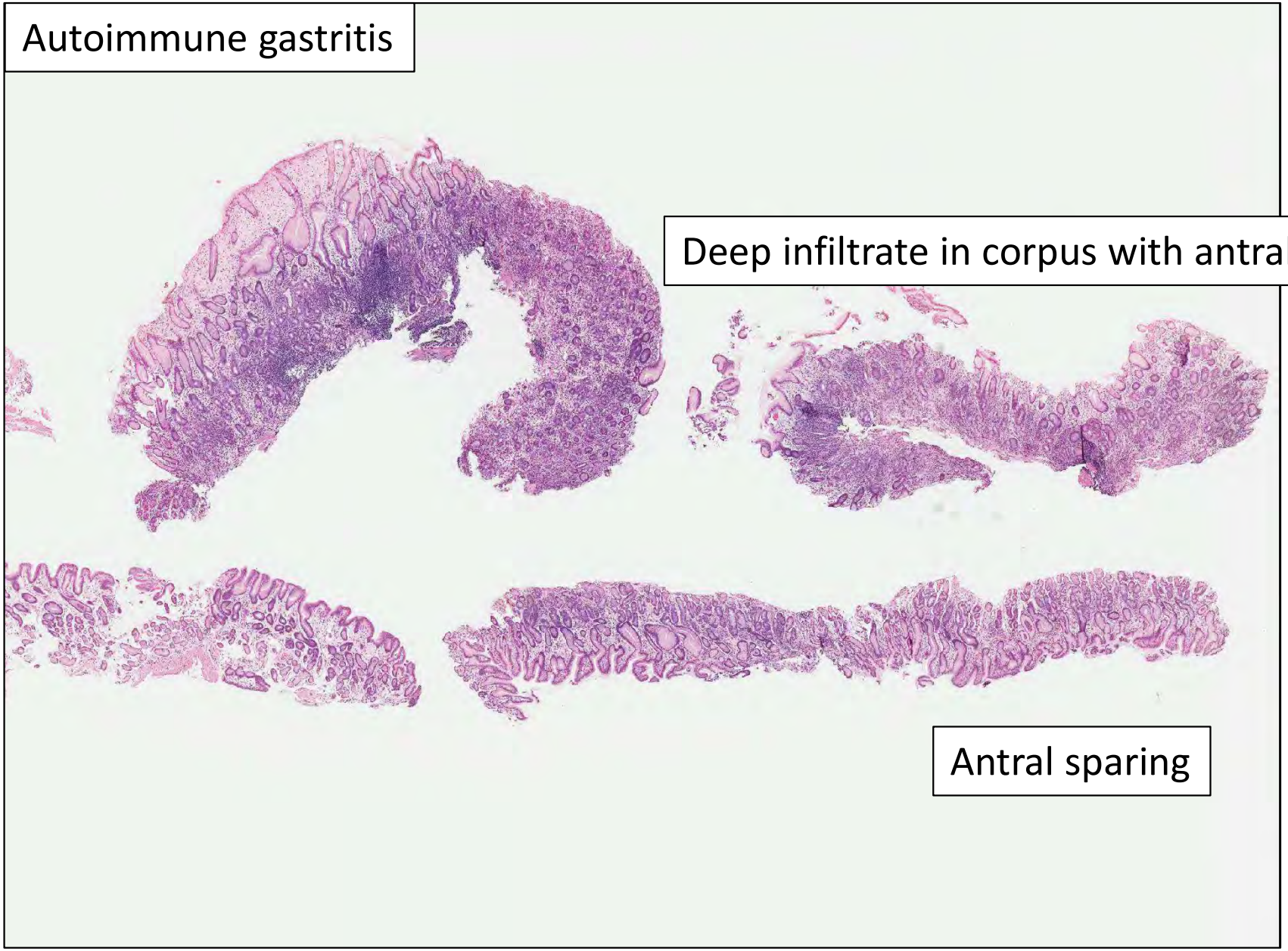


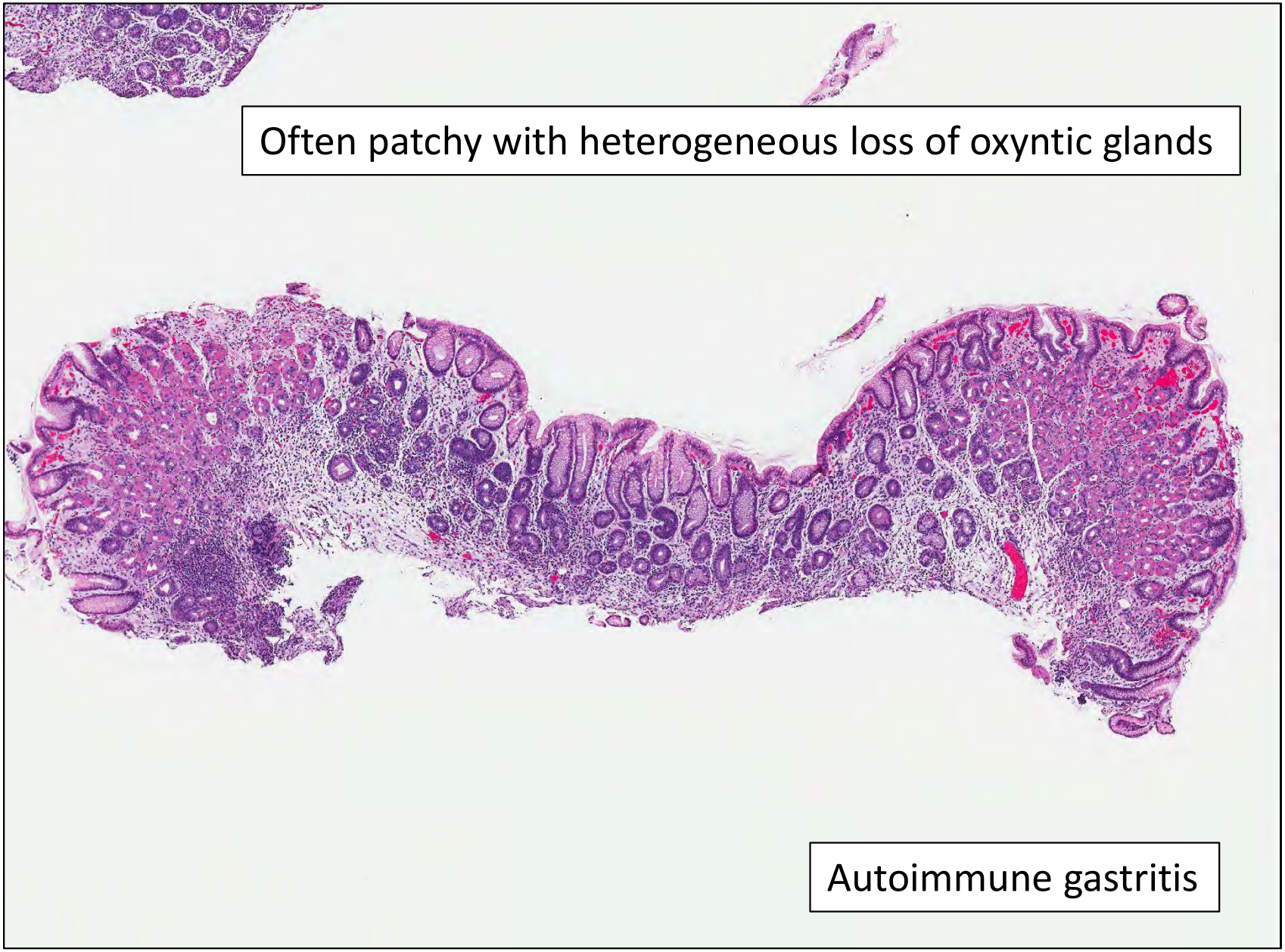
Plasma cell-rich inflammation of superficial mucosa or full thickness

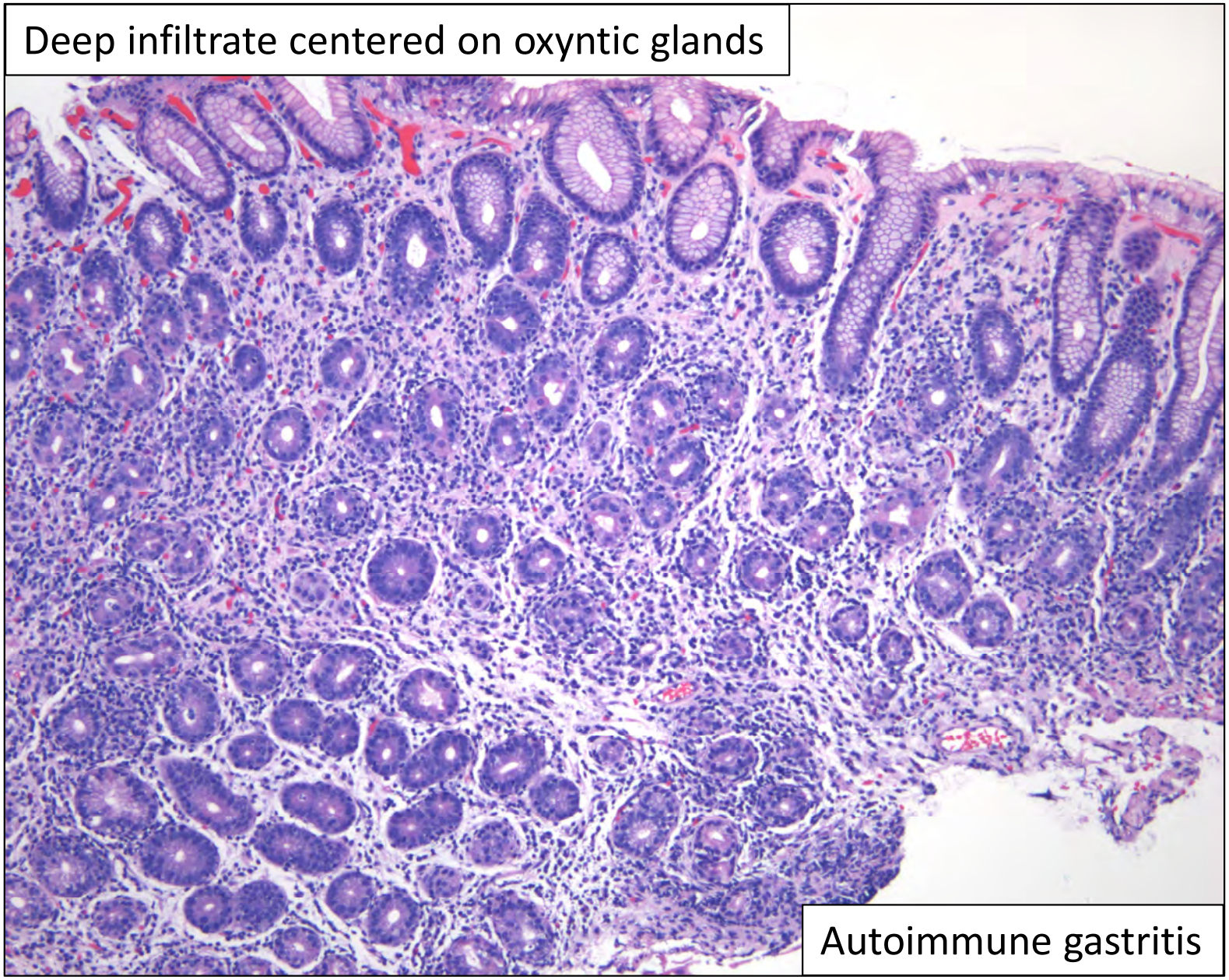
Autoimmune gastritis

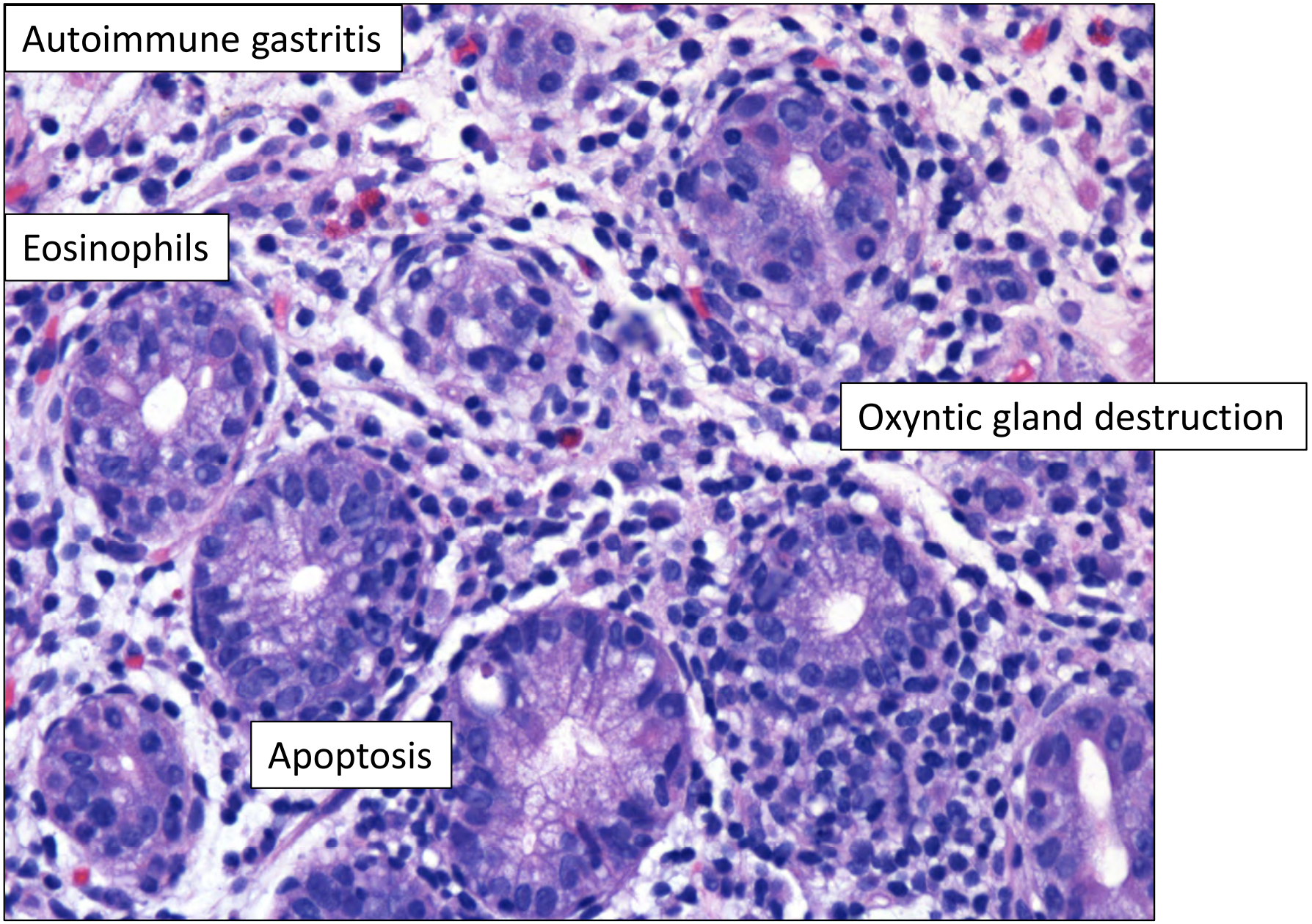


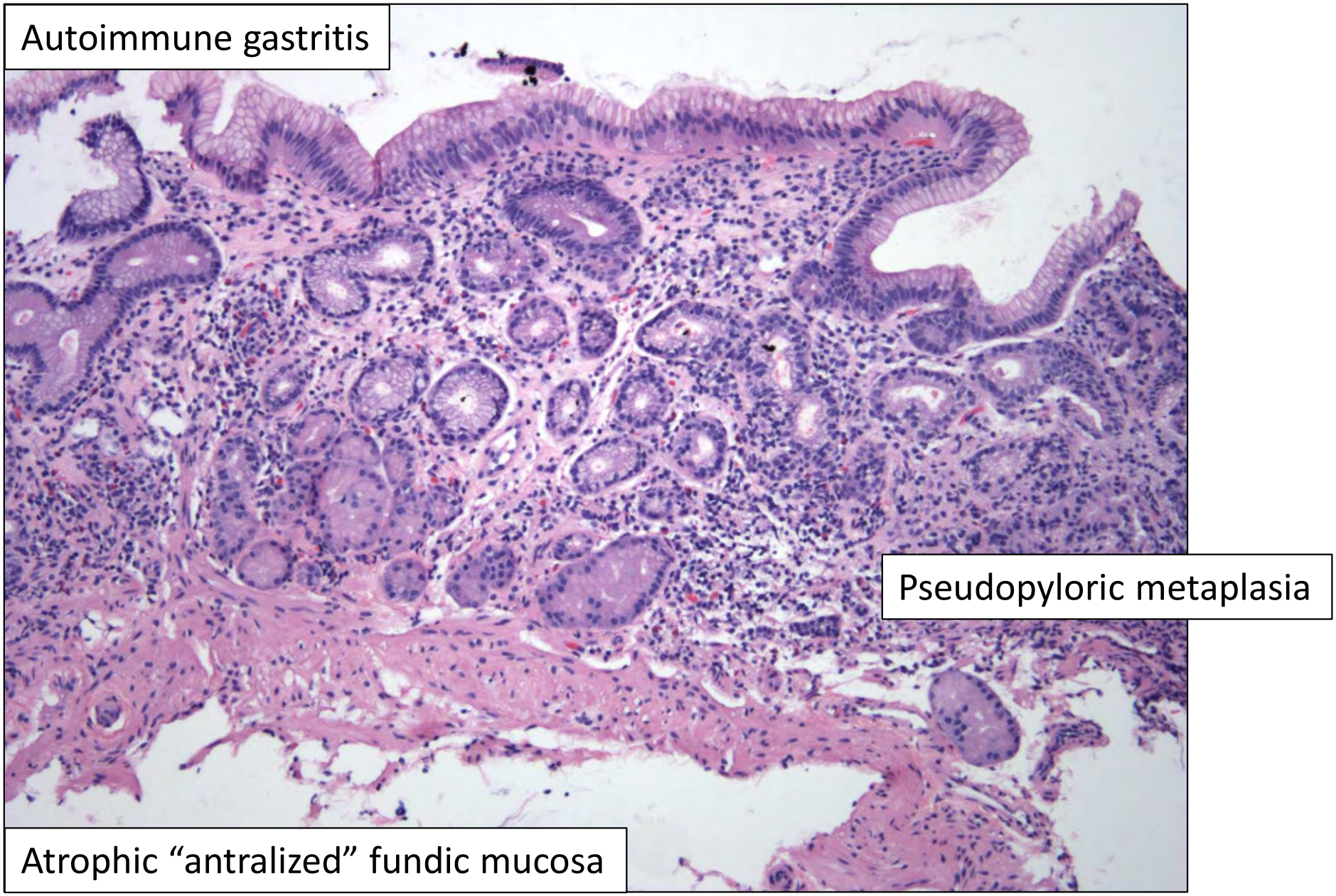
Autoimmune gastritis



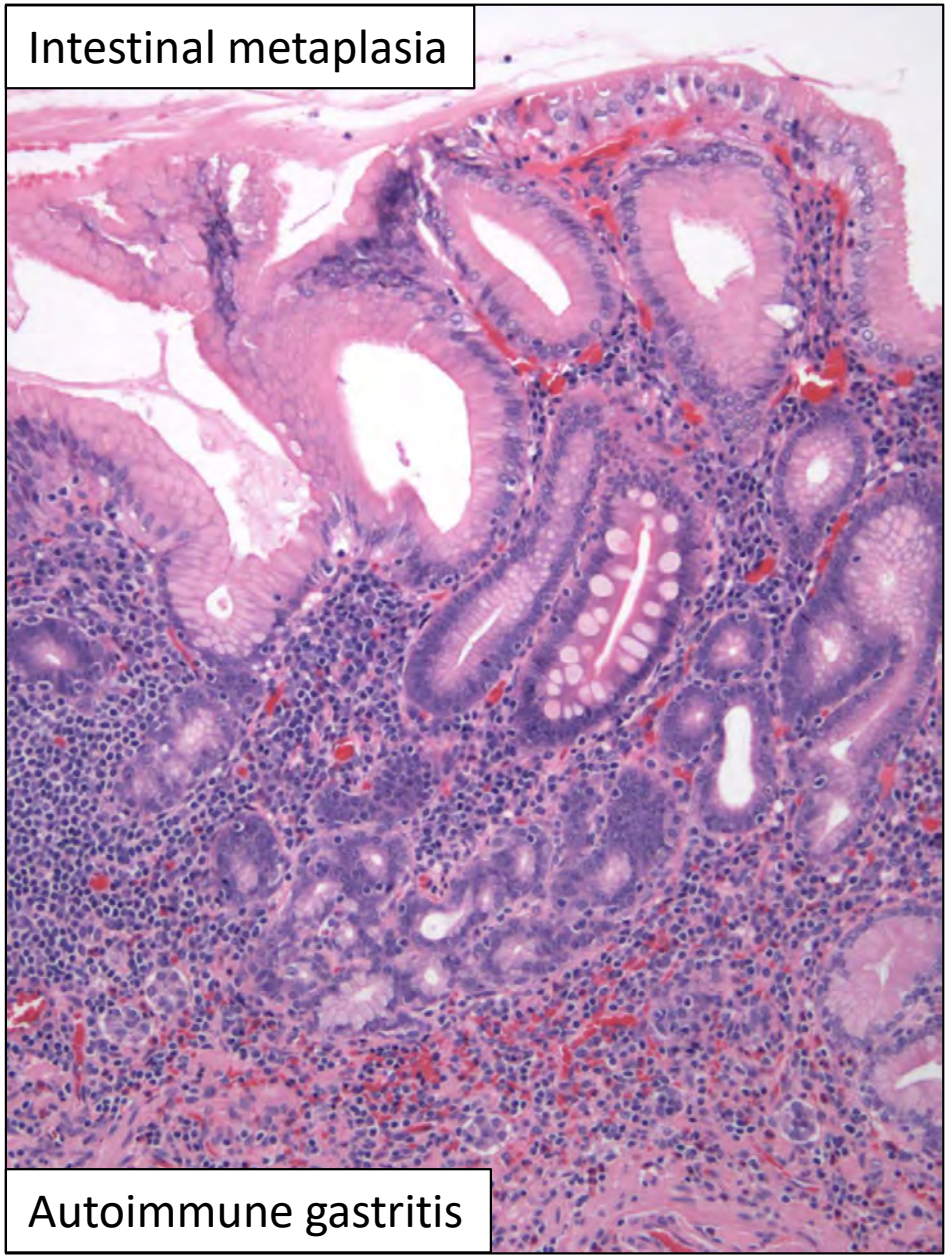

Often patchy with heterogeneous loss of oxyntic glands
Autoimmune gastritis


Deep infiltrate centered on oxyntic glands
Autoimmune gastritis


Autoimmune gastritis
Eosinophils
Oxyntic gland destruction
Apoptosis

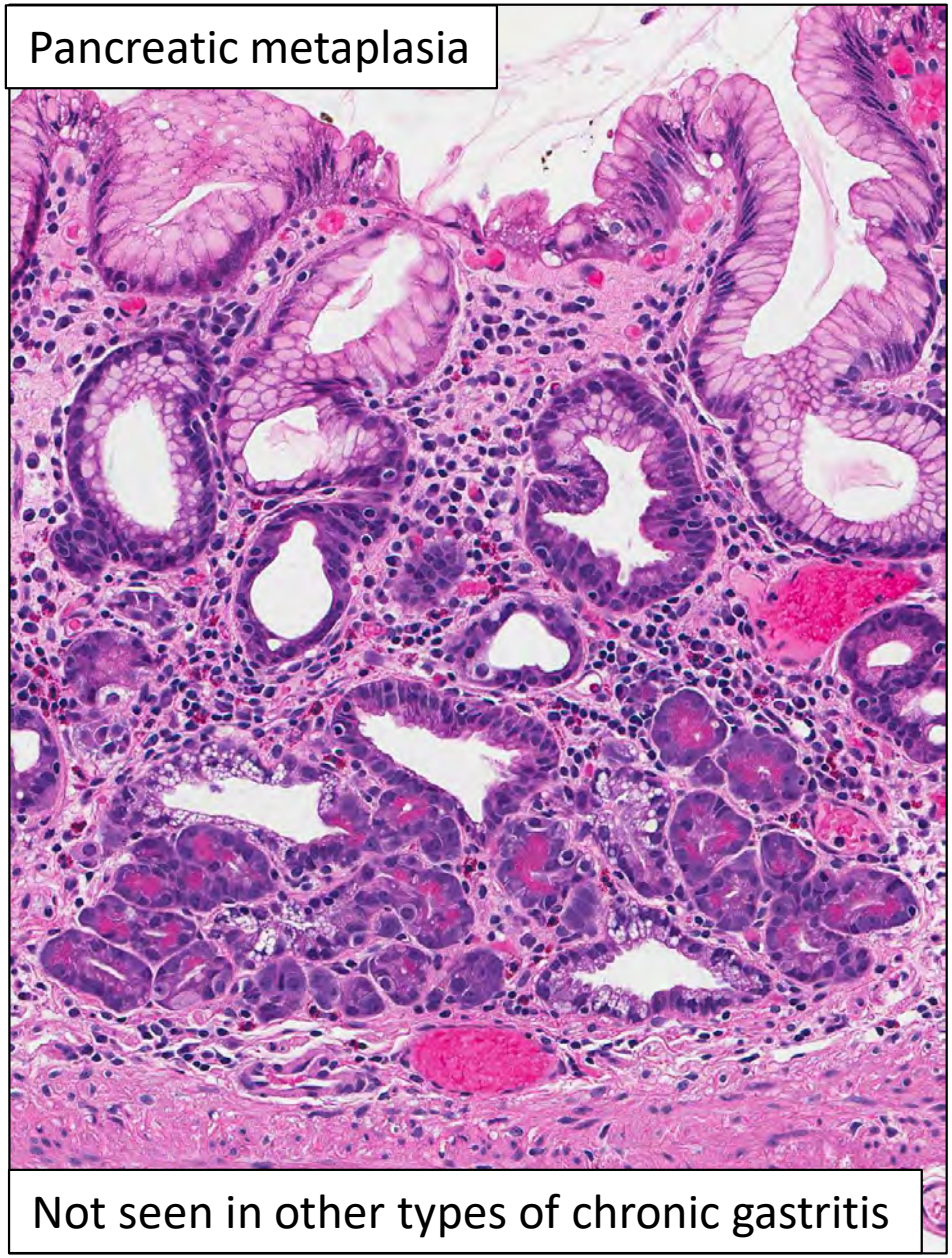

Autoimmune gastritis
Pseudopyloric metaplasia
Atrophic “antralized” fundic mucosa

Intestinal metaplasia

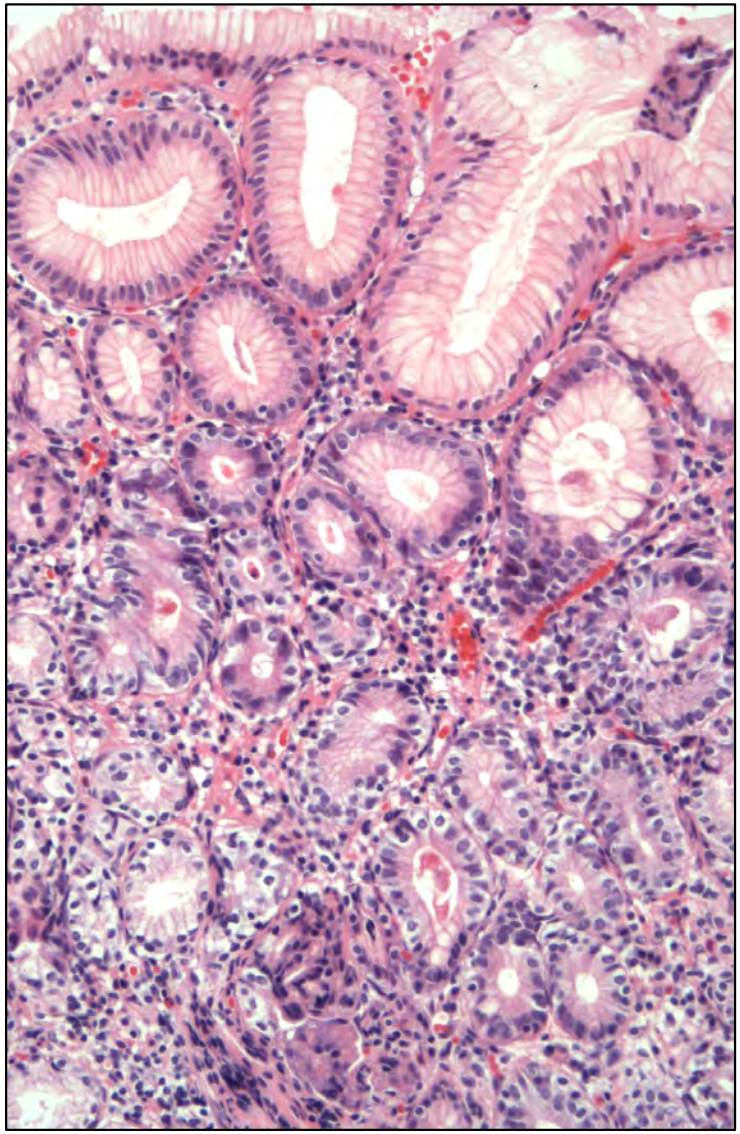


Autoimmune gastritis

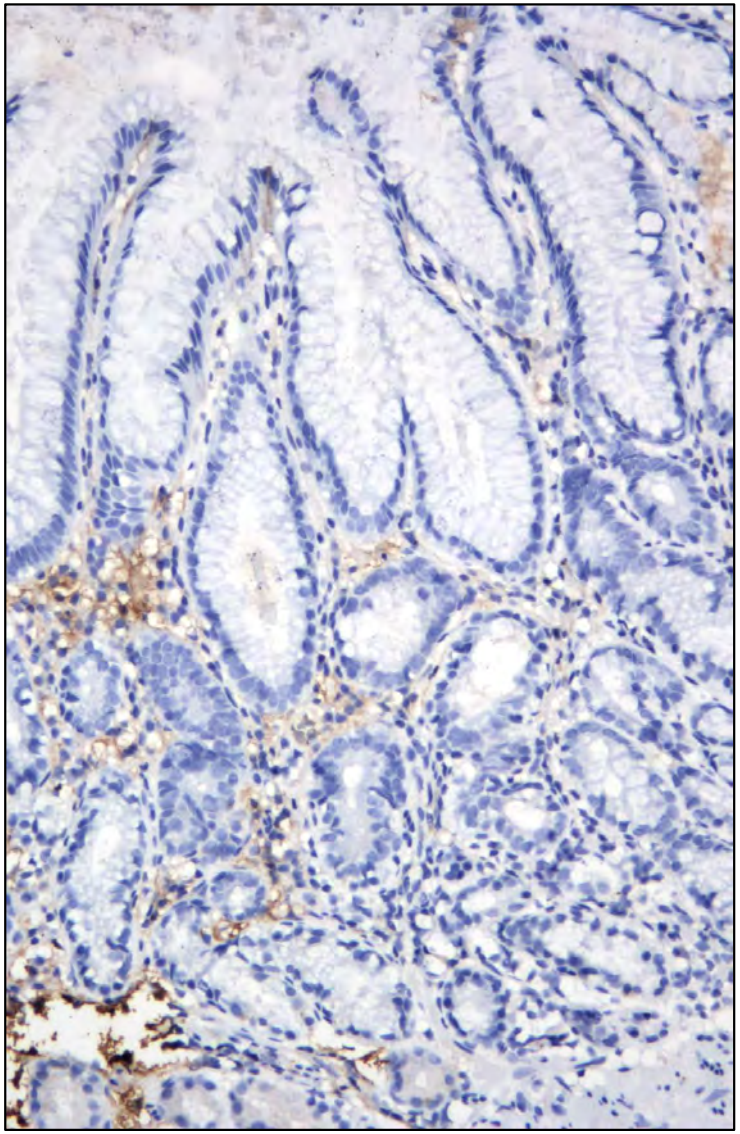
Pancreatic metaplasia



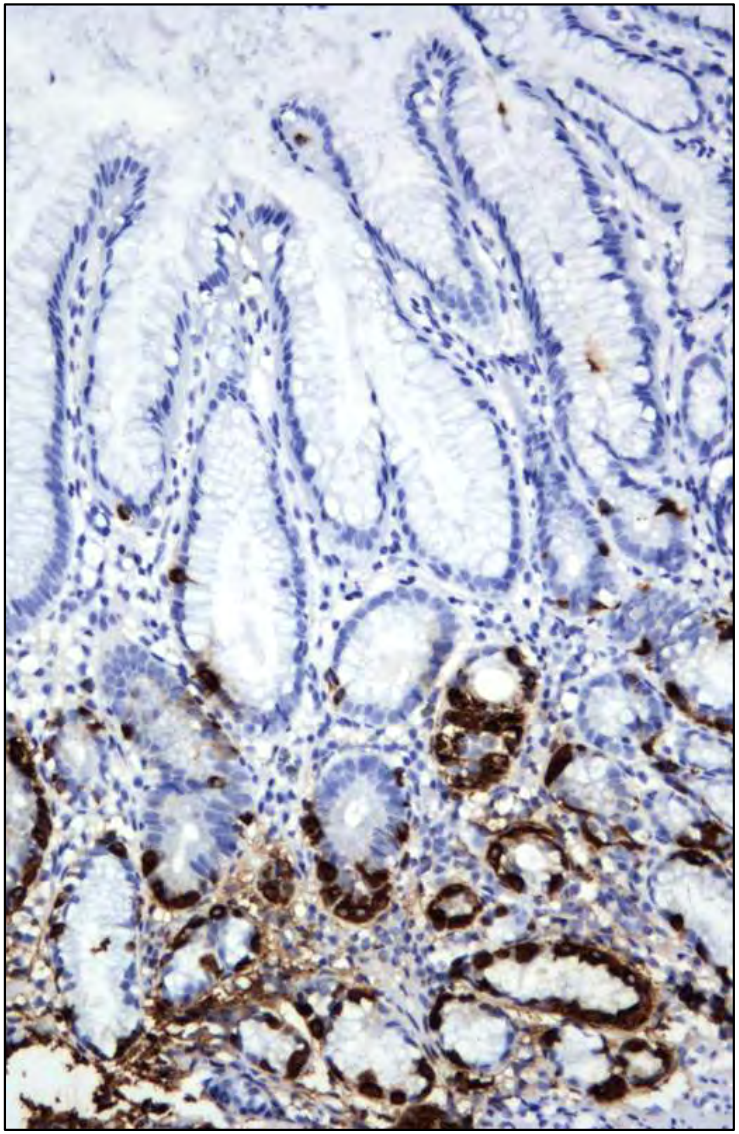
Not seen in other types of chronic gastritis



ECL cell hyperplasia

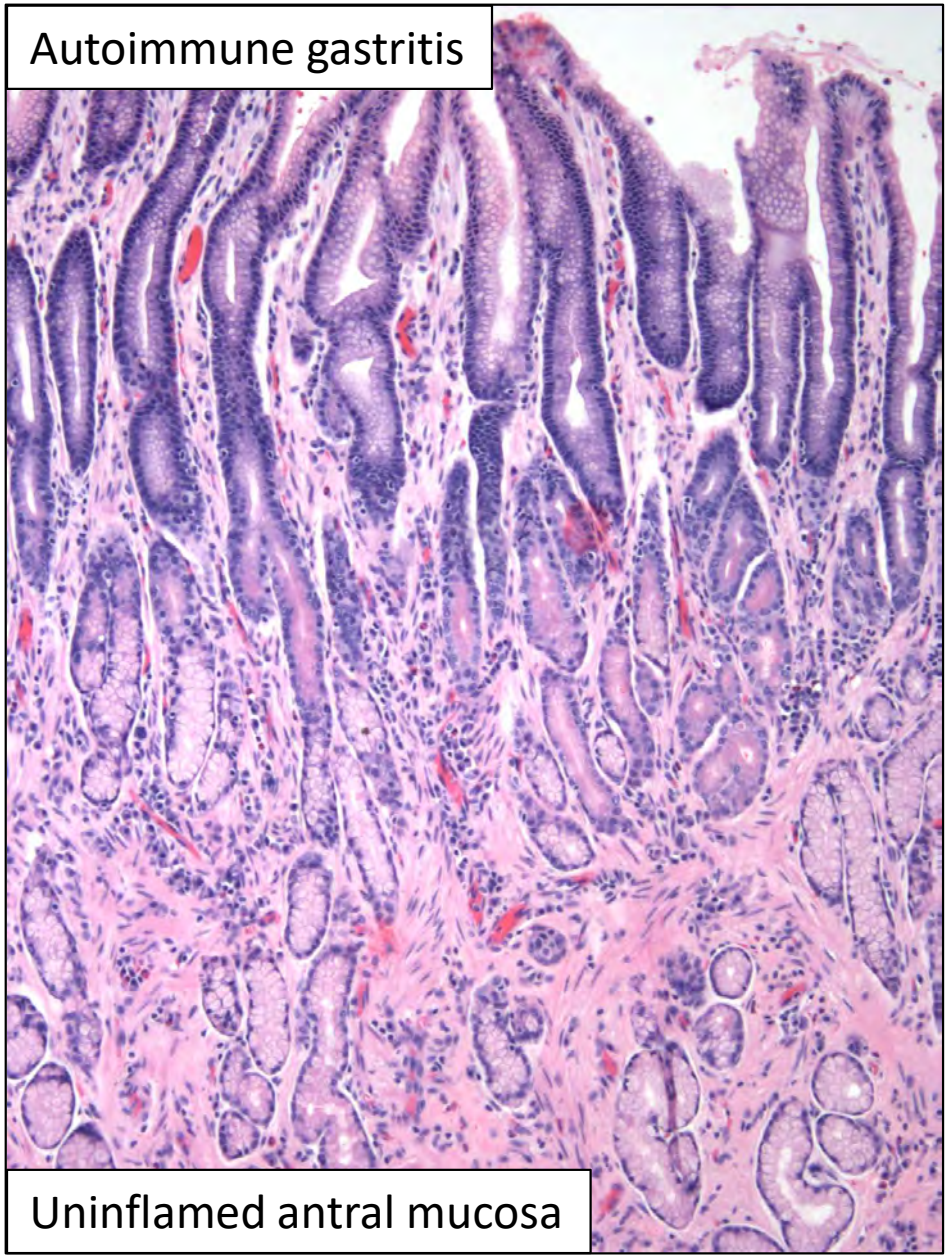


Gastrin immunostain

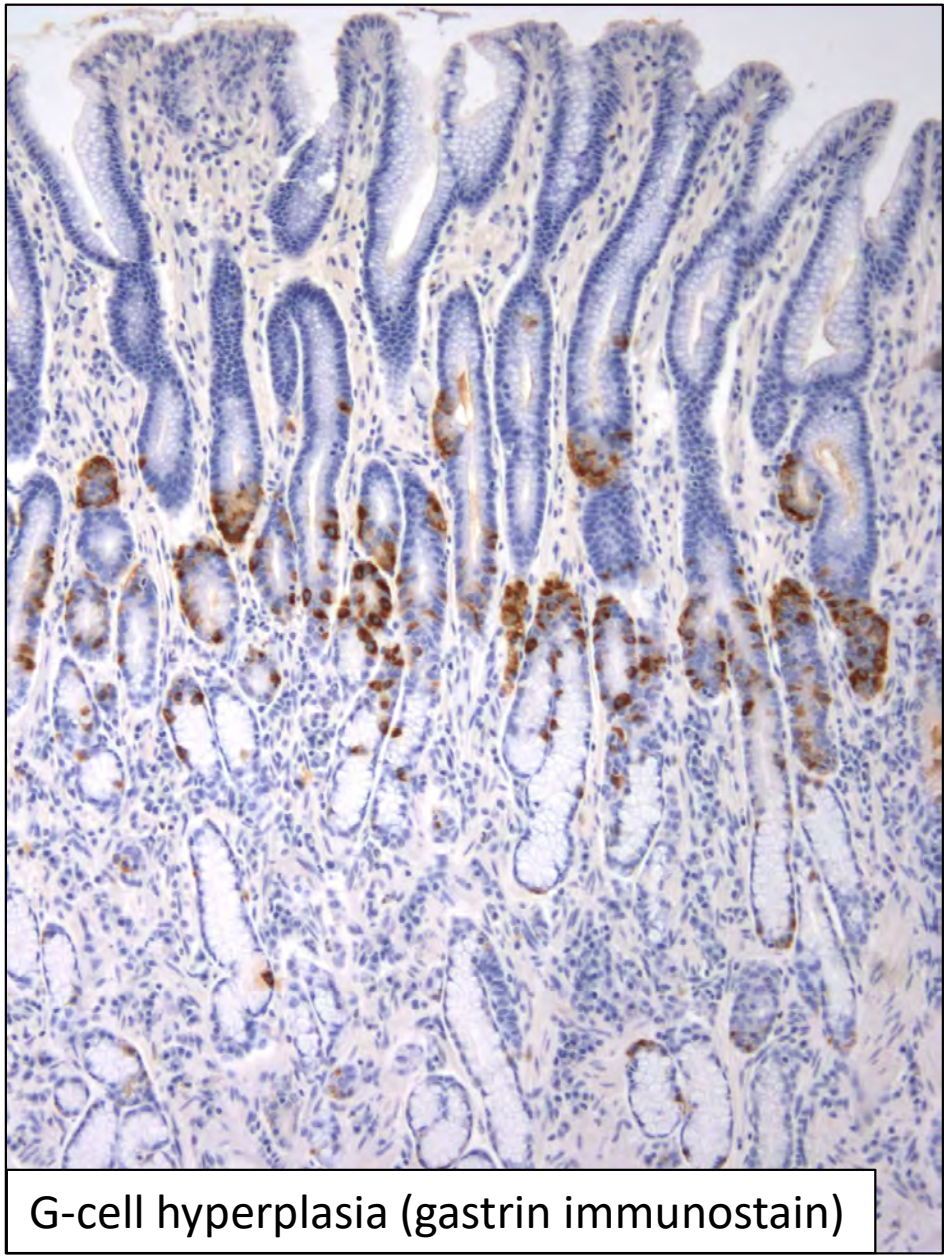


Chromogranin immunostain

Autoimmune gastritis



Uninflamed antral mucosa

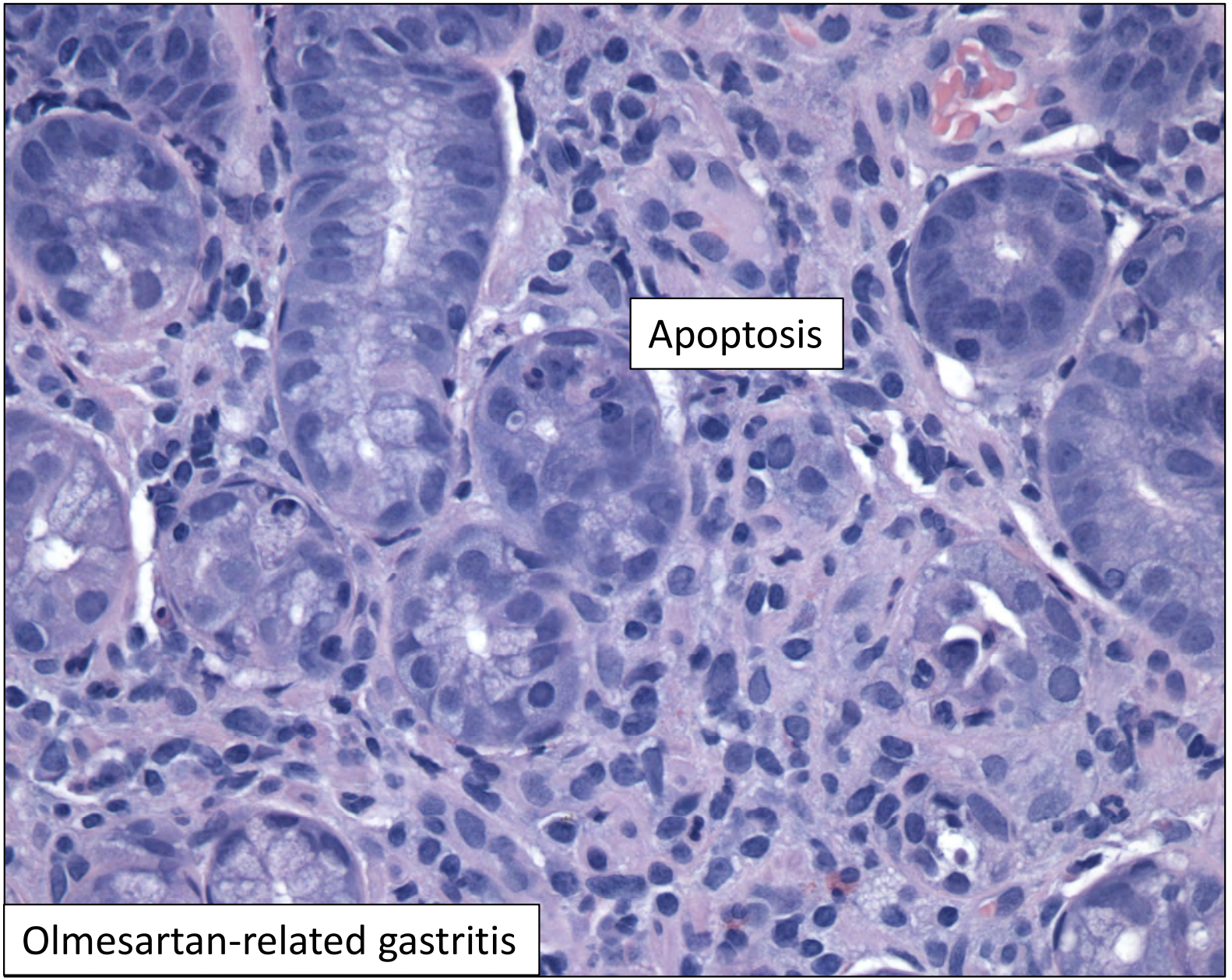


G-cell hyperplasia (gastrin immunostain)

What about *H. pylori*-negative Gastritis that Isn't Autoimmune Gastritis?

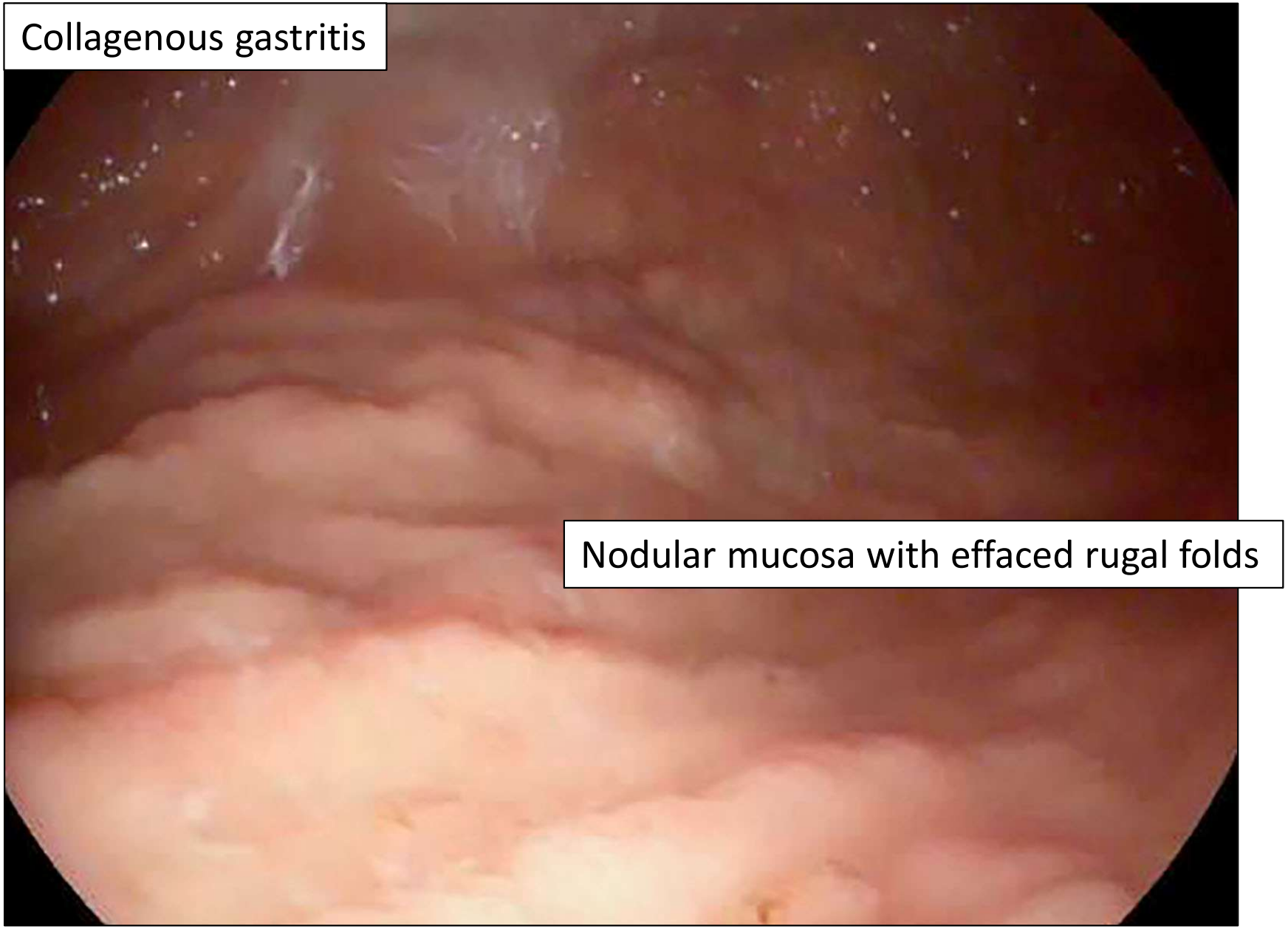
- Some patients with *H. pylori* don't have organisms (incompletely treated)
- Medications
  - Olmesartan
- Other immune-mediated conditions
  - Collagenous gastritis
  - Lymphocytic gastritis
  - Crohn disease
- Non-*H. pylori* infections

Chronic active gastritis without detectable organisms probably isn't *H. pylori*-related

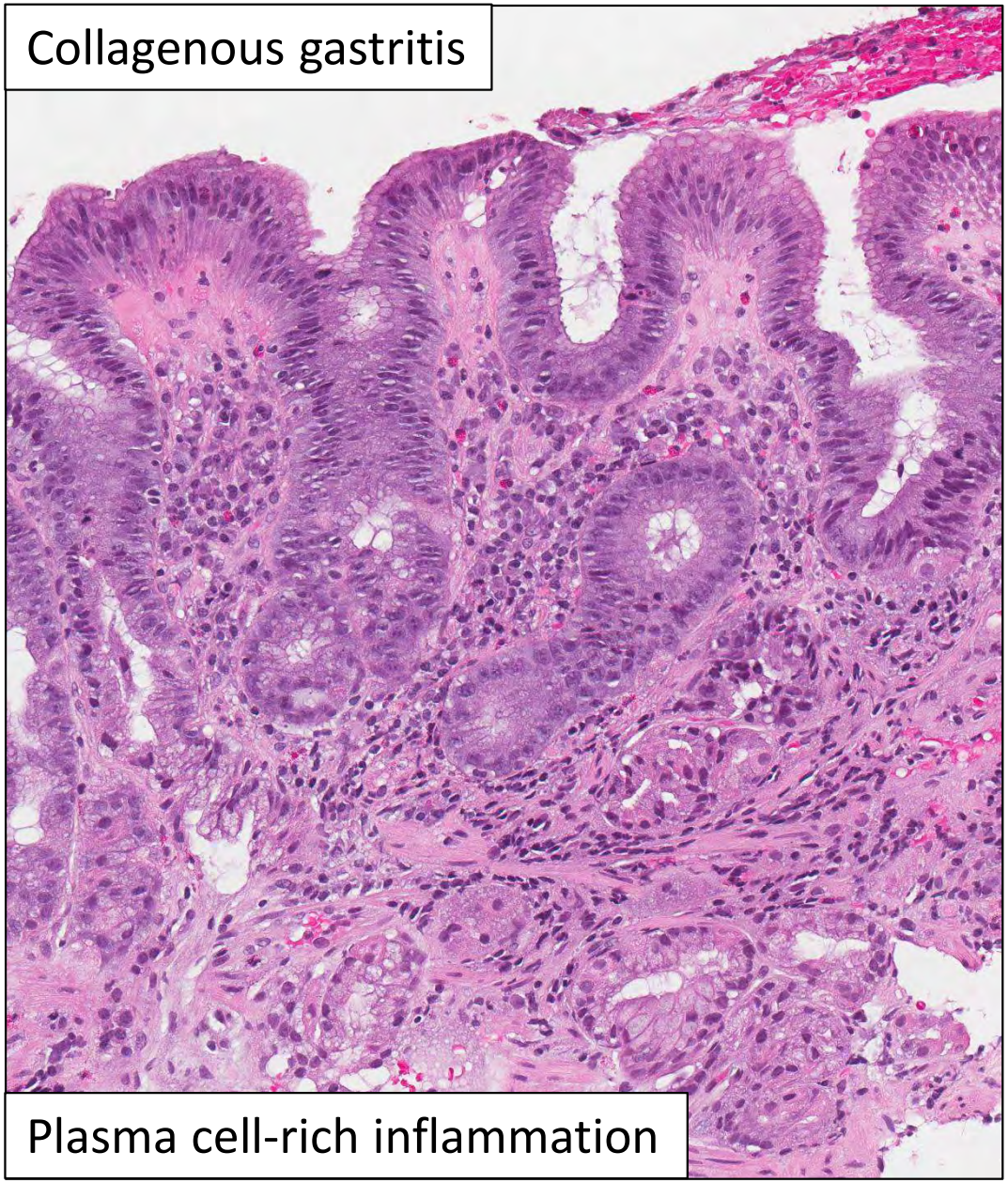

Apoptosis
Olmesartan-related gastritis

Collagenous Gastritis

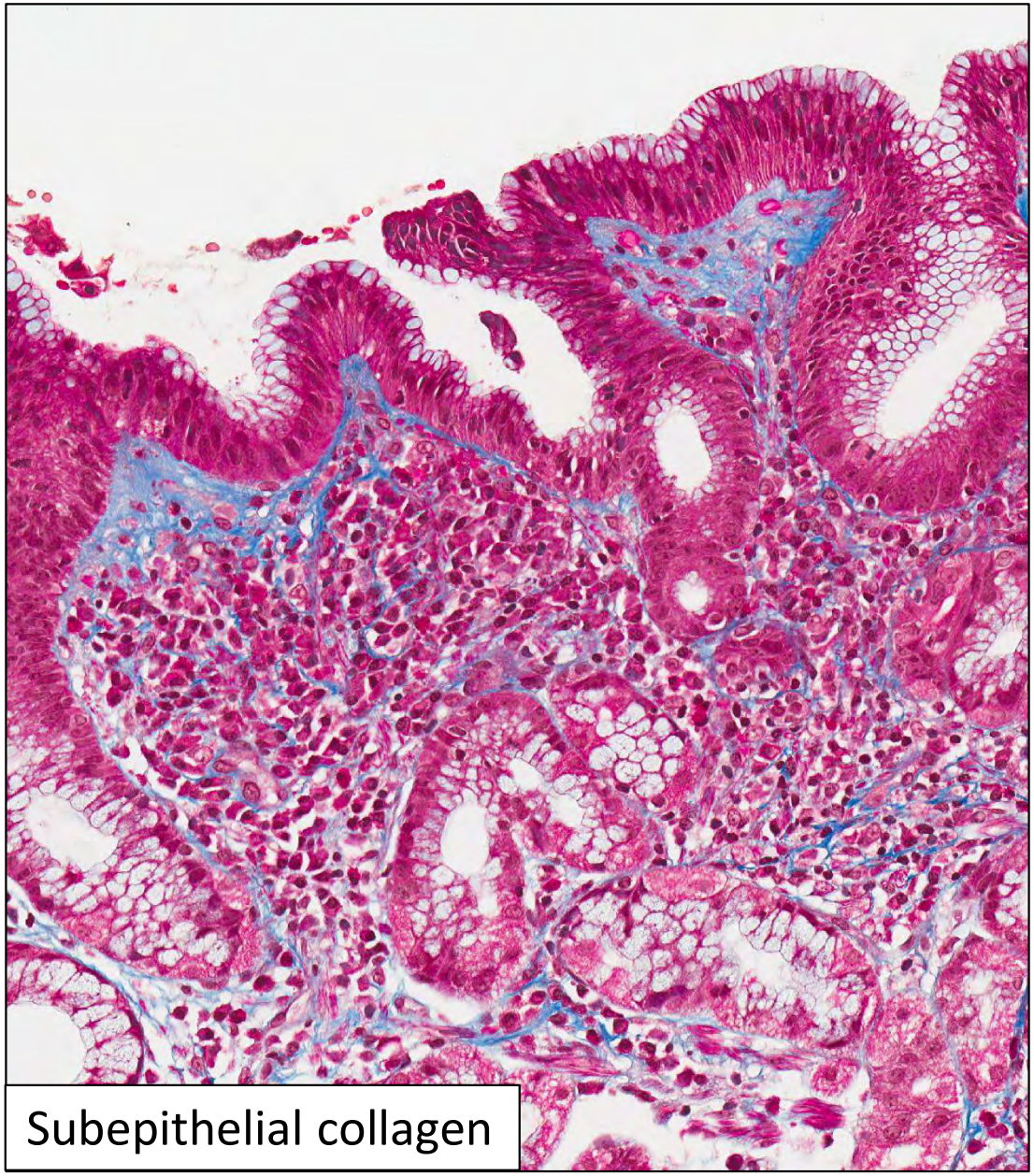
- Etiologies
  - Associated immune-mediated diseases, medications (Olmesartan), isolated finding
- Early data suggested two forms
  - Children with anemia, nodular mucosa, and gastric disease only
  - Adults with watery diarrhea and diffuse collagen deposits throughout gastrointestinal tract
  - Enough overlap between phenotypes that subclassifying is not useful


