Gastric Polyps & Dysplasia:
A review of an ever expanding list

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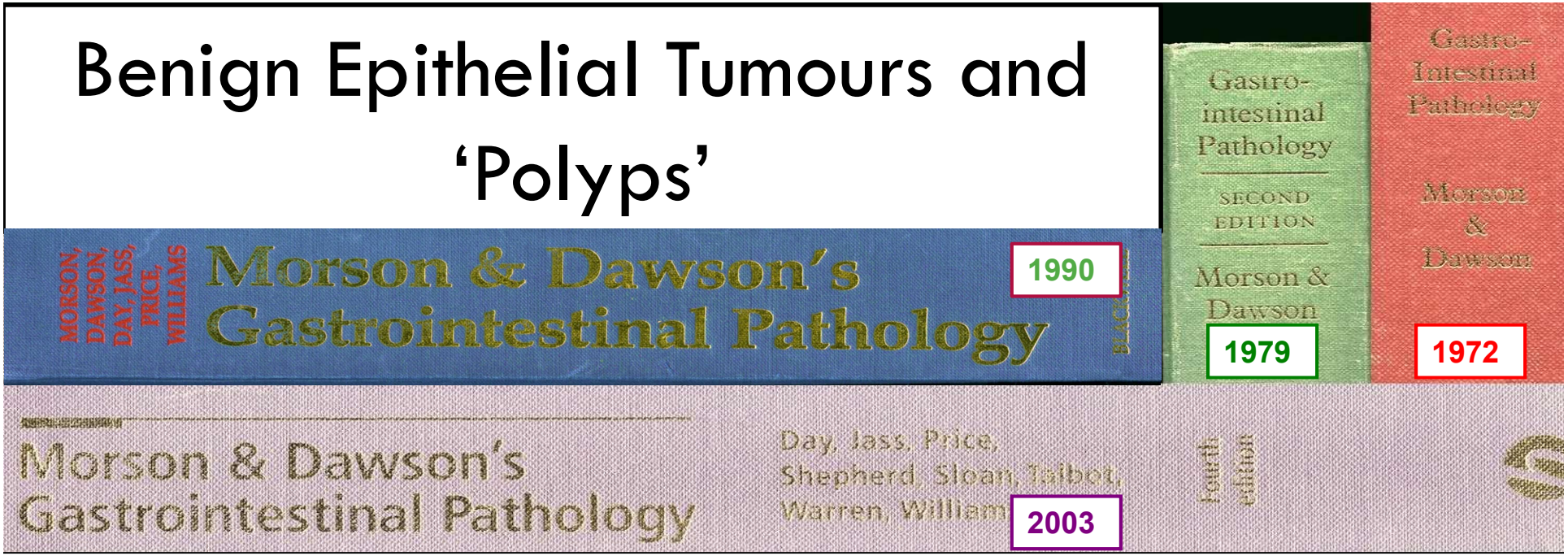
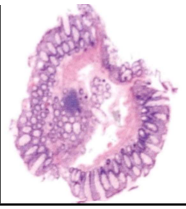
Benign Epithelial Tumours and 'Polyps'



- **Heterotopia or Hamartomatous**
- **Regenerative or Inflammatory**
- **Neoplastic (Adenoma/papilloma/papillary adeoma)**
- **Cystic Polyps**
- **Miscellaneous (Cronkhite-Canada) / Fundic Glandular cysts)**
  - **Heretoropic pancreas**
  - **Cystic Inflammatory Fibroid polyp**
  - **Xanthelasma**
  - **Others**

Benign Epithelial Tumours and 'Polyps'



MORSON AND DAWSON'S **Gastrointestinal Pathology** 2013 FIFTH EDITION

General category	Subtype	Usual location	Malignant potential
Epithelial			
Hyperplastic/inflammatory	Hyperplastic (and variants)	Antrum and lower body	Low[a]
Hamartomatous	Peutz–Jeghers		Low
	Juvenile		Low[a]
	Cowden		Unknown
Neoplastic	Fundic gland polyp	Body fundus	Low[b]
	Polypoid dysplasia (adenoma)	Antrum and body fundus	High
	Neuro-endocrine tumor	Body fundus	Low to moderate
Mesenchymal			
	Inflammatory fibroid polyp	Antrum	None
	Others[c]		
Miscellaneous			
	Cronkhite–Canada		Unknown
	Xanthoma		None
	Gastric heterotopic pancreas		Very low

[a]The risk increases with the size of the polyp.
[b]The risk is higher in syndromic polyps than in sporadic lesions.
[c]These include: gastrointestinal stromal tumour (GIST), smooth muscle tumour, glomus tumour, inflammatory myofibroblastic tumour,

- Incidental findings
- Prevalence of 3.75% (200,000 endoscopies-US)
  - Rare: hemorrhage / outflow obstruction

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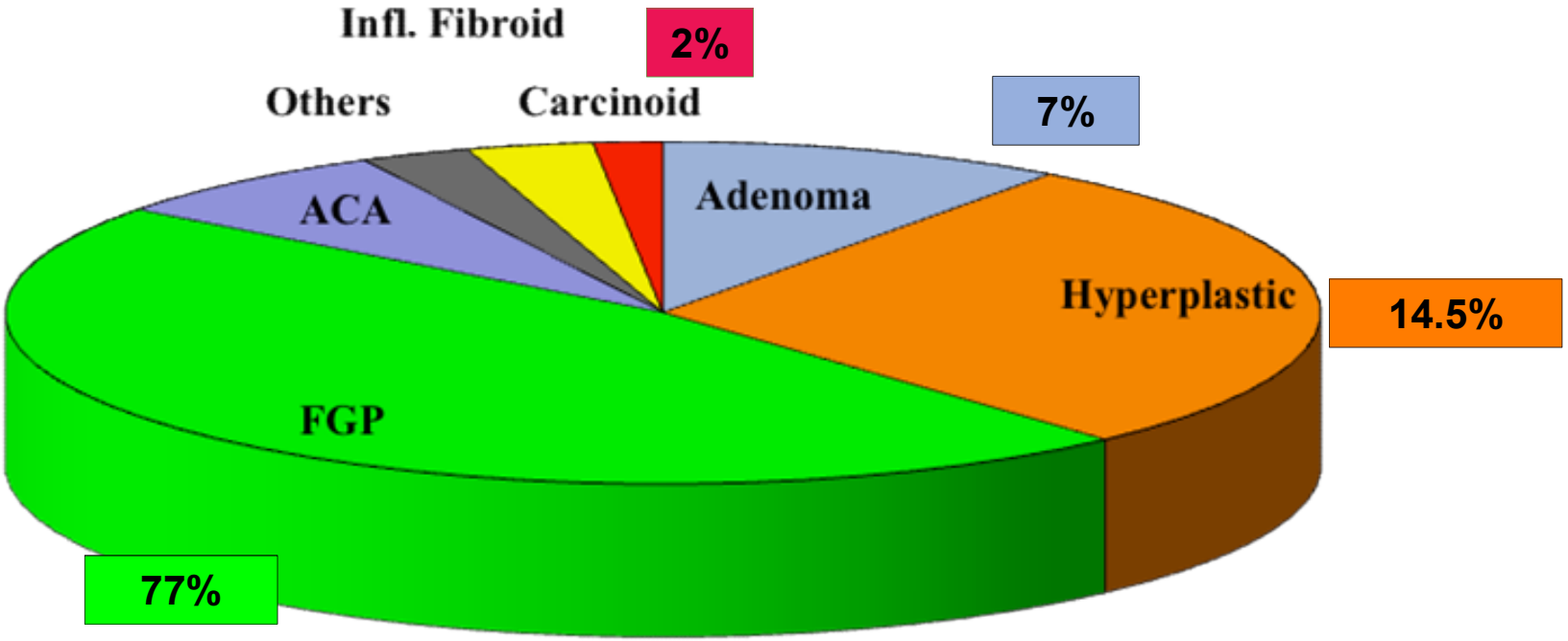
Prevalence of gastric polyps



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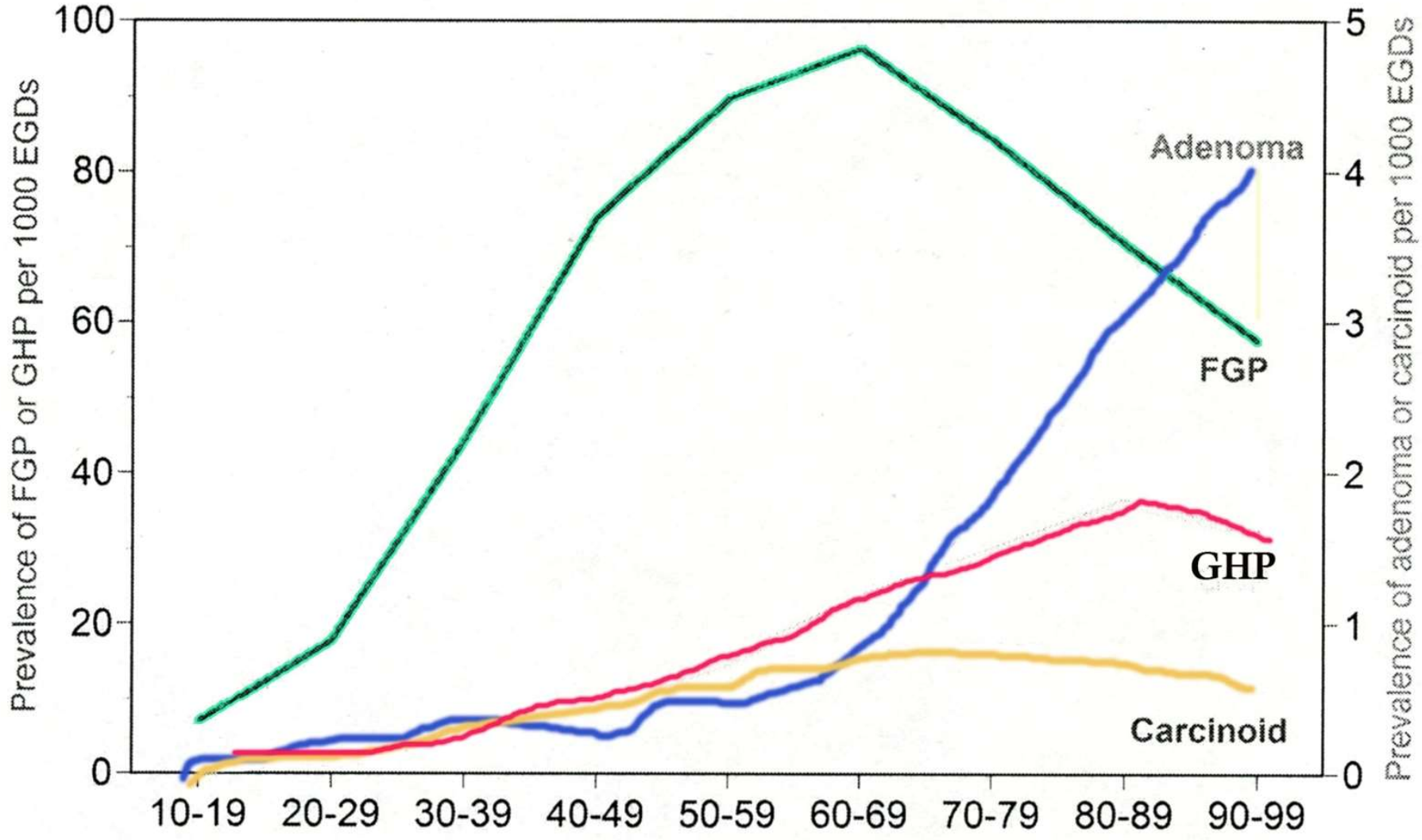
Sonnenberg A., Digestive and Liver Disease 47 (2015)

Prevalence of gastric polyp / age



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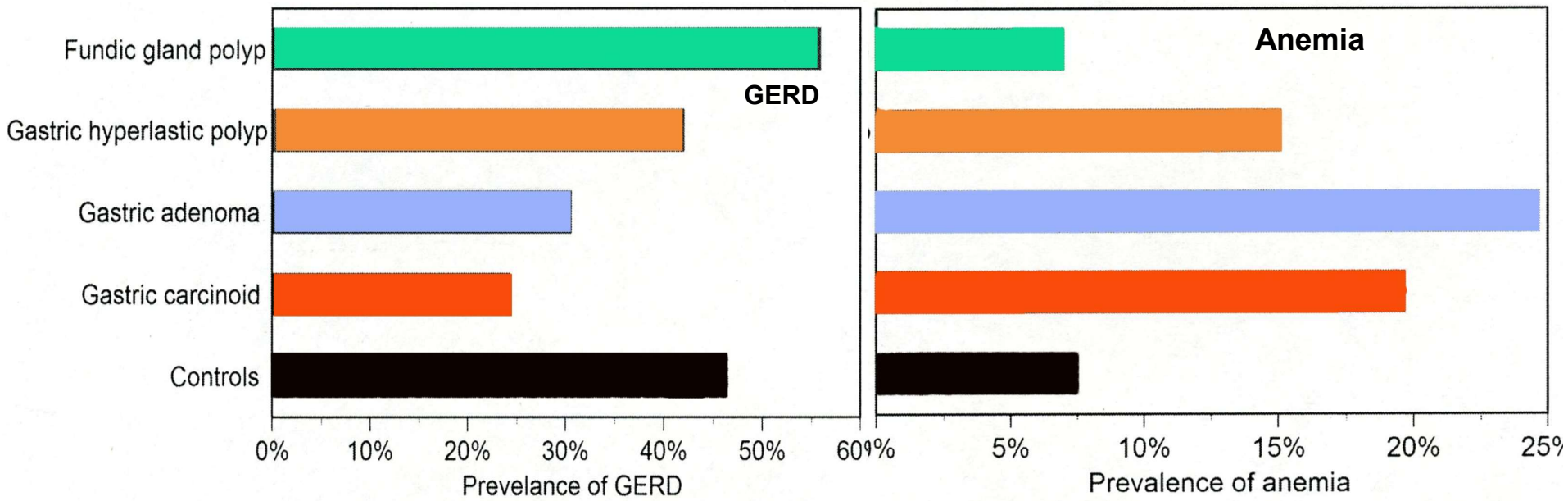
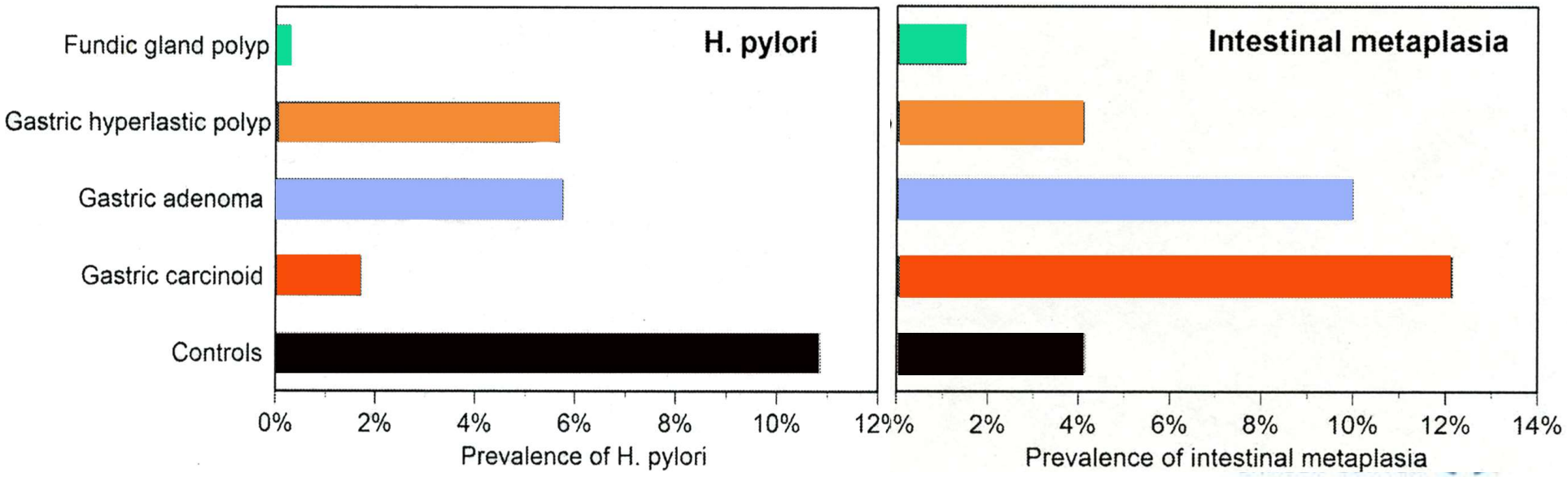
FGP: Fundic Gland Polyp; GHP:Gastric Hyperplastic Polyp

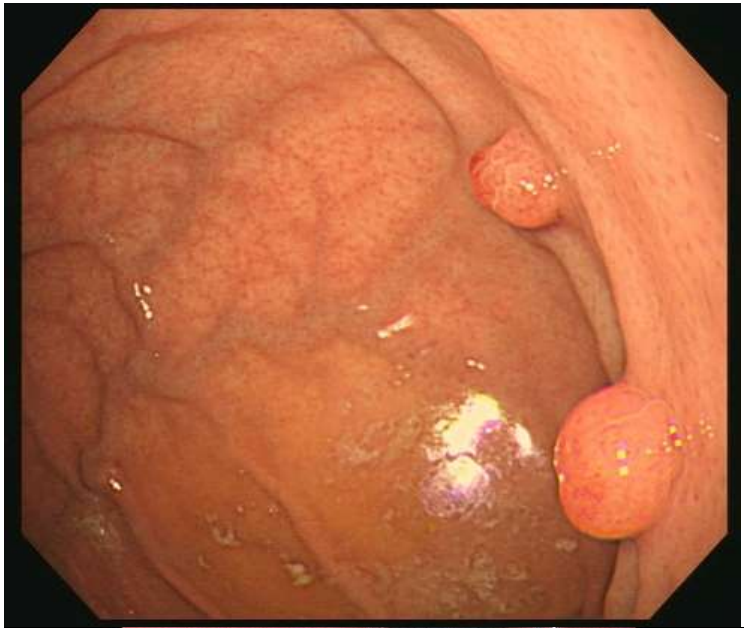
Clinical associations of gastric polyps

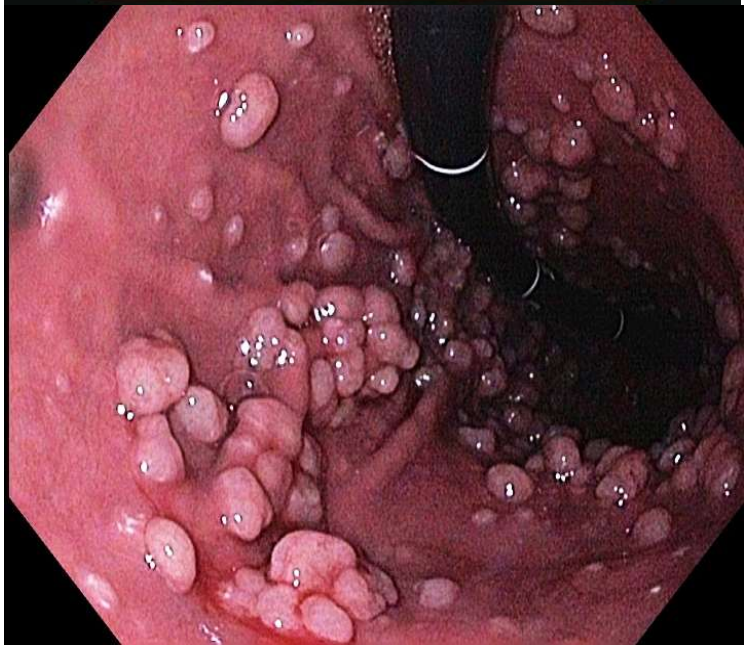




Sonnenberg A., Digestive and Liver Disease 47 (2015)

Fundic Gland Polyps





- Oxyntic mucosa
- Sessile: 1-5 mm
- Multiple (40-60%)
- Over time 40-50% are labile

- Sporadic (0.09 to 5% of endoscoped pts; Female +).
- FAP
- Proton pump inhibitors
- GAPPS (Gastric Adenocarcinoma and Proximal Polyposis)

