XXIV CONGRESO SOCIEDAD CHILENA DE ANATOMIA PATOLOGICA 2020

Lesiones precursoras de cáncer gástrico. Displasias gástricas

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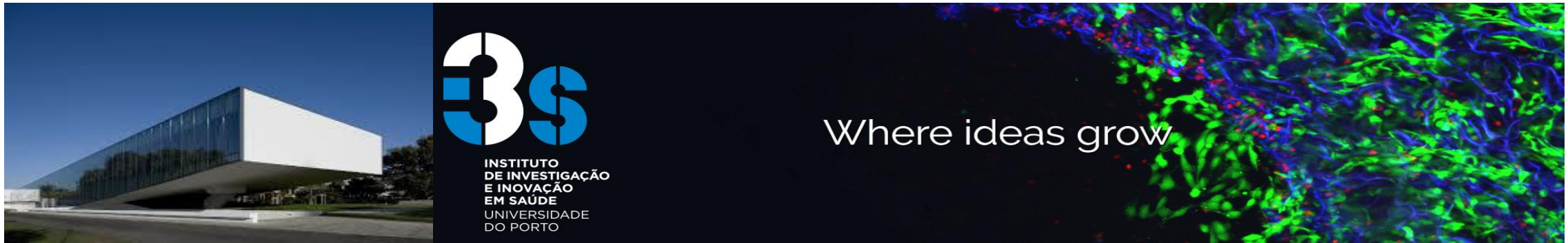


Precancerous conditions

- Chronic atrophic gastritis and intestinal metaplasia (IM) are considered to be precancerous conditions

because

- They independently confer a risk for development of gastric cancer and constitute the background in which dysplasia and adenocarcinoma may occur.
- Atrophic gastritis should be defined as significant (moderate to marked) atrophy or as IM (as the best and more reliable marker of atrophy).

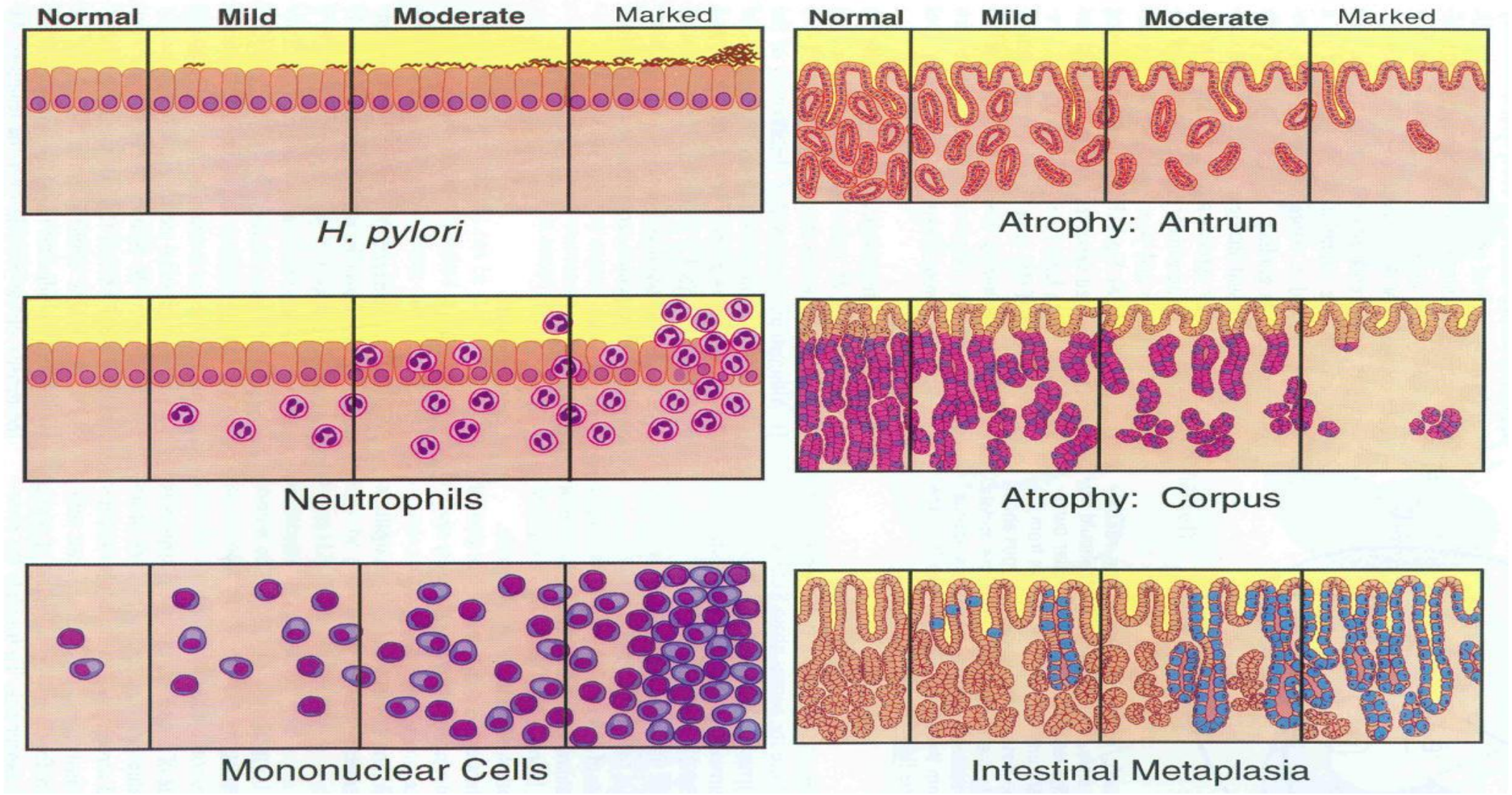
Precancerous lesion

- Dysplasia is a direct neoplastic precancerous lesion

TABLE 1. *Classification of chronic gastritis based on topography morphology and etiology*

Type of gastritis	Etiologic factors	Gastritis synonyms
Nonatrophic	*Helicobacter pylori* ?Other factors	Superficial Diffuse antral gastritis (DAG) Chronic antral gastritis (CAG) Interstitial—follicular Hypersecretory Type B[a]
Atrophic		
Autoimmune	Autoimmunity	Type A[a] Diffuse Corporal Pernicious anemia-associated
Multifocal atrophic	*Helicobacter pylori* Dietary ?Environmental factors	Type B,[a] type AB[a] Environmental Metaplastic
Special forms		
Chemical[b]	Chemical irritation Bile NSAIDs ? Other agents	Reactive Reflux NSAID Type C[a]
Radiation	Radiation injury	
Lymphocytic	Idiopathic? Immune mechanisms Gluten Drug (ticlopidine) ? *H. pylori*	Varioliform (endoscopic) Celiac disease-associated
Noninfectious granulomatous	Crohn's disease Sarcoidosis Wegener's granulomatosis and other vasculitides Foreign substances Idiopathic	Isolated granulomatous
Eosinophilic	Food sensitivity ? Other allergies	Allergic
Other infectious gastritides	Bacteria (other than *H. pylori*) Vlruses Fungi Parasites	Phlegmonous

Dixon MF et al: Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994.
Am J Surg Pathol 20(10):1161, 1996



Dixon MF et al: Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994.
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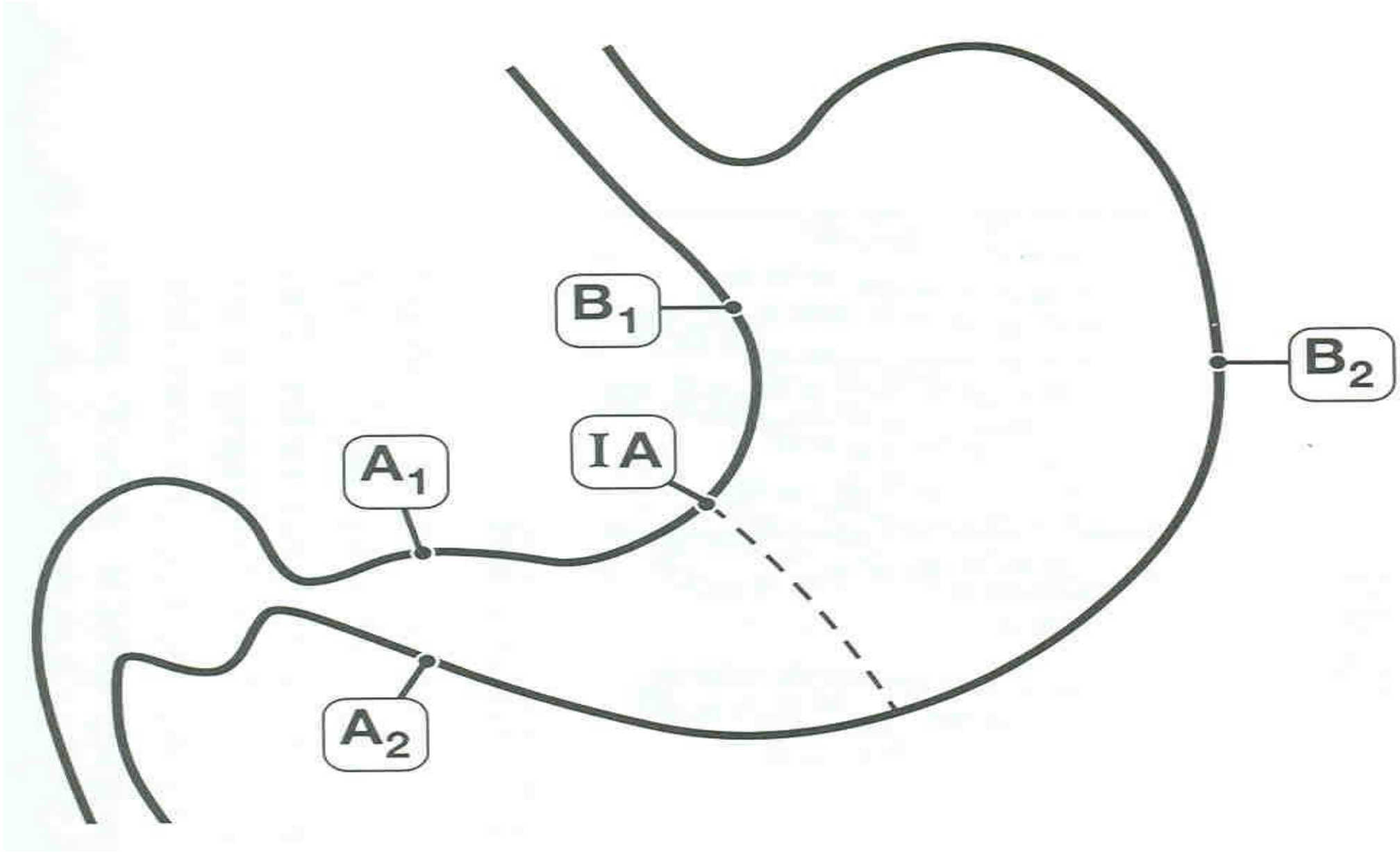
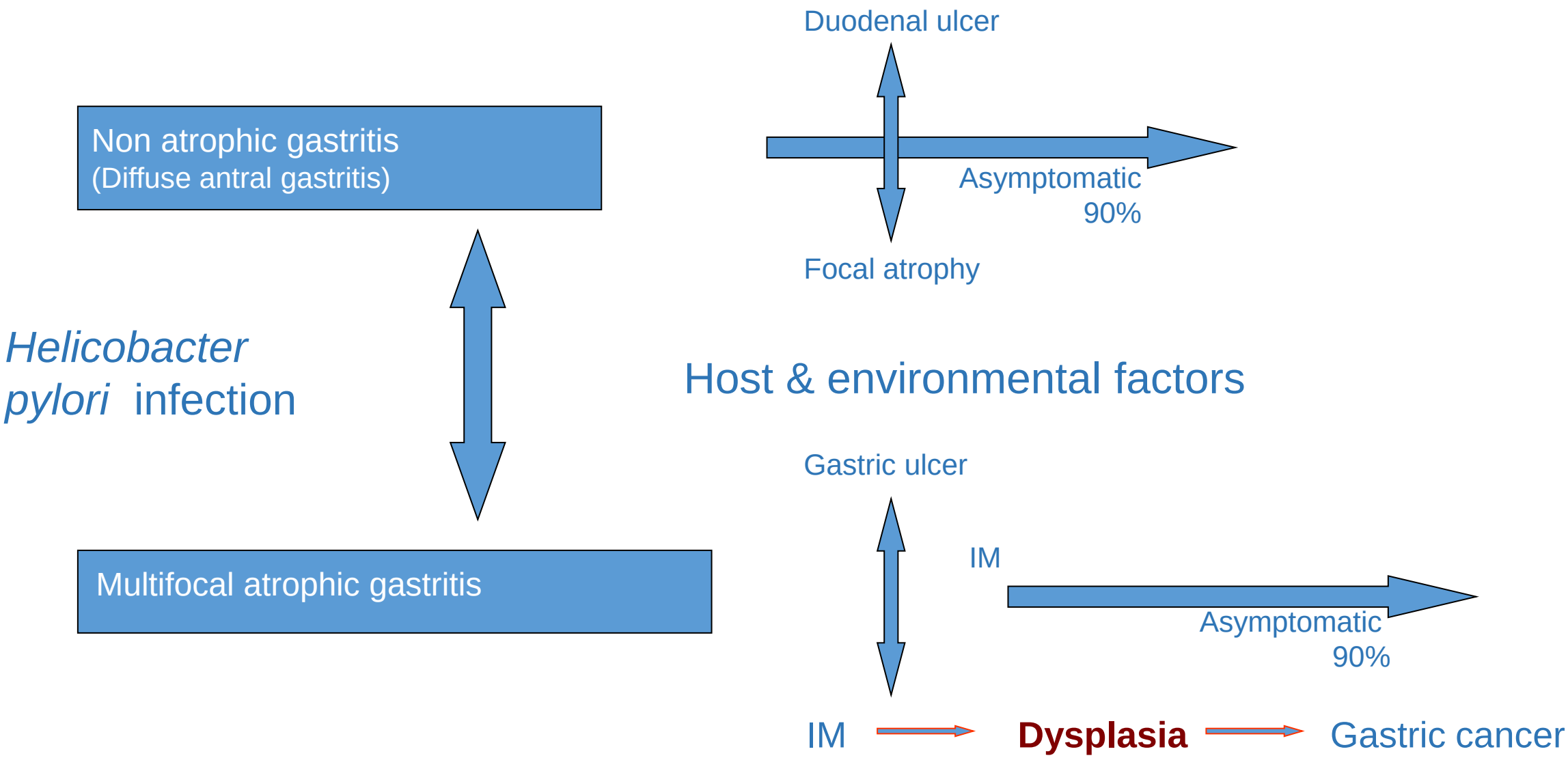

B1
B2
IA
A1
A2


Non atrophic gastritis
(Diffuse antral gastritis)
Duodenal ulcer
Asymptomatic
90%
Focal atrophy
Helicobacter pylori infection
Host & environmental factors
Gastric ulcer
IM
Asymptomatic
90%
Multifocal atrophic gastritis
IM
Dysplasia
Gastric cancer

REVIEW

Gut Microbes 4:6, 505–531; November/December 2013; © 2013 Landes Bioscience

The role of the gastrointestinal microbiome in *Helicobacter pylori* pathogenesis

Alexander Sheh and James G Fox*

Division of Comparative Medicine; Massachusetts Institute of Technology; Cambridge, MA USA

Keywords: *Helicobacter pylori*, gastric, stomach, microbiota, cancer, hypochlorhydria, bacterial colonization

The discovery of *Helicobacter pylori* overturned the conventional dogma that the stomach was a sterile organ and that pH values < 4 were capable of sterilizing the stomach. *H. pylori* are an etiological agent associated with gastritis, hypochlorhydria, duodenal ulcers, and gastric cancer. It is now appreciated that the human stomach supports a bacterial community with possibly 100s of bacterial species that influence stomach homeostasis. Other bacteria colonizing the stomach may also influence *H. pylori*-associated gastric pathogenesis by creating reactive oxygen and nitrogen species and modulating inflammatory responses. In this review, we summarize the available literature concerning the

of the GI tract, in contrast to the high bacterial counts (10^{10} to 10^{12} CFU/g) observed in the colon.[12-14] The low bacterial densities within this portion of the GI tract are due to the effects of rapid peristalsis, low pH and/or high bile concentration.[15] As *H. pylori* are directly implicated as an etiological agent in several gastric diseases, including gastric atrophy and cancer,[16] it is important to determine the contributions made by other bacteria in gastric health and disease.

