

# Gastritis (and gastropathy)

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# Topics for discussion

- ▶ Classification of gastritis
- ▶ Minimal diagnostic criteria for 'gastritis'
- ▶ H.pylori negative active chronic gastritis
- ▶ Routine use of special stains in gastric biopsies
- ▶ Assessment of atrophy
- ▶ Lymphocytic gastritis
- ▶ Gastritis in Crohn's disease
- ▶ Uncommon/newly described forms of gastritis
- ▶ Open discussion

# General points

- ▶ Gastritis and gastropathy may represent
  - ▶ specific condition eg Hp gastritis, autoimmune gastritis
  - ▶ a tissue reaction pattern with many possible causes e.g. reactive gastropathy, lymphocytic gastritis and granulomatous gastritis

# Classification scheme

## Gastritis

Diffuse

H. pylori

Autoimmune

Eosinophilic

Lymphocytic

Collagenous

Infection - non HP

Focal

Focally enhanced

Granulomatous

## Gastropathy

Reactive gastropathy

Vascular gastropathies - GAVE, PHG, congestive

Medication related - doxycycline, sartans,  
biologics

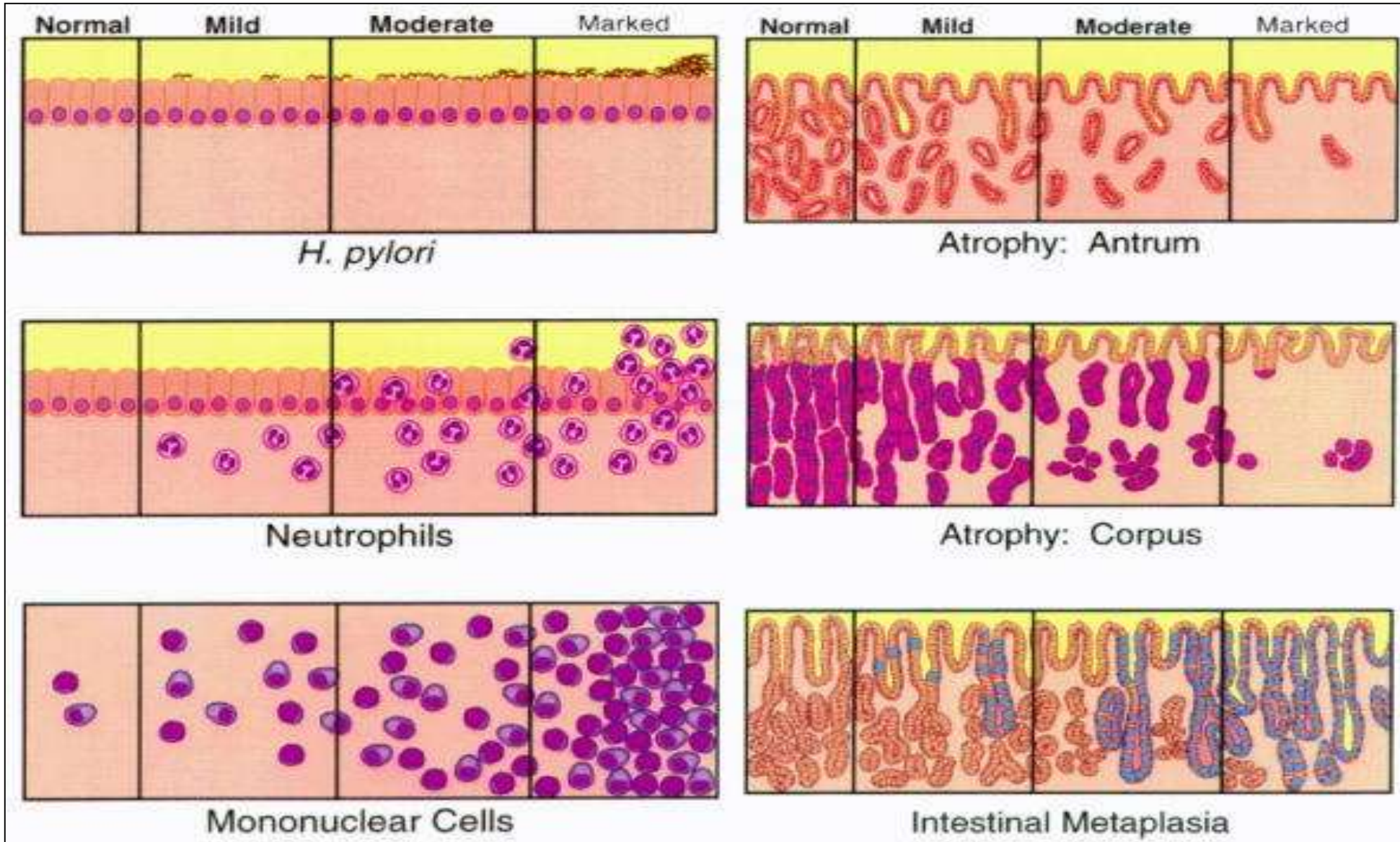
Radiation

GVHD

Other - osmoprep, ischaemia, siderosis

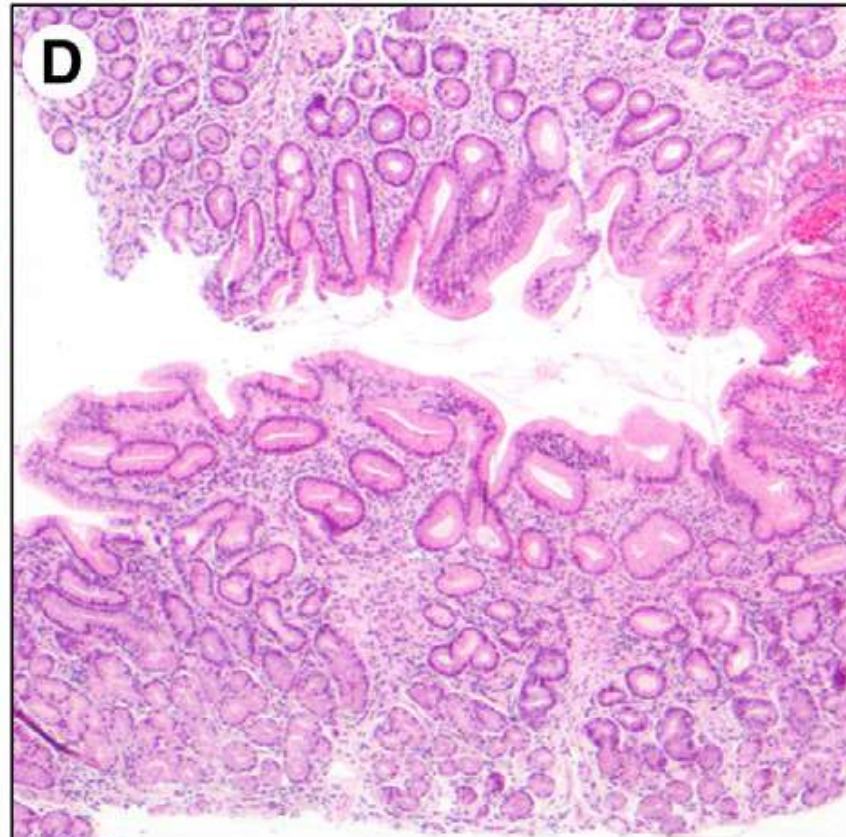
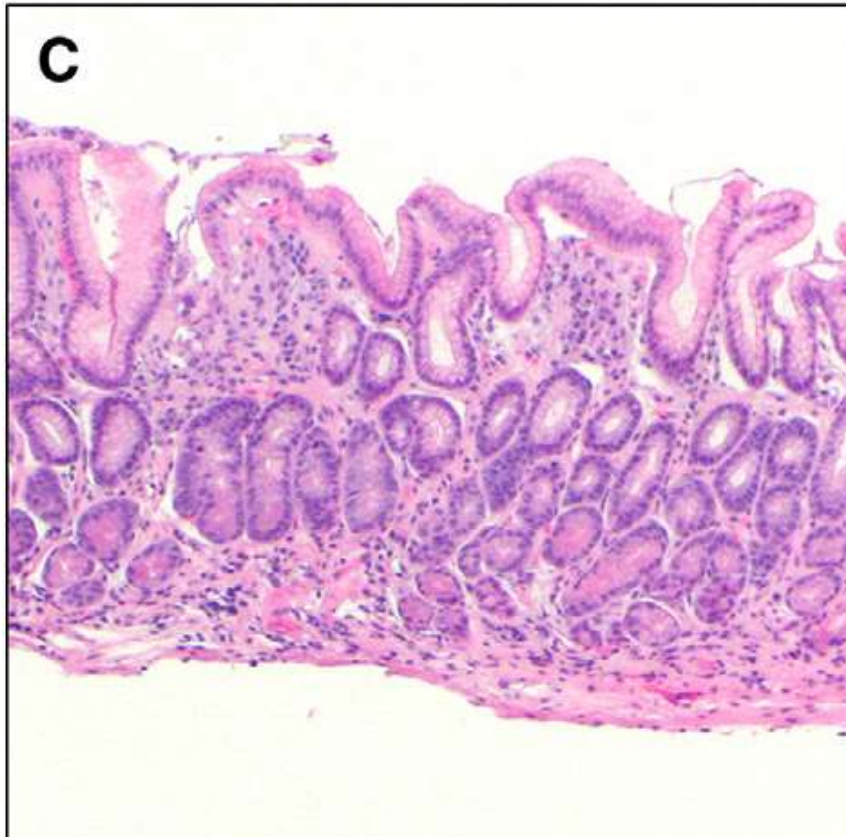
# Minimal criteria for ‘gastritis’