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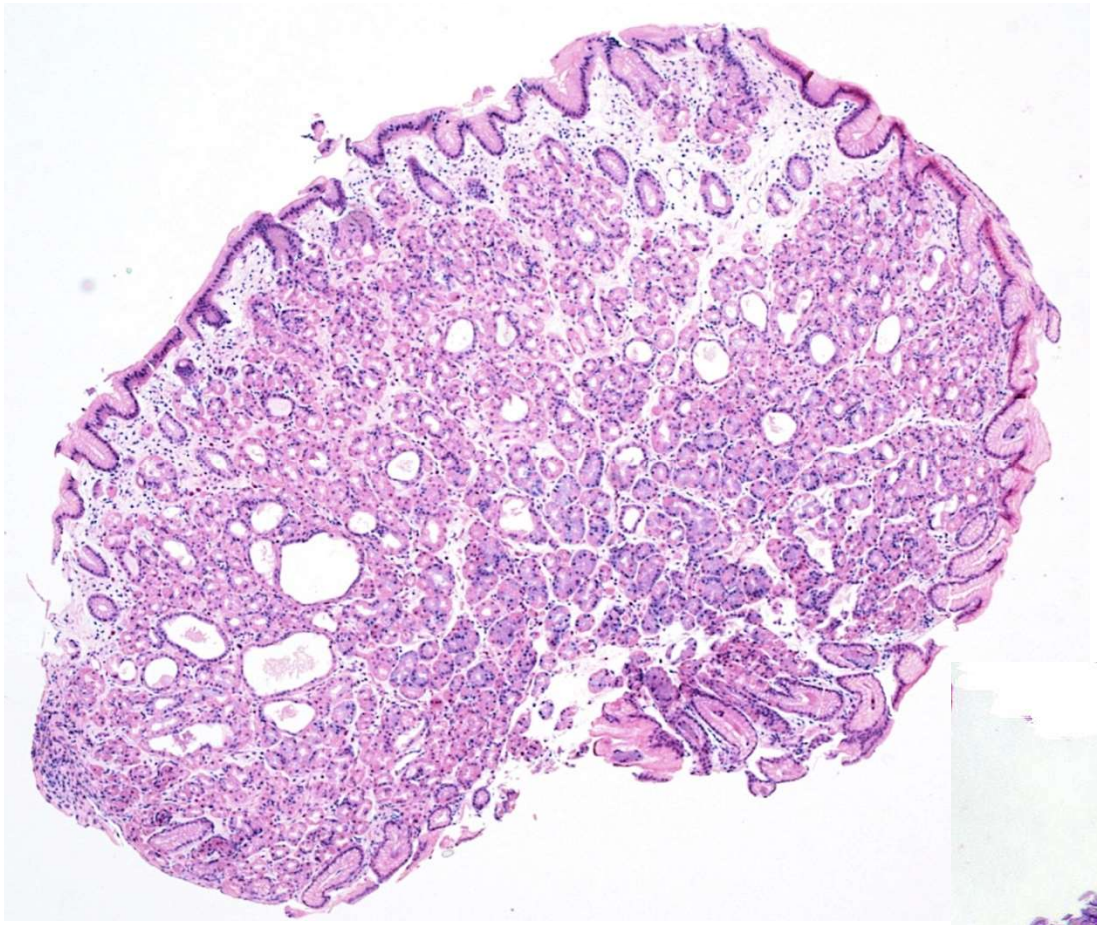
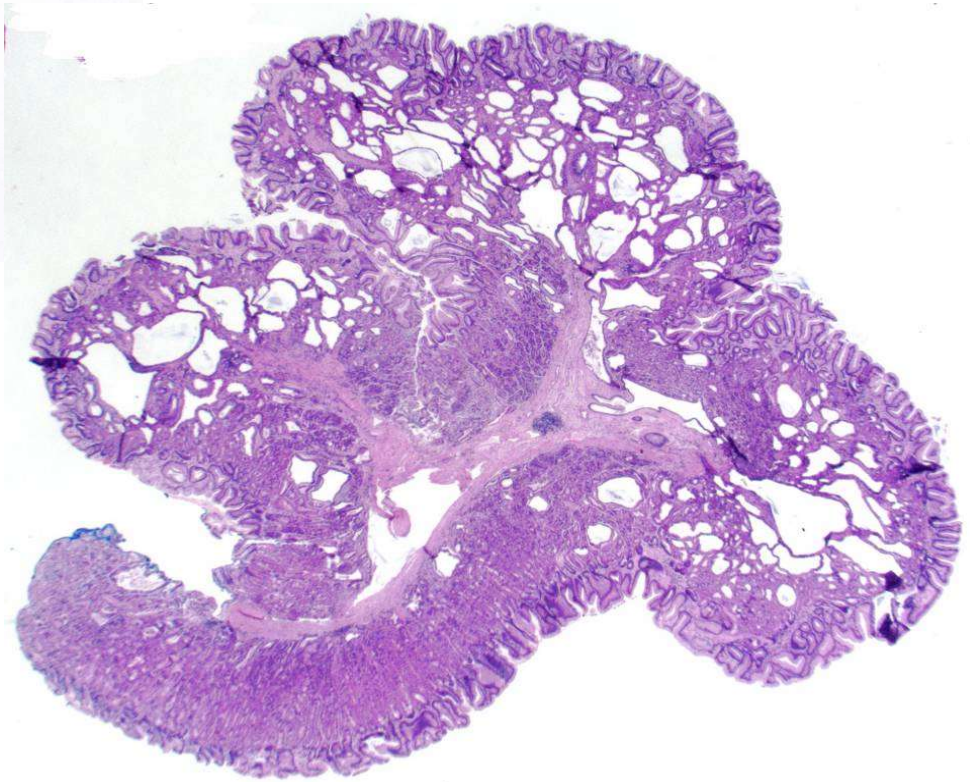
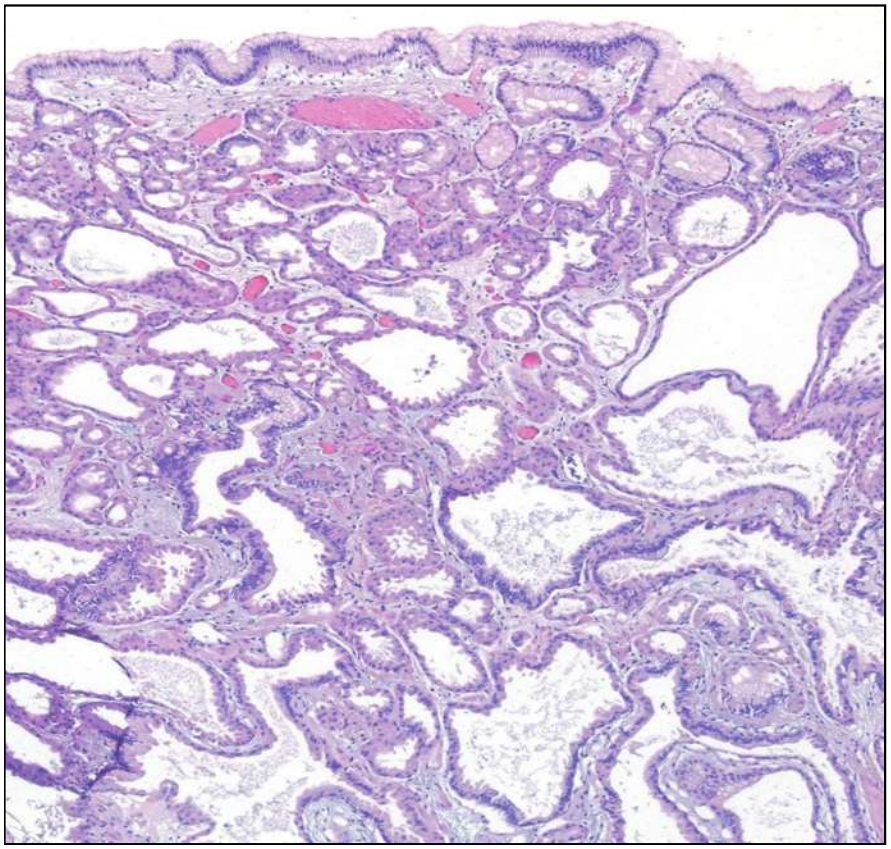
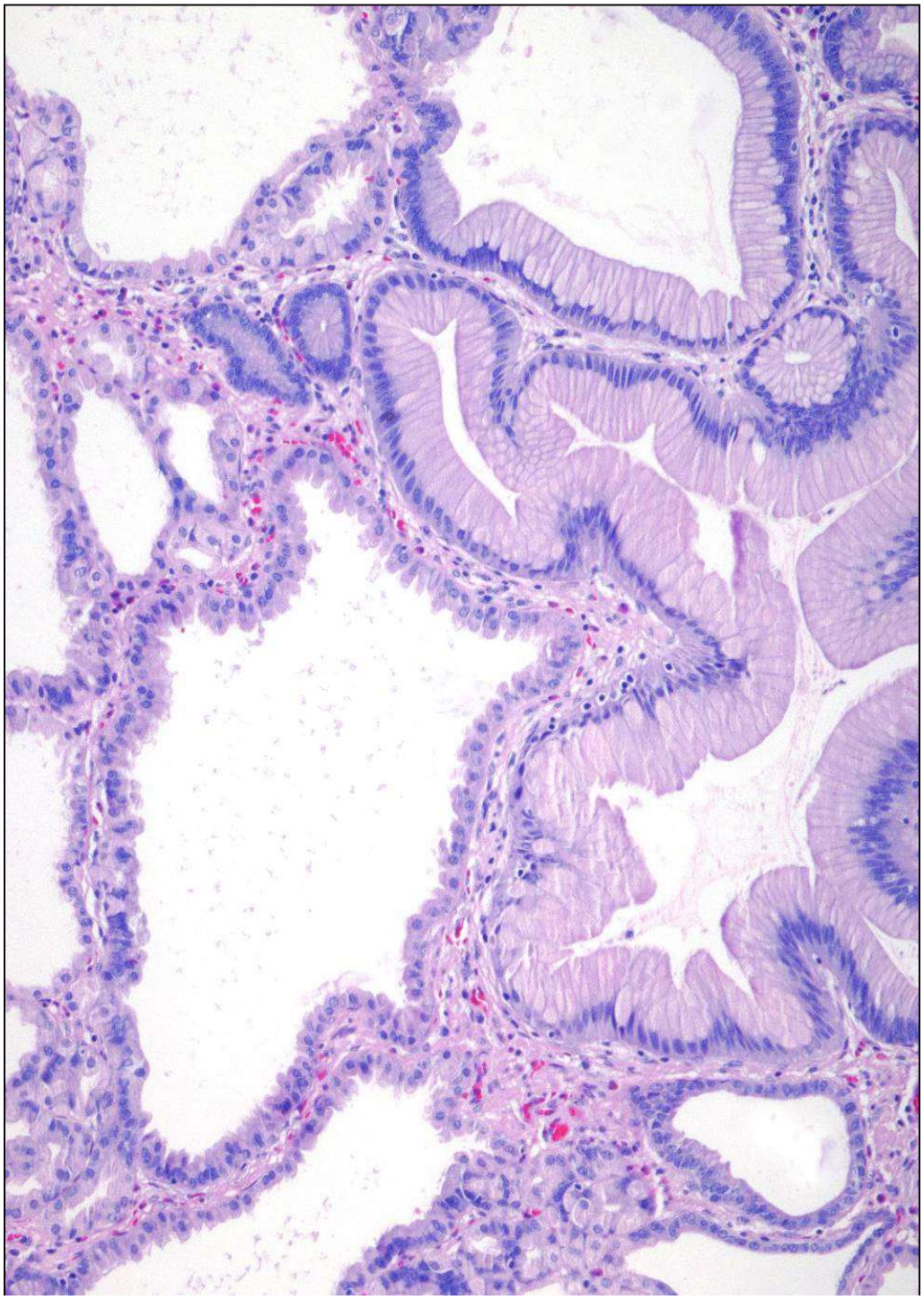
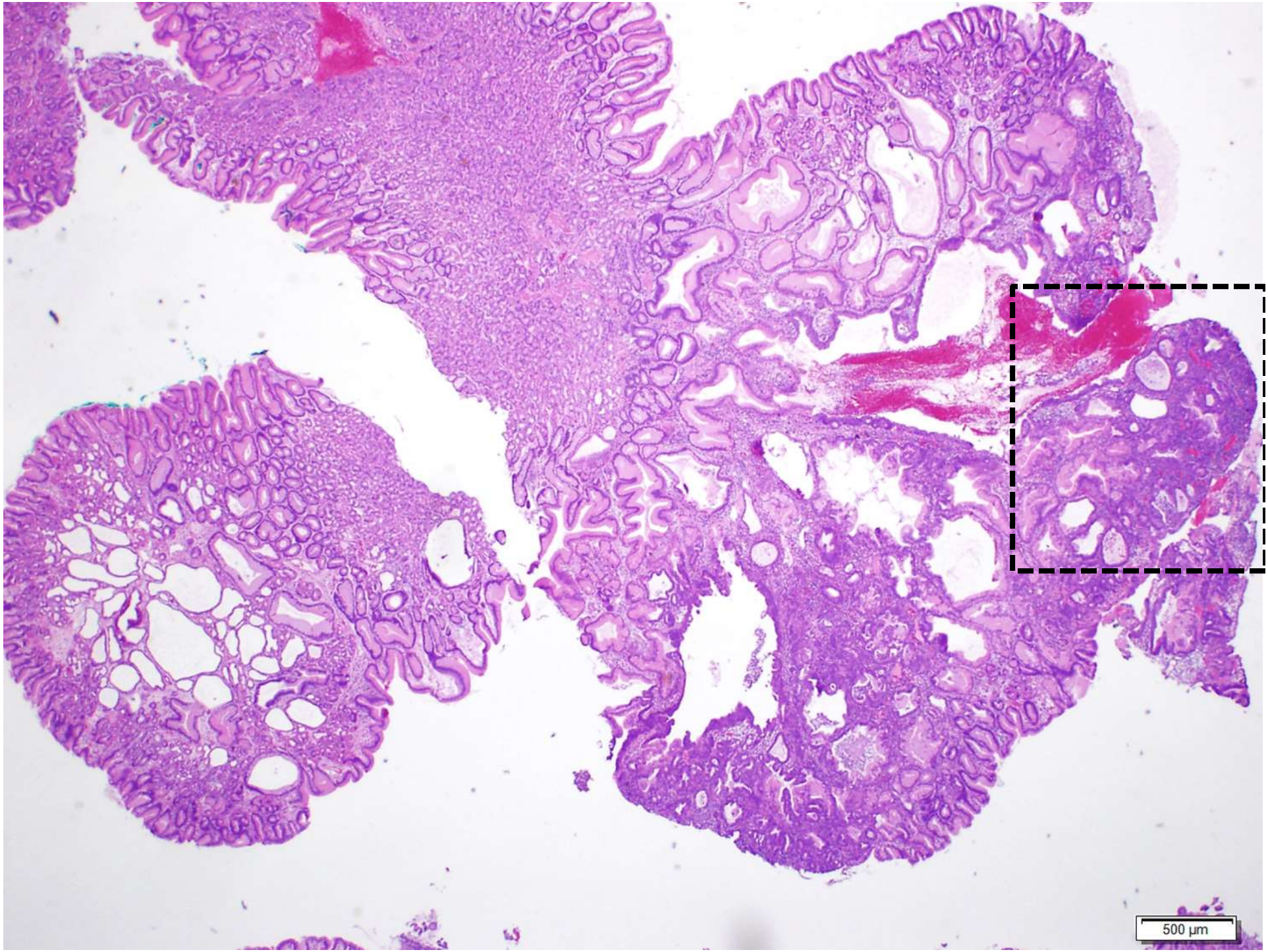








- FAP: inactivating *APC* / chr 5q allelic loss
- Sporadic: activating β catenin mutation (60%-90%)


500 µm

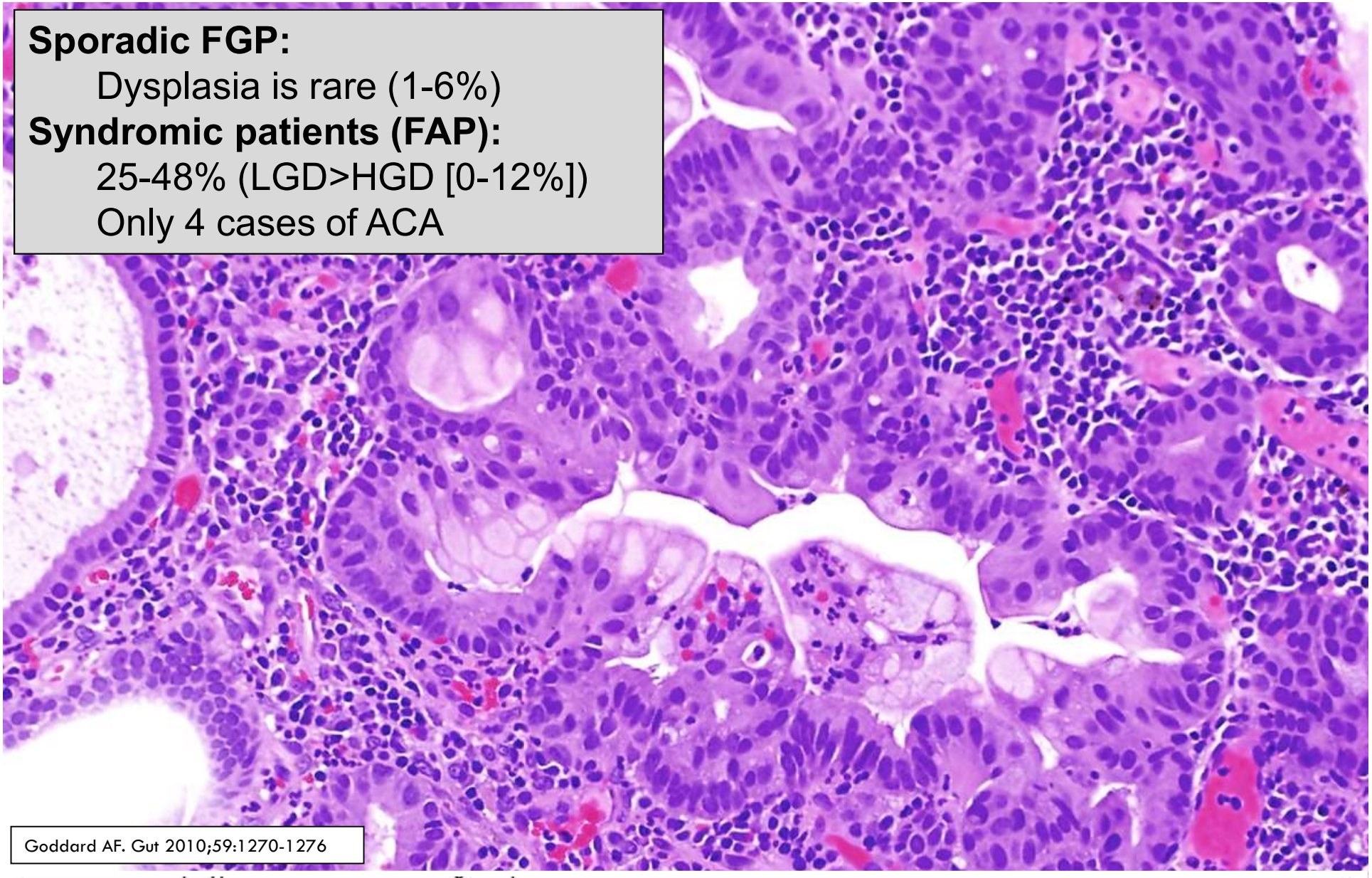
Sporadic FGP:

Dysplasia is rare (1-6%)

Syndromic patients (FAP):

25-48% (LGD>HGD [0-12%])

Only 4 cases of ACA



Goddard AF. Gut 2010;59:1270-1276

Polyp type	Usual number and size	Usual site	Malignant potential of polyp	Malignant potential of background mucosa	Management
Sporadic fundic gland polyp	Multiple 1–5 mm	Upper and lower body	Very low	Very low	Biopsy to confirm nature of polyp No follow-up needed

Morphology and natural history of familial adenomatous polyposis-associated dysplastic fundic gland polyps

Thomas Arnason,[1,2,*] Wen-Yih Liang,[3,4,*] Eduardo Alfaro,[1] Paul Kelly,[1,5] Daniel C Chung,[6] Robert D Odze[7] & Gregory Y Lauwers[1]

Histopathology 2014,

- 24 pts (9M/15F;mean age of 35 yrs)
  - Total of 57 dysplastic FGPs.
  - Most had multifocal dysplastic FGPs.
    - 1 w/ concurrent antral adenoma.
  - 96% LGD; 4% (n=1) HGD
- Evolution: [mean follow-up of 6 years].
  - 54% stable "persisted" (n=13)
  - 33% "regressed" (n=8)
  - 13% "progressed" to HGD/IMC (n=3)

(sporadic GED progression rate: LGD: 5-14% and HGD:24-37%)

- Recommendations:
  - *Follow q. 2/3 years:*
    - Look for large polyps (>1cm)
    - Sample extensively

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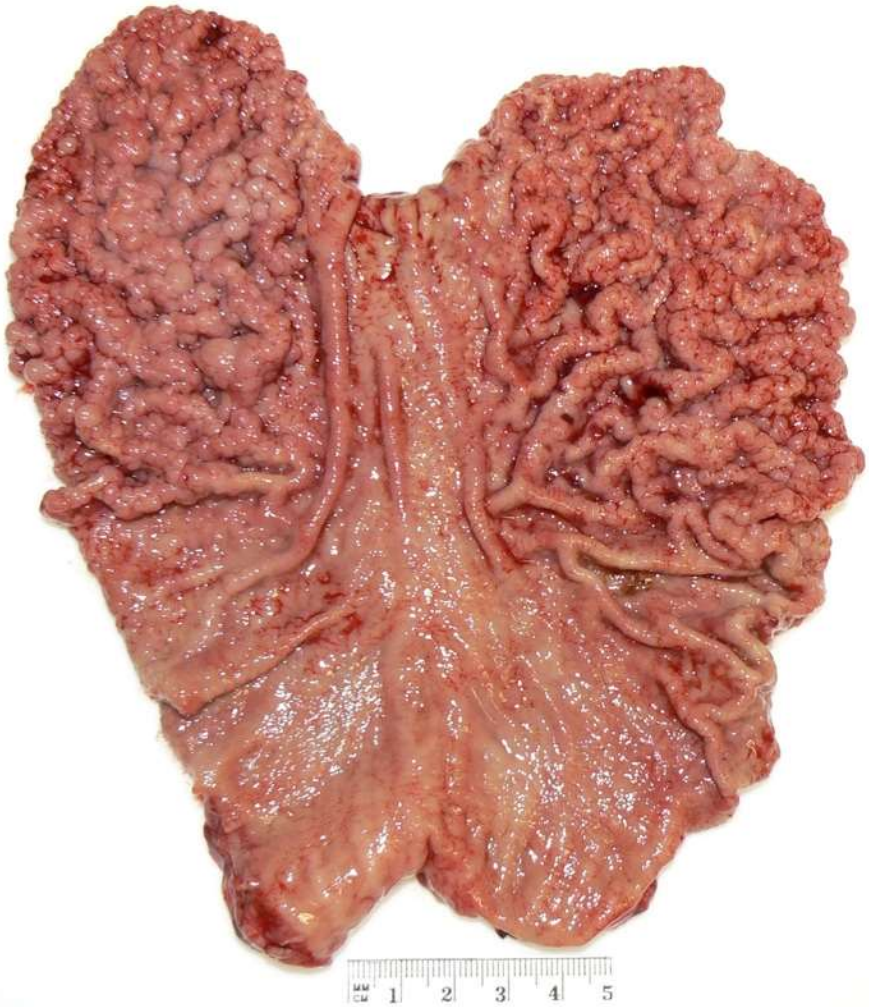
Gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS): a new autosomal dominant syndrome

D L Worthley,[1] K D Phillips,[2] N Wayte,[3] K A Schrader,[4] S Healey,[5] P Kaurah,[4]