Stomach Anatomy

European *Helicobacter* Study Group

2015

European *Helicobacter* and Microbiota Study group

Helicobacter ISSN 1523-5378
doi: 10.1111/hel.12145

Differences in Gastric Mucosal Microbiota Profiling in Patients with Chronic Gastritis, Intestinal Metaplasia, and Gastric Cancer Using Pyrosequencing Methods

Chang Soo Eun,*,[1] Byung Kwon Kim,[†,1] Dong Soo Han,* Seon Young Kim,[‡] Kyung Mo Kim,[§] Bo Youl Choi,[¶] Kyu Sang Song,** Yong Sung Kim[‡] and Jihyun F. Kim[‡‡]

OLGA staging

(Operative Link for Gastritis Assessment)

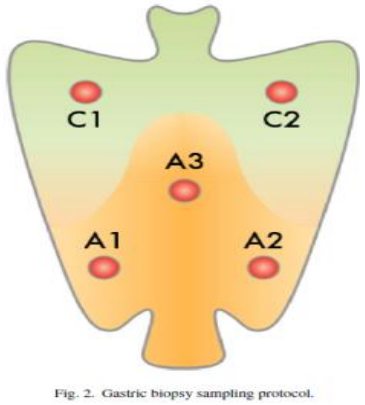
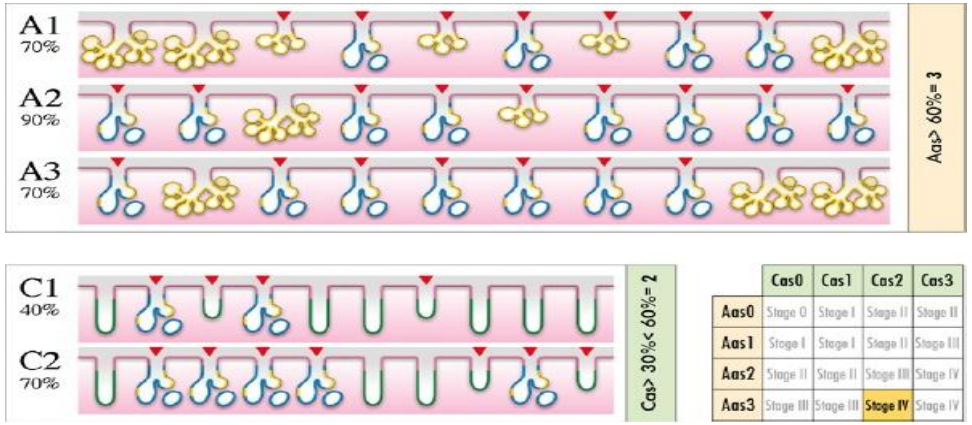


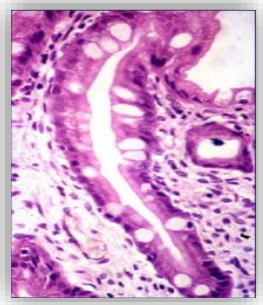
Fig. 2. Gastric biopsy sampling protocol.



Atrophy Score		Corpus			
		No Atrophy (score 0)	Mild Atrophy (score 1)	Moderate Atrophy (score 2)	Severe Atrophy (score 3)
Antrum	No Atrophy (score 0) (including *incisura angularis*)	STAGE 0	STAGE I	STAGE II	STAGE II
	Mild Atrophy (score 1) (including *incisura angularis*)	STAGE I	STAGE I	STAGE II	STAGE III
	Moderate Atrophy (score 2) (including *incisura angularis*)	STAGE II	STAGE II	STAGE III	STAGE IV
	Severe Atrophy (score 3) (including *incisura angularis*)	STAGE III	STAGE III	STAGE IV	STAGE IV

"… strong association between OLGA stages III/IV and Gastric Cancer…"

Rugge M, et al, OLGA staging for gastritis: A tutorial, Dig Liver Dis. 2008



Classification of chronic gastritis
OLGIM staging

The staging of gastritis with the OLGA system by using intestinal metaplasia as an accurate alternative for atrophic gastritis

Lisette G. Capelle, MD, Annemarie C. de Vries, MD, PhD, Jelle Haringsma, MD, Frank Ter Borg, MD, PhD, Richard A. de Vries, MD, PhD, Marco J. Bruno, MD, PhD, Herman van Dekken, MD, PhD, Jos Meijer, MD, Nicole C. T. van Grieken, MD, PhD, Ernst J. Kuipers, MD, PhD

TABLE 2. Proposal for the OLGIM staging system

		Corpus			
	IM score	**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.

Capelle L *et al*. Gastrointest Endosc 71: 1150, 2010

Thieme

Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European *Helicobacter* and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019

3 Definitions and prevention aims

3.1 Gastric carcinogenesis

STATEMENT

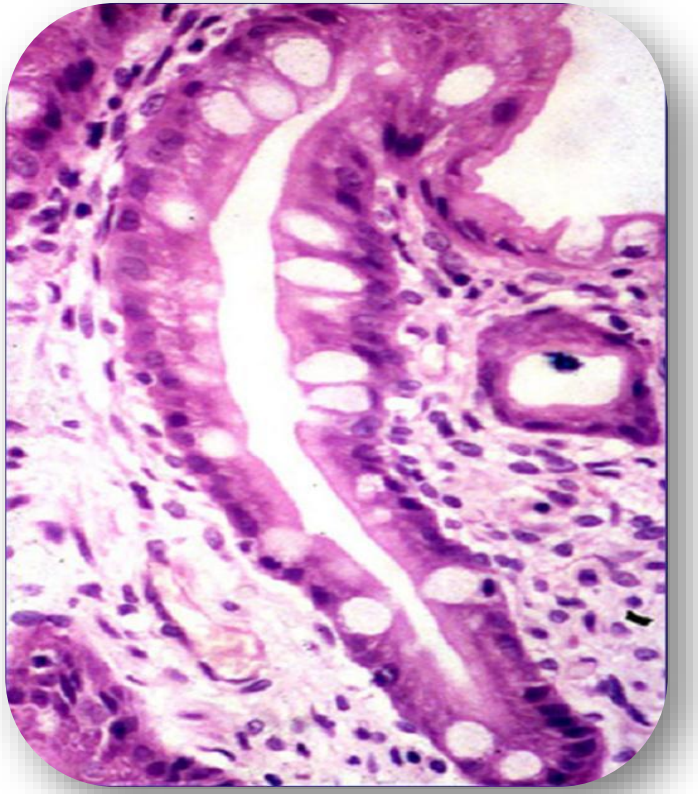
1 Patients with chronic atrophic gastritis
metaplasia are at risk for gastric adenocarc
High quality evidence (100% agree [94
moderately agree]).

STATEMENT

2 Histologically confirmed intestinal metaplasia is the most reliable marker of atrophy in gastric mucosa.
High quality evidence (100% agree [100% strongly or moderately agree]).

RECOMMENDATION

3 Patients with advanced stages of gastritis, that is, atrophy and/or intestinal metaplasia affecting both antral and corpus mucosa, should be identified as they are considered to be at higher risk for gastric adenocarcinoma.
Moderate quality evidence, strong recommendation (94% agree [94% strongly or moderately agree]).

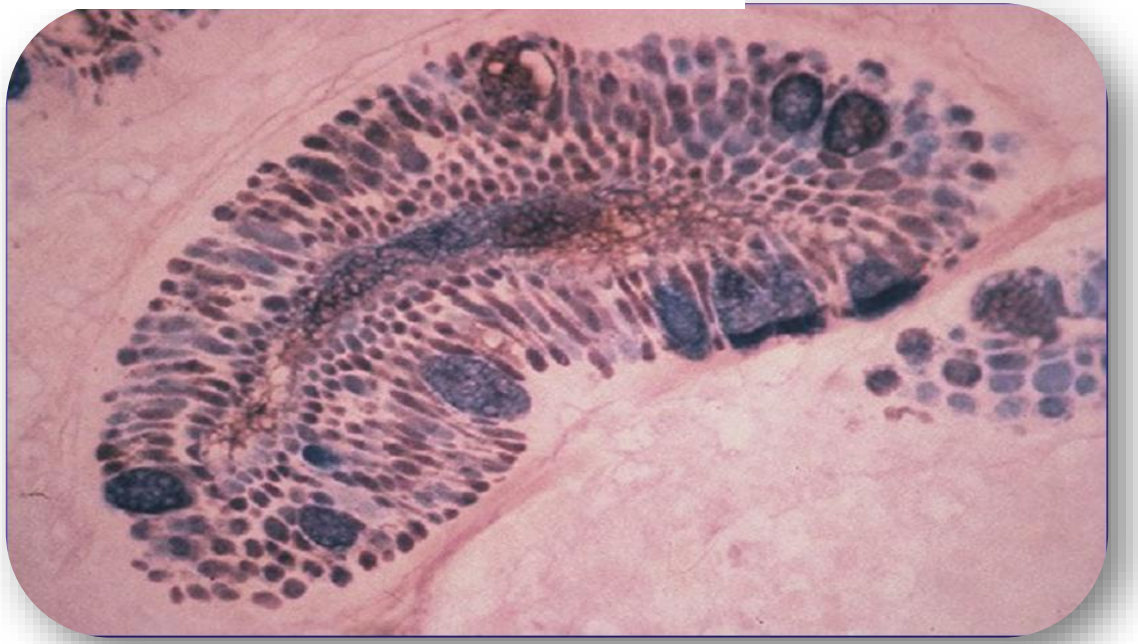


Intestinal Metaplasia (IM)