Collagenous gastritis
Nodular mucosa with effaced rugal folds

Collagenous gastritis



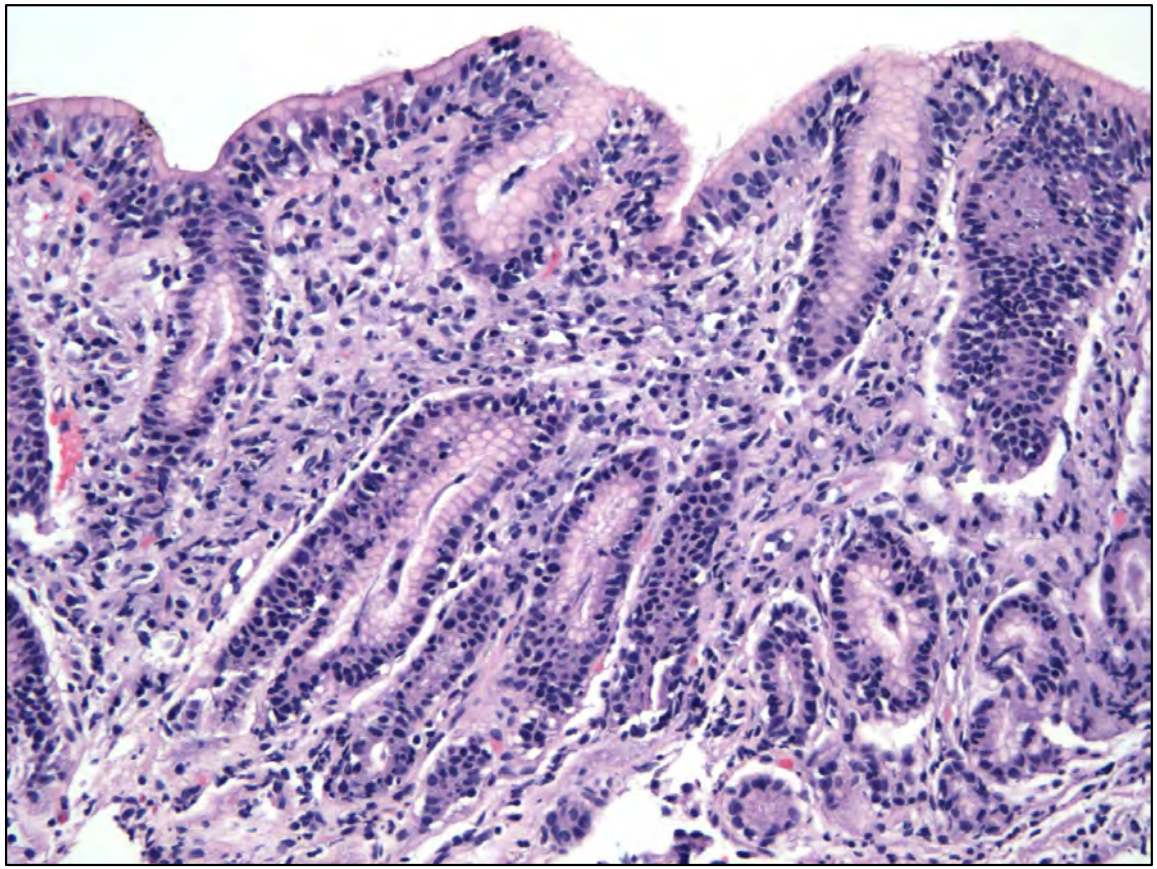
Plasma cell-rich inflammation

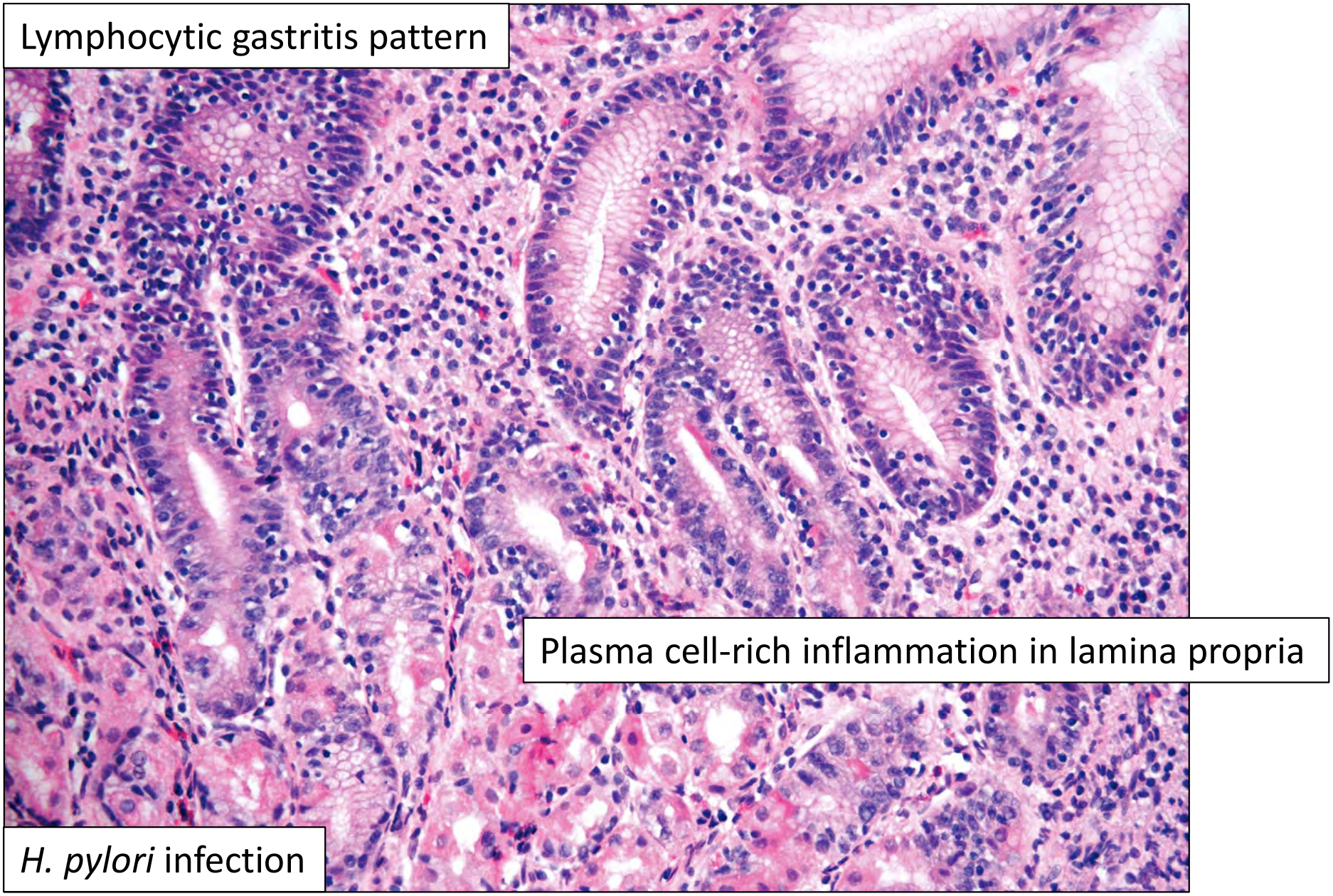


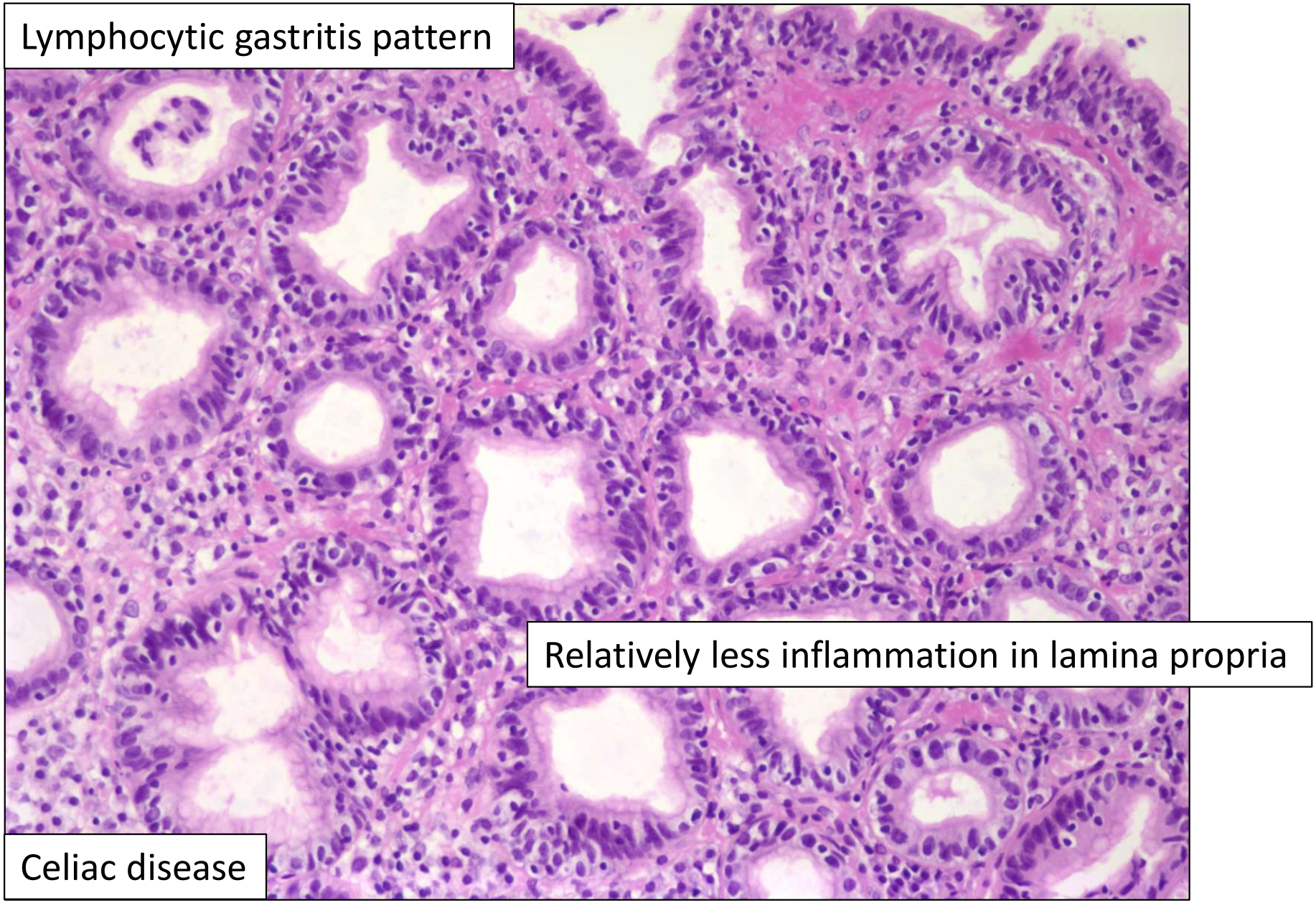
Subepithelial collagen

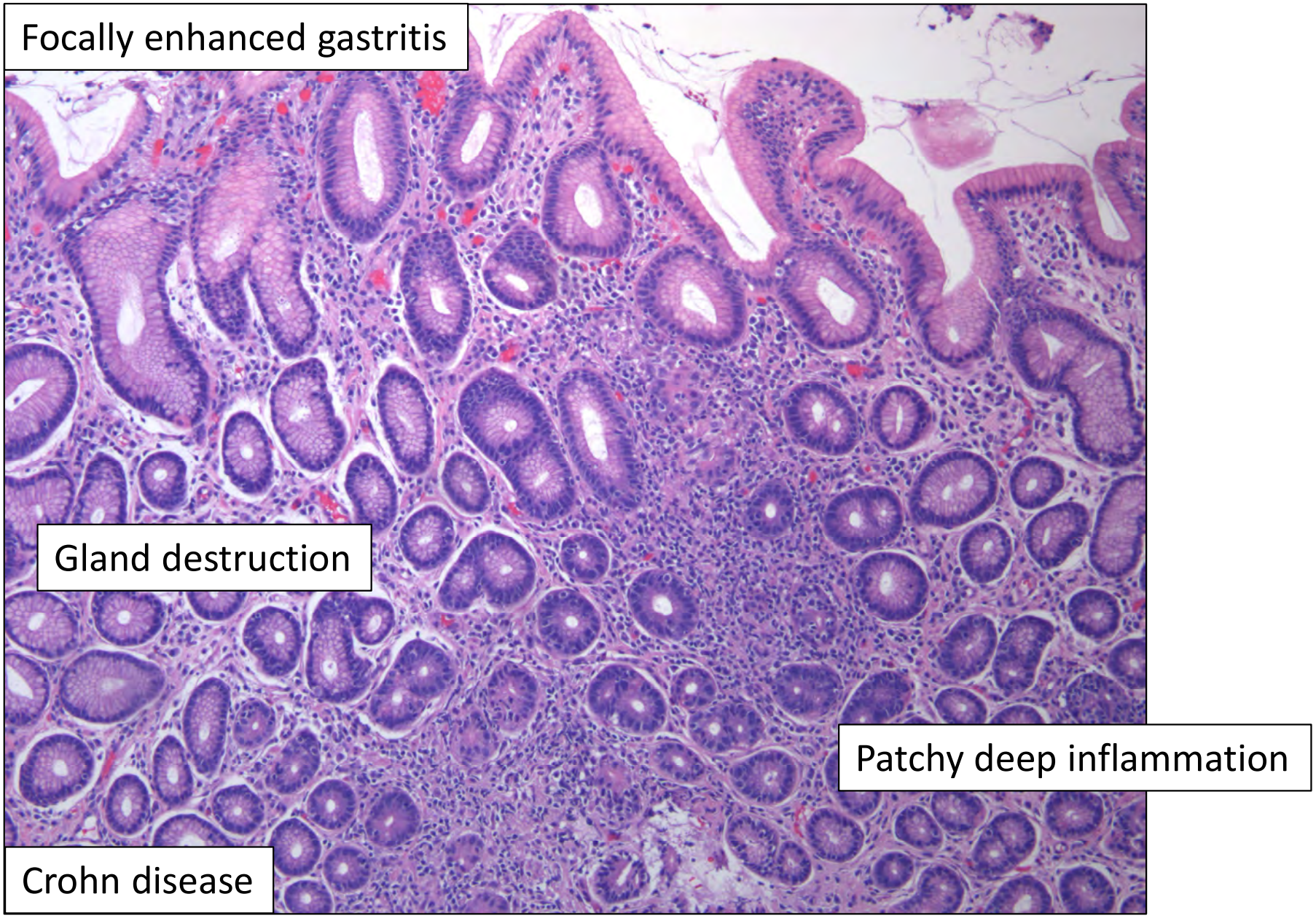
Lymphocytic Gastritis Pattern

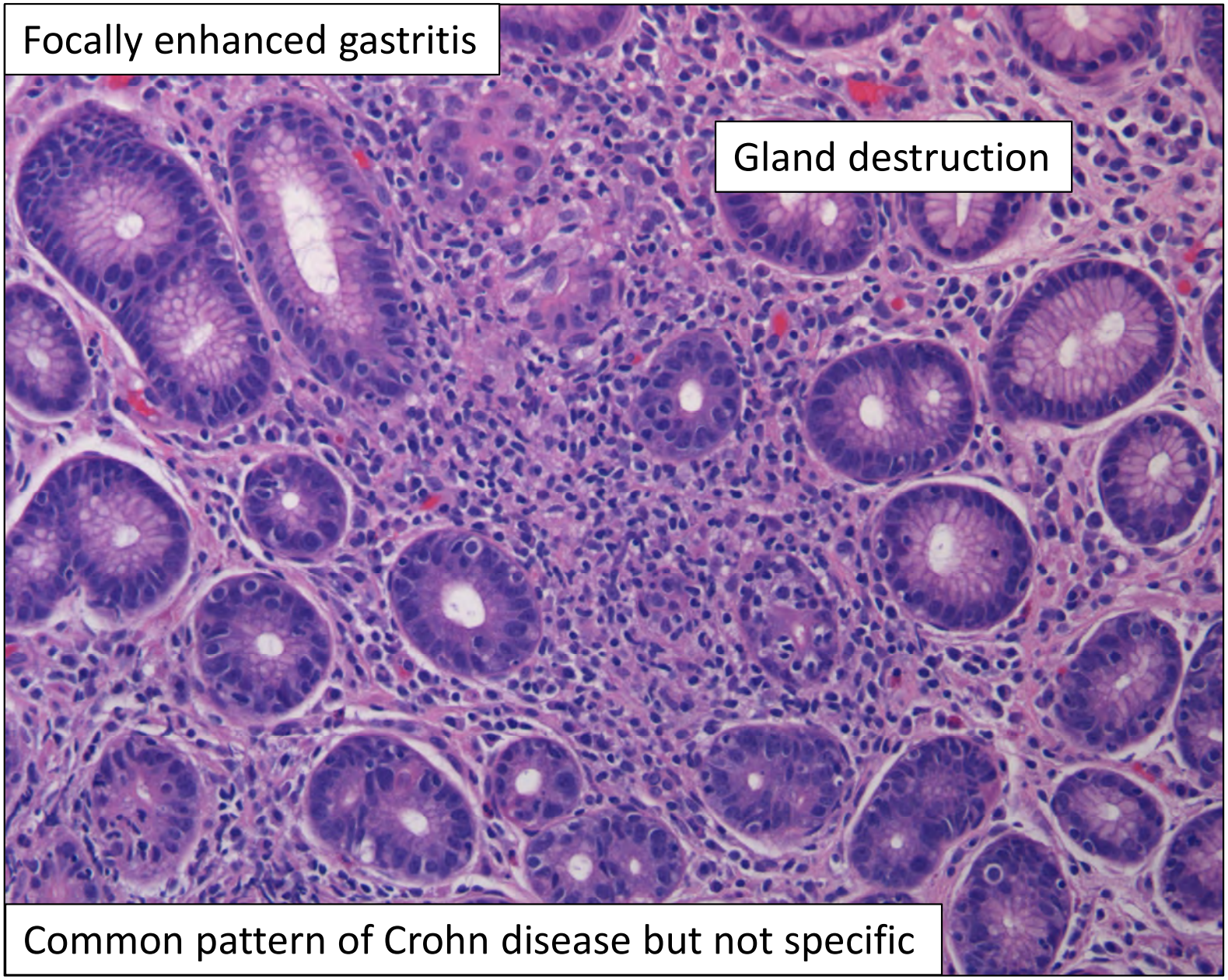
- *H. pylori*
- Celiac disease
- Ménétrier disease
- Lymphocytic colitis
- Medications
  - NSAIDs
  - Olmesartan

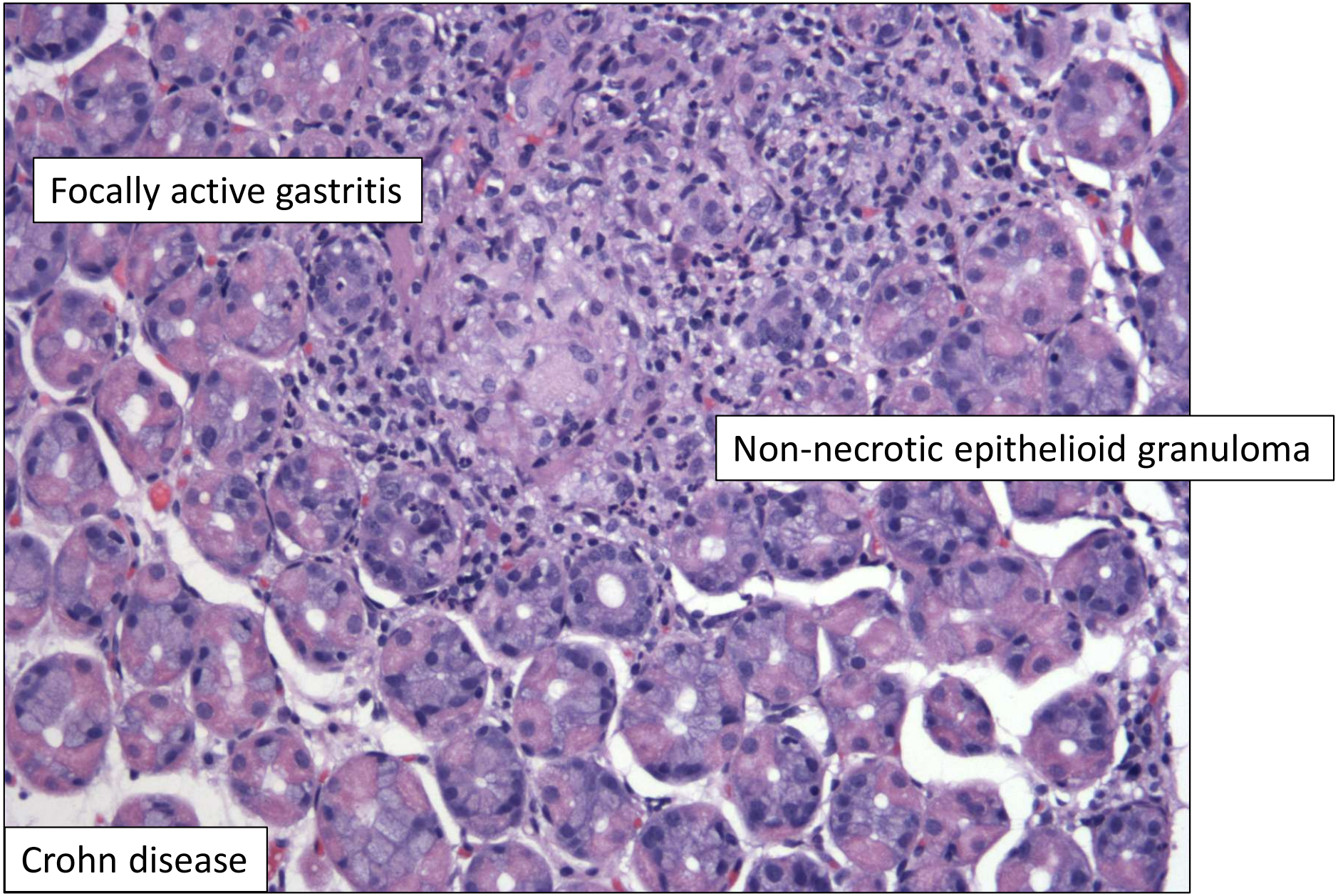



Lymphocytic gastritis pattern
Plasma cell-rich inflammation in lamina propria
H. pylori infection


Lymphocytic gastritis pattern
Relatively less inflammation in lamina propria
Celiac disease

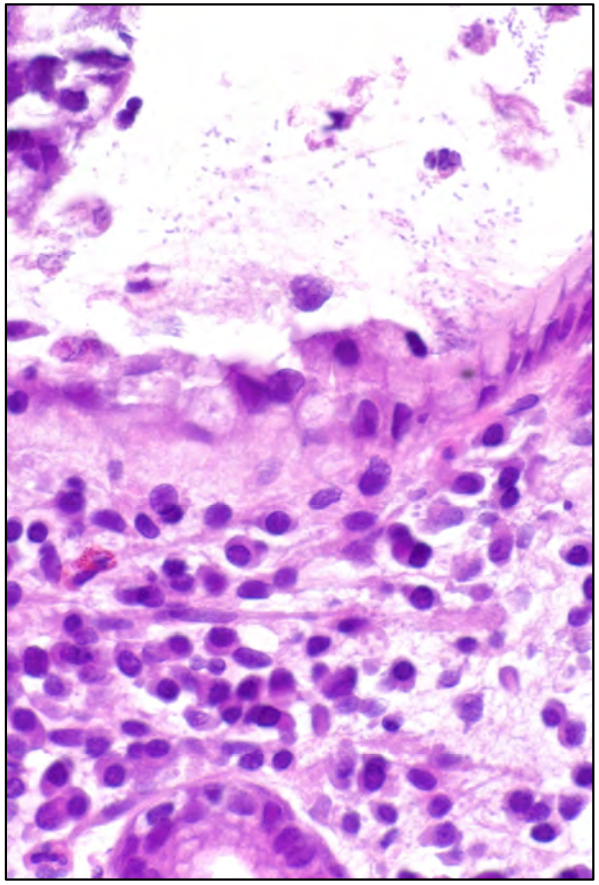

Focally enhanced gastritis
Gland destruction
Patchy deep inflammation
Crohn disease


Focally enhanced gastritis
Gland destruction
Common pattern of Crohn disease but not specific


Focally active gastritis
Non-necrotic epithelioid granuloma
Crohn disease

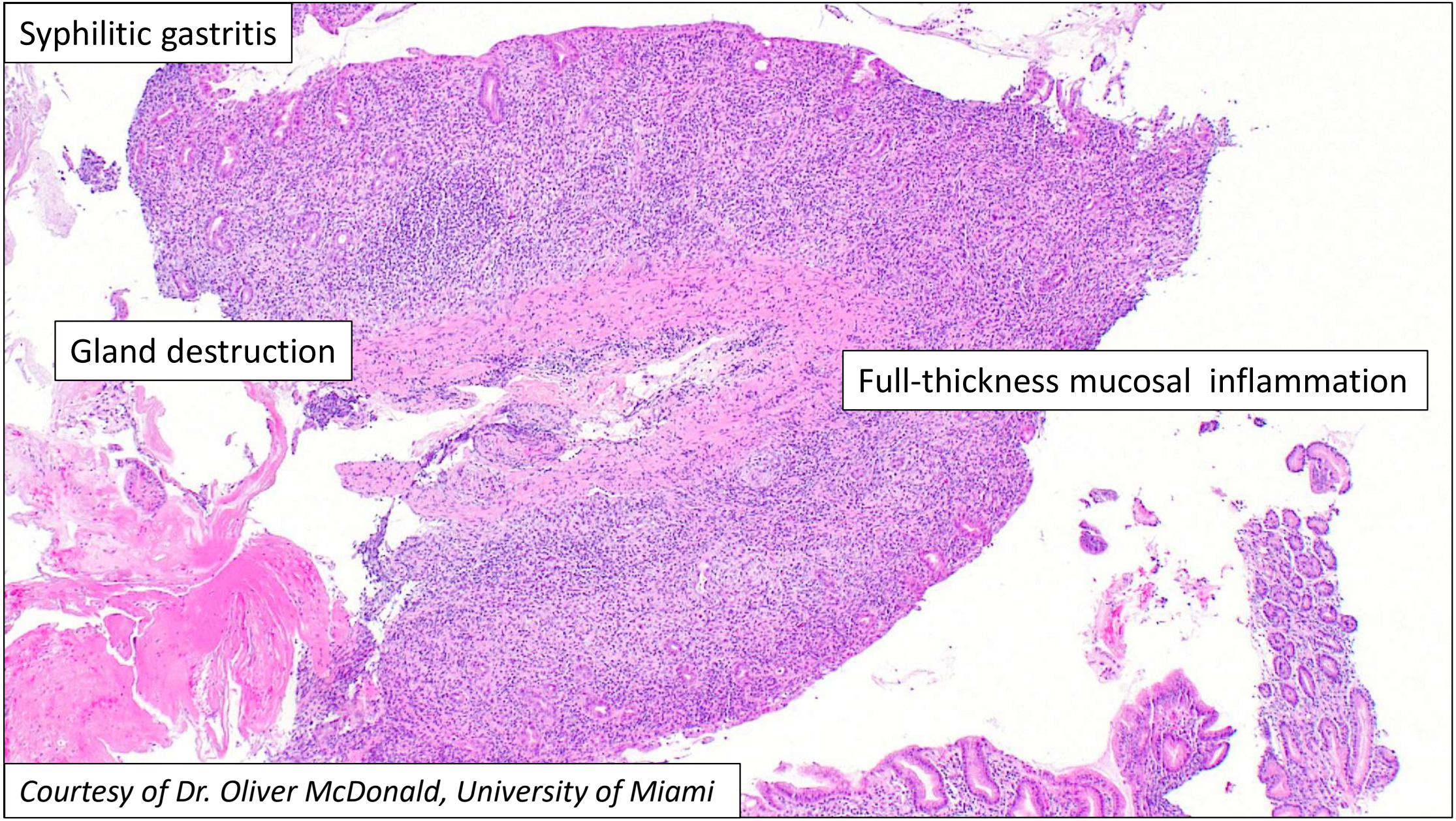
Non-Helicobacter Infections

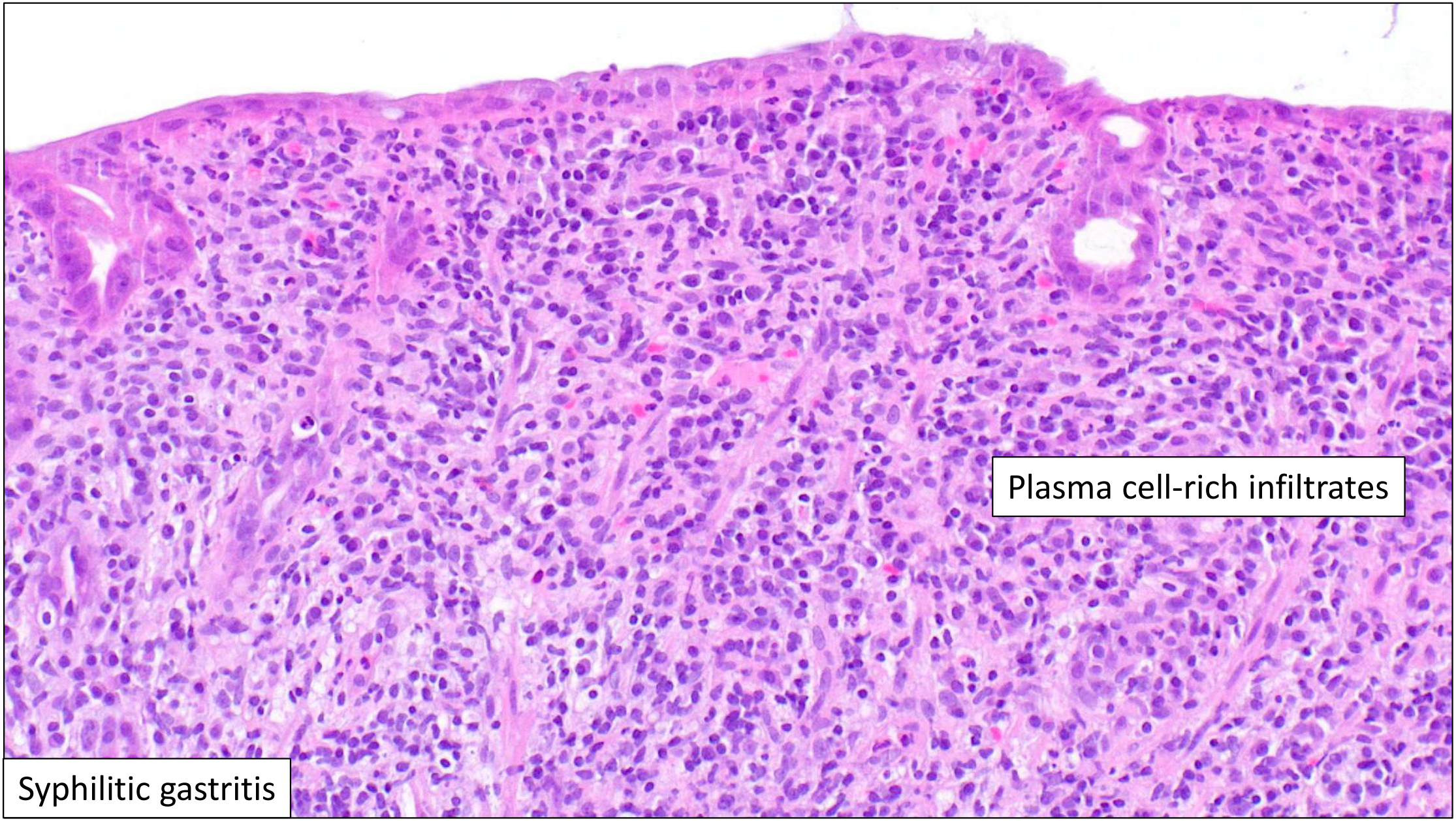
- Major role of stomach is acidification and sterilization of contents
- Extensive intestinal metaplasia and hypochlorhydria result in failed sterilization of luminal contents
- Opportunity for bacteria to grow in gastric juices
  - *Campylobacter*
    - May cross-react with *H. pylori* immunostain
  - *Enterococcus*

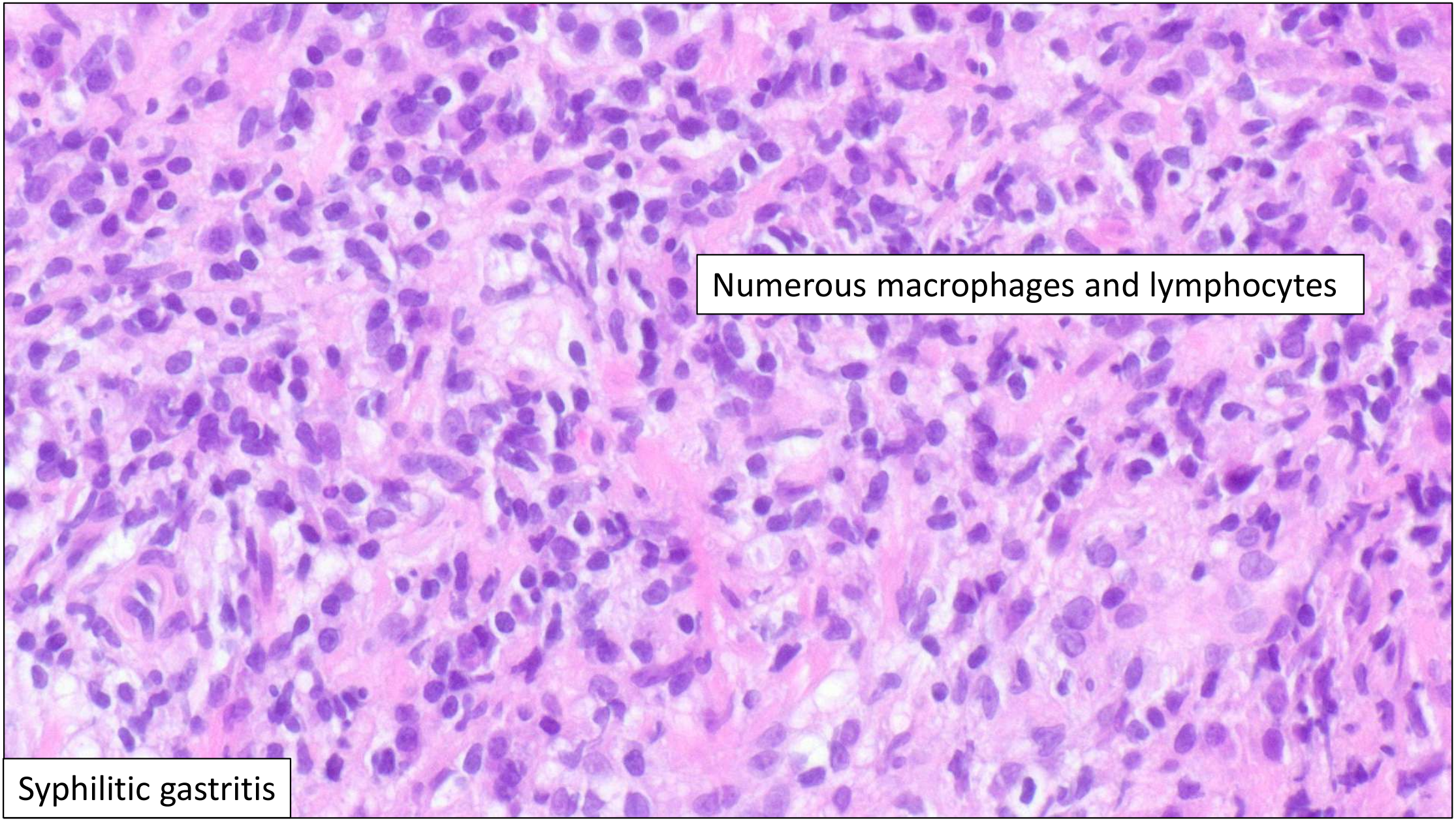


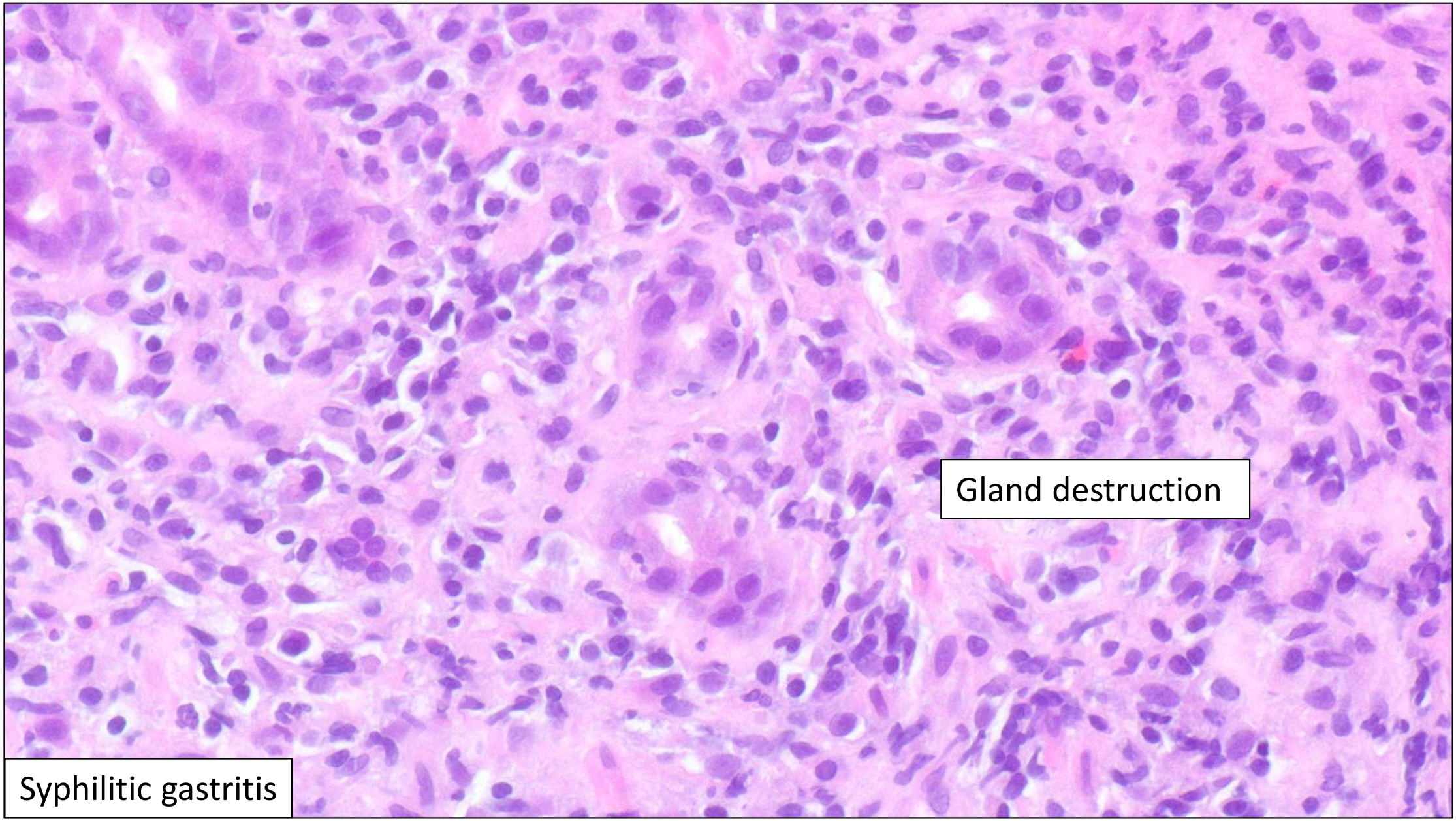
Gastric Syphilis

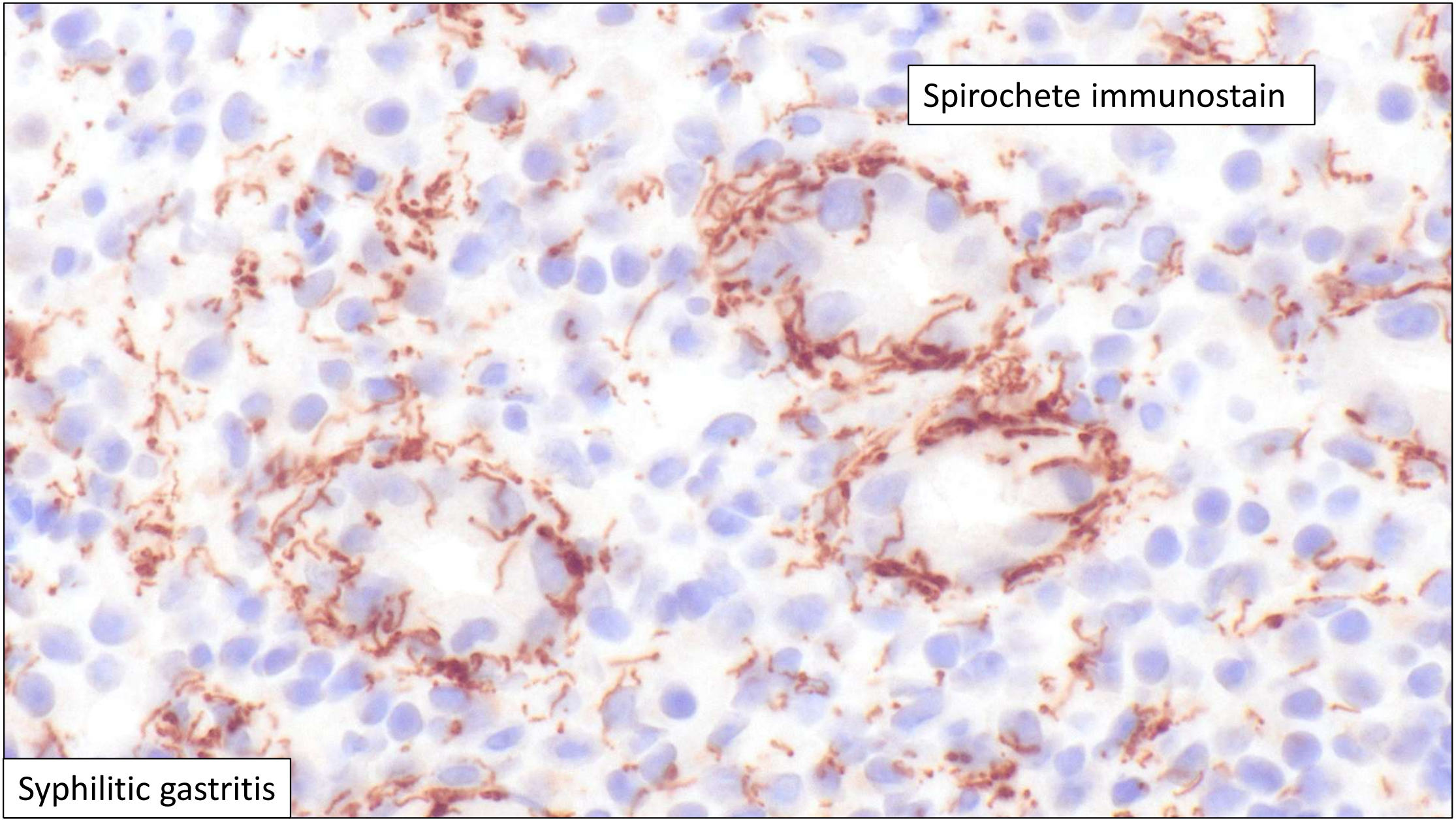
- Gastric infection is second most common site
- Bleeding from the upper gastrointestinal tract
- Nausea and anorexia
- Indurated inflammatory masses that can simulate a malignancy


Syphilitic gastritis
Gland destruction
Full-thickness mucosal inflammation
Courtesy of Dr. Oliver McDonald, University of Miami


Plasma cell-rich infiltrates
Syphilitic gastritis


Numerous macrophages and lymphocytes
Syphilitic gastritis

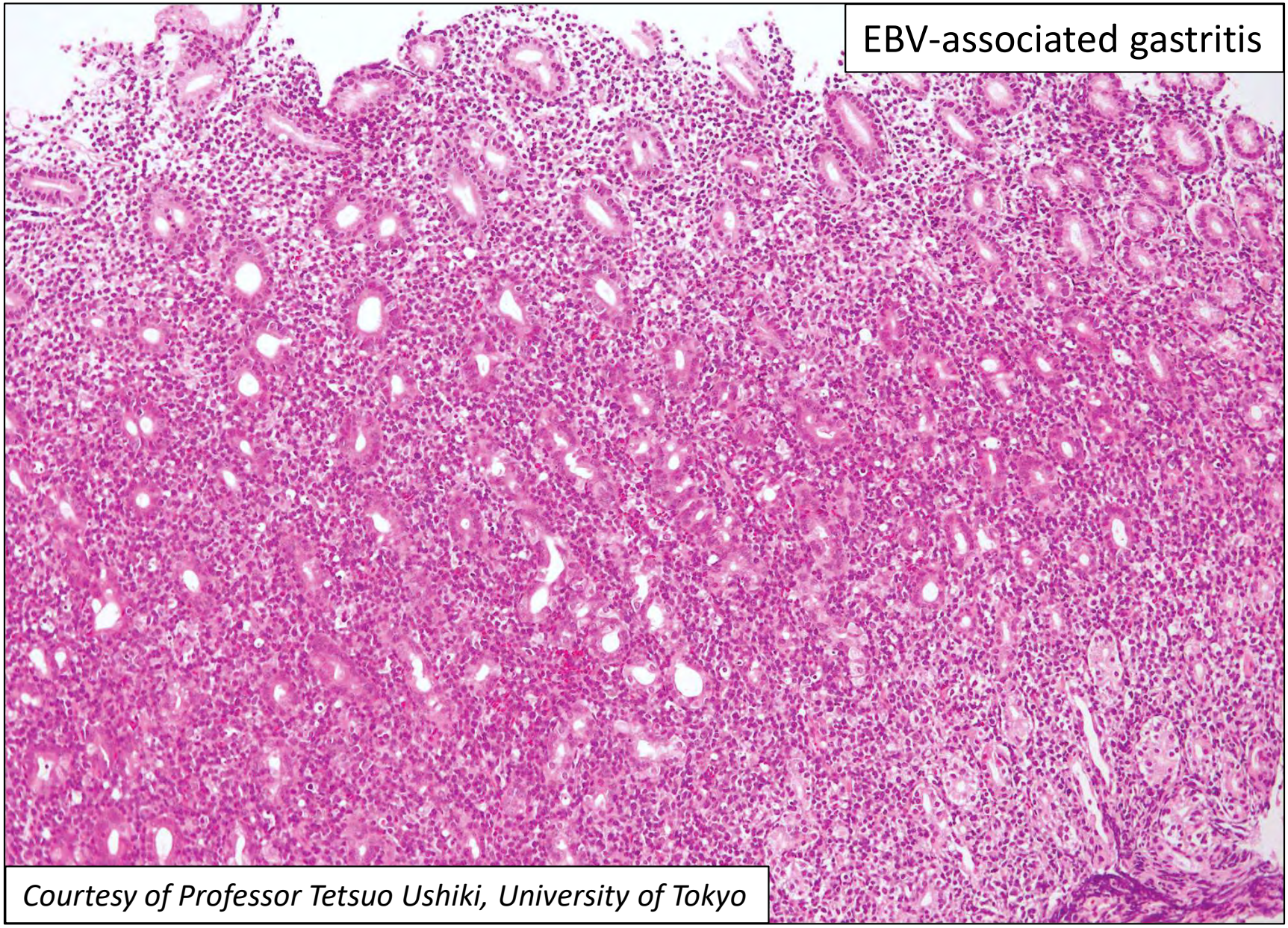

Gland destruction
Syphilitic gastritis


Spirochete immunostain
Syphilitic gastritis

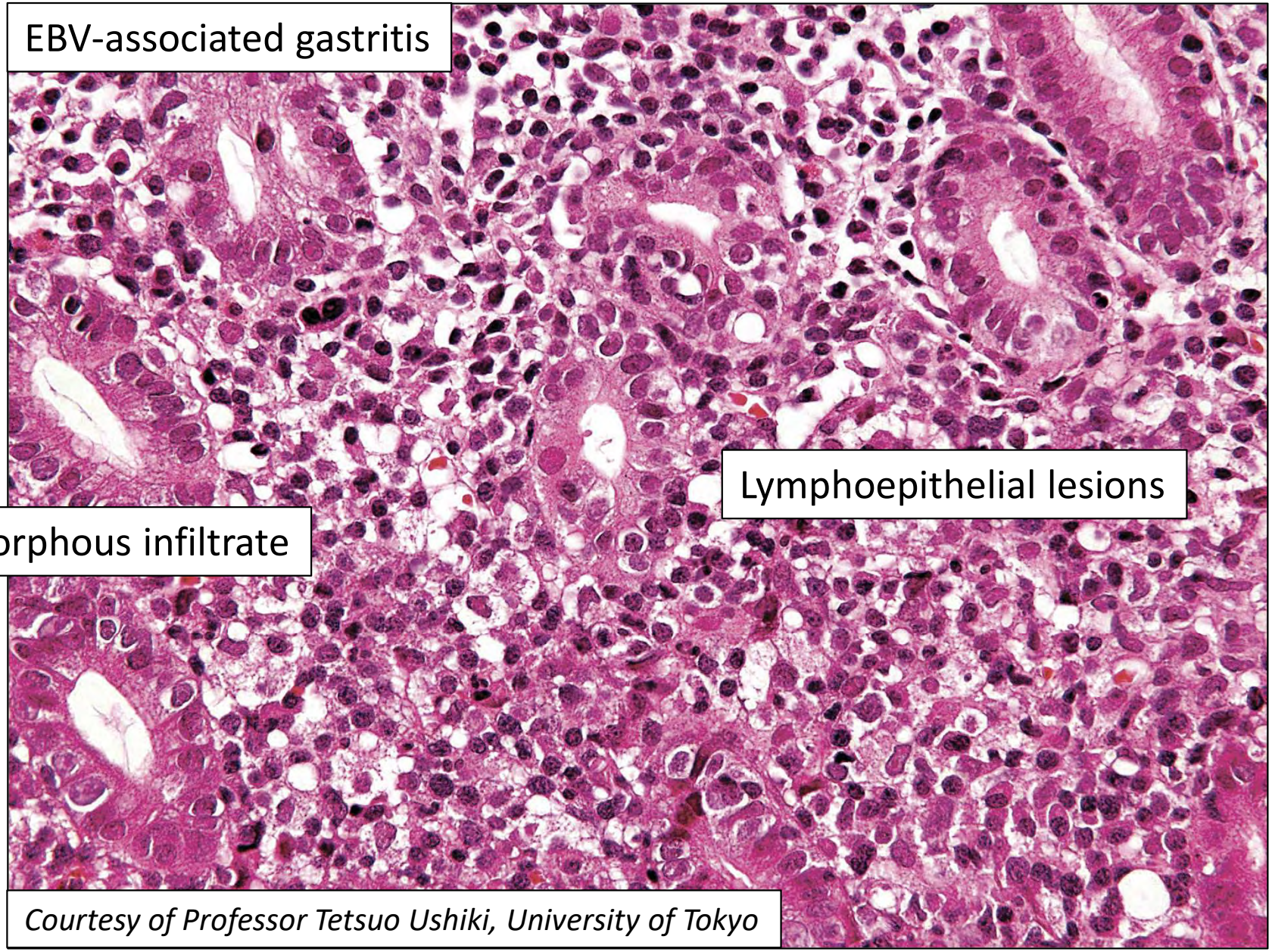
EBV-Related Gastritis

- Patients with primary infection and infectious mononucleosis
  - Positive monospot test and IgM to viral capsid antigen
  - Uncommon, but likely underrecognized
  - Self-limited in immunocompetent patients
  - T-cell mediated injury to EBV-infected B-cells
- Chronic active EBV-related gastritis (increased in Asian populations)
  - Infectious mononucleosis-type symptoms
  - EBV DNA copies in peripheral blood persisting for >3 month

Tian, *et al. Am J Surg Pathol* 2019; 43(9): 1253-1263.
Dursun, *et al. Turk J Gastroenterol* 2020; 31(3): 205-210


EBV-associated gastritis
Courtesy of Professor Tetsuo Ushiki, University of Tokyo

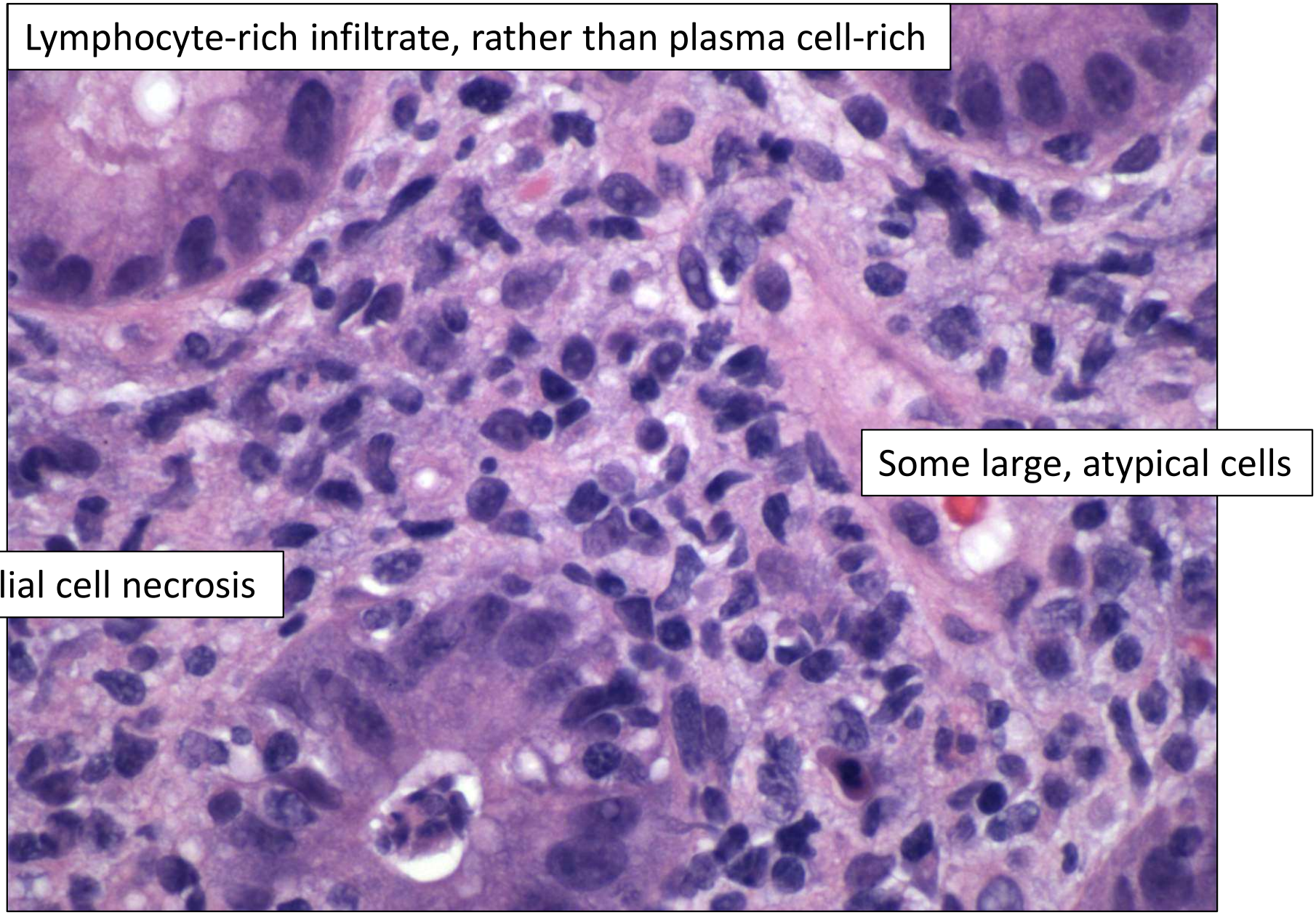
EBV-associated gastritis



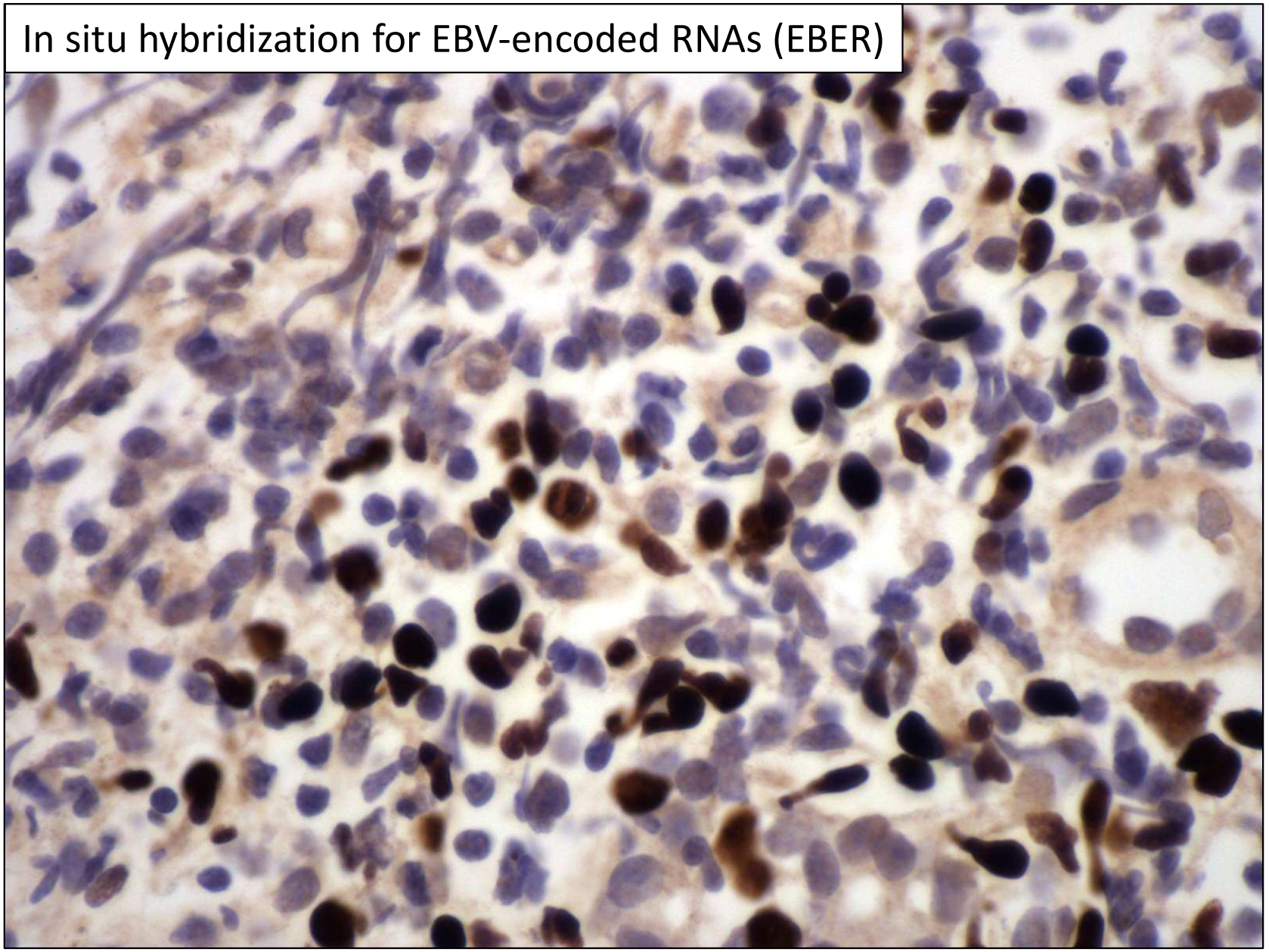
Lymphoepithelial lesions

Polymorphous infiltrate

Courtesy of Professor Tetsuo Ushiki, University of Tokyo


Lymphocyte-rich infiltrate, rather than plasma cell-rich
Some large, atypical cells
Epithelial cell necrosis

In situ hybridization for EBV-encoded RNAs (EBER)



Evaluating Gastric Samples for Gastric Injury *Take Home Points*

- Chemical gastropathy alone is probably not so important but it is often seen in combination with specific types of injury that should be recognized
- Site and severity of chronic gastritis can be clues to etiology
  - *H. pylori* causes superficial infiltrate with lots of plasma cells
  - Any other cell type in abundance should raise the possibility of an alternative diagnosis
  - Lymphocytosis and collagen deposits suggest a drug or immune-mediated injury
  - Extensive gland destruction is not *H. pylori*-related


Intermission
You look like you could use a snack!
Mr. Pops
We'll meet you in the lobby.