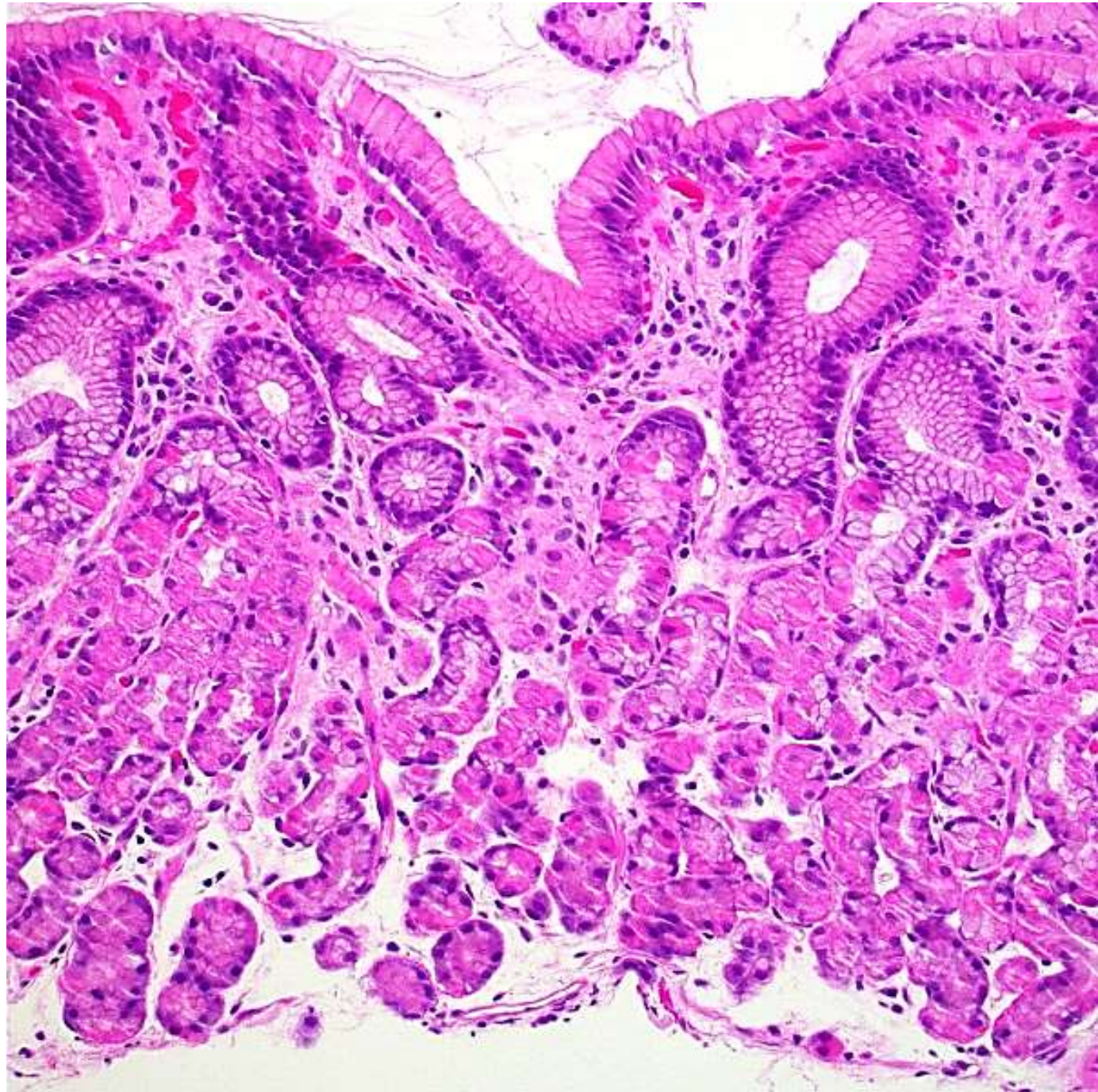
- ▶ “A few mononuclear leukocytes are always present in the lamina propria of the gastric mucosa; however, a precise definition of chronic inflammation is **hampered by lack of a universal standard for the quantity of mononuclear inflammatory cells in the normal mucosa**. The latter can be heavily influenced by geographic location and other demographic variables of the persons studied and by observers' subjective impressions. From a pragmatic standpoint, it may be useful to think in terms of an “expected” rather than a “normal” level of chronic inflammatory cell infiltration”.
- ▶ “the normal number of gastric mucosal mononuclear leukocytes in the lamina propria is viewed as a **maximum of 2 to 5 lymphocytes, plasma cells and and macrophages per high power (×40 objective) microscopic field or, by another approach, two or macrophages per high power (×40 objective)three lymphocytes or plasma cells between foveolae** (the area in which chronic inflammatory cells are most often found). Plasma cells are sparse or absent from the stomach of healthy persons; so their presence is an especially important indicator of a chronic inflammatory response. **Some observers consider chronic inflammation to be present even when there are as few as one or two plasma cells per high-power field”**.



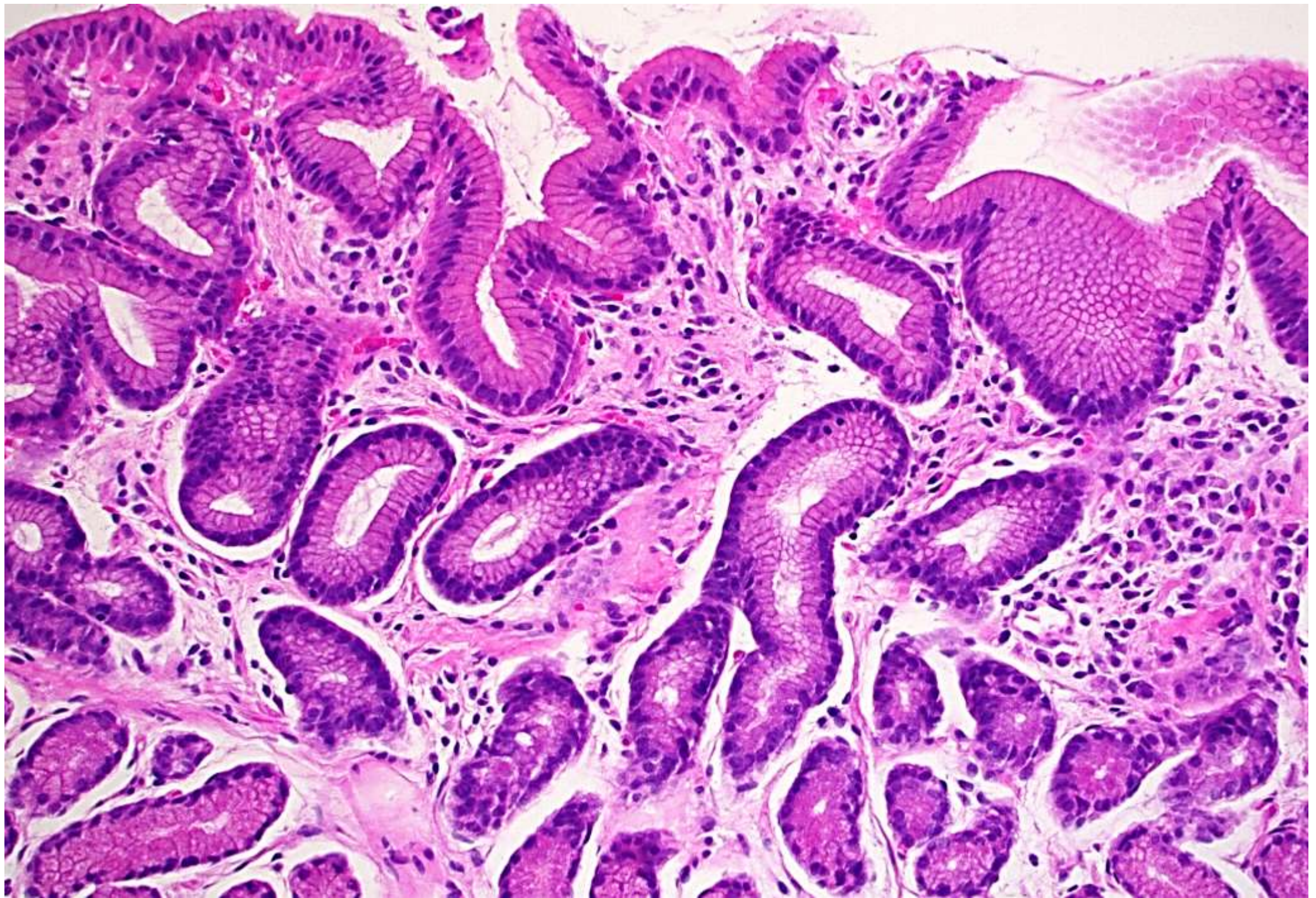
# Criteria in Human Pathology Dec 2016 paper

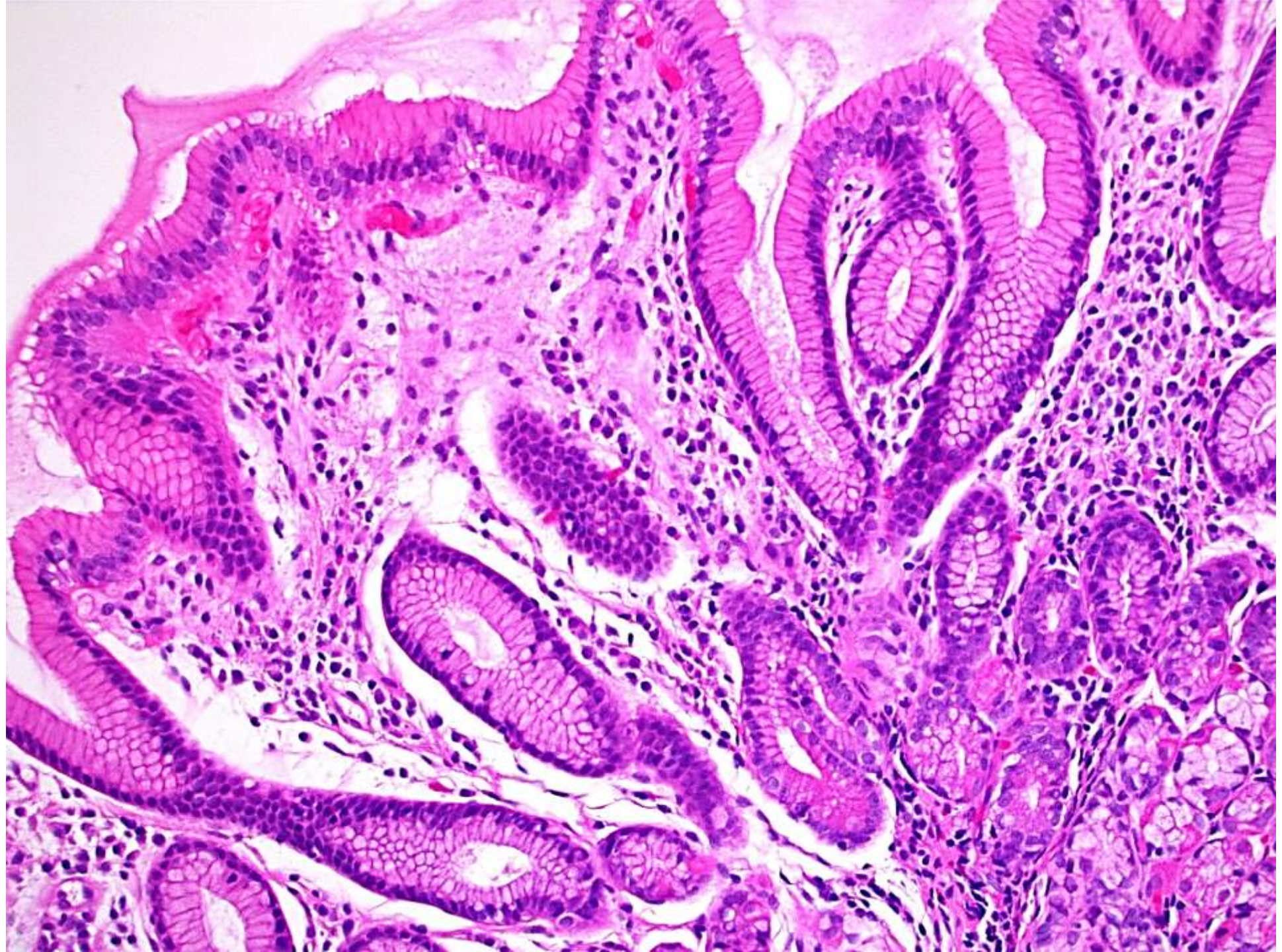
- ▶ Chronic inflammation = ‘increased inflammation, predominantly plasma cells, within the lamina propria in a patchy, loose distribution; no destruction or involvement of epithelium; ×10 needed to identify clusters’
- ▶ Inactive chronic gastritis = dense lymphoplasmacytic infiltrate of the lamina propria easily identifiable on ×4; includes infiltration and destruction of epithelium