Sub-types of IM

Type I - complete
Type II - incomplete
Type III - incomplete

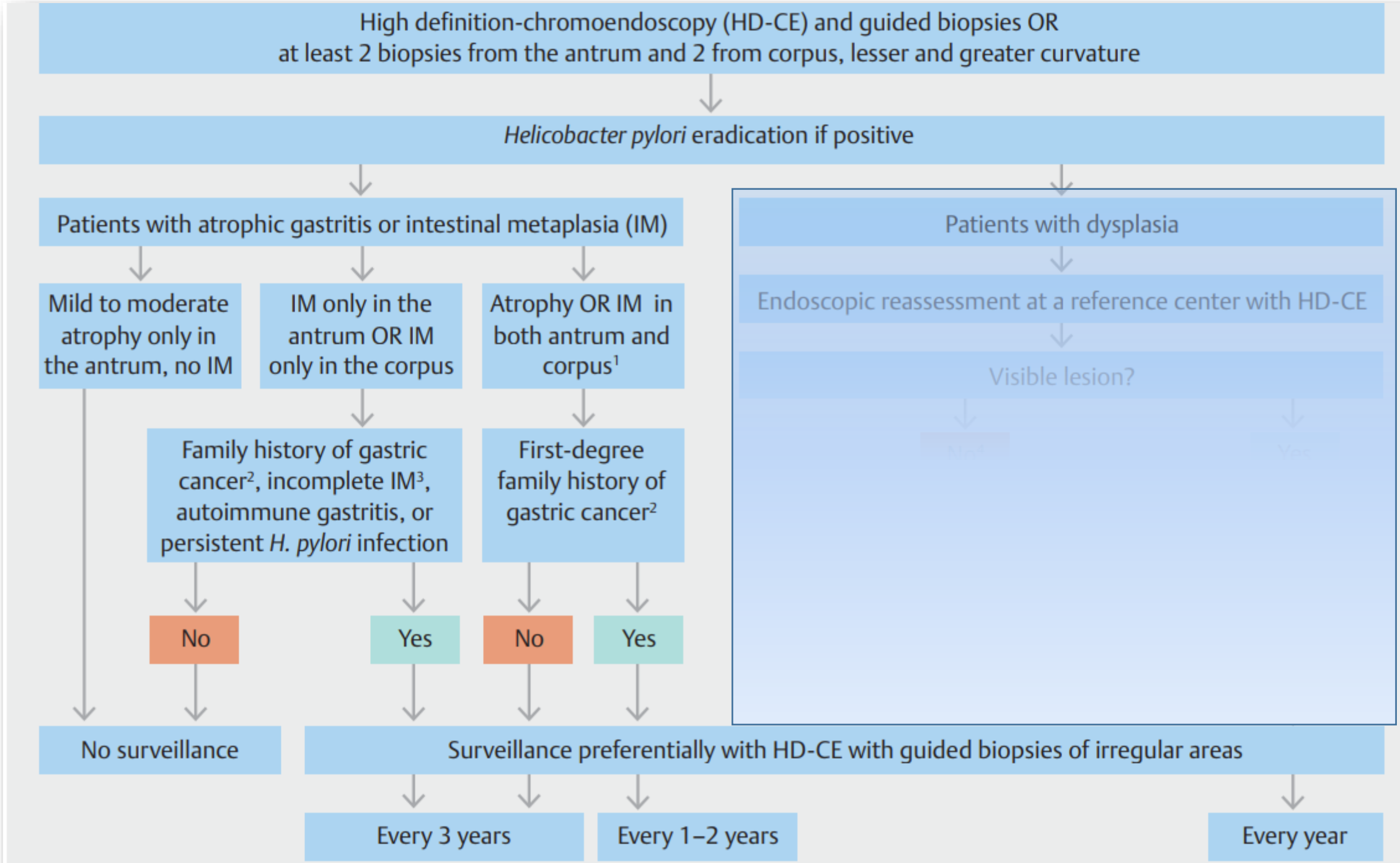
Risk of gastric cancer development

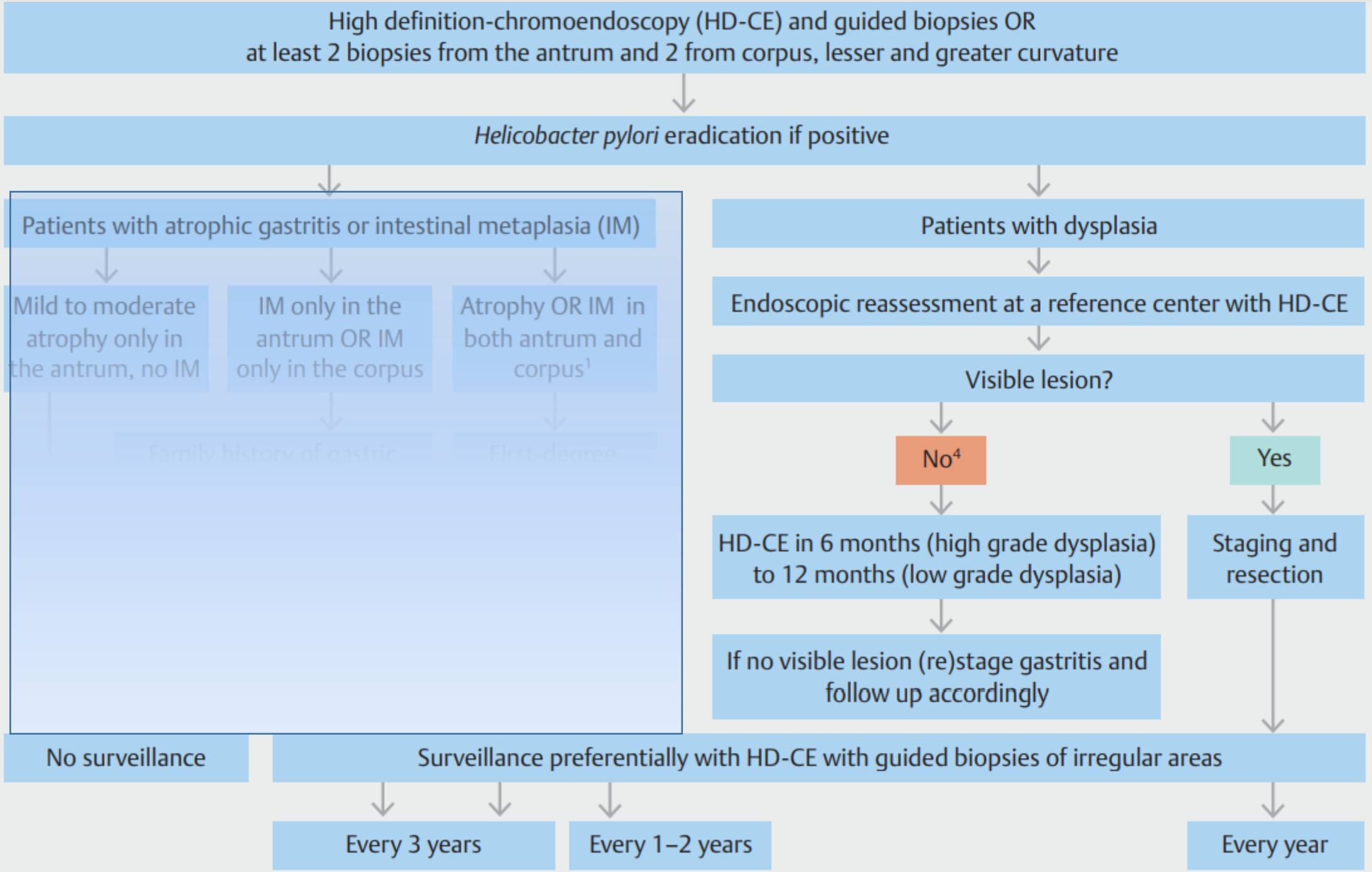


•A systematic review in 10 follow-up studies, incomplete **type III IM was associated with significantly higher risk** of **gastric cancer** with a **6 – 11-fold higher risk.**

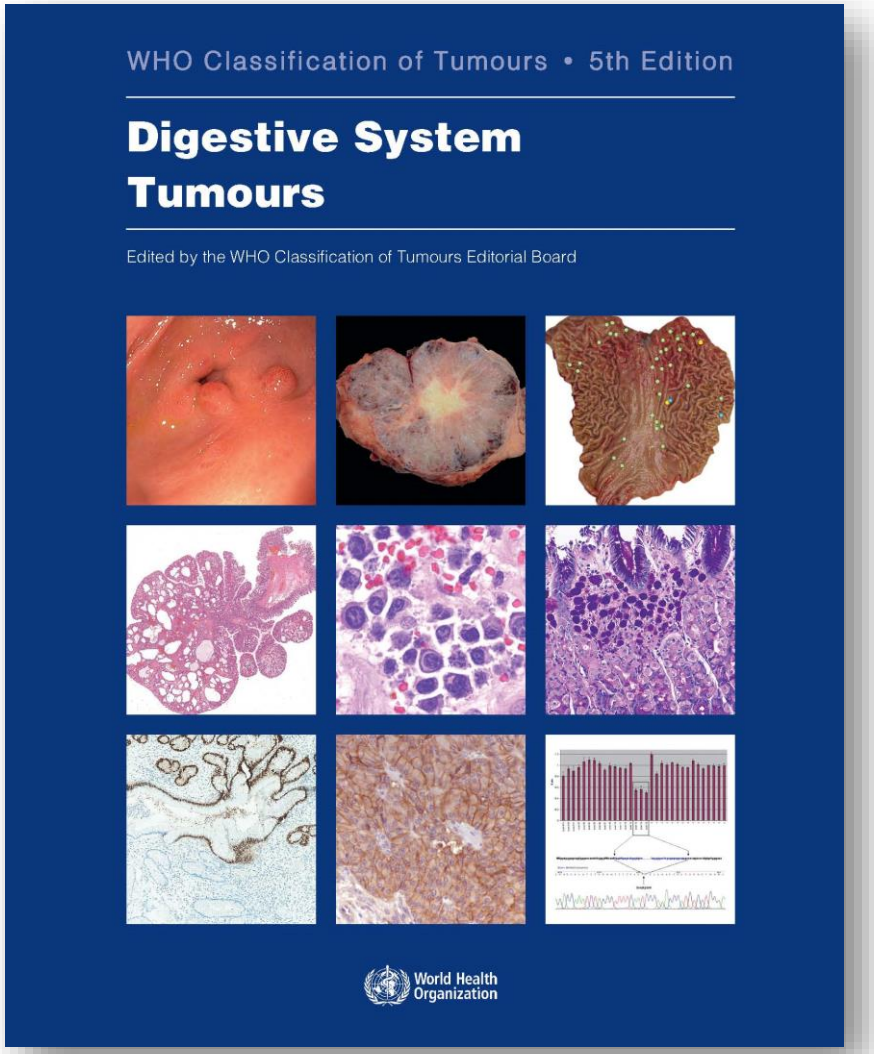
•A follow-up of 16 years also showed that incomplete-type IM was associated with a higher risk of progression to cancer than the complete type (**OR 11.3**, 95 %CI 1.4 – 91.4)

Filipe F *et al.* Int J Cancer 57: 324, 1994


High definition-chromoendoscopy (HD-CE) and guided biopsies OR
at least 2 biopsies from the antrum and 2 from corpus, lesser and greater curvature
Helicobacter pylori eradication if positive
Patients with atrophic gastritis or intestinal metaplasia (IM)
Mild to moderate atrophy only in the antrum, no IM
IM only in the antrum OR IM only in the corpus
Atrophy OR IM in both antrum and corpus[1]
Family history of gastric cancer[2], incomplete IM[3], autoimmune gastritis, or persistent H. pylori infection
First-degree family history of gastric cancer[2]
No
Yes
No
Yes
No surveillance
Surveillance preferentially with HD-CE with guided biopsies of irregular areas
Every 3 years
Every 1–2 years
Every year
Patients with dysplasia
Endoscopic reassessment at a reference center with HD-CE
Visible lesion?


High definition-chromoendoscopy (HD-CE) and guided biopsies OR
at least 2 biopsies from the antrum and 2 from corpus, lesser and greater curvature
Helicobacter pylori eradication if positive
Patients with atrophic gastritis or intestinal metaplasia (IM)
Mild to moderate atrophy only in the antrum, no IM
IM only in the antrum OR IM only in the corpus
Atrophy OR IM in both antrum and corpus[1]
Family history of gastric
First-degree
Patients with dysplasia
Endoscopic reassessment at a reference center with HD-CE
Visible lesion?
No[4]
Yes
HD-CE in 6 months (high grade dysplasia) to 12 months (low grade dysplasia)
Staging and resection
If no visible lesion (re)stage gastritis and follow up accordingly
No surveillance
Surveillance preferentially with HD-CE with guided biopsies of irregular areas
Every 3 years
Every 1–2 years
Every year

WHO Classification of Tumours of the Digestive System, 5th edition, 2019



Gastric dysplasia

Definition

Gastric dysplasia consists of unequivocal neoplastic changes of the gastric epithelium without evidence of stromal invasion

Related terminology

Acceptable: intraepithelial neoplasia

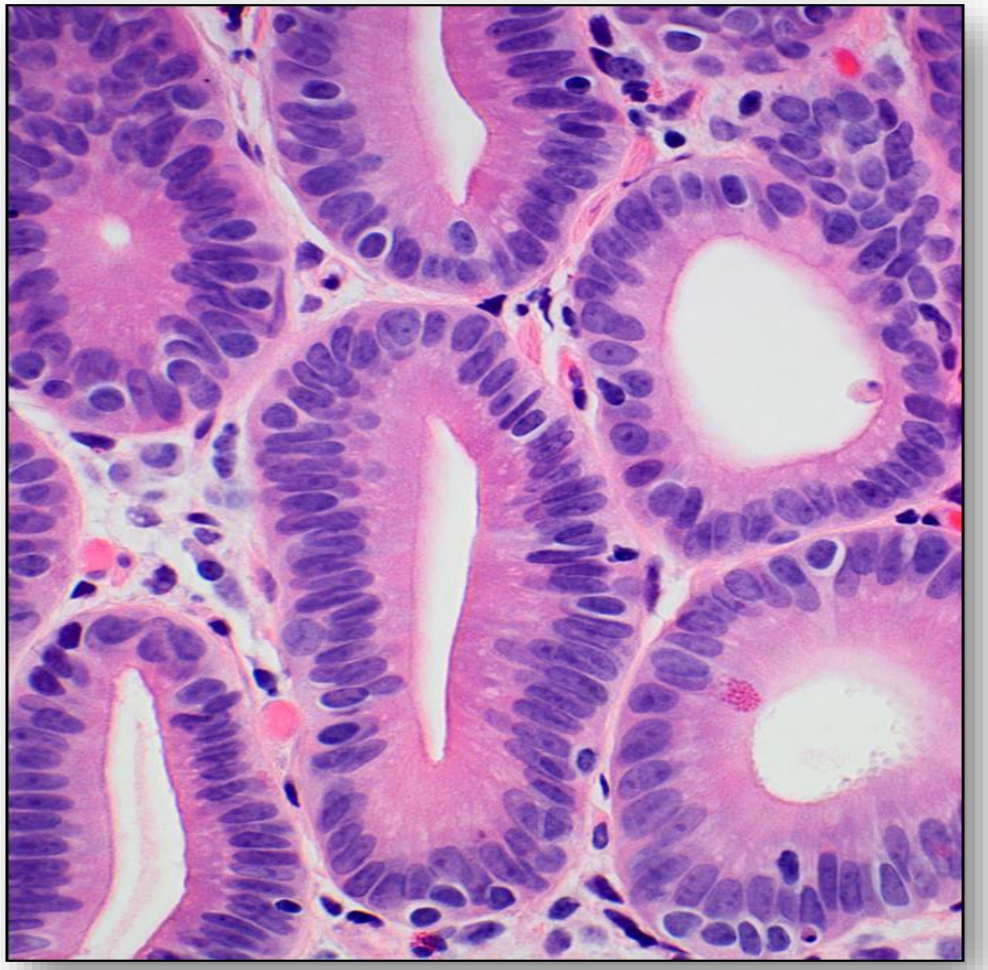
Subtype(s)

Intestinal-type dysplasia; foveolar-type (gastric-type) dysplasia; gastric pit/crypt dysplasia; serrated dysplasia

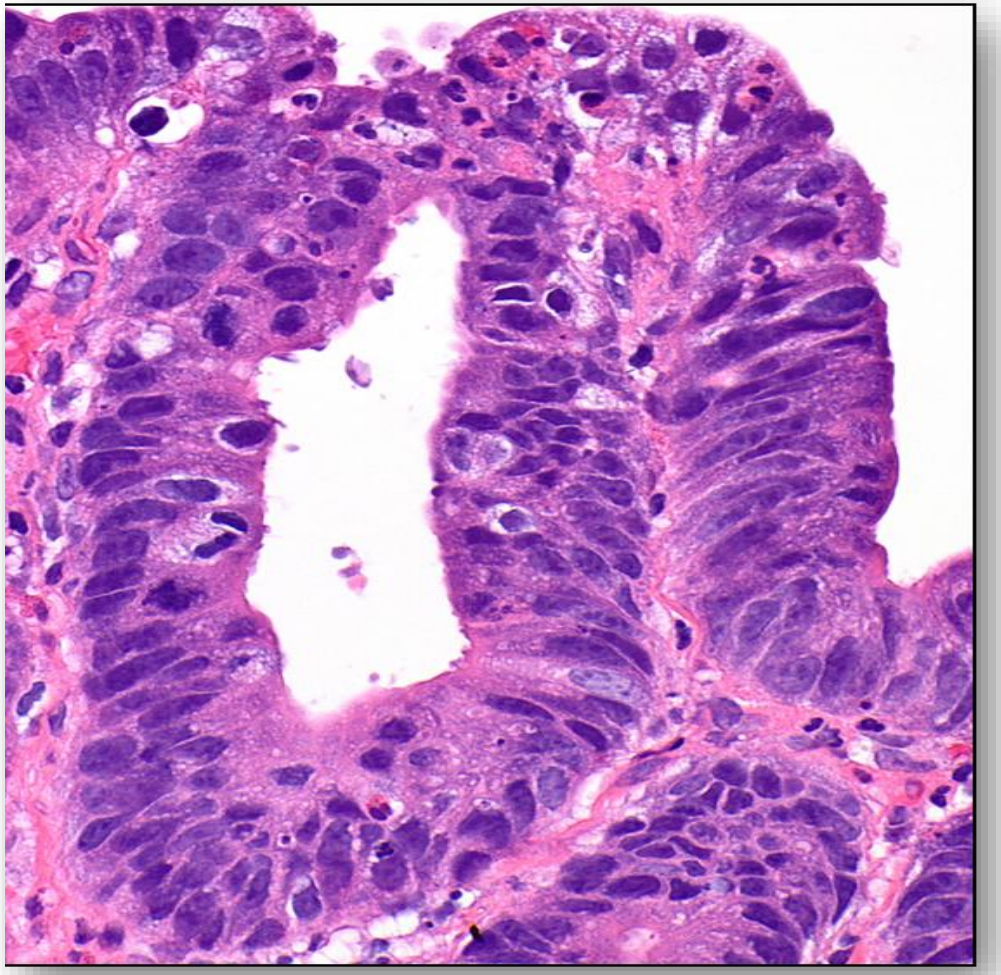
WHO Classification of Tumours of the Digestive System, 5th edition, 2019