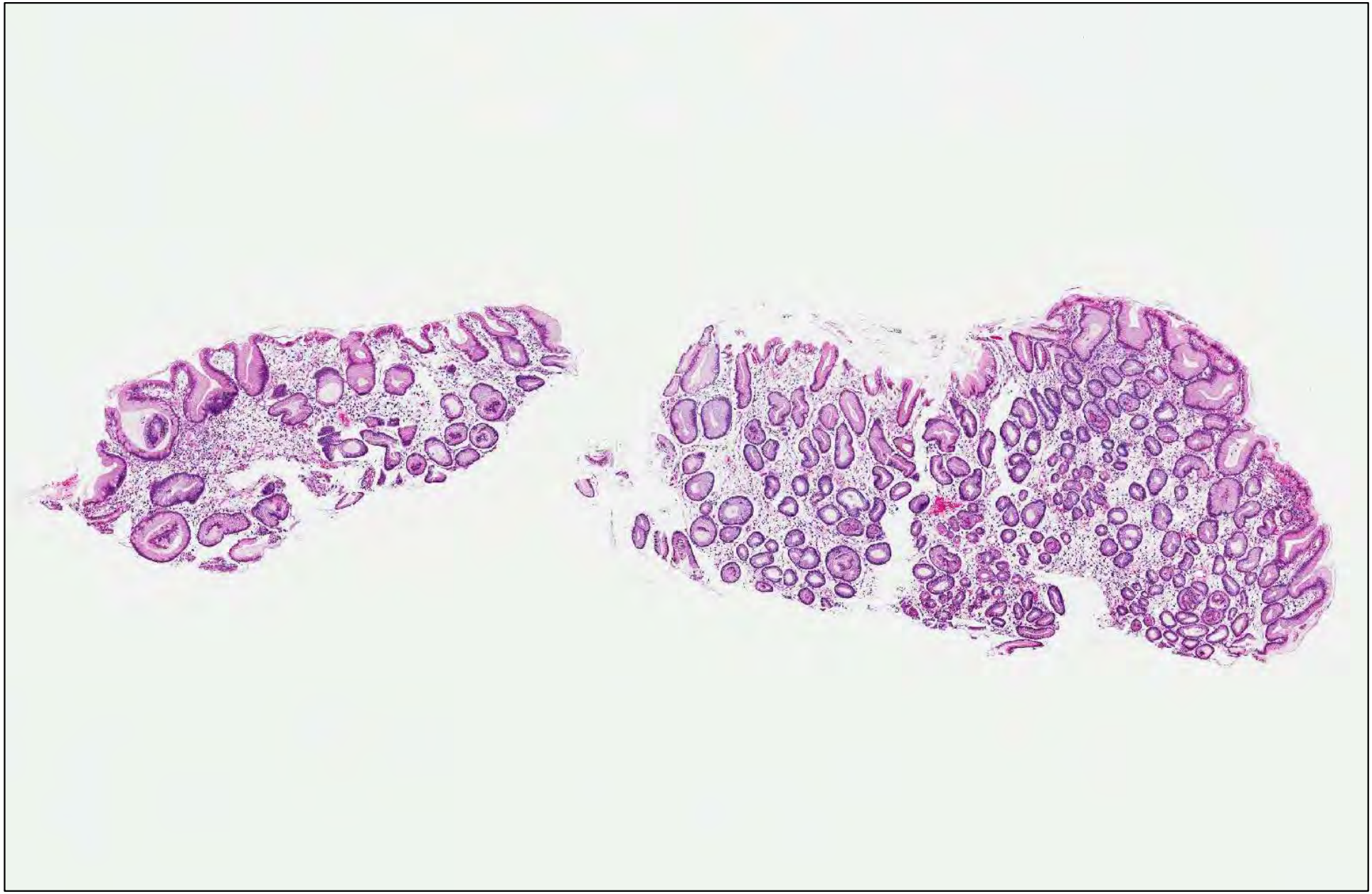
CASES THAT KEEP YOU UP AT NIGHT

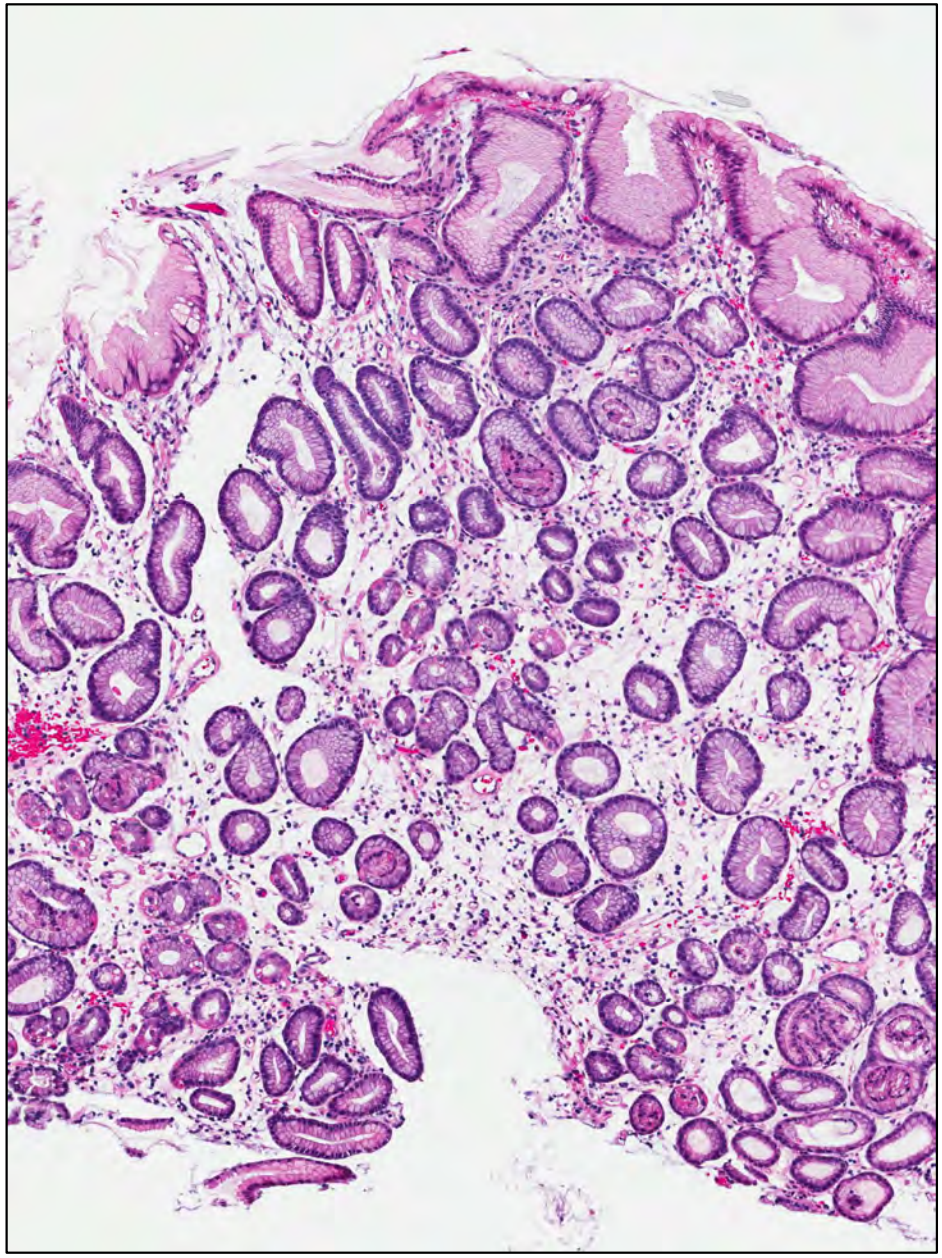
UHealth
UNIVERSITY OF MIAMI HEALTH SYSTEM
UNIVERSITY OF MIAMI
MILLER SCHOOL
of MEDICINE

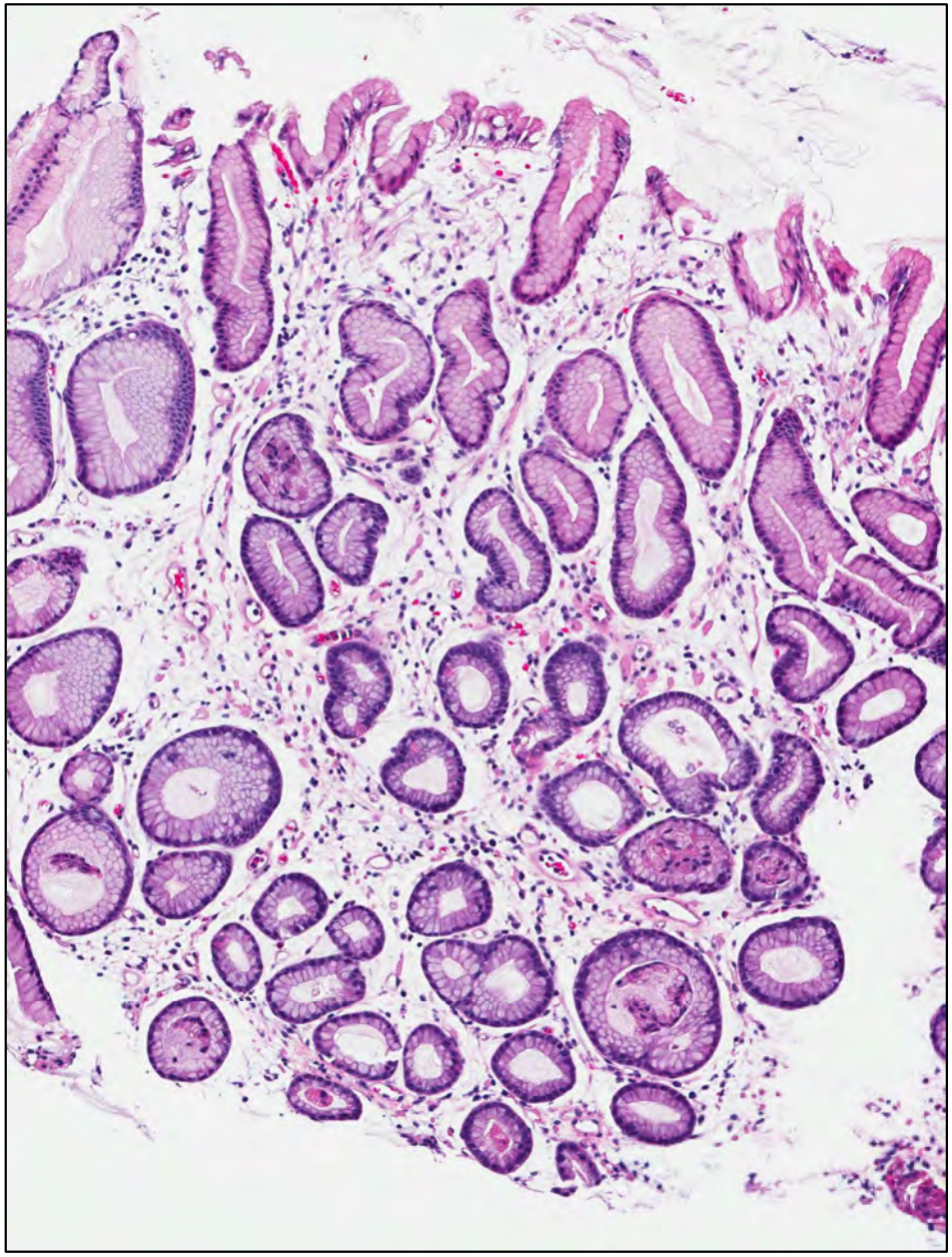
PATHOLOGY & LABORATORY MEDICINE

Here is a case to keep you up at night

- 33-year-old woman with gastric outlet obstruction due to superior mesenteric artery syndrome
- Seen for stent revision and removal
- Biopsies obtained to rule out *H. pylori*





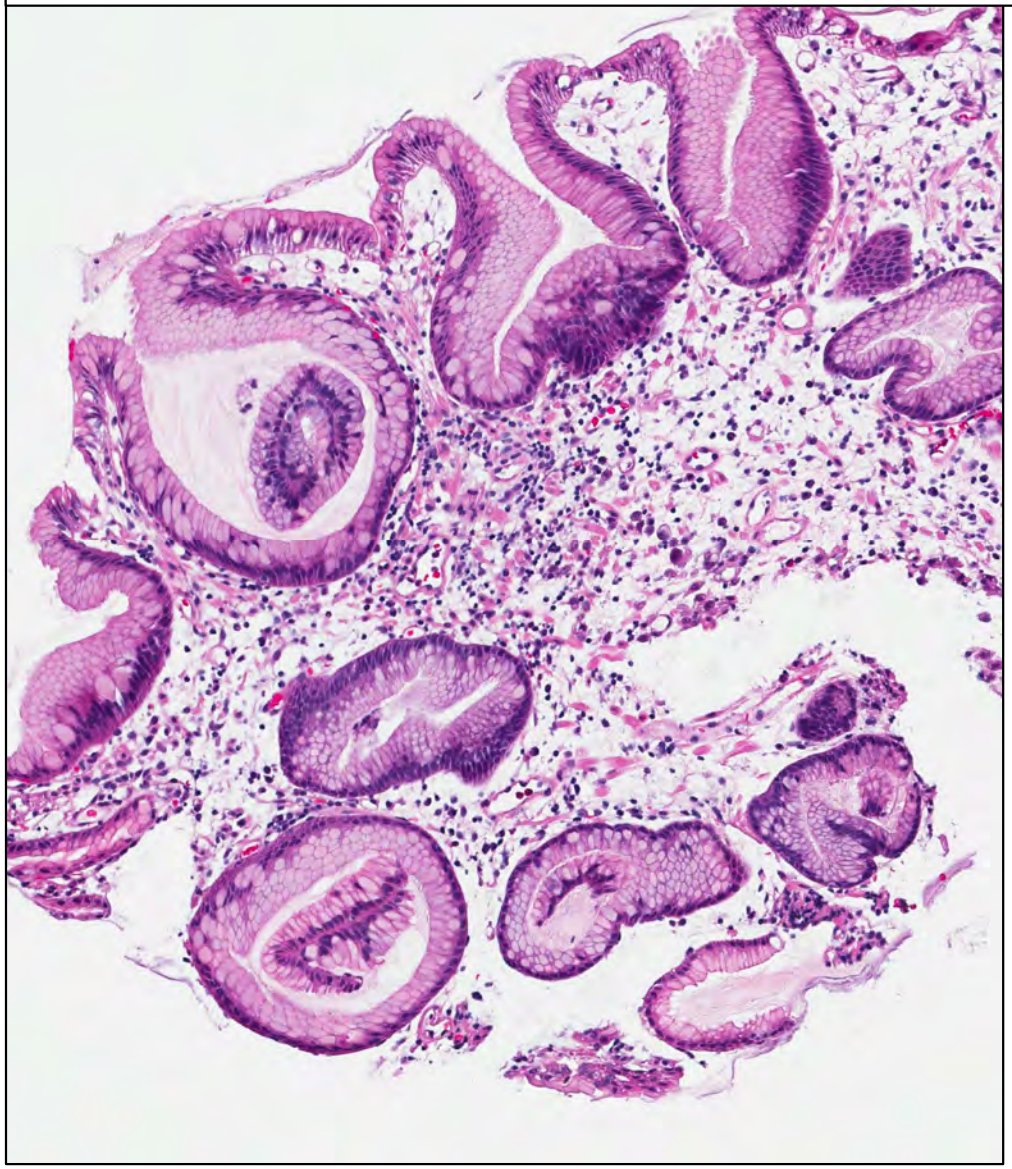


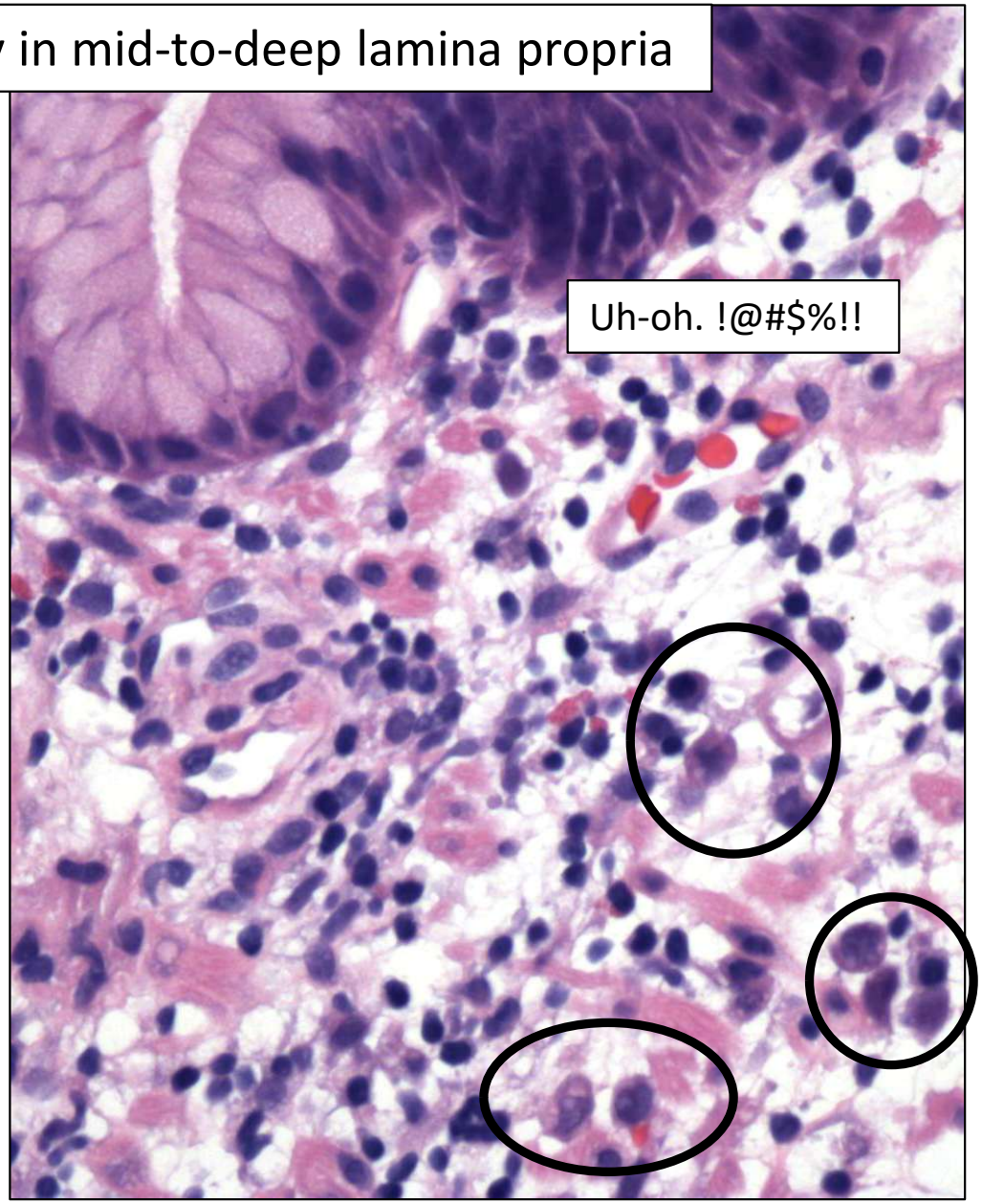
Signed out as ”Gastric antral mucosa with regenerative foveolar hyperplasia”

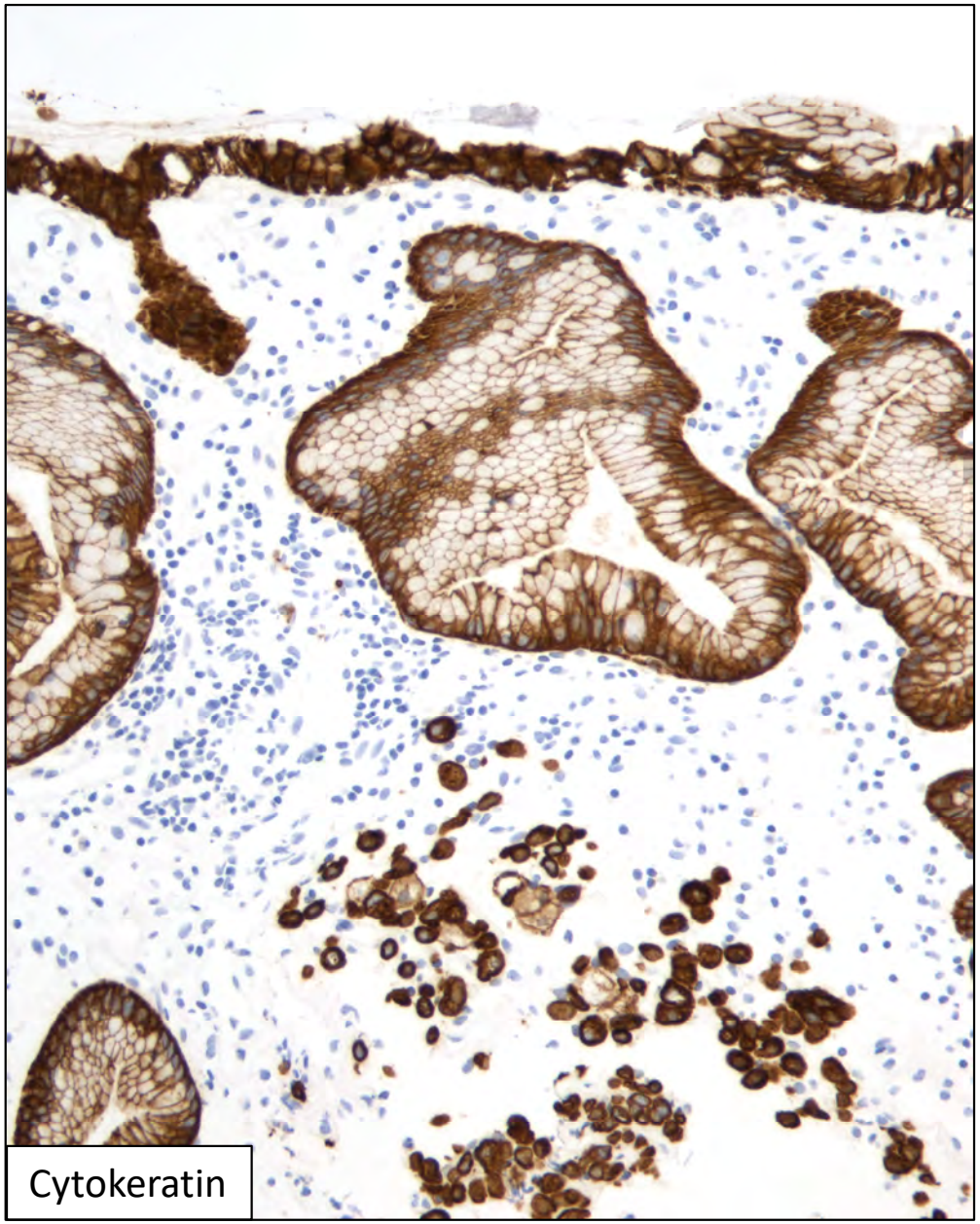
Follow-Up

- Patient re-presented with an ovarian mass and ascites a few months later
- Clinical suspicion for ovarian carcinoma or lymphoma
- Ascites fluid sent to cytology
  - Signet ring cell carcinoma

Clues at low magnification: Patchy cellularity in mid-to-deep lamina propria

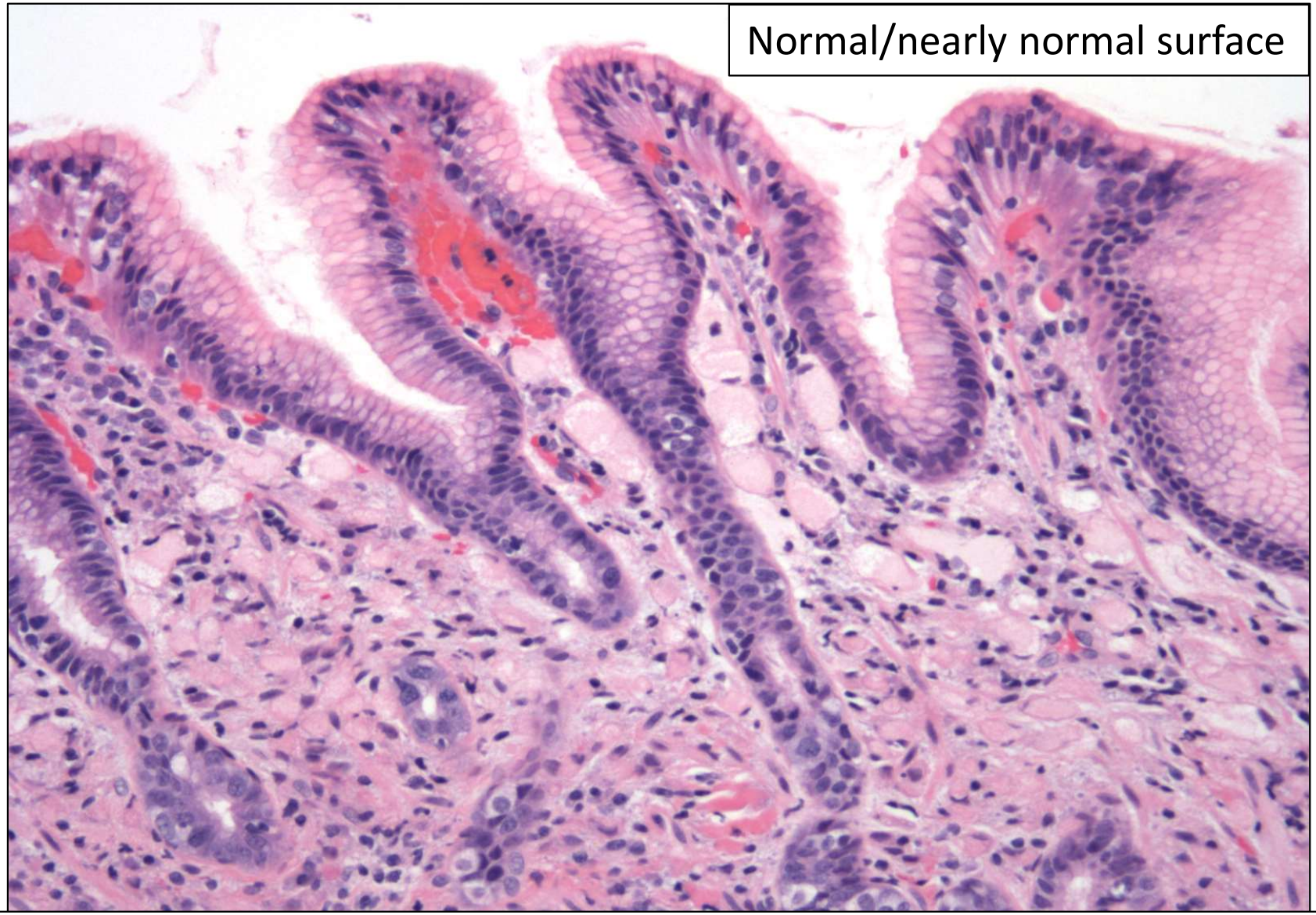




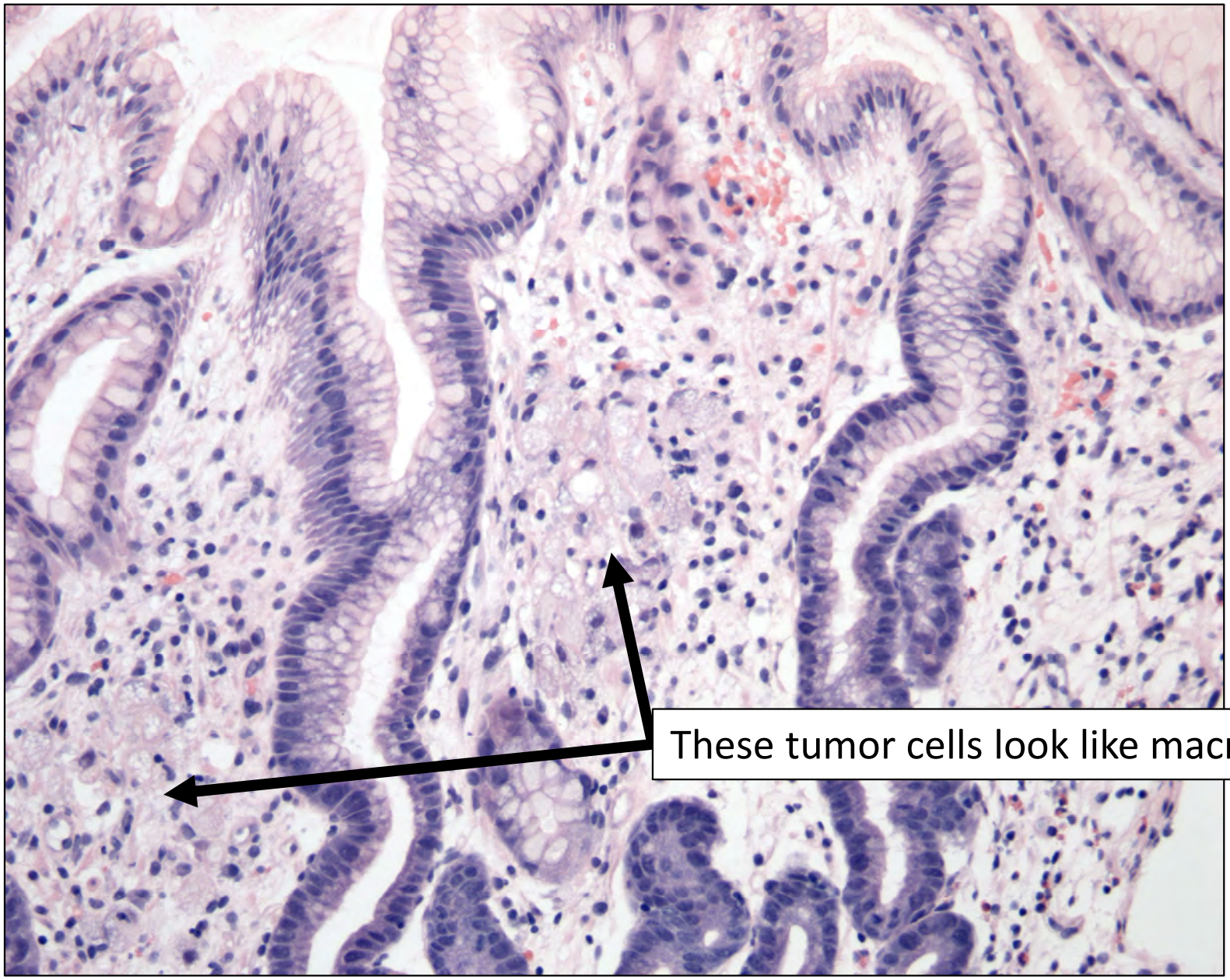

Cytokeratin

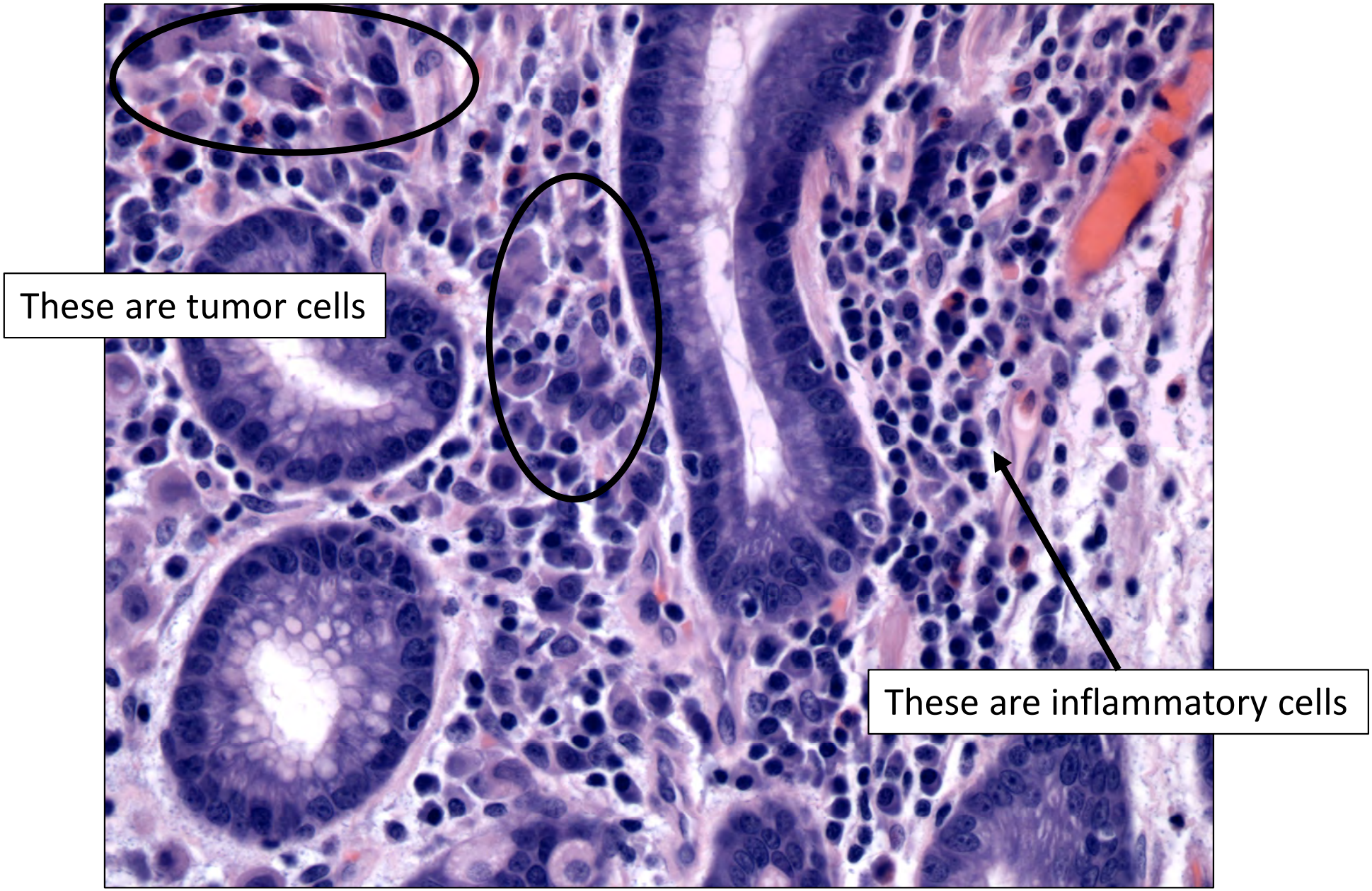
Types of Pathologists

- Those who have missed diffuse type gastric carcinoma in a biopsy
- Those who are going to miss diffuse type gastric carcinoma in a biopsy



Infiltrating signet ring cells unassociated with gland architectural distortion or stromal reaction


These tumor cells look like macrophages!

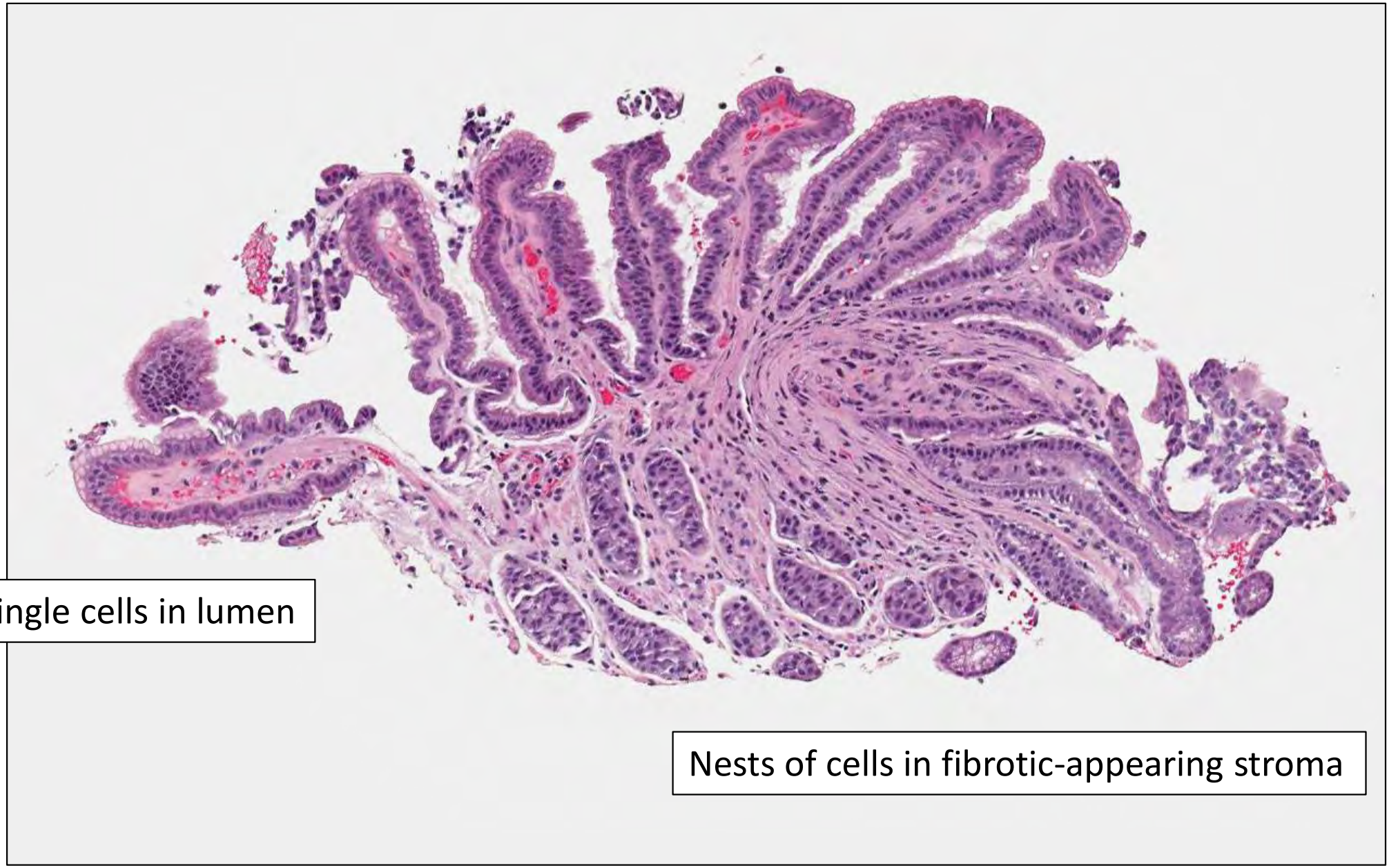

These are tumor cells
These are inflammatory cells

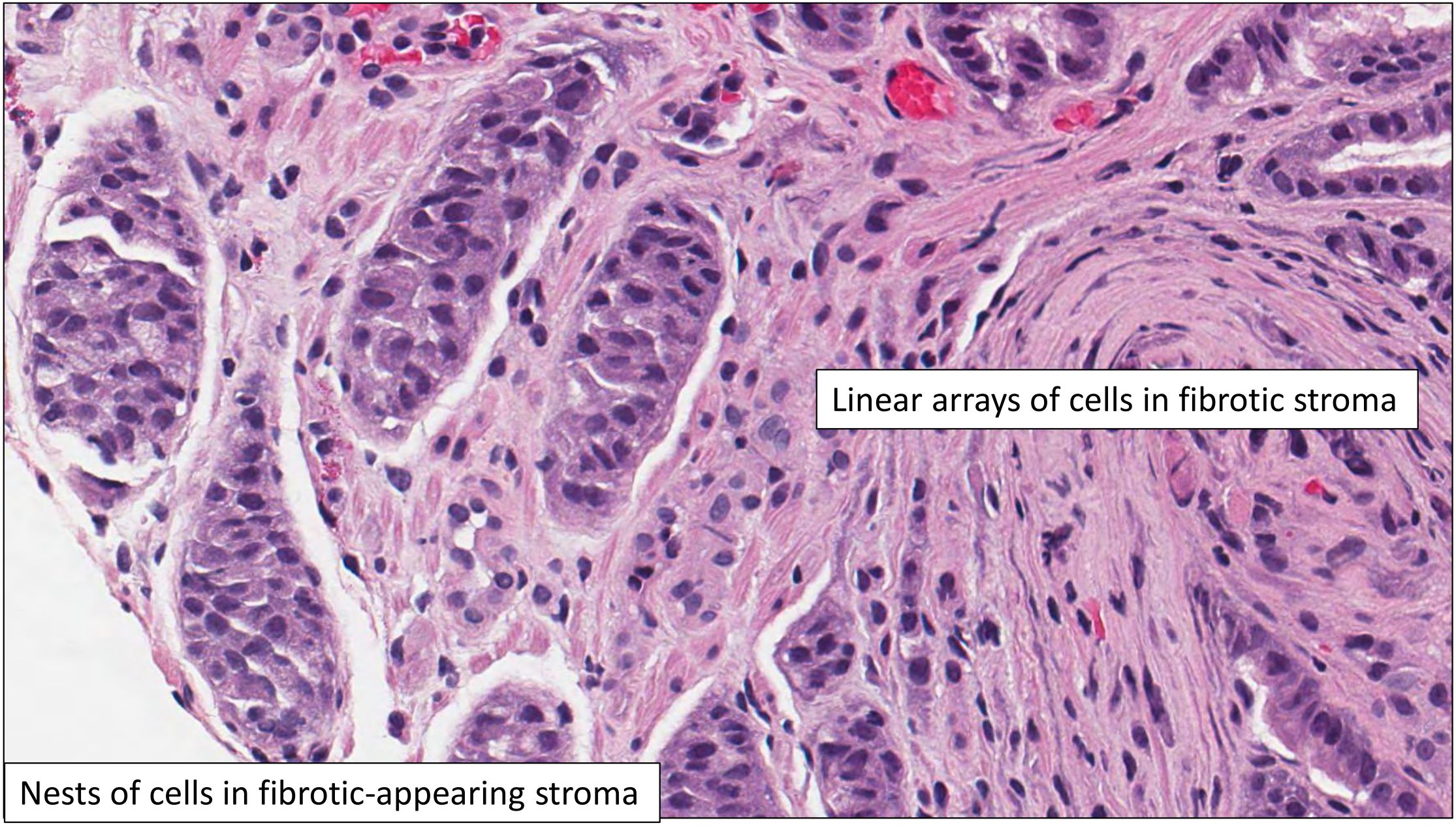
Discussion for Today

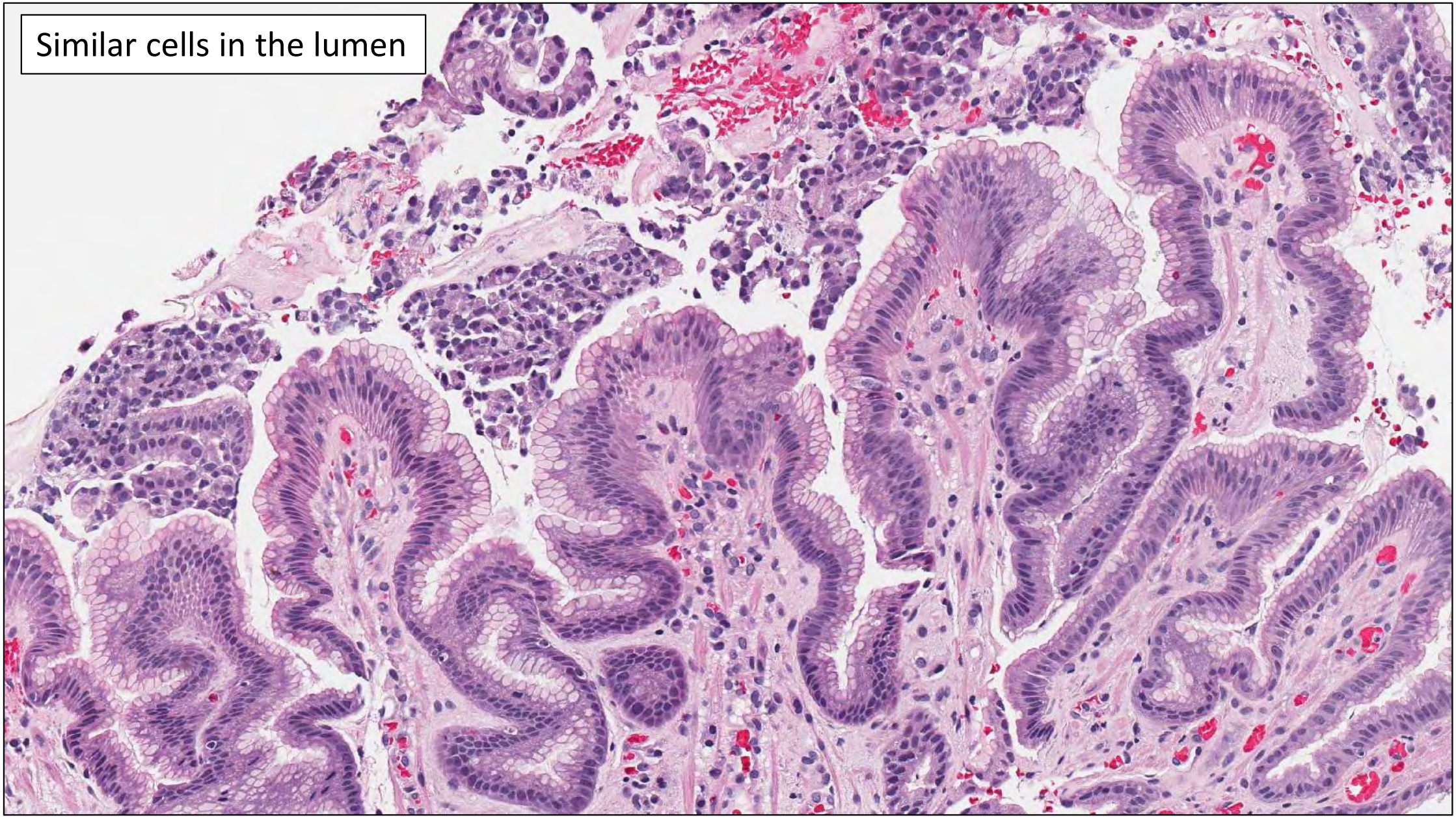
- Benign mimics of poorly cohesive gastric cancer in biopsy samples
  - Macrophages
  - Epithelium
- Carcinomas that simulate benign conditions
  - Poorly cohesive gastric carcinoma
  - Tubular type gastric carcinoma

Case

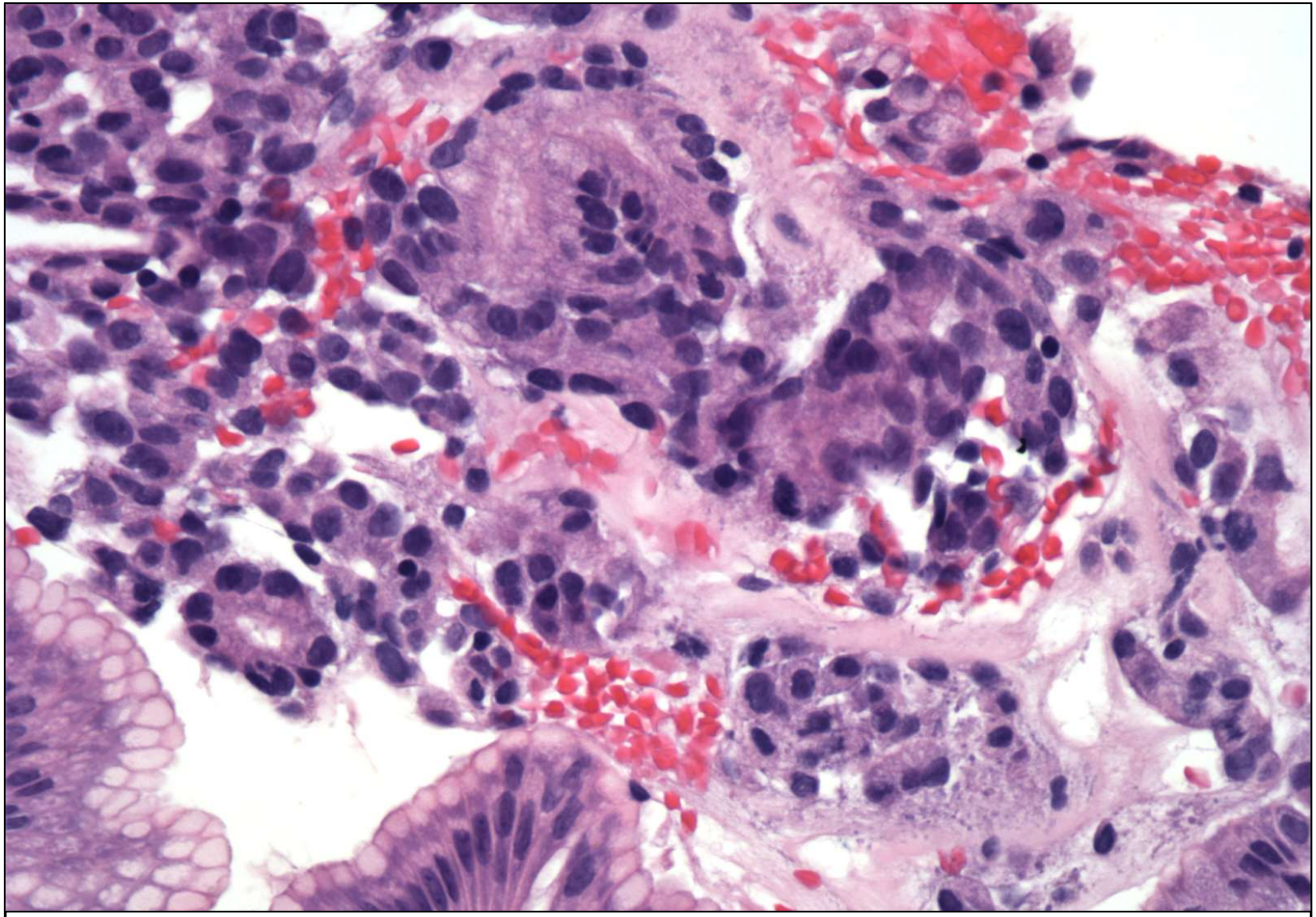
- 49-year-old female with gastric ulcer
- Biopsy interpreted to be suspicious for carcinoma
- Referred for surgery


Single cells in lumen
Nests of cells in fibrotic-appearing stroma

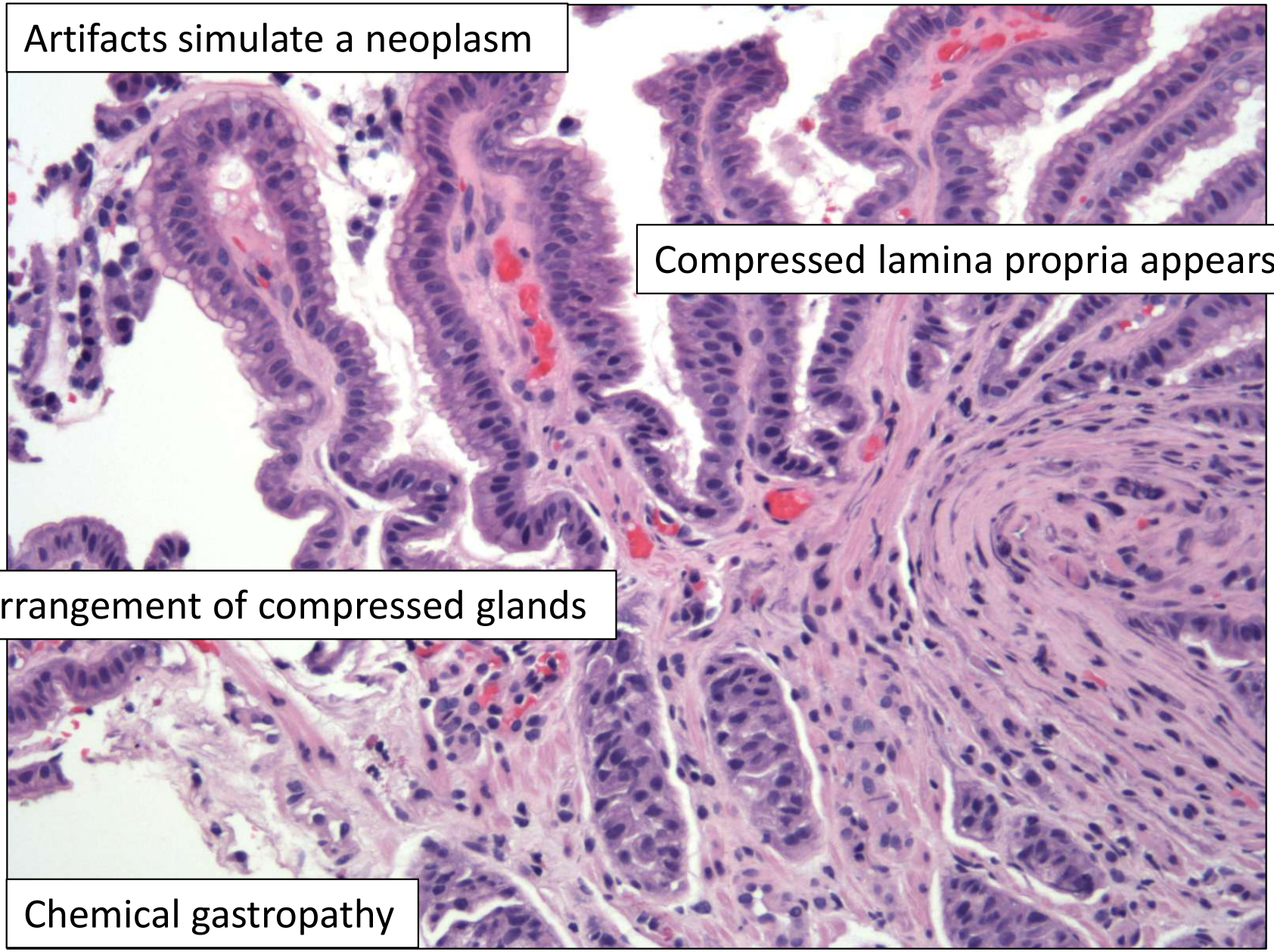

Linear arrays of cells in fibrotic stroma
Nests of cells in fibrotic-appearing stroma