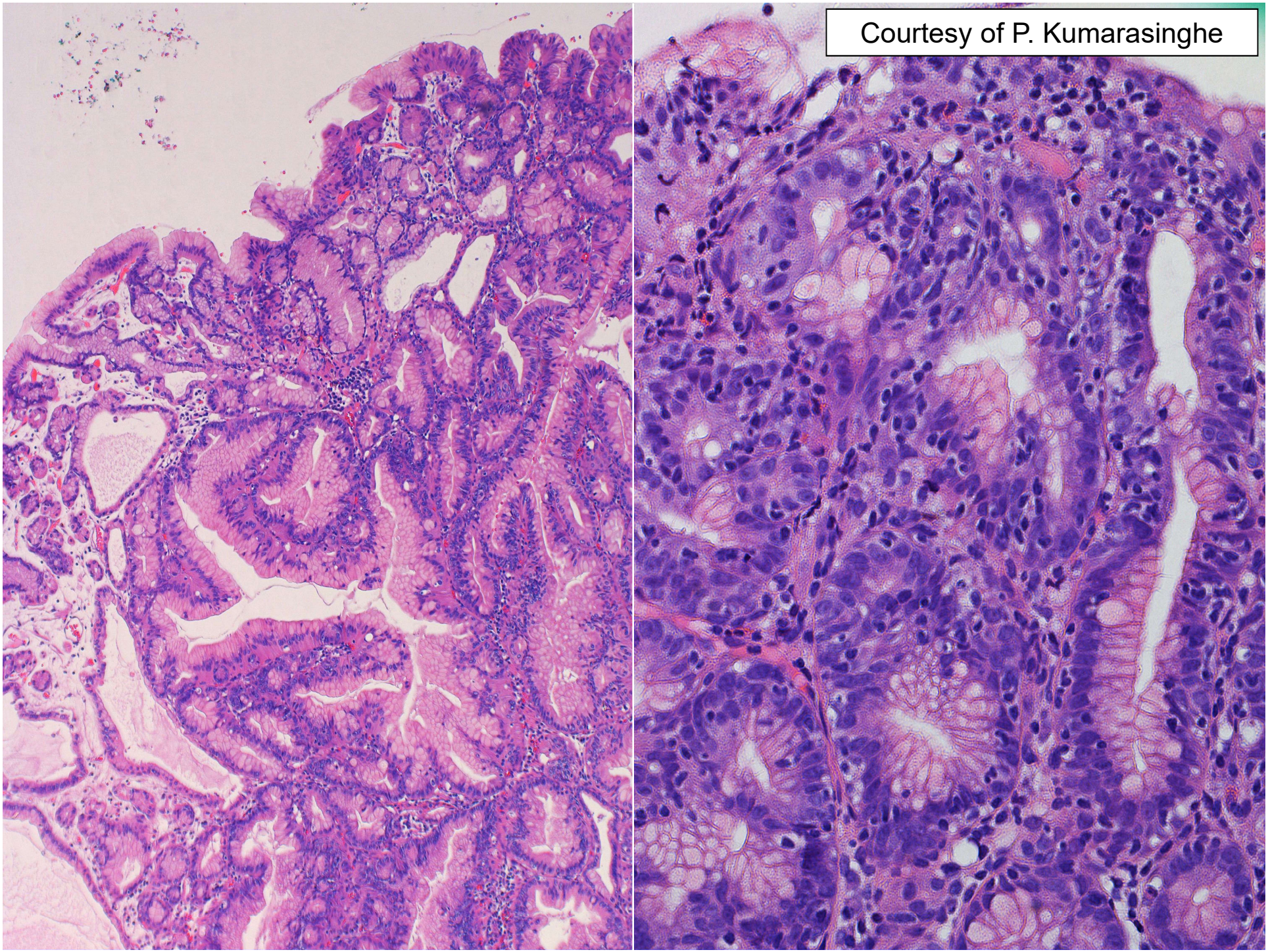


✧ ***Key features:***

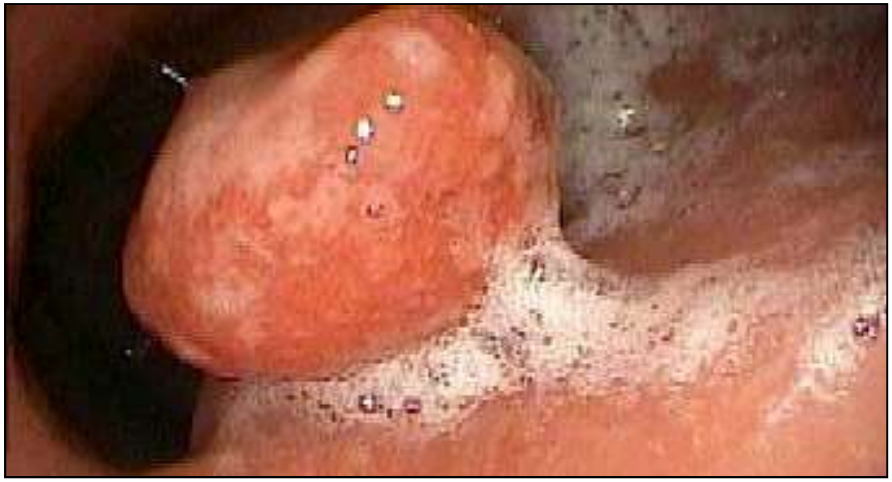
- FG polyposis w/occasional hyperplastic & adenomatous polyps,
  - sparing the antrum
  - devt. of intestinal type GCA
- Autosomal dominant inheritance (Incomplete penetrance).
- No colonic polyps
- *MUTYH, CDH1, SMAD4, BMPR1A, STK11* and *PTEN* mutations are excluded.
- Point mutation in exon 1B of *APC*

The American Journal of Human Genetics 98, 1–13, May 5, 2016

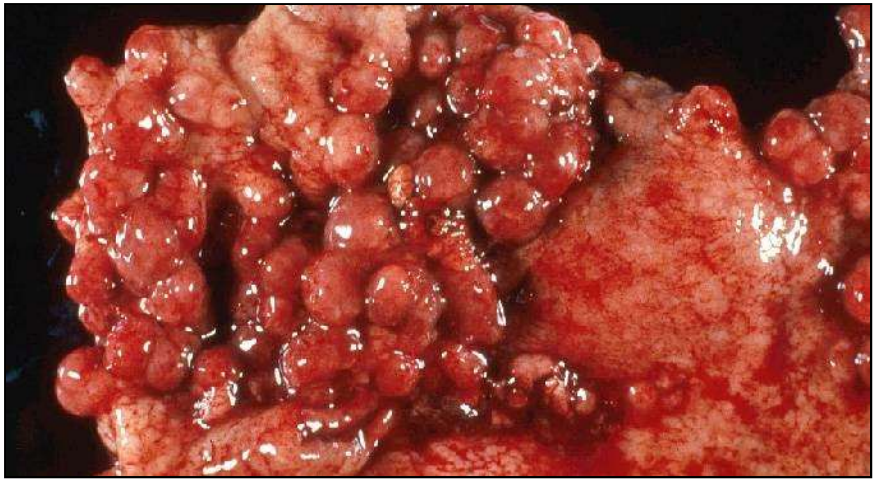
Gut 2012, 61:774-779


Courtesy of P. Kumarasinghe

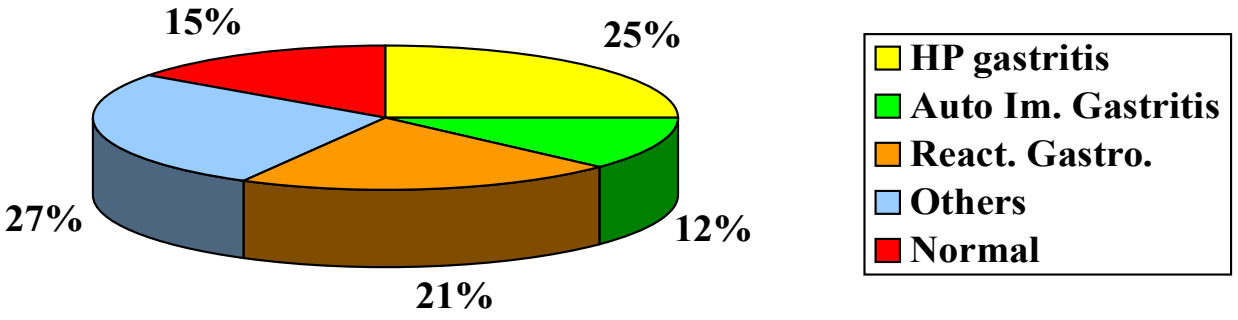
Hyperplastic Polyps



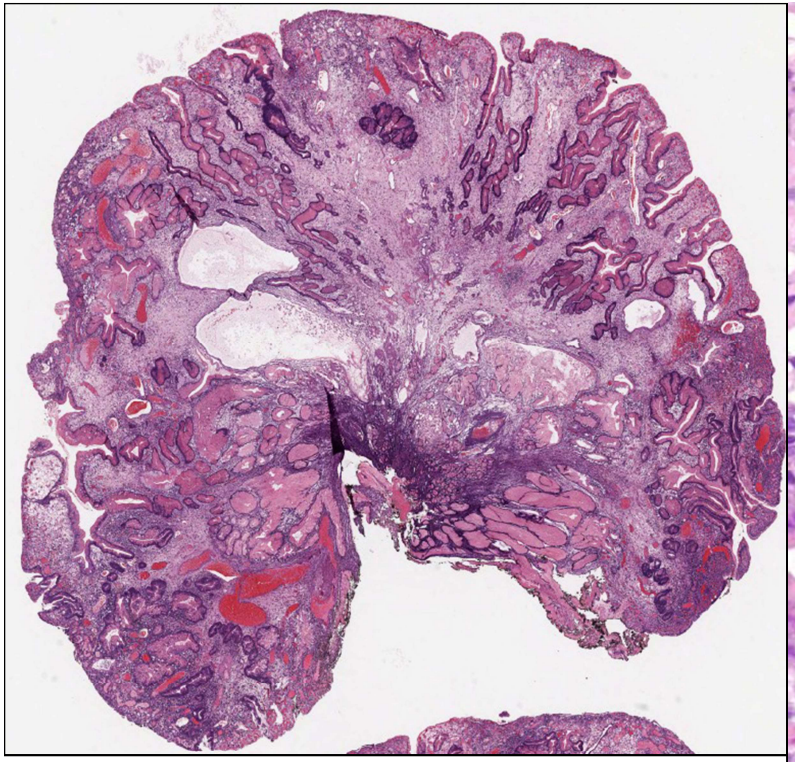
Mean age: 65yrs -Sessile/pedunculate -Antrum:60%.

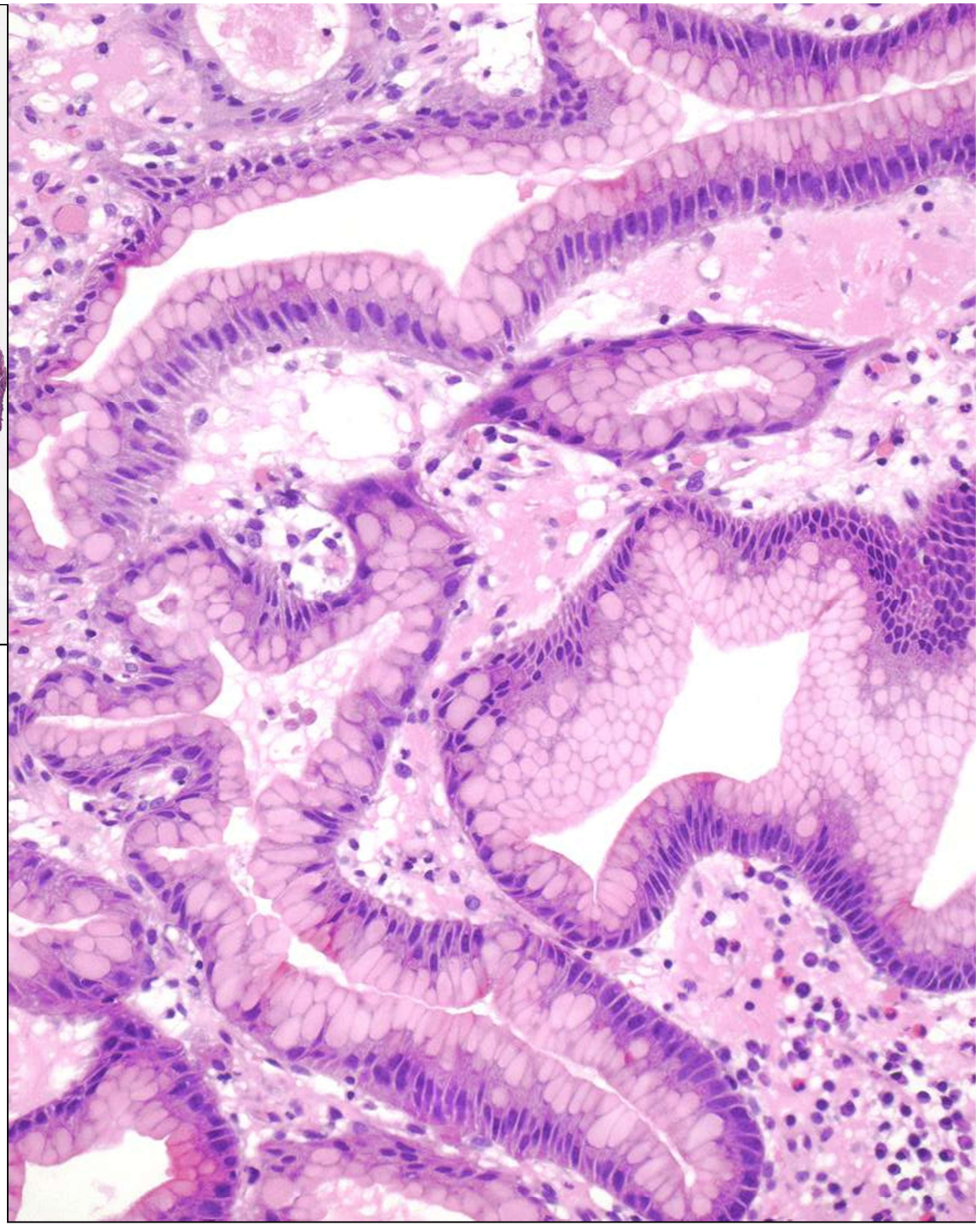


Multiplicity: 20%.



Mucosal background

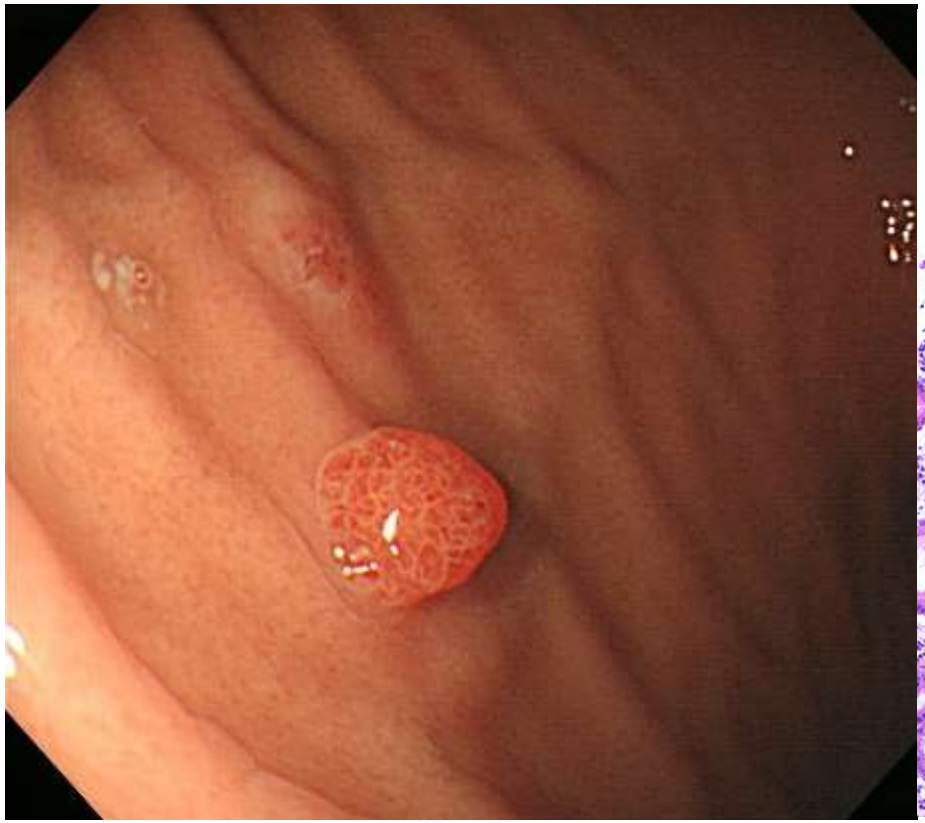


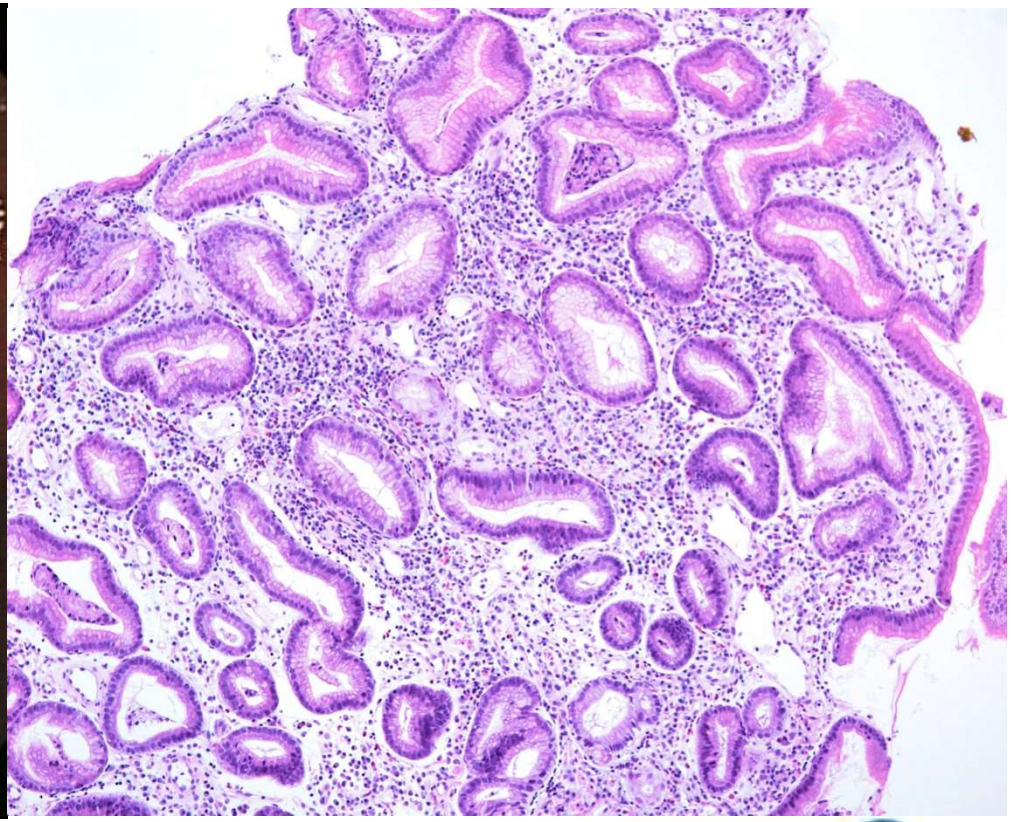


- Sessile or pedunculated
- Size is variable

Polypoid foveolar hyperplasia

<1cm





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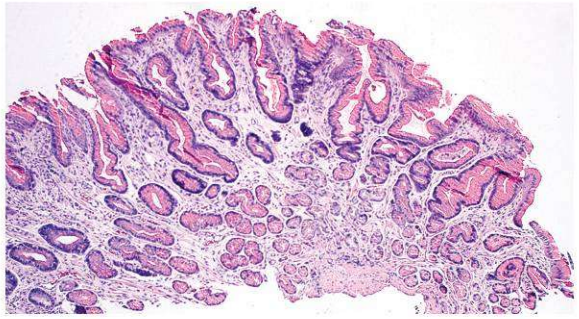
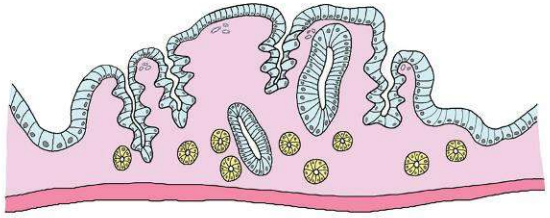
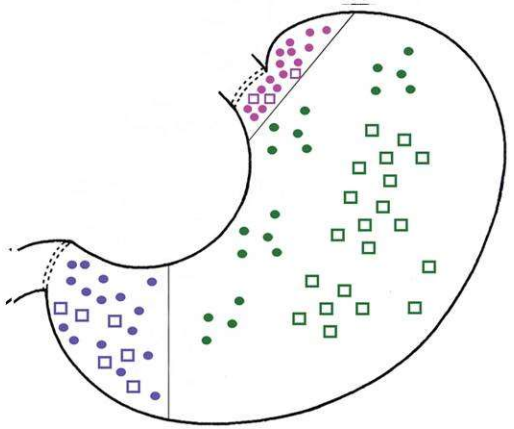
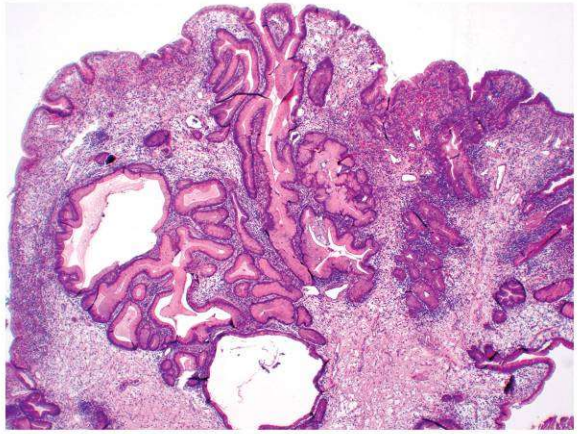
208 polypoid lesions reported as *hyperplastic* polyps