Padova International	Vienna	Revised Vienna	Japanese Diagnostic Framework (Biopsy)	WHO (2019)
Category 1: Negative for dysplasia	**Category 1:** Negative for dysplasia	**Category 1:** Negative for dysplasia	**Group 1:** Normal/non-neoplastic	**Negative for dysplasia/IEN**
Category 2: Indefinite for dysplasia	**Category 2:** Indefinite for dysplasia	**Category 2:** Indefinite for dysplasia	**Group 2:** Indefinite for neoplasia	**Indefinite for dysplasia/IEN**
Category 3.1: Low-grade dysplasia (low-grade NiN)	**Category 3:** Non-invasive low-grade neoplasia (low-grade adenoma/dysplasia)	**Category 3:** Low-grade adenoma/dysplasia	**Group 3:** Adenoma	**Low-grade dysplasia/IEN** (low-grade adenoma/dysplasia)
Category 3.2: High-grade dysplasia (high-grade NiN)	**Category 4:** High-grade neoplasia **4.1:** High-grade adenoma/dysplasia **4.2:** Non-invasive carcinoma **4.3:** Suspicious for invasive carcinoma	**Category 4:** High-grade neoplasia **4.1:** High-grade adenoma/dysplasia **4.2:** Non-invasive carcinoma **4.3:** Suspicious for invasive carcinoma **4.4:** Intramucosal carcinoma	**Group 4:** Suspicious for carcinoma	**High-grade dysplasia/IEN** (high-grade adenoma/dysplasia)
Category 4: Suspicious for invasive carcinoma			**Group 5:** Carcinoma (non-invasive or invasive)	
Category 5: Invasive adenocarcinoma	**Category 5:** Invasive neoplasia **5.1:** Intramucosal carcinoma			**Intramucosal invasive neoplasia** (intramucosal carcinoma)

Low- and high-grade dysplasia

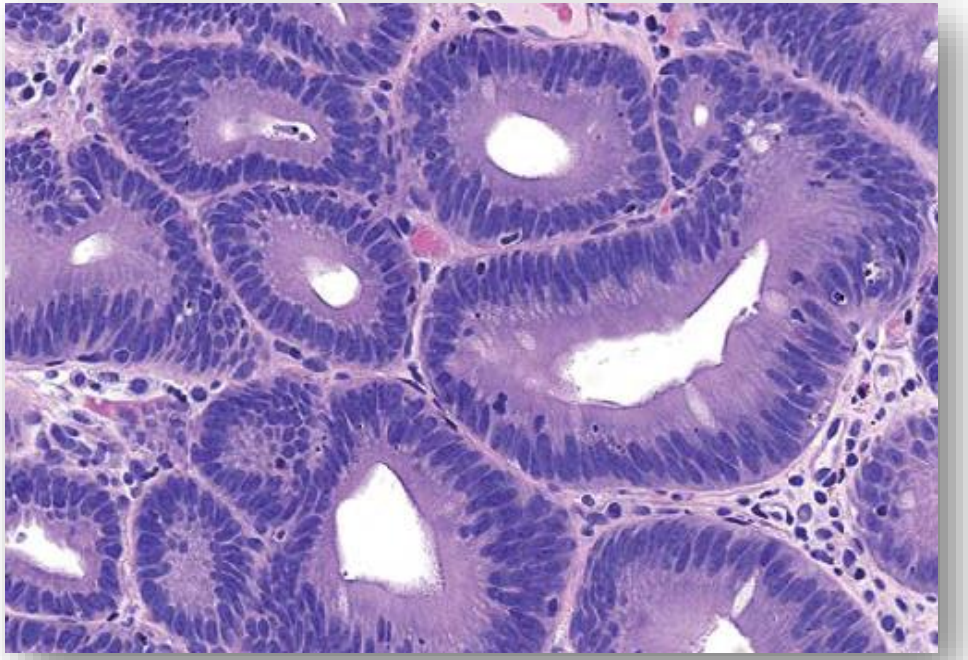


- **Minimal** architectural disarray
- Mild/moderate cytological atypia
- Nuclei are elongated, polarised, basally located
- Mitotic activity is mild/moderate.

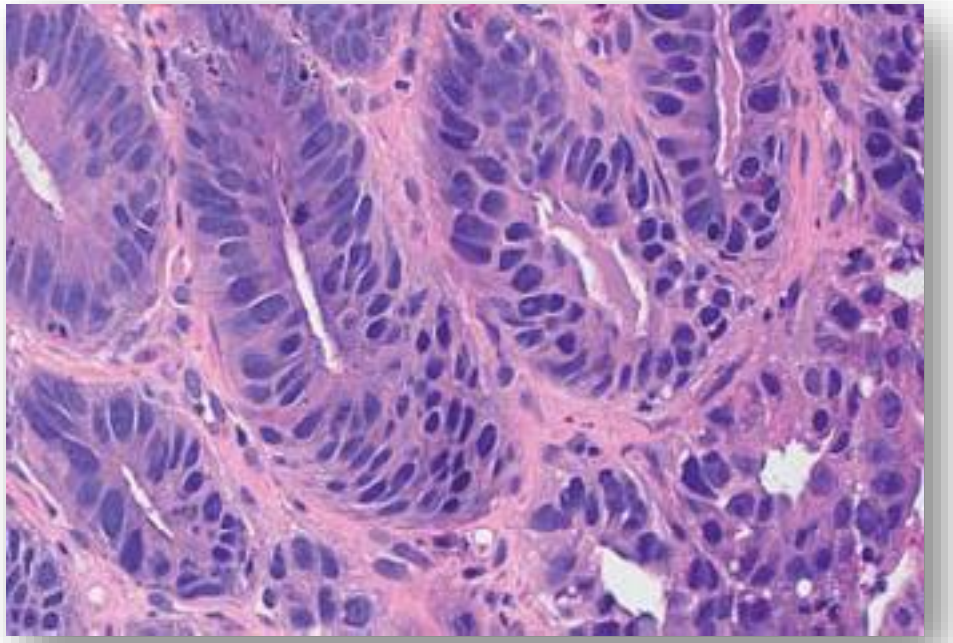


- **Pronounced** architectural disarray
- High nucleus:cytoplasm ratio
- Numerous mitoses, often atypical
- Nuclei frequently extend towards the luminal half of the gland

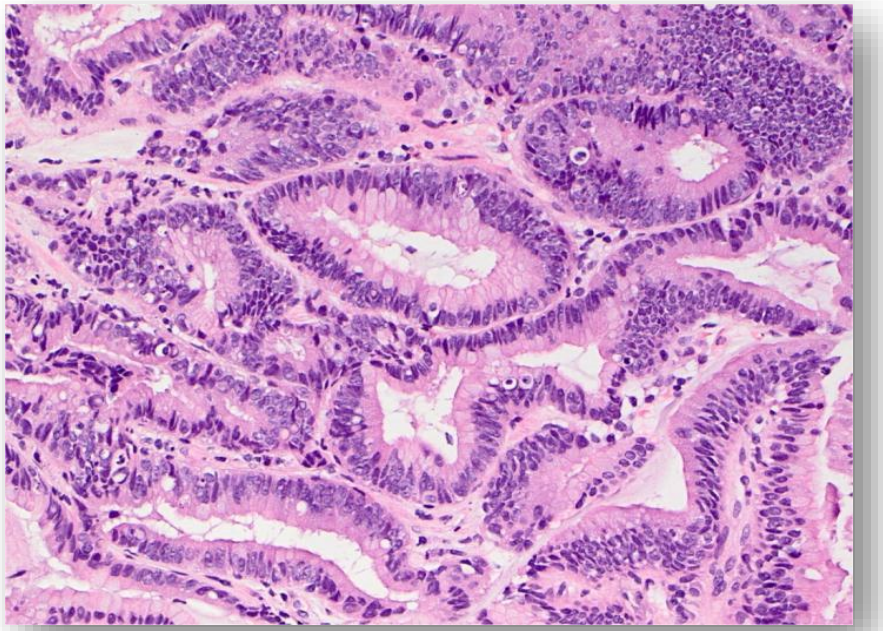
Intestinal phenotype
(adenomatous, type I)



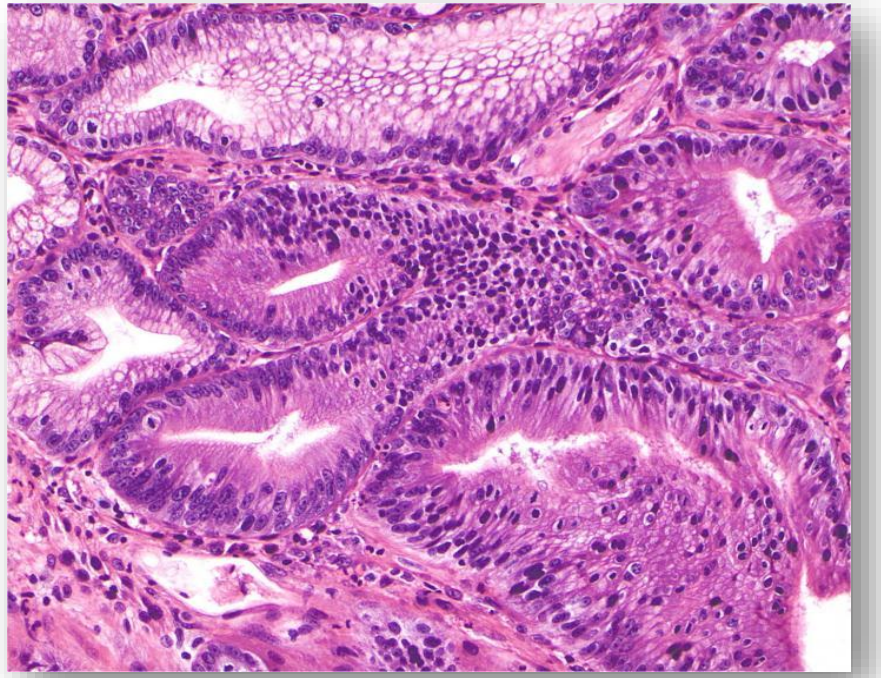
Overlapping, pencillate, hyperchromatic and/or pleomorphic nuclei, with pseudo-stratification and inconspicuous nucleoli, mucin depletion, and lack of surface maturation.



Gastric phenotype
(foveolar or pyloric, type II)

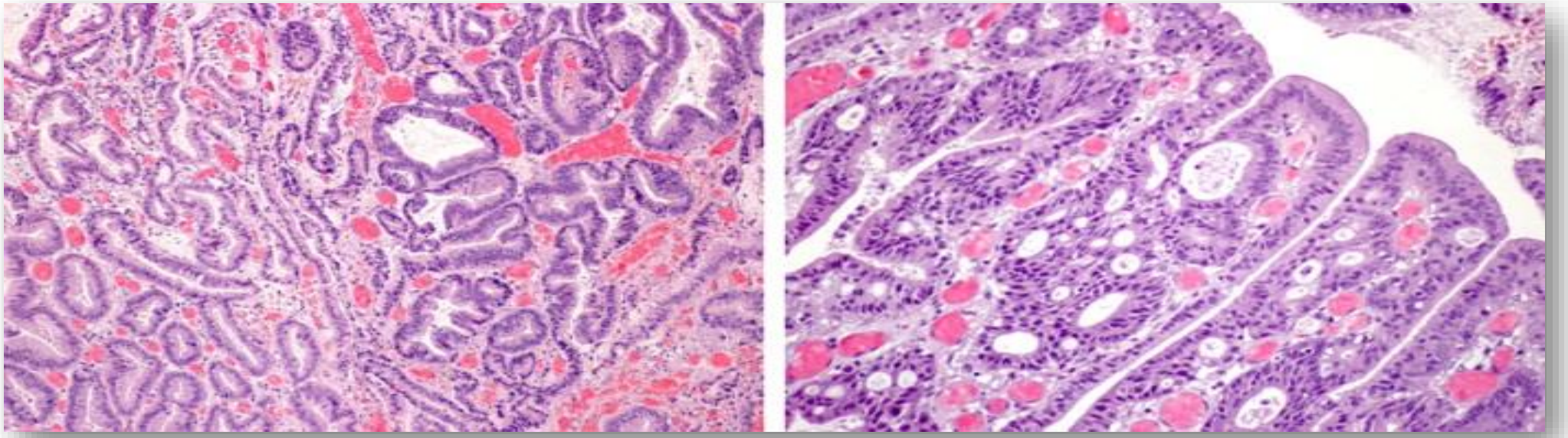


Cuboidal or low columnar cells, with clear or eosinophilic cytoplasm, and round to oval nuclei.



- The use of the term carcinoma *in situ* for columnar precursor lesions is strongly discouraged (included in high grade dysplasia).