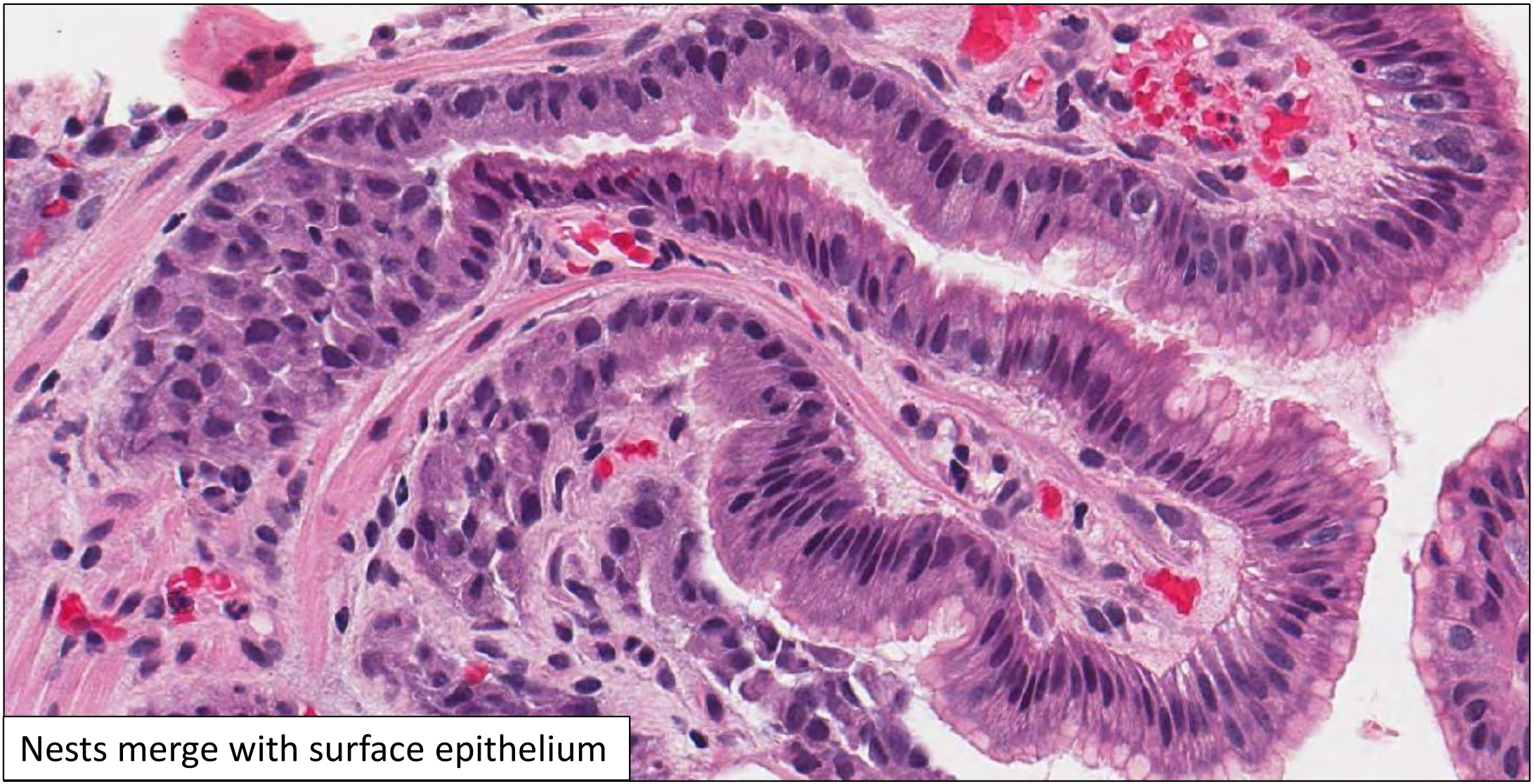

Similar cells in the lumen

Poorly cohesive/diffuse-type gastric cancer is not nested and should be present in intact tissue, not the lumen



Atypical cells out in lumen (not a pattern of signet ring cell carcinoma)

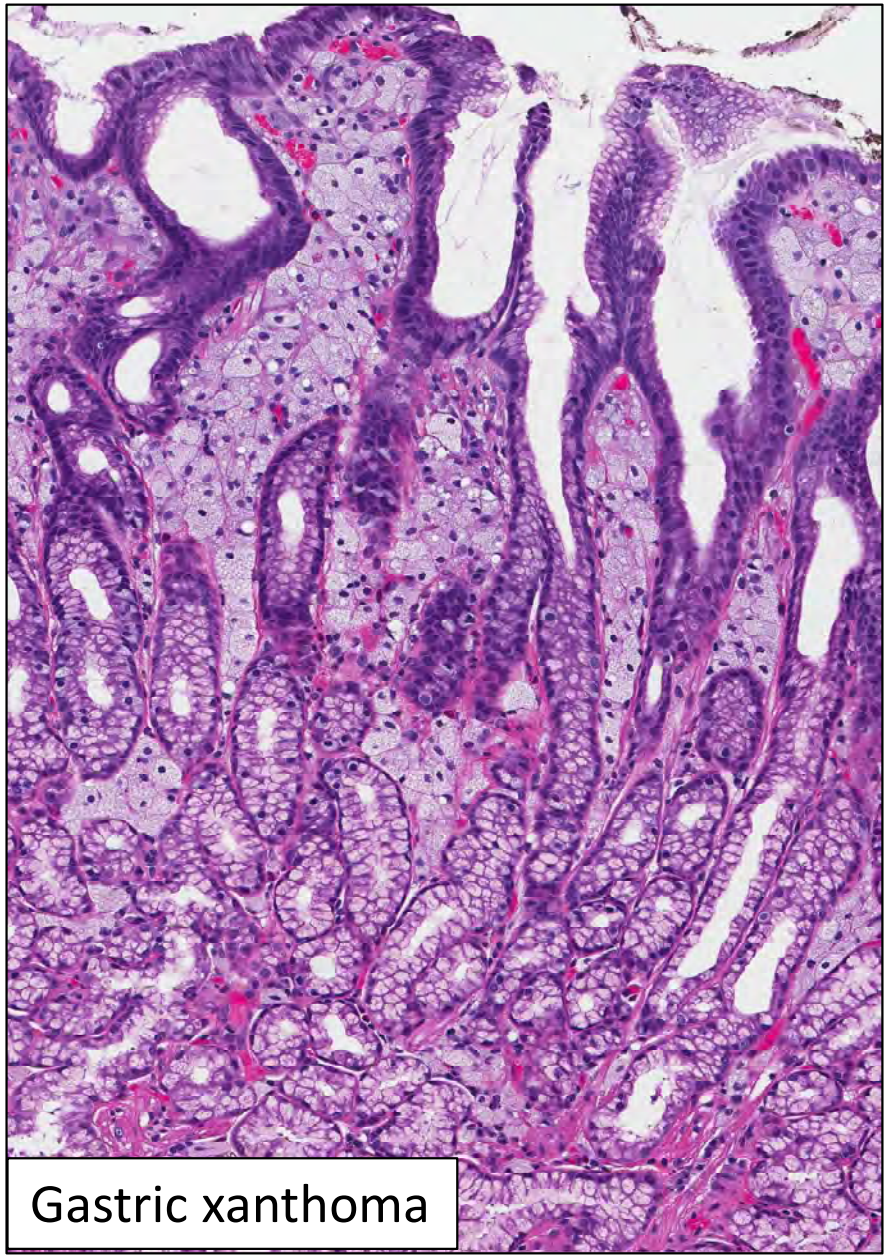

Artifacts simulate a neoplasm
Compressed lamina propria appears fibrotic
Nested arrangement of compressed glands
Chemical gastropathy

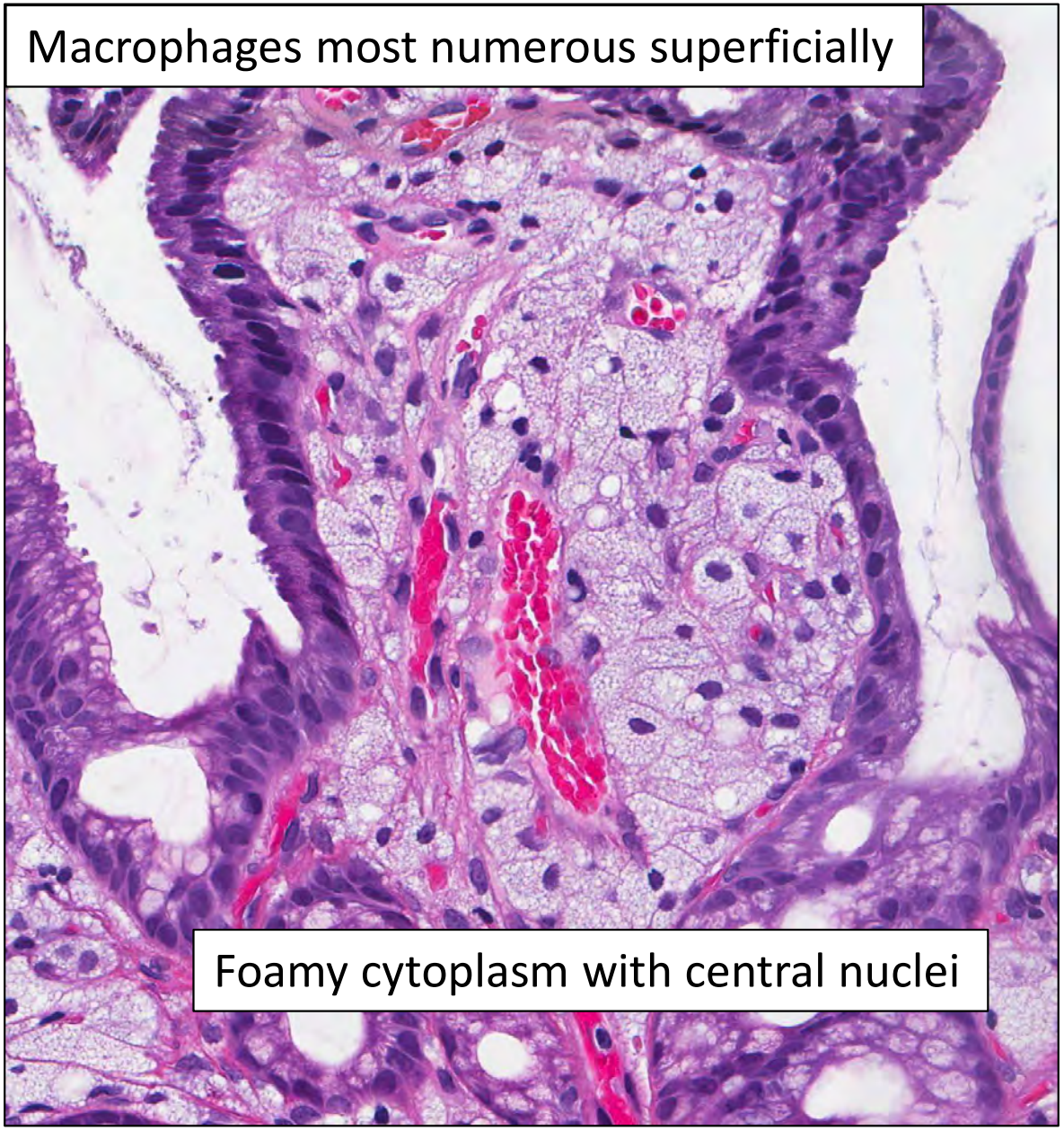


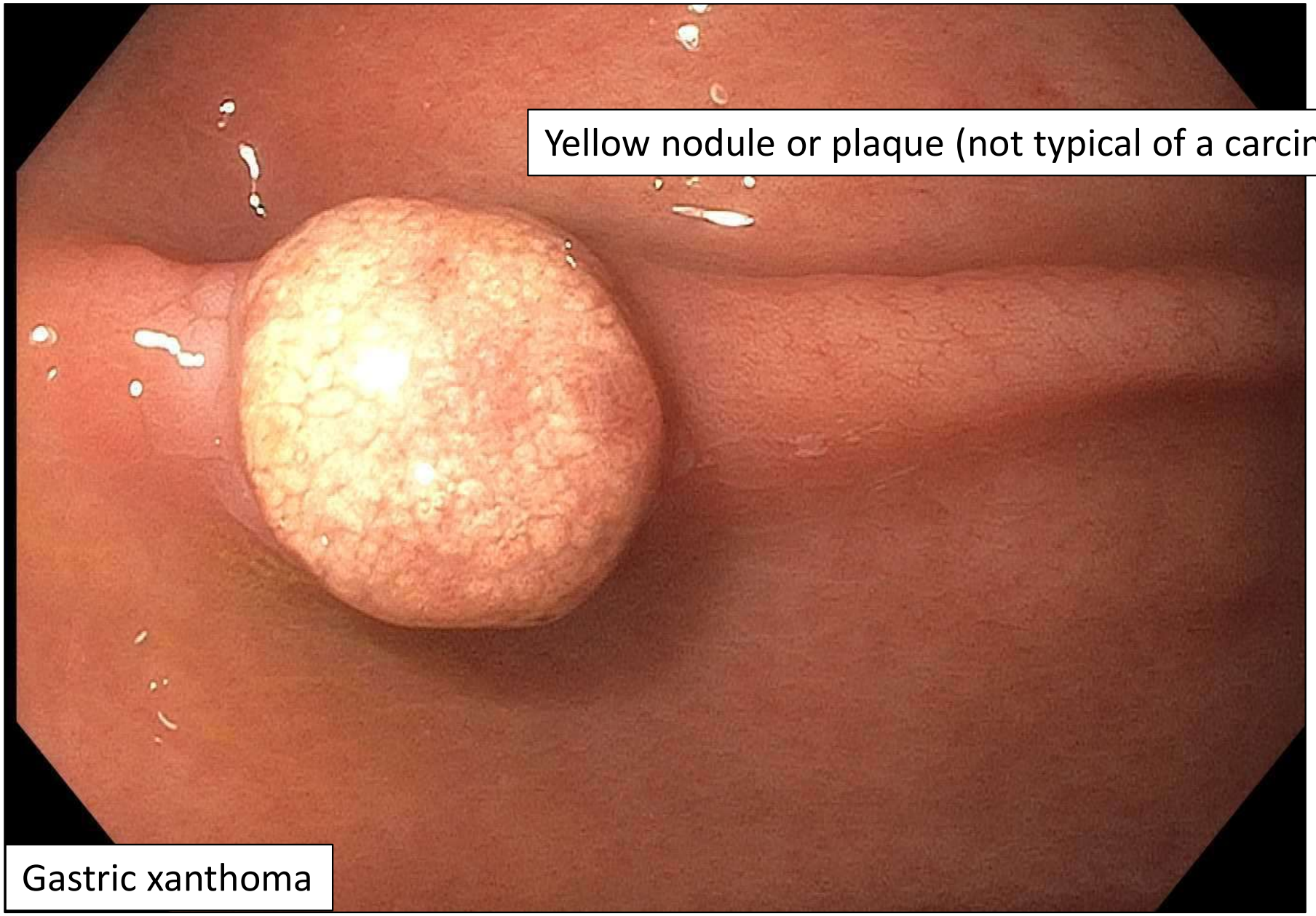
Nests merge with surface epithelium

Benign Mimics of Diffuse Gastric Cancer

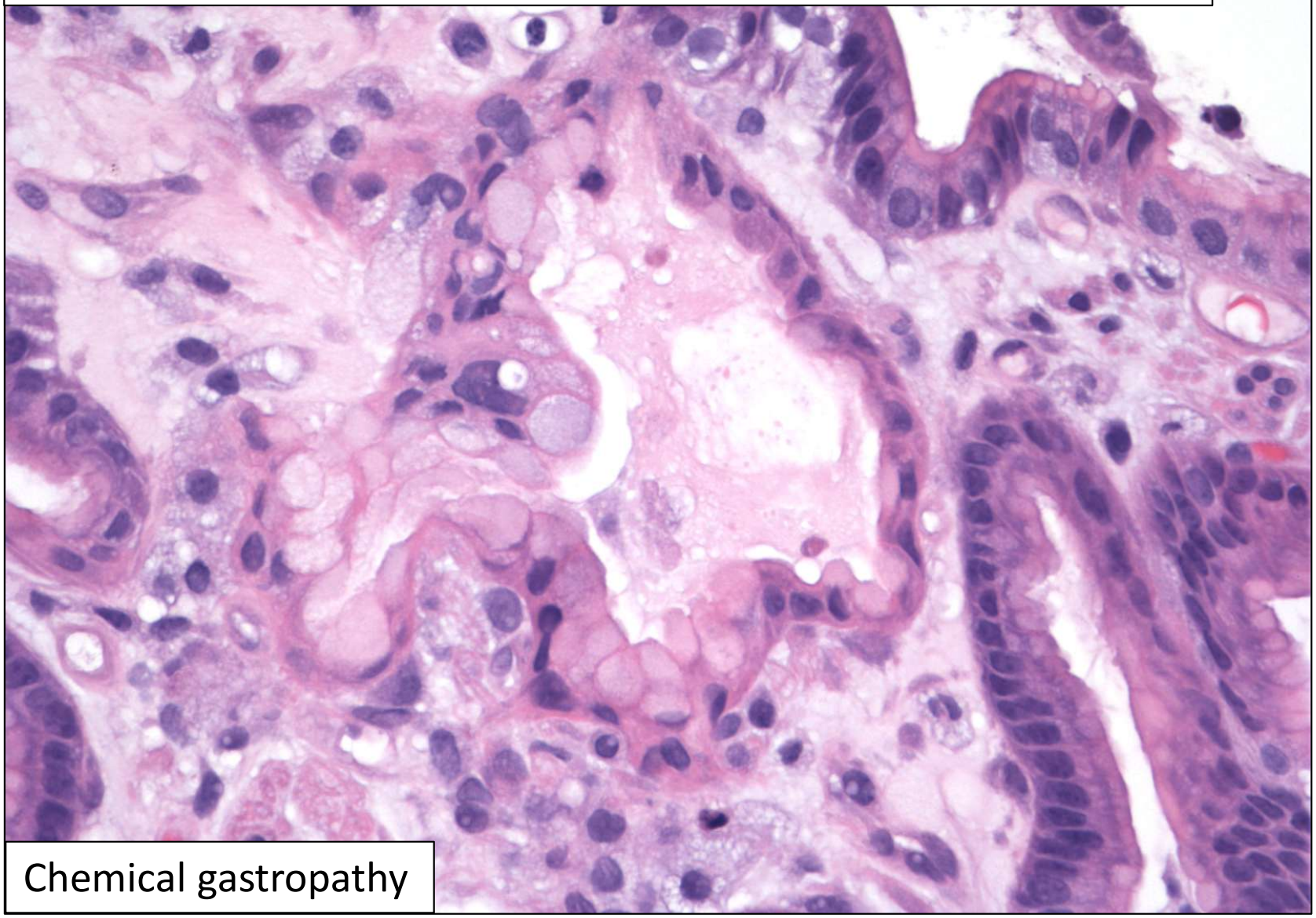
- Macrophages
  - Often associated with ruptured glands
  - Extruded mucin
  - Xanthomas
- Epithelial cells (benign signet ring cell change)
  - Stripped or tunneled foveolar cells
  - Mucus neck cells
  - Degenerative change associated with ulcers and ischemia


Gastric xanthoma


Macrophages most numerous superficially
Foamy cytoplasm with central nuclei

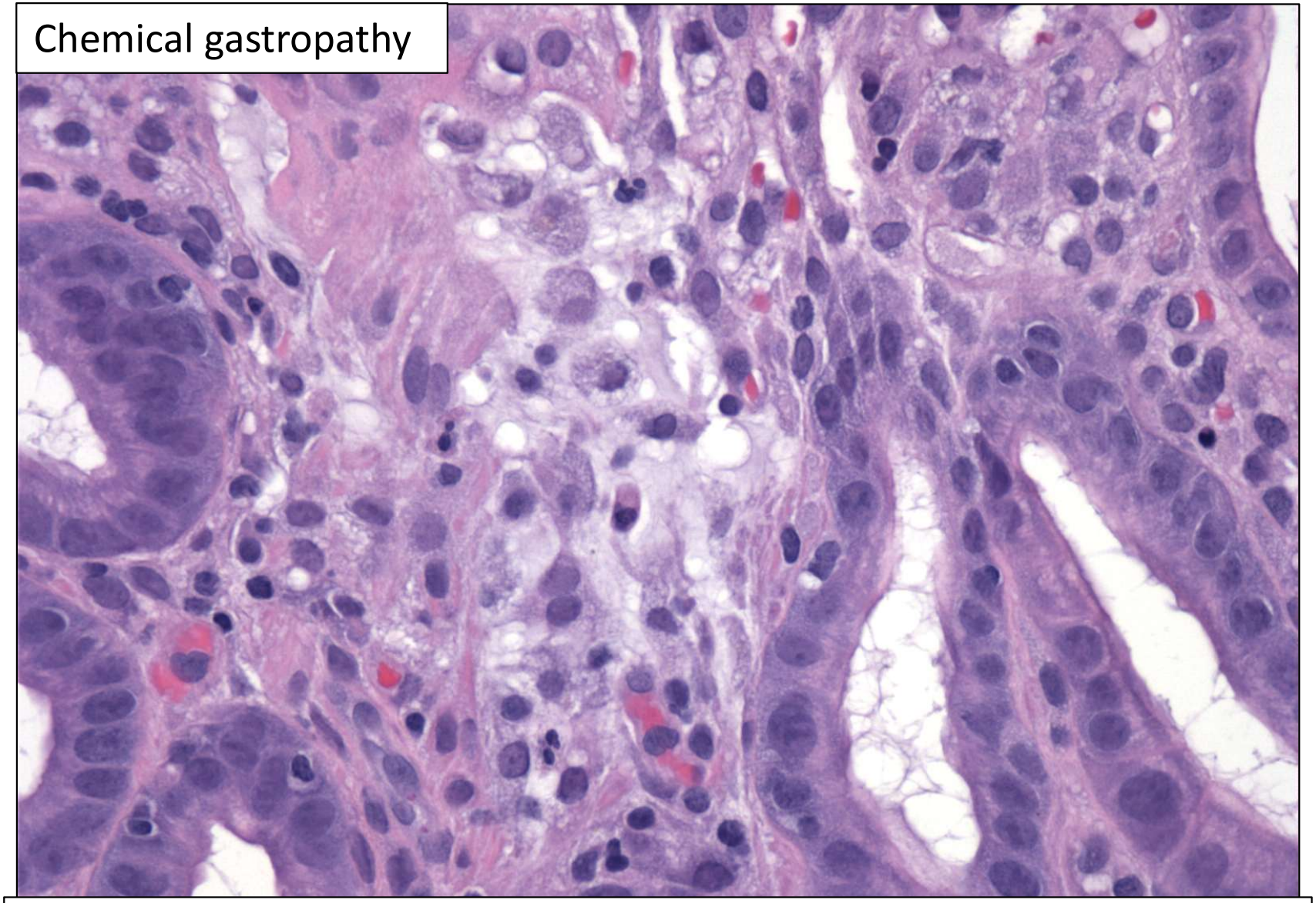

Yellow nodule or plaque (not typical of a carcinoma)
Gastric xanthoma

Injured glands rupture and extrude mucin, eliciting macrophages



Chemical gastropathy

Chemical gastropathy



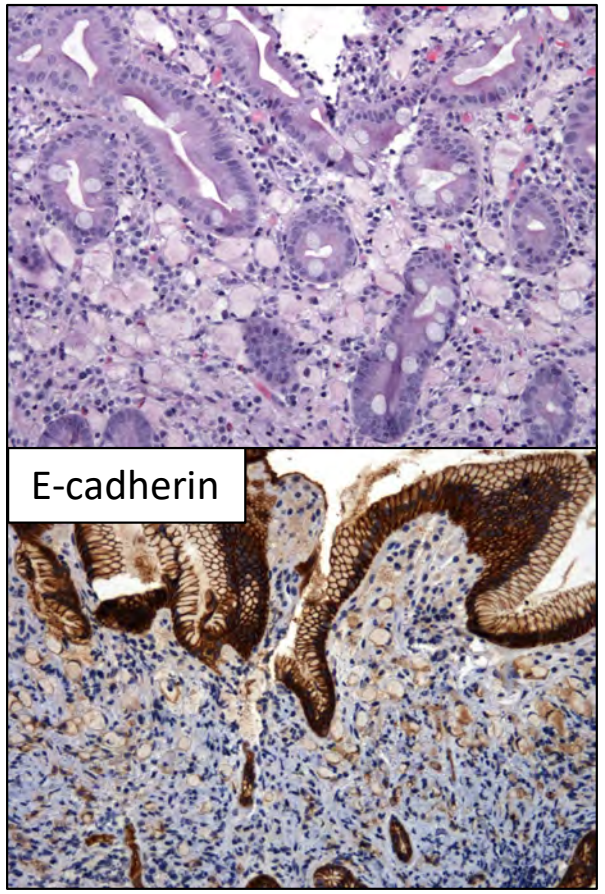
Muciphages often associated with extracellular mucin and inflammation

Benign Mimics of Diffuse Gastric Cancer

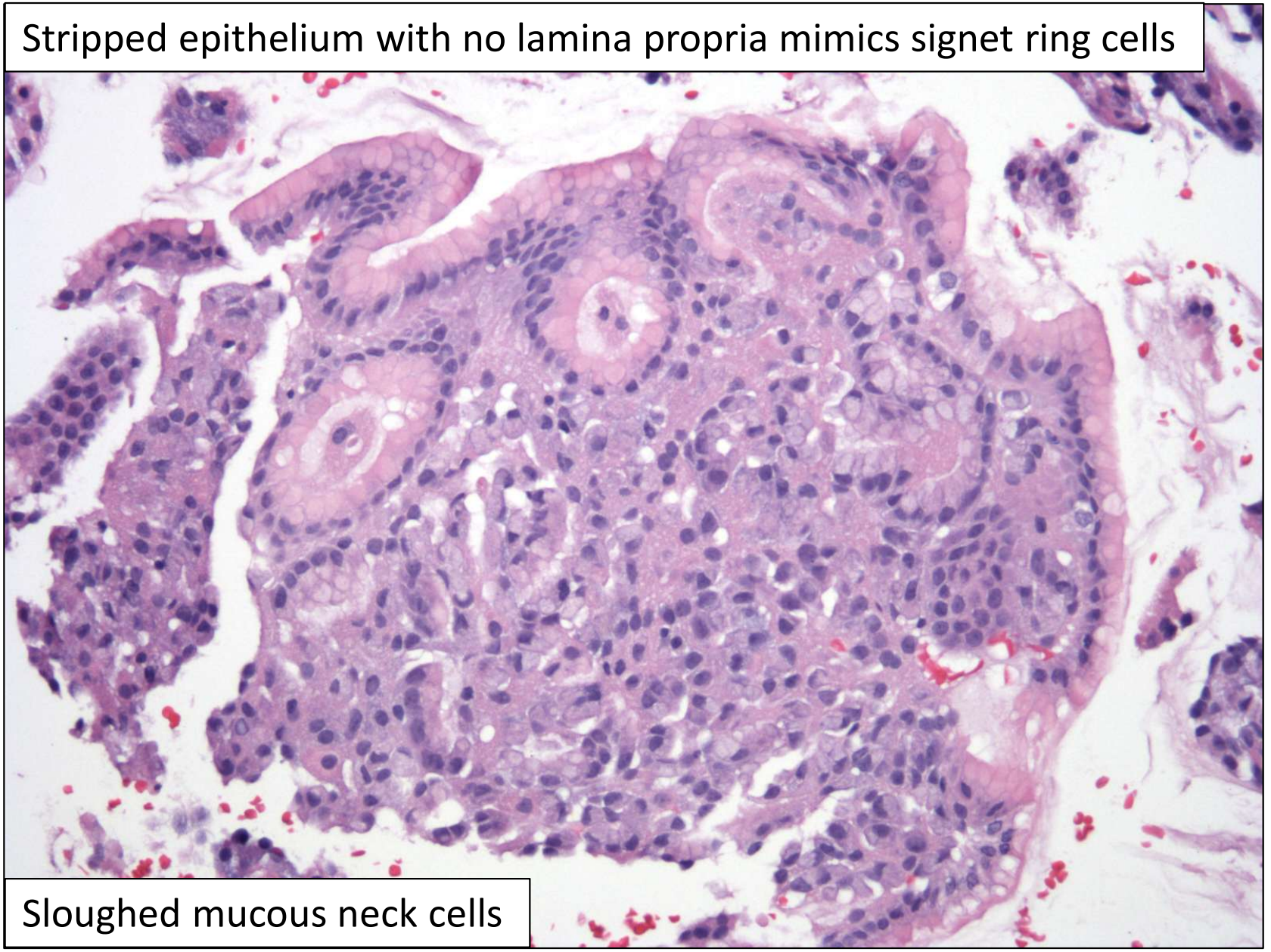
- Macrophages
  - Often associated with ruptured glands
  - Extruded mucin
  - Xanthomas
- Epithelial cells (benign signet ring cell change)
  - Stripped or tunneled foveolar cells
  - Mucus neck cells
  - Degenerative change associated with ulcers and ischemia

Rules of Diffuse Gastric Cancer

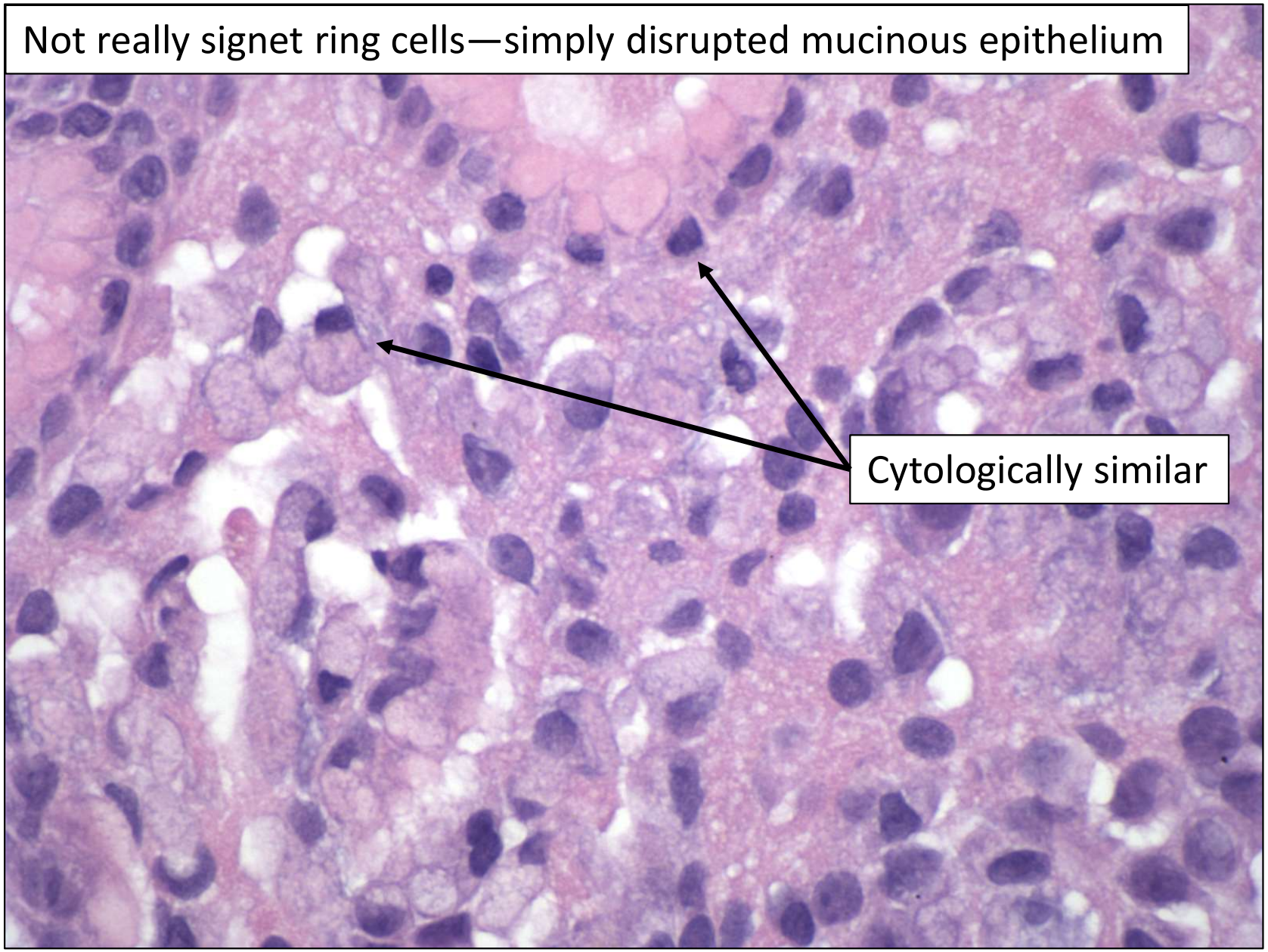
- Cells are not in the lumen
- Lamina propria should be visible between tumor cells
- Infiltrates lamina propria as single cells
- Not nested
- Decreased/absent E-cadherin

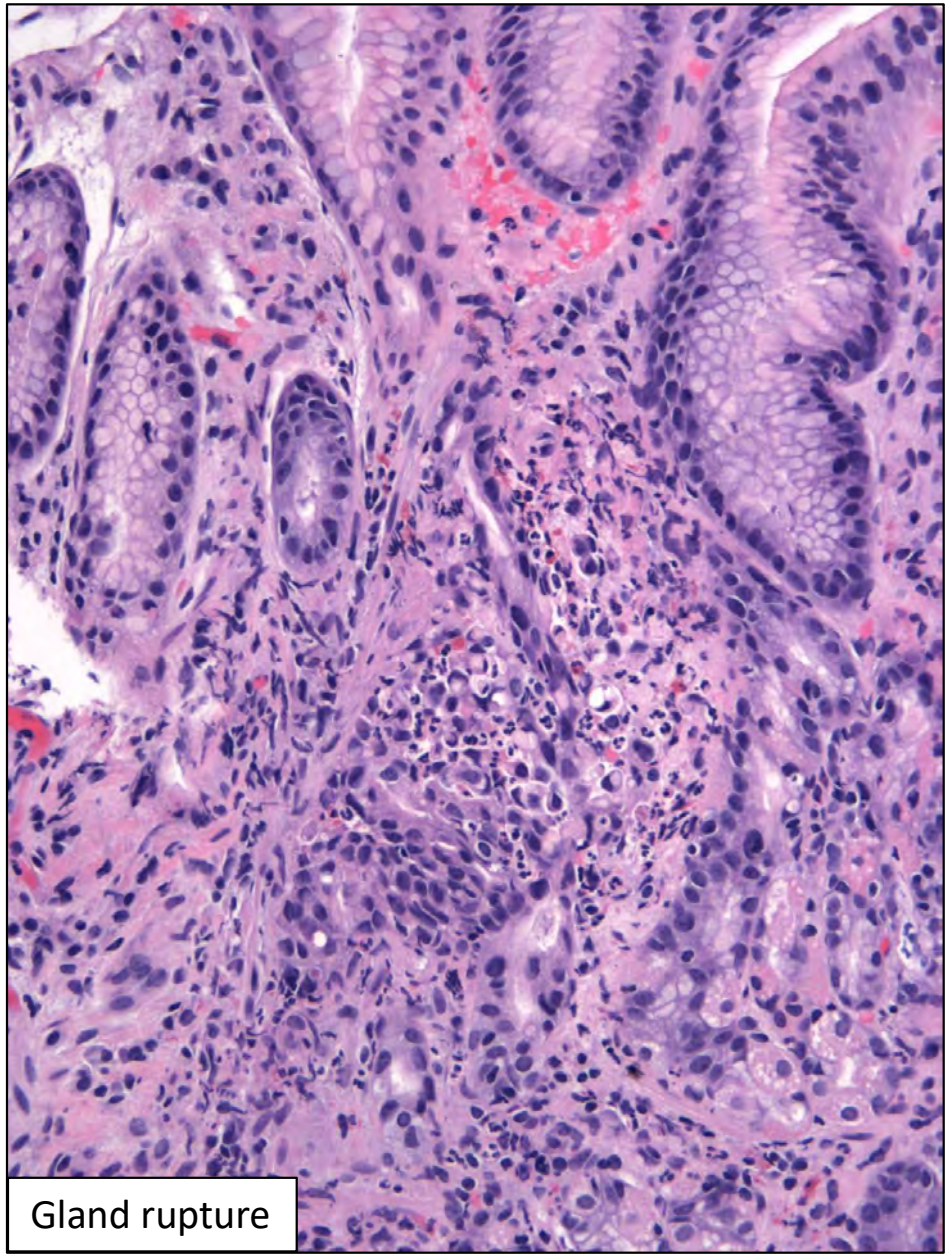


Stripped epithelium with no lamina propria mimics signet ring cells

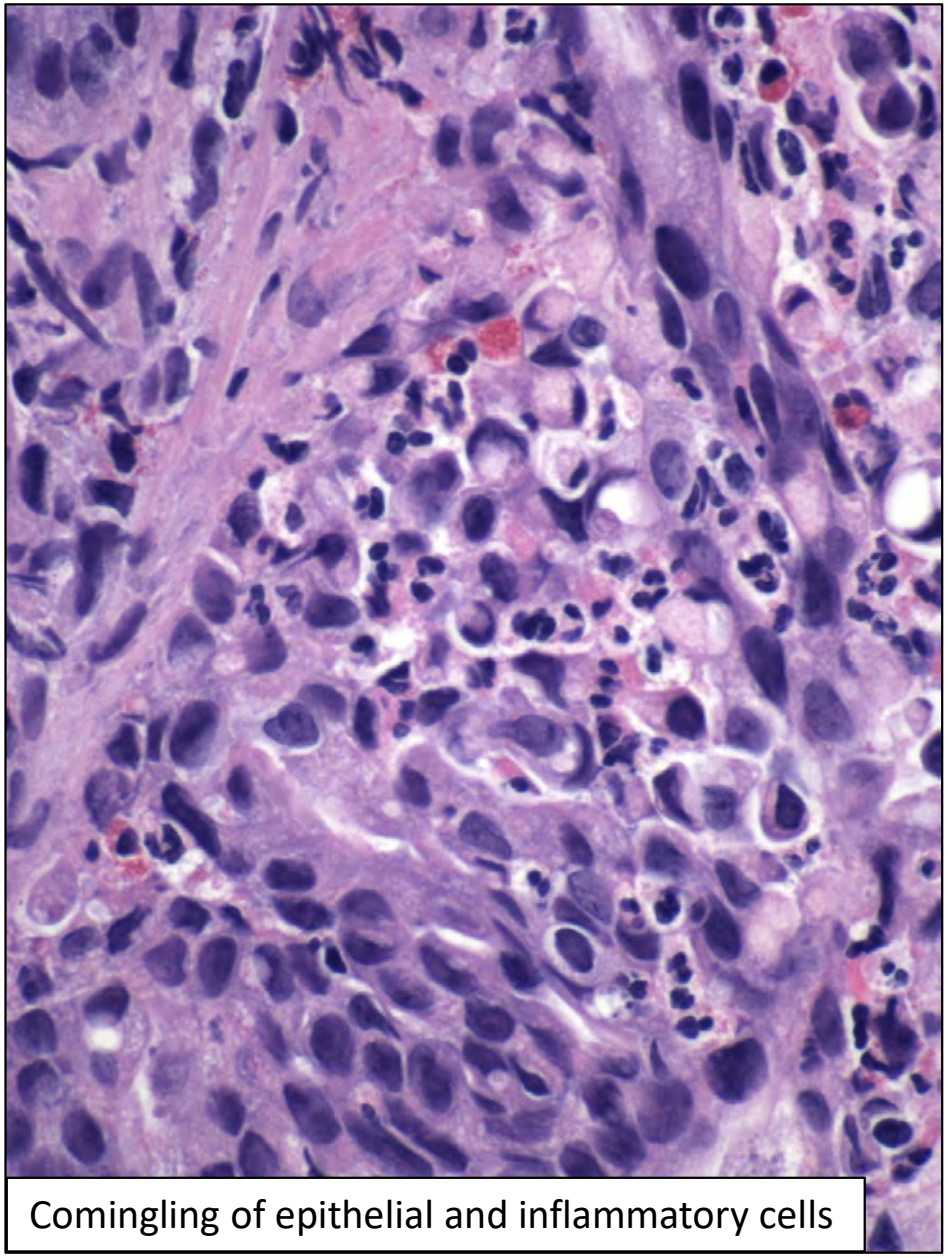


Sloughed mucous neck cells


Not really signet ring cells—simply disrupted mucinous epithelium
Cytologically similar

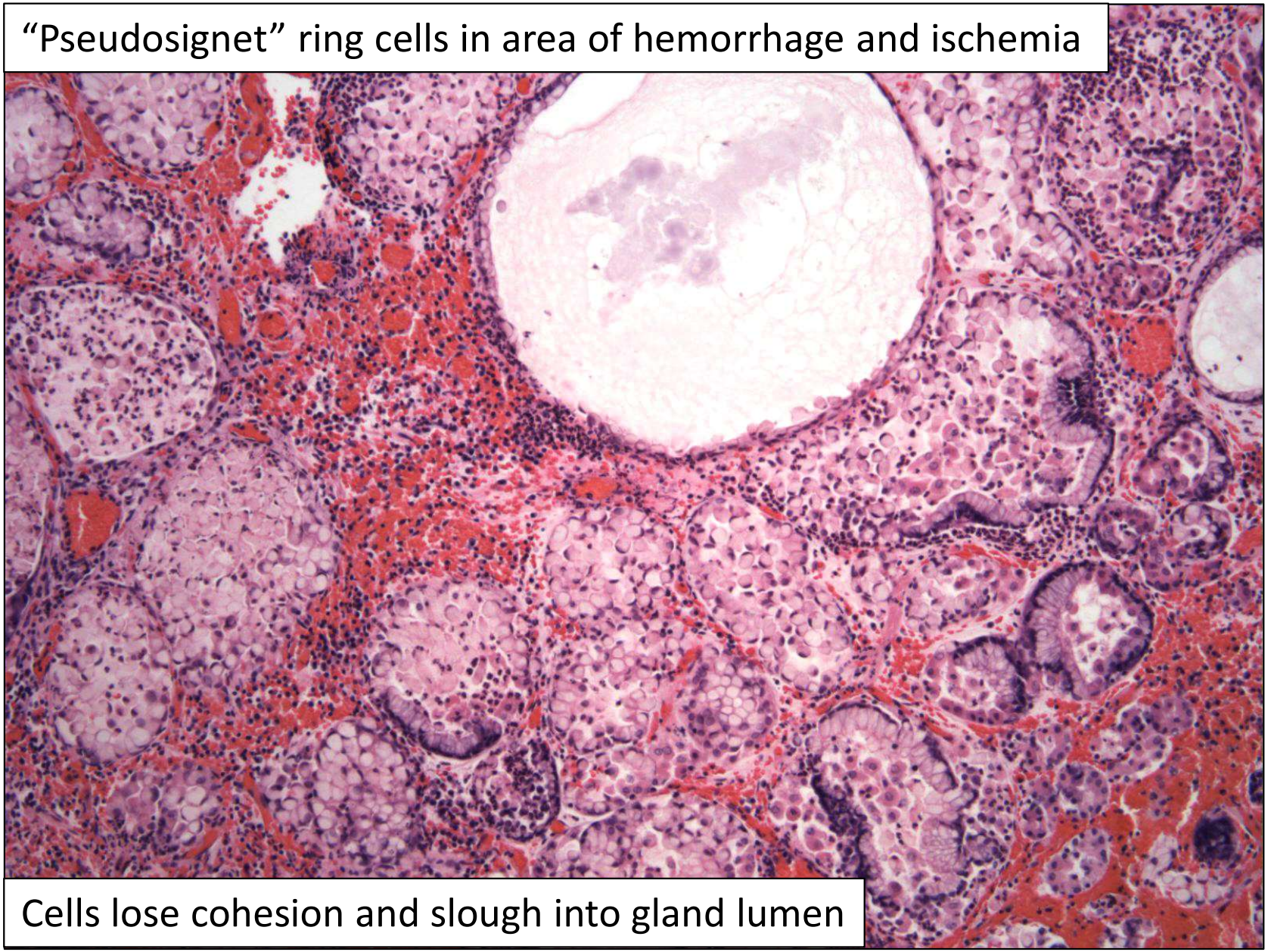


Gland rupture

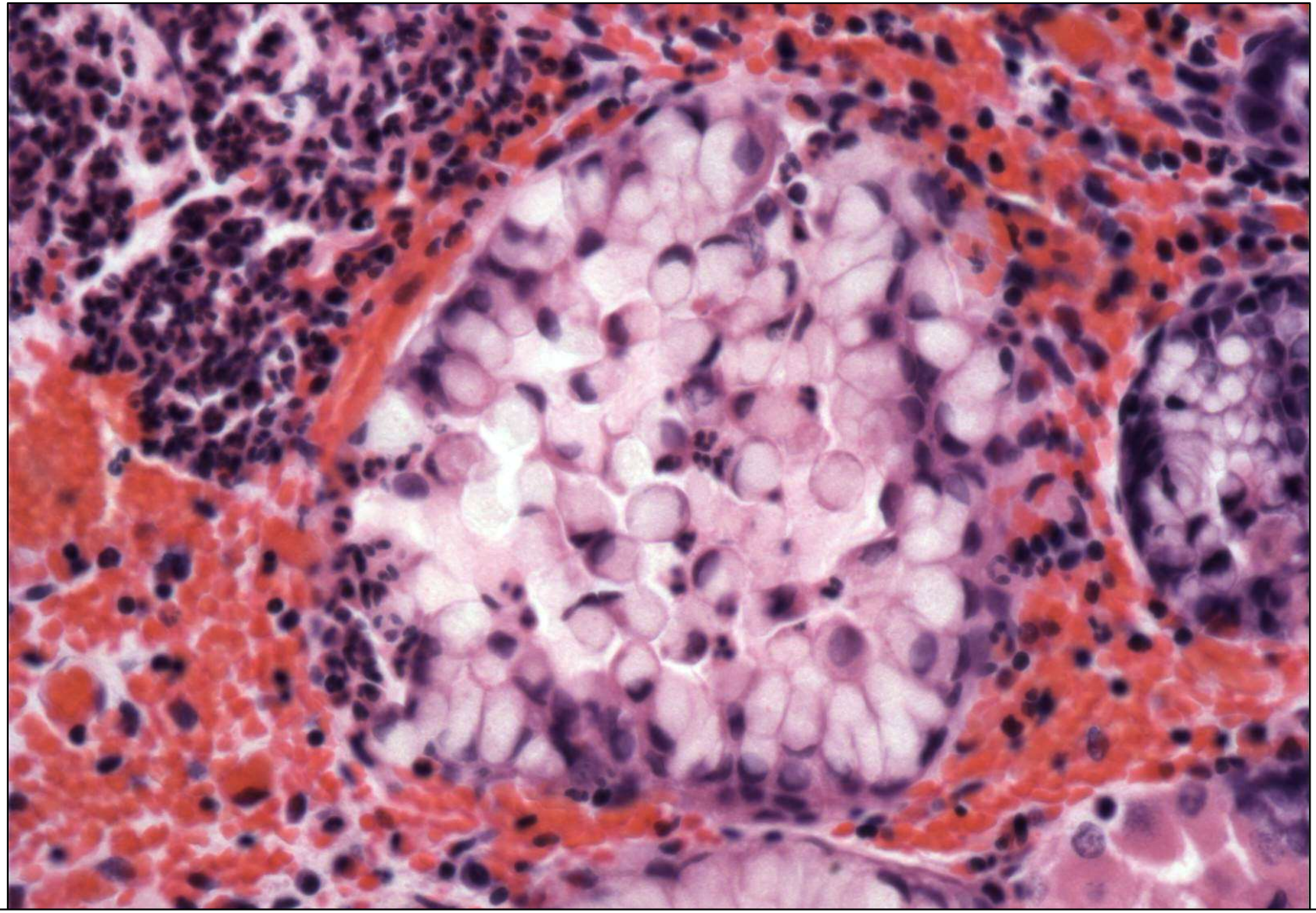


Comingling of epithelial and inflammatory cells

“Pseudosignet” ring cells in area of hemorrhage and ischemia

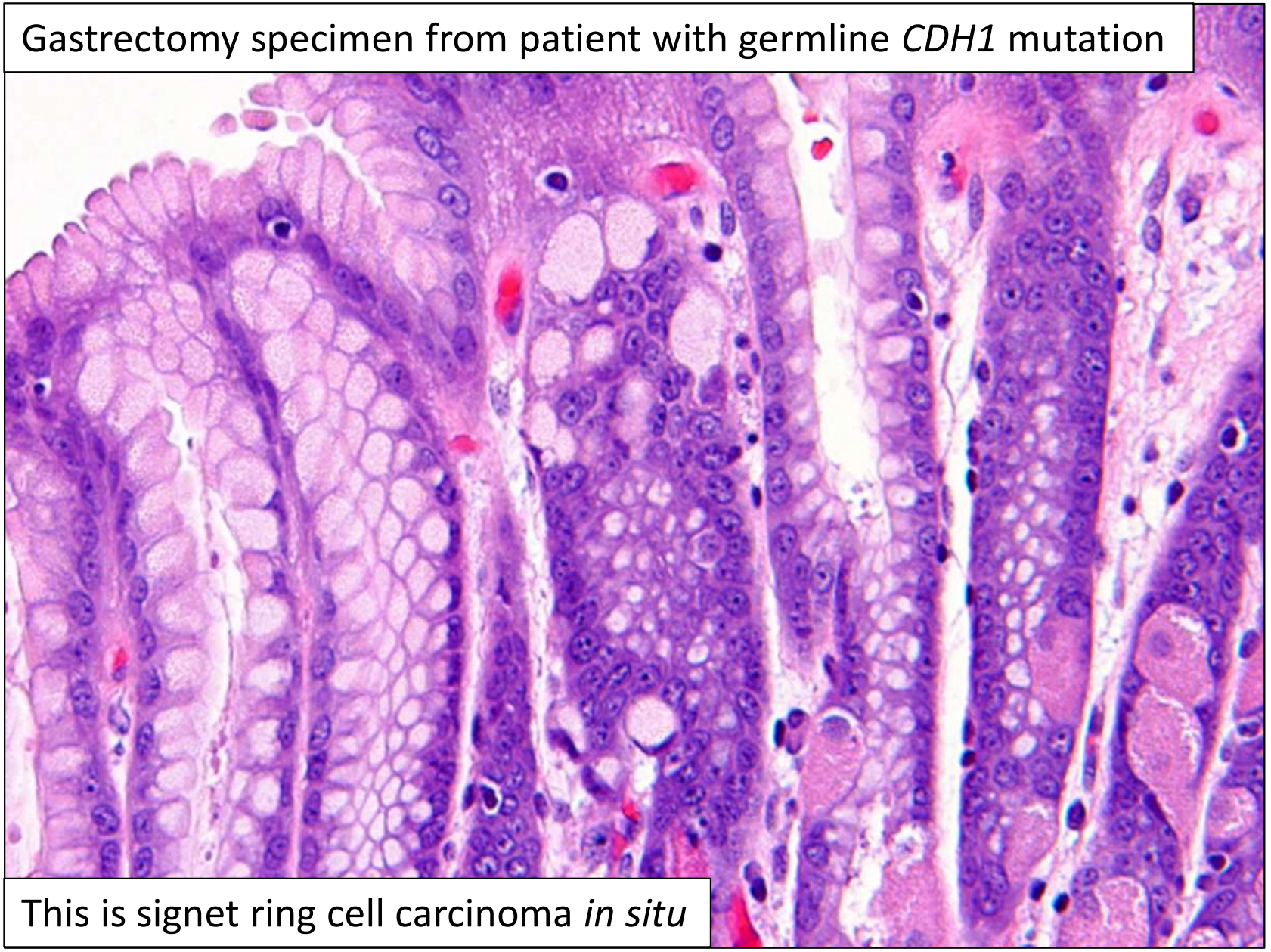


Cells lose cohesion and slough into gland lumen



Pseudosignet ring cells confined to glands (E-cadherin staining is retained)

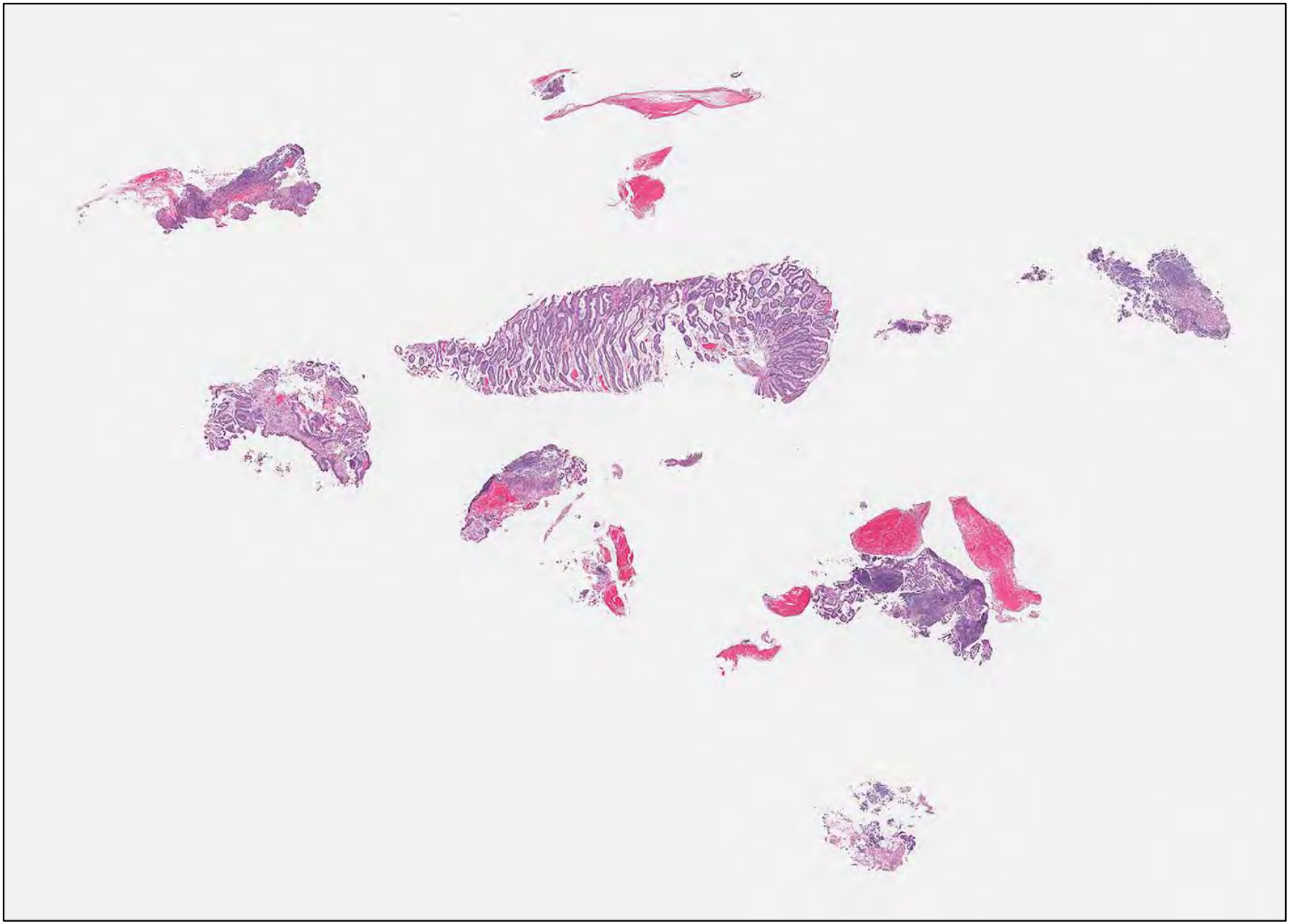
Gastrectomy specimen from patient with germline *CDH1* mutation