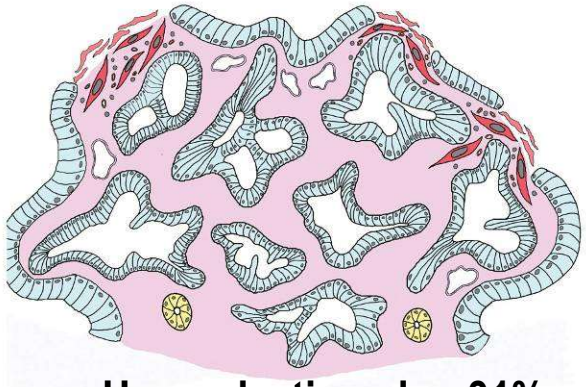


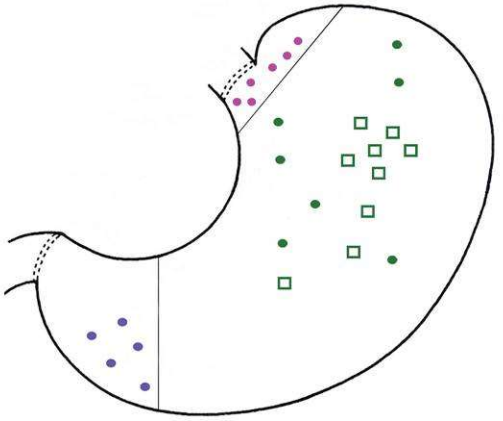




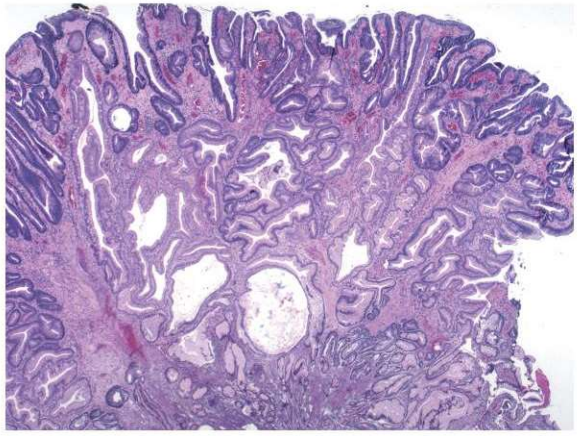
Polypoid fov. hyperplasia:49%

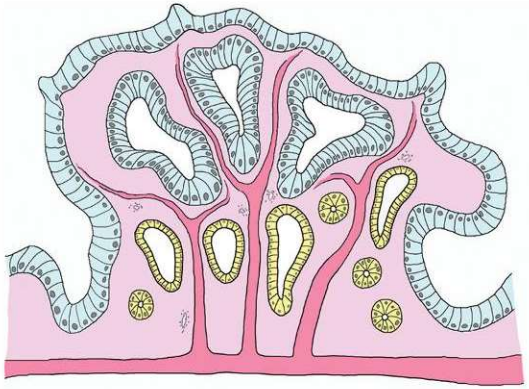


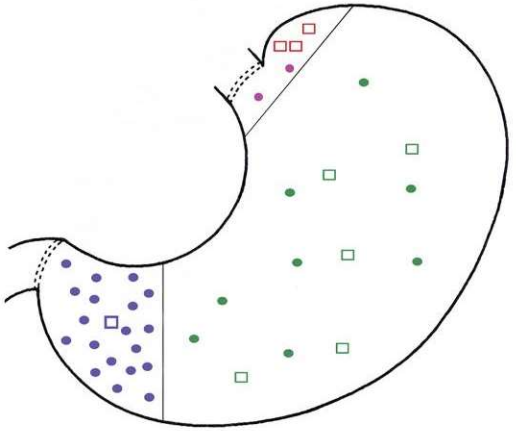




Hyperplastic polyp:31%

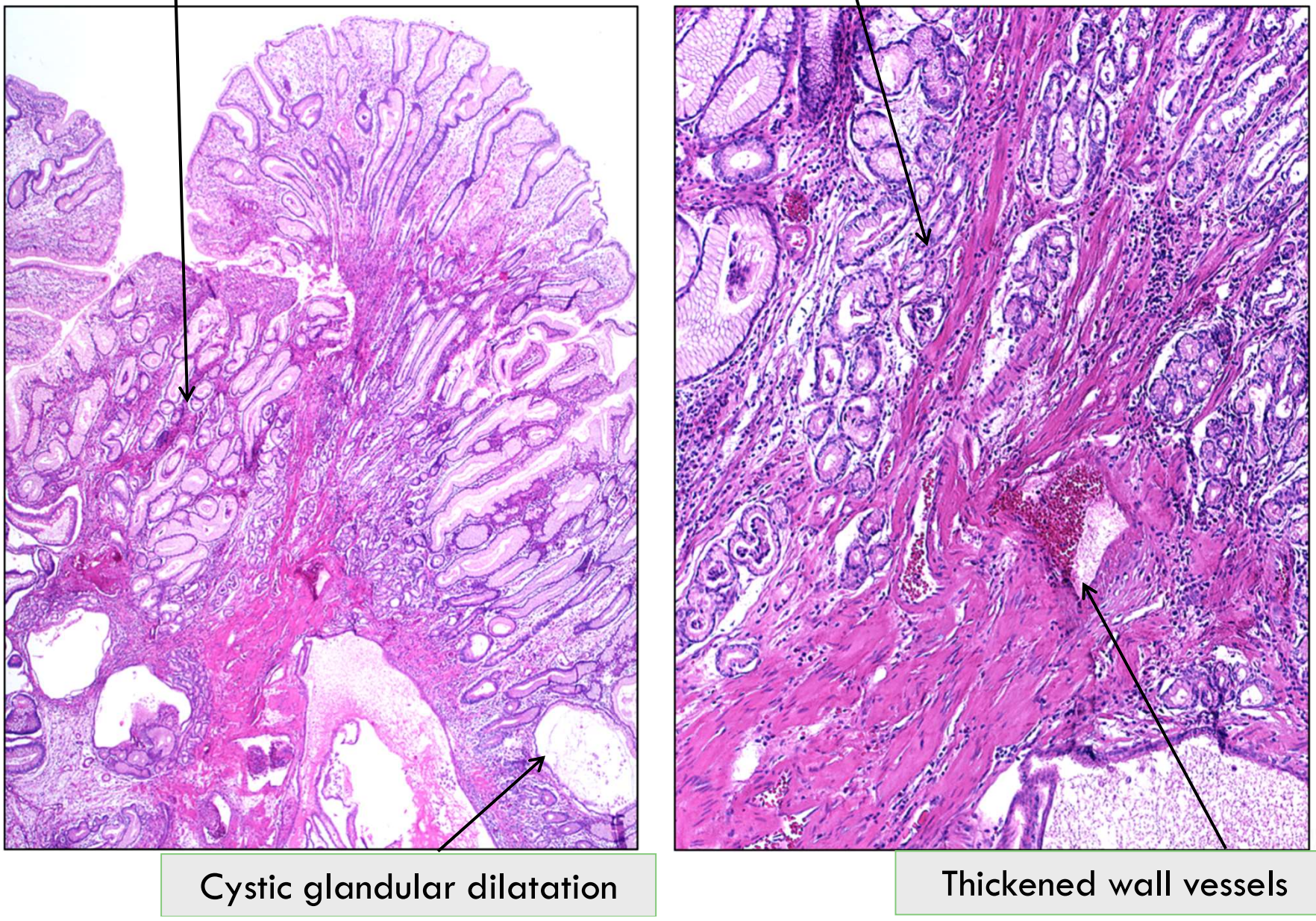




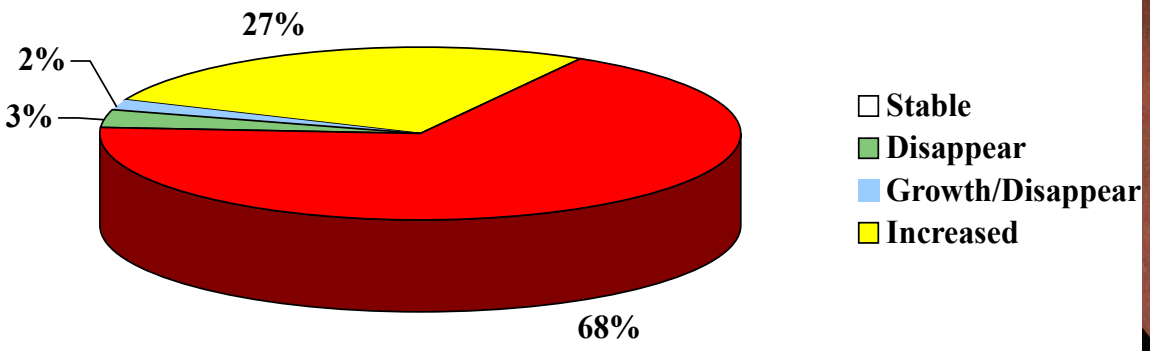


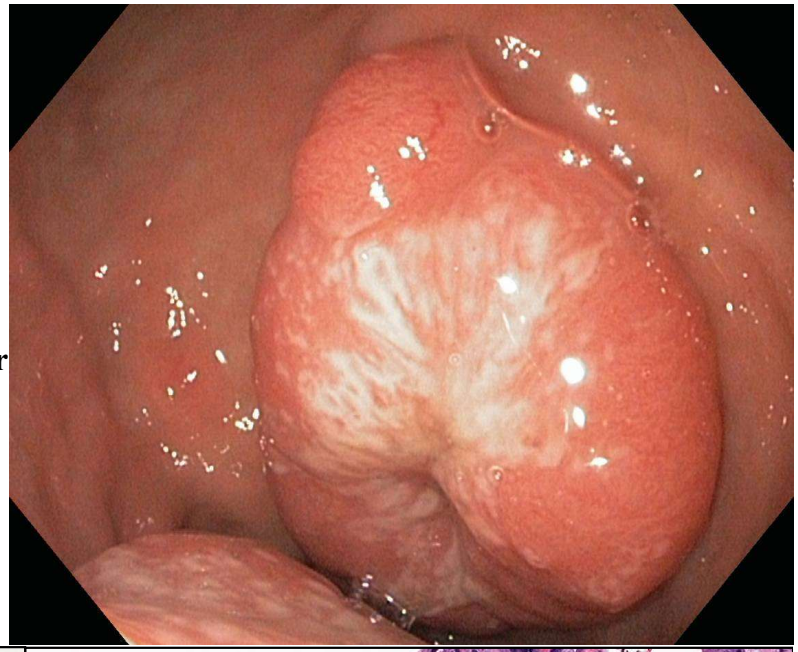
Prolapse polyp:20%

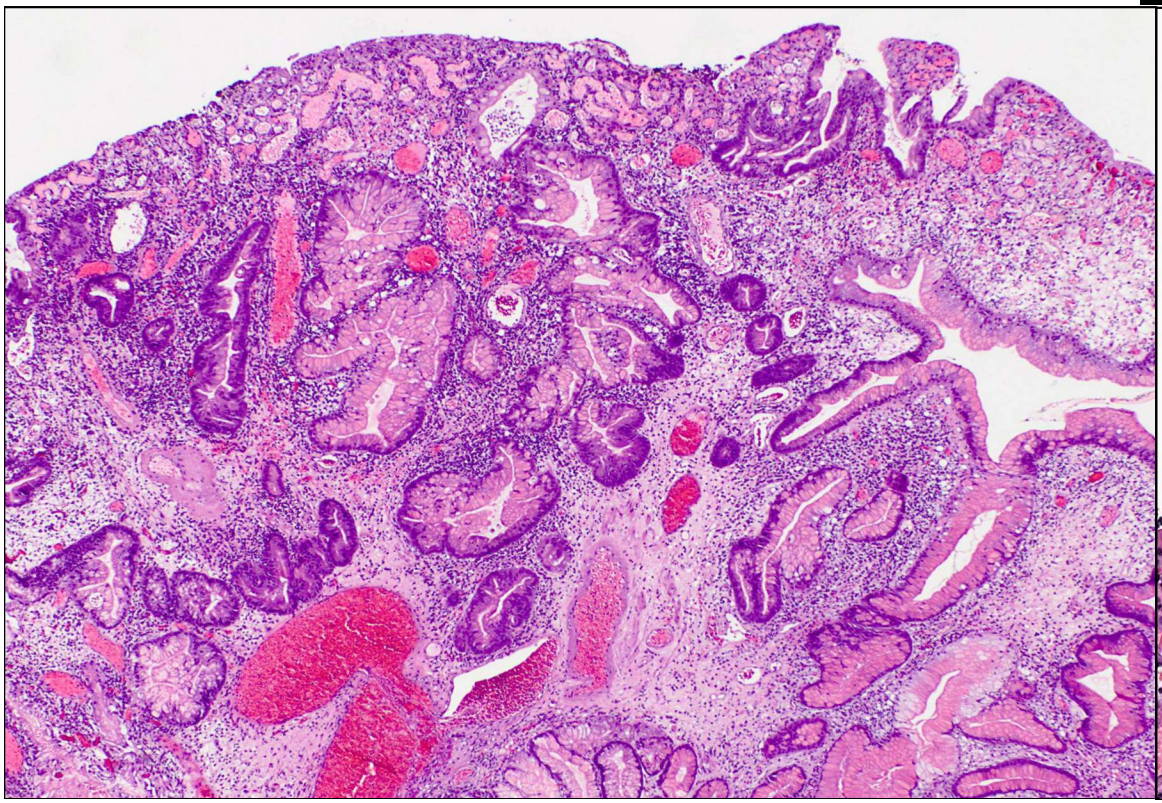
Prolapse variant (of hyperplastic polyp)

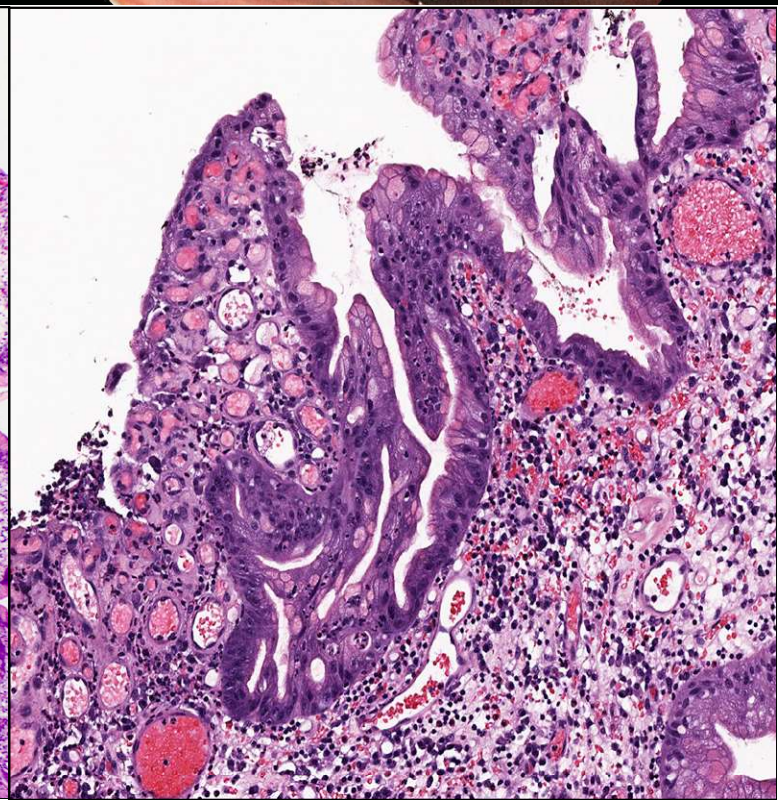


Natural history of hyperplastic polyps

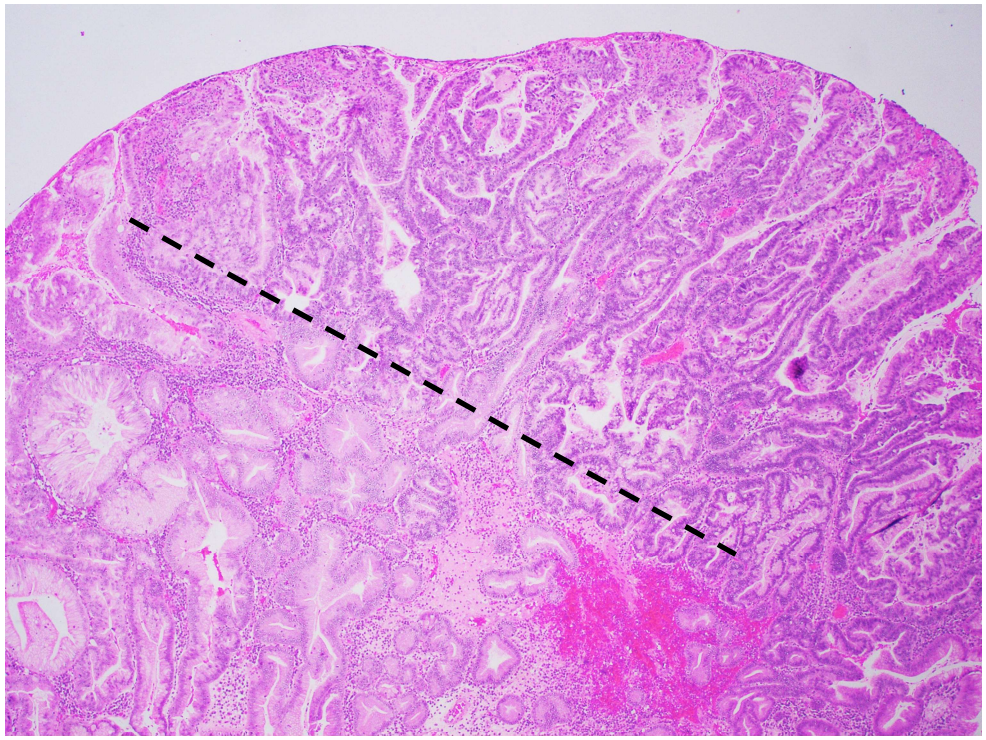


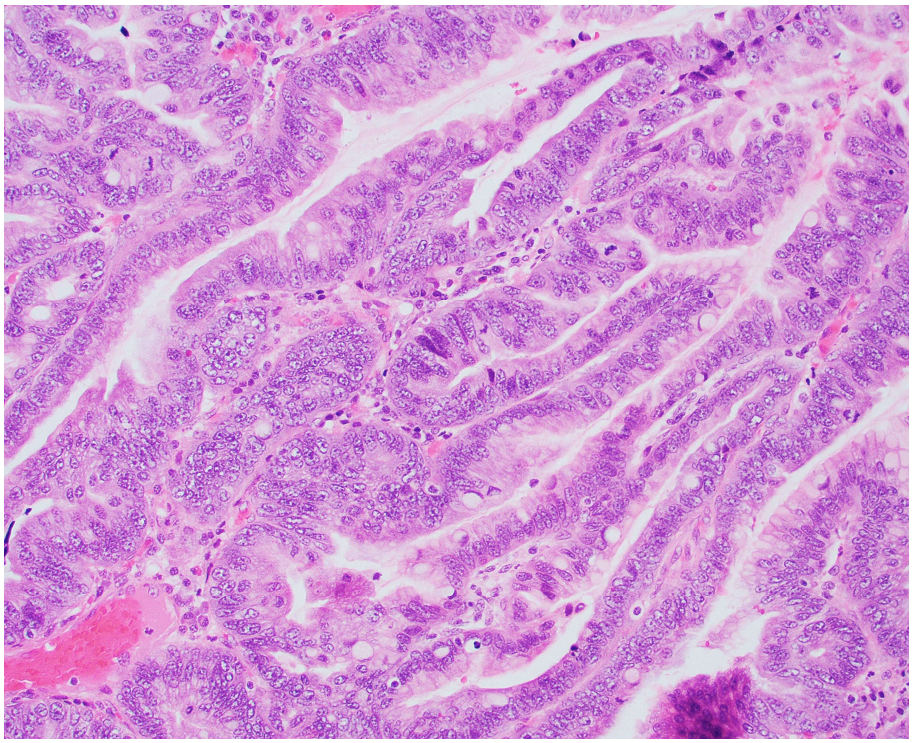






Dysplasia:1.8-16.4%; Carcinoma:0.3-7.1% (avg 2.1%) (> 2.0 cm)