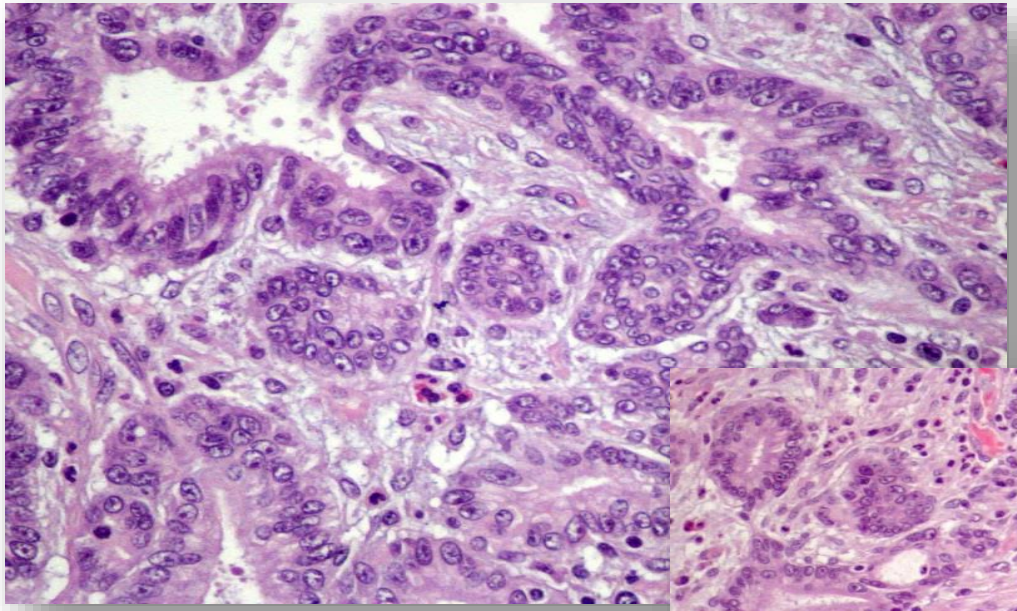
- Intramucosal adenocarcinoma is the term used for lesions that show invasion into the lamina propria or muscularis mucosa but not into the submucosa (what qualifies as evidence of invasion?).



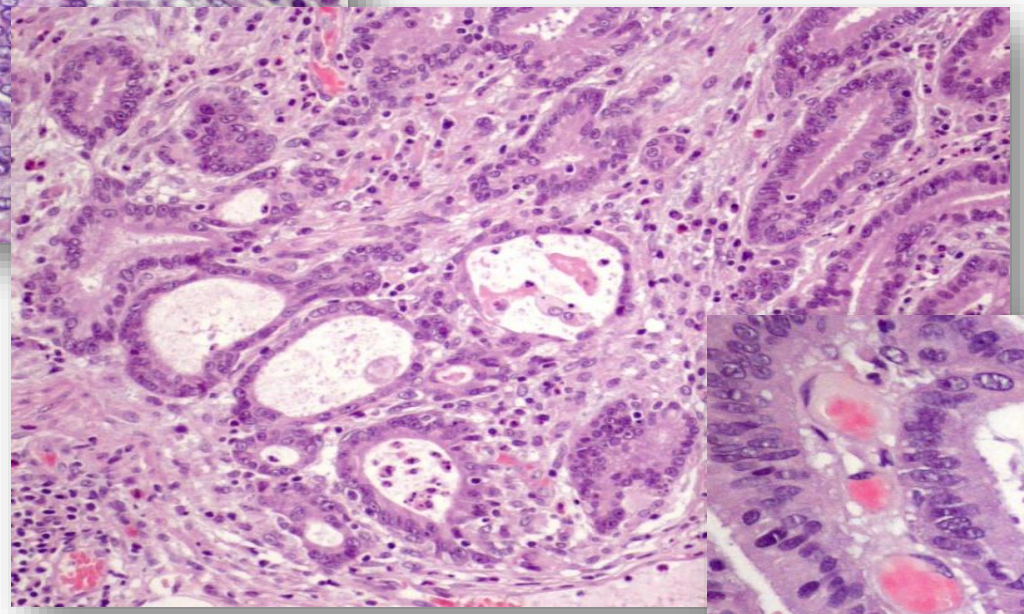
Low & high grade dysplasia

Intramucosal carcinoma

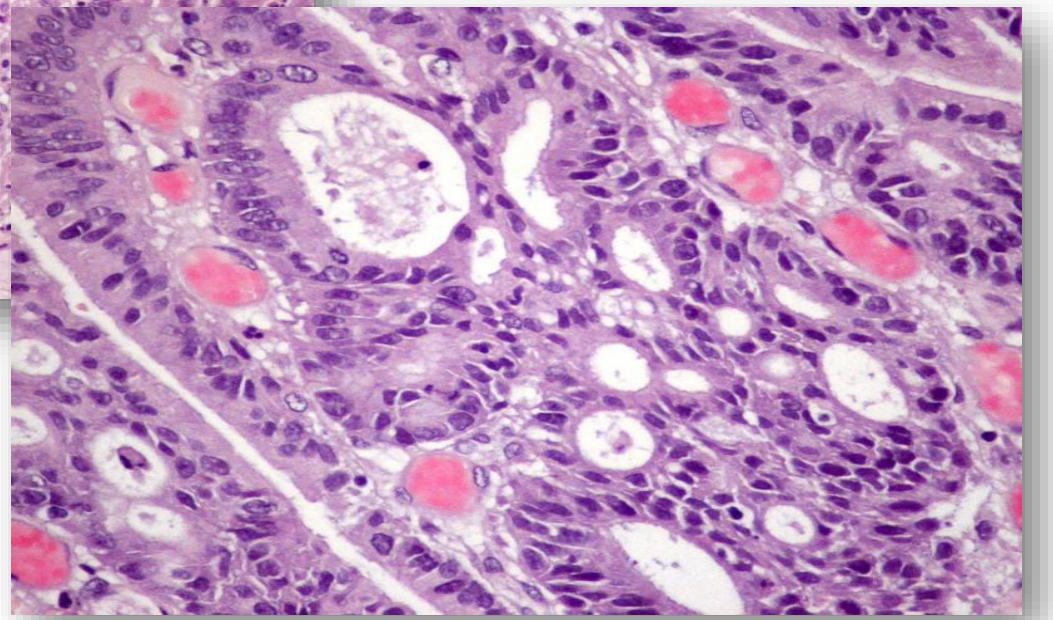
Intramucosal invasive neoplasia/intramucosal carcinoma



Branching and budding of glands

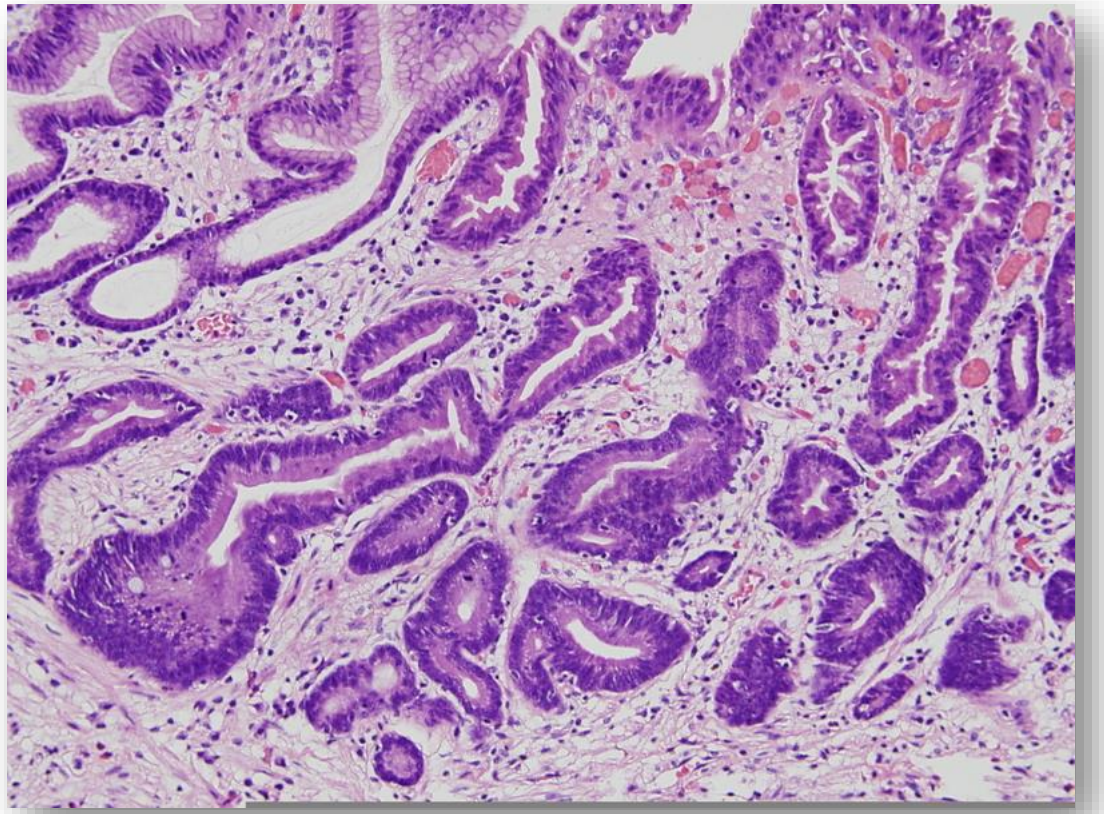


Intraluminal necrotic debris



Fused or cribriforming glands

Gastric pit/crypt dysplasia



Dysplasia at the basal portion of gastric pits. The glandular structures show maturation to the surface epithelial cells.

It has been reported at the periphery of traditional neoplasia in 49–72% of cases, and it is believed to be an independent predictor of cancer progression.

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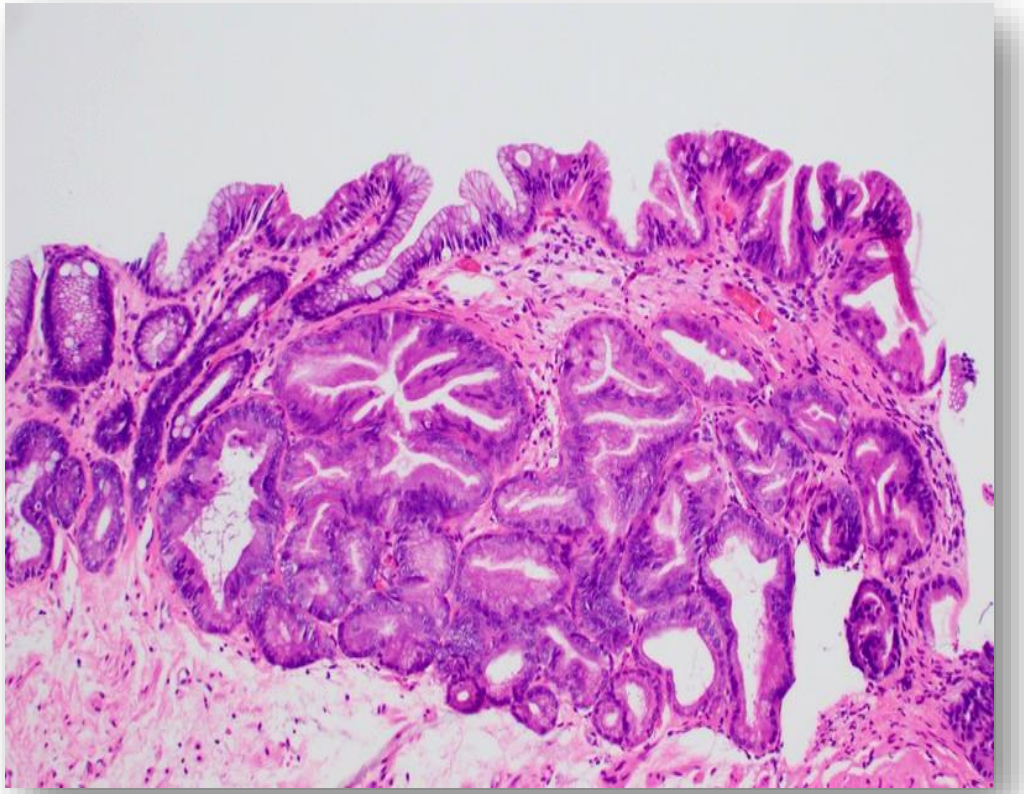
Serrated dysplasia



Serrated dysplasia is characterized by its distinctive topography (pit region); it frequently features a micropapillary pattern, extending to the mucosal surface and exhibiting MUC5AC expression.

This phenotype has also been reported as serrated adenoma and frequently coexists with adenocarcinoma.

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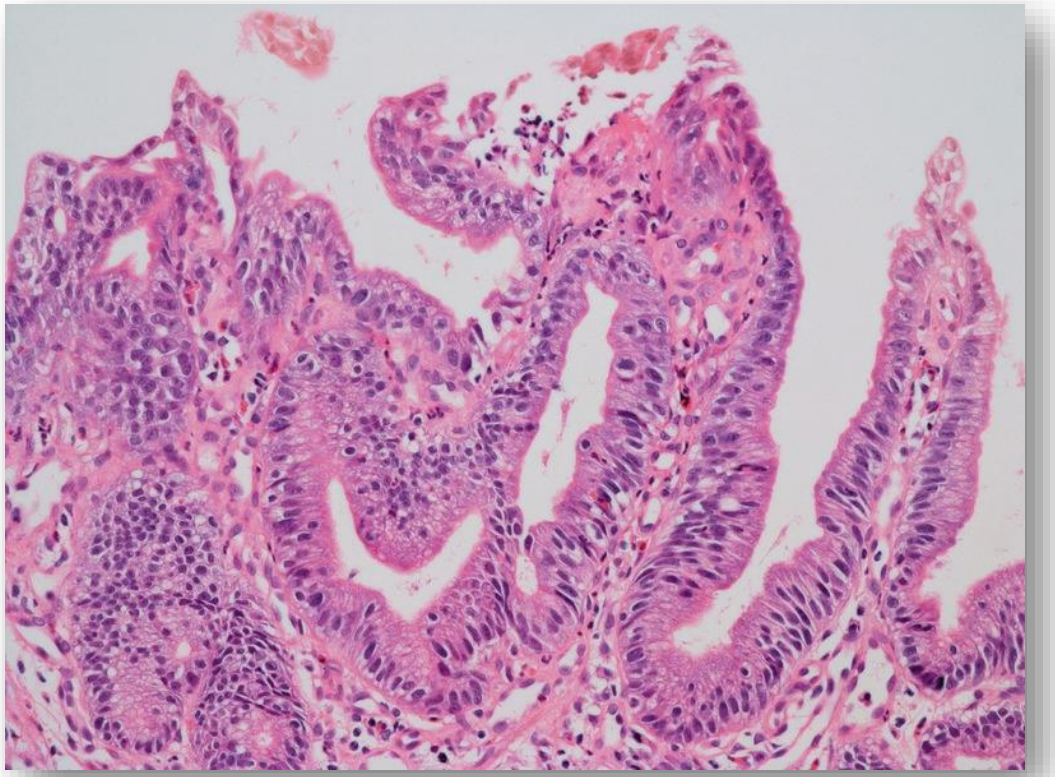
Regenerative atypia



Surface maturation of epithelium
with inflammatory background.