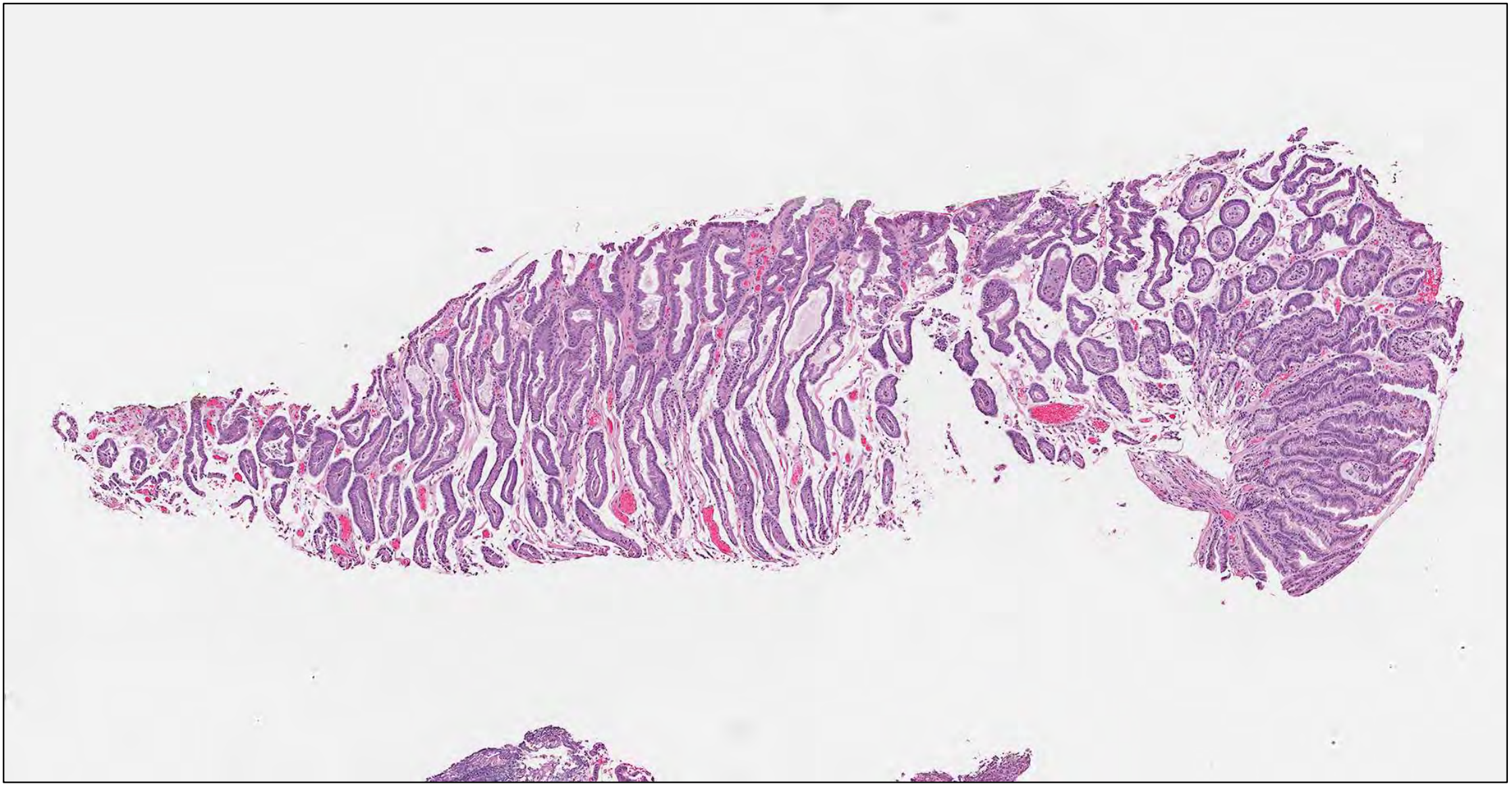


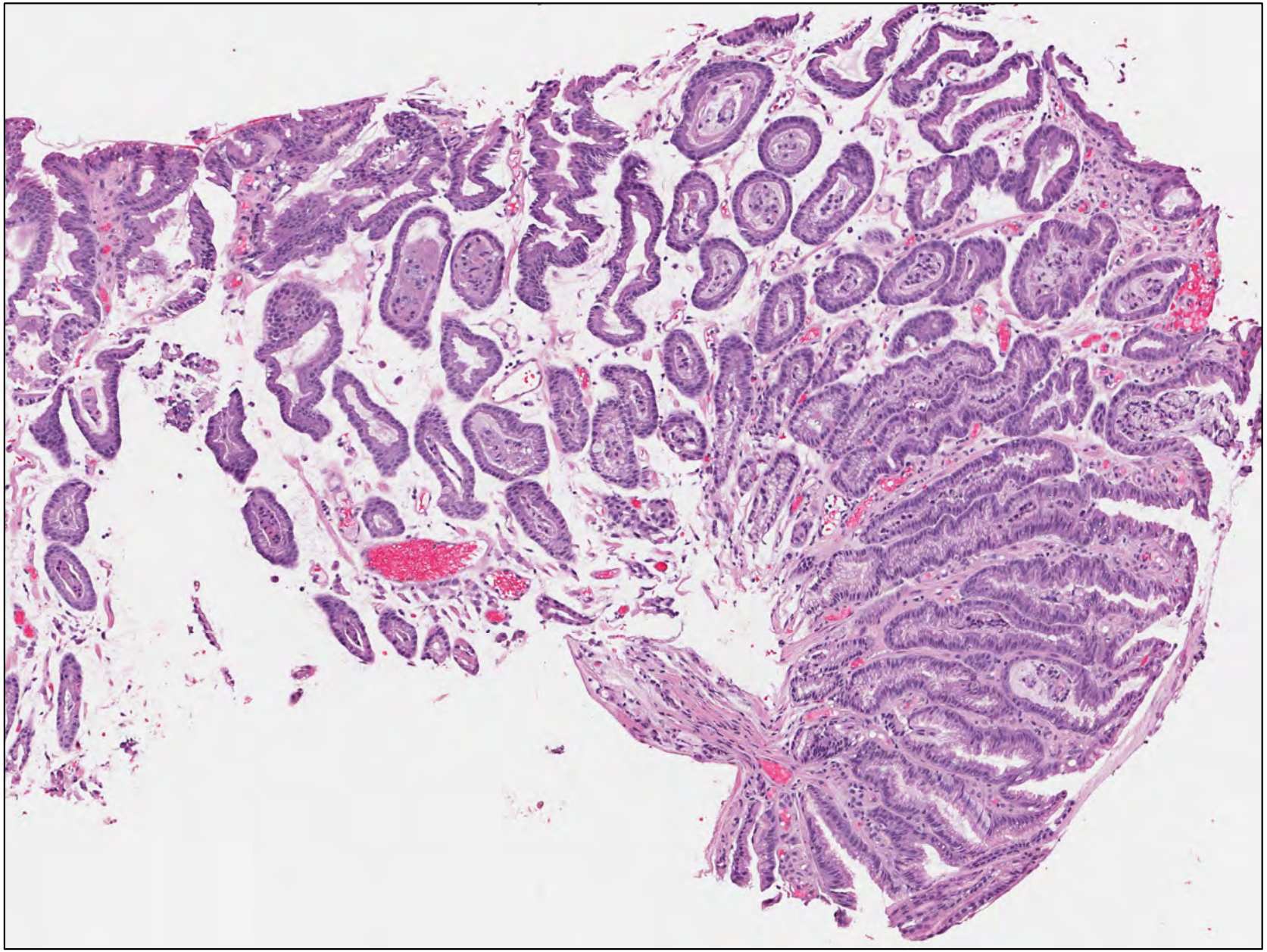
This is signet ring cell carcinoma *in situ*

Case

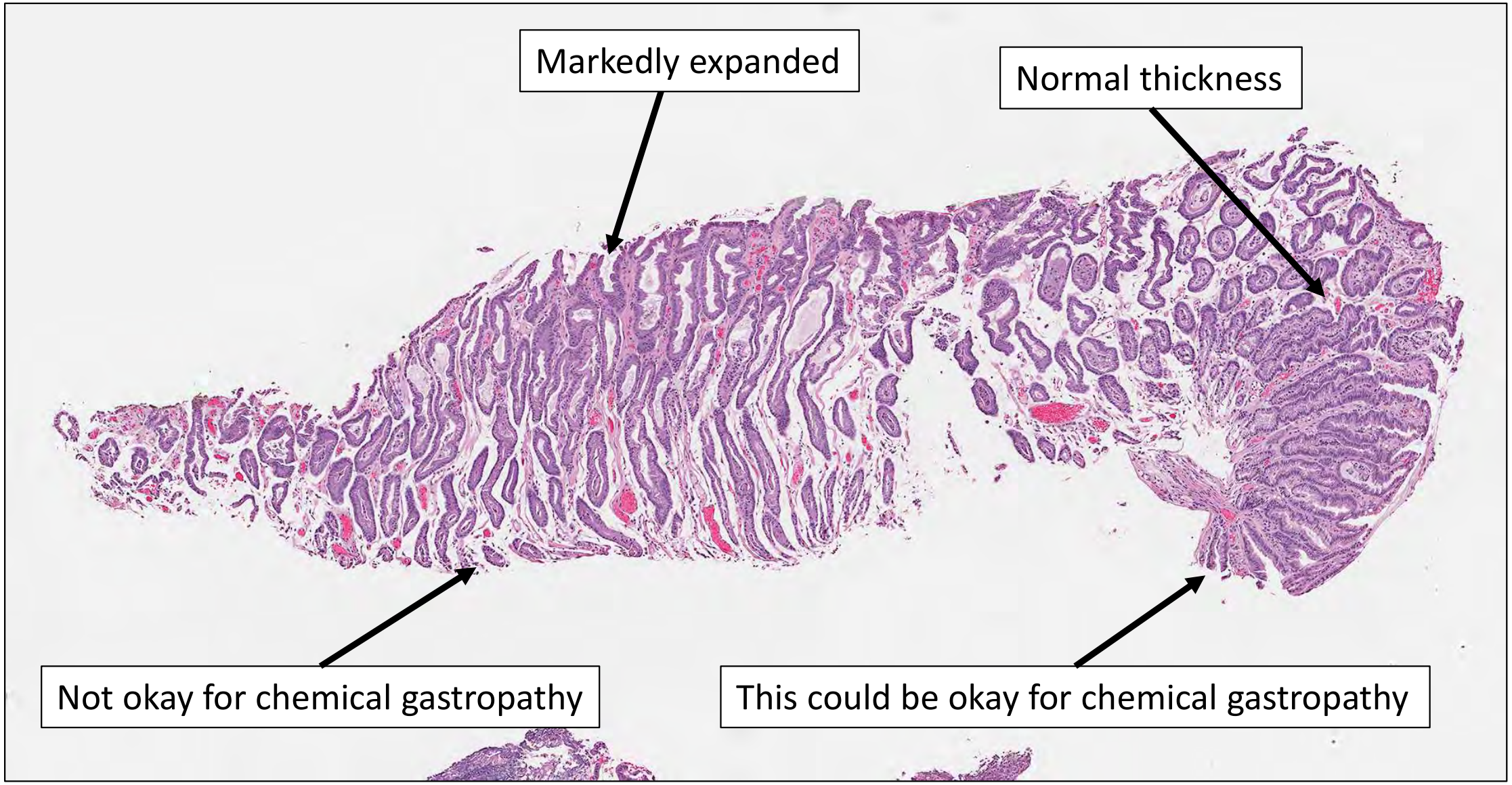
- 50-year-old male with vague abdominal pain and weight loss
- Upper endoscopy
  - Ulcer
  - Thickened surrounding folds



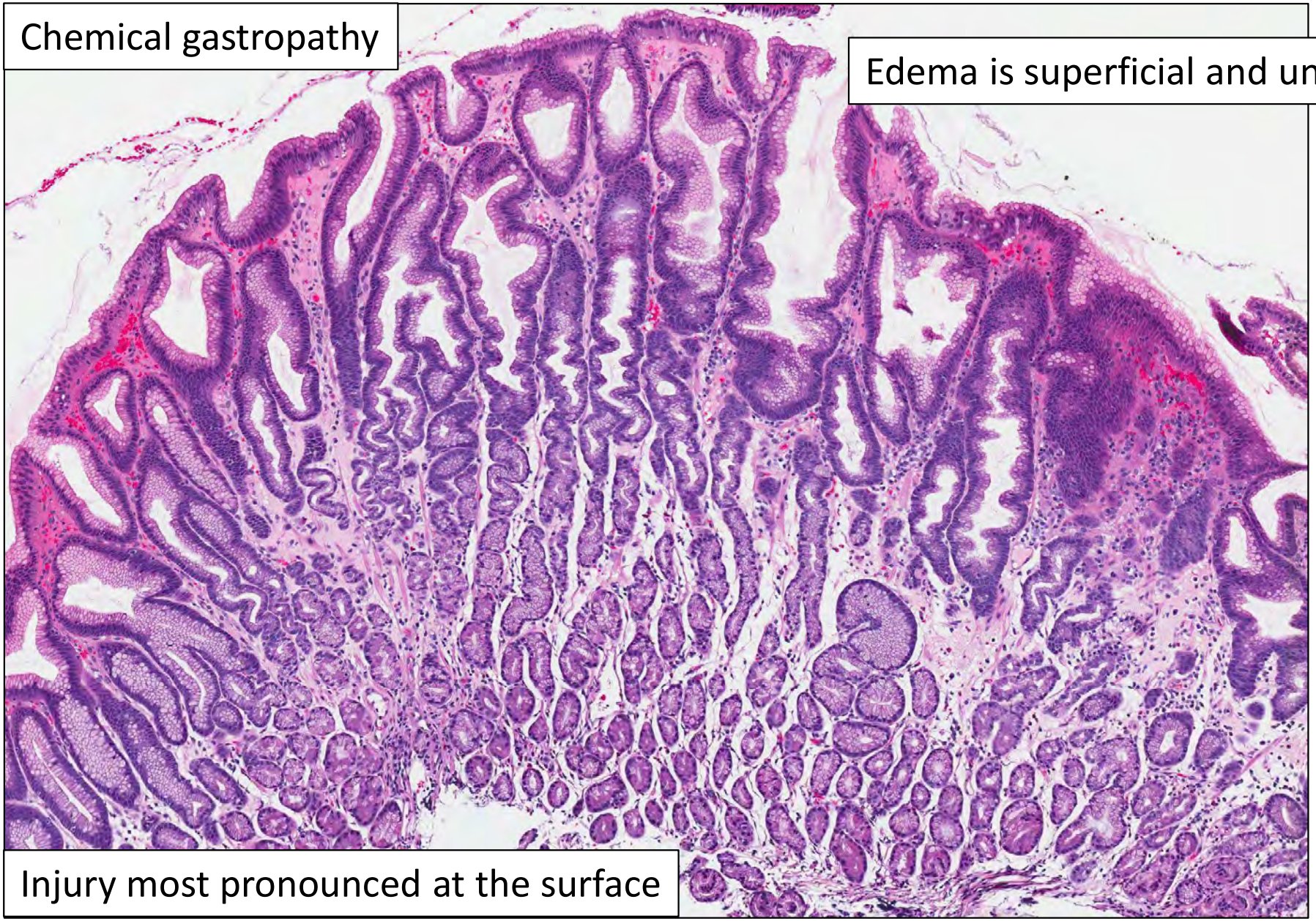




Look more closely when you see patchy edema or cellularity, especially if deep

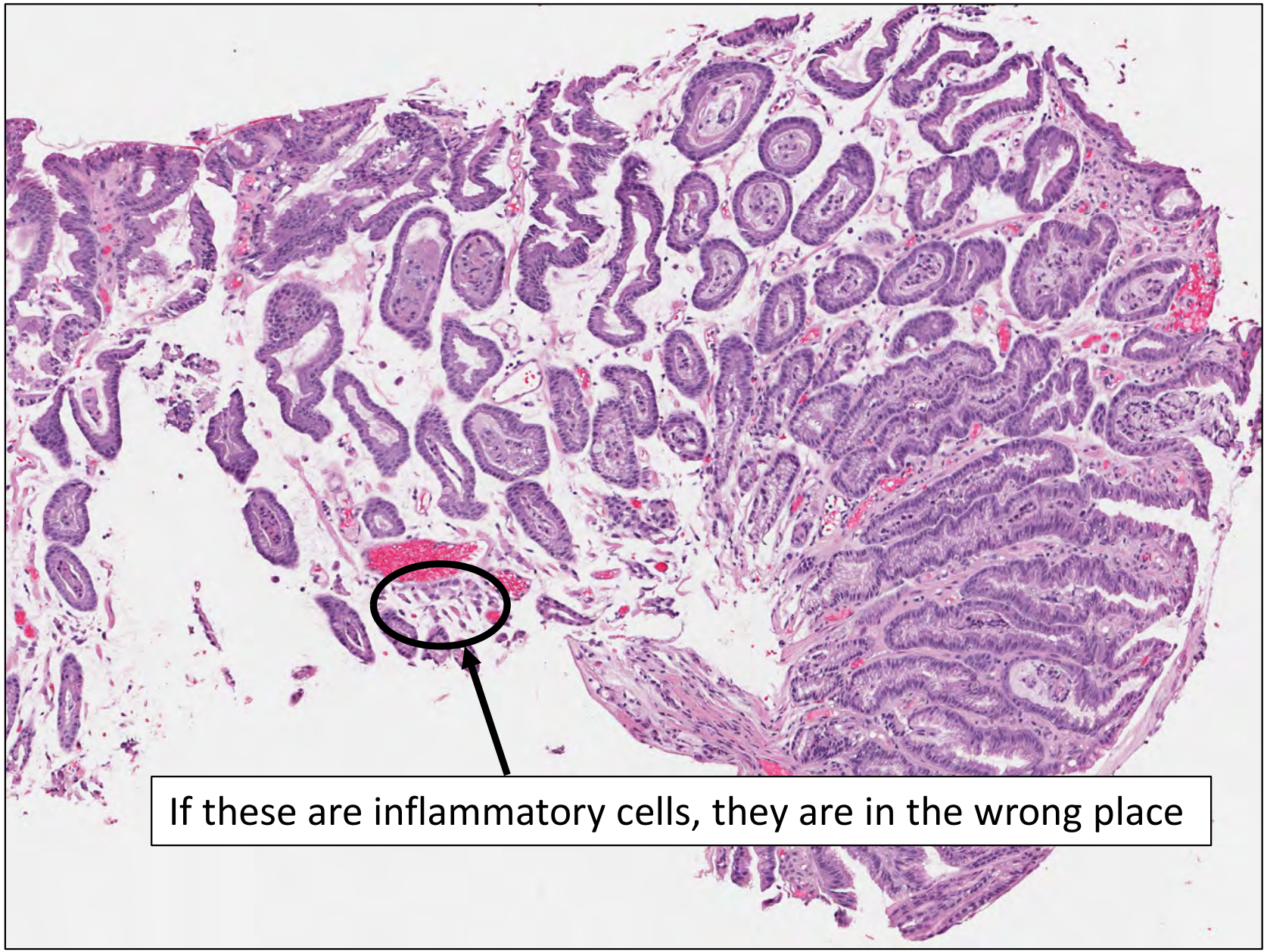

Markedly expanded
Normal thickness
Not okay for chemical gastropathy
This could be okay for chemical gastropathy

Chemical gastropathy

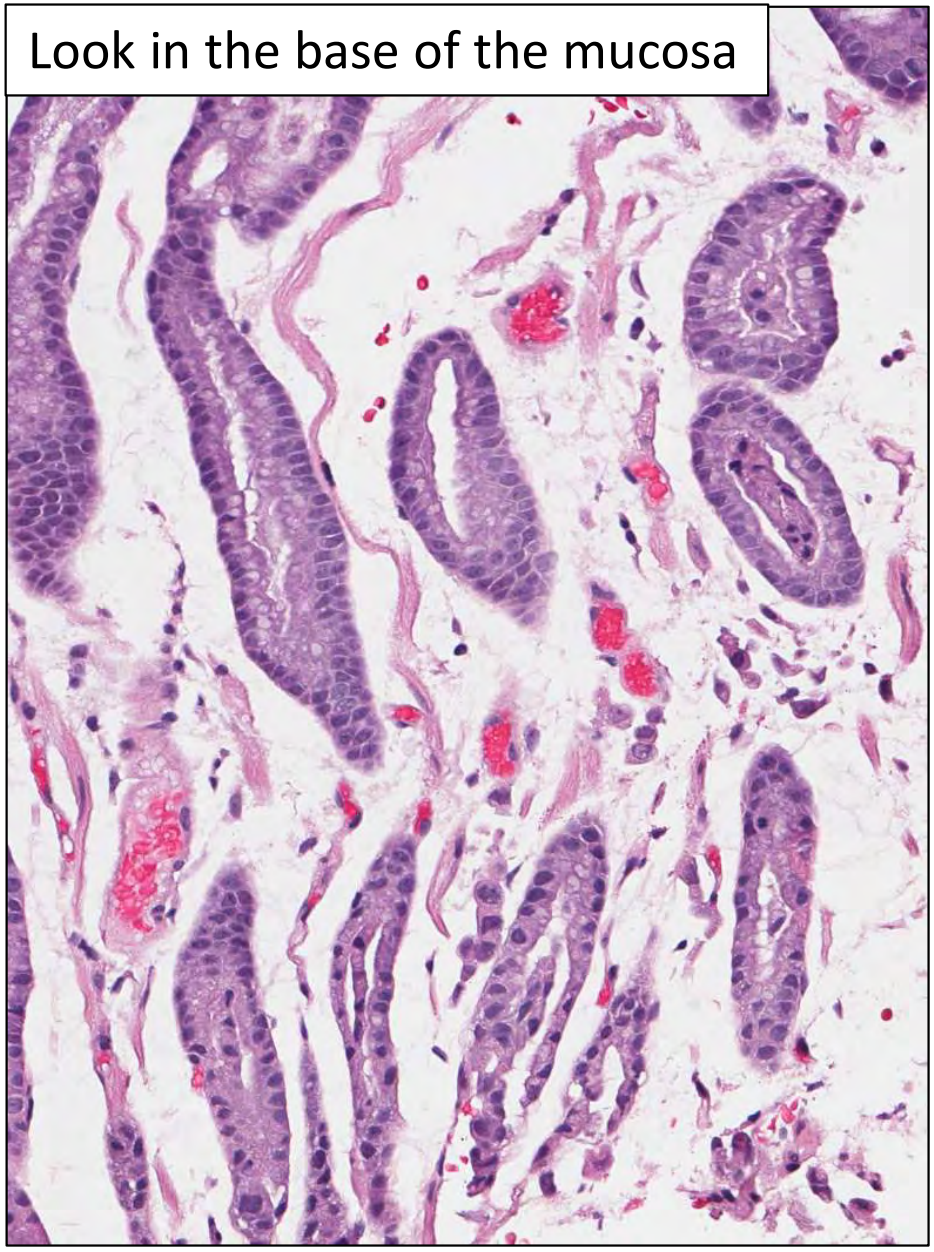


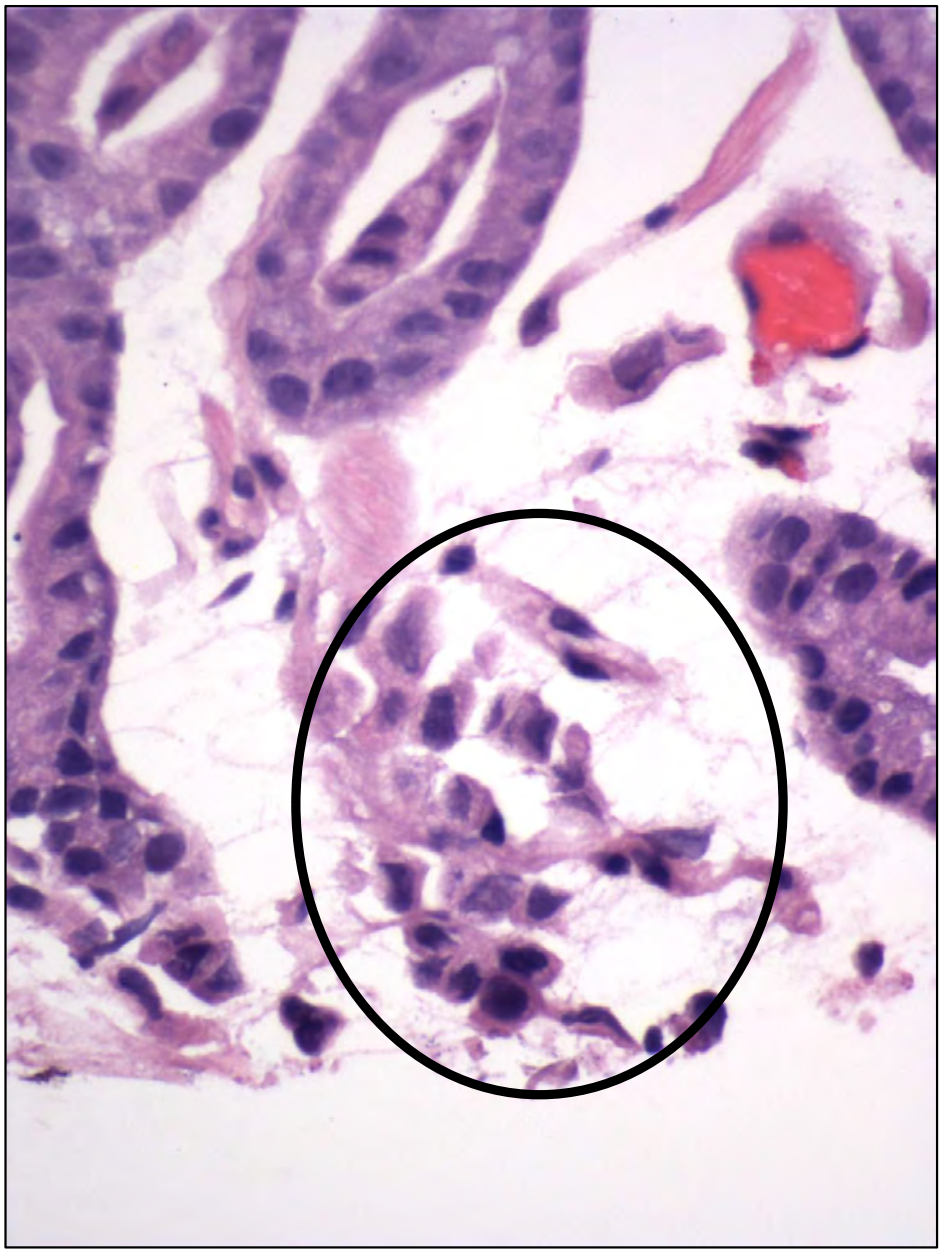
Edema is superficial and uniform

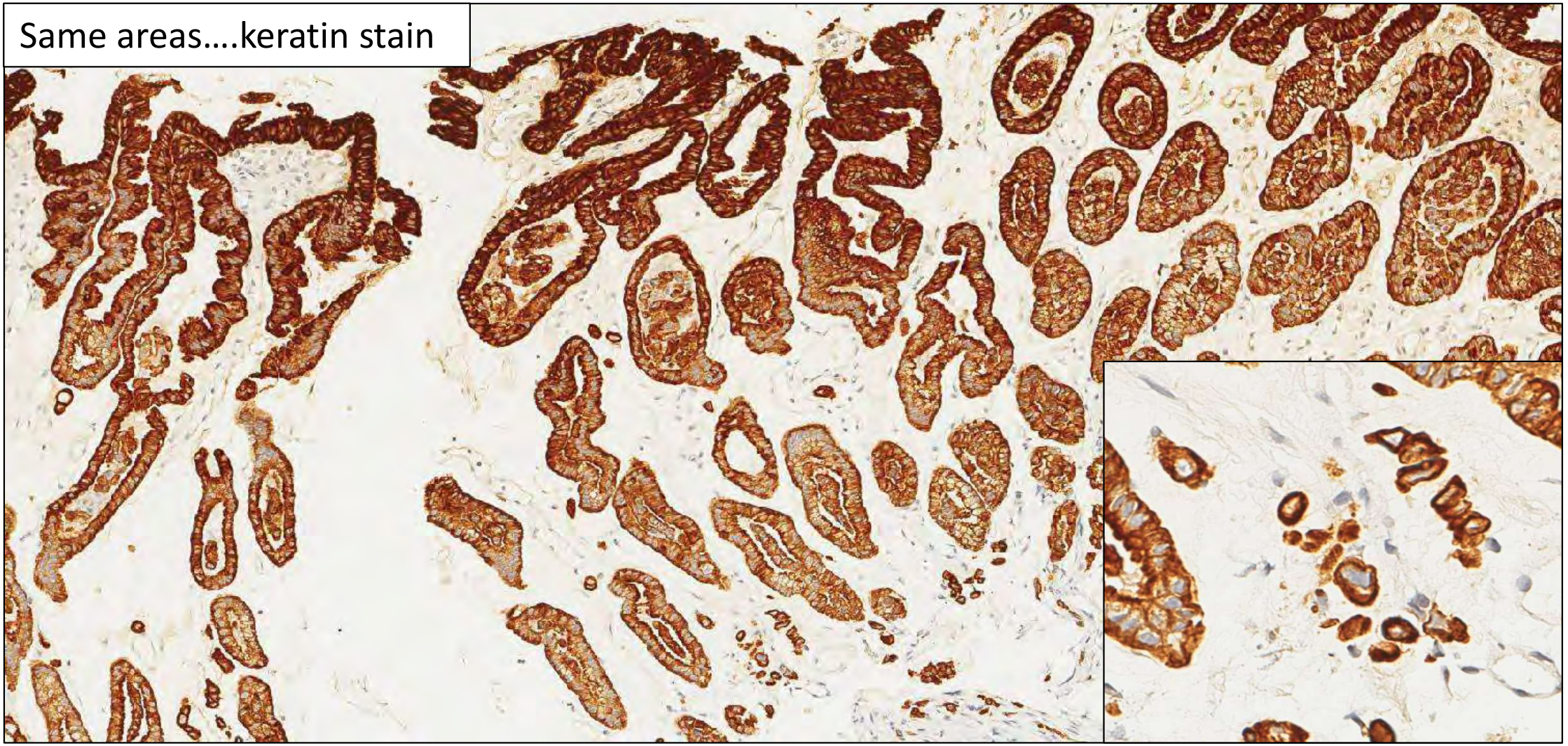
Injury most pronounced at the surface

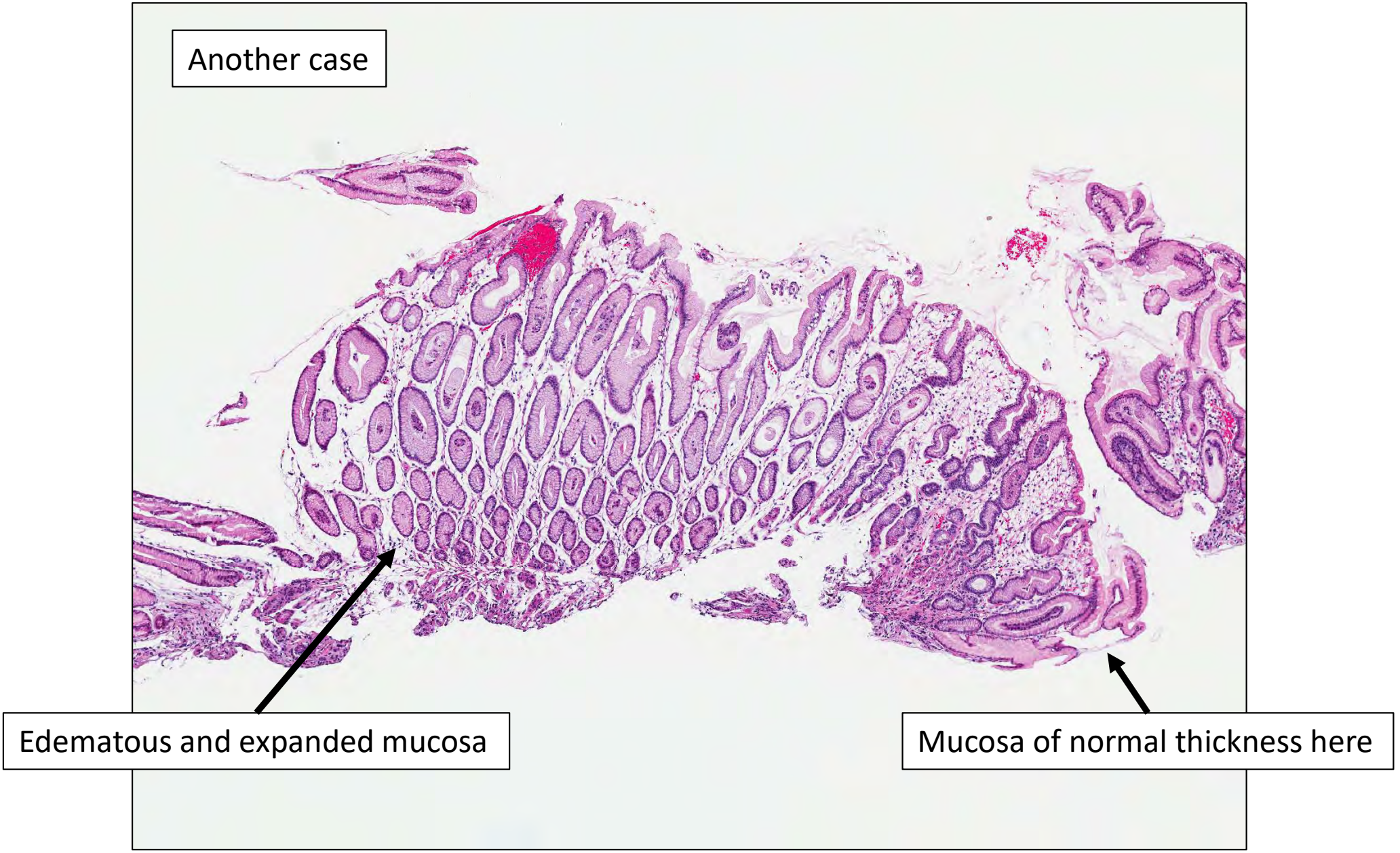

If these are inflammatory cells, they are in the wrong place

Look in the base of the mucosa

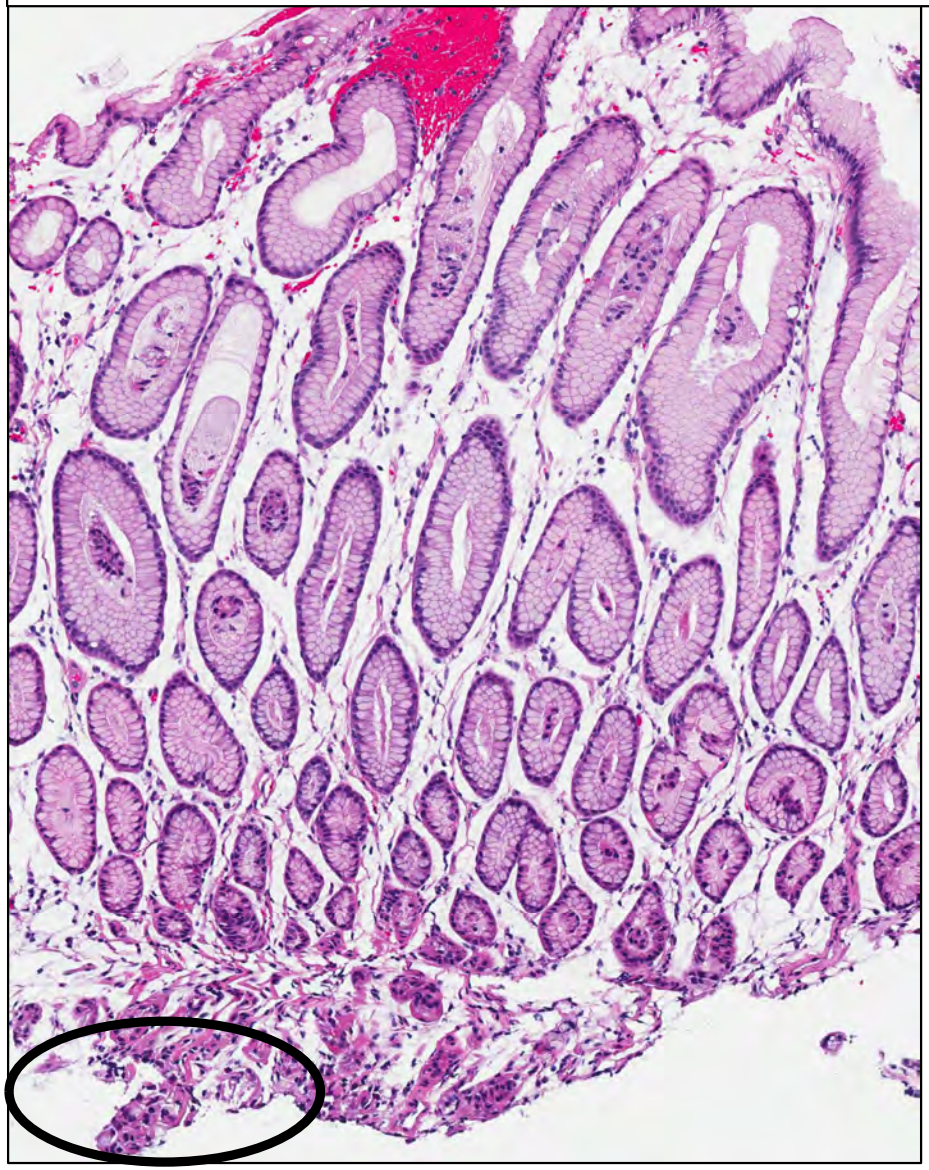


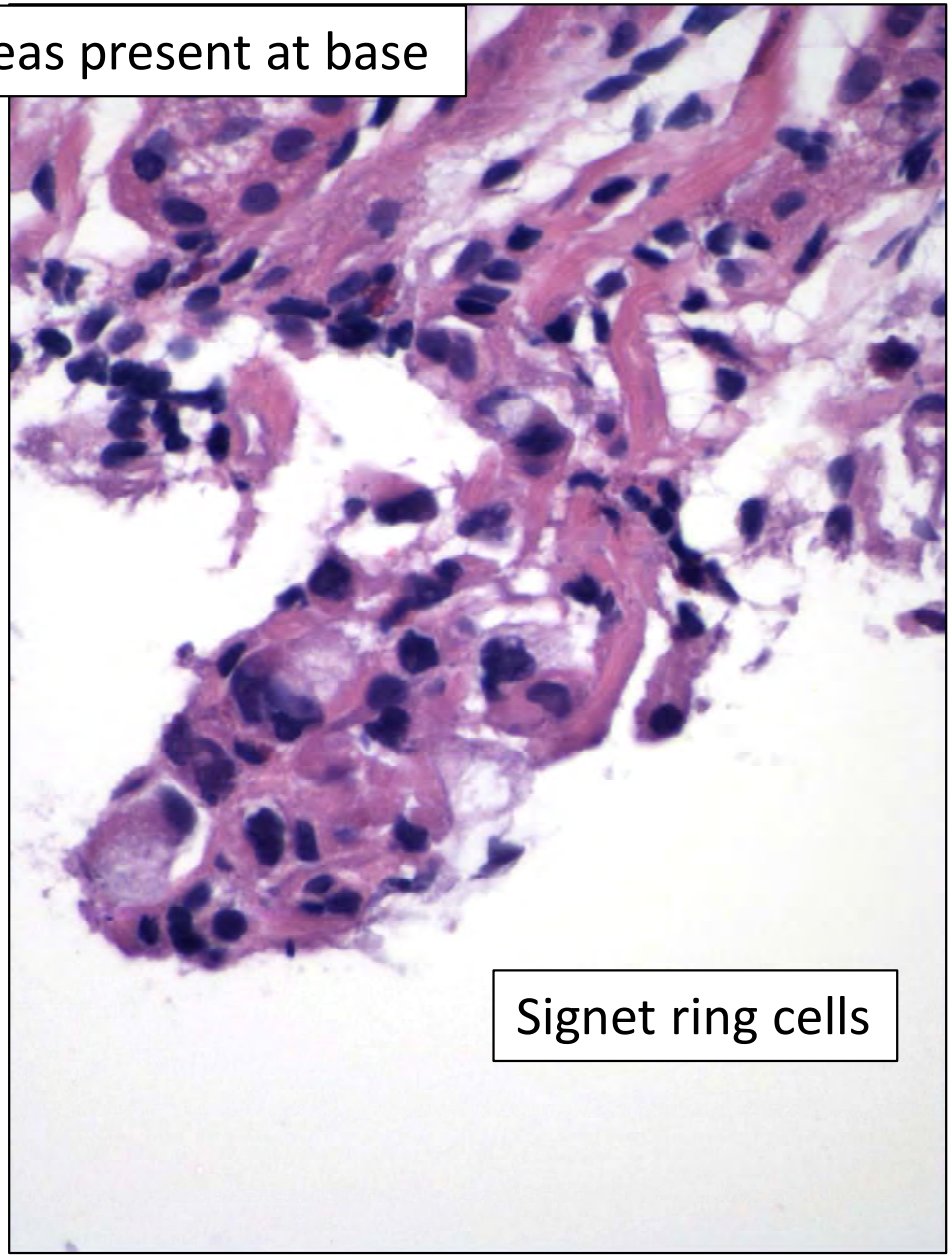



Same areas….keratin stain


Another case
Edematous and expanded mucosa
Mucosa of normal thickness here

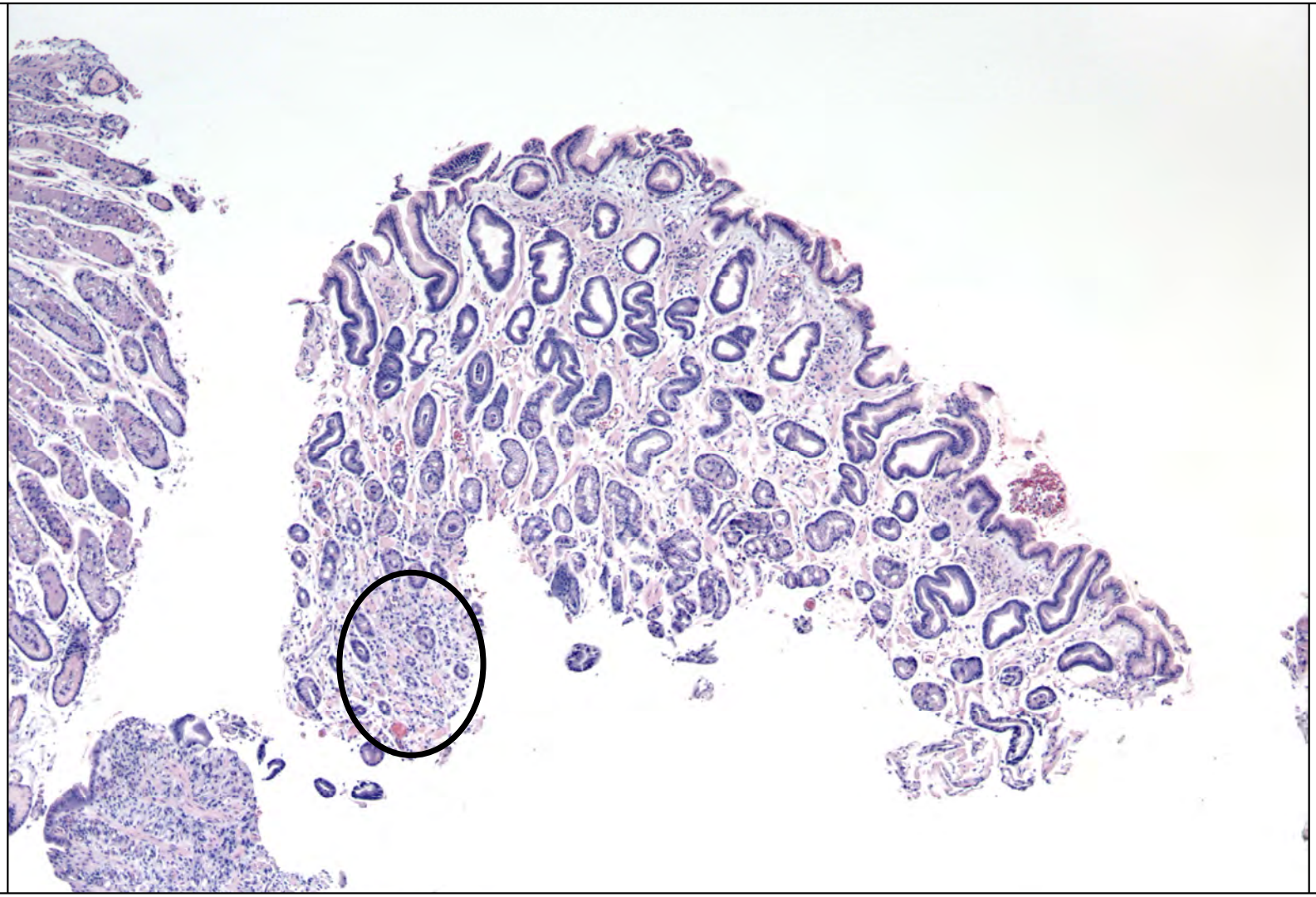
Edematous mucosa is empty, but cellular areas present at base



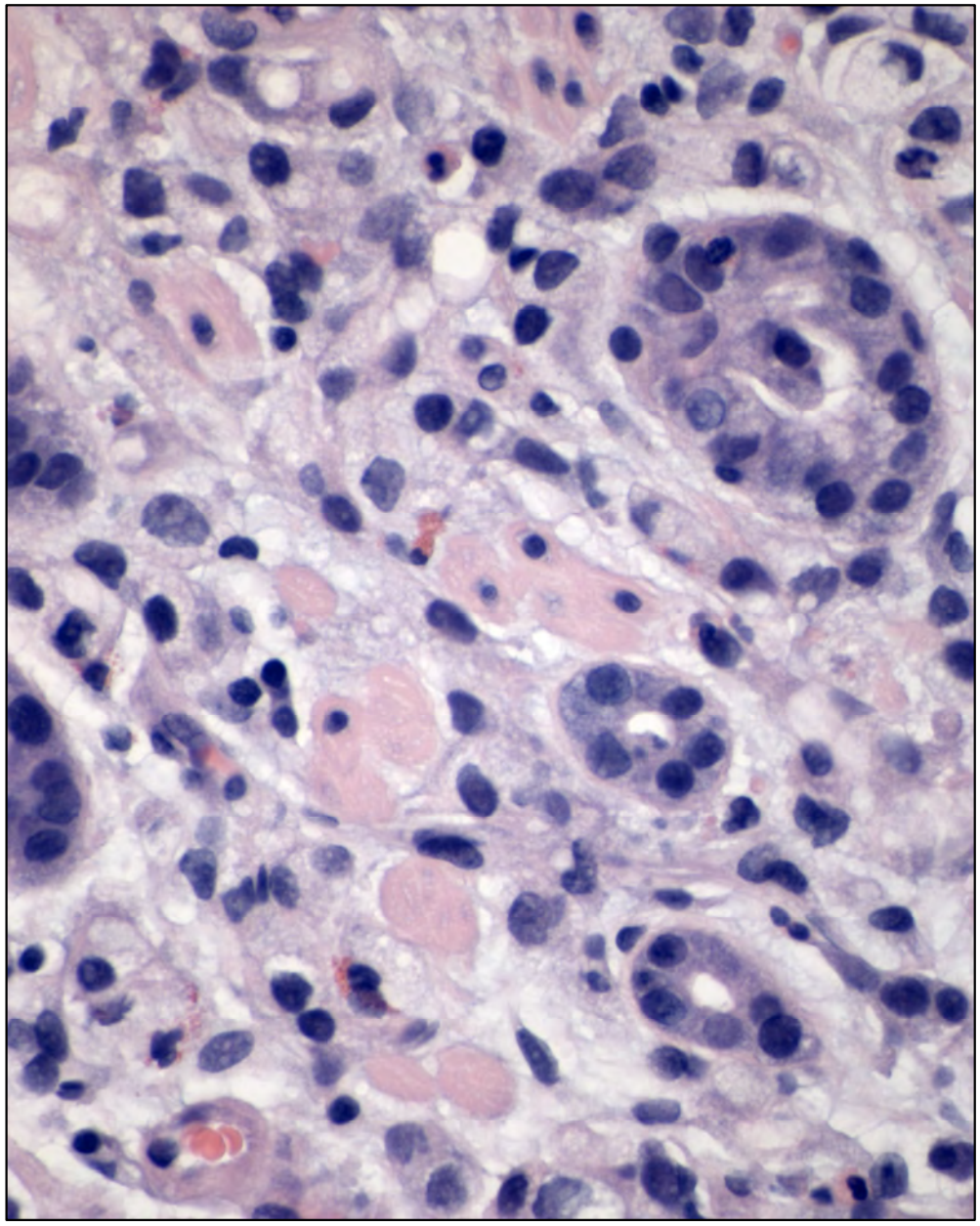


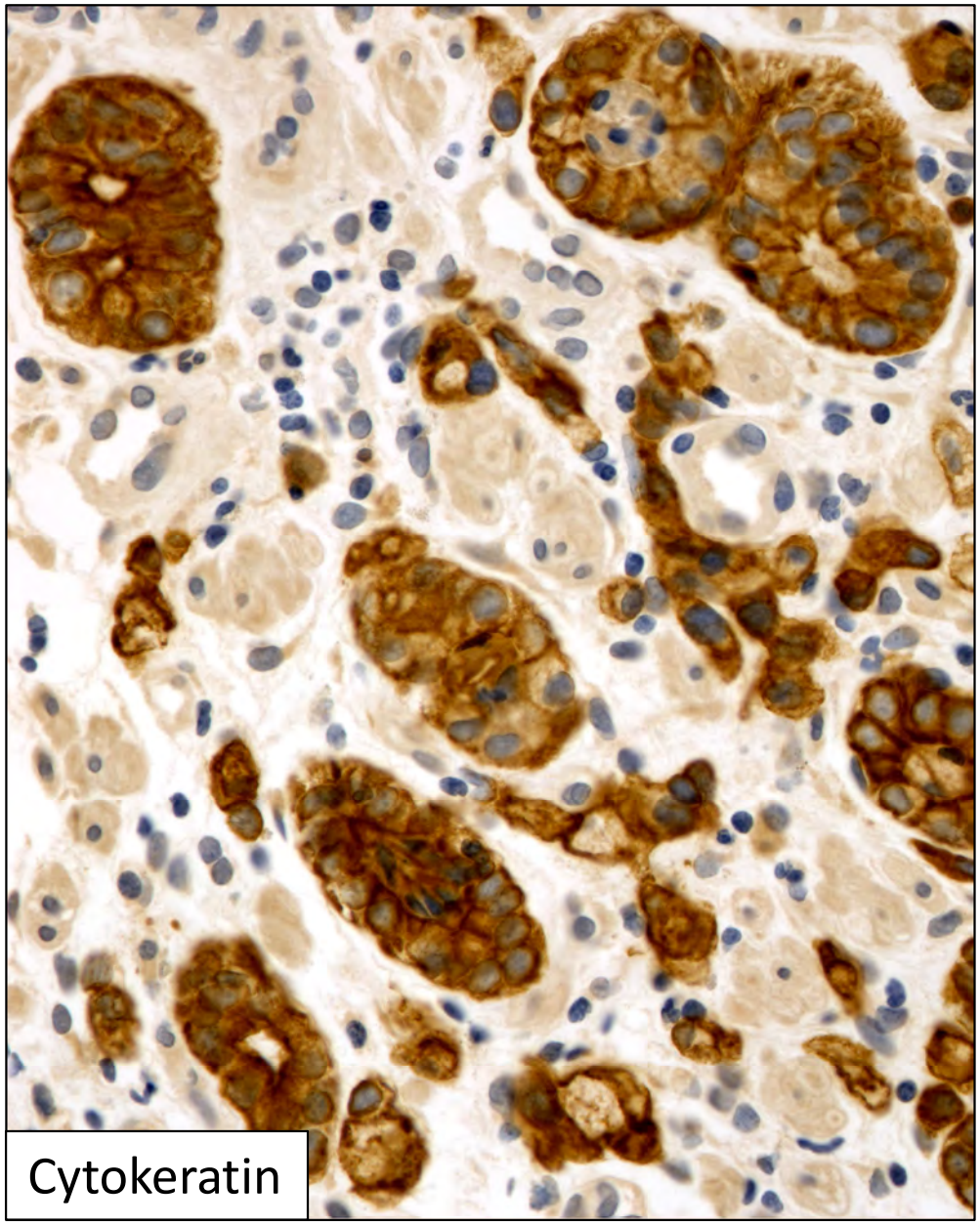
Signet ring cells

Patchy cellularity, especially in deep mucosa, prompts a second look



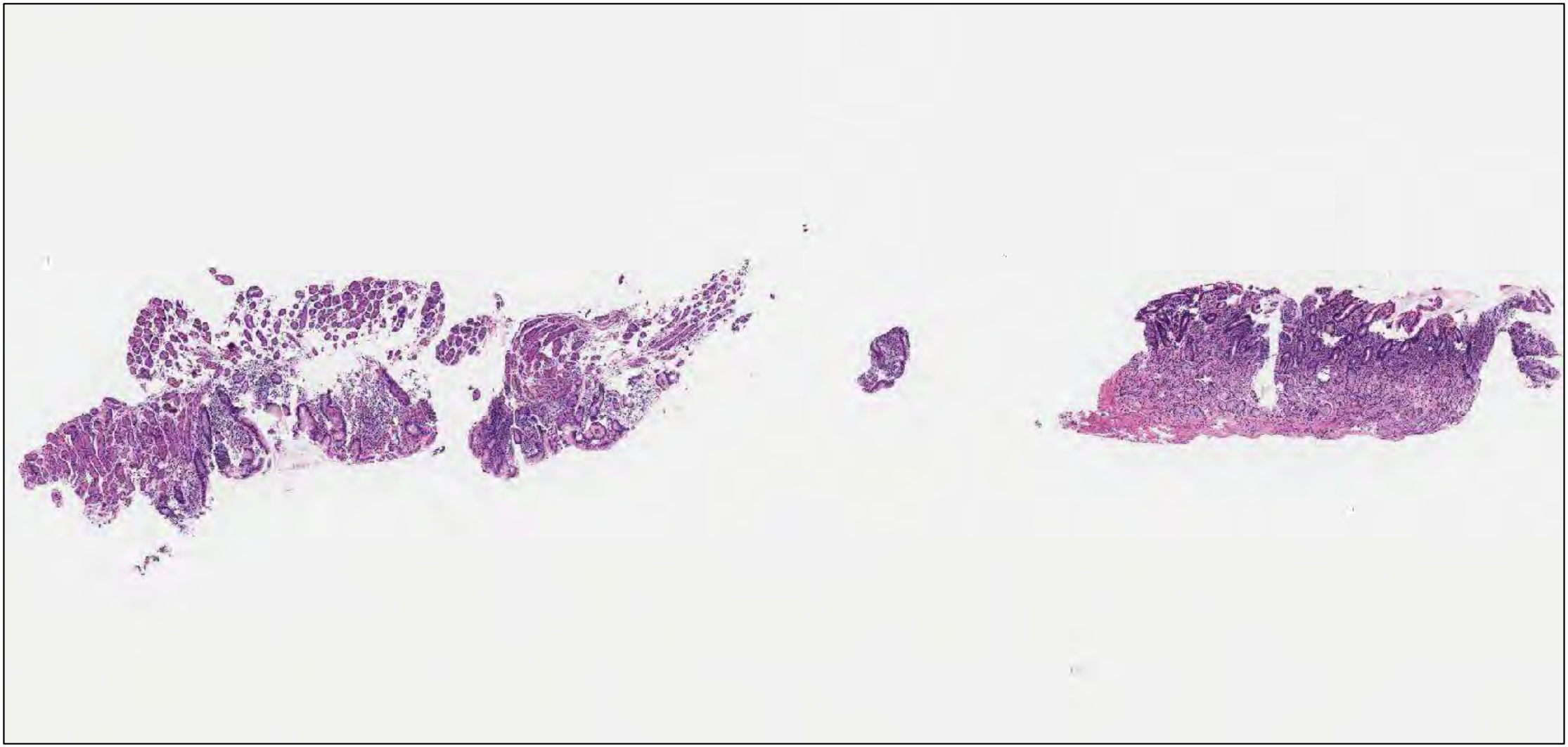
Sort of looks like chemical gastropathy with a little chronic inflammation

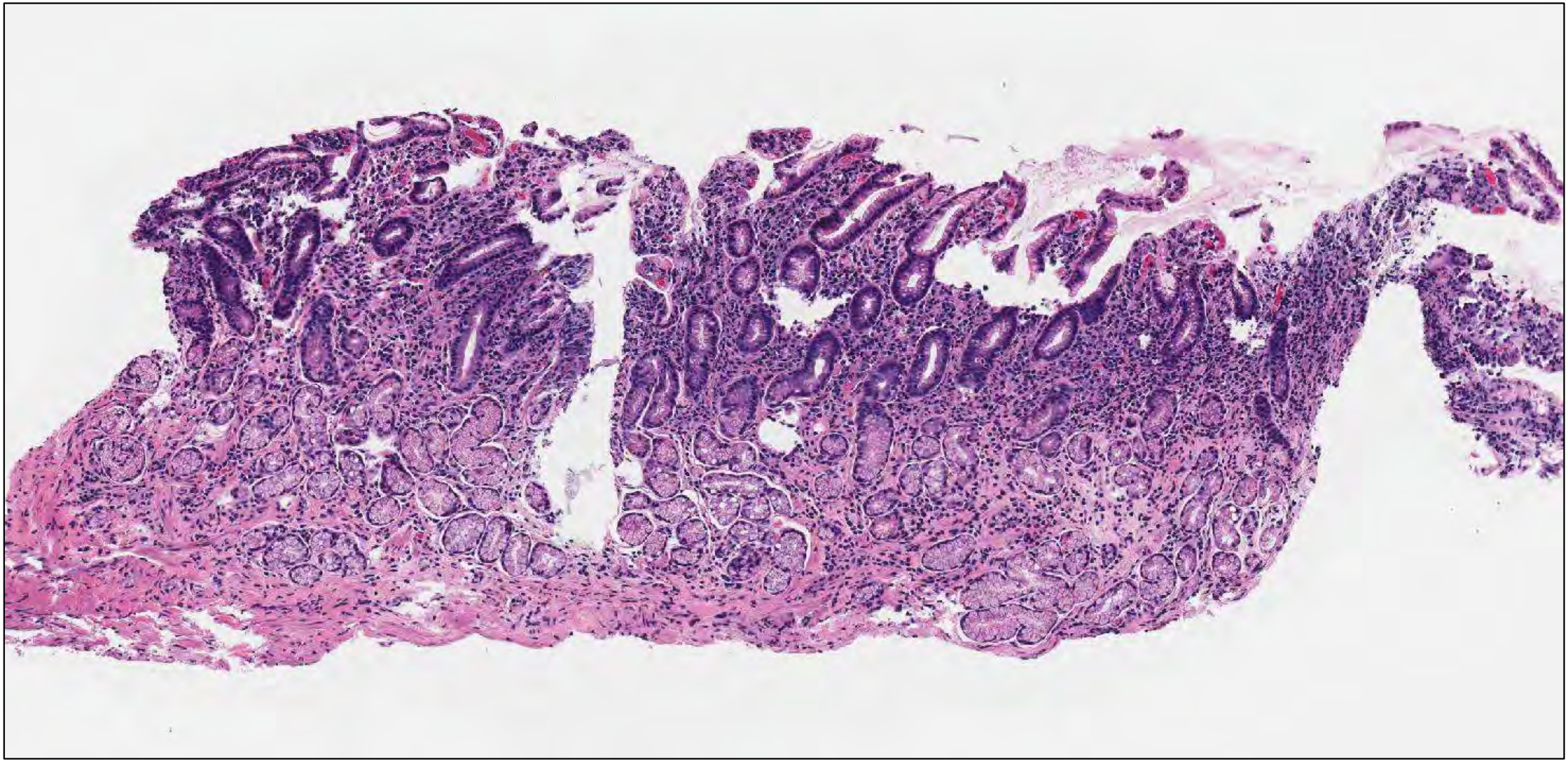



Cytokeratin

Case

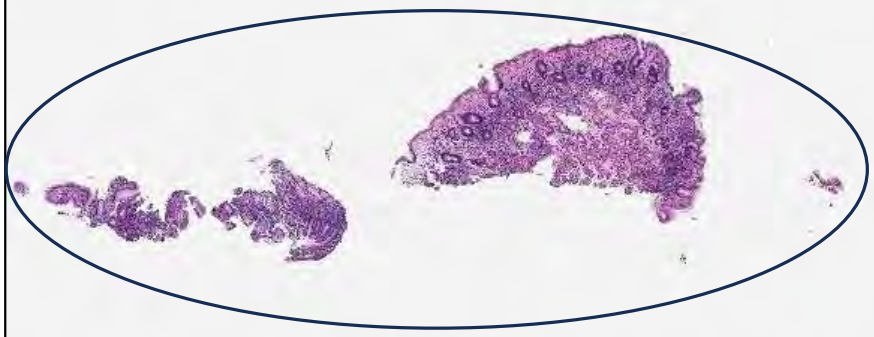
- 54-year-old female with upper endoscopy
- Complaints of abdominal pain
- Increasing abdominal girth