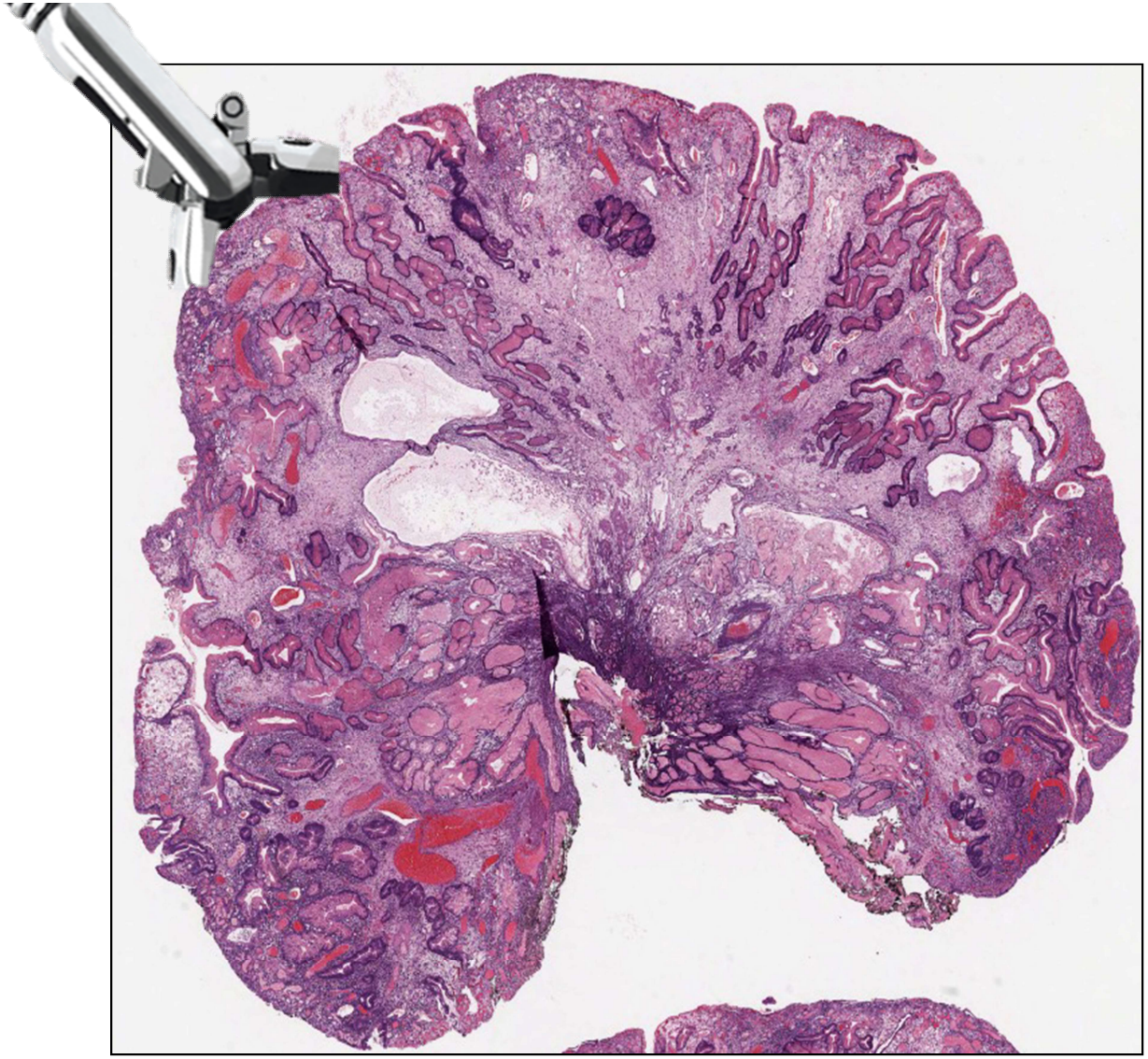




Polyp type	Usual number and size	Usual site	Malignant potential of polyp	Malignant potential of background mucosa	Management
Hyperplastic	Single 1–2 cm	Antrum	Low but significant	Low	Remove polyp if dysplastic Eradicate *H pylori* Repeat OGD 1 year
	Multiple <1 cm	Lower body	Low but significant	Low	Eradicate *H pylori* Repeat OGD 1 year

Goddard AF. Gut 2010;59:1270-1276

Differential diagnosis of hyperplastic polyps is challenging on a superficial pinch biopsies



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Hyperplastic Polyps – Diff. Dx

	Juvenile polyposis	Peutz-Jeghers Syndrome	Cowden's Disease	Cronkhite-Canada Syndrome
Inheritance	autosomal dominant	autosomal dominant	autosomic dominant	non-inherited (sporadic)
Gene	SMAD4 or BMPR1A	STK11/LKB1	PTEN	None
Gastric location	infrequent (15~25%)	25~50%	common	common
Location of polyp	antrum > body or fundus	random	random	random
Size of polyp	variable	usually small (<1cm)	usually small (<1cm)	variable
Lifetime risk of gastric Ca.	**15~20%**	**30%**	**rare**	**about 10%**

- Other differential dx:
  - Menetrier's disease
  - Bile reflux/ post surgery gastritis
  - Gastritis Polyposa Cystica

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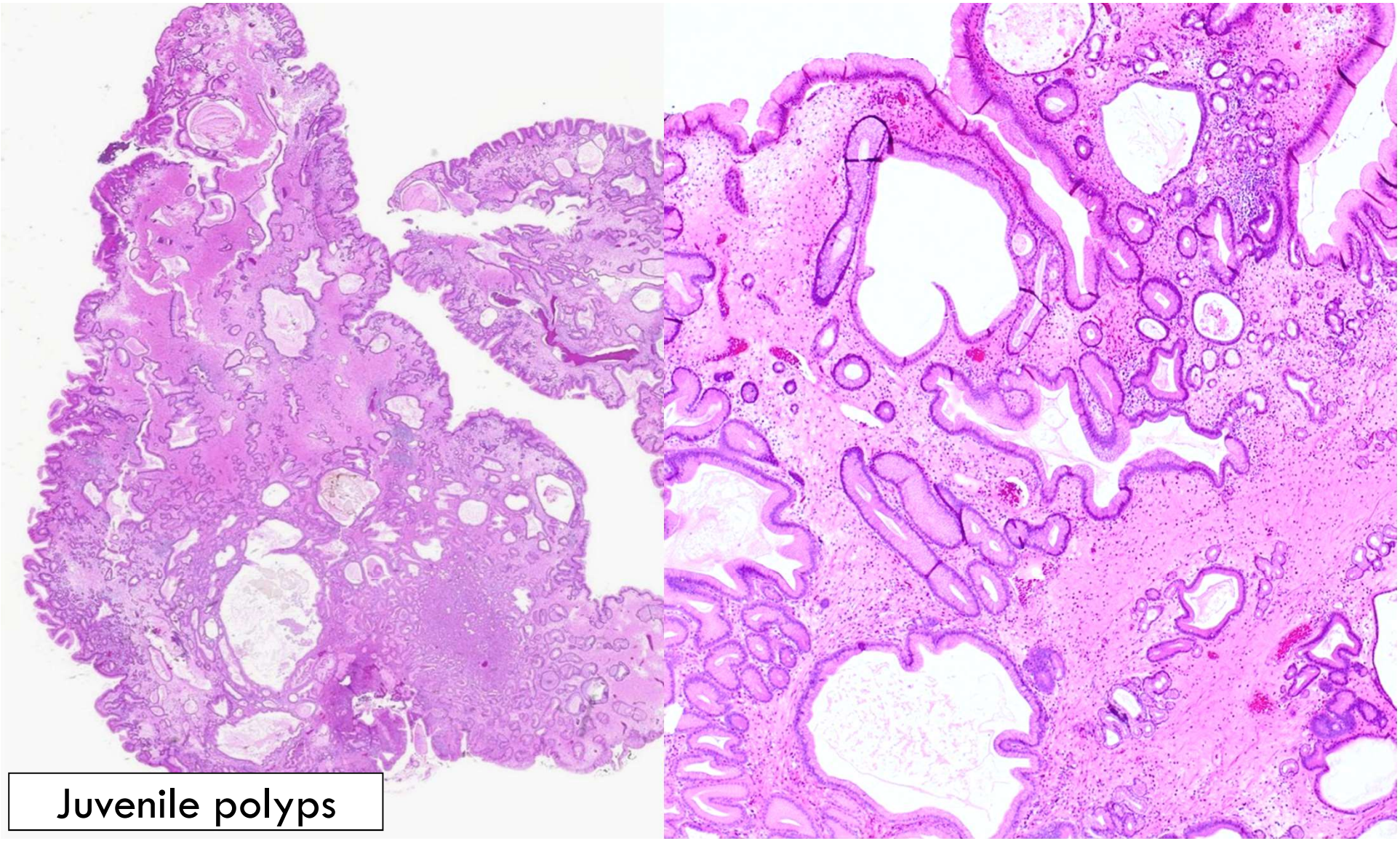
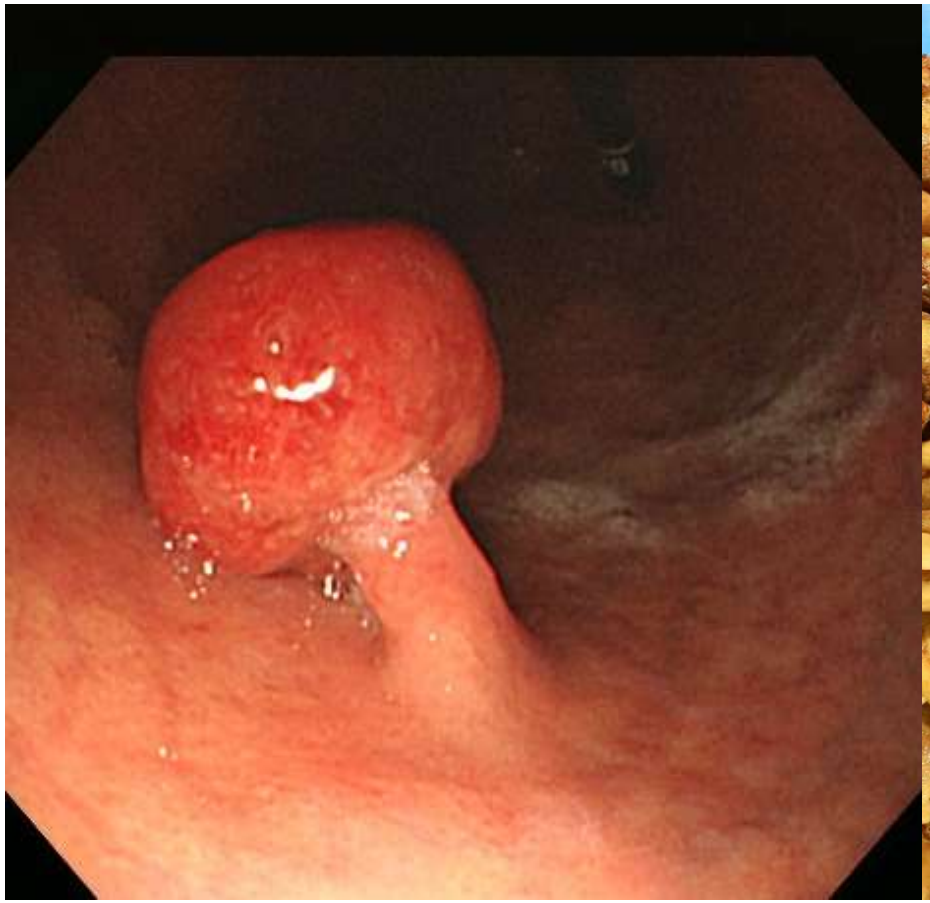
- Disorganized pits / glands of varying sizes & shapes.
- Edematous L propria (w/ granulation tissue)
- No smooth muscle fibers



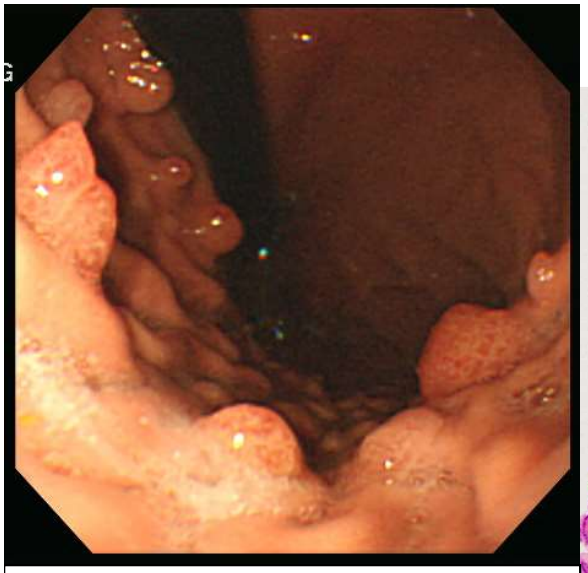
Juvenile polyps

Juvenile polyps (polyposis)

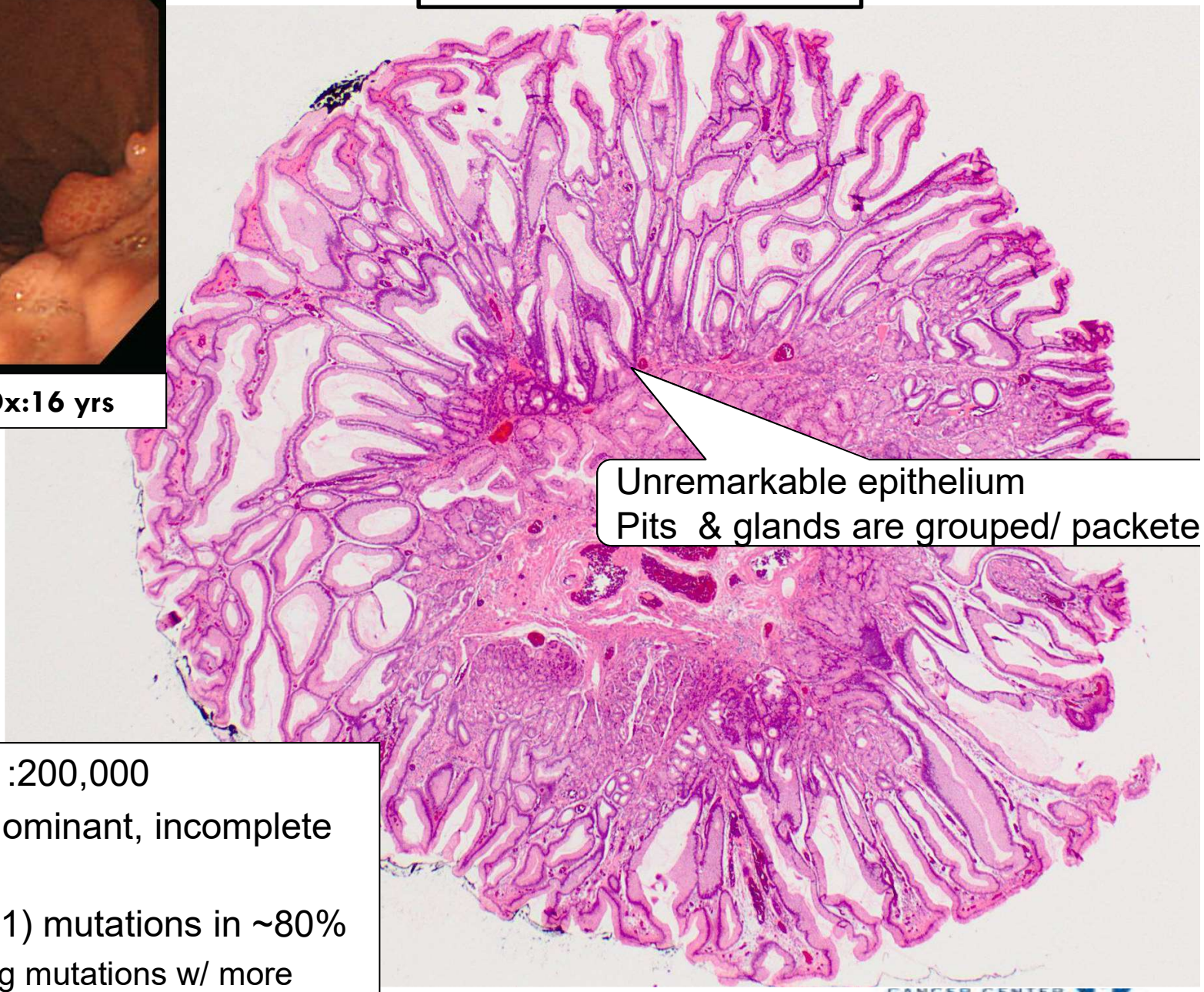


- Family history in 50% pts. Extra-colonic polyps almost always syndromic
- Median age of pts presenting with gastric polyps ~40 years
- Rounded and sessile when small but pedunculated with a lobular appearance as they enlarge.

PEUTZ-JEGHERS



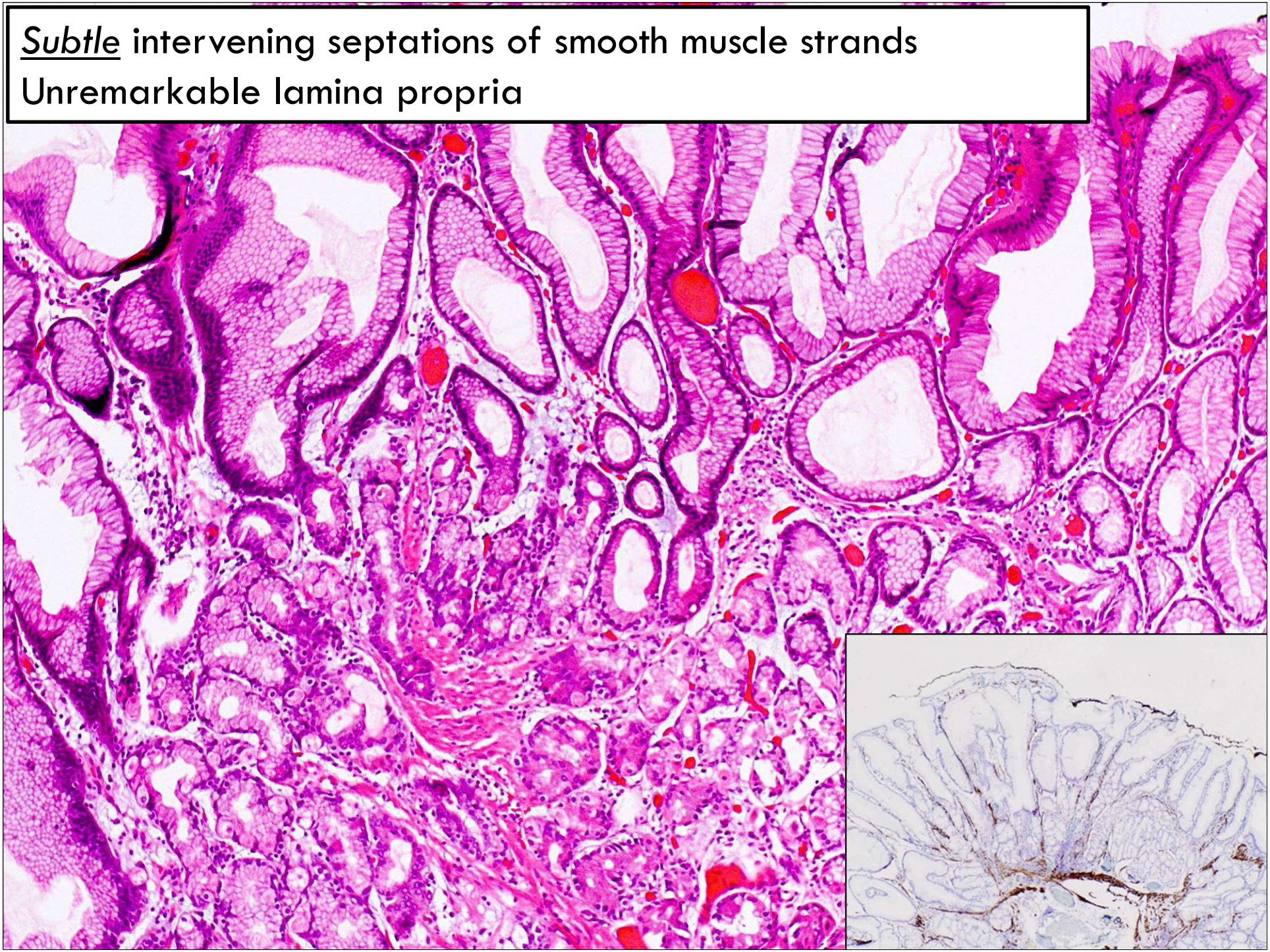
Median age of Dx:16 yrs



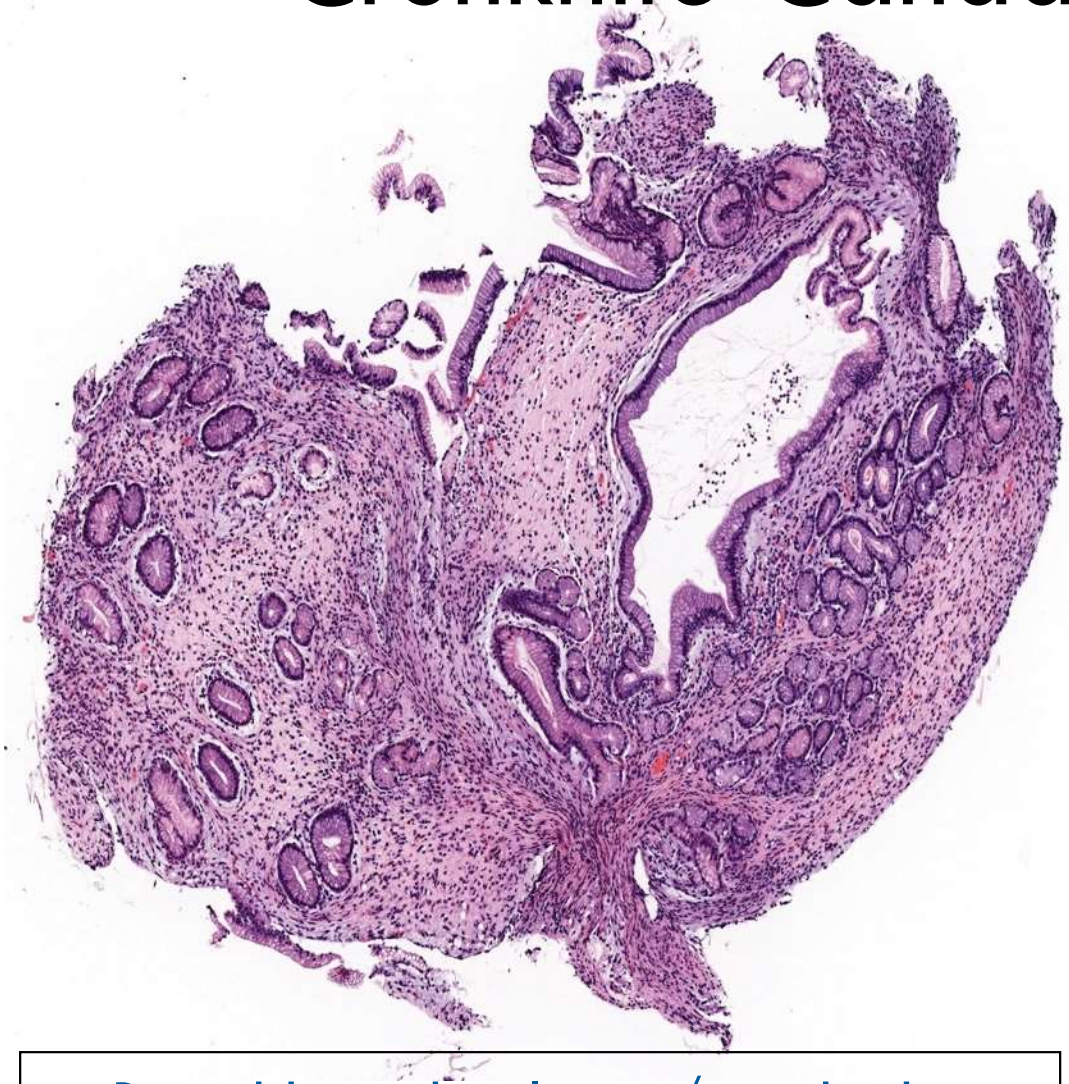
- Incidence : 1:200,000
- Autosomal dominant, incomplete penetrance
- LKB1 (STK11) mutations in ~80%
  - Truncating mutations w/ more severe disease

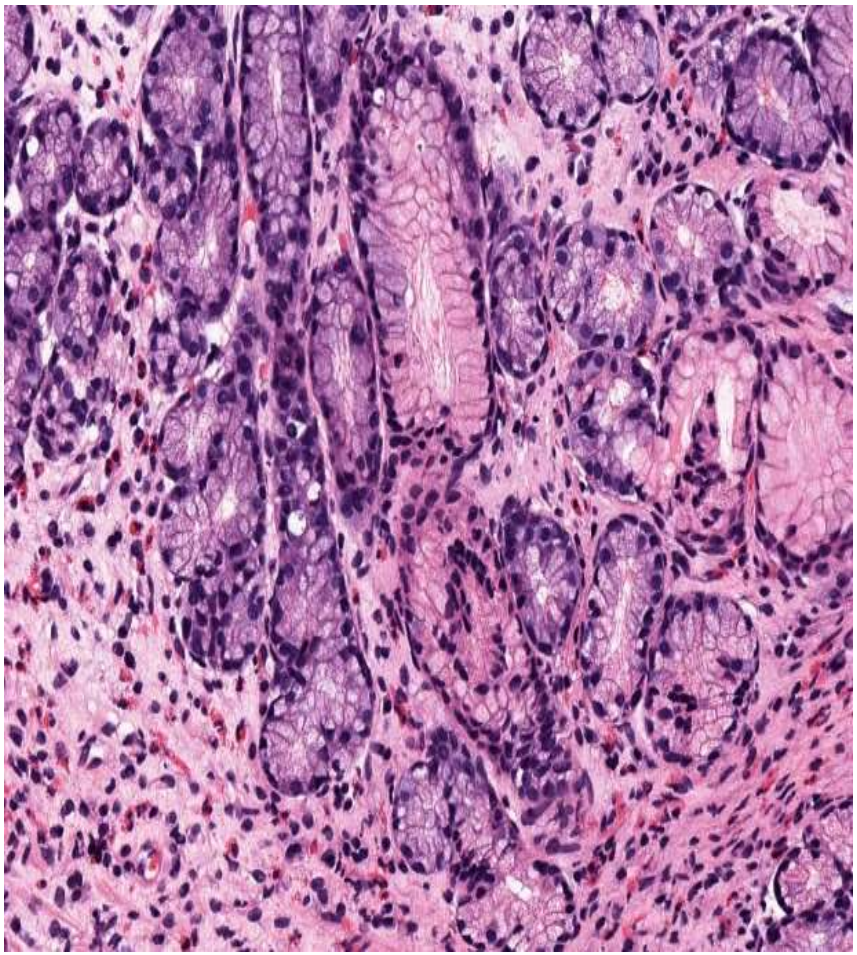
Subtle intervening septations of smooth muscle strands

Unremarkable lamina propria



Cronkhite-Canada Syndrome





- Broad based polyp w/ marked stromal edema & unevenly spaced glands.

- Mixed inflammatory infiltrate w/ prominent eosinophilia

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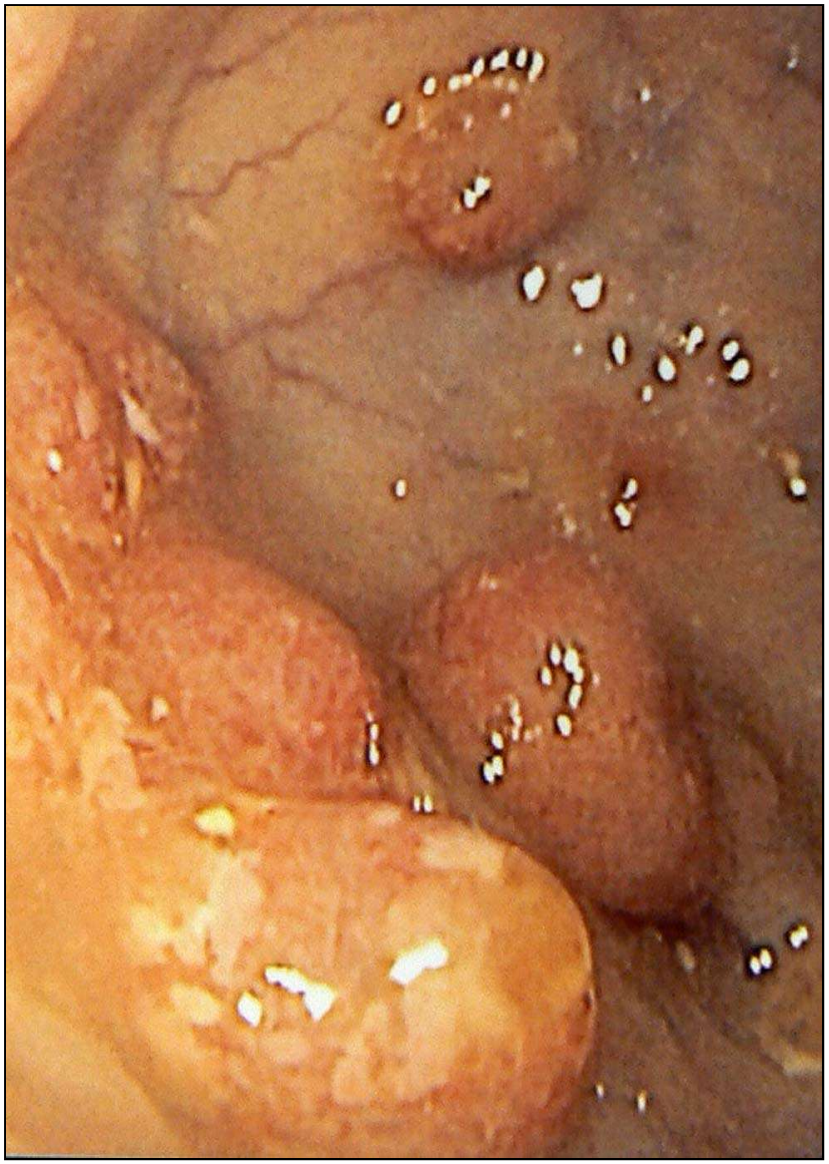
Cronkhite-Canada Syndrome



- Protein-losing enteropathy.
- Ectodermal changes
- Hamartomatous polyposis.
- (IgG4 related condition?)
- Variable natural history
  - 50-60% mortality
  - Electrolytes imbalance, GI bleeding, opportunistic infections
- Malignant potential~10%

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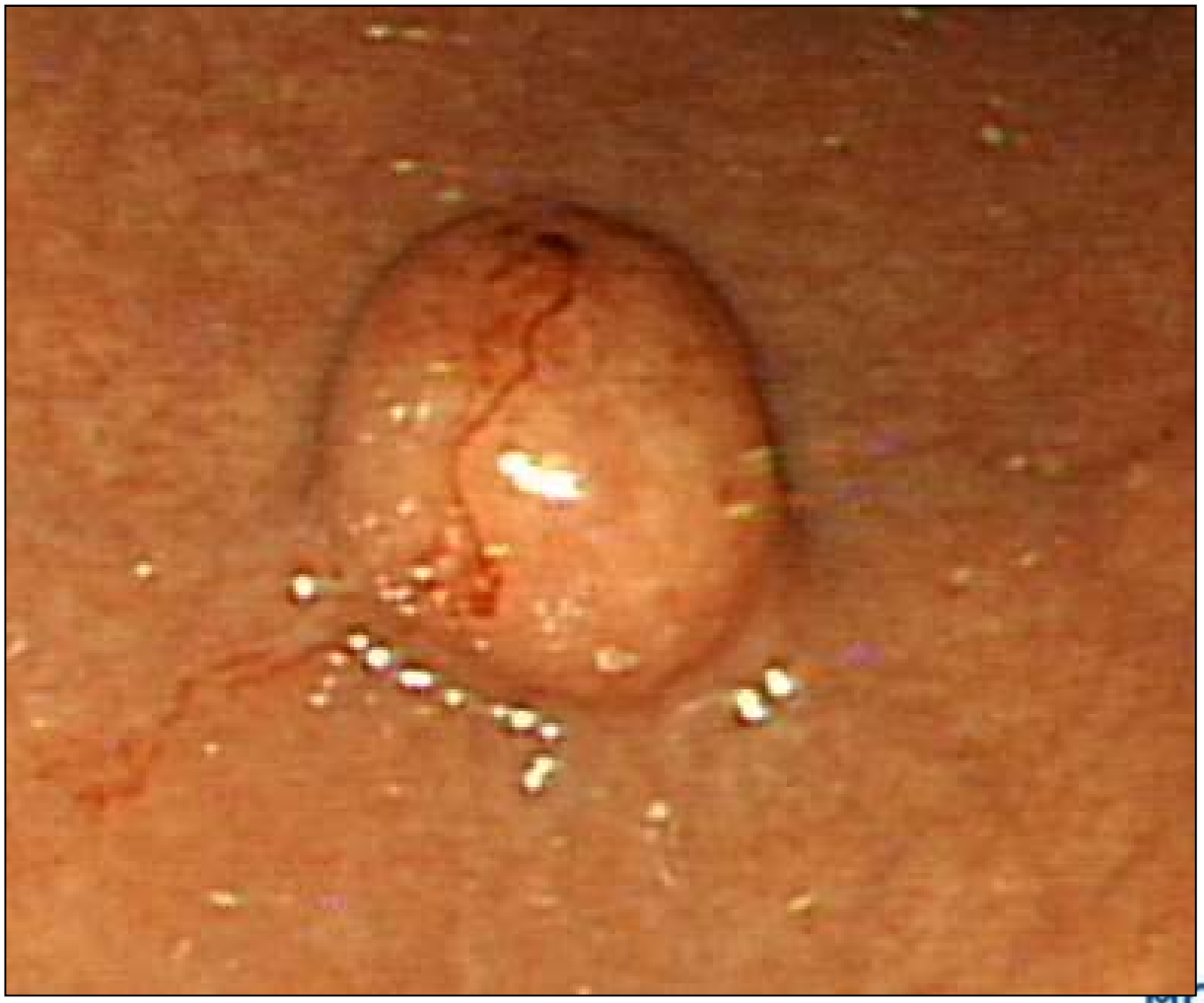
Gastric Adenoma

- Nodule of dysplastic epithelium, i.e., *"Unequivocal neoplastic (non invasive) process"*



- ***Single in 82% of cases; 80-90% < 2cm***

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Architectural & Cytologic Features of Gastric Epithelial Dysplasia

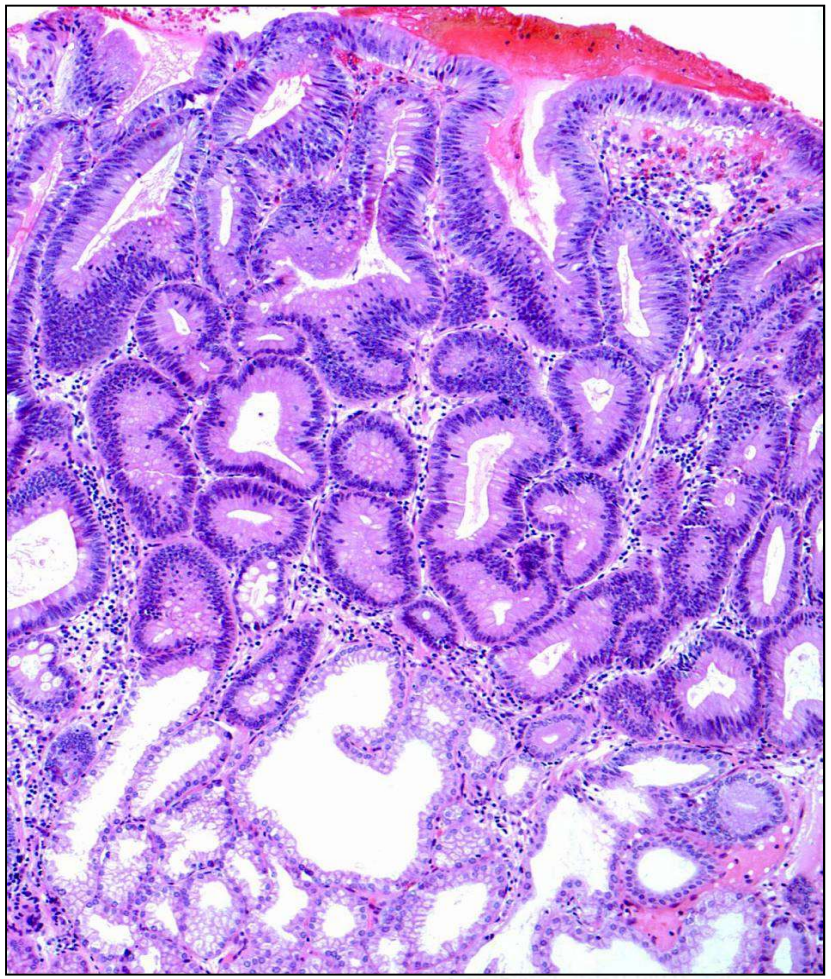
Glandular disarray,budding, branching and dilatation

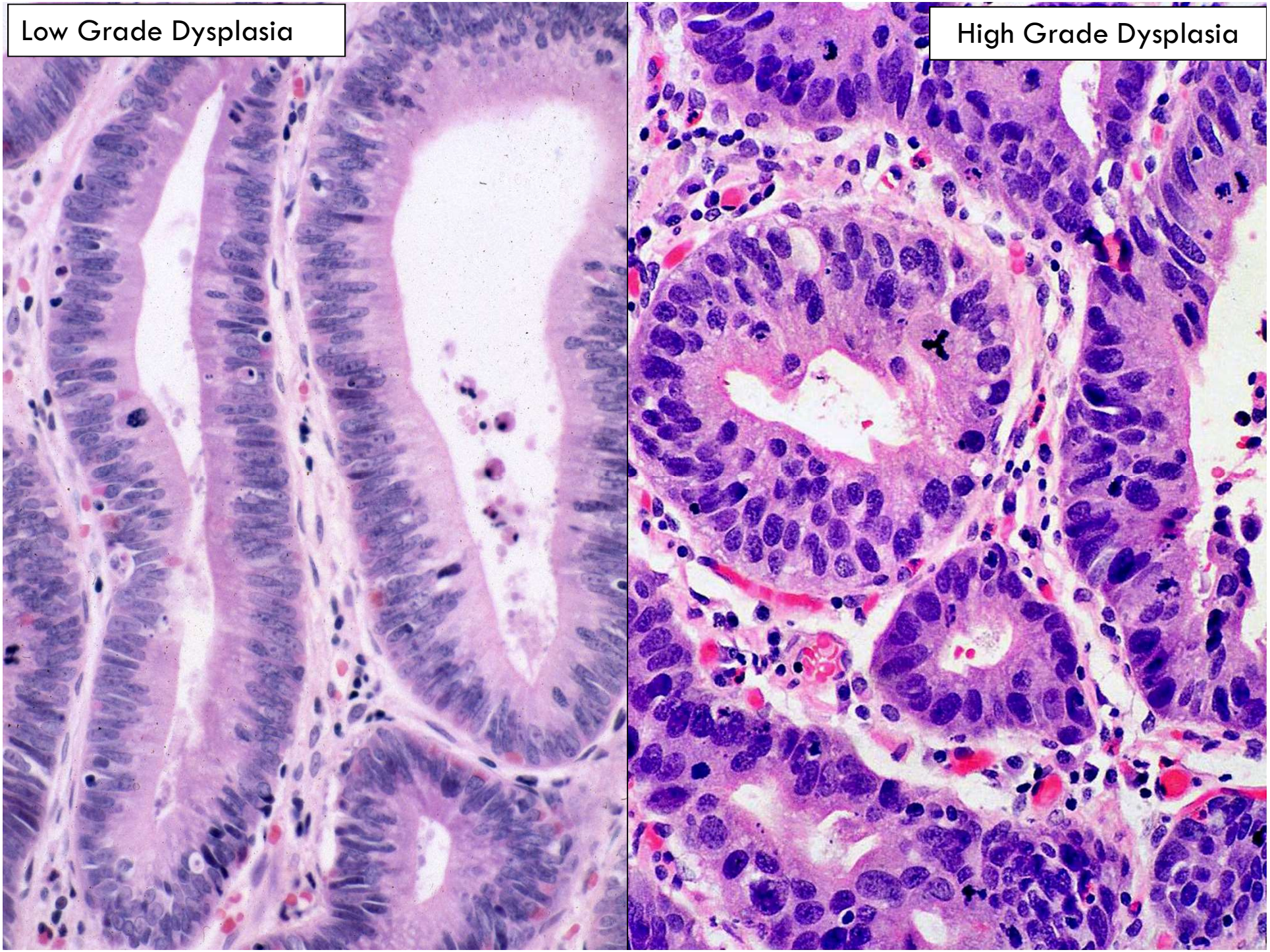
Nuclear pleomorphism

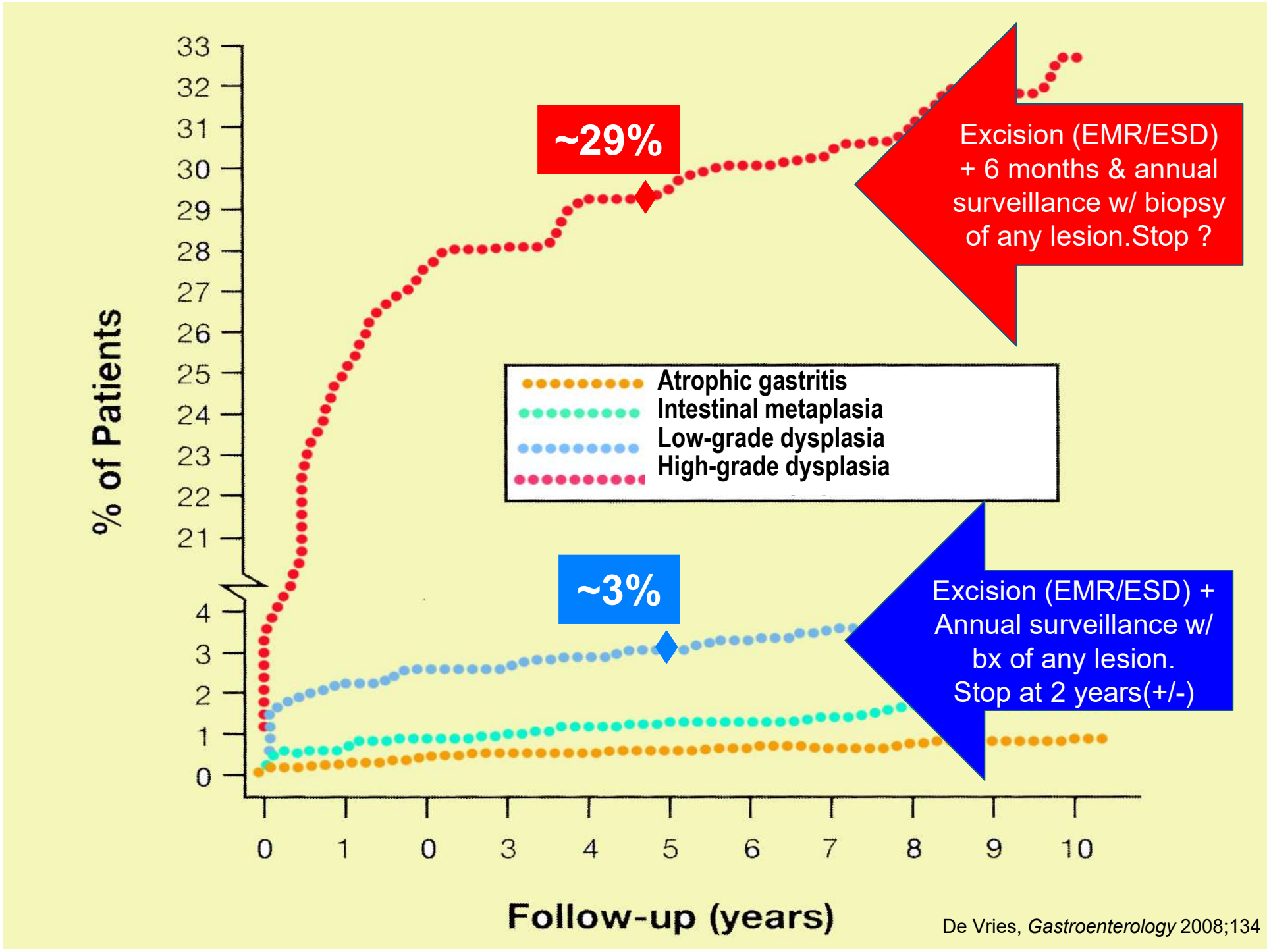
High N/C ratio

Loss of nuclear polarity w/ pseudostratification

Lack of differentiation w/ mucus depletion

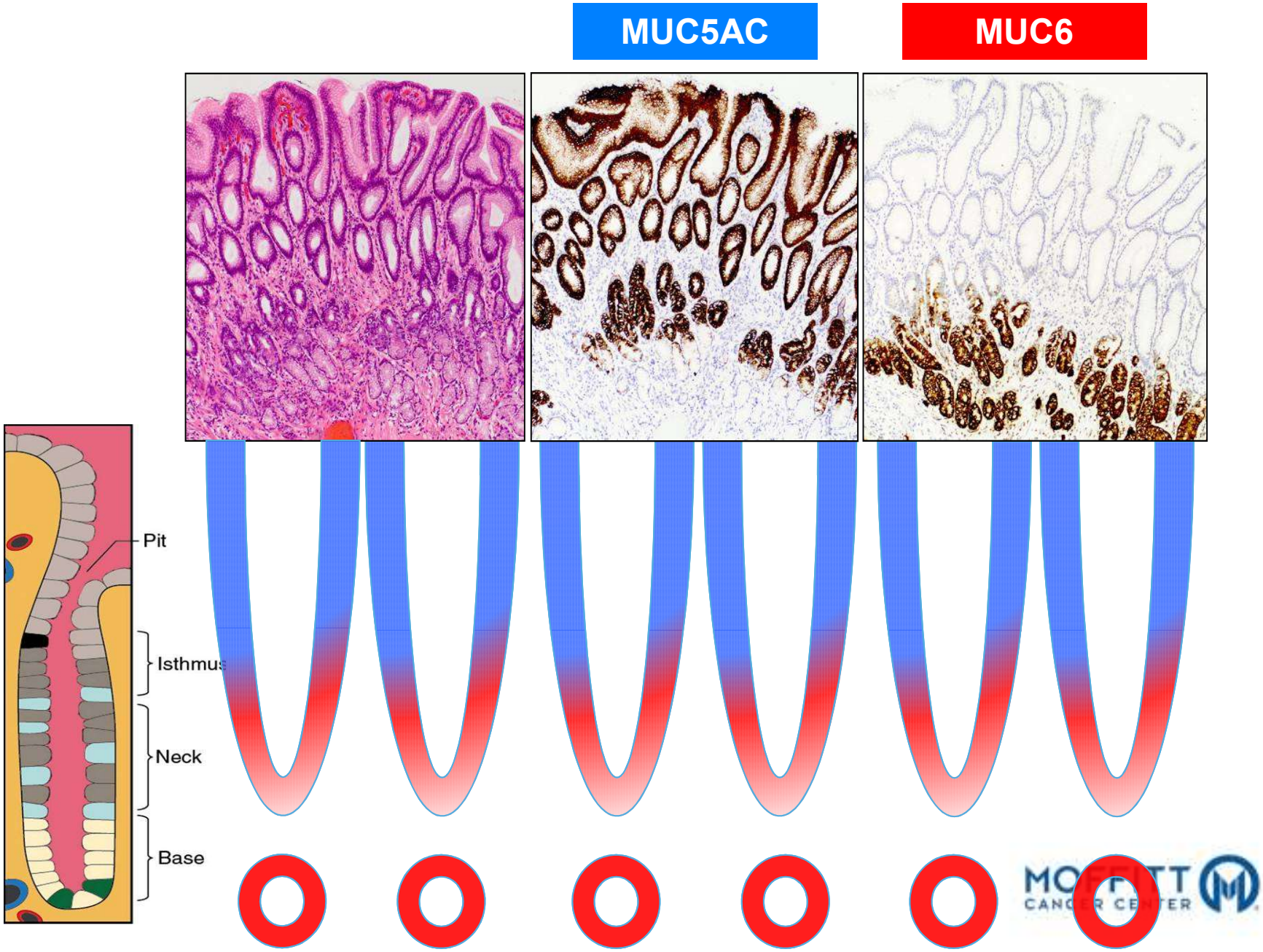



Low Grade Dysplasia
High Grade Dysplasia



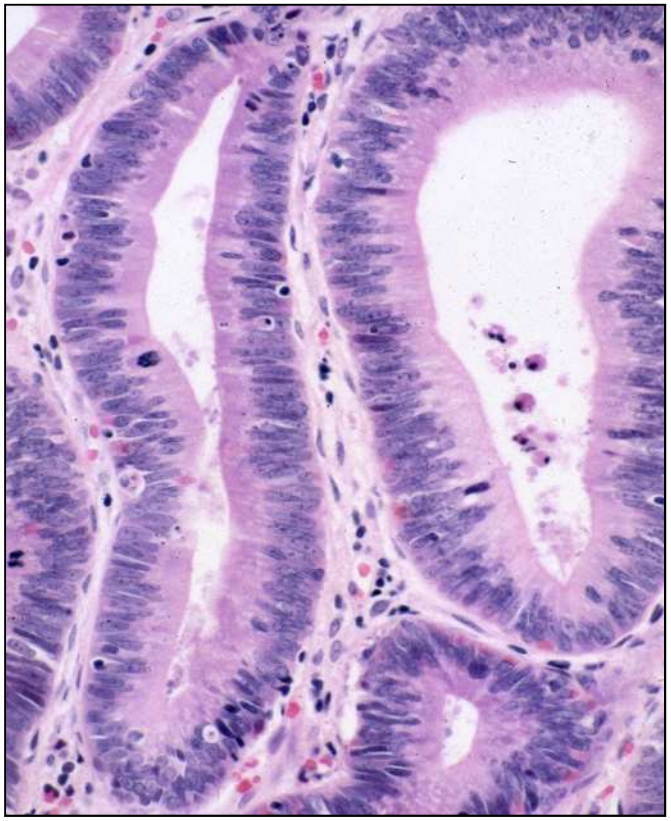
De Vries, *Gastroenterology* 2008;134

Normal gastric mucosa shows cell-type specific expression of Muc-5AC, Muc-6 glycoproteins.

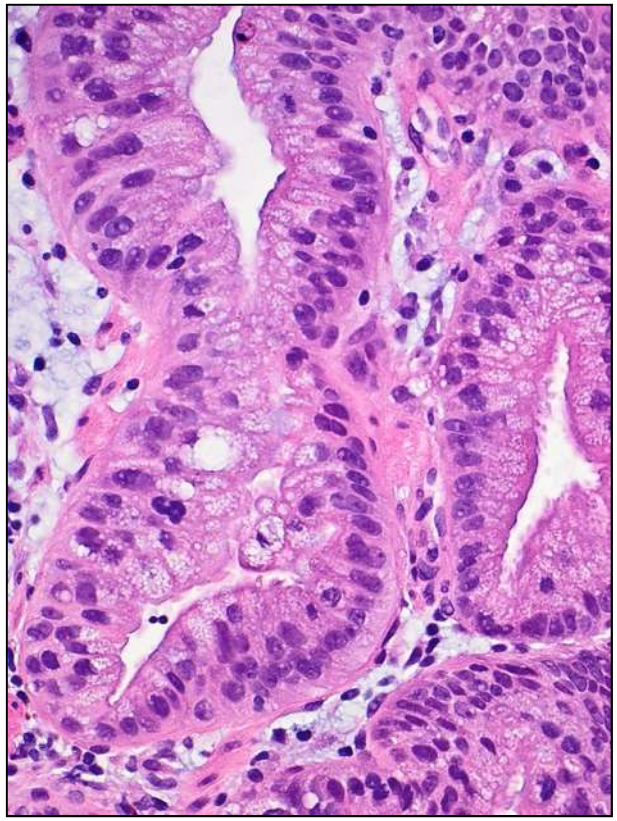


Phenotypic Diversity of Gastric Dysplasia

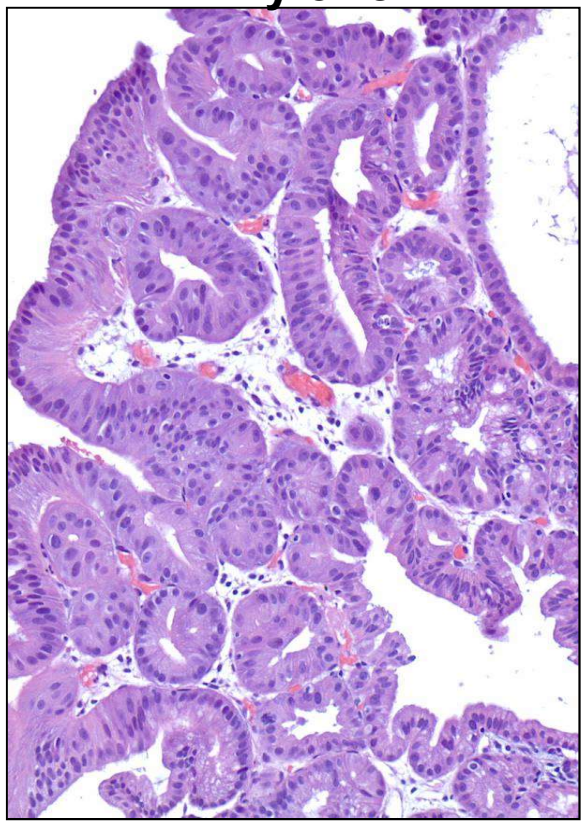
Adenomatous



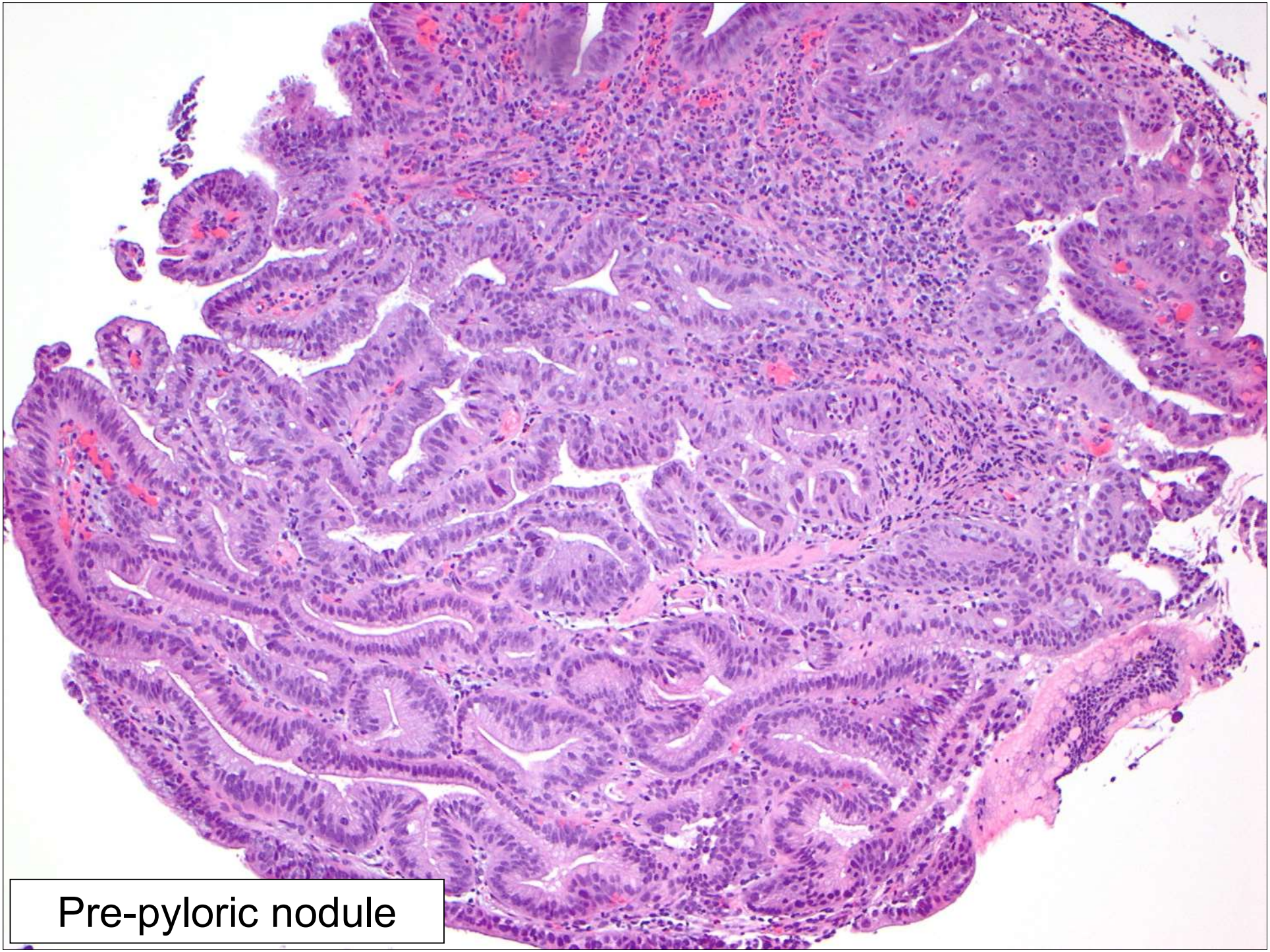
Foveolar

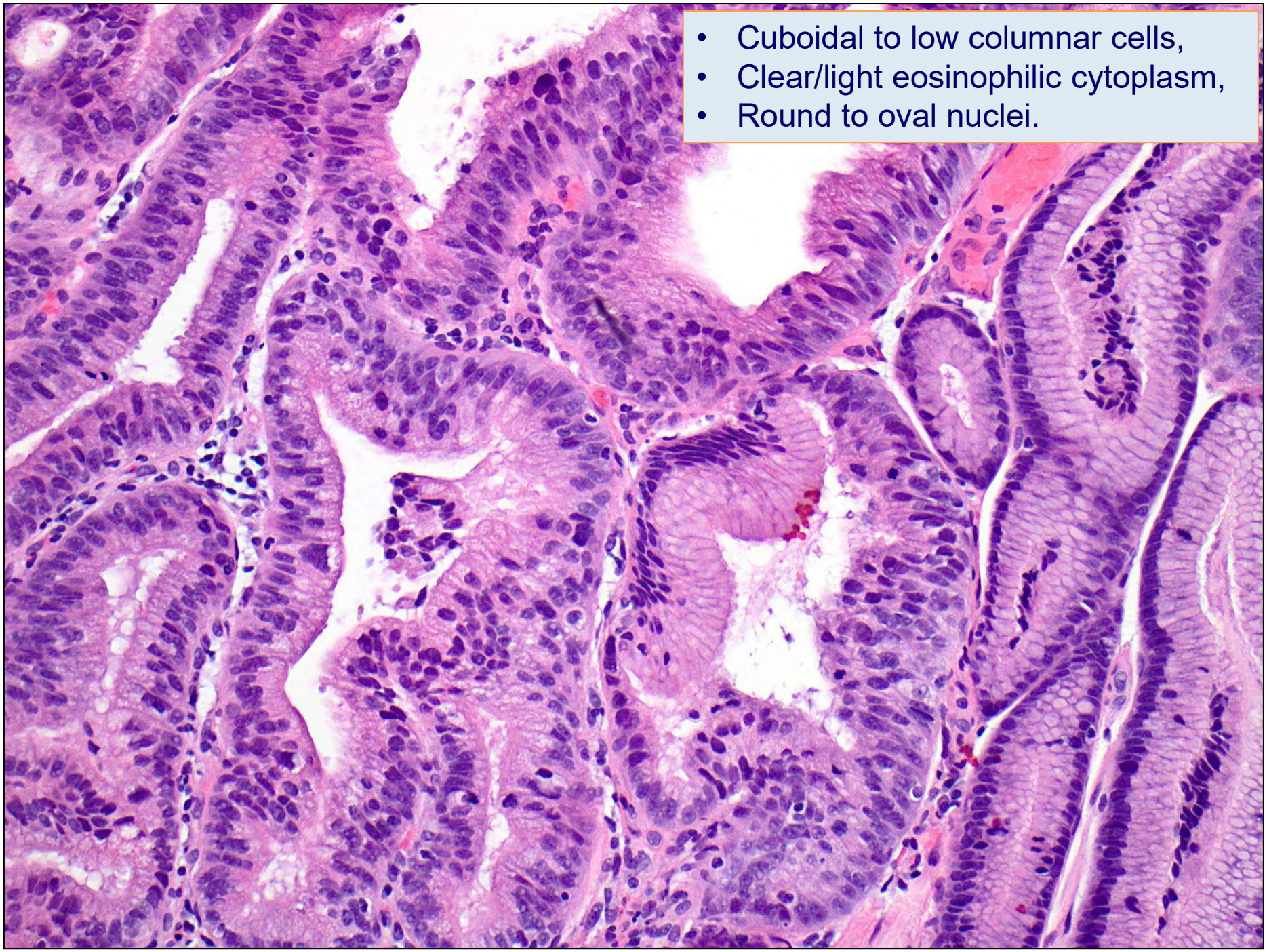


Pyloric



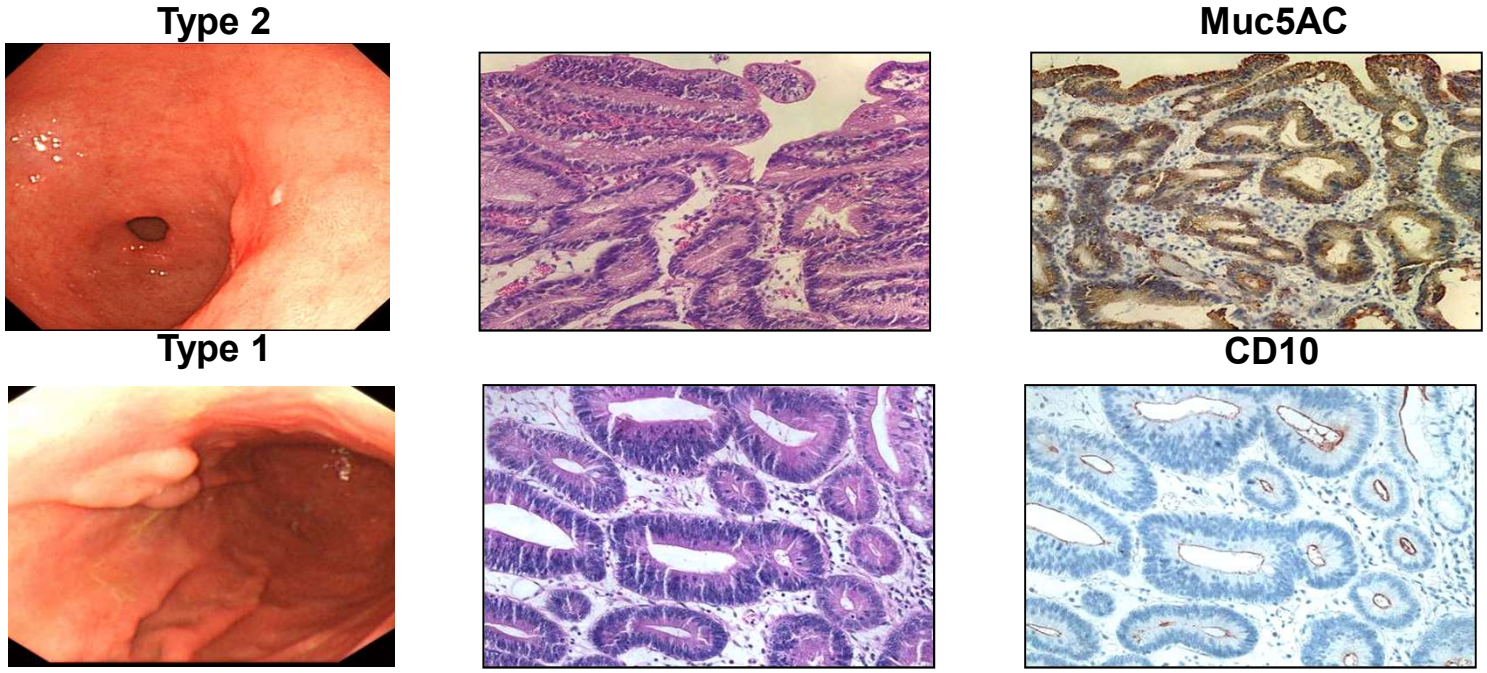
	CD10	MUC2	MUC5AC	MUC6
Intestinal	(+) (Apical membrane)	(+) (Goblet cells)	(-)	(-)
Foveolar	(-)	(-)	(+)	(+/-) (glands)
Pyloric	(-)	(-)	(+) (surface)	(+) (glands)


Pre-pyloric nodule


• Cuboidal to low columnar cells,
• Clear/light eosinophilic cytoplasm,
• Round to oval nuclei.

Park DY. AJSP 2008

Prevalence of foveolar GED: 22% (Adenomatous: 45%, hybrid 33%) (n=69)



- Foveolar GED is often depressed/flat and associated w/ HGD (p= 0.046).
- HGD associated w/ MUC5AC expression regardless of the type (p=0.026).

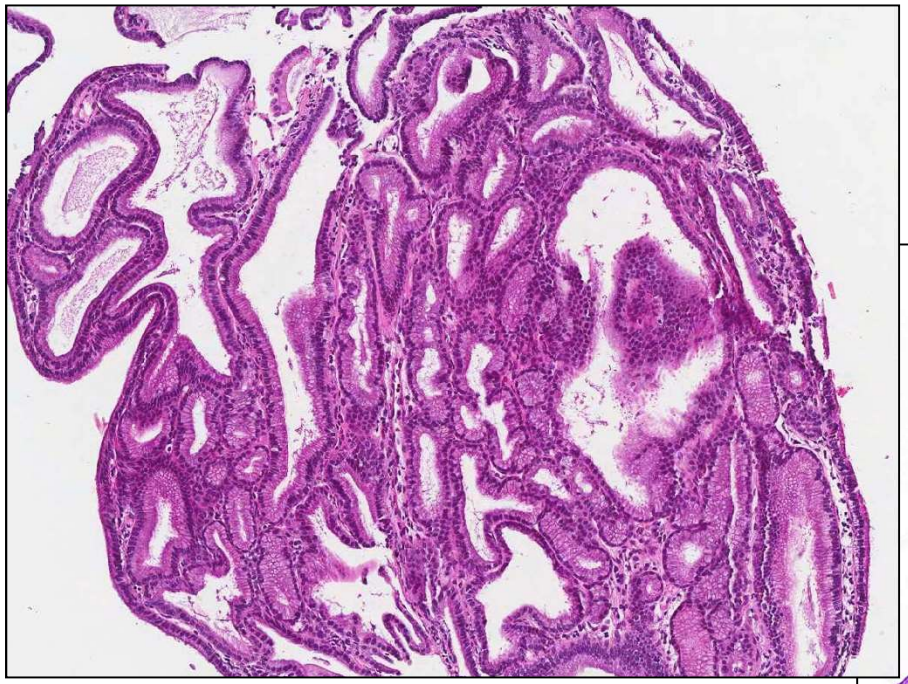
Grade	Immunophenotype			p value
	Foveolar (n=24)	Intestinal (n=22)	Hybrid (n=14)	
HGD (n=25)	15* (63%)	4 (18%)	6 (43%)	
Low grade (n=35)	9 (37%)	18 (82%)	8 (57%)	0.010

* coexistent intramucosal carcinoma in 8 cases

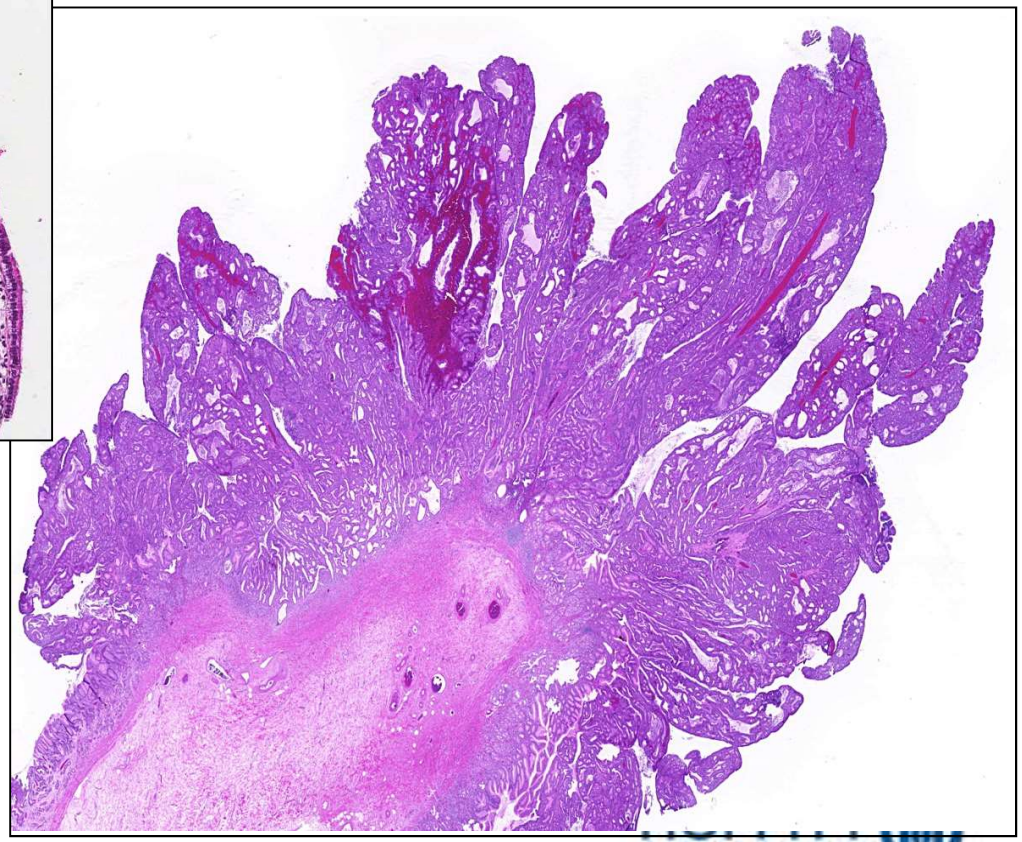
Foveolar differentiation is associated w/ HGD & coexistence of IMC

Valente P; Gastric Cancer 2014

PYLORIC GLAND ADENOMA



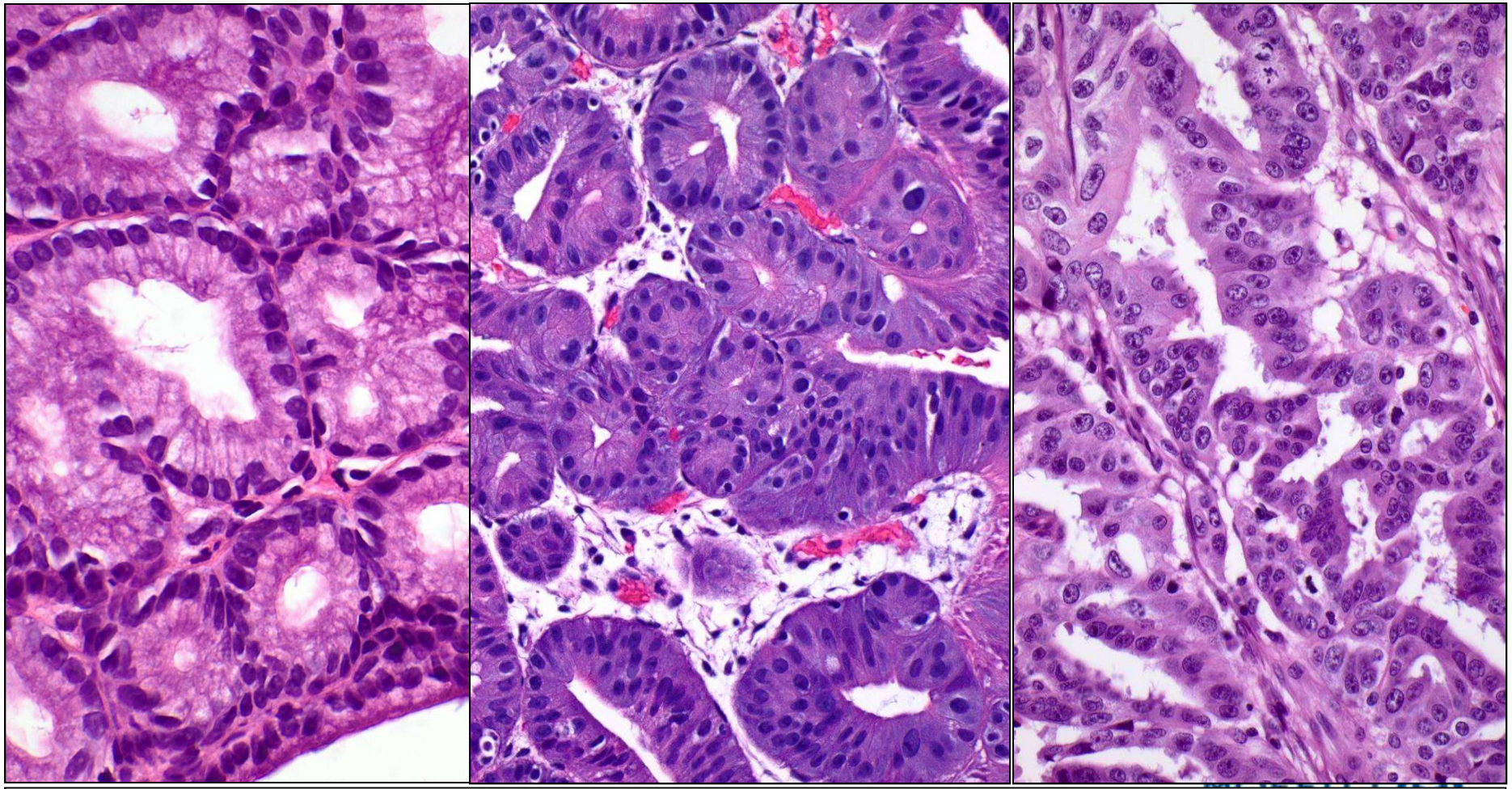
- Older pts (mean age: 70 yrs)
- Females > males (3:1)



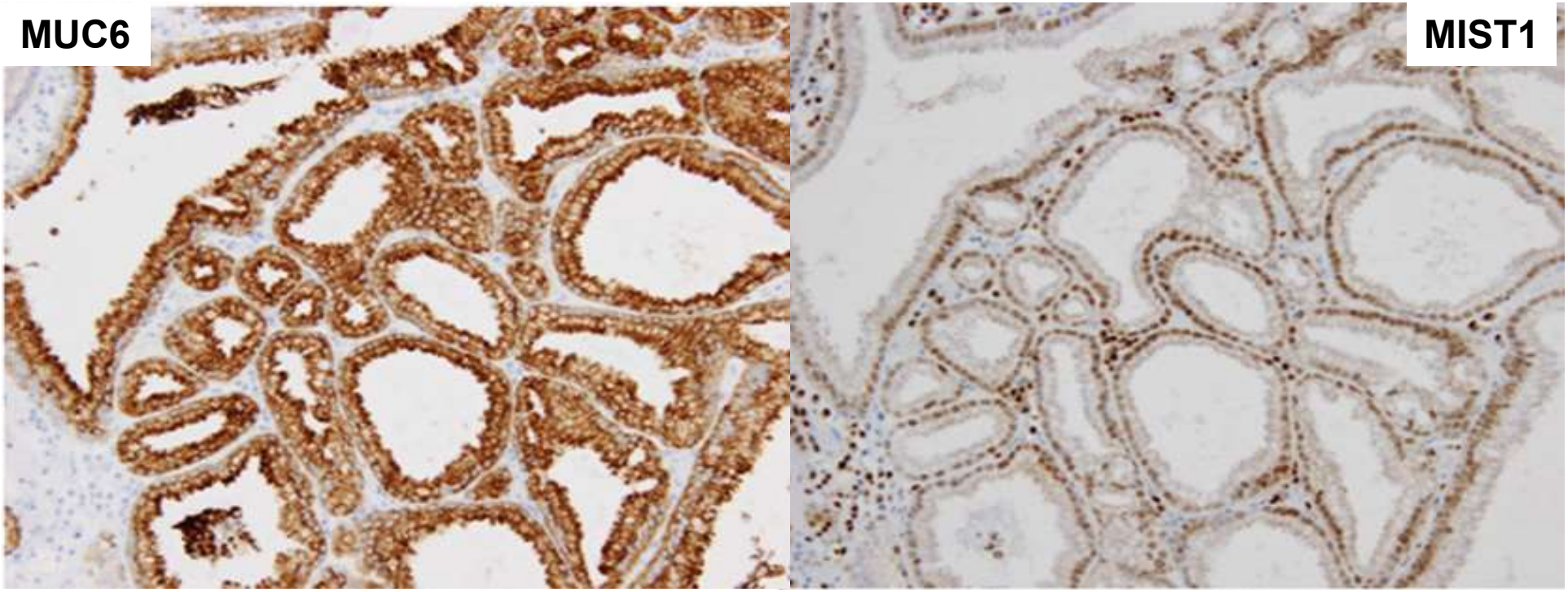
- Oxyntic mucosa
- Autoimmune gastritis +
- FAP; no sex predominance (6%)

“dysplasia” in pyloric gland adenoma

~1/3 w/ HGD



Dysplasia ranges to very subtle to appreciable (HGD)



Journal of Pathology
J Pathol 2013; **229:** 579–587
Published online 4 February 2013 in Wiley Online Library
(wileyonlinelibrary.com) DOI: 10.1002/path.4153

ORIGINAL PAPER

Frequent *GNAS* and *KRAS* mutations in pyloric gland adenoma of the stomach and duodenum

Akiko Matsubara,[1] Shigeki Sekine,[2]* Ryoji Kushima,[1] Reiko Ogawa,[2] Hirokazu Taniguchi,[1] Hitoshi Tsuda[1] and Yae Kanai[2]

GNAS mutation in 48% of cases (not in intestinal and foveolar type dysplasia)
KRAS mutation in 41% of cases

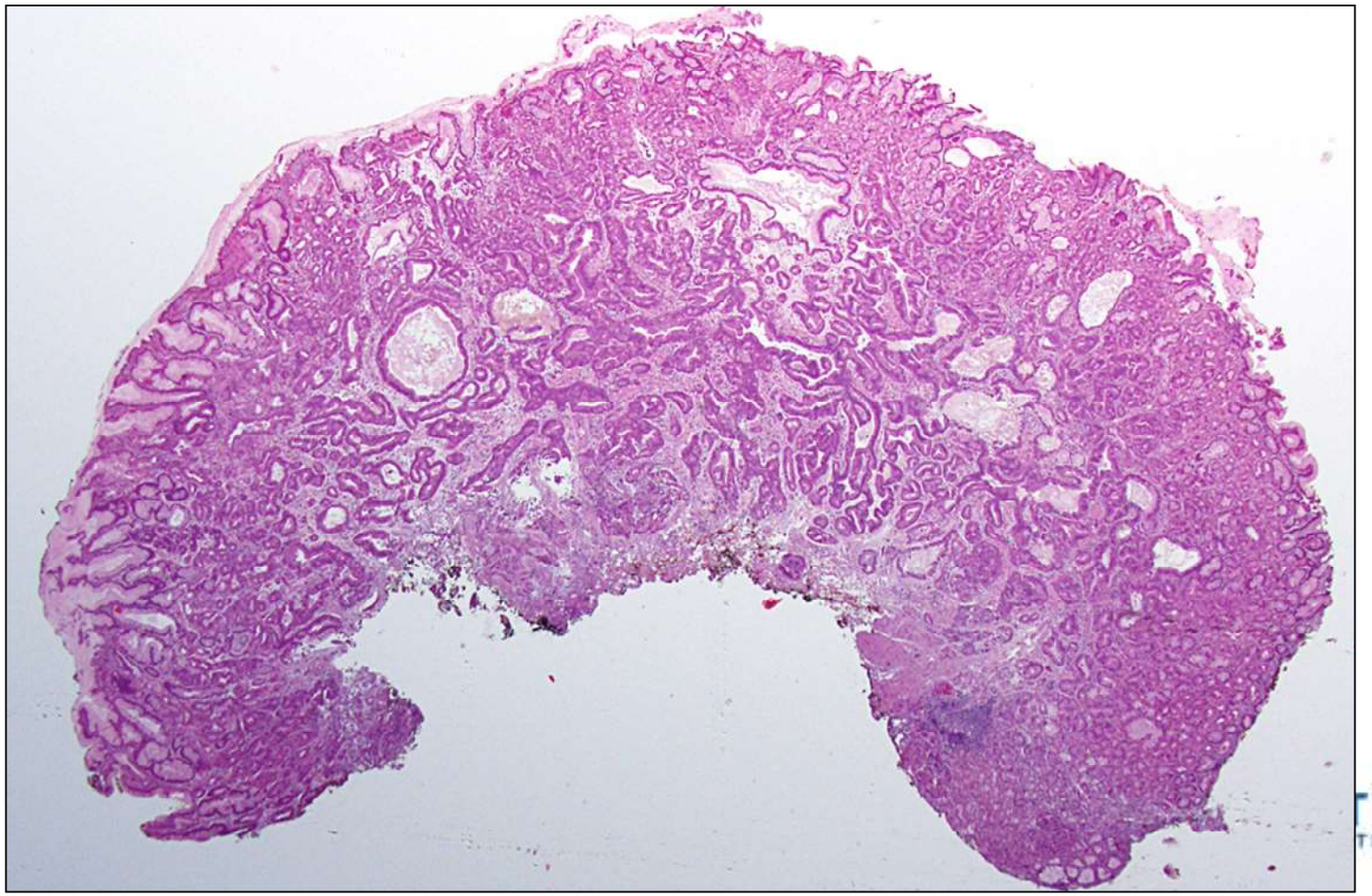
Gastric Adenocarcinoma of Fundic Gland Type (Chief Cell Predominant Type): Proposal for a New Entity of Gastric Adenocarcinoma

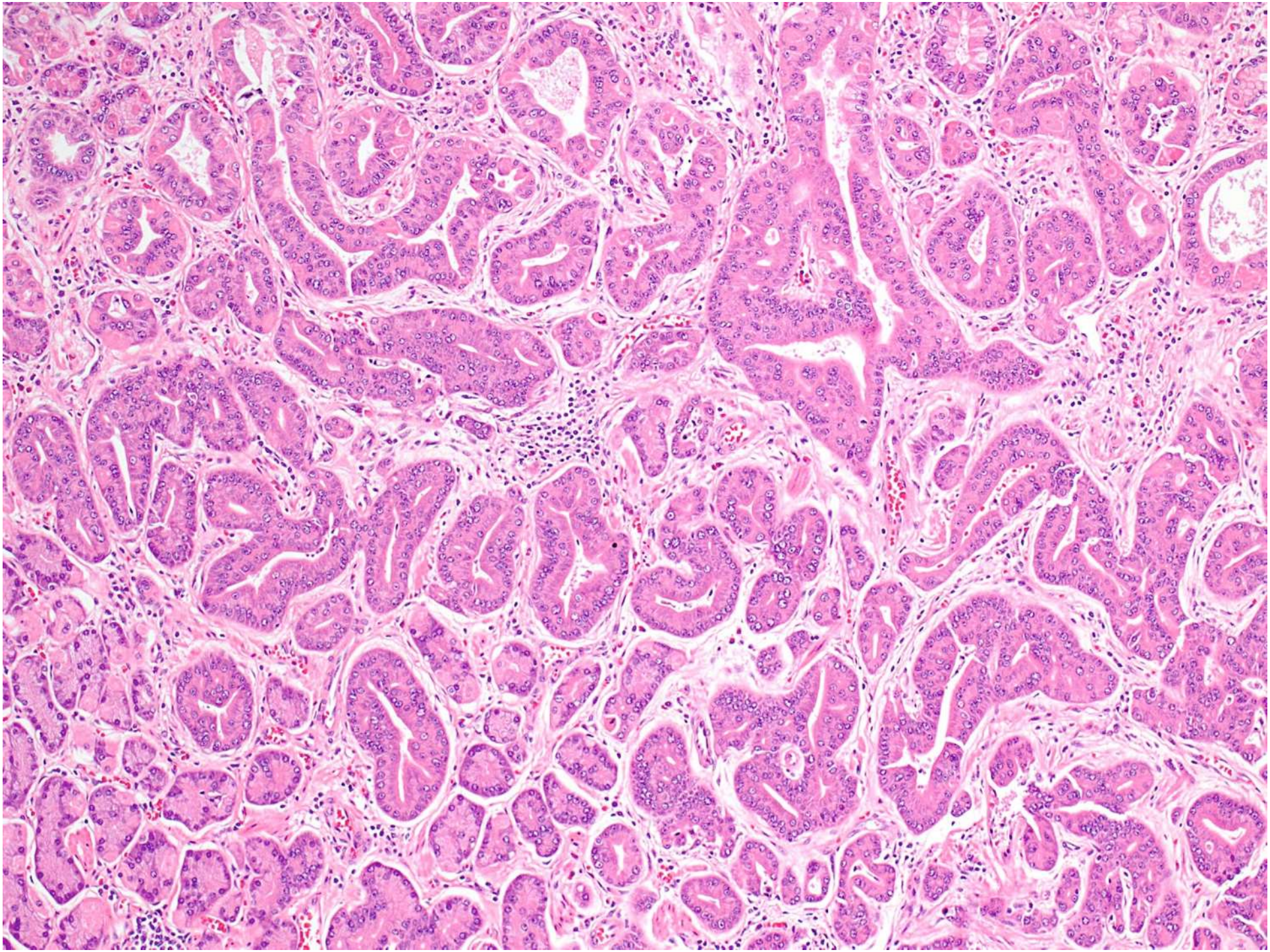
Uyema H AJSP. 2010;609-619.

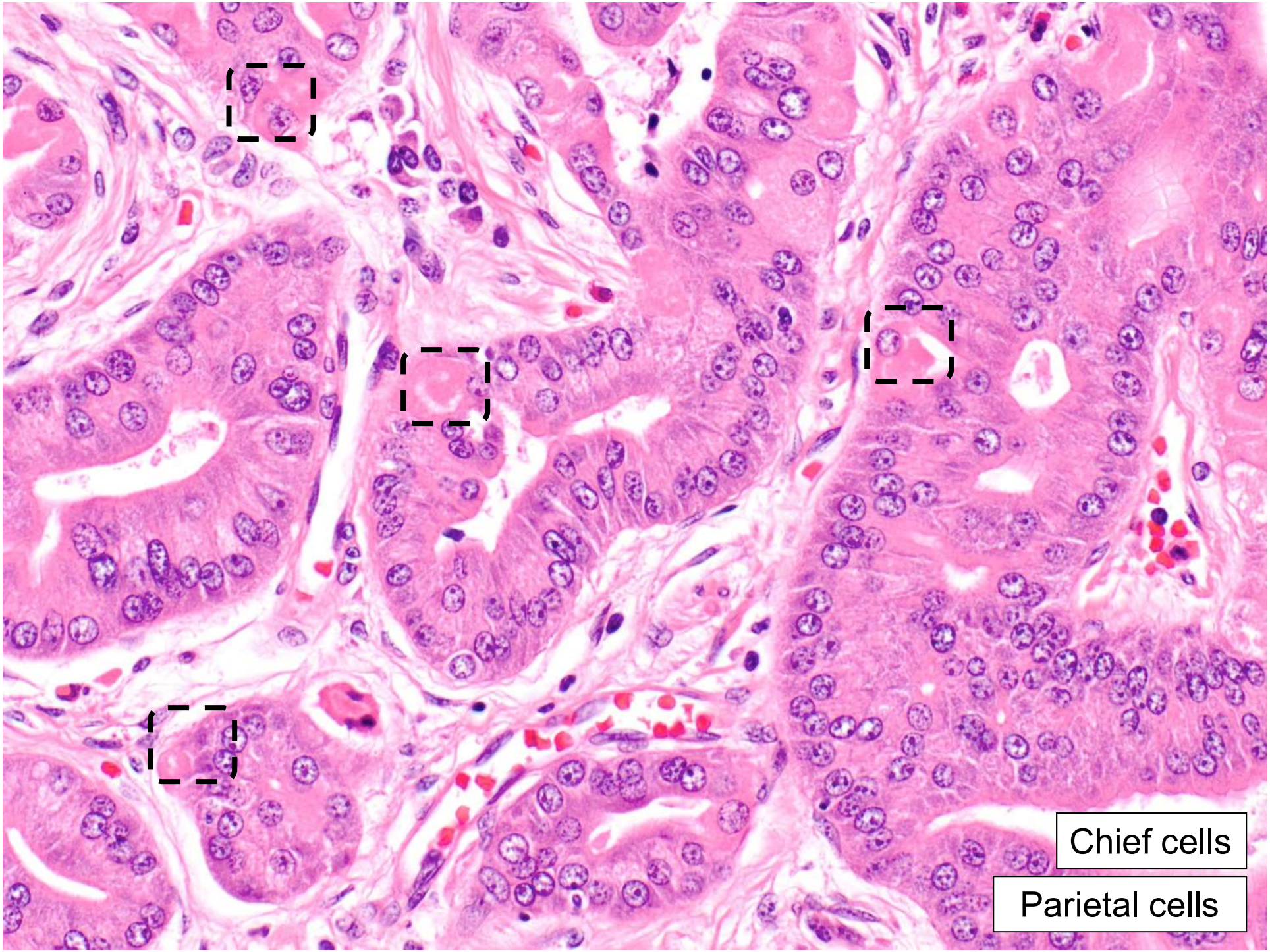
Gastric Adenocarcinoma With Chief Cell Differentiation