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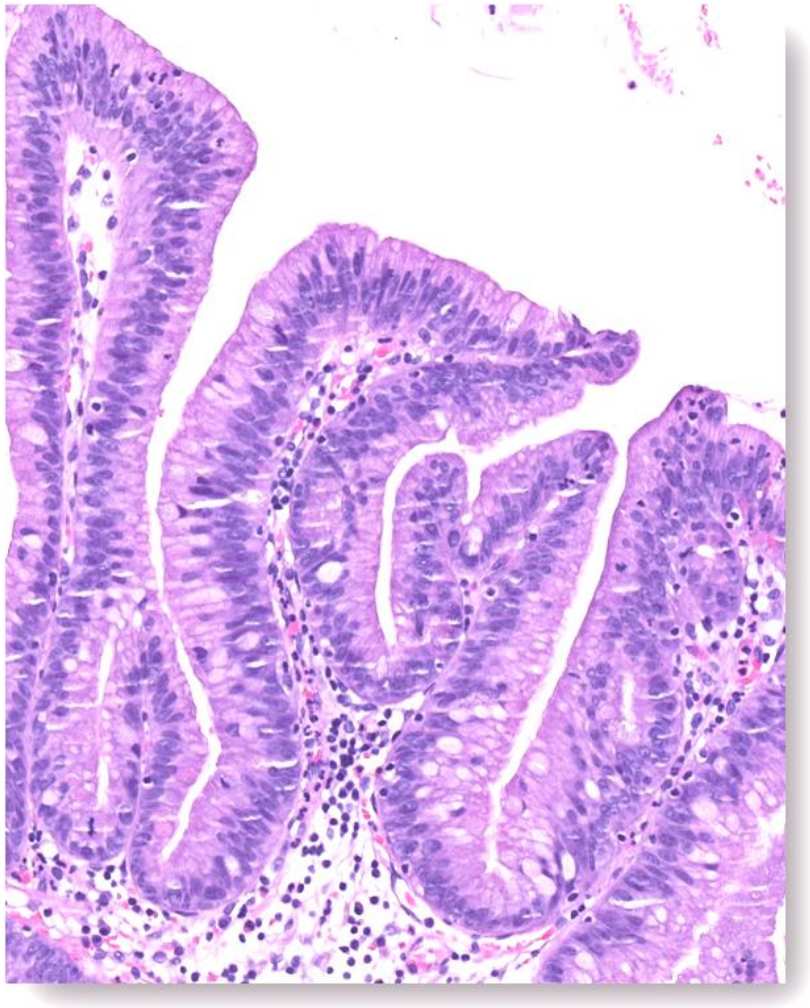
Epithelial tumours

3.1.2: Benign epithelial tumours and precursors

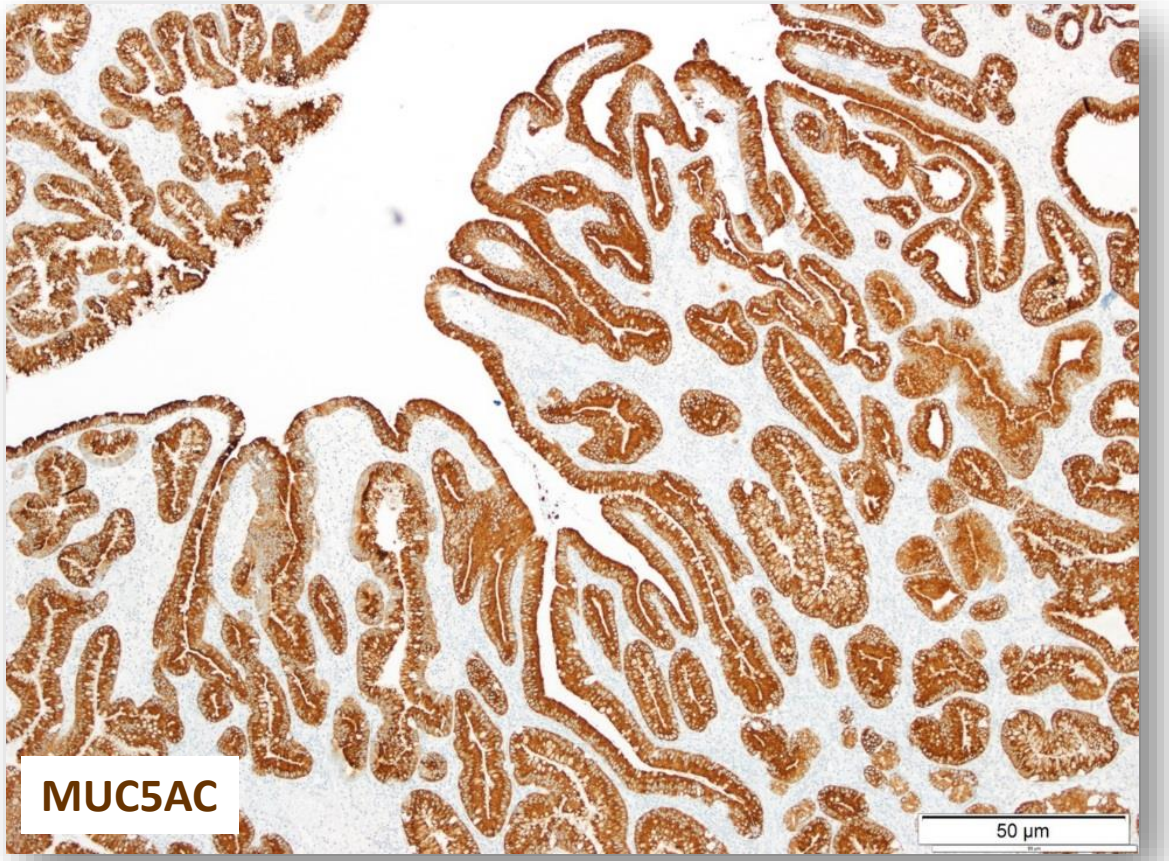
- 3.1.2.1: Fundic gland polyps
- 3.1.2.2: Gastric hyperplastic polyps
- 3.1.3.1: Gastric dysplasia
- 3.1.4.1: Intestinal-type gastric adenoma
- 3.1.4.2: Foveolar-type adenoma
- 3.1.4.3: Gastric pyloric gland adenoma
- 3.1.4.3: Oxyntic gland adenoma

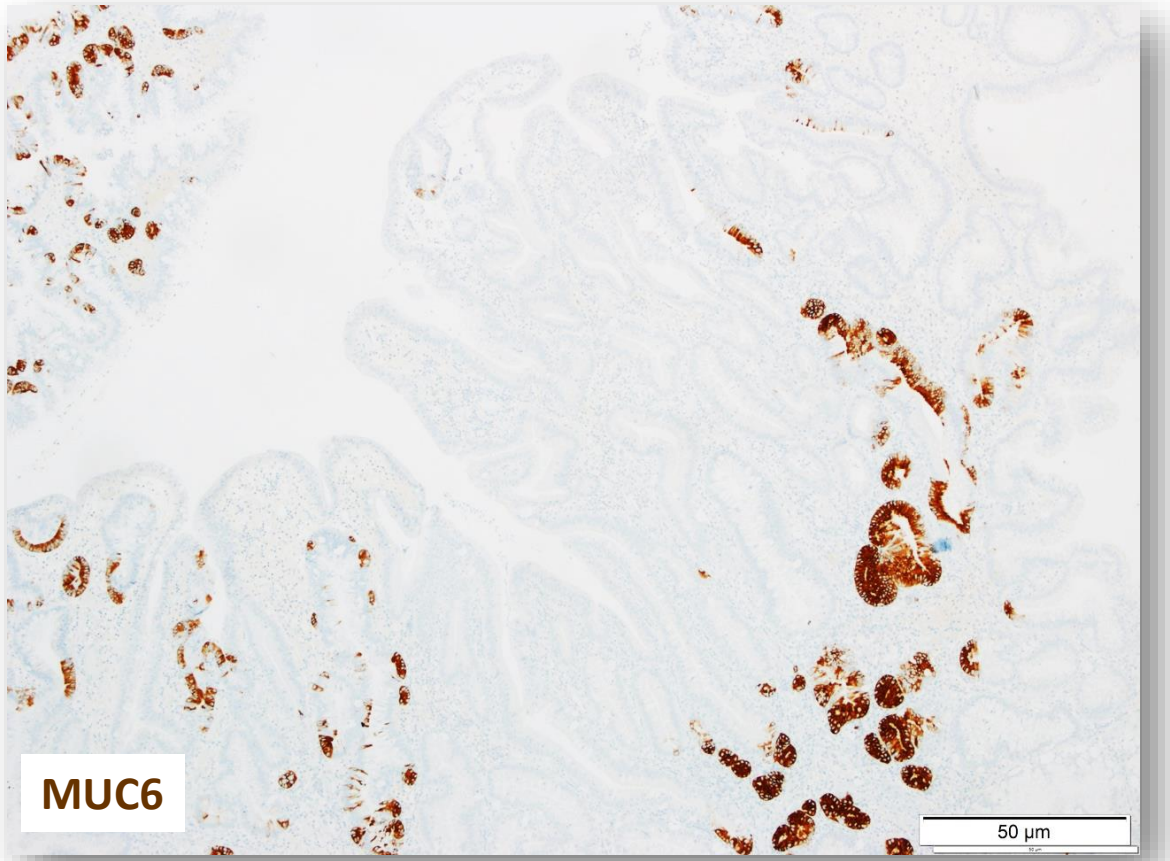
Foveolar-type adenoma



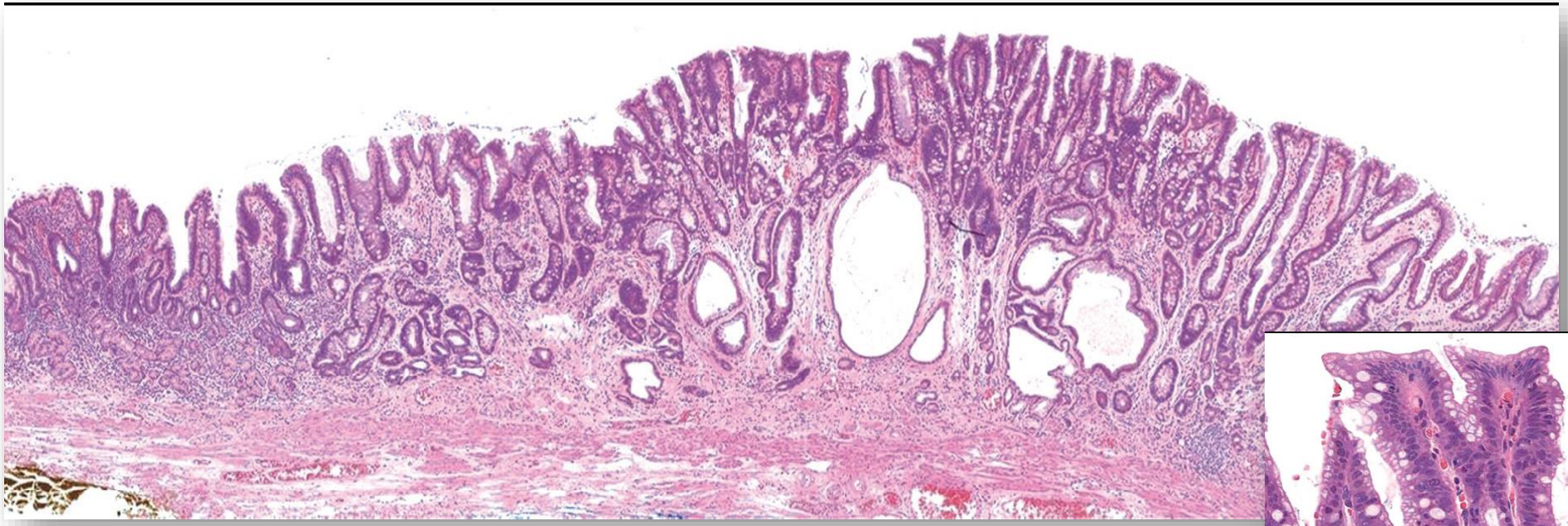
Essential and desirable diagnostic criteria

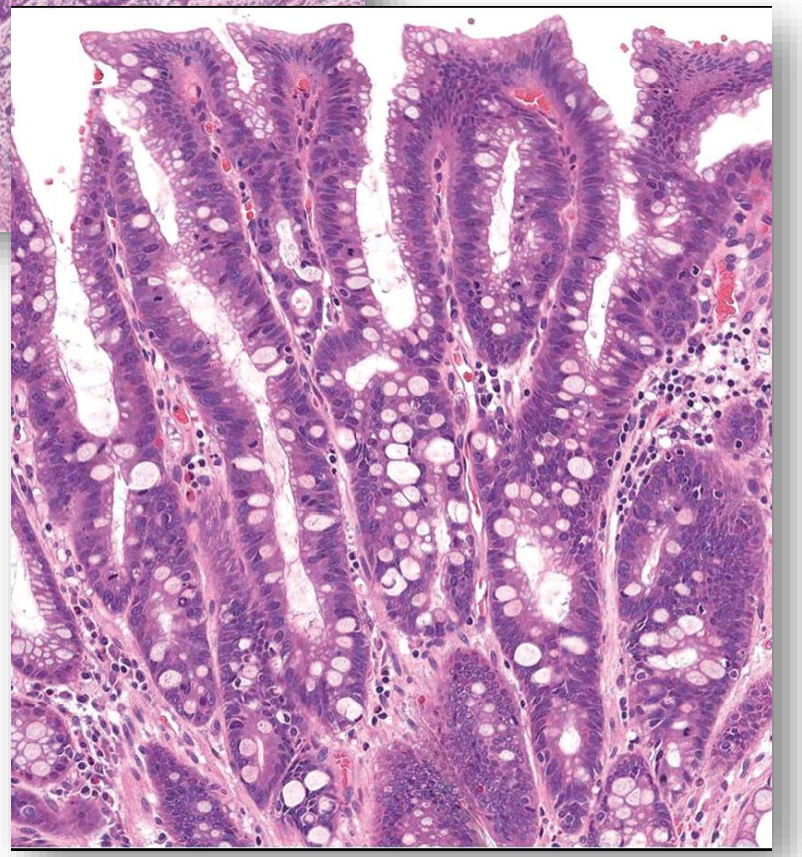
• polypoid growth of dysplastic columnar epithelia with a foveolar-cell phenotype, with a distinctive apical cap of neutral mucins.