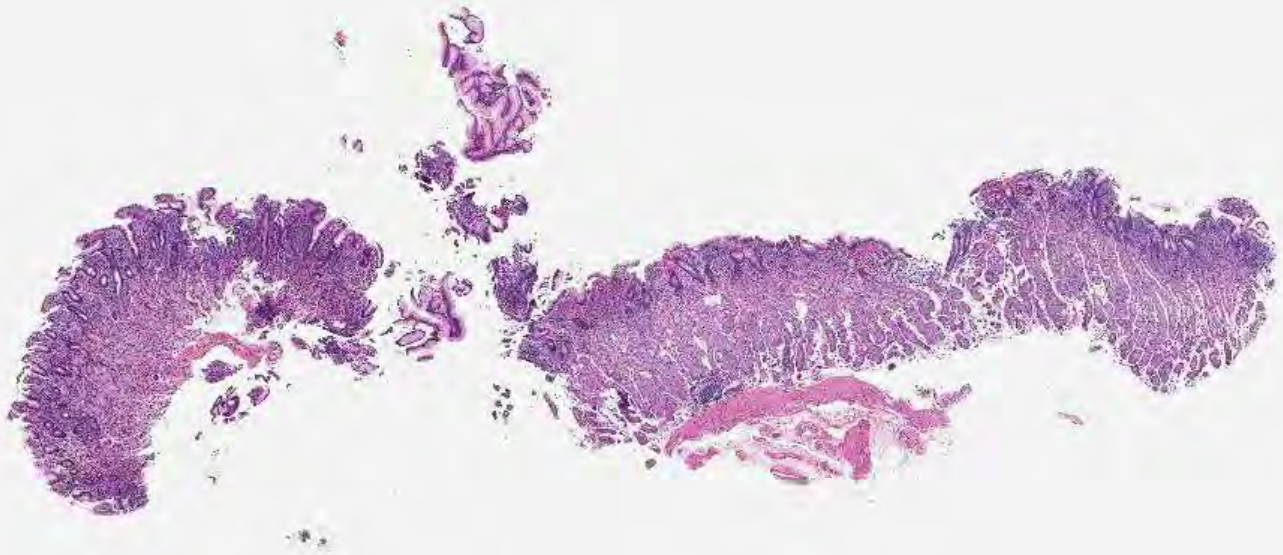


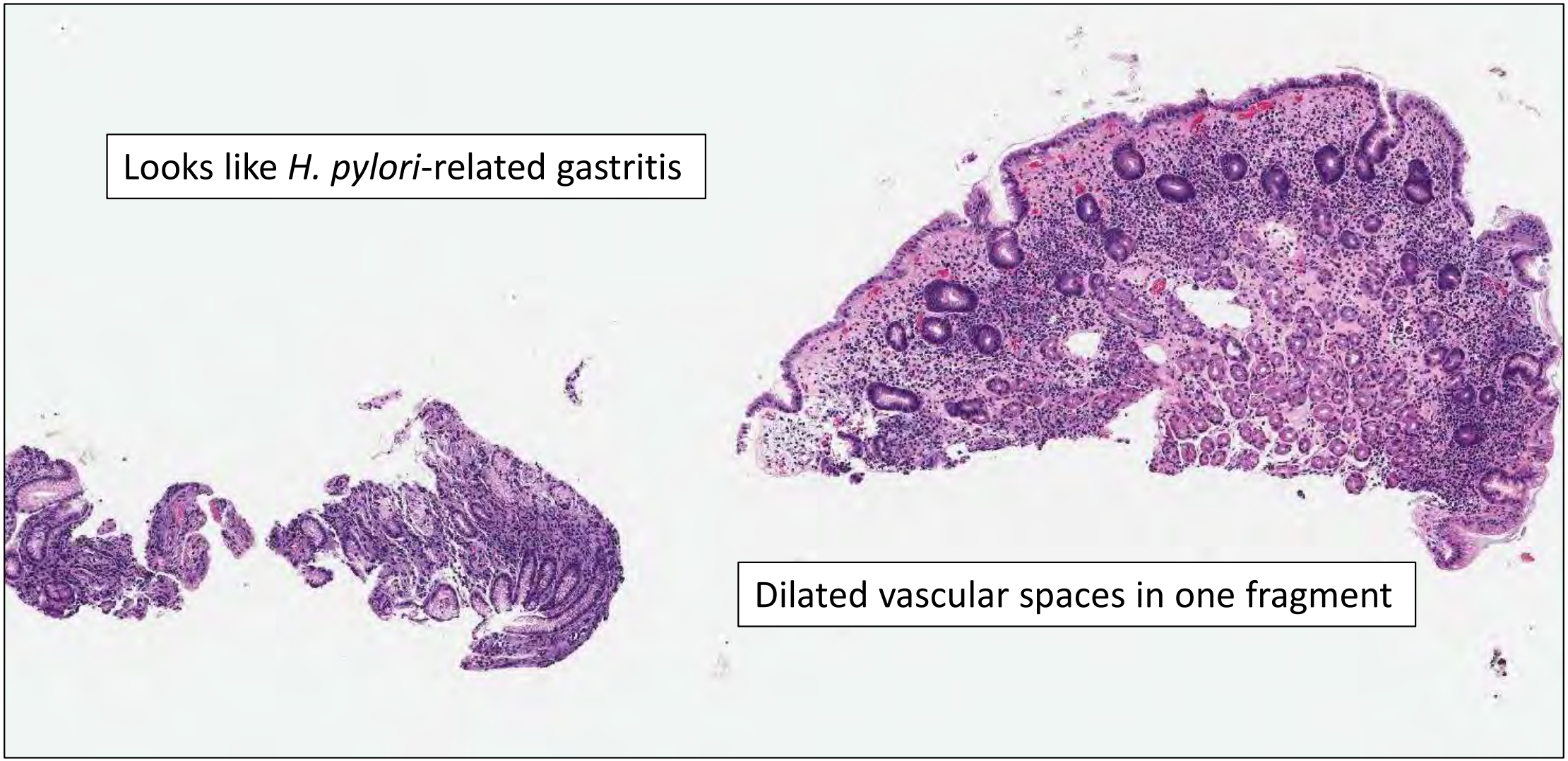


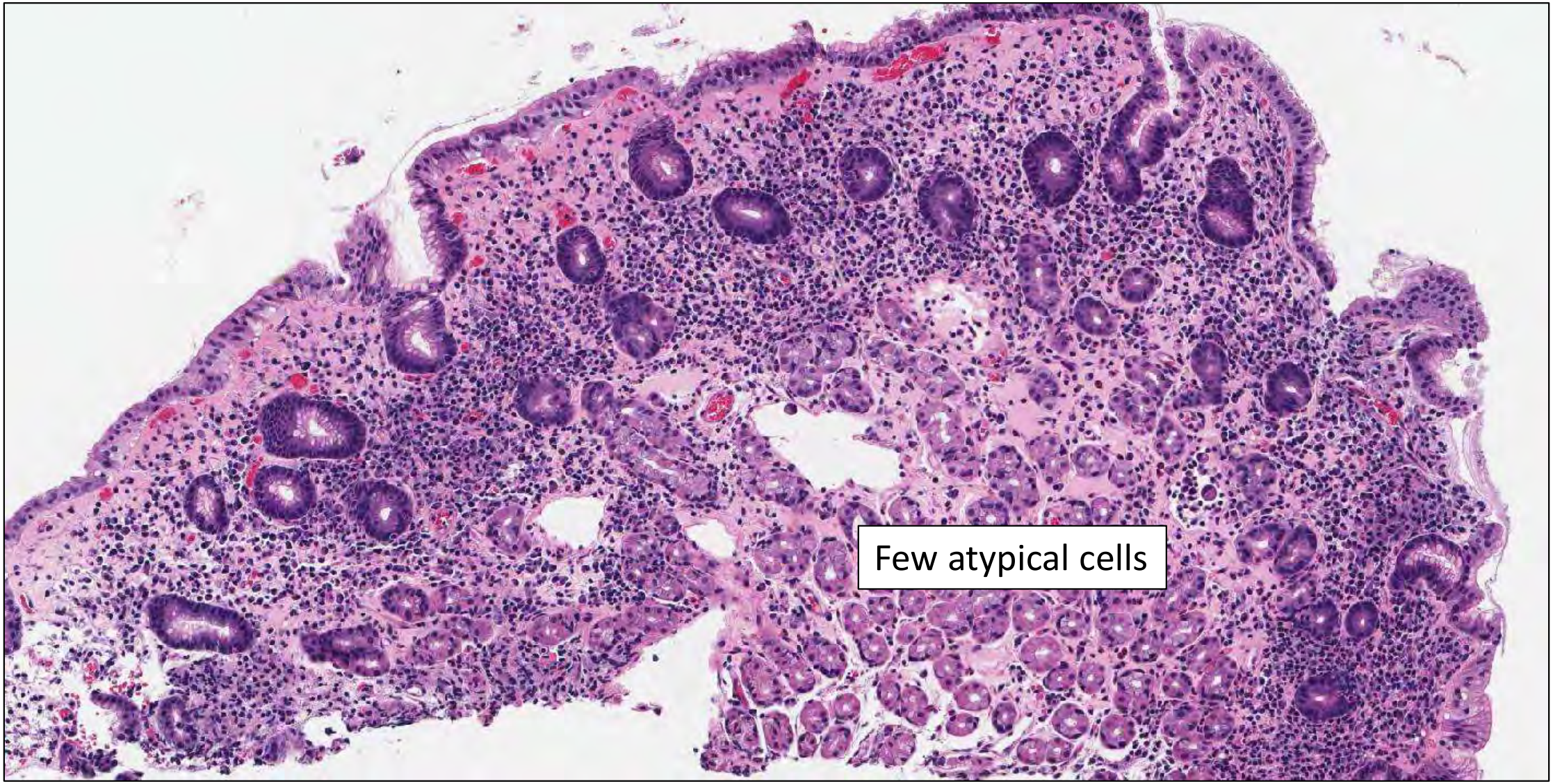
Chronic gastritis does not explain cancer symptoms

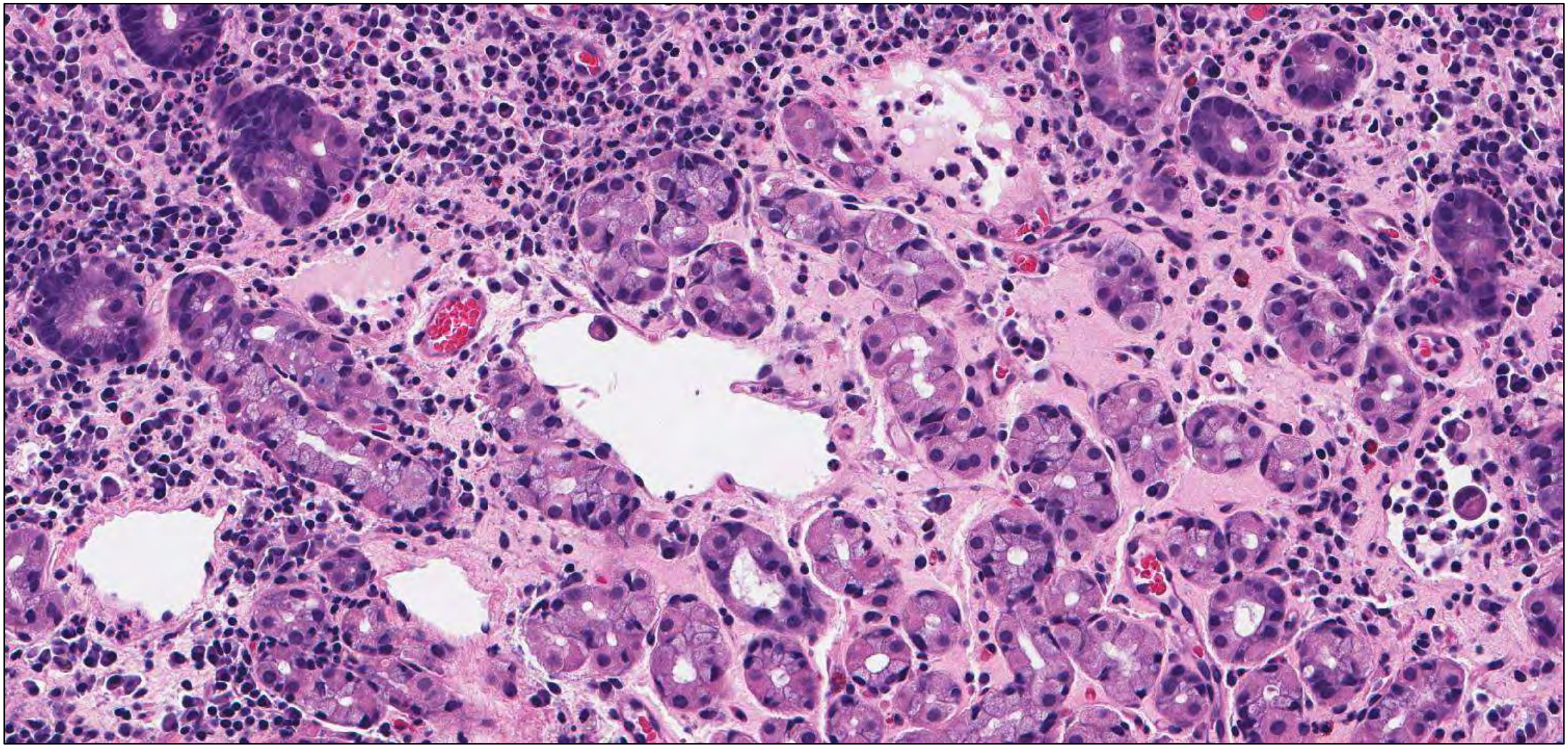
More tissue in second slide

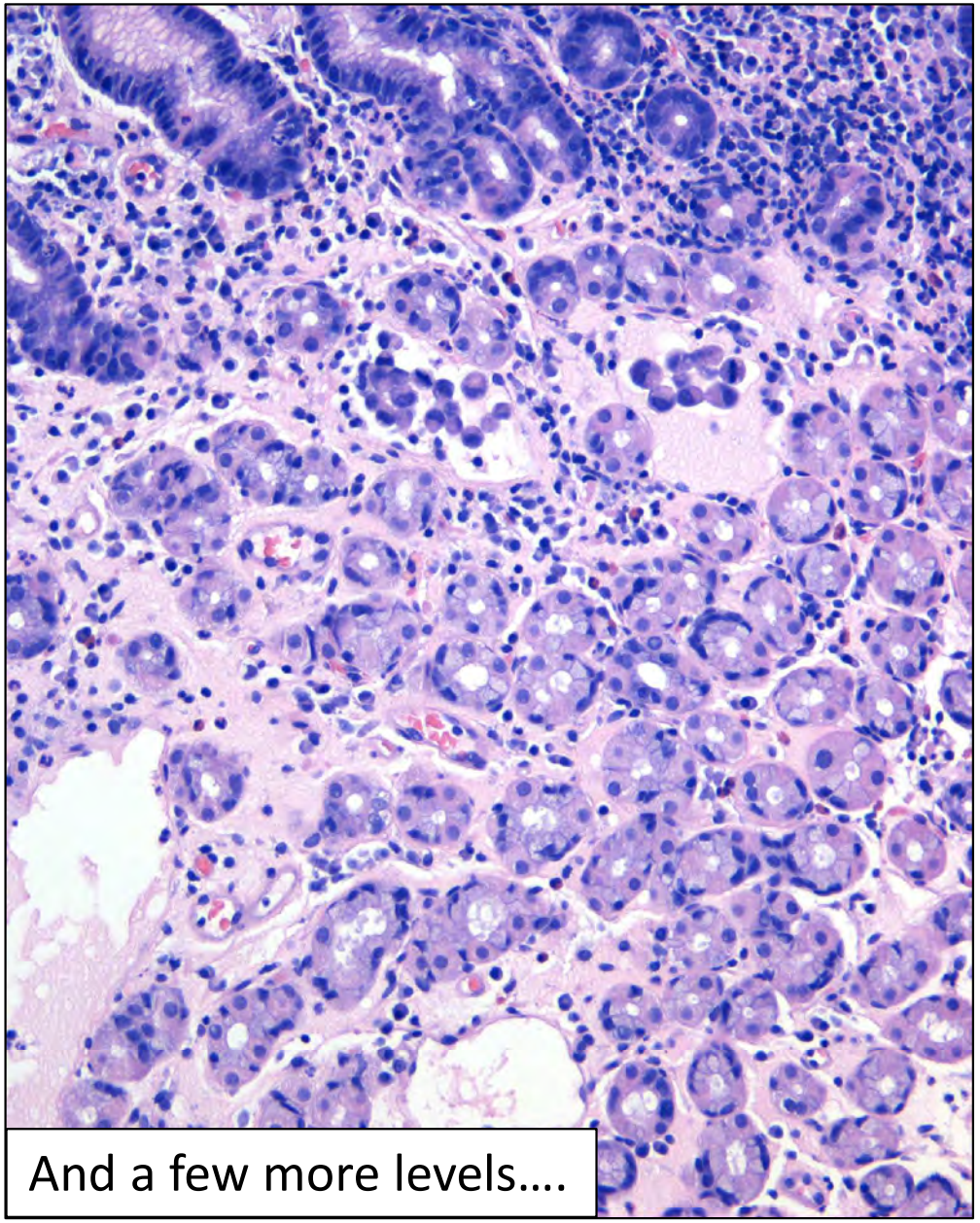




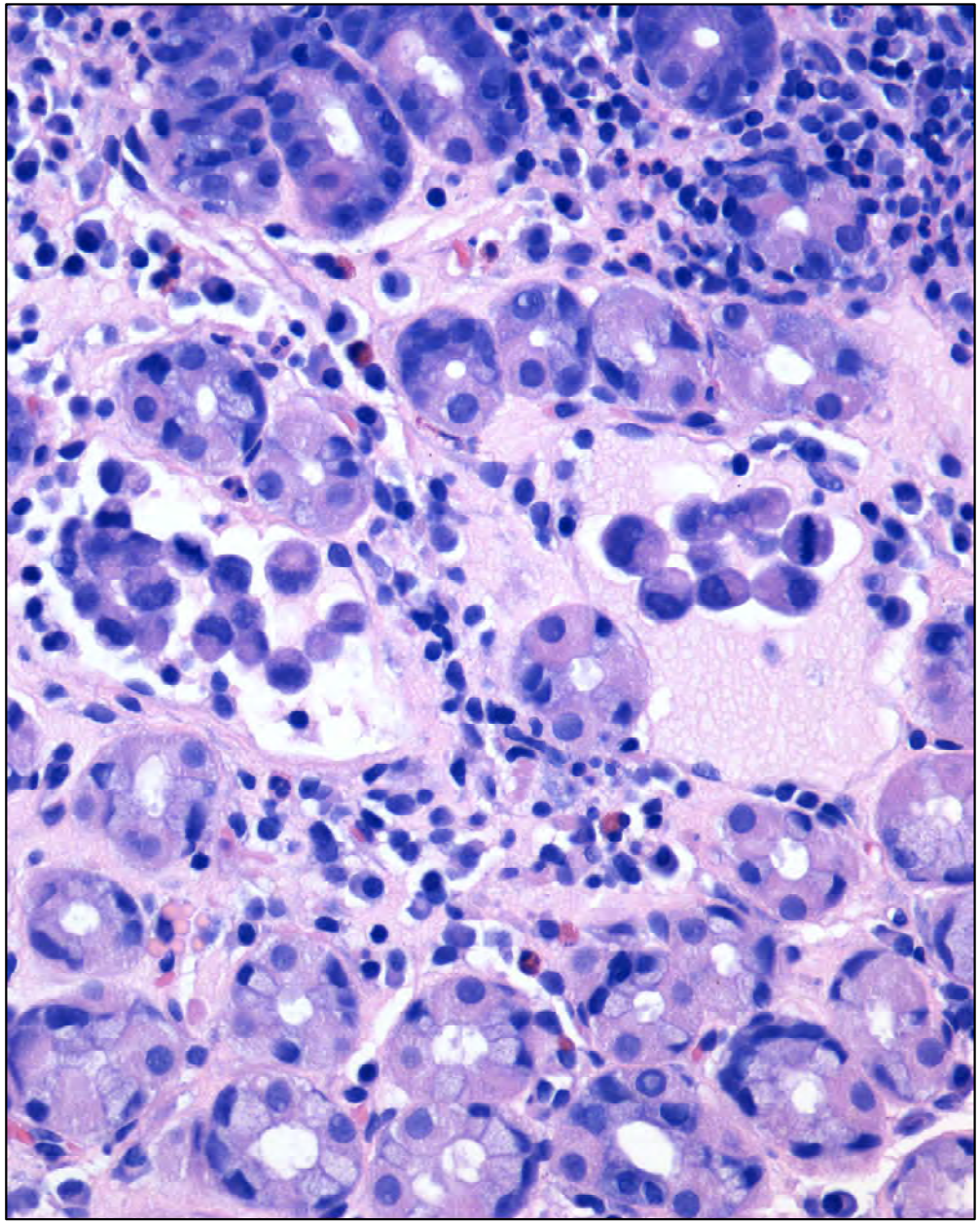

Looks like *H. pylori*-related gastritis
Dilated vascular spaces in one fragment


Few atypical cells

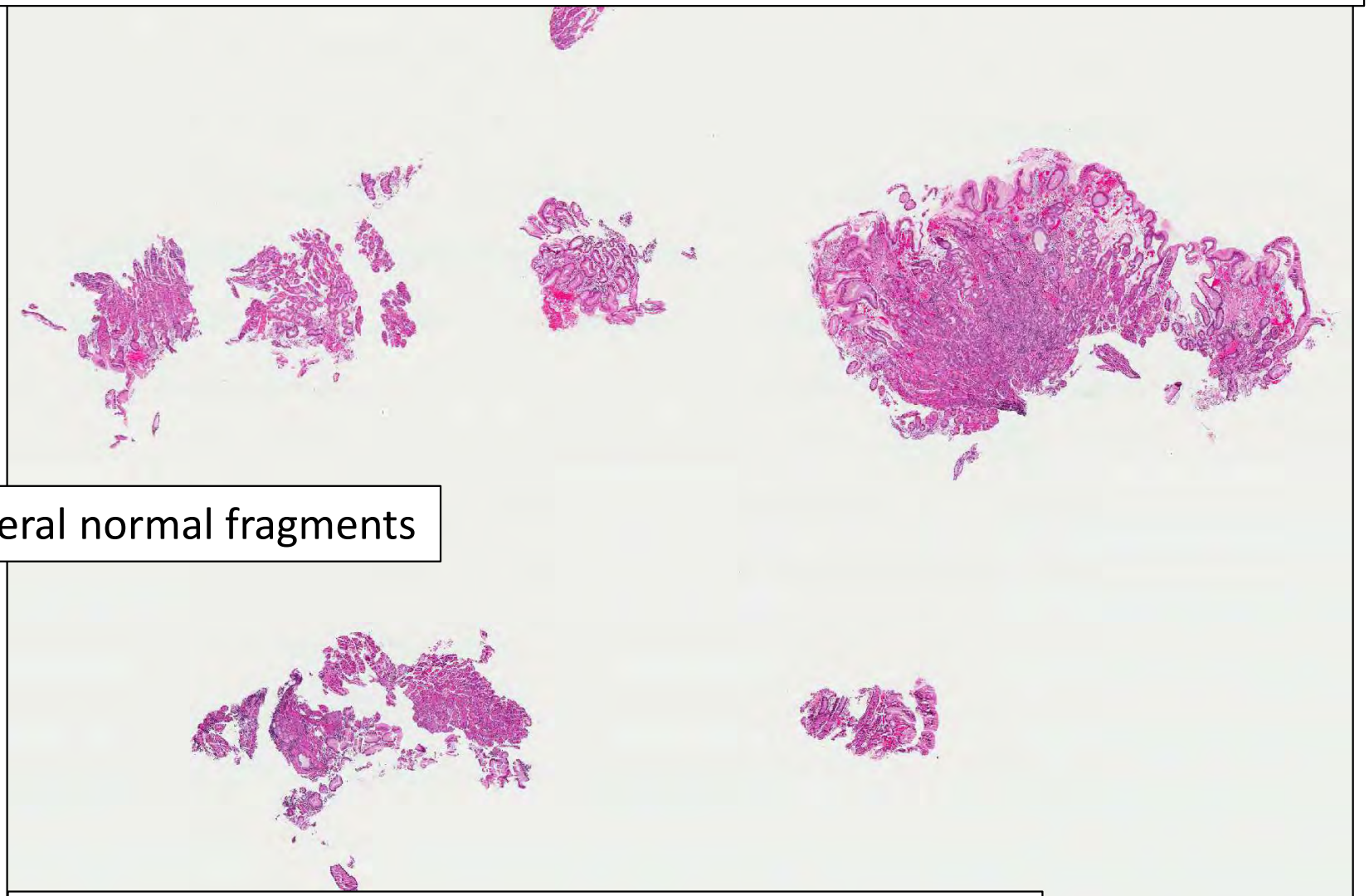




And a few more levels….



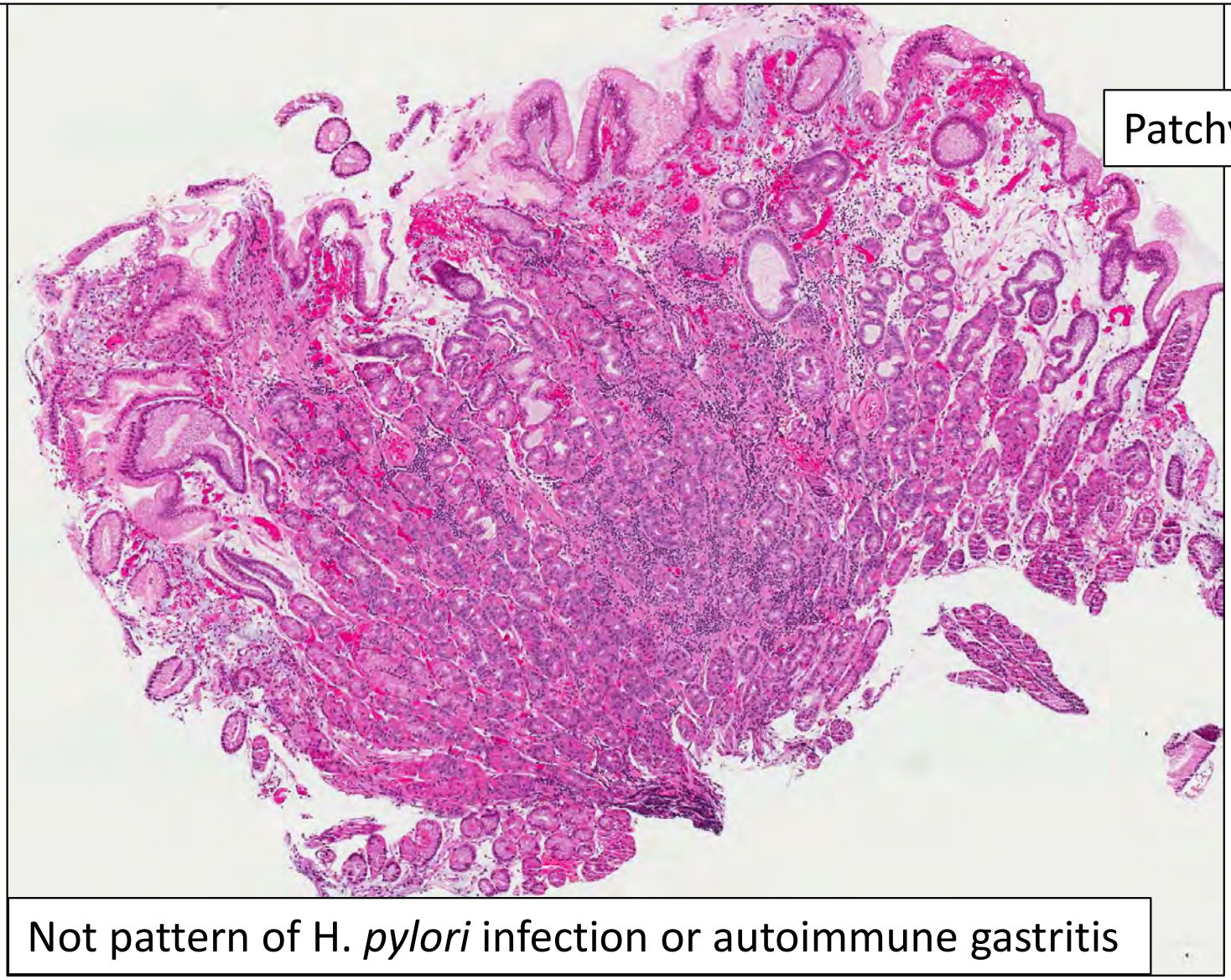
58-year-old woman with abdominal pain and suspected linitis plastica



Several normal fragments

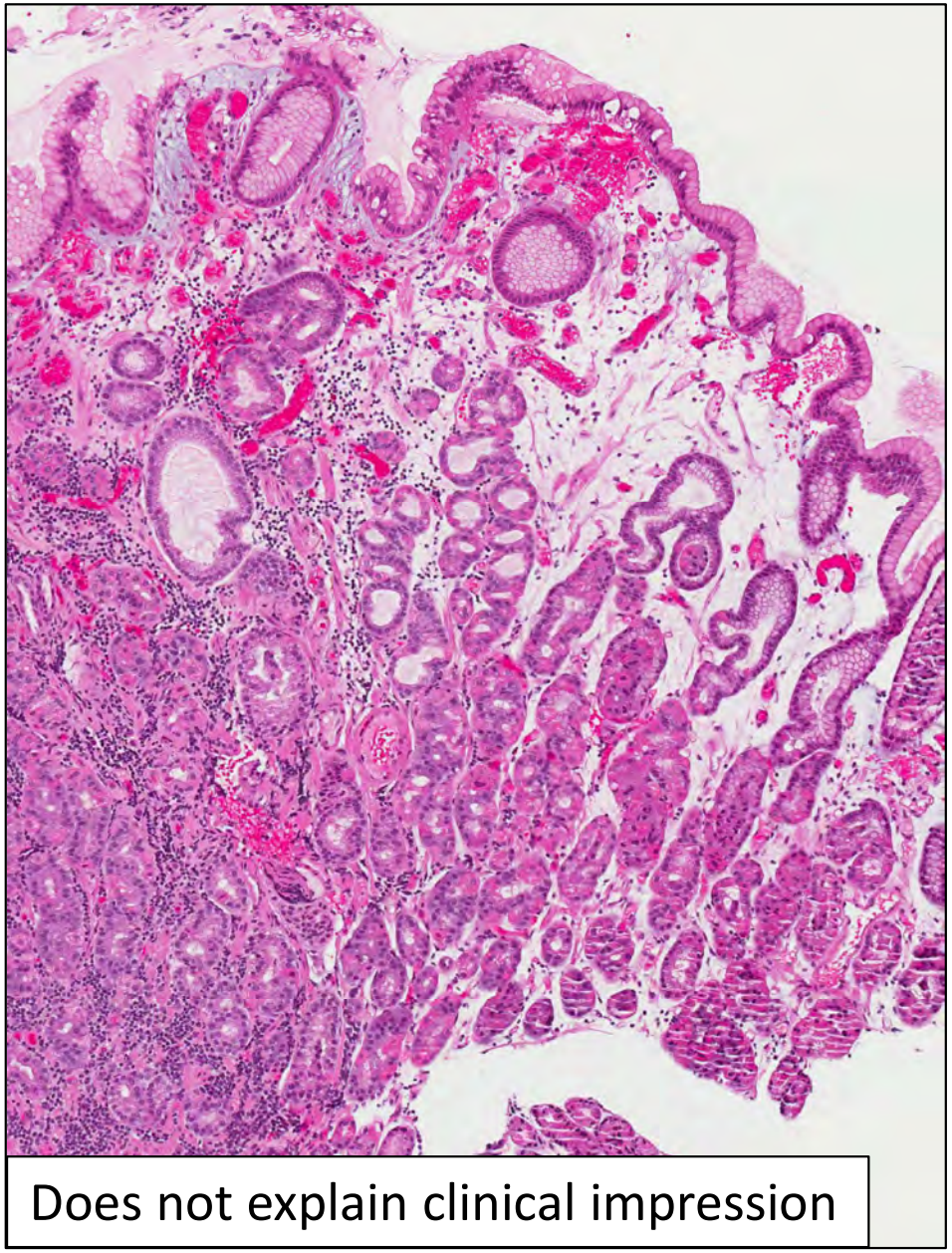
Case courtesy of Dr. Jinru Shia, MSKCC, New York, NY

58-year-old woman with abdominal pain and suspected linitis plastica

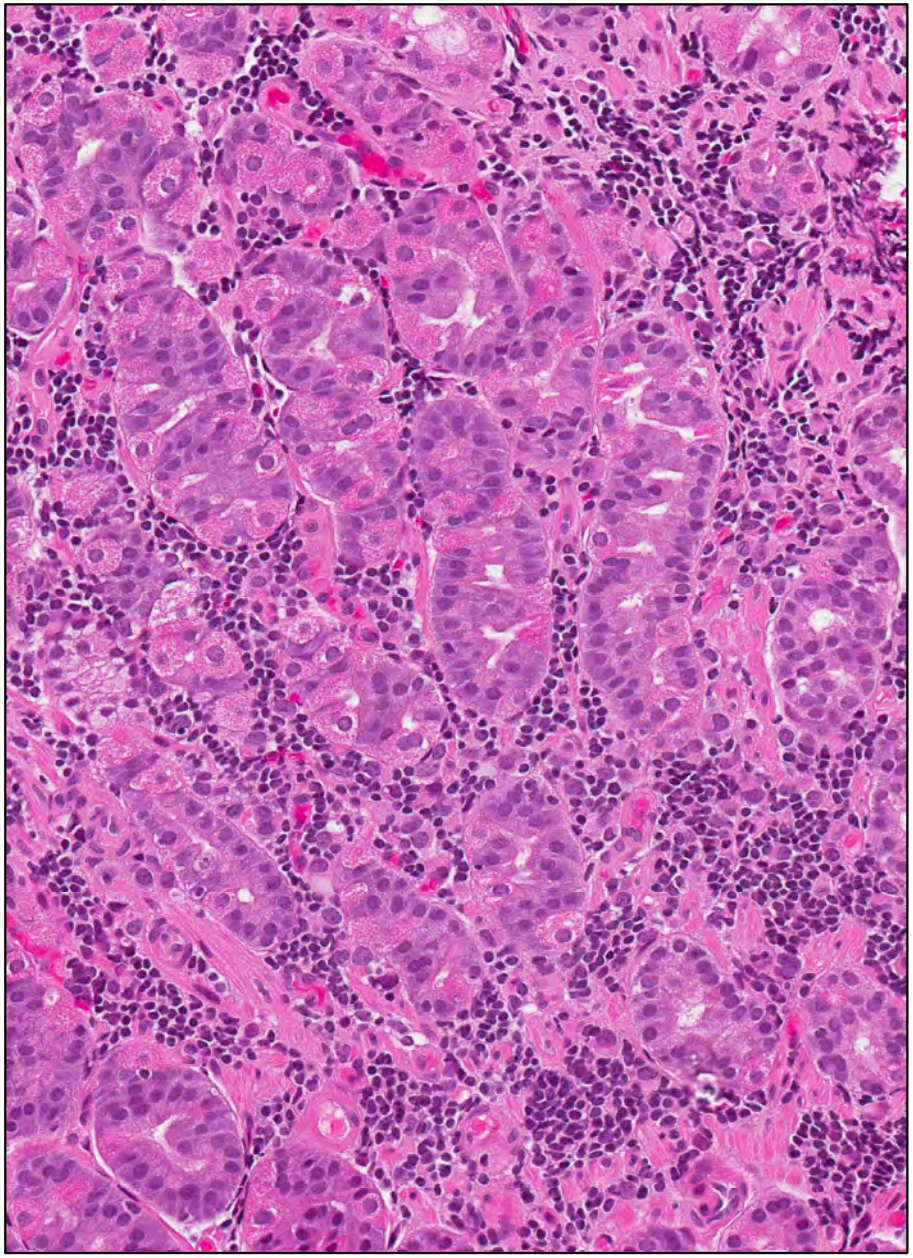


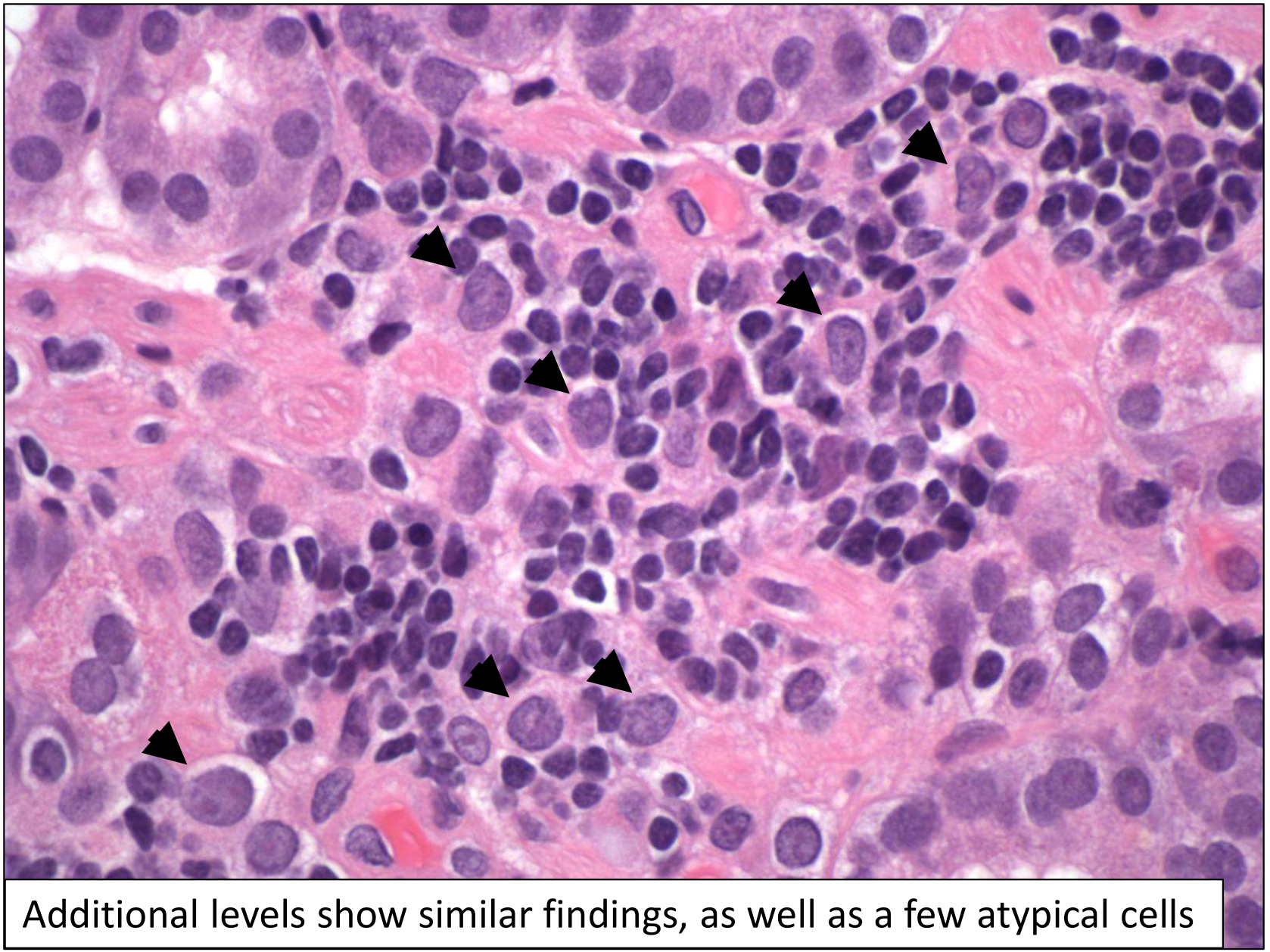
Patchy edema (bad)

Not pattern of H. *pylori* infection or autoimmune gastritis



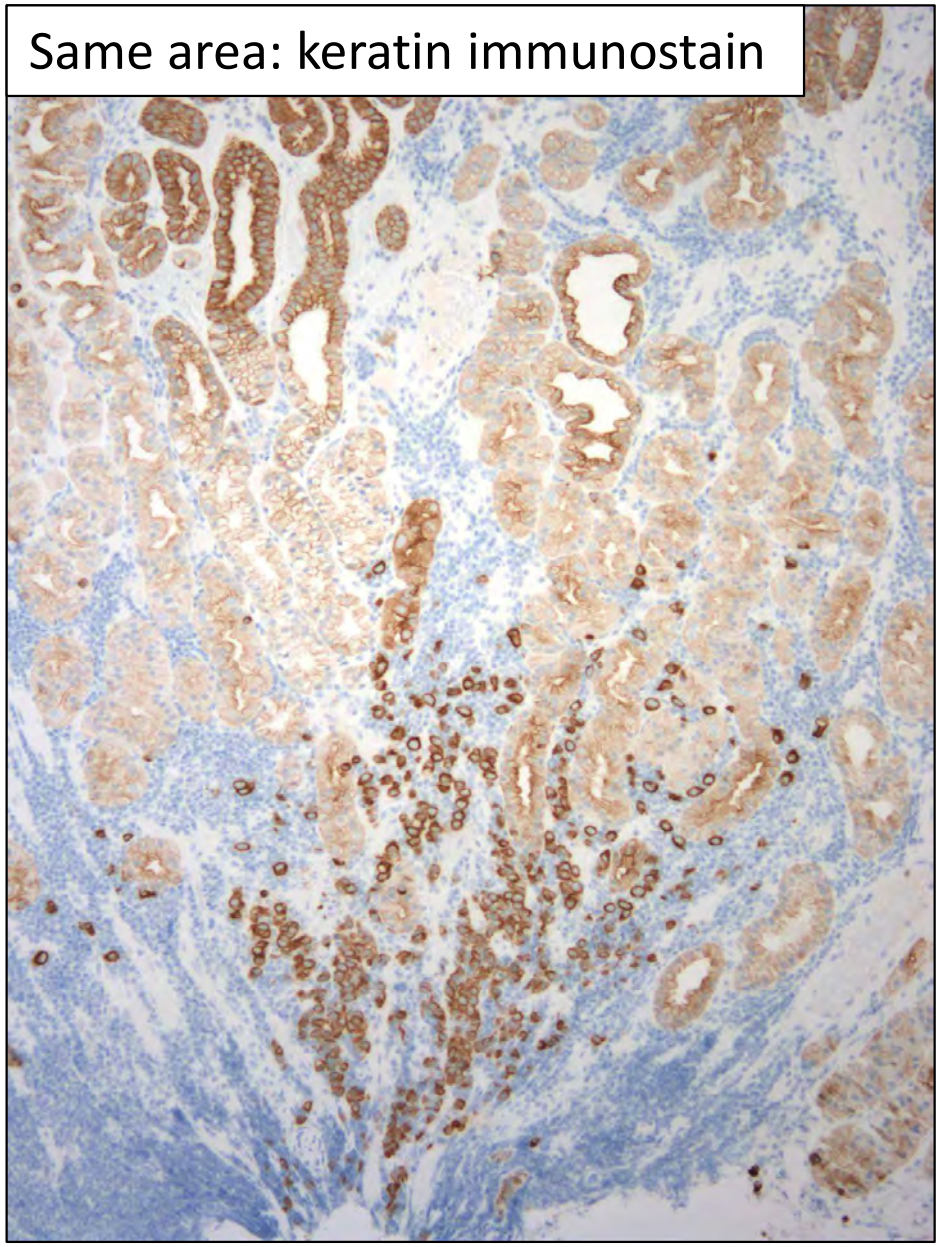
Does not explain clinical impression

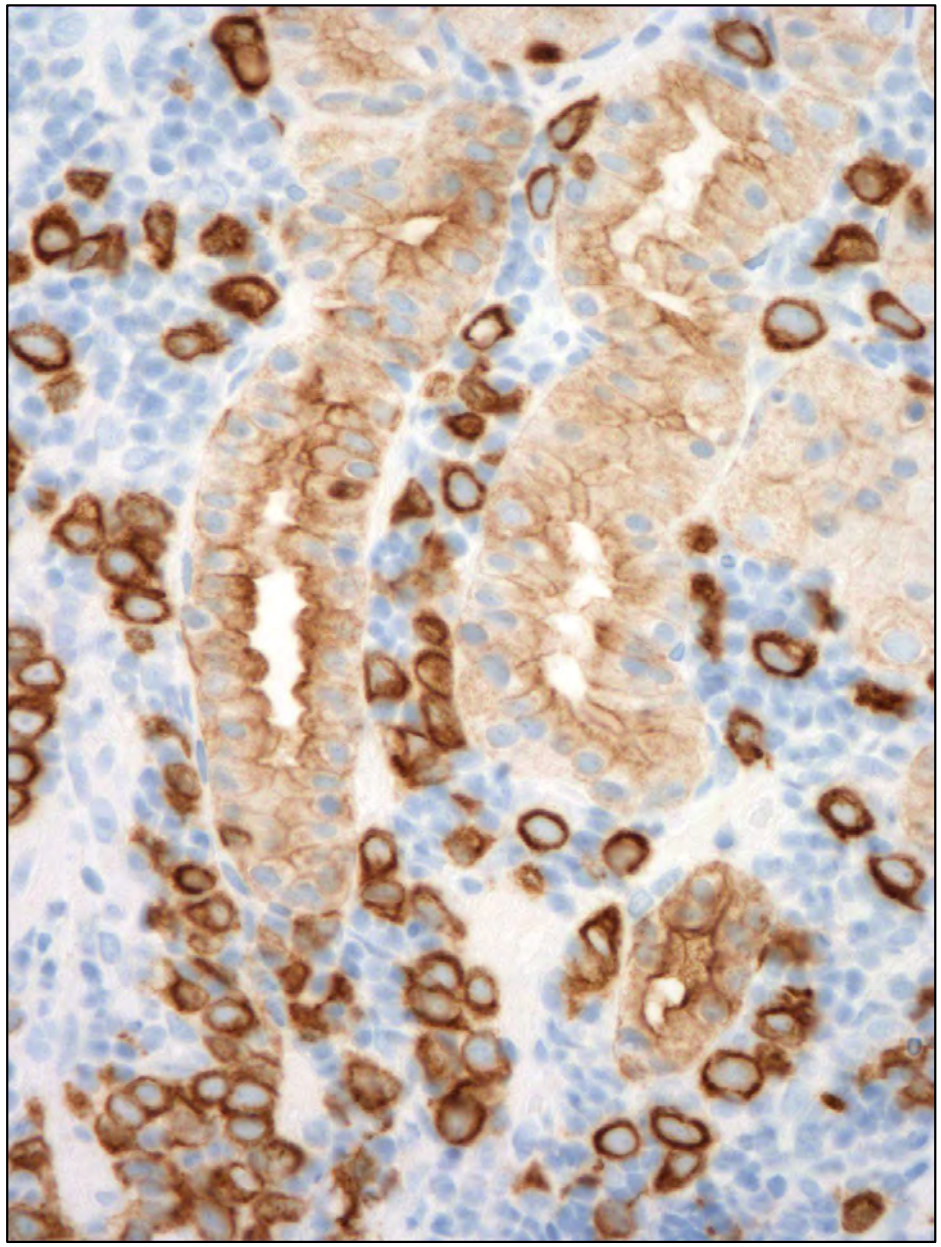




Additional levels show similar findings, as well as a few atypical cells

Same area: keratin immunostain

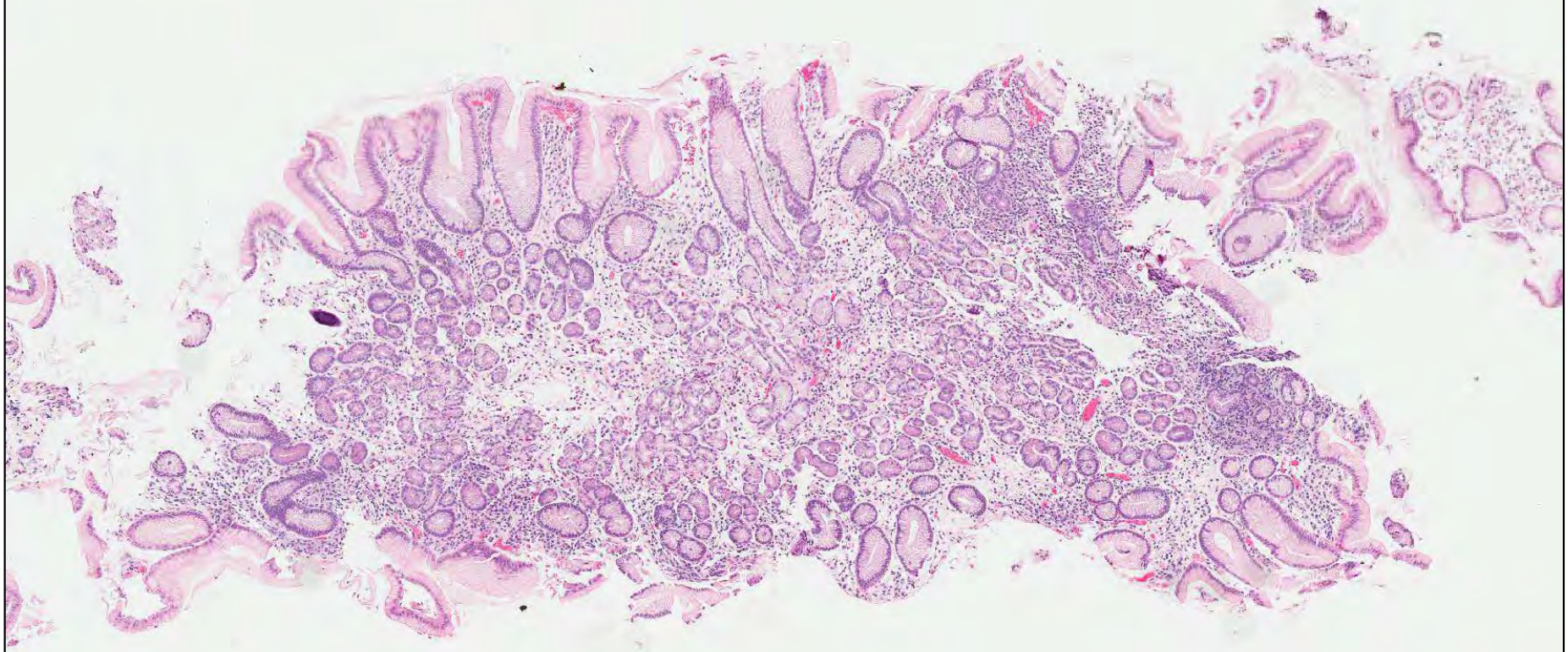




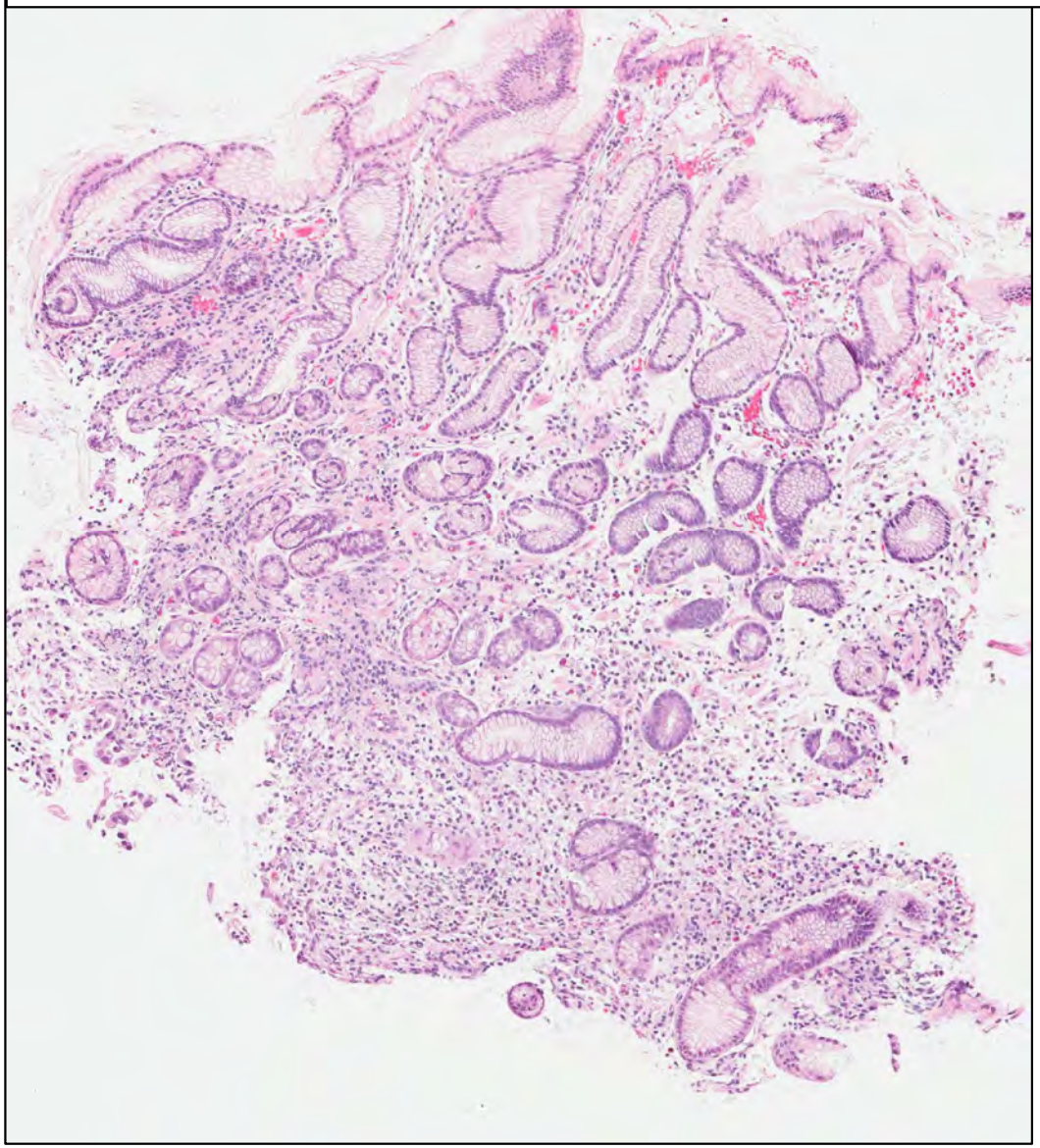
Case

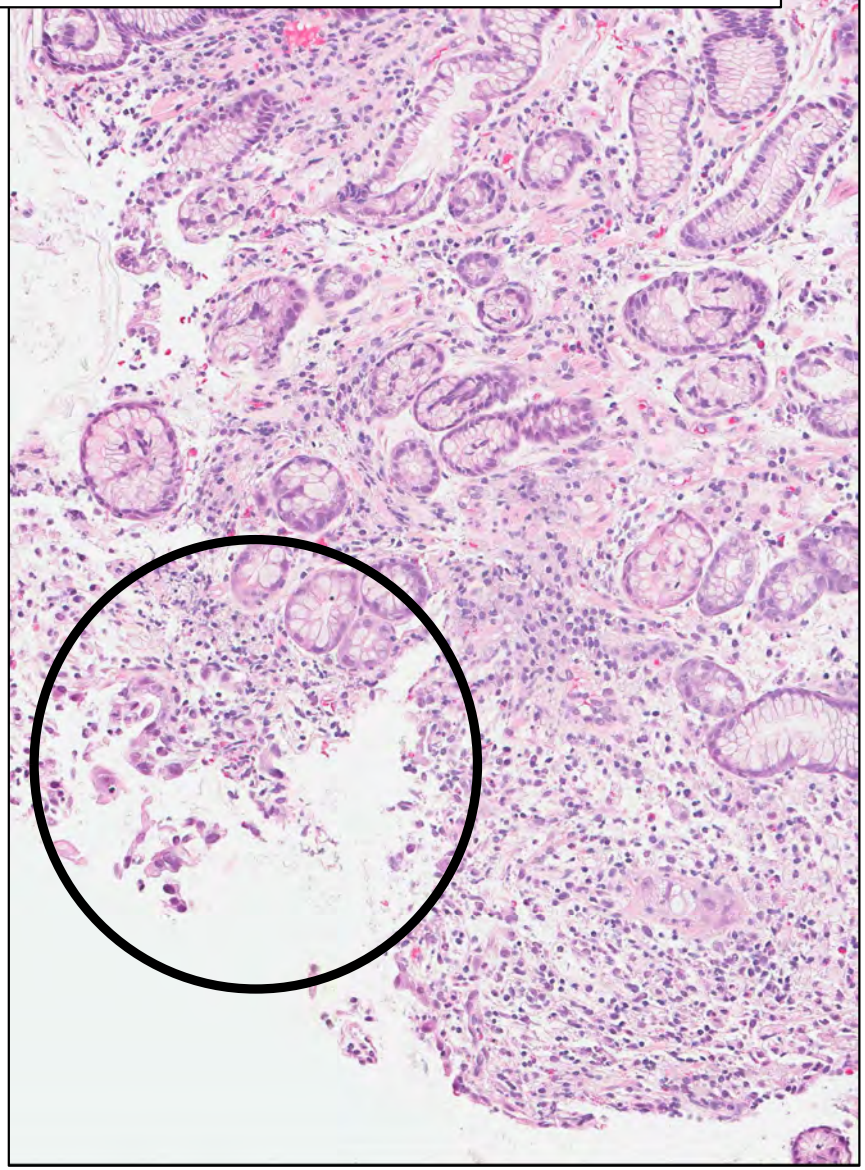
- 62-year-old male with gastric outlet obstruction
- *H. pylori*-related gastritis six months previously

Chronic inactive gastritis, not unusual for treated *H. pylori* infection

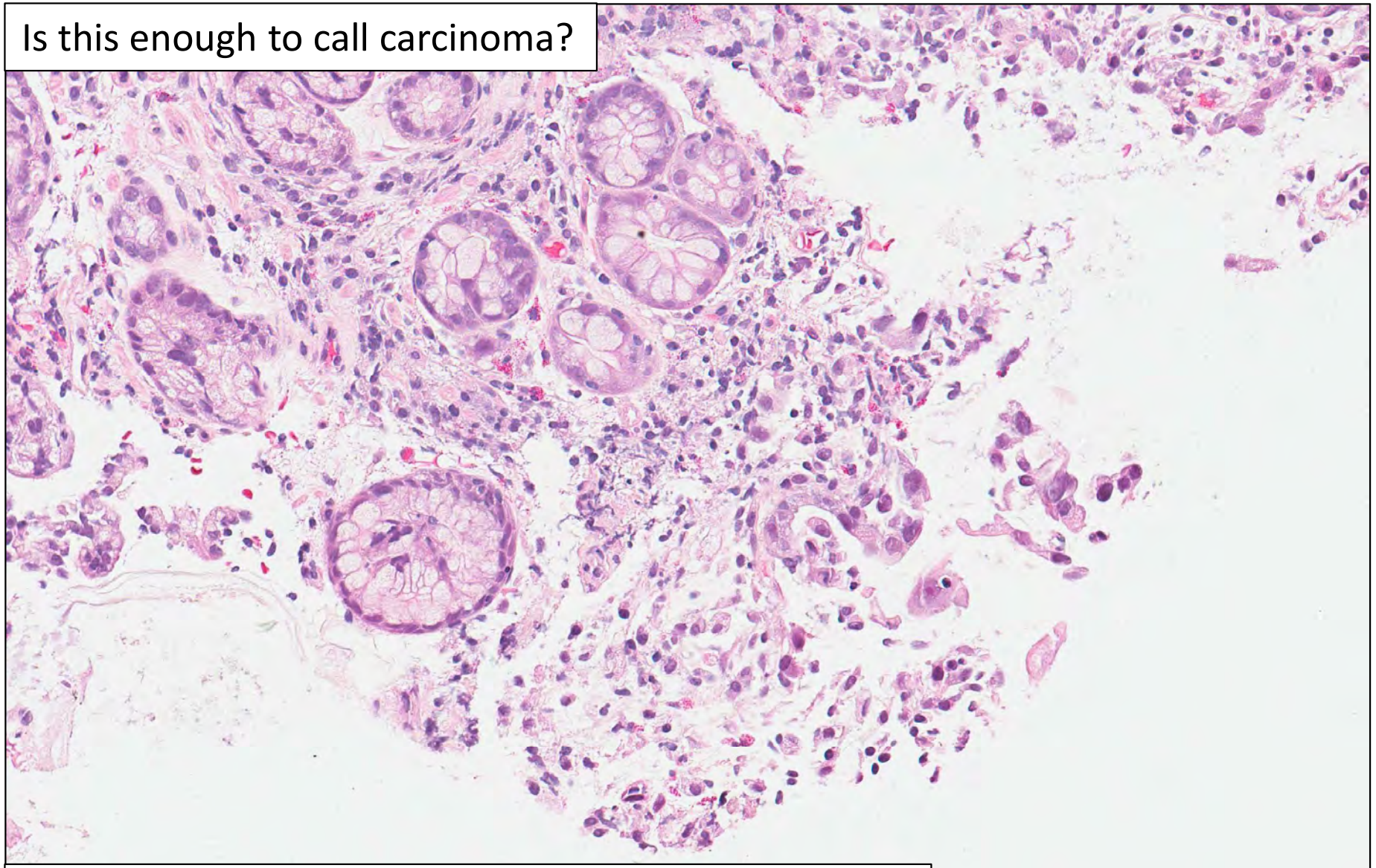


But remember chronic gastritis does not explain clinical suspicion for malignancy



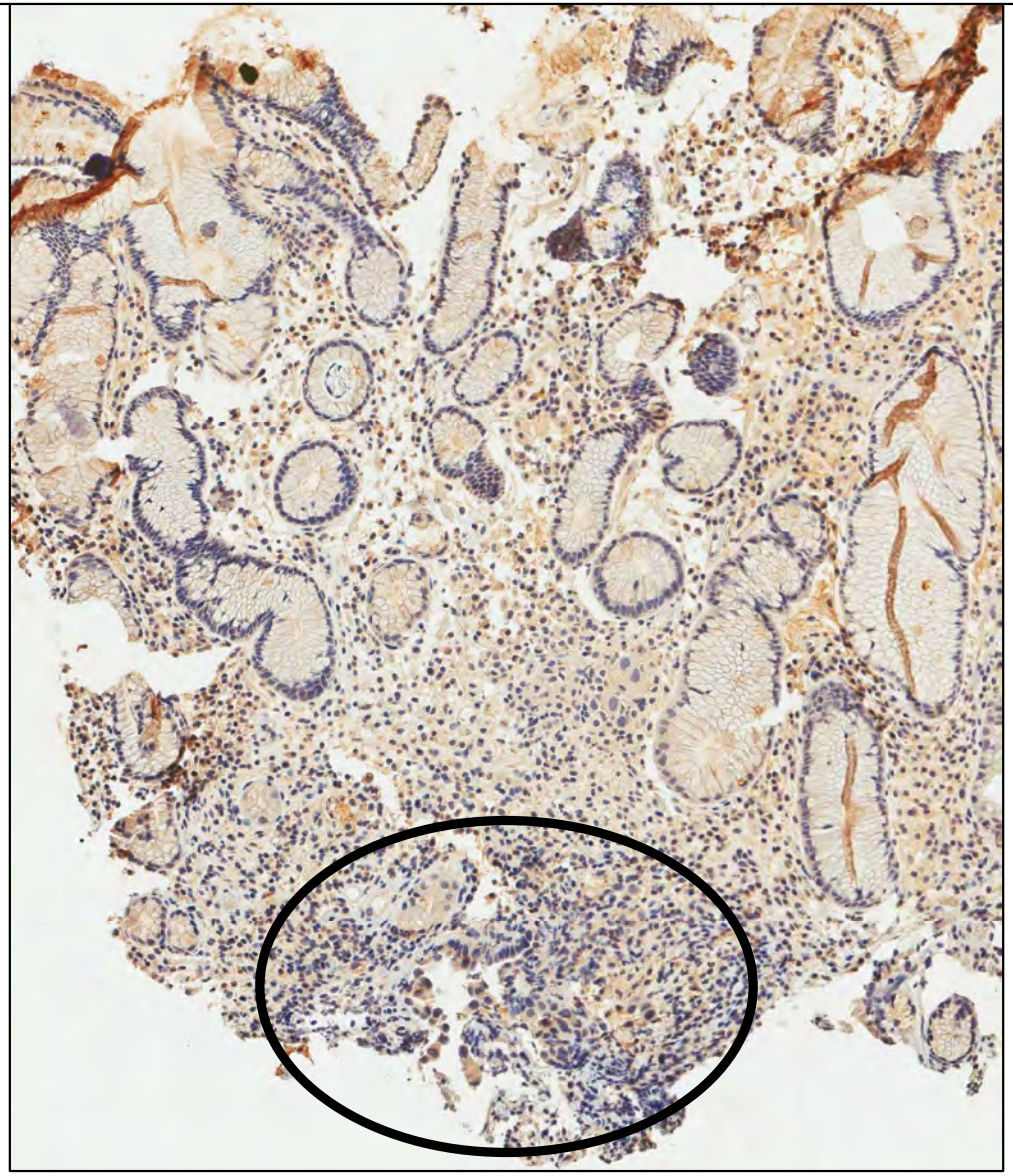


Is this enough to call carcinoma?