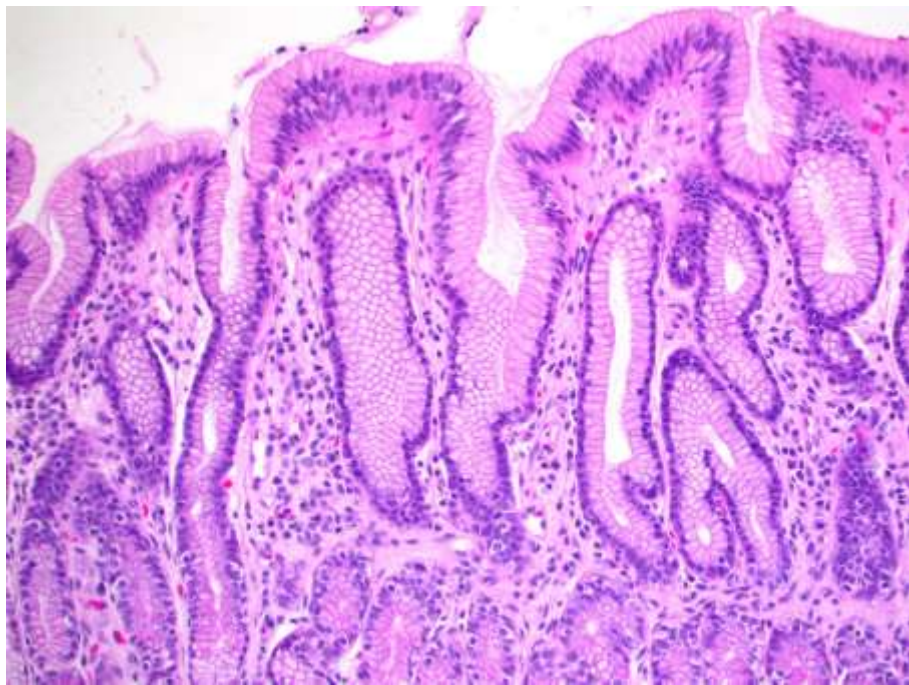
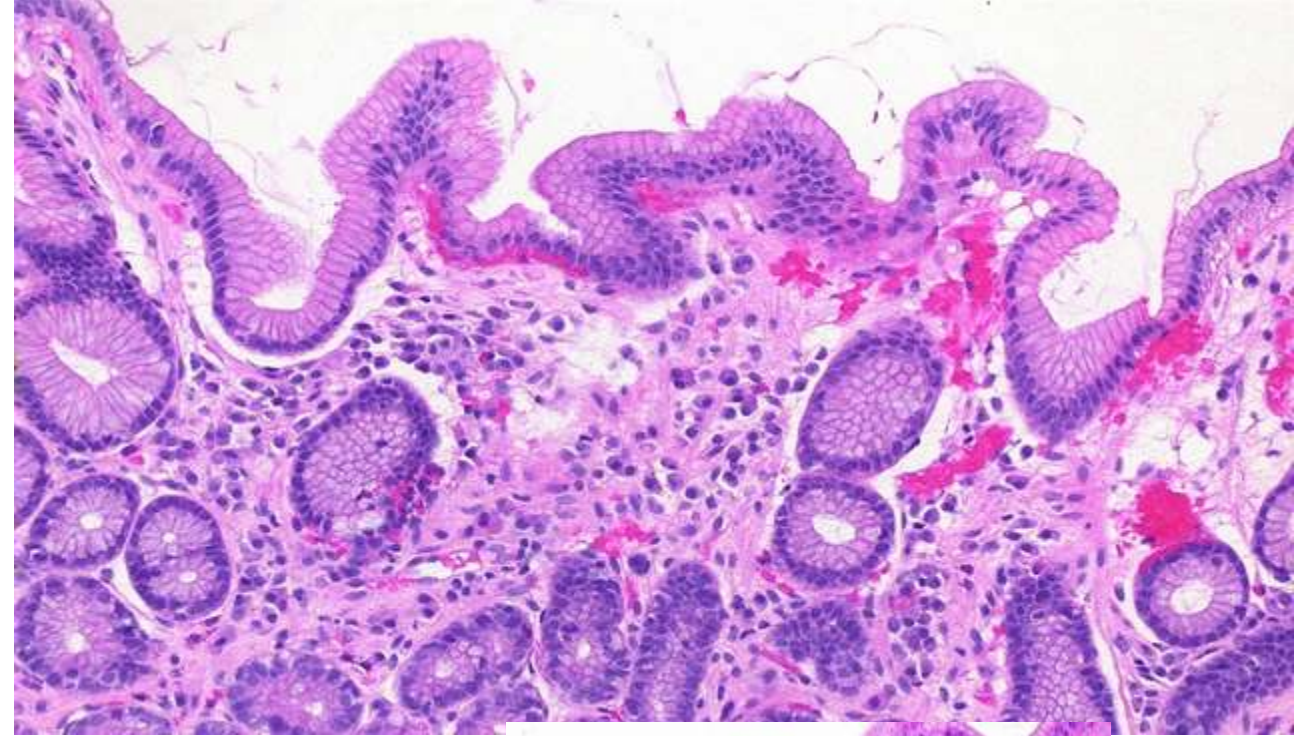
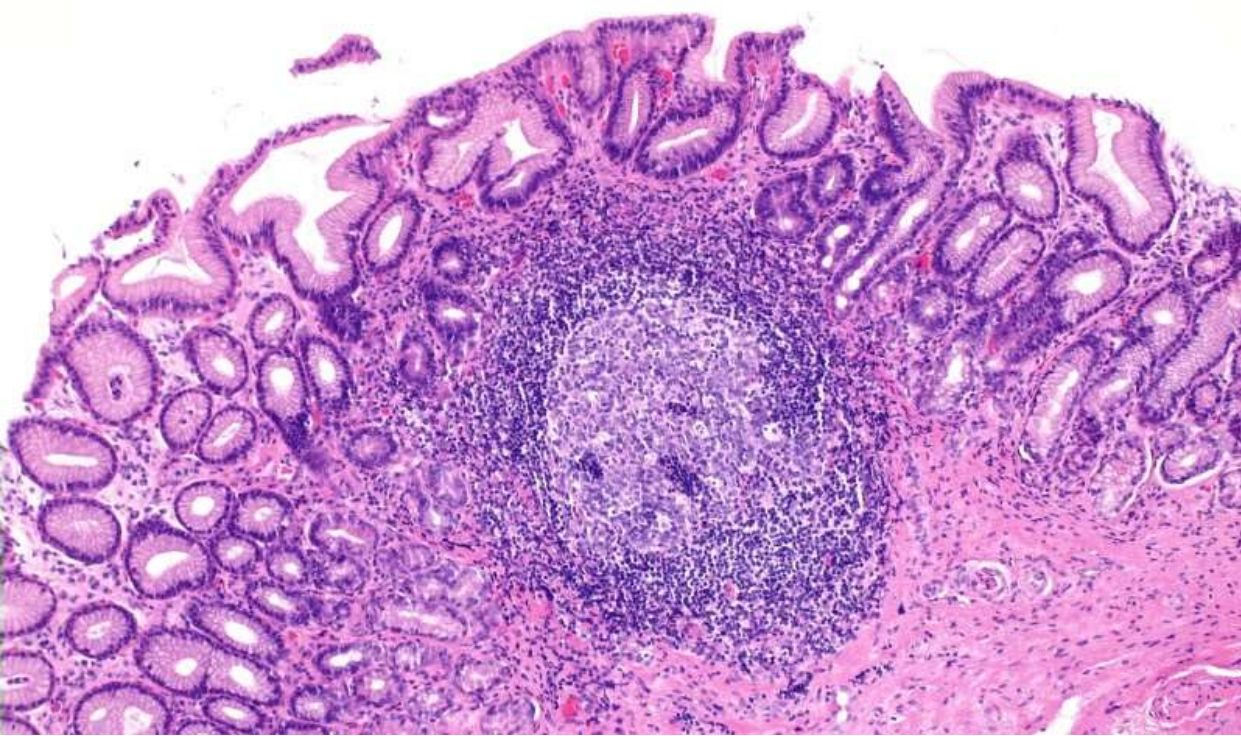




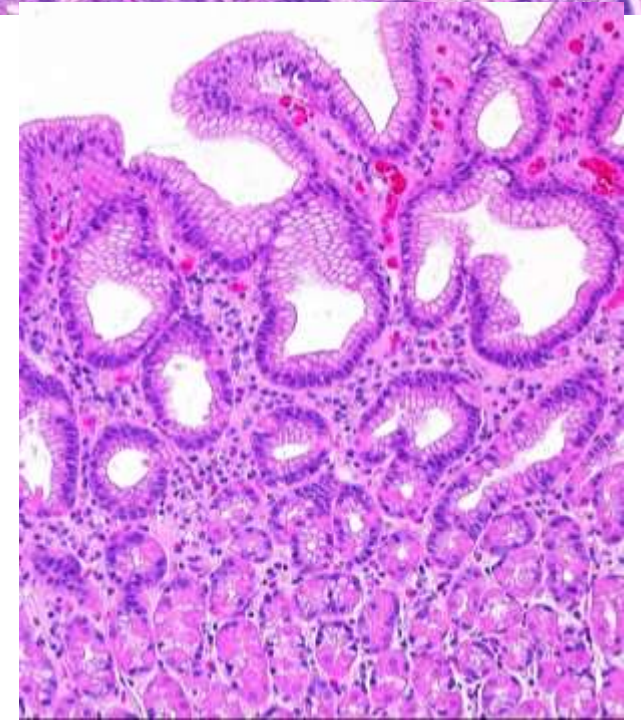






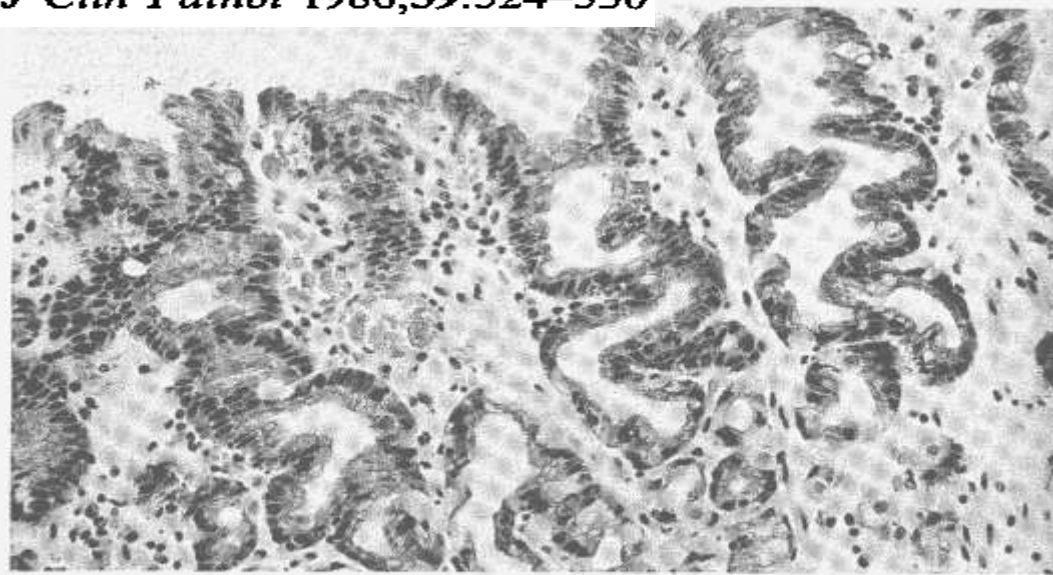


Paediatric  
'gastritis'