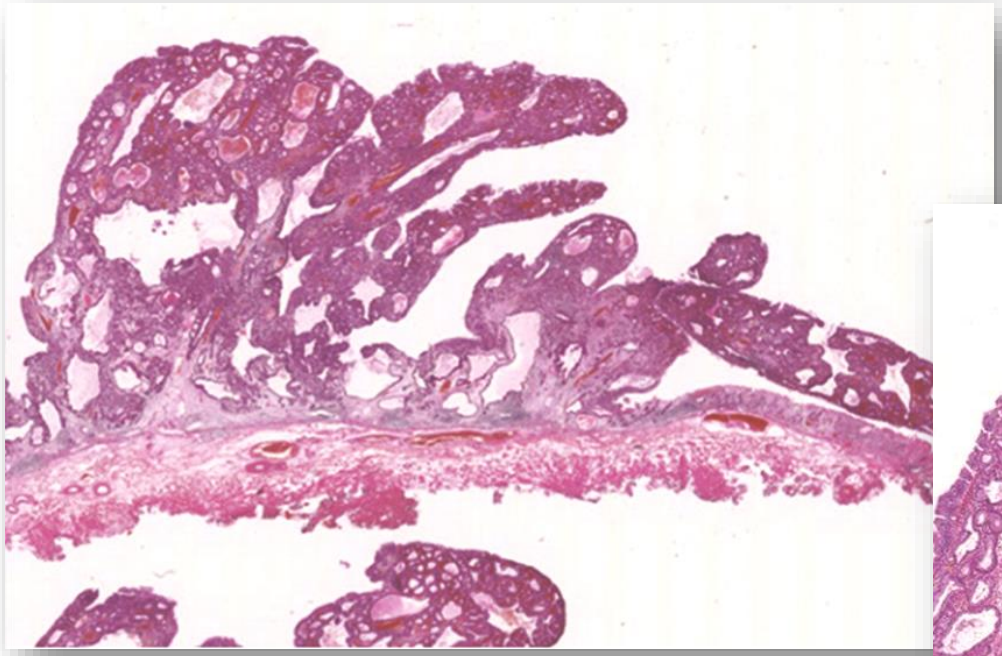
Foveolar-cell phenotype

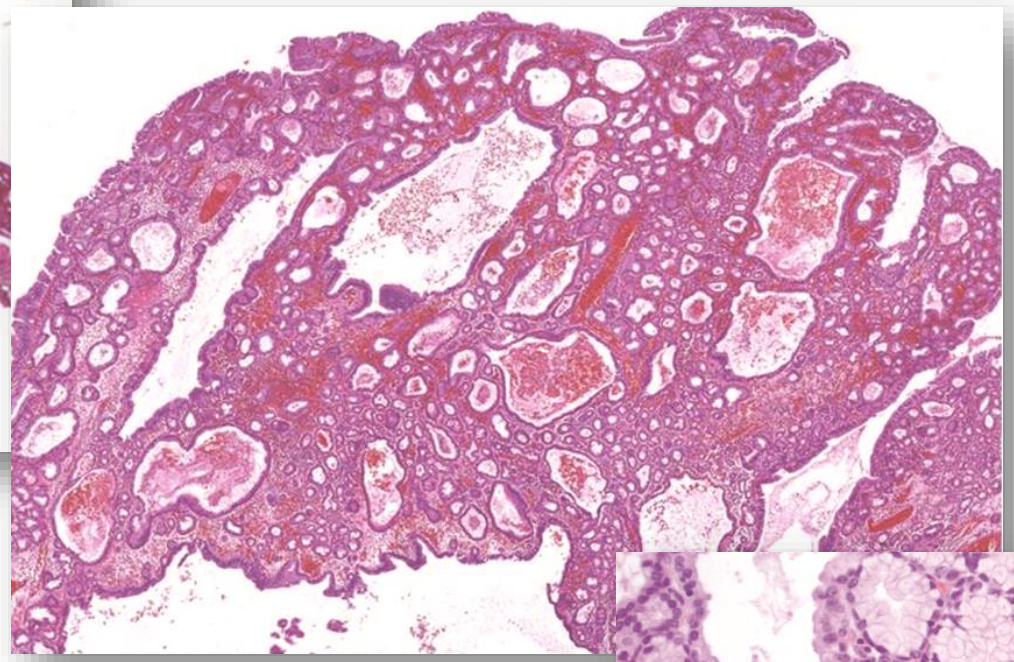


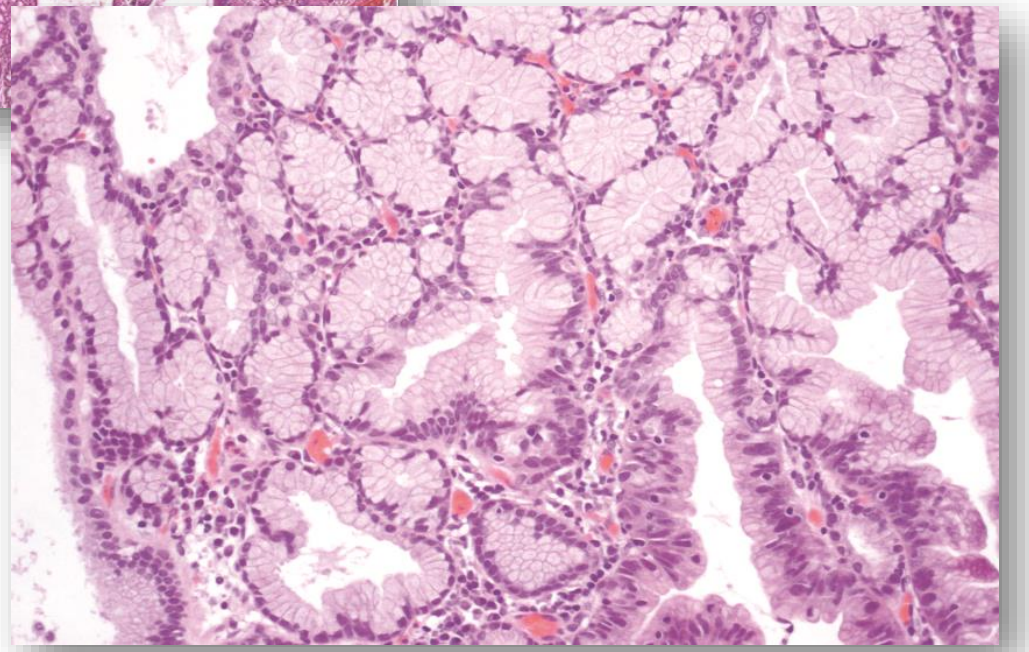


Intestinal type adenoma

Pyloric gland adenoma



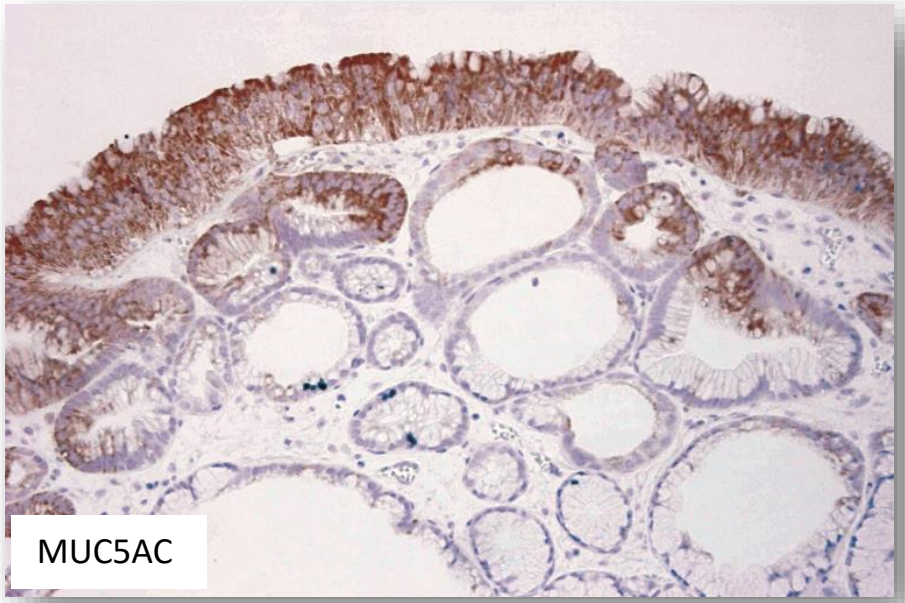


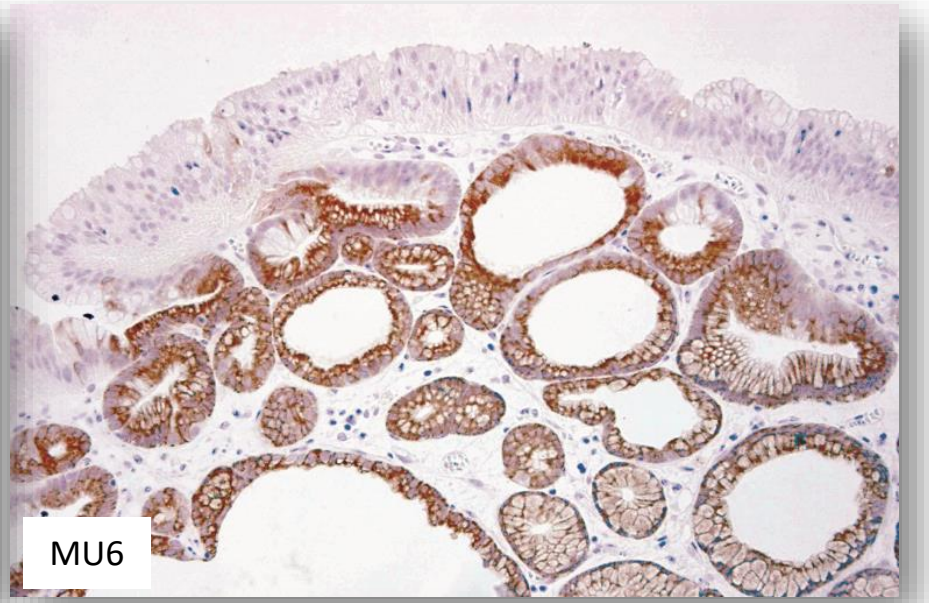


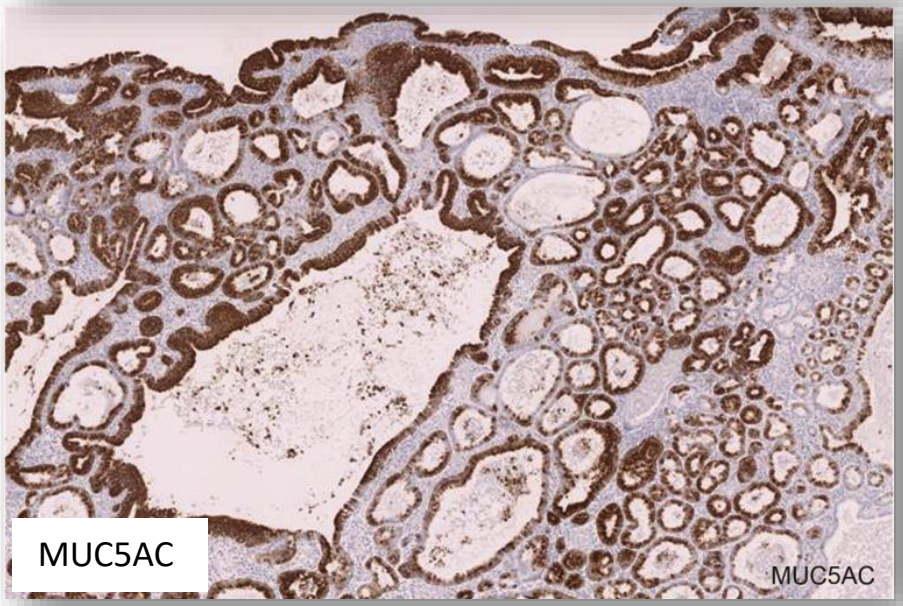
Pyloric gland adenoma (PGA)

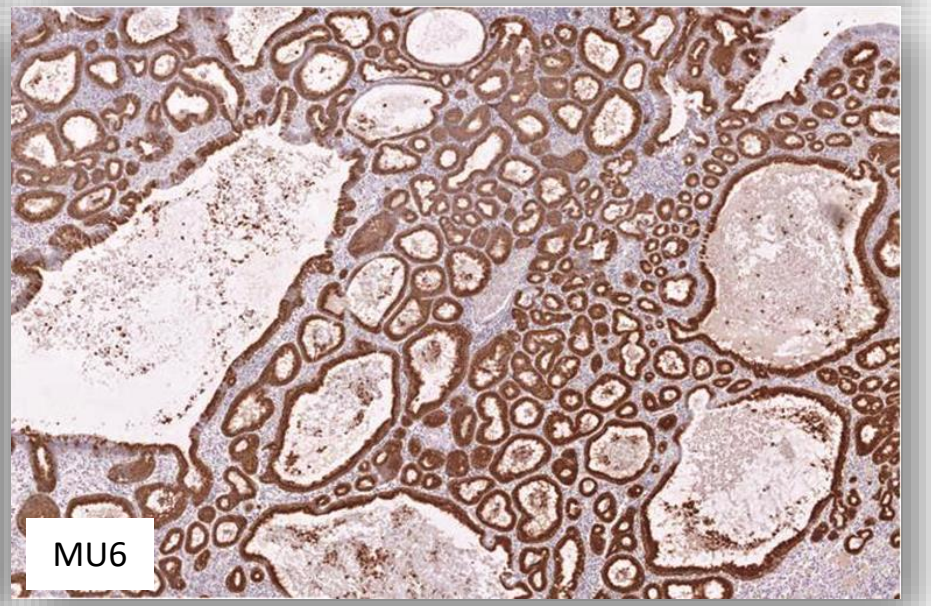
- rare lesions (less than 3 % of all gastric polyps)
- increased risk of malignancy
- proliferation of closely packed pyloric-type glands lined by a monolayer of cuboidal to low columnar epithelial cells with round nuclei and pale to eosinophilic cytoplasm with a “ground glass” appearance
- cystic dilatation of the glands is observed occasionaly