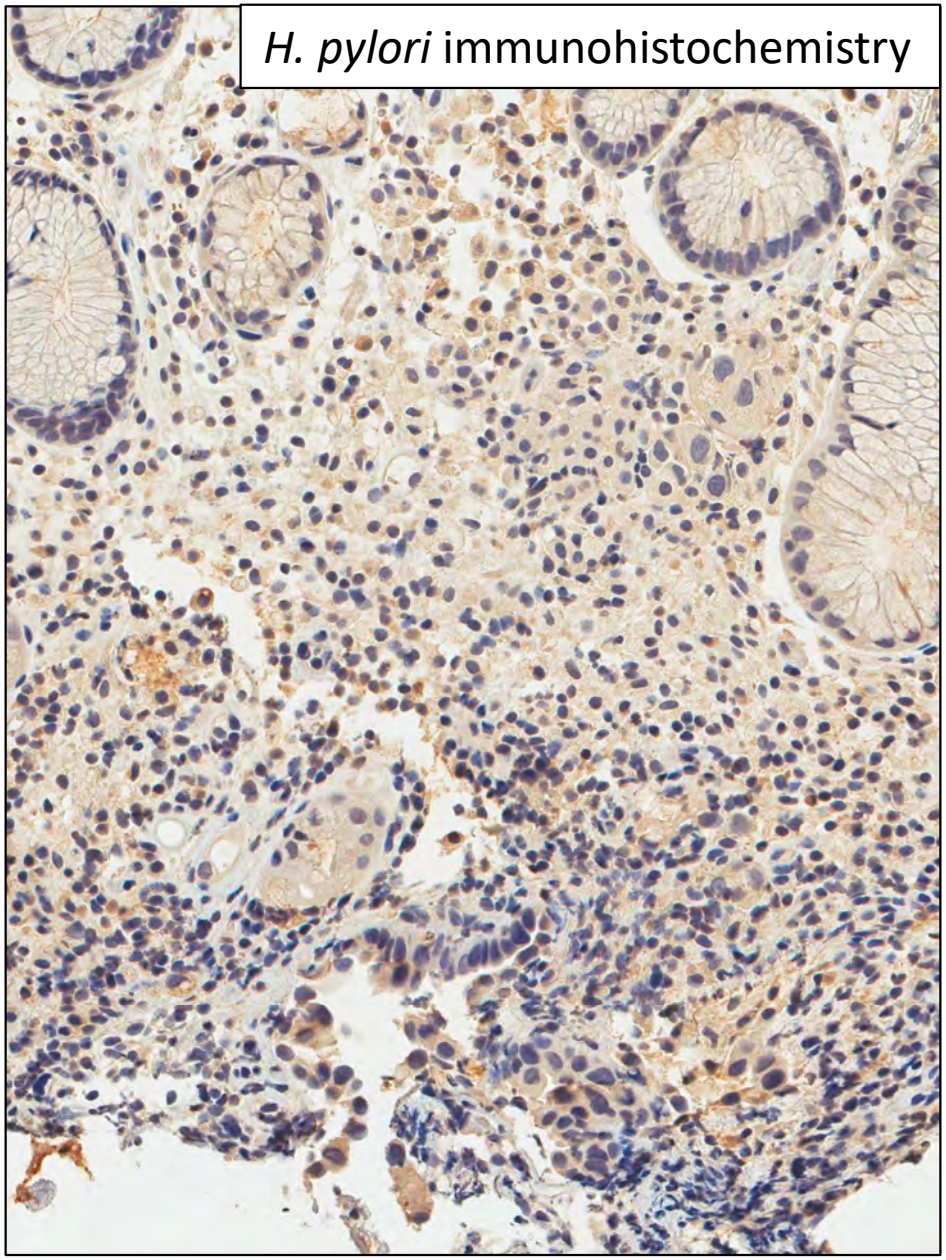


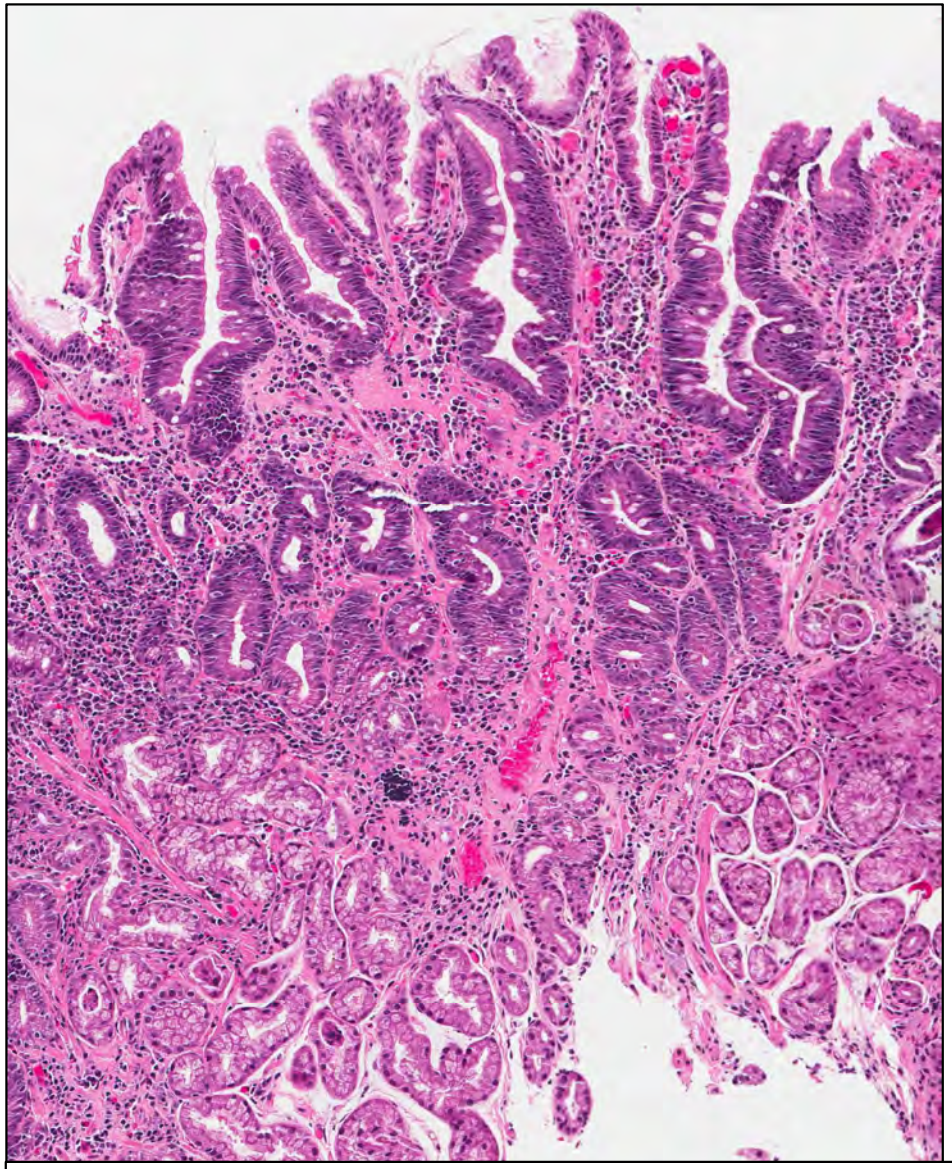
Gone in deeper tissue levels….now what do you do?

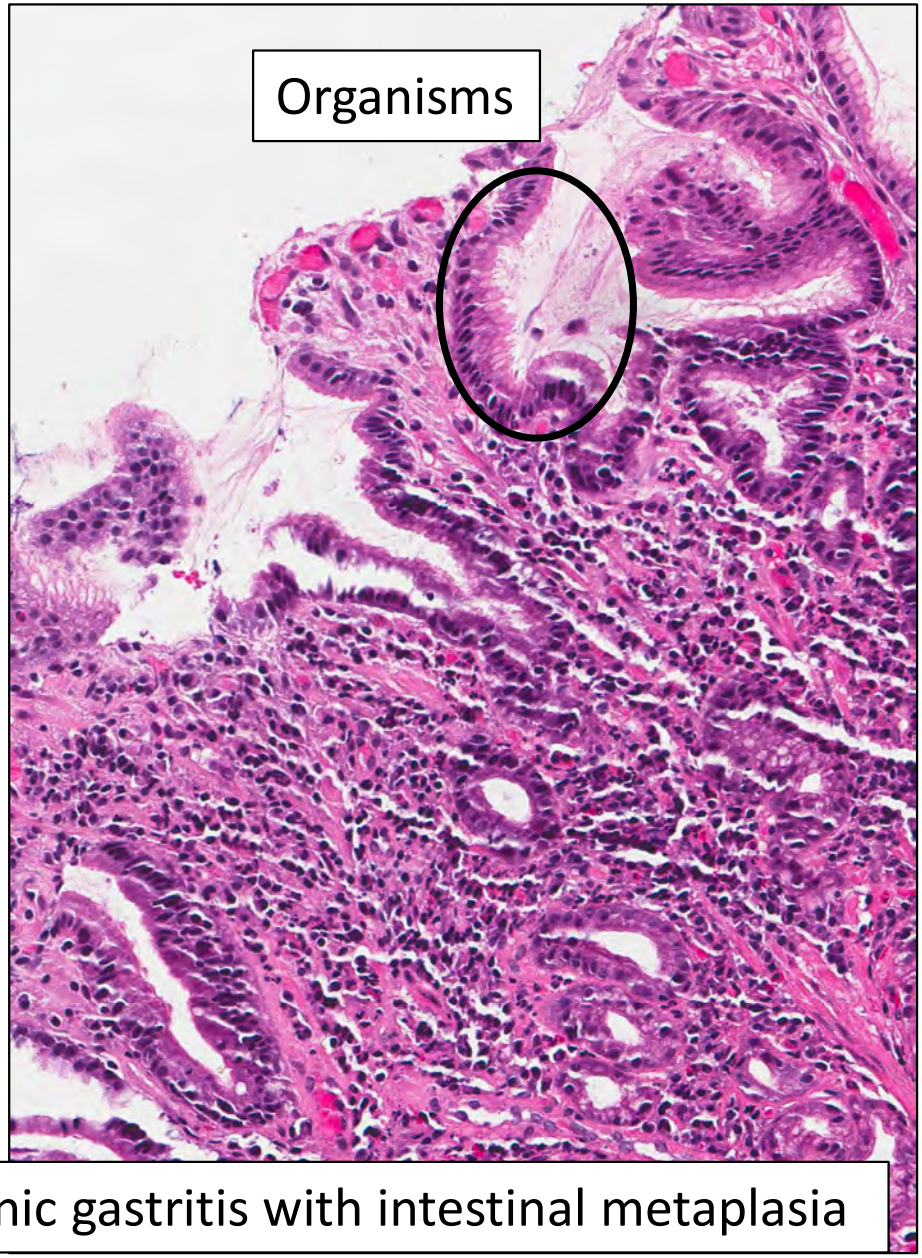
Immunostains can serve as a tissue level in a pinch



H. pylori immunohistochemistry

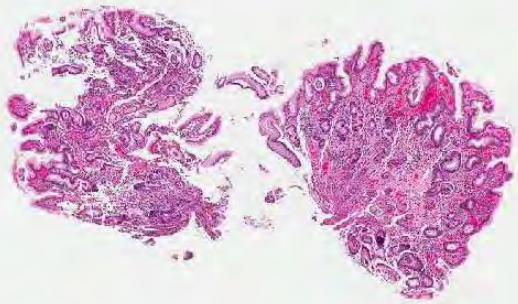


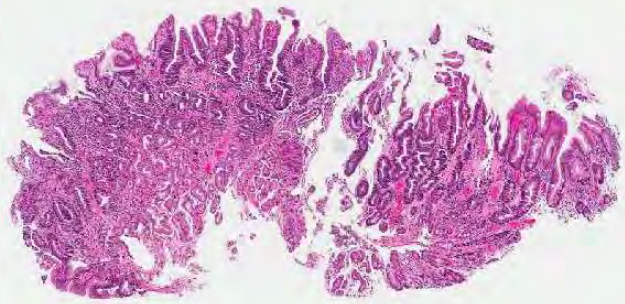


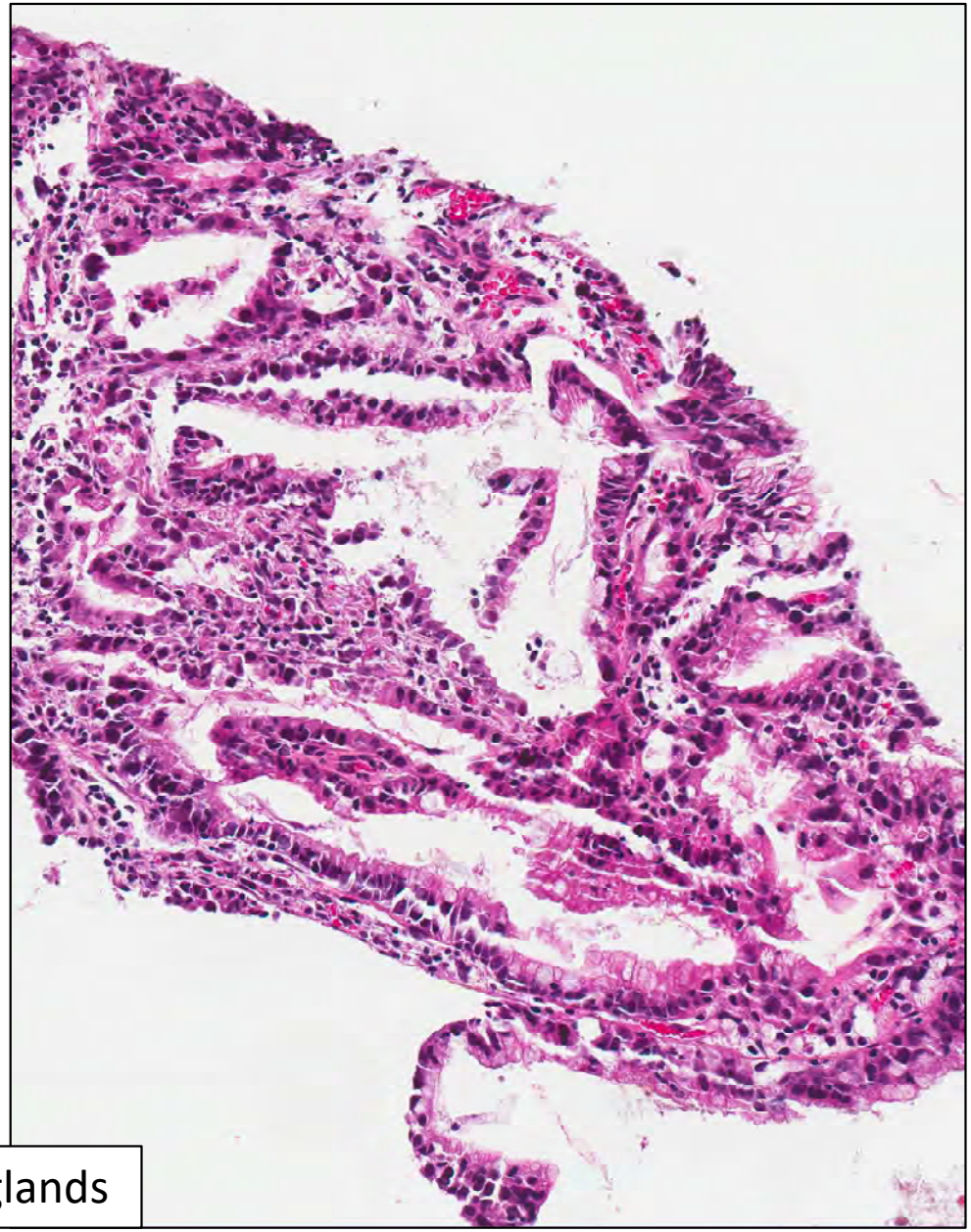


Prior biopsies show *H. pylori*-associated chronic gastritis with intestinal metaplasia

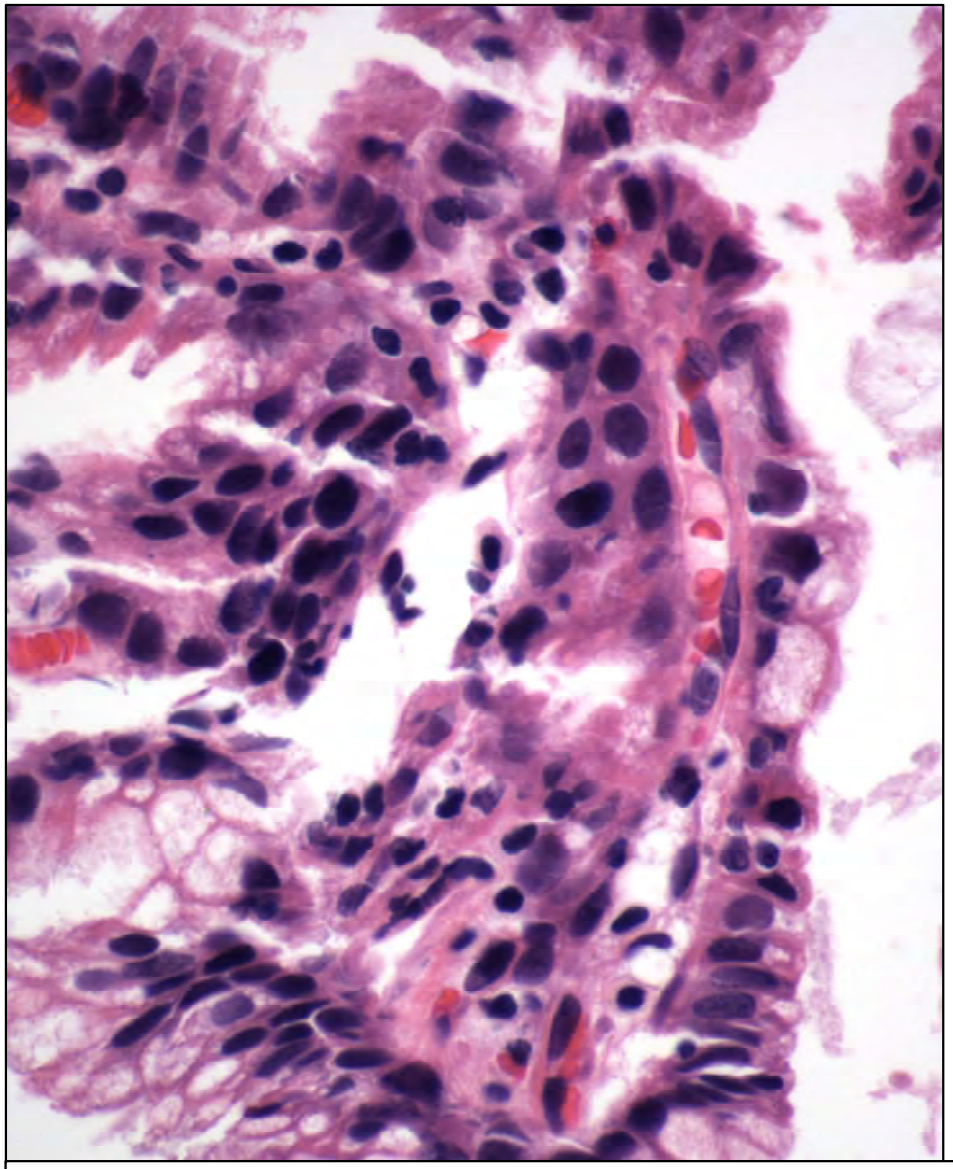
But then there were these two pieces off to the side…

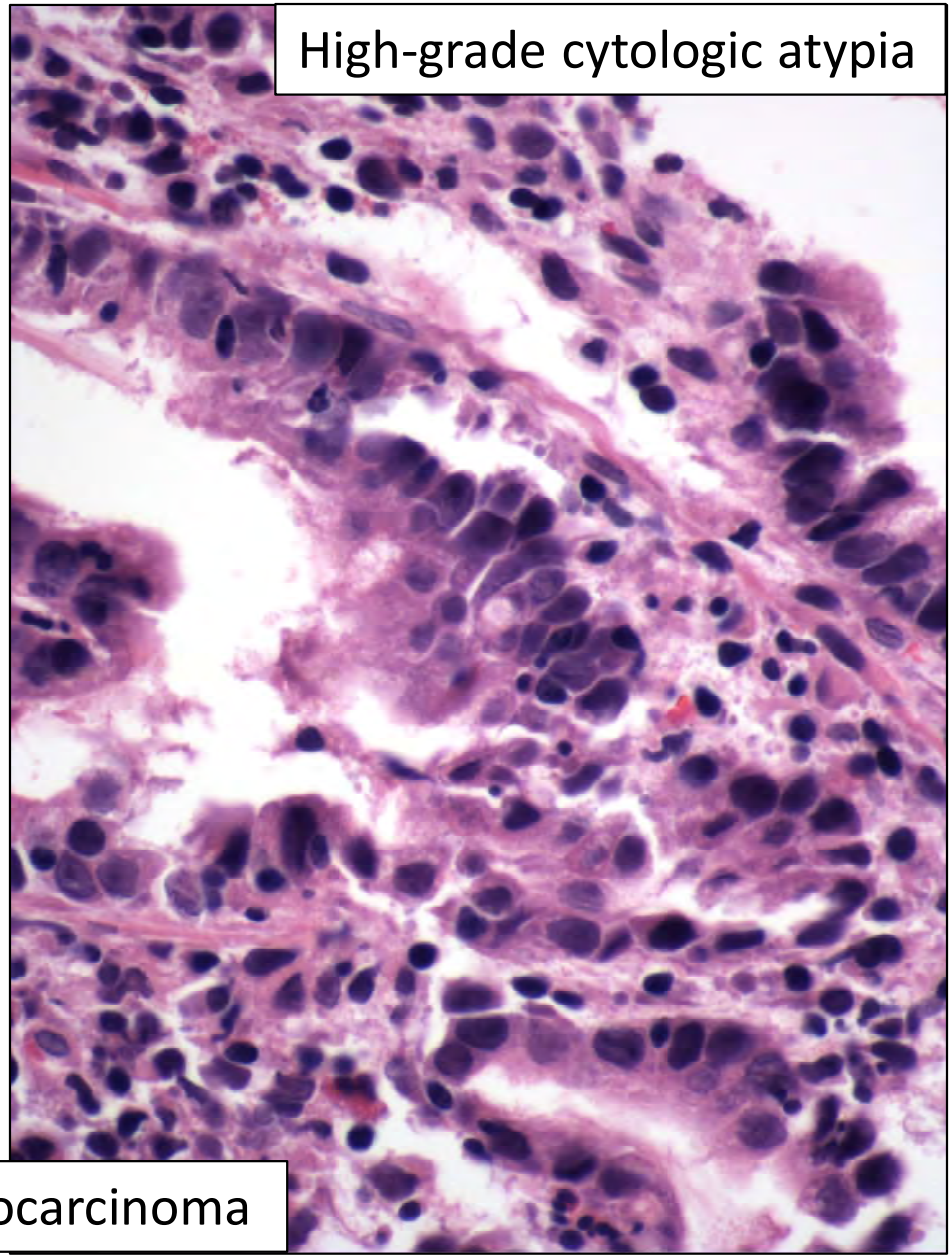






Architecturally complex proliferation of abnormal glands



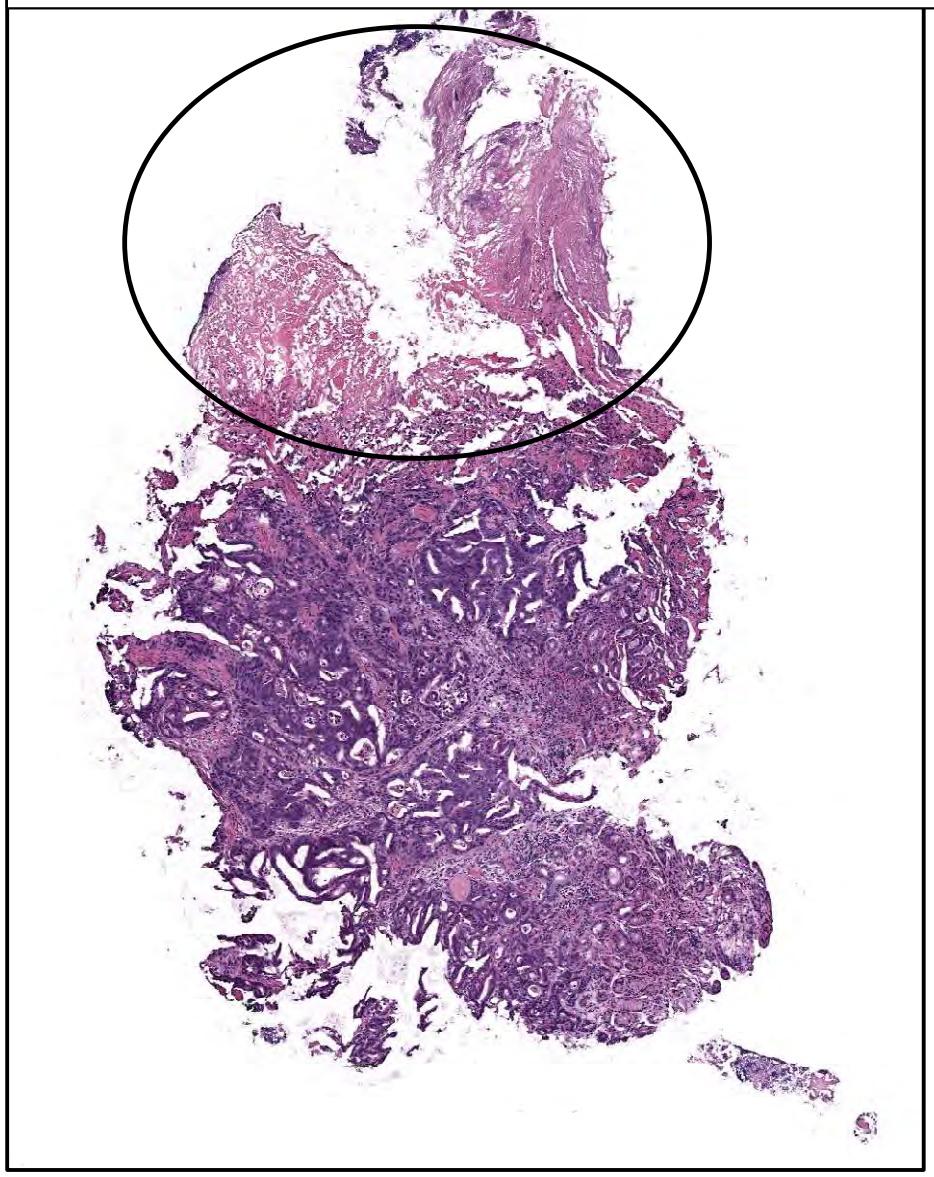


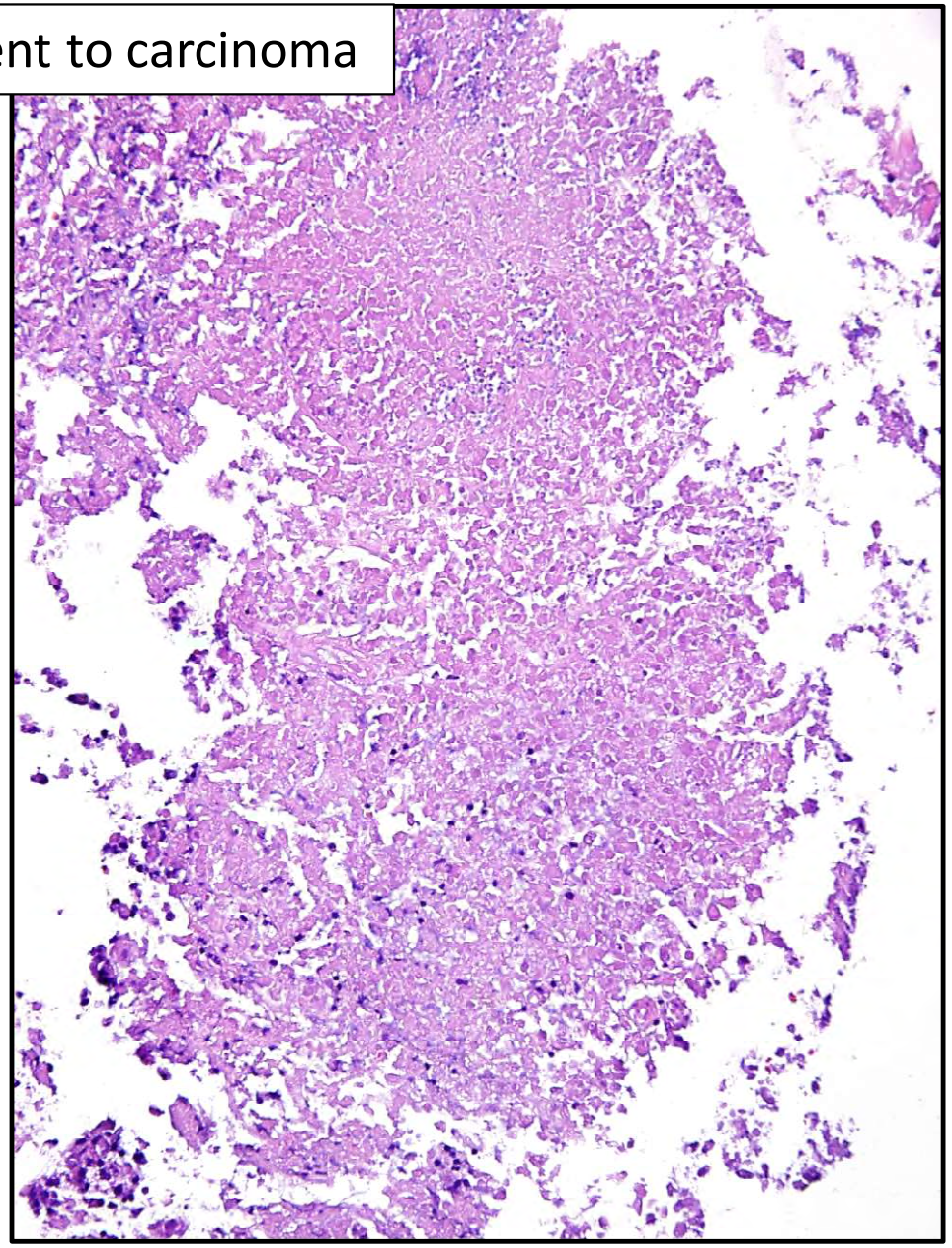
Patient proved to have a pT3, N1 gastric adenocarcinoma

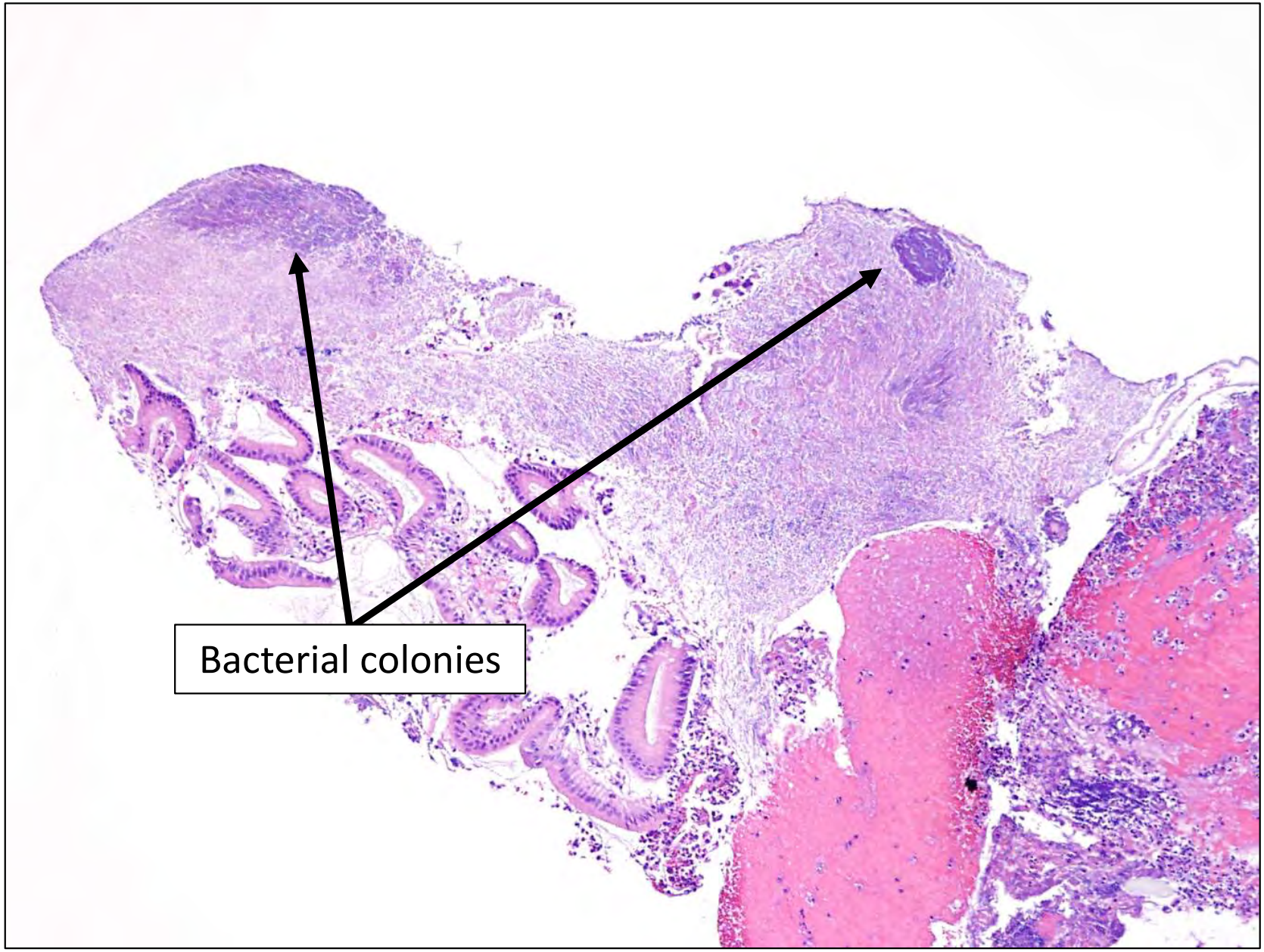
Detecting Small Volume Cancers

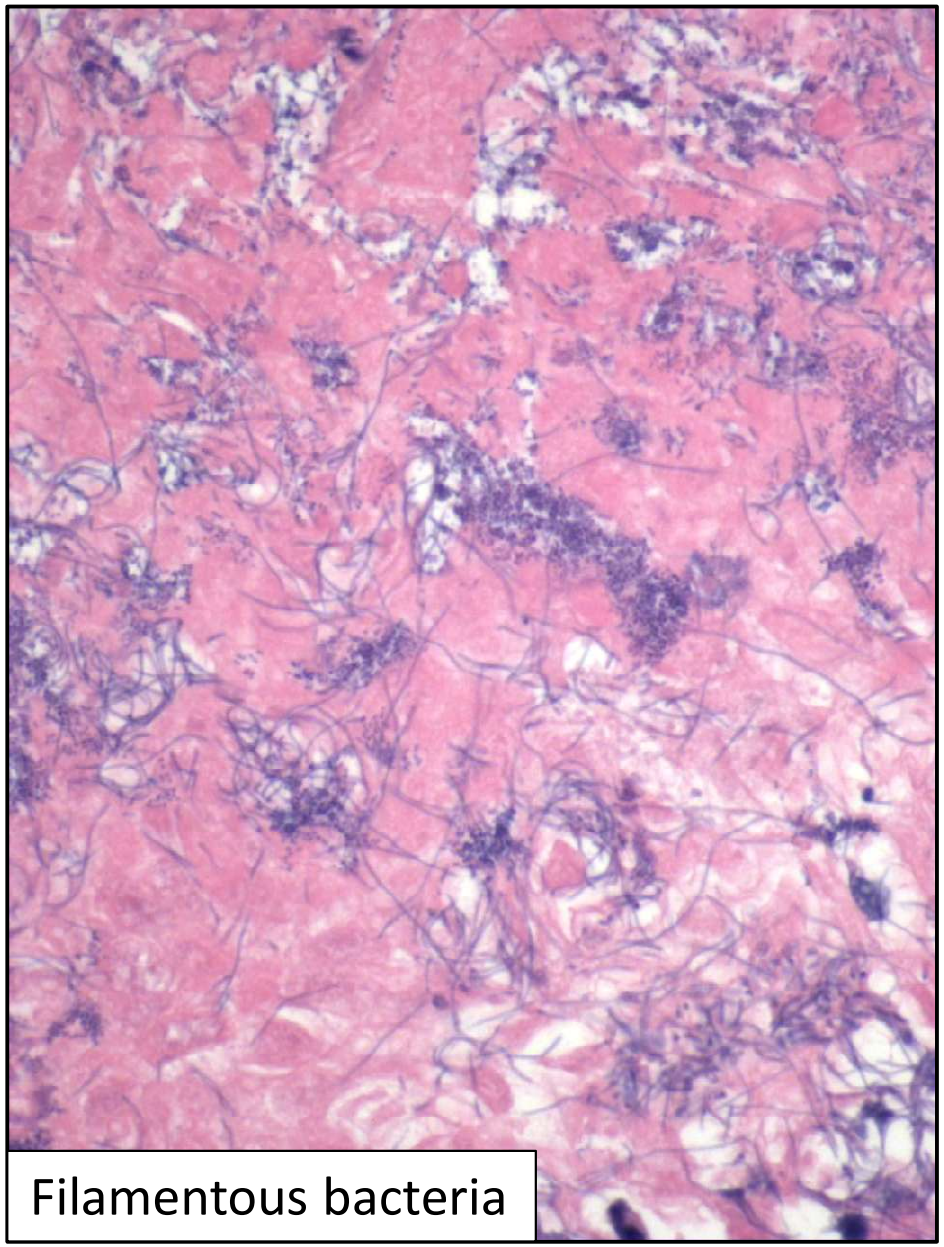
- Gastric cancers develop in a background of intestinal metaplasia and atrophy
  - *H. pylori*-associated gastritis
  - Autoimmune gastritis
  - Chronic bile reflux
  - Other types of chronic injury
- Atrophy leads to hypochlorhydria and decreased sterilization of gastric contents
- Swallowed bacteria and yeast survive
  - Colonize necrotic tissue (like ulcers and tumors)

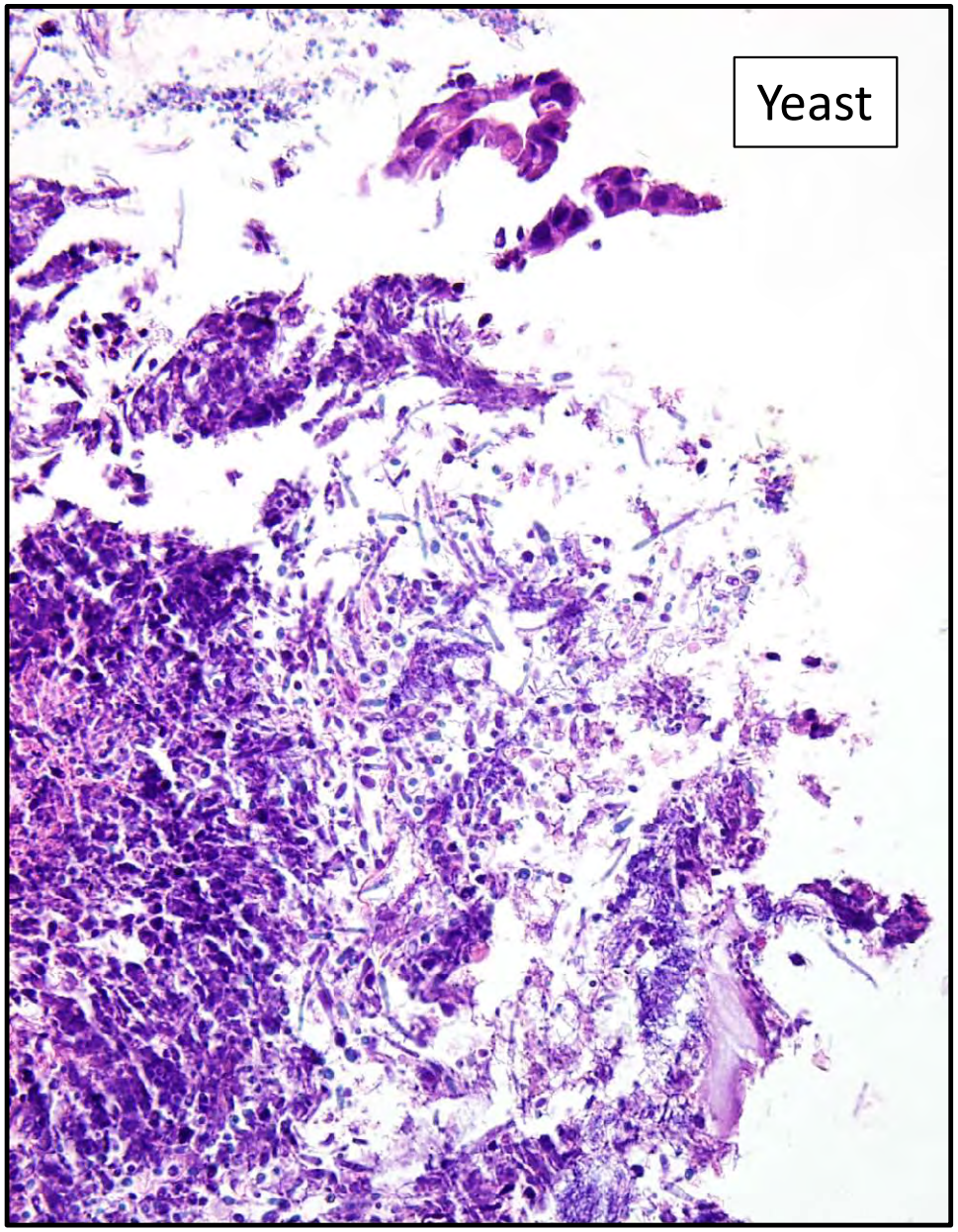
Luminal material and ulcer debris adherent to carcinoma






Bacterial colonies


Filamentous bacteria


Yeast

Findings in Exudates Distinguish Benign Ulcers from Ulcerated Gastric Carcinomas

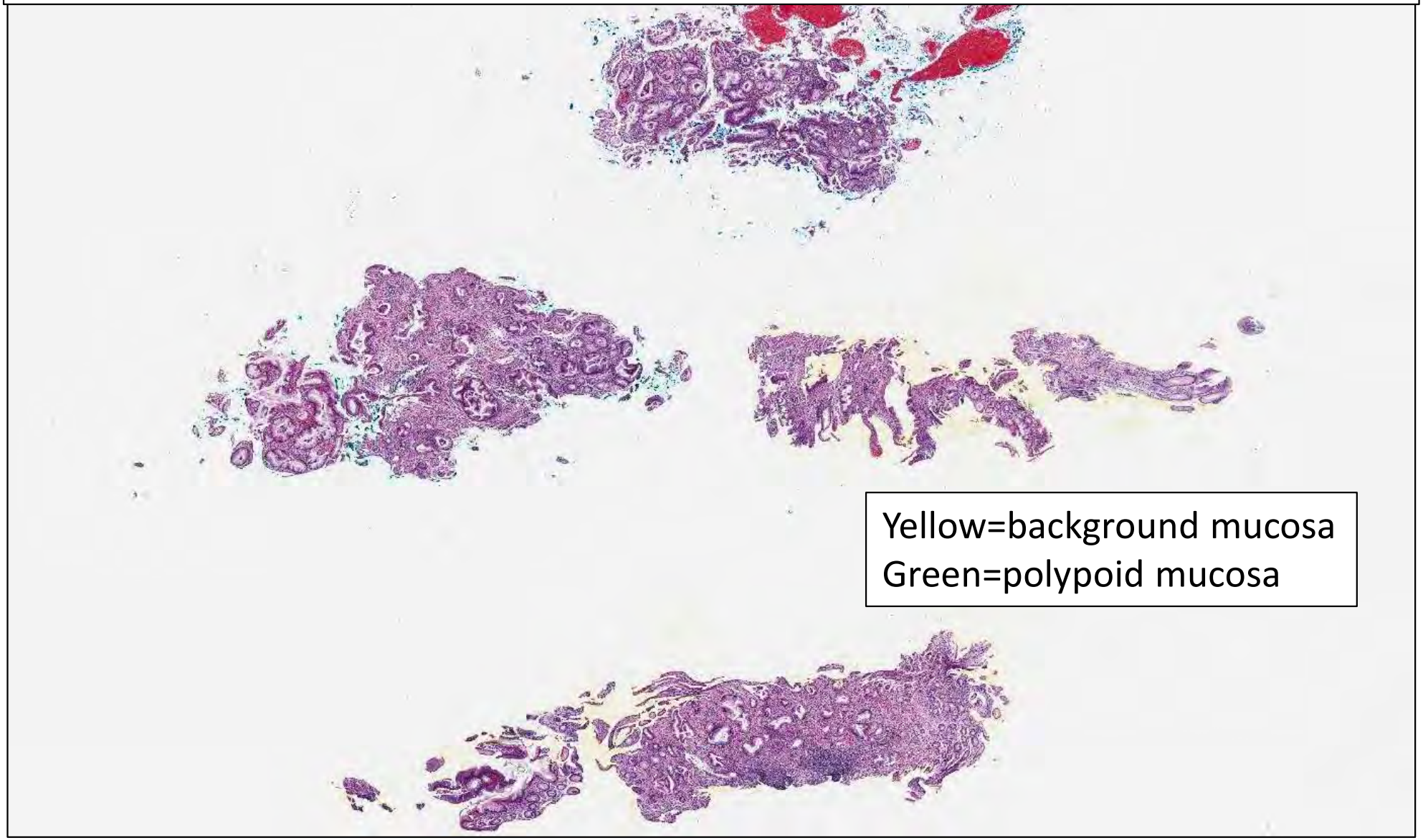
	Carcinoma cases	Benign ulcer cases	P value
Necrotic cellular debris	38 (76%)	37 (74%)	p > 0.05
Blood and/or fibrin	48 (96%)	48 (96%)	p > 0.05
Non-*H. pylori* bacteria	38 (76%)	5 (10%)	p < 0.01
Filamentous bacteria	8 (16%)	1 (2%)	p = 0.02
Fungi	9 (18%)	1 (2%)	p = 0.02
Background mucosa			
H. pylori gastritis	6 (12%)	10 (20%)	p > 0.05
Chemical gastropathy	5 (10%)	26 (52%)	p < 0.01
Intestinal metaplasia	25 (50%)	14 (28%)	p = 0.04
Autoimmune gastritis	4 (8%)	1 (2%)	p > 0.05
H. pylori-negative gastritis	9 (18%)	8 (16%)	p > 0.05

Hissong, *et al. Histopathology*. 2018; 73(2): 215-219.