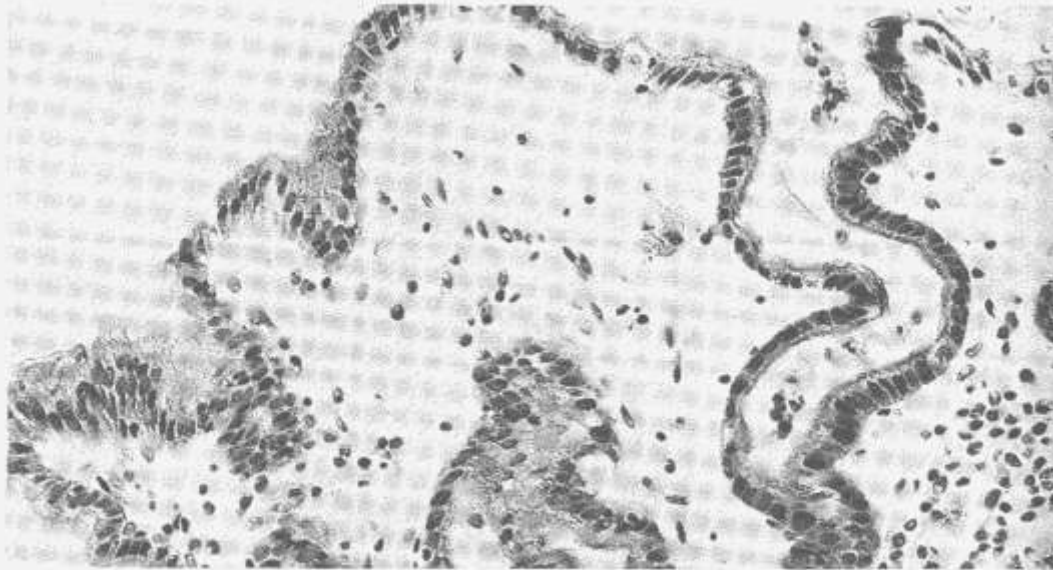


# Minimum criteria for reactive gastropathy

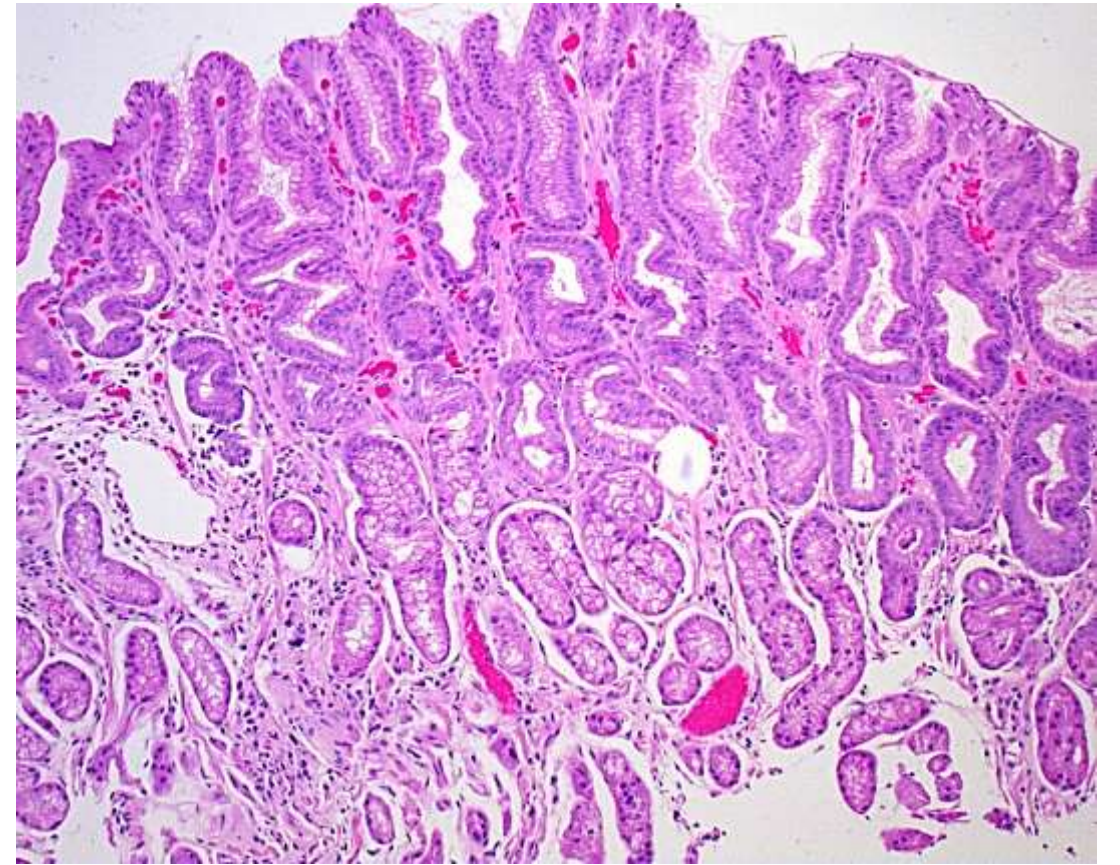
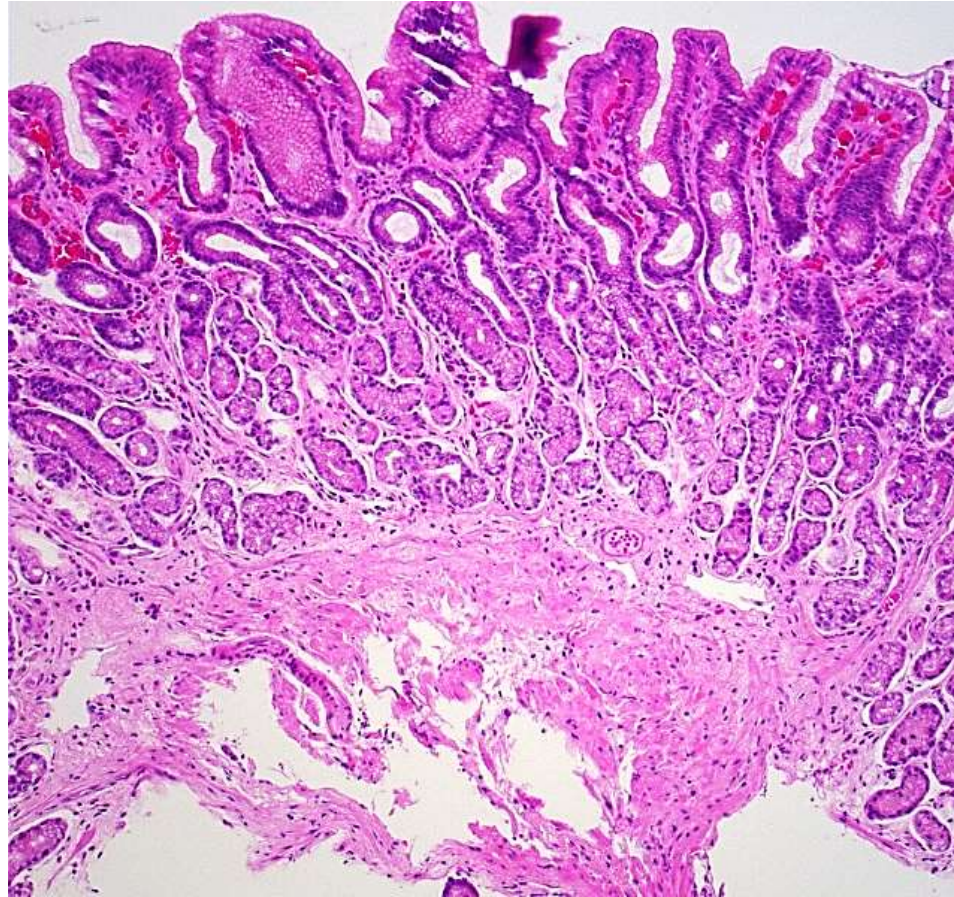
- ▶ Dixon *J Clin Pathol* 1986;**39**:524–530
- ▶ Score 0-3 for the following elements
  - ▶ Foveolar hyperplasia
  - ▶ Oedema and smooth muscle fibres in LP
  - ▶ Vascular congestion
  - ▶ Absence of acute inflammation
  - ▶ Absence of chronic inflammation
- ▶ Score >10 = ‘bile reflux gastritis’ (confirmed by higher gastric pH and bile acid concentration in gastric contents)



*Fig. 2* Biopsy specimen showing marked foveolar hyperplasia (grade 3), moderate oedema and smooth muscle fibres in the lamina propria (2), severe capillary congestion (3), paucity of chronic inflammatory cells (3), and absence of polymorphs (3). (Haematoxylin and eosin.)  $\times 224$ .



*Fig. 3* In this biopsy specimen there is striking lamina propria oedema (grade 3), severe foveolar hyperplasia (3), and slight increase in chronic inflammatory cells (2), but absent polymorphs (3). Capillary congestion was seen elsewhere in specimen. (Haematoxylin and eosin.)  $\times 280$ .



# Helicobacter negative active chronic gastritis

- ▶ Pediatric non-*Helicobacter pylori* atrophic gastritis: a case series. [Am J Surg Pathol. 2015 Jun;39\(6\):786-92.](#)
- ▶ [Helicobacter-negative gastritis: a distinct entity unrelated to Helicobacter pylori infection.](#) [Aliment Pharmacol Ther. 2015 Jan;41\(2\):218-26.](#)
- ▶ [Helicobacter pylori-negative gastritis: prevalence and risk factors.](#) [Am J Gastroenterol. 2013 Jan;108\(1\):65-71.](#)
- ▶ *Helicobacter pylori*-negative gastritis: seek, yet ye shall not always find. [Am J Surg Pathol 2010; 34: e25-34](#)

# Helicobacter negative active chronic gastritis

- ▶ 10% of active chronic gastritis = H. pylori negative on biopsy material
- ▶ Causes:
  - Failure to recognise the H.pylori
  - Biopsies near an ulcer e.g. NSAID induced
  - Carditis secondary to acid reflux
  - Other infections e.g. CMV
  - Other gastritis type - autoimmune/immune dysfunction, lymphocytic, collagenous, IBD associated
  - Idiopathic



# Helicobacter negative active chronic gastritis

## Reasons for not identifying H. pylori:

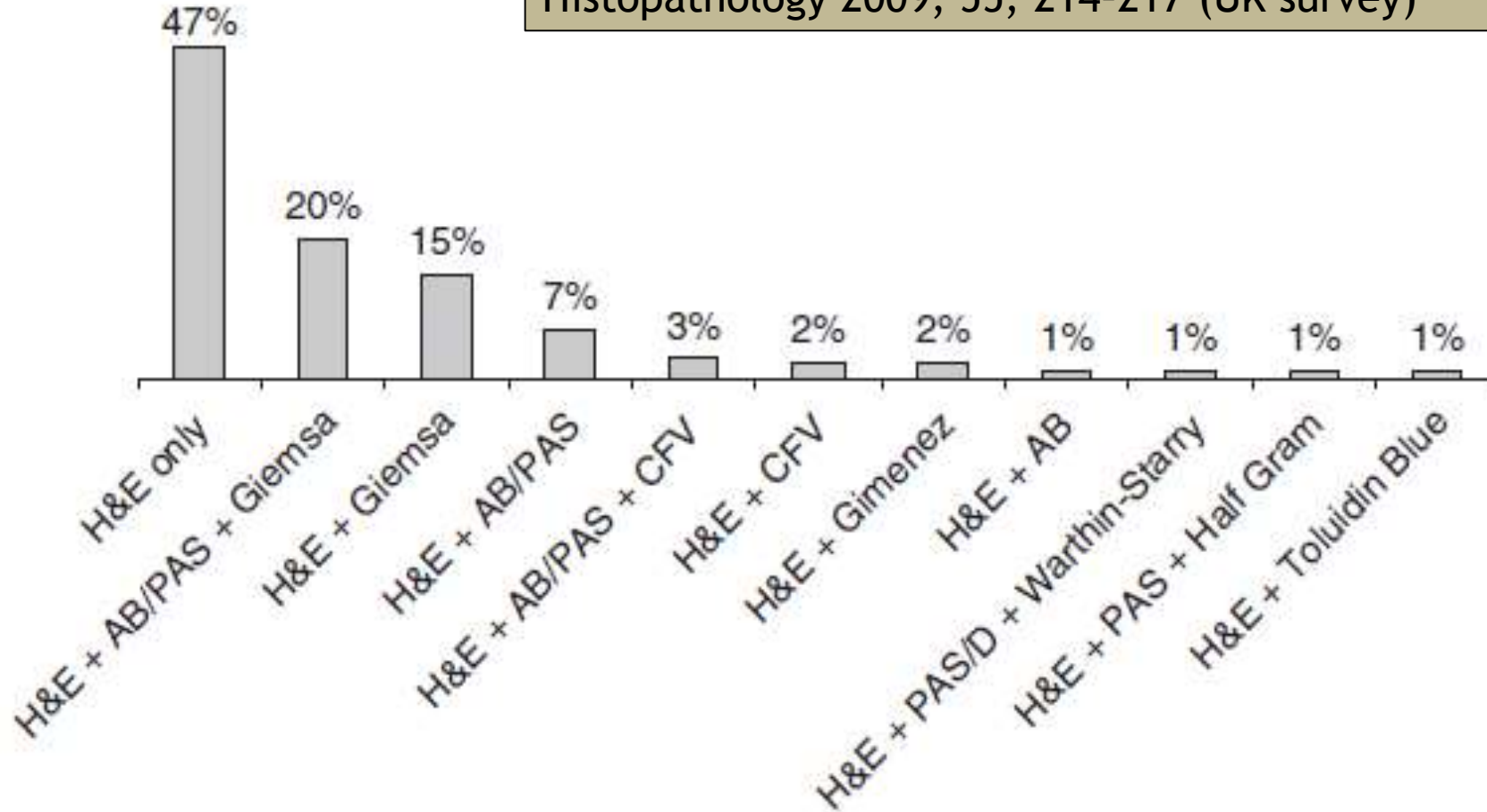
- 1) Proton pump inhibitor treatment
  - Helicobacter:
    - move from antrum to body
    - move deeper into gastric glands
    - reduce in number
- 2) Ulceration
- 3) Superimposed reactive gastropathy
- 4) Recent antibiotic treatment

# ‘invasive H.pylori’

- ▶ Prepublication Human Pathology 2016 (Hum Pathol. 2016 Oct 19. pii: S0046-8177(16)30254-4. doi)
- ▶ 18 cases
- ▶ Mostly detected on routine H.pylori IHC
- ▶ Intercellular deep crypt location
- ▶ Chronic inflammation but activity in  $< \sim 1/2$
- ▶ Body > antrum
- ▶ 2/3 on PPI

# Use of routine special stains

Histopathology 2009, 55, 214-217 (UK survey)



Am J Surg Pathol 2013;37:e12-e22

50% of US GIPS members routinely use at least one special stain for H.pylori detection

# Use of routine special stains

- ▶ Am J Surg Pathol 2006;30:357-361
- ▶ ~600 consecutive biopsies
  - ▶ 70% HP negative on H&E and confirmed on Tol Blue in 100%
  - ▶ 10% HP positive on H&E and confirmed on Tol Blue in 95%
  - ▶ 20% inconclusive on H&E and Tol blue positive in 15%
- ▶ Alcian blue identifies goblet cells not seen in the H&E in <0.5%
- ▶ ‘We conclude that routine special stains for all gastric and/or esophageal biopsies are not required, and hematoxylin and eosin assessment combined with selective ordering of these stains will identify virtually all cases of H. pylori gastritis and intestinal metaplasia’.

# Johns Hopkins experience

- ▶ ‘Prospective identification of Helicobacter pylori in routine gastric biopsies without reflex ancillary stains is cost-efficient for our healthcare system.’ Human Pathology December 2016;58:90-96
- ▶ 1 month period - cost benefit of reflex Diff-Quik stain
- ▶ 379 gastric biopsies

	Envoi last week
▶ Normal - 50%	73%
▶ H.pylori gastritis - 7%	4.5%
▶ Active chronic gastritis (H.pylori IHC negative) - 3%	0%
▶ Chemical gastropathy - 14%	5.5%
▶ Chronic gastritis - 19%	4.5%
▶ Inactive chronic gastritis - 6%	
▶ Other - 1%	12.5%
- ▶ 25 cases H.pylori - 21 identified on H&E, 2 further on Diff-Quik and another 2 on IHC.
- ▶ One normal biopsy had H.pylori on IHC (but on review were visible on H&E)
- ▶ Reimbursement: Diff-Quik USD 98.12 (1 month routine = \$37452.78), H.pylori IHC USD 107.41 (1 month PRN = \$2148.20)

# Use of routine special stains

- ▶ Am J Surg Pathol 2013;37:e12-e22
  - ▶ Rodger C. Haggitt Gastrointestinal Pathology Society recommendations
  - ▶ ‘Pathologists rarely, if ever, detect H. pylori in “normal” biopsies, but readily observe them in optimally stained hematoxylin and eosin sections from infected patients. Therefore, we suggest that use of ancillary stains is appropriate when biopsies show chronic, or chronic active, gastritis without detectable H. pylori in hematoxylin and eosin stained sections, but **performing them “up front” on all gastric biopsies is generally unnecessary**’
  - ▶ Favour IHC as the special stain for H.pylori detection: ‘most histochemical stains, including H&E, have sensitivities in the 60% to 90% range compared with immunohistochemistry’.

**TABLE 2. Utility of Key Findings and Stains in Detecting *H. pylori* in Gastric Biopsies**

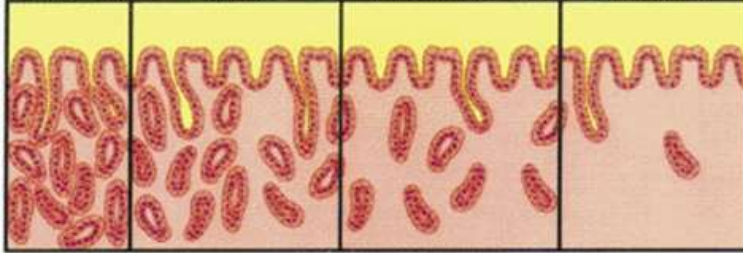


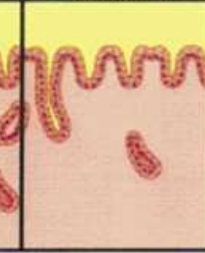



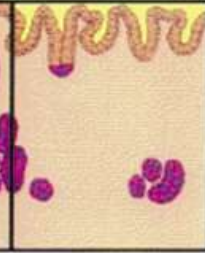
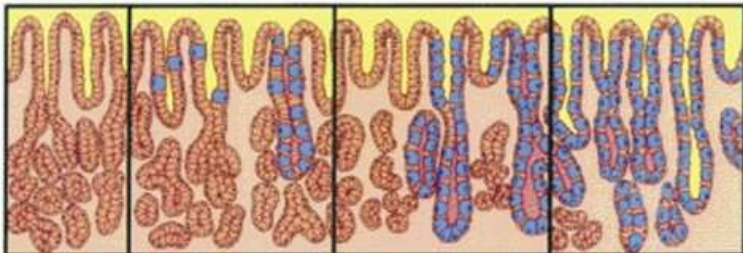
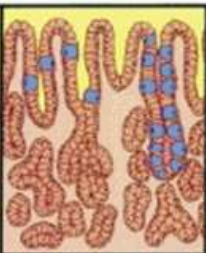
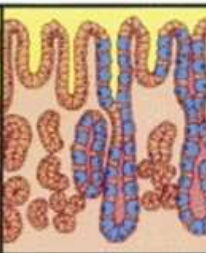

Study Findings	Hartman and Owens <sup>8</sup> (%)	Smith et al <sup>10</sup> (%)	Wang et al <sup>24</sup> (%)
Sensitivity of moderate to severe gastritis	97	94	93
Specificity of moderate to severe gastritis	98	88	91
Sensitivity of H&E	93	91	95-100
Specificity of H&E	100	100	100
Sensitivity of immunohistochemistry	97-100	100	100
Specificity of immunohistochemistry	100	100	100

Morphologic Findings	GIPS Recommendations For Special Stains*
Normal gastric mucosa	Not indicated
Chemical (reactive) gastropathy	Not indicated if chemical injury is only abnormality Appropriate if superimposed chronic gastritis is present
Chronic active gastritis	Not indicated if H&E demonstrates organisms Appropriate if H&E is negative for <i>H. pylori</i> Low yield if serologic studies are known to be negative
Chronic inactive gastritis	Not indicated if serologic studies are known to be negative, but probably justified in most other cases Appropriate if gastroduodenal ulcers are present Appropriate if gastric MALT-type lymphoma or adenocarcinoma is present Appropriate if duodenal lymphocytosis is present Appropriate in patients with prior <i>H. pylori</i> treatment Appropriate in high-risk demographic areas
Lymphocytic gastritis	Appropriate



# Assessment of atrophy

Human Pathology 2011; Sydney classification AJSP October 2006

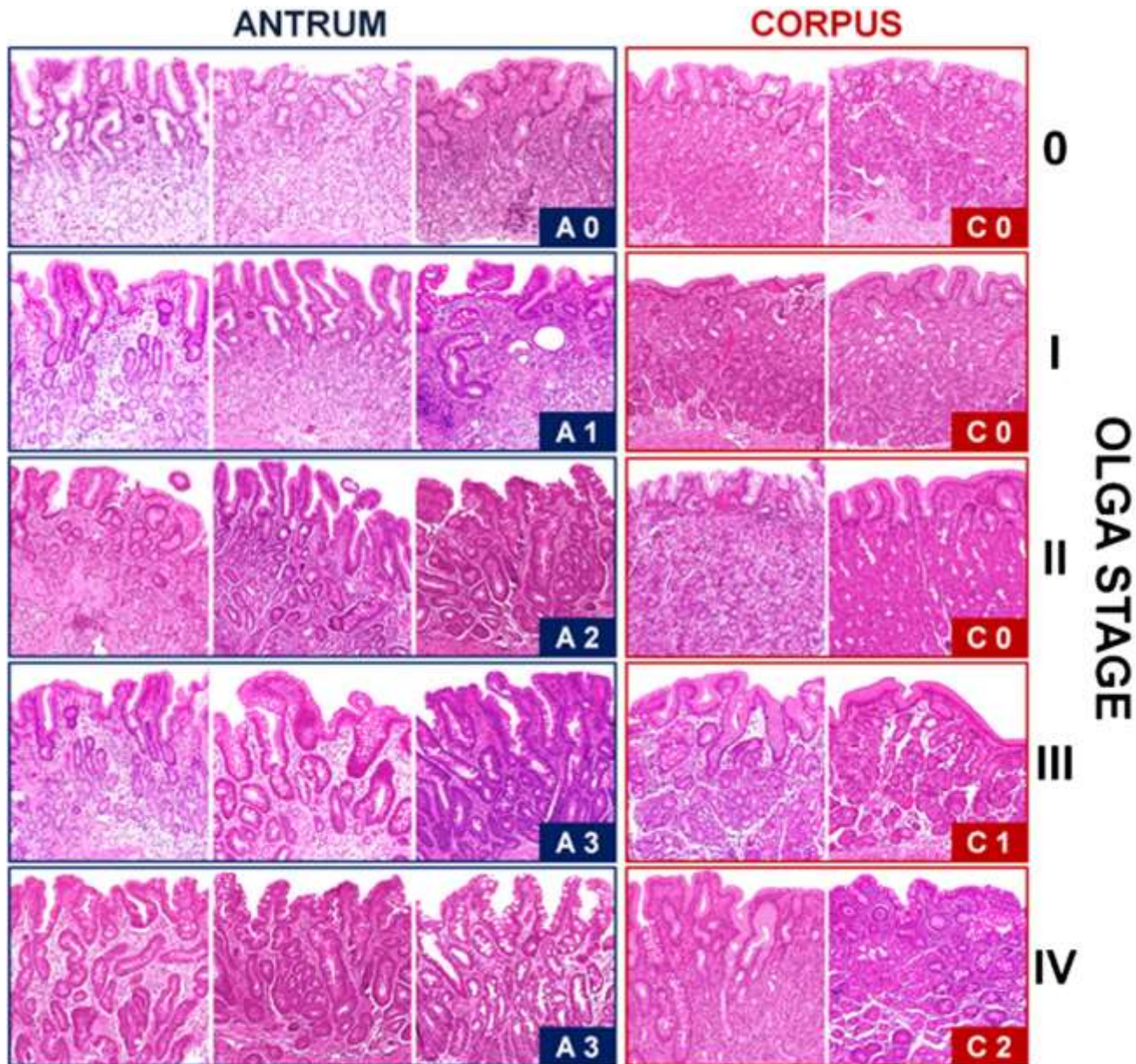
Grade	0	1	2	3
				
	Atrophy: Antrum			
				
	Atrophy: Corpus			
				
	Intestinal Metaplasia			

**TABLE 1. The OLGA staging system<sup>a</sup>**

		Corpus			
		Not fat: no atrophy (score 0)	Mild atrophy (score 1)	Moderate atrophy (score 2)	Severe atrophy (score 3)
	Atrophy score				
<b>Antrum (including incisura angularis)</b>	No atrophy (score 0)	Stage 0	Stage I	Stage II	Stage II
	Mild atrophy (score 1)	Stage I	Stage I	Stage II	Stage III
	Moderate atrophy (score 2)	Stage II	Stage II	Stage III	Stage IV
	Severe atrophy (score 3)	Stage III	Stage III	Stage IV	Stage IV

<sup>a</sup>OLGA, Operative link on gastritis assessment.

# OLGA



- Interobserver variability is significant
- Dysplasia and carcinoma risk rises when stage 3 or 4

More reproducible

Autoimmune gastritis

**TABLE 2. Proposal for the OLGIM staging system**

	IM score	Corpus			
		Not fat: no IM (score 0)	Mild IM (score 1)	Moderate IM (score 2)	Severe IM (score 3)
Antrum (including incisura angularis)	No IM (score 0)	Stage 0	Stage I	Stage II	Stage II
	Mild IM (score 1)	Stage I	Stage I	Stage II	Stage III
	Moderate IM (score 2)	Stage II	Stage II	Stage III	Stage IV
	Severe IM (score 3)	Stage III	Stage III	Stage IV	Stage IV

IM, Intestinal metaplasia; OLGIM, operative link on gastric intestinal metaplasia assessment.

# What causes lymphocytic gastritis?

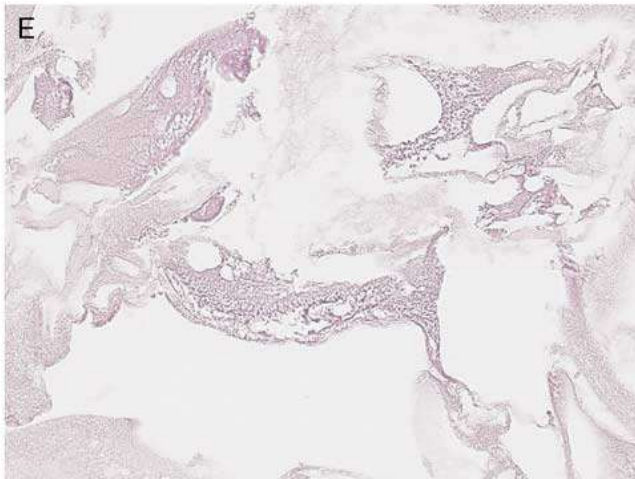
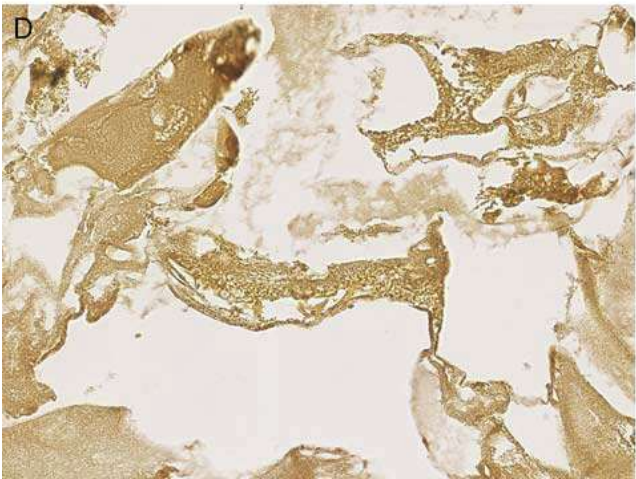
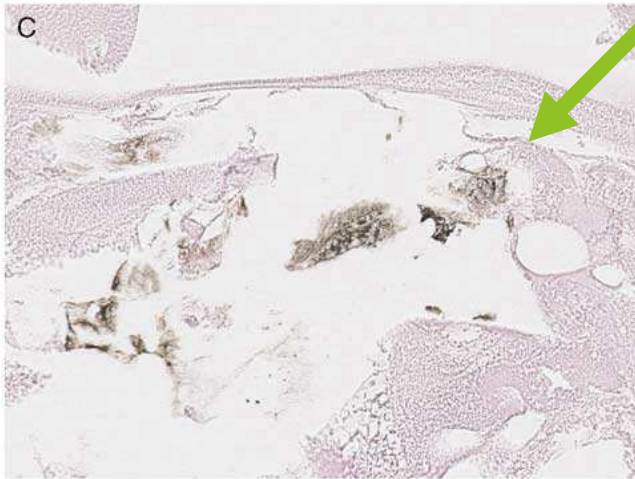
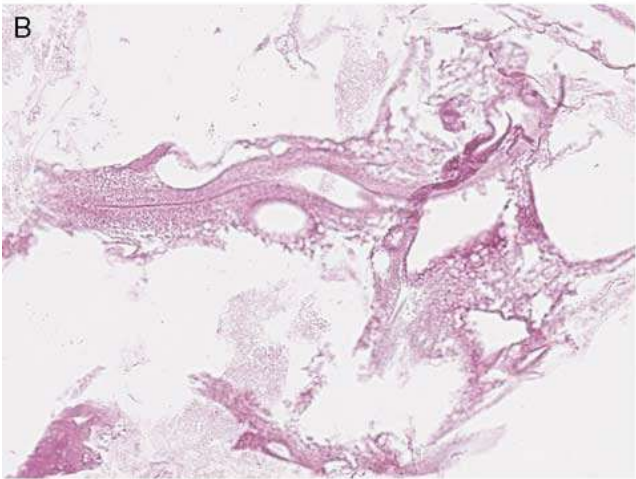
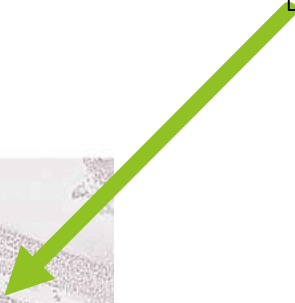
- ▶ Coeliac disease
- ▶ H.pylori infection
- ▶ Other infections e.g. viral gastroenteritis, [Propionibacteria!!]
- ▶ Hypertrophic gastropathy (Menetrier like giant folds - cytokine mediated)
- ▶ Immune disorders eg CVID, autoimmune enteropathy
- ▶ Collagenous gastritis (1/3 of cases have increased IELs)
- ▶ Drugs e.g. Sartan's, biologics
- ▶ Crohn disease
- ▶ **Idiopathic**

# OsmoPrep associated gastritis AJSP 2016;40(11):1550-1556

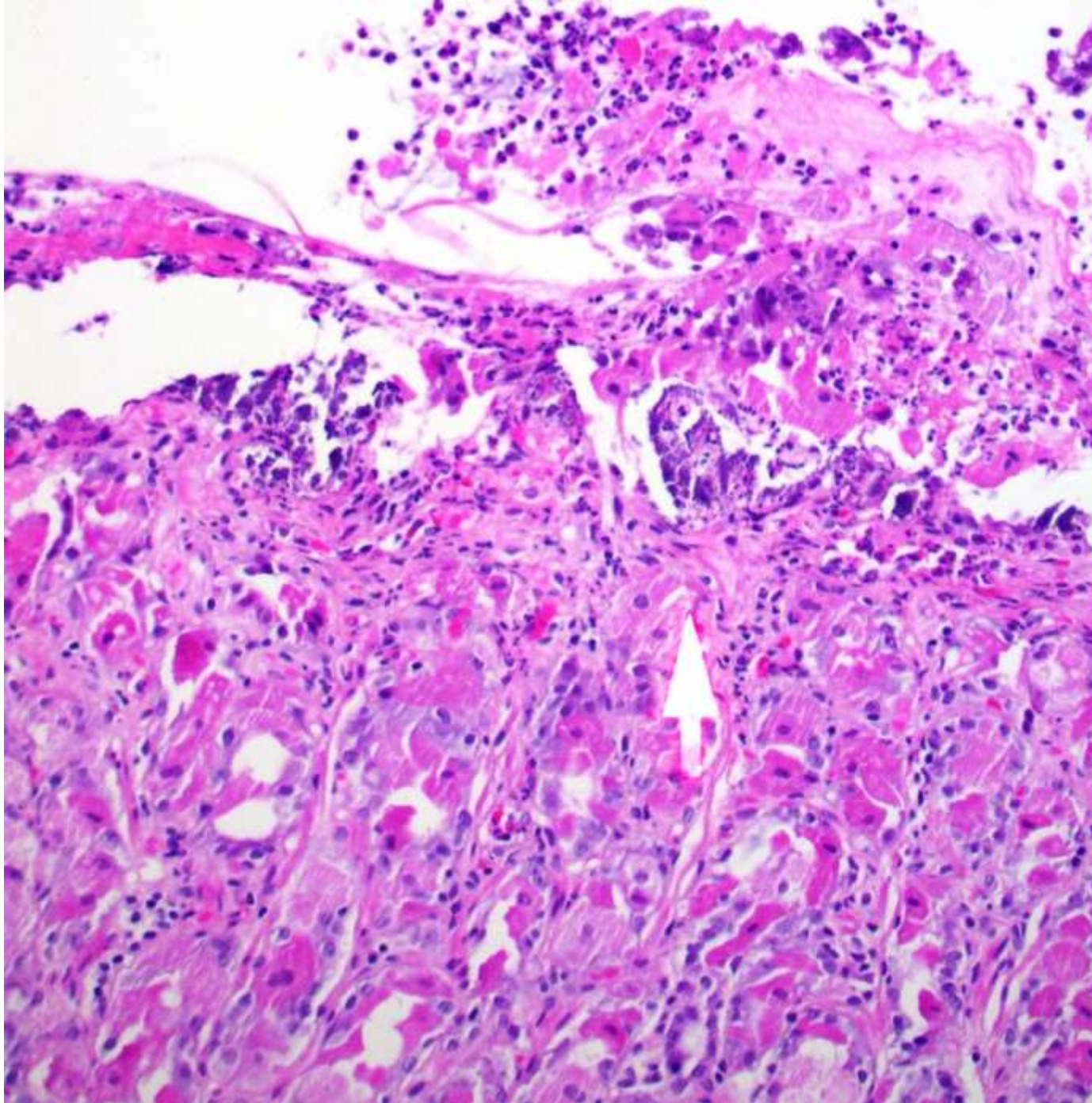
- ▶ OsmoPrep, a tablet form of sodium phosphate, used for colonoscopy preparation.
  - ▶ 32 tablets and 2 litres combined night before and day of endoscopy
- ▶ 8 cases
- ▶ Histology: “purple to black granular deposits in the superficial mucosa associated with marked reactive epithelial changes”
  - ▶ ‘No erosions or inflammation’
  - ▶ Von Kossa positive, Perls negative
- ▶ DDx = mucosal calcinosis



Von Kossa



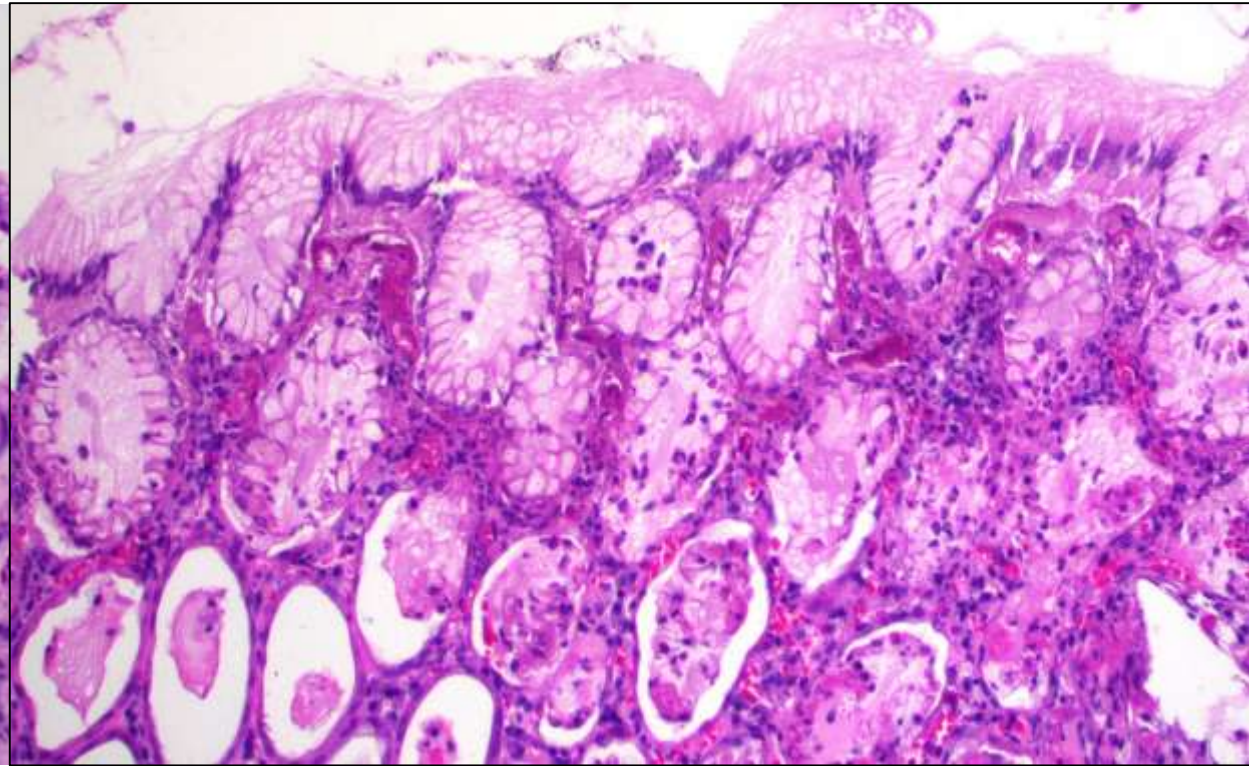
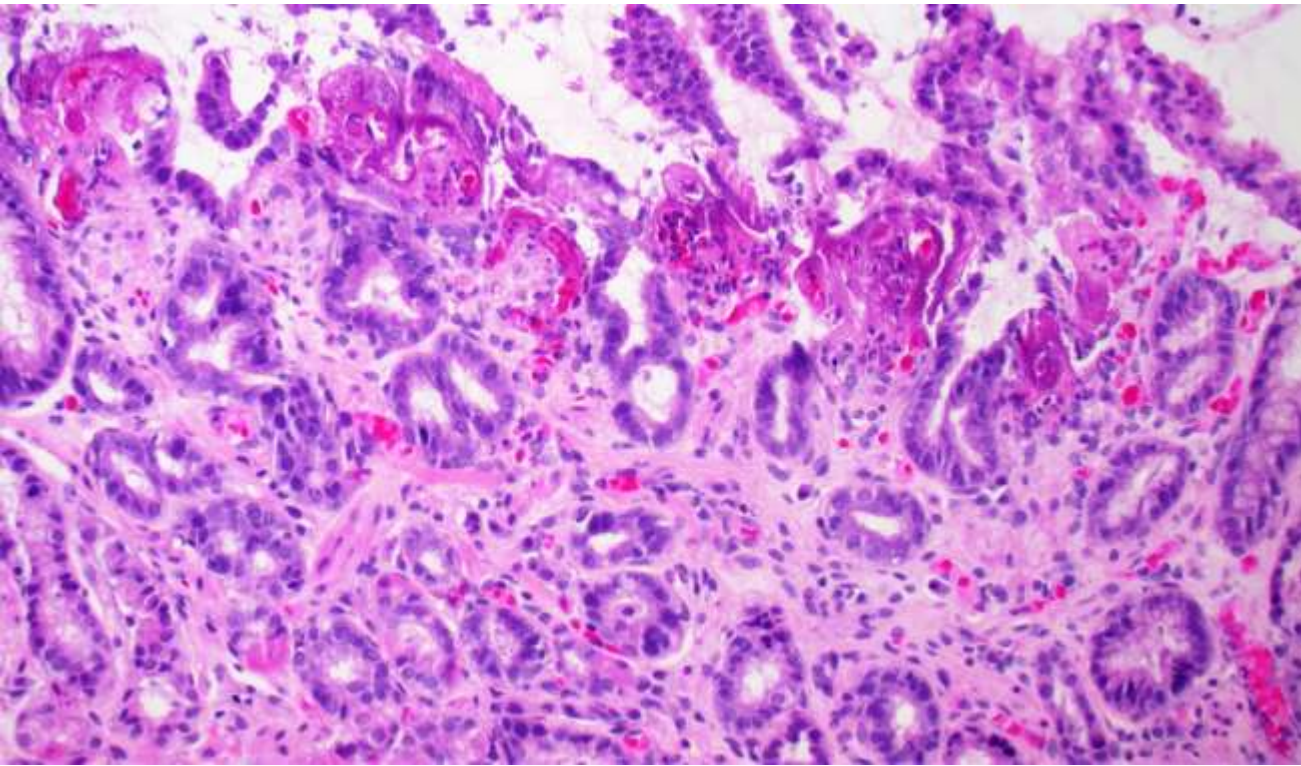
Note: erosion in some of our local cases





# Doxycycline gastritis/gastropathy

- ▶ *Gastric Mucosal Necrosis With Vascular Degeneration Induced by Doxycycline*. Am J Surg Pathol. 2013;37(2):259-63.
- ▶ ‘background of chemical gastropathy with foveolar hyperplasia, with superimposed active inflammation, superficial mucosa necrosis, fibrosis in the superficial lamina propria, microthrombi in capillaries, and capillary wall degeneration’.



Both cases are elderly patients taking doxycycline for acne rosacea

# Medication induced inflammatory reaction patterns in stomach

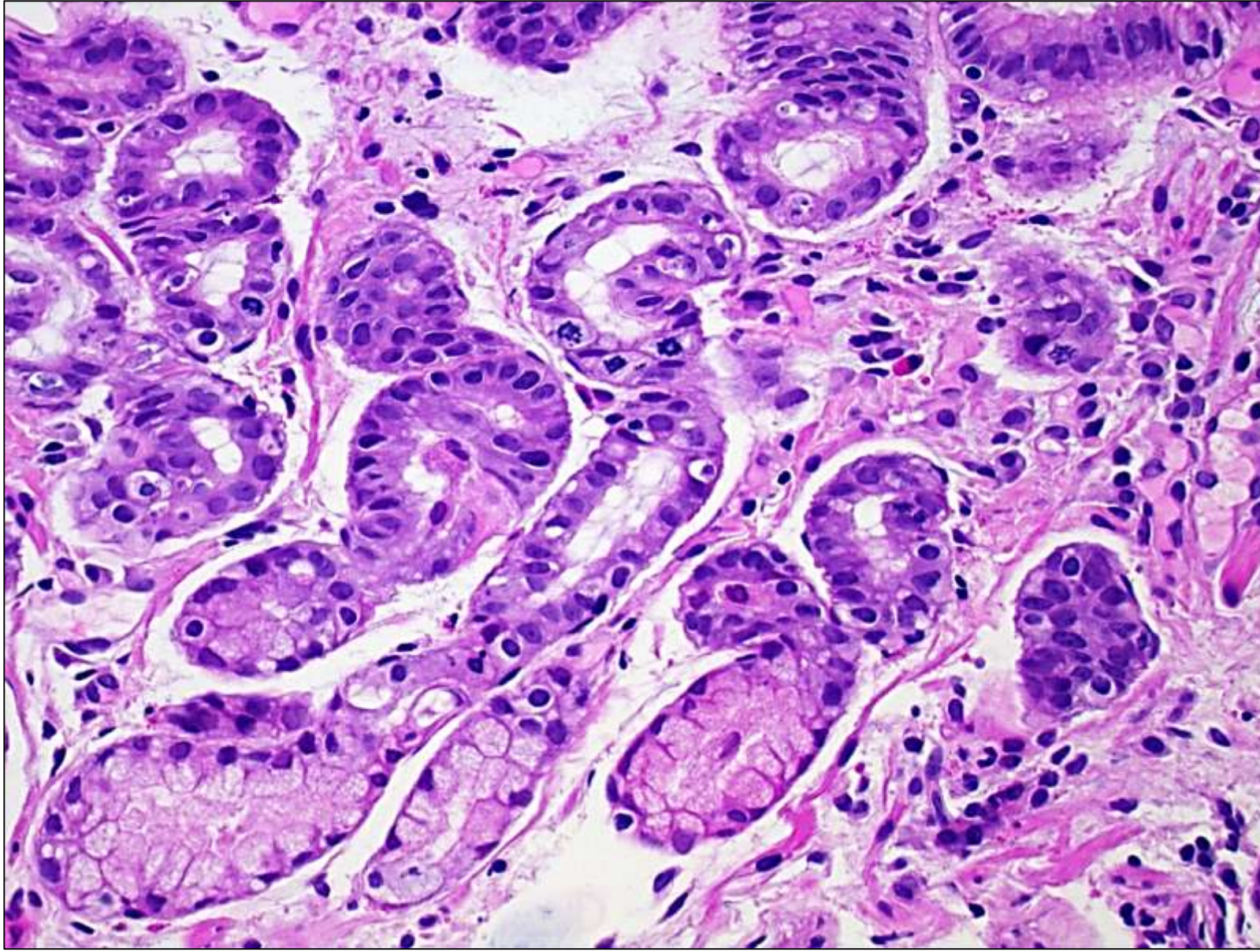
- ▶ Acute inflammation
  - ▶ Focal or Diffuse
- ▶ Active chronic inflammation
  - ▶ Focal or Diffuse
- ▶ Chronic inflammation
- ▶ Intraepithelial lymphocytosis
- ▶ Subepithelial collagen deposition

- ▶ Eosinophil infiltration
- ▶ Granulomatous
- ▶ Epithelial apoptosis
- ▶ Ischemic pattern
- ▶ Toxic injury pattern
- ▶ Mixed patterns
- ▶ Depositions

# Medication injury - Stomach

- ▶ Focal inflammation/erosion
  - ▶ Antibiotics - cyclines and mycins, NSAIDs, Biphosphonates, Salts - KCl, Fe preparations, Chemotherapy (taxanes, others), colchicine, Sartans, biologics
- ▶ Intraepithelial lymphocytosis
  - ▶ Sartan's, biologics
- ▶ Eosinophils
  - ▶ NSAID's, Gold, L-Tryptophan, Carbamazepine, Methotrexate, Tacrolimus, Azothioprine, Rifampicin, Clozapine, Enalapril, Mycophenolate, biologics
- ▶ Granulomas
  - ▶ ? (probably more than reported)
- ▶ Apoptosis
  - ▶ Chemotherapy eg 5-FU, Taxane, Colchicine, Immunomodulatory medications eg Ipilimumab, Mycophenolate
- ▶ Ischaemic injury
  - ▶ Chemotherapy, SIR spheres
- ▶ Depositions
  - ▶ Iron, Kayexalate (and other resins)

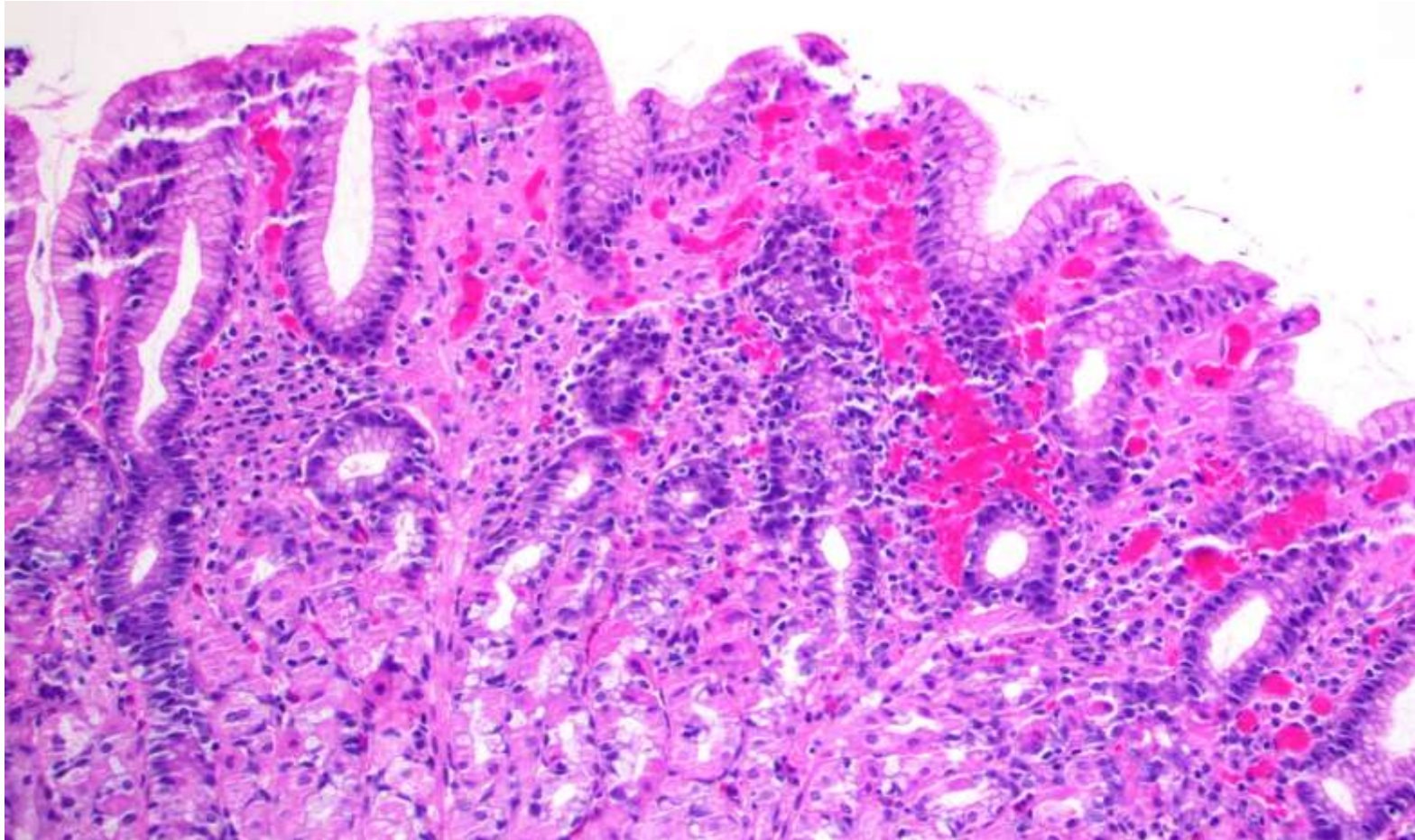
Colchicine toxicity - making a comeback in younger patients as treatment for pericarditis



# Gastritis in Crohn's disease

- ▶ Focally enhanced gastritis ( $\pm$  granuloma)
- ▶ Granuloma/granulomatous gastritis
- ▶ Diffuse active chronic gastritis (H.pylori negative)
- ▶ Lymphocytic gastritis
- ▶ Combination - FEG, granuloma, IELs

# LG pattern of gastric Crohn disease - initial presentation

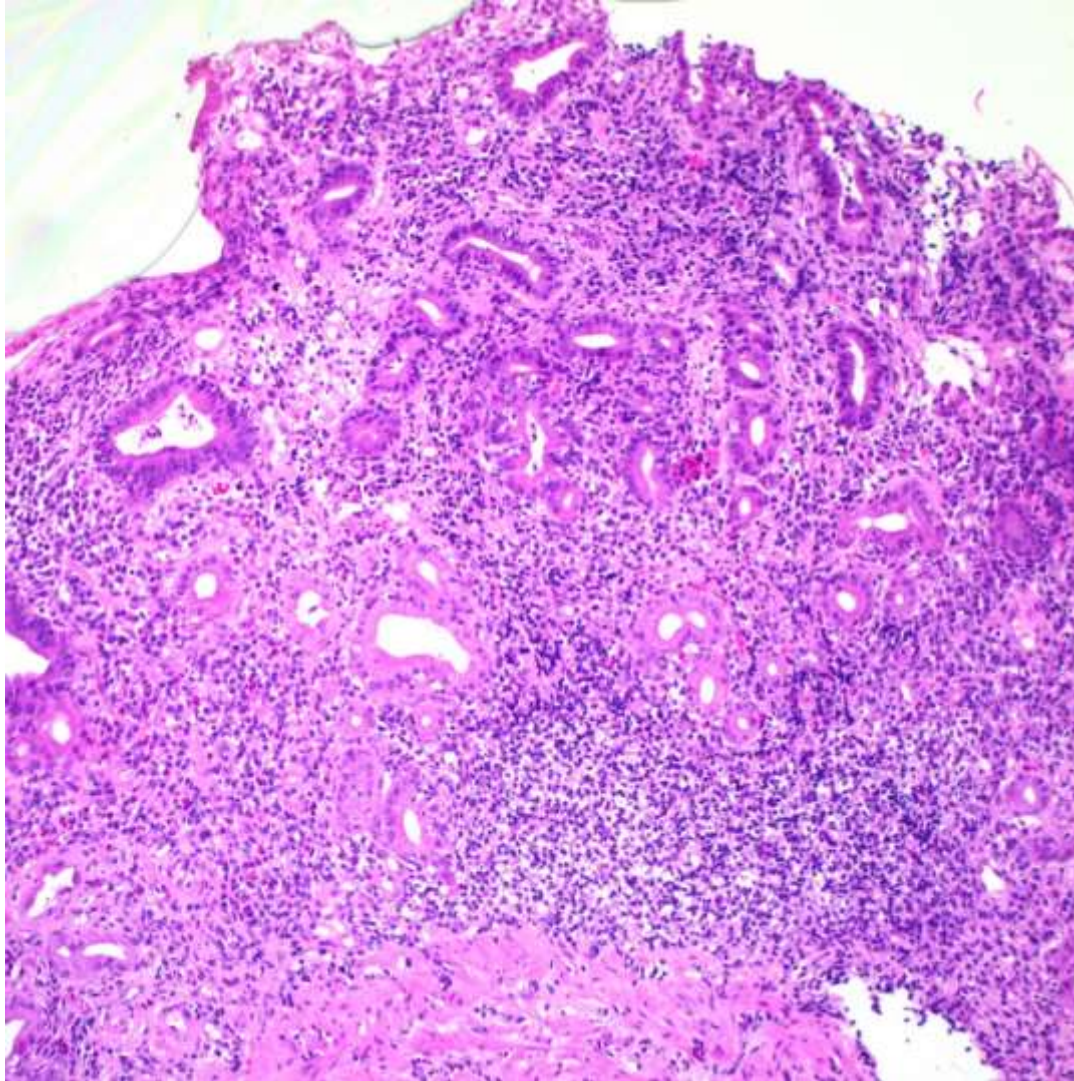


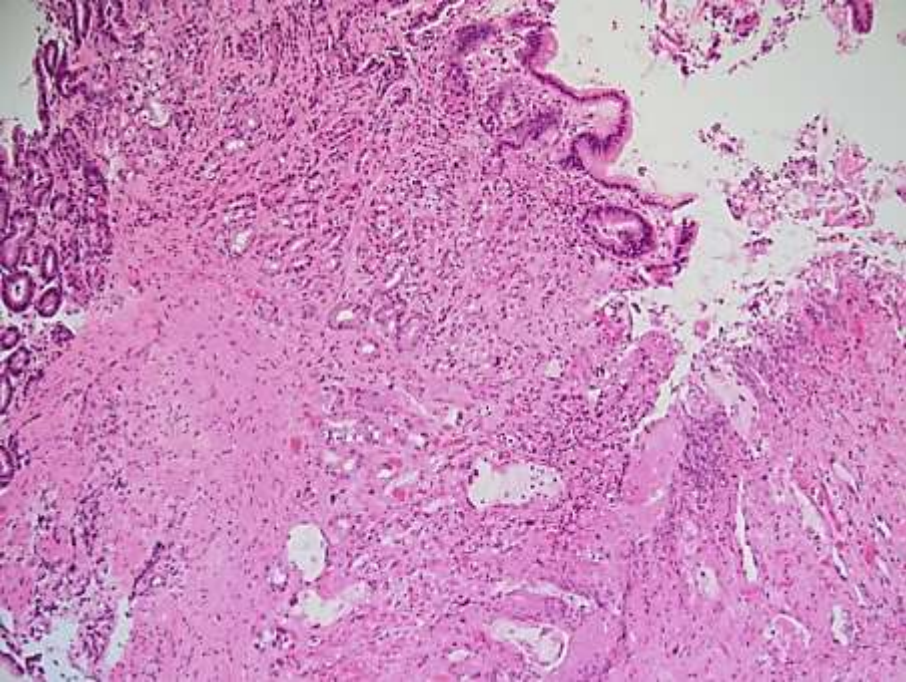
# Severe active chronic gastritis

- Infection
  - Viral - Herpes viridae - CMV, HSV, HZV, EBV
  - Bacterial - syphilis, mycobacteria (typical and atypical)
  - Fungi - candida, mucomycosis, aspergillus
  - (Parasitic - anisarkiasis, Schistosoma)
- Medications
  - Sartans, biologics (including immune modulator drugs)
- Topical injury
- Immune - CVID, Autoimmune enteropathy



# Severe gastritis in autoimmune enteropathy





HZV gastritis