Pyloric gland adenoma

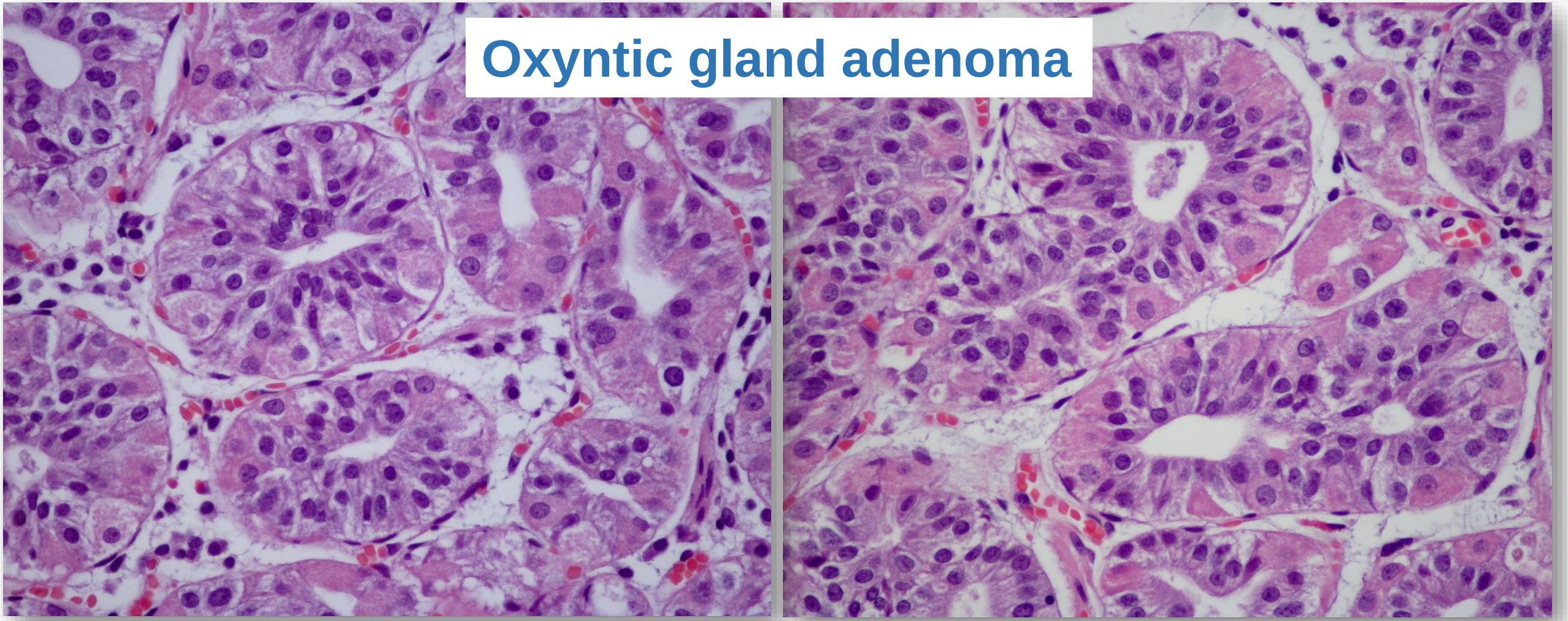








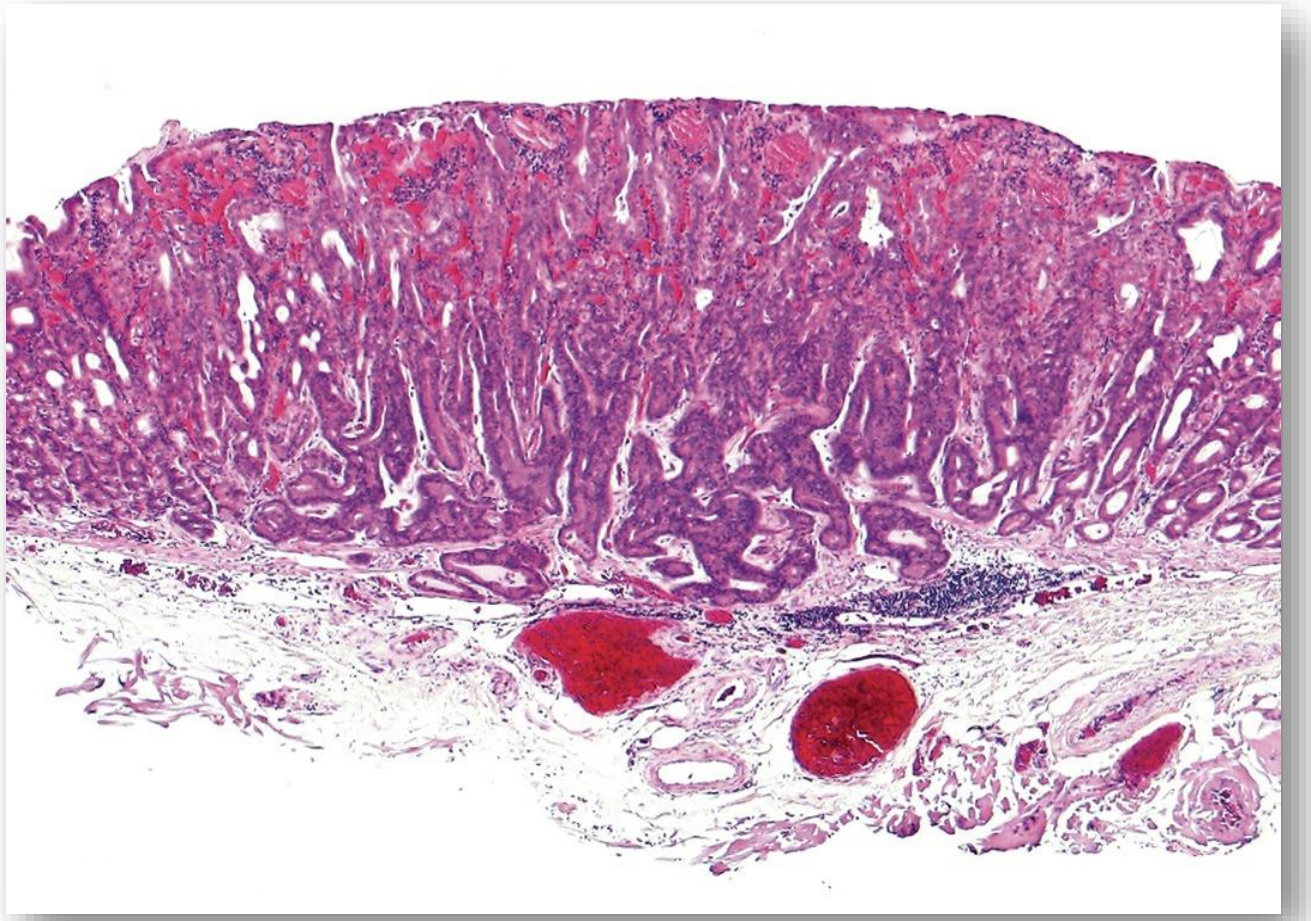
Oxyntic gland adenoma

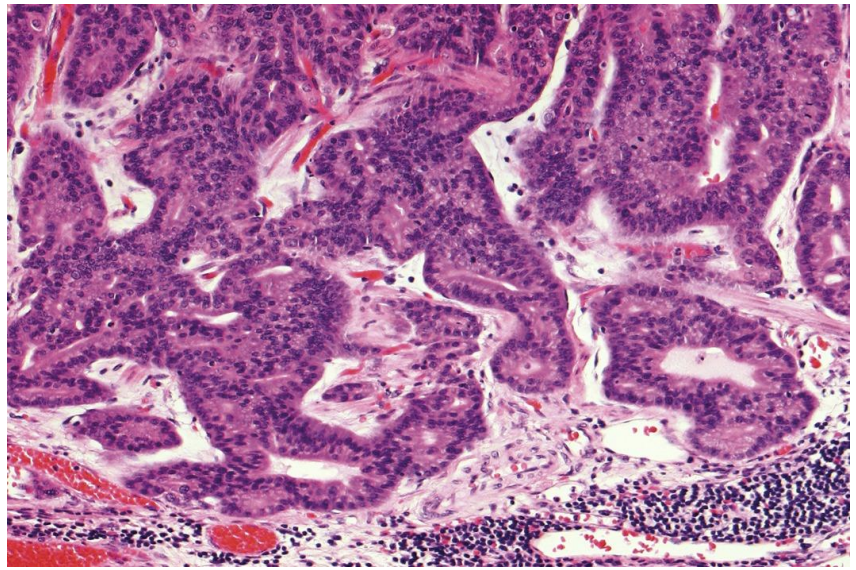


(OGA) is composed of highly differentiated columnar cells with pale basophilic cytoplasm and mild nuclear atypia, mimicking the oxyntic (fundic) gland (mainly chief cell). The tumour consists of irregular architectures, such as tubular fusion and lateral expansion of glands.

The differentiation to the components of oxyntic (fundic) gland is confirmed by immunohistochemistry, such as pepsinogen I (chief cell) and H^+/K^+ ATPase (parietal cell).

Gastric adenocarcinoma of fundic-gland type

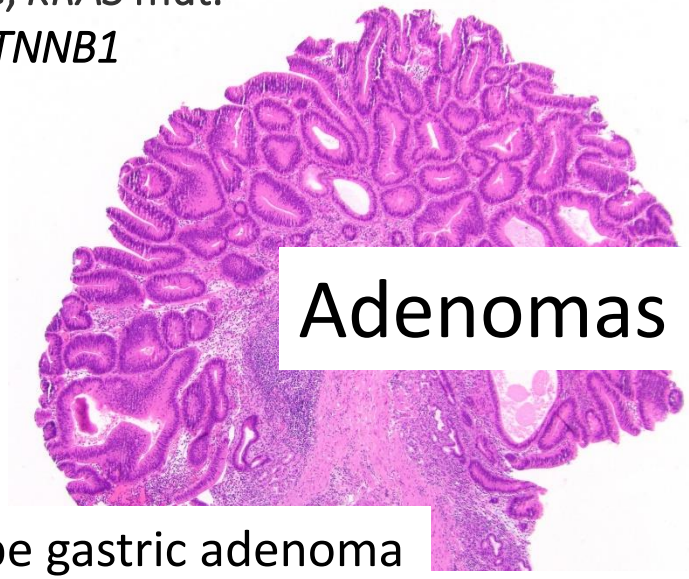




Oxyntic gland adenoma
is a precursor of
Gastric adenocarcinoma of fundic-gland type
Submucosal invasion in the central portion of the tumor Neoplastic cells of immature fundic-gland type

Adenomas of the superficial epithelium

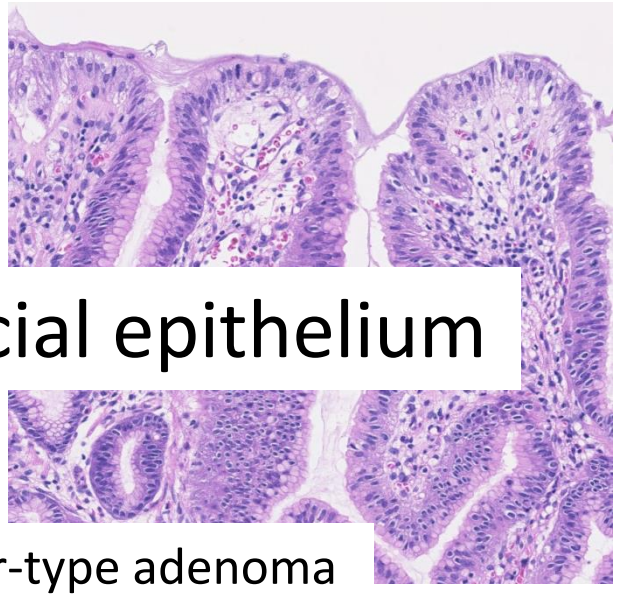
Frequent *APC*, *KRAS* mut.
NO mut. in *CTNNB1*

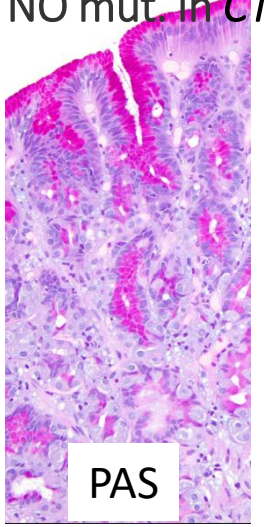


Intestinal-type gastric adenoma

Unequivocal neoplastic changes in a polypoid lesion consisting of gastric intestinalized glands; no evidence of invasion.

Rare *APC*, *KRAS* mut
NO mut. in *CTNNB1*



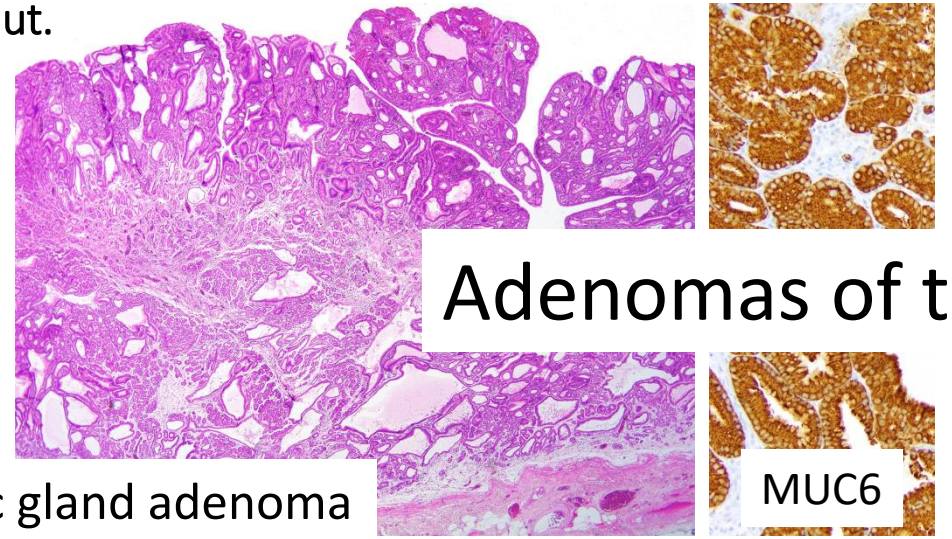


Foveolar-type adenoma

Polypoid growth of dysplastic columnar epithelia with a foveolar-cell phenotype, with a distinctive apical cap of neutral mucins

Adenomas of the glandular epithelium

APC, *KRAS* mut.
GNAS mut.

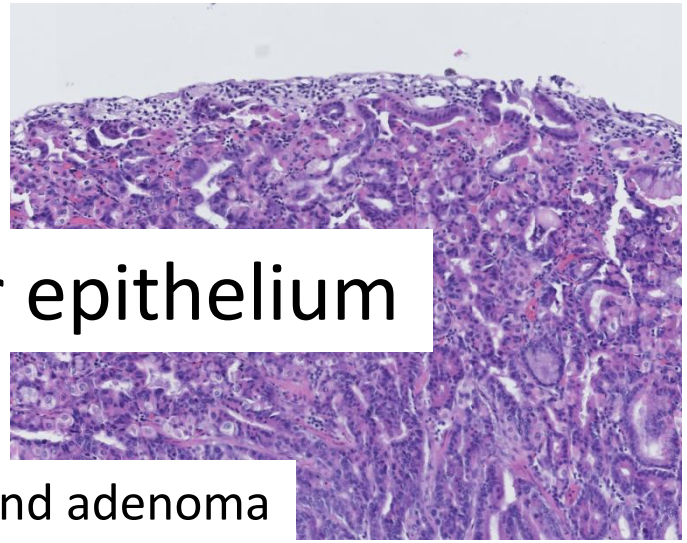


Pyloric gland adenoma

Proliferation of pyloric-type glands consisting of cuboidal/ columnar cells with foamy, ground-glass cytoplasm; no well-formed apical mucin cap.

APC, *AXIN1-2*

OGA –GA-FG
(*GNAS* mut.)



Oxyntic gland adenoma

Intramucosal proliferation of differentiated columnar cells with pale basophilic cytoplasm and mild nuclear atypia, mimicking the oxyntic (fundic) gland.

Obrigada pela atenção