Case

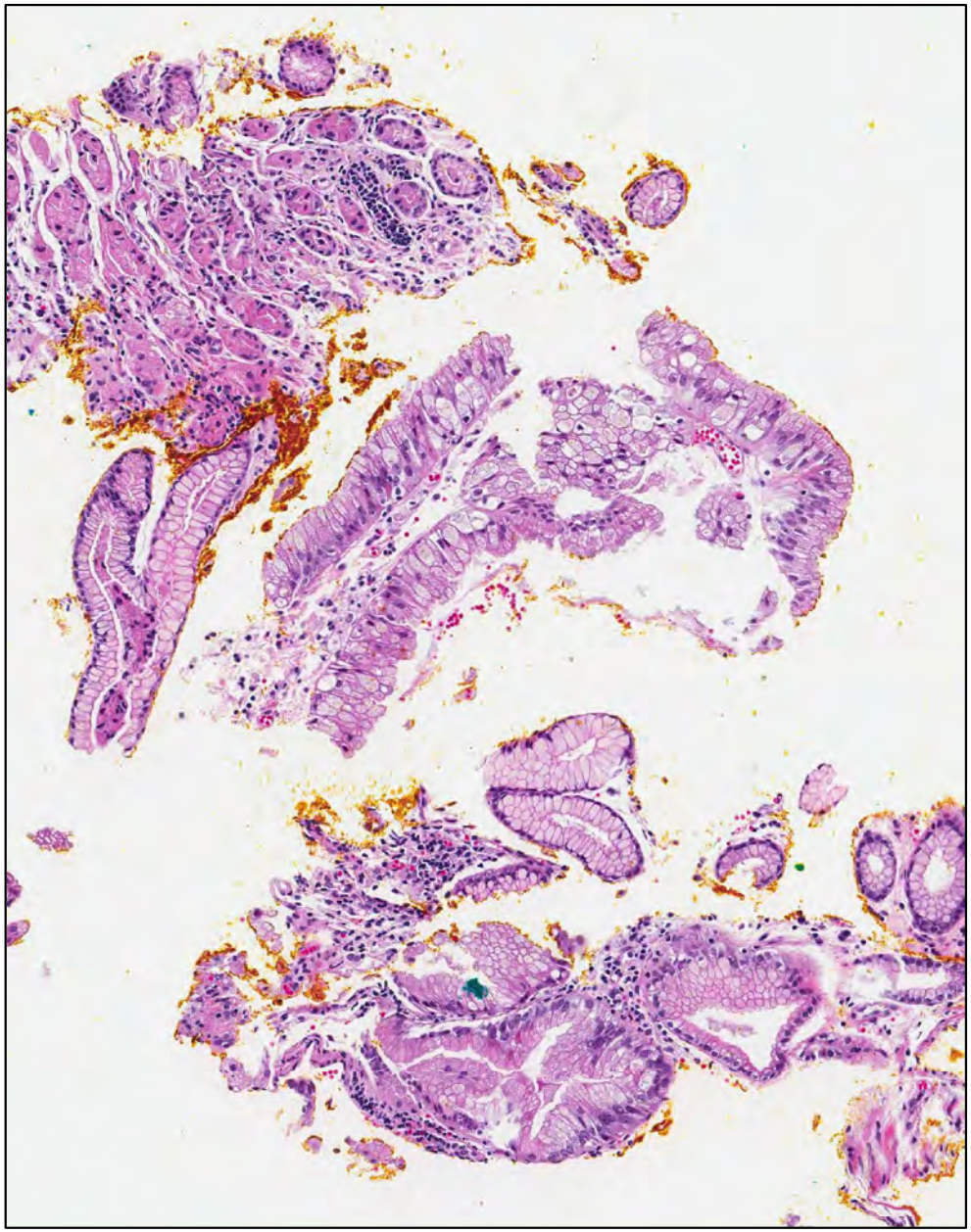
- 60-year-old female with recently diagnosed autoimmune gastritis and gastric polyps
- Biopsies from a gastric mass interpreted to be hyperplastic polyps
- Reviewed because the polyps “looked a little funny”

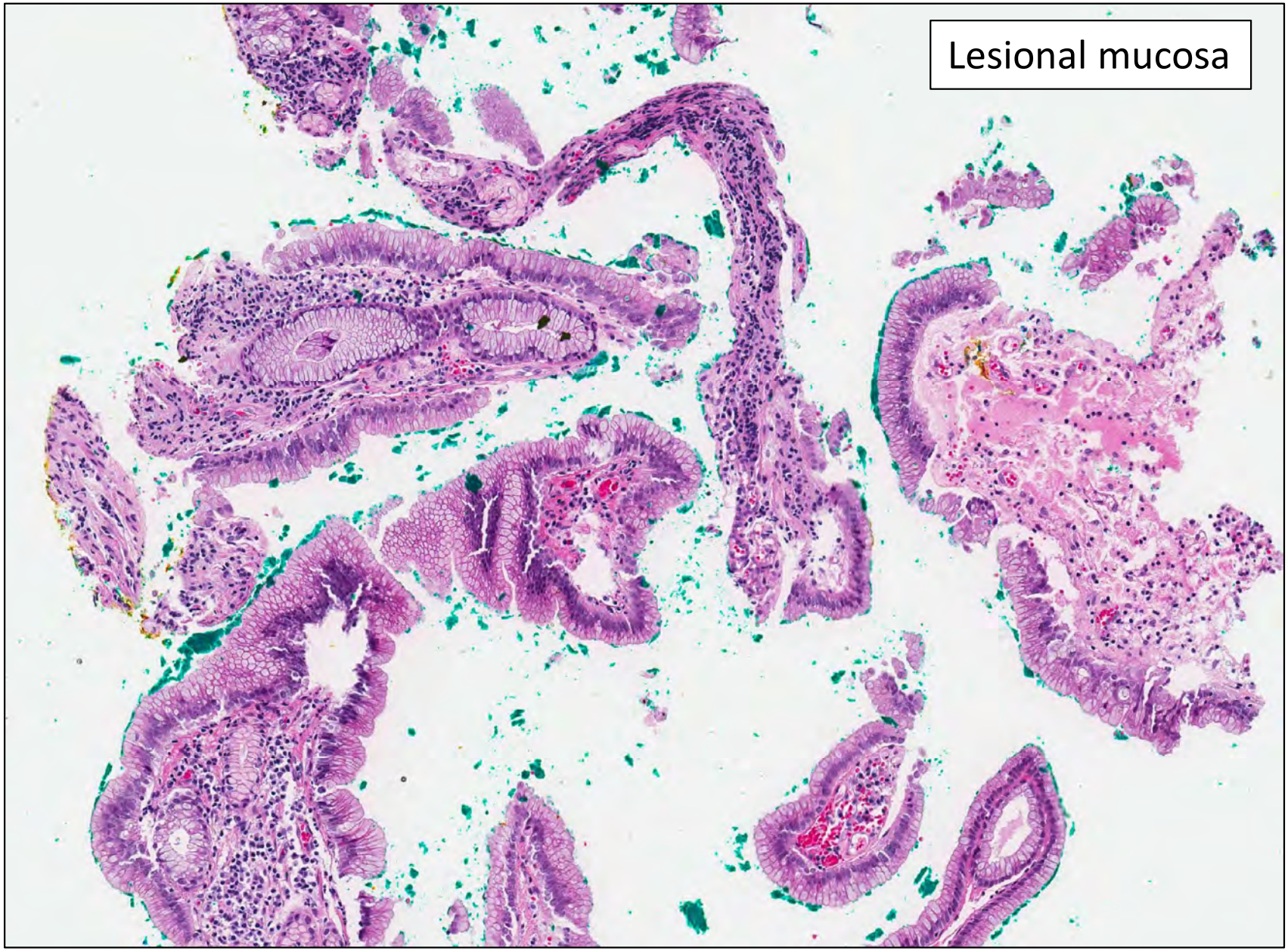
60-year-old woman with recently diagnosed autoimmune gastritis and gastric polyps

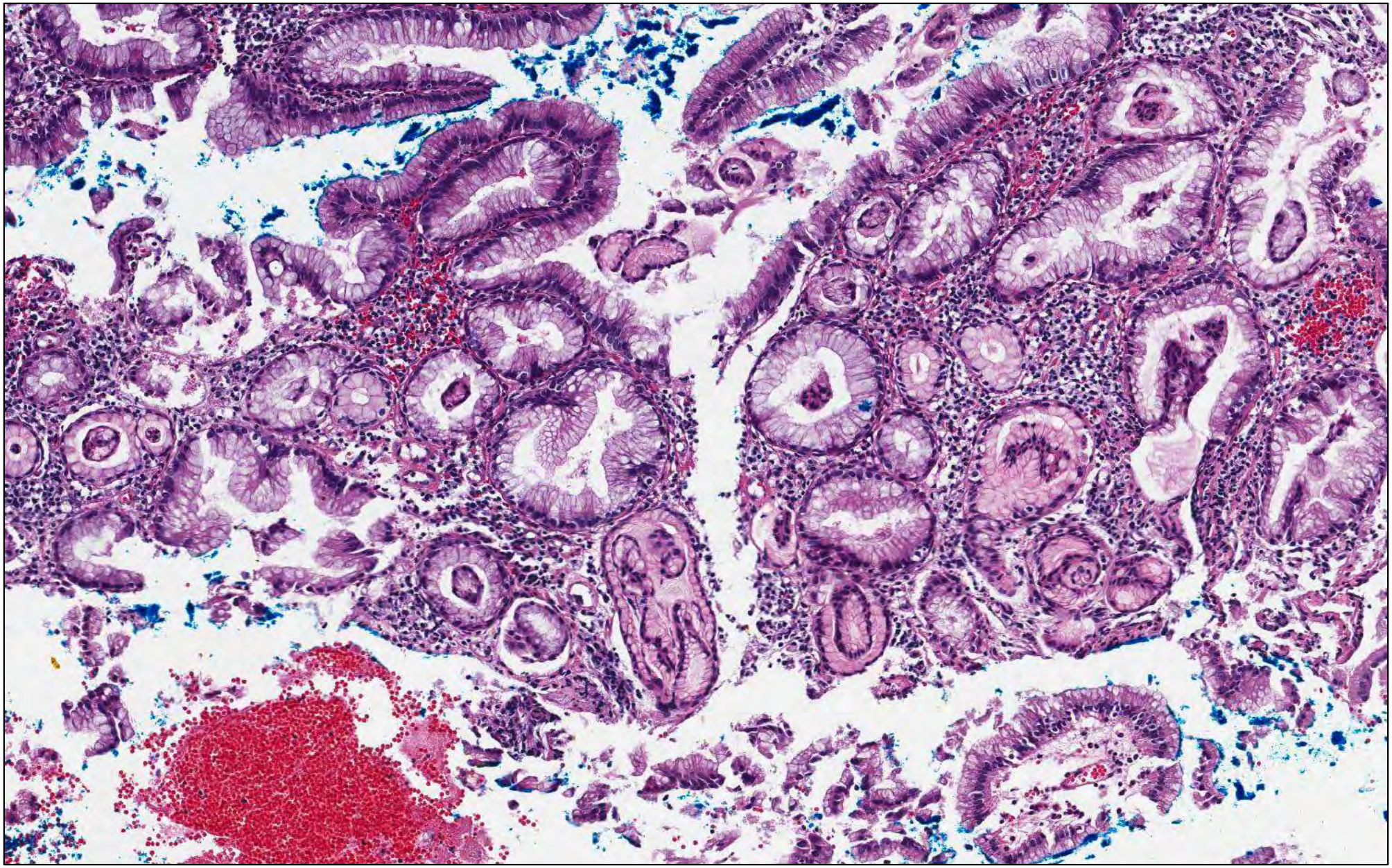


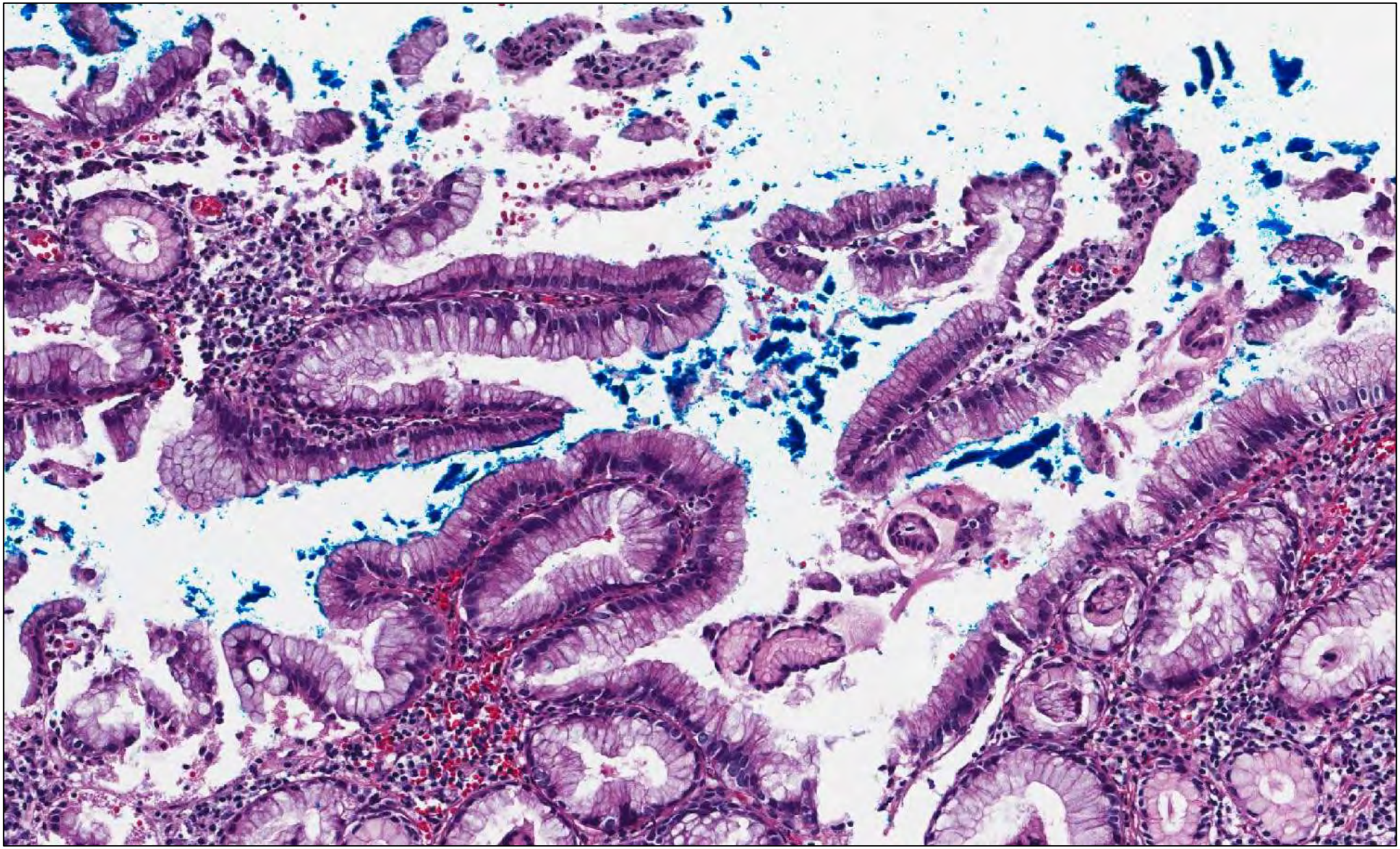

Background mucosa


Background mucosa



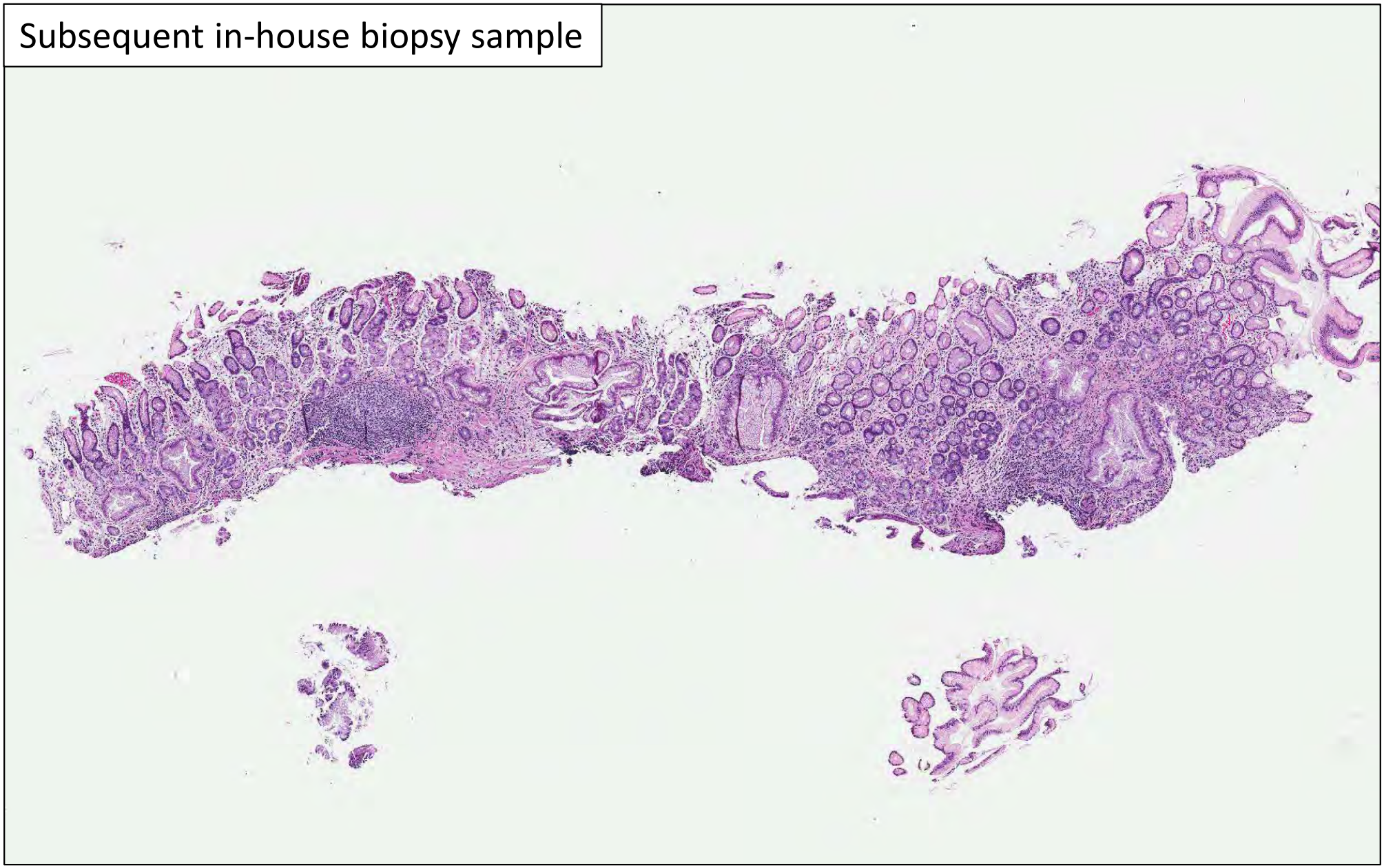

Lesional mucosa



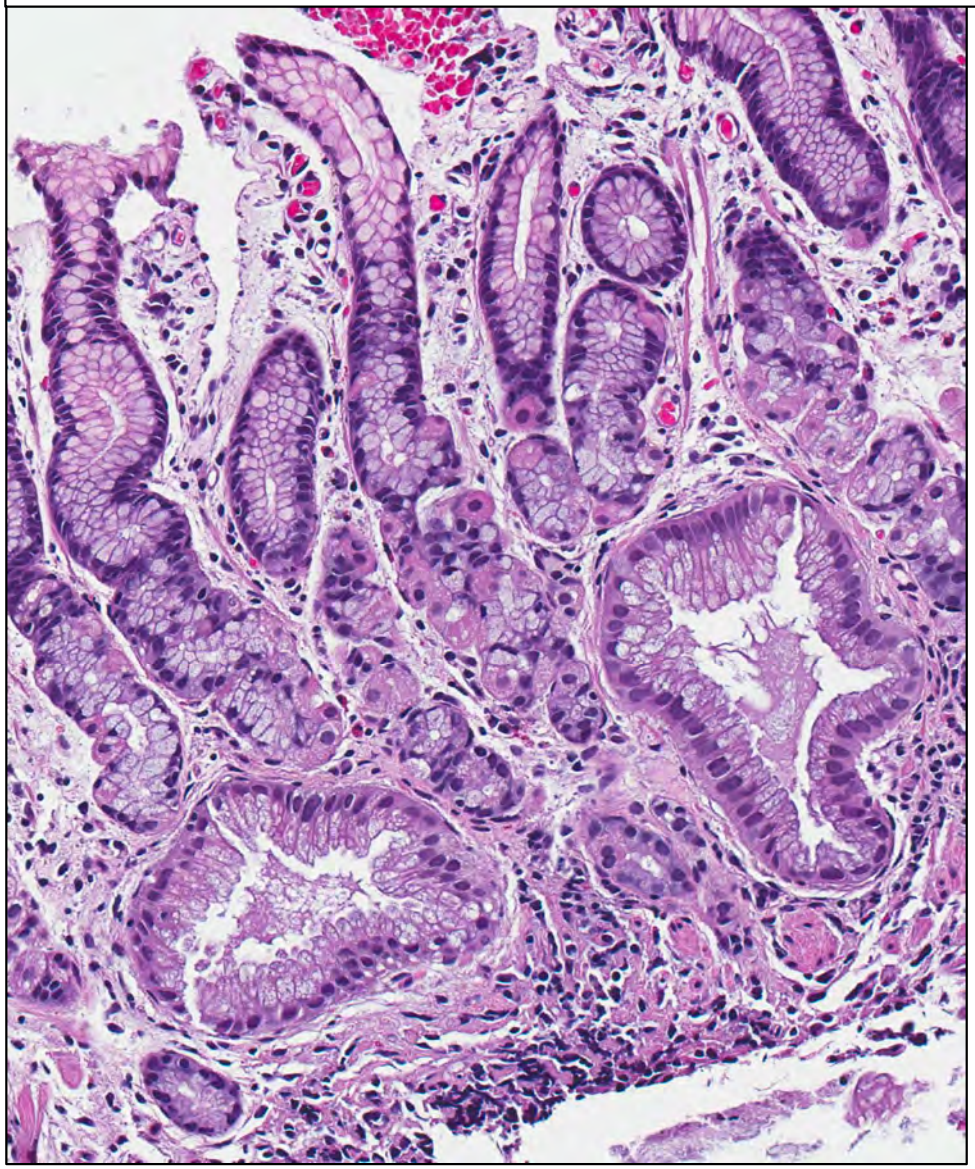


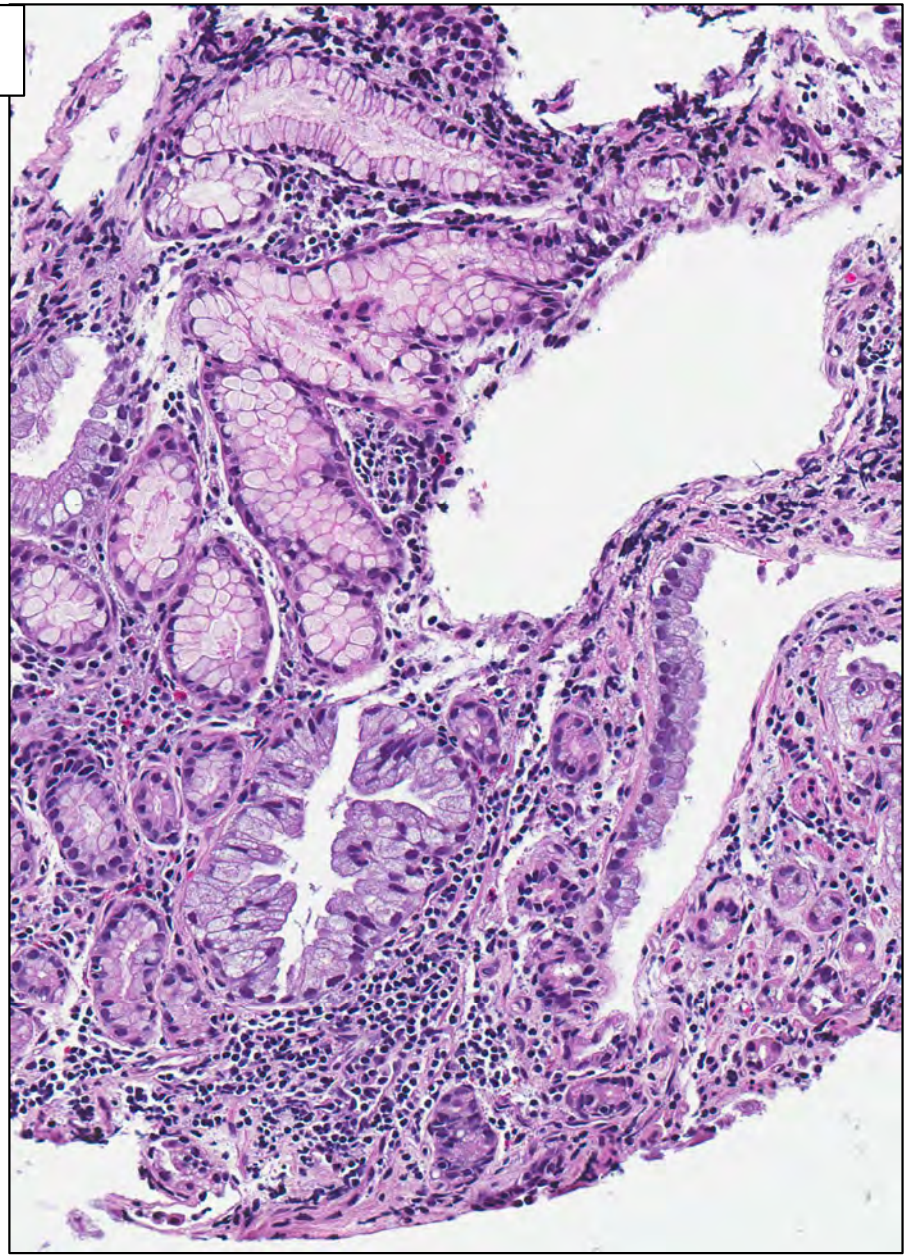
Diagnosis: Mucosal hyperplasia/hyperplastic polyps in association with autoimmune gastritis

Subsequent in-house biopsy sample

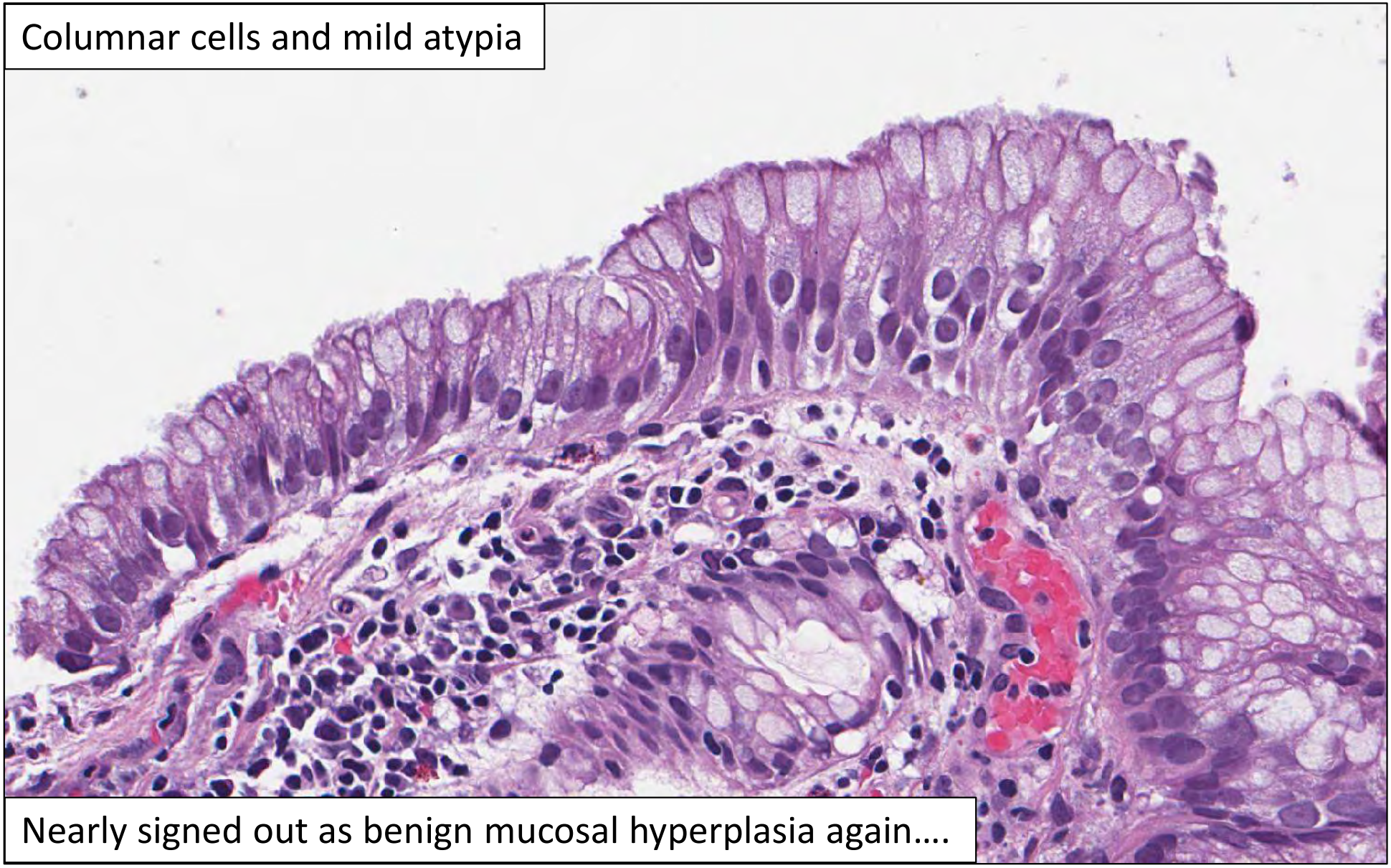


Chronic gastritis with funny mucinous glands

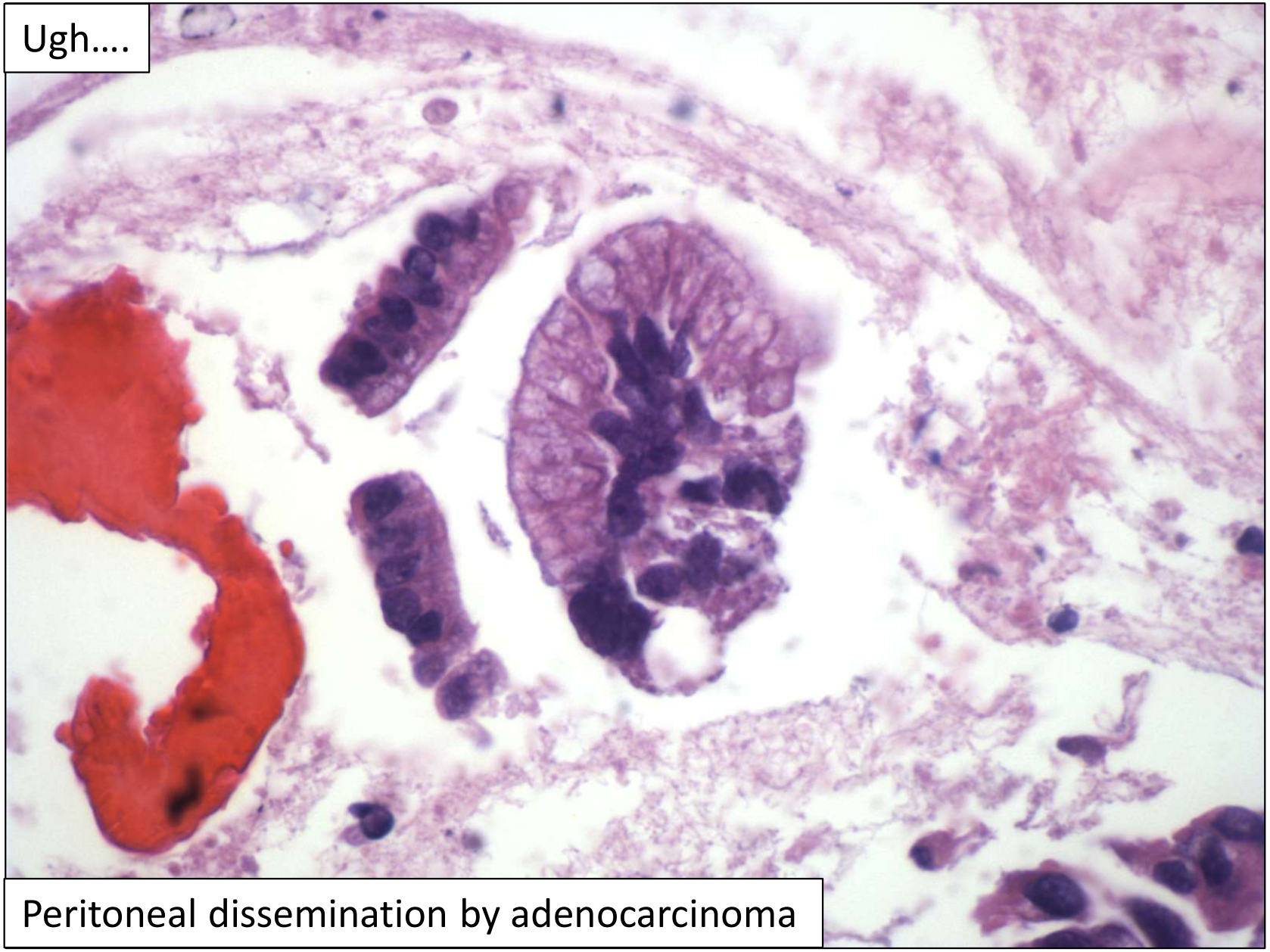




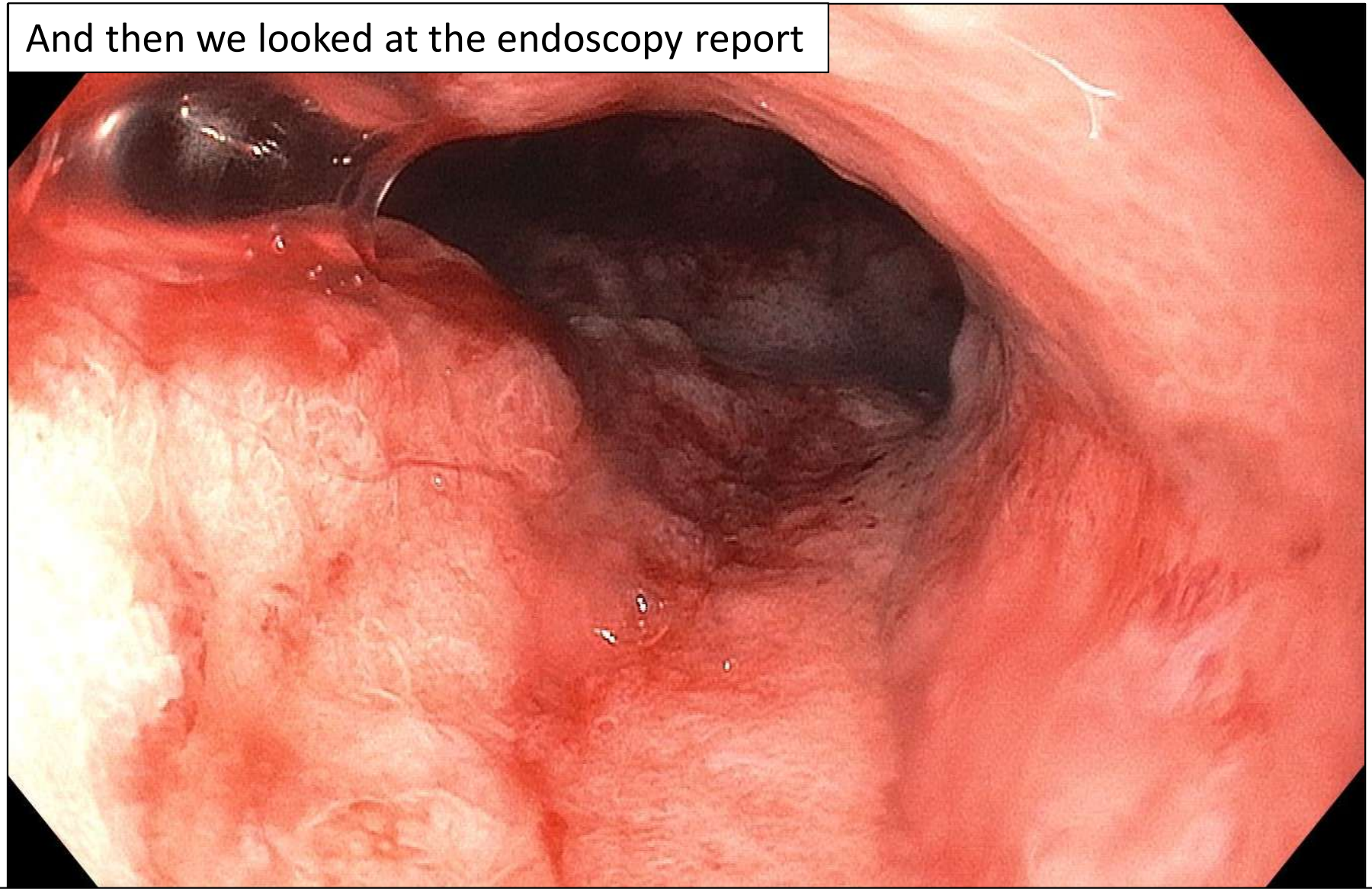
Columnar cells and mild atypia



Nearly signed out as benign mucosal hyperplasia again….

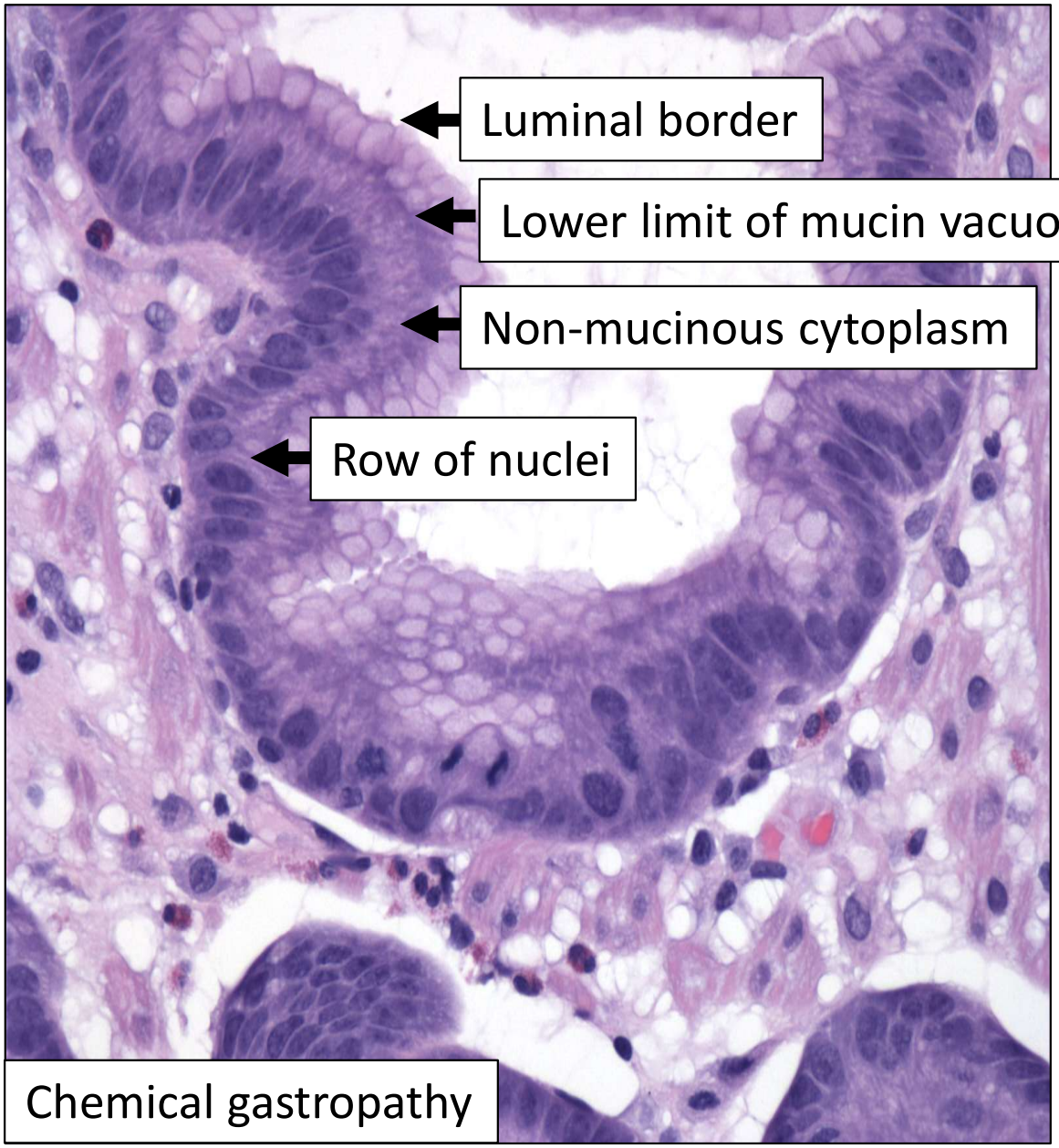

Ugh….
Peritoneal dissemination by adenocarcinoma

And then we looked at the endoscopy report

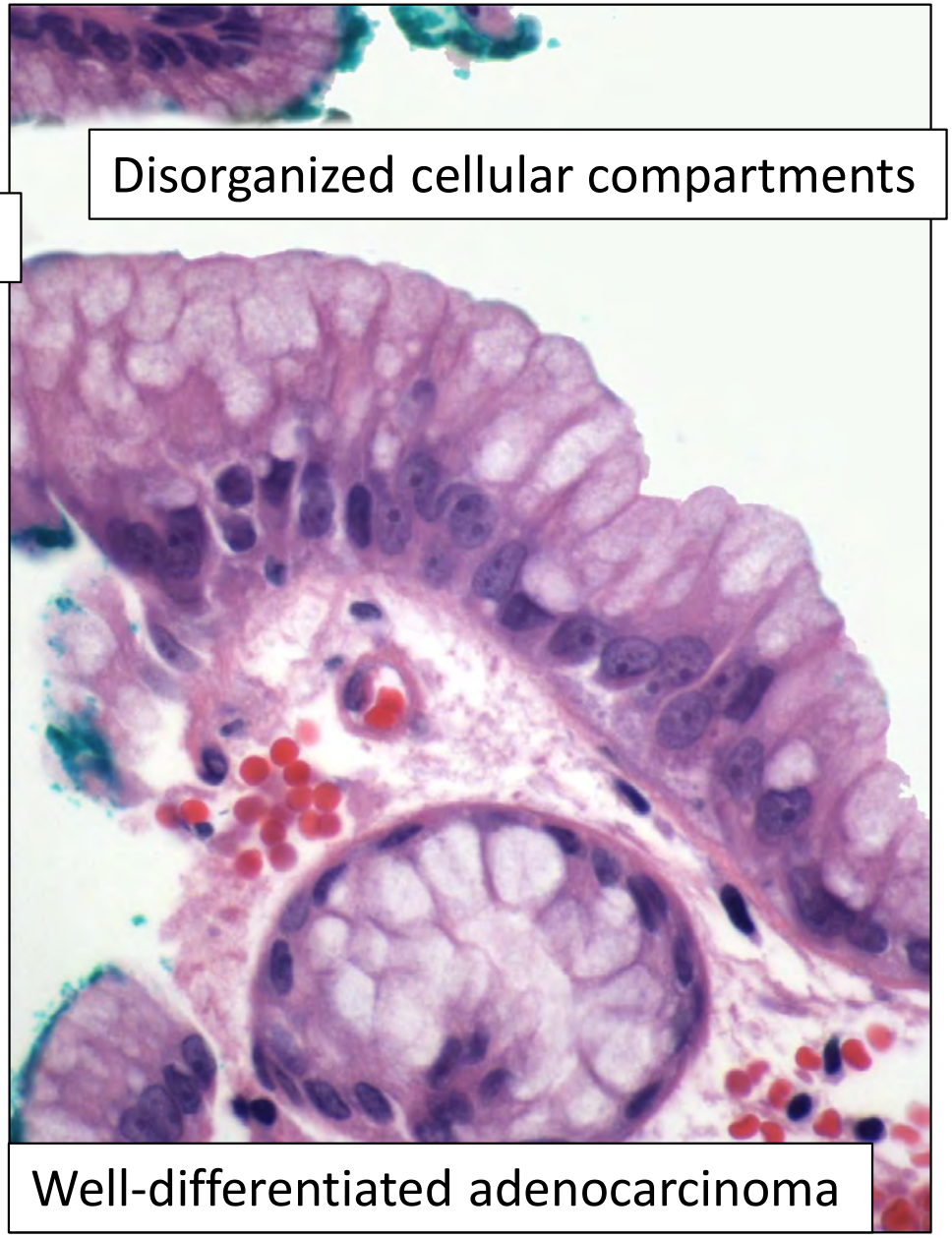


Endoscopic findings of a cancer, not a hyperplastic polyp or benign mucosal abnormality

Don’t force unusual cases into pre-existing categories without getting the full story

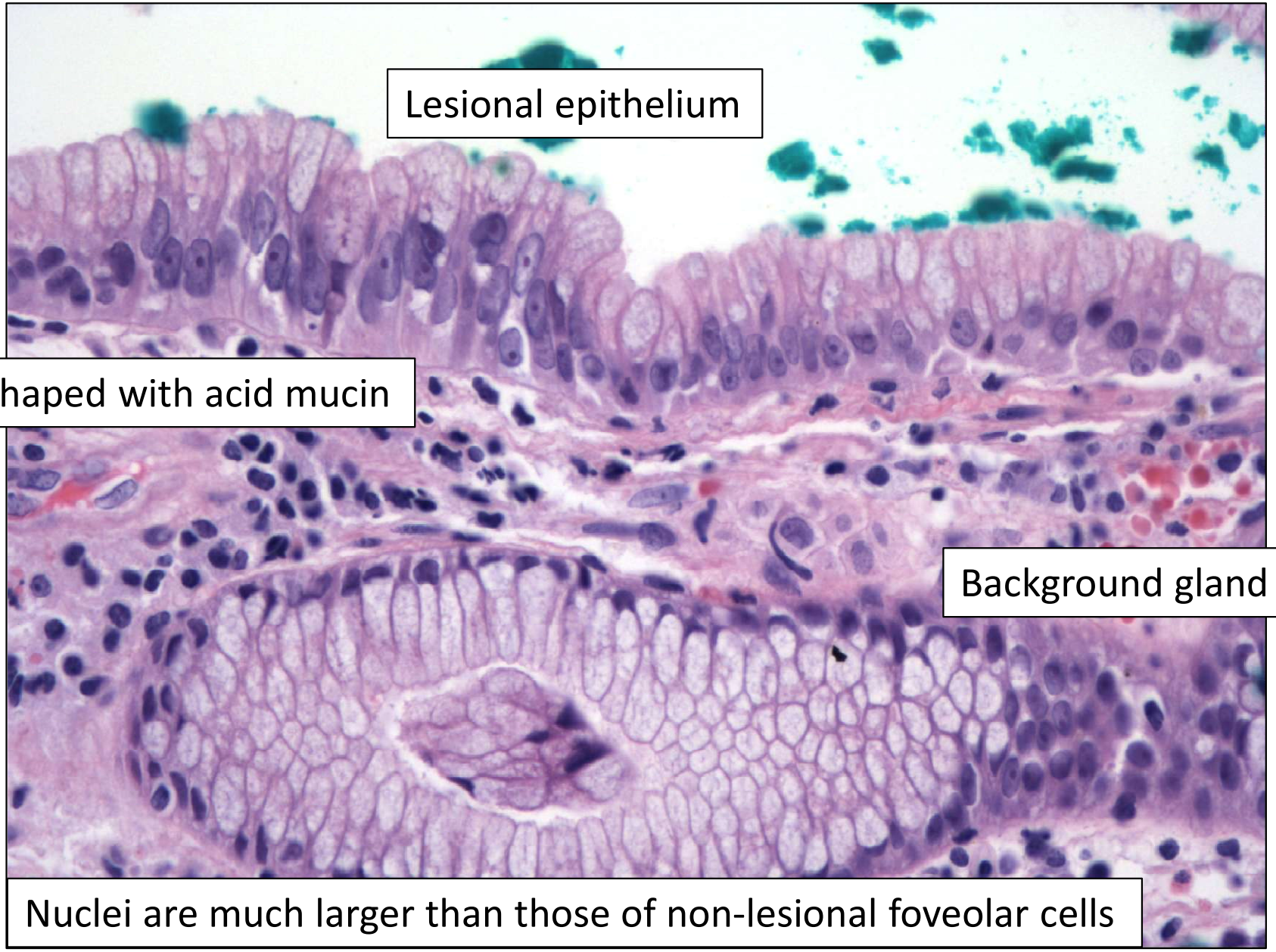


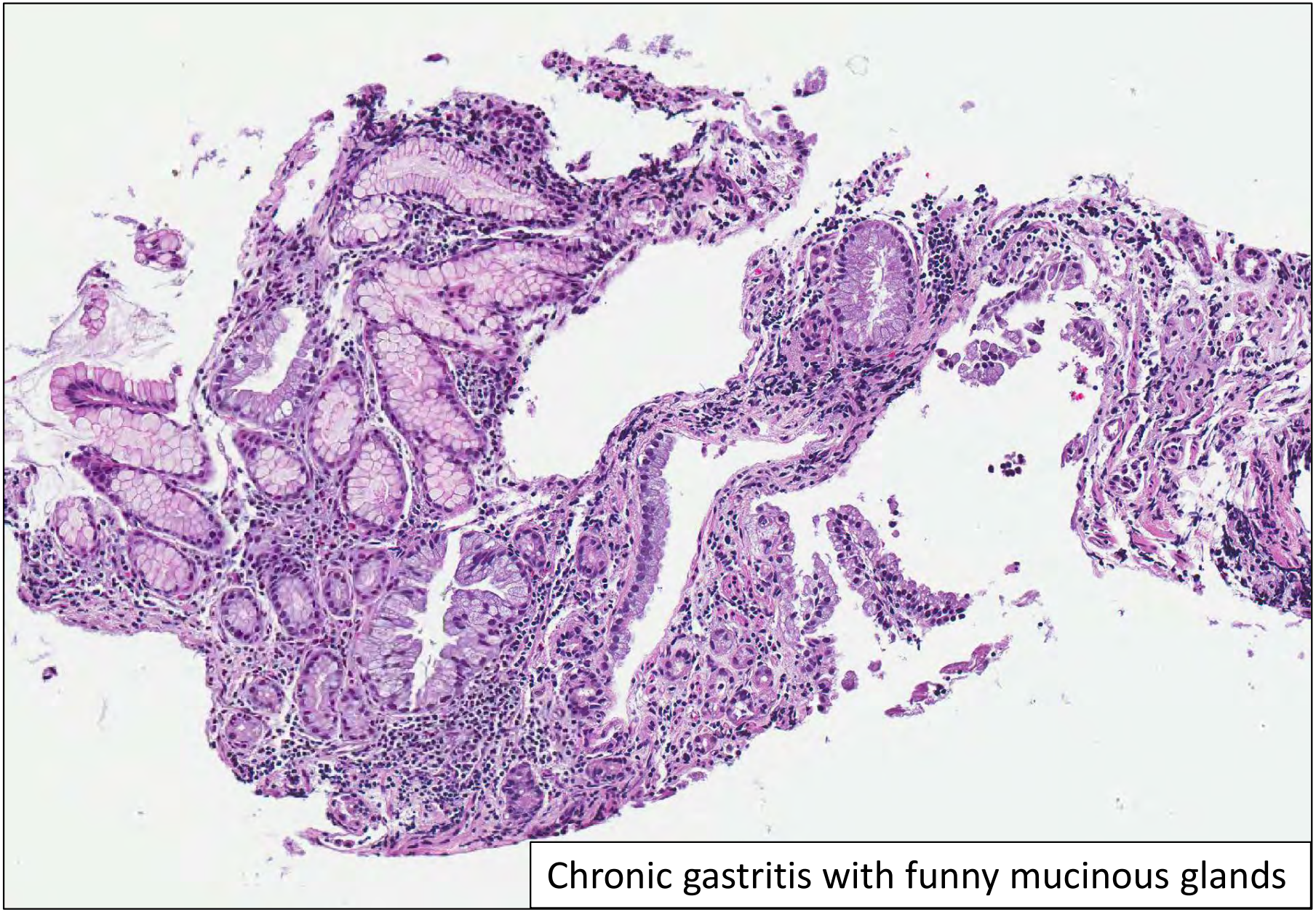
Chemical gastropathy



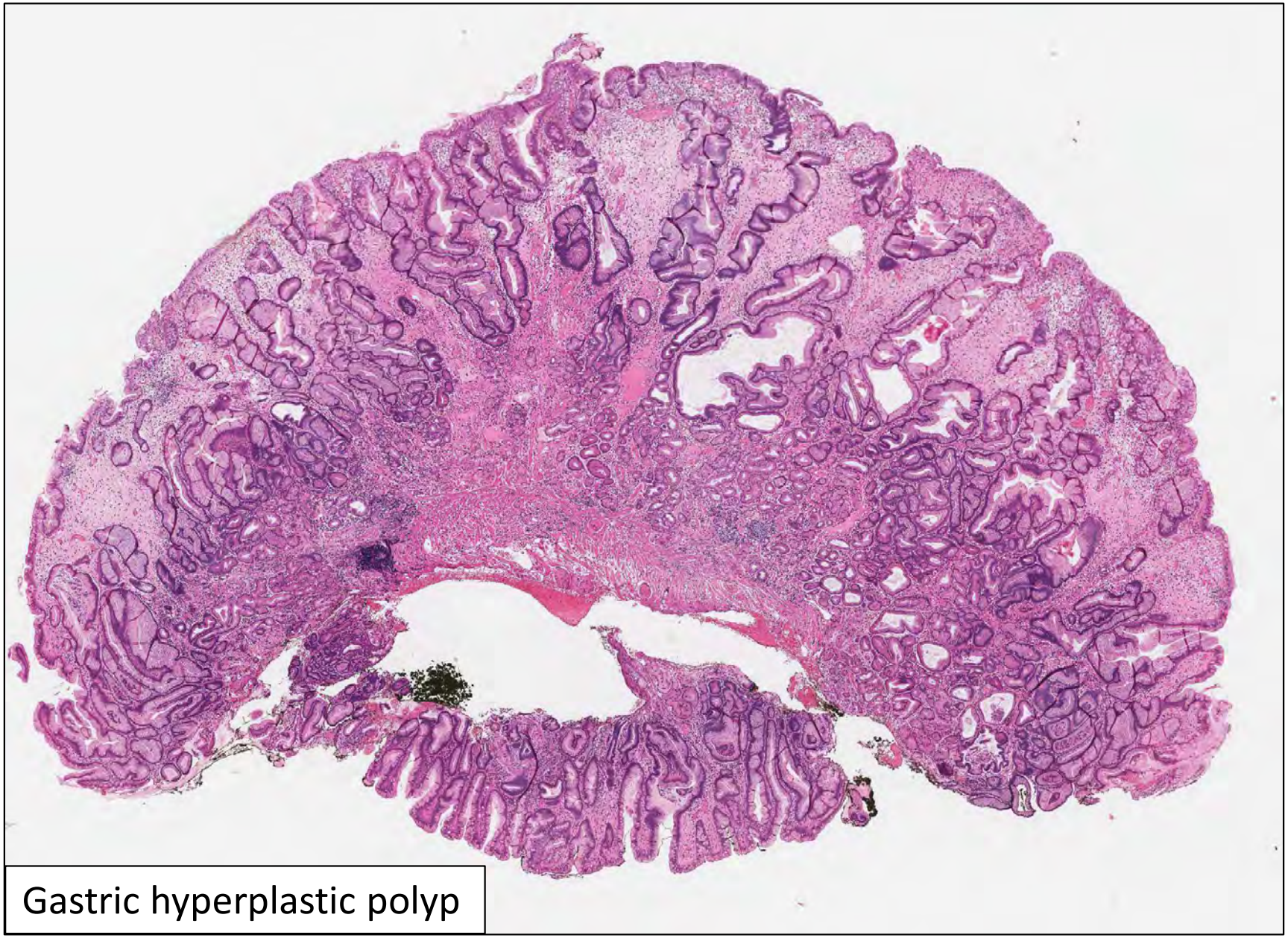
Well-differentiated adenocarcinoma

Back to the case


Lesional epithelium
Barrel-shaped with acid mucin
Background gland
Nuclei are much larger than those of non-lesional foveolar cells



Chronic gastritis with funny mucinous glands



Gastric hyperplastic polyp

Gastric hyperplastic polyp

Papillary surface of cancer

Extremely Well-Differentiated Adenocarcinoma of Gastric Phenotype

World Journal of Surgical Oncology

BioMed Central

Case report

Open Access

Gastric extremely well differentiated adenocarcinoma of gastric phenotype: as a gastric counterpart of adenoma malignum of the uterine cervix

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Published: 23 May 2005
World Journal of Surgical Oncology 2005, 3:28 doi:10.1186/1477-7819-3-28
Received: 09 March 2005
Accepted: 23 May 2005
This article is available from: http://www.wjso.com/content/3/1/28

Abstract

Background: Most of gastric adenocarcinoma can be simply diagnosed by microscopic examination of biopsy specimen. Rarely the structural and cellular atypia of tumor cells is too insignificant to discriminate from benign foveolar epithelium.

Case presentation: A 67-year-old male presented with a gastric mass incidentally found on the abdominal computed tomography (CT) for routine medical examination. Gastric endoscopic examination revealed a huge fungating mass at the cardia and mucosal biopsy was performed. Microscopically the biopsy specimen showed proliferation of bland looking foveolar epithelia in the inflammatory background and diagnosed as foveolar epithelial hyperplasia. Because the clinical and endoscopic features of this patient were strongly suggestive of malignancy, the patient underwent radical total gastrectomy. The resected stomach revealed a huge fungating tumor at the cardia. The cut surface of the tumor was whitish gelatinous. Microscopically the tumor was sharply demarcated from surrounding mucosa and composed of very well formed glandular structures without significant cellular atypia, which invaded into the whole layer of the gastric wall. Tumor glands were occasionally complicated or dilated, and glandular lumina were filled with abundant mucin. Immunohistochemically the tumor cells revealed no overexpression of p53 protein but high Ki-67 labeling index. The tumor cells and intraluminal mucin were diffusely expressed MUC1 and MUC5AC and only focally expressed MUC2. On abdominal CT taken after 12 months demonstrated peritoneal carcinomatosis and multiple metastatic foci in the lung.

Conclusion: The clinicopathologic profiles of gastric extremely well differentiated adenocarcinoma of gastric phenotype include cardiac location, fungating gross type, very similar histology to foveolar epithelial hyperplasia, foveolar mucin phenotype, lack of p53 overexpressoin and high proliferative index.

Background

Most of gastric adenocarcinoma can be simply diagnosed by microscopic examination of biopsy specimen. Extremely well differentiated adenocarcinoma (EWDA) of the stomach is histologically too bland and too similar to benign foveolar epithelium to make a diagnosis as

- Non-goblet, acid mucin-containing cells with mild cytologic atypia
- No/minimal mitotic activity
- No necrosis
- P53 generally negative
- Ki-67 often shows some labeling
- Almost impossible to diagnose in biopsy samples alone
- Largely diagnosed at resection following multiple biopsy procedures

How to Avoid Missing or Over-Diagnosing Gastric Cancer

- Be cautious with malignant diagnoses when disrupted glands are present
- Cancers growing in mucosa can be sneaky
  - Edema and deep cellularity are clues
  - Lots of non-*H. pylori* organisms should prompt a closer look, levels
- Tissue levels are often revealing and buy time
- High index of suspicion; knowledge of clinical findings
  - Don’t try to force unusual cases into pre-existing categories

THANK YOU

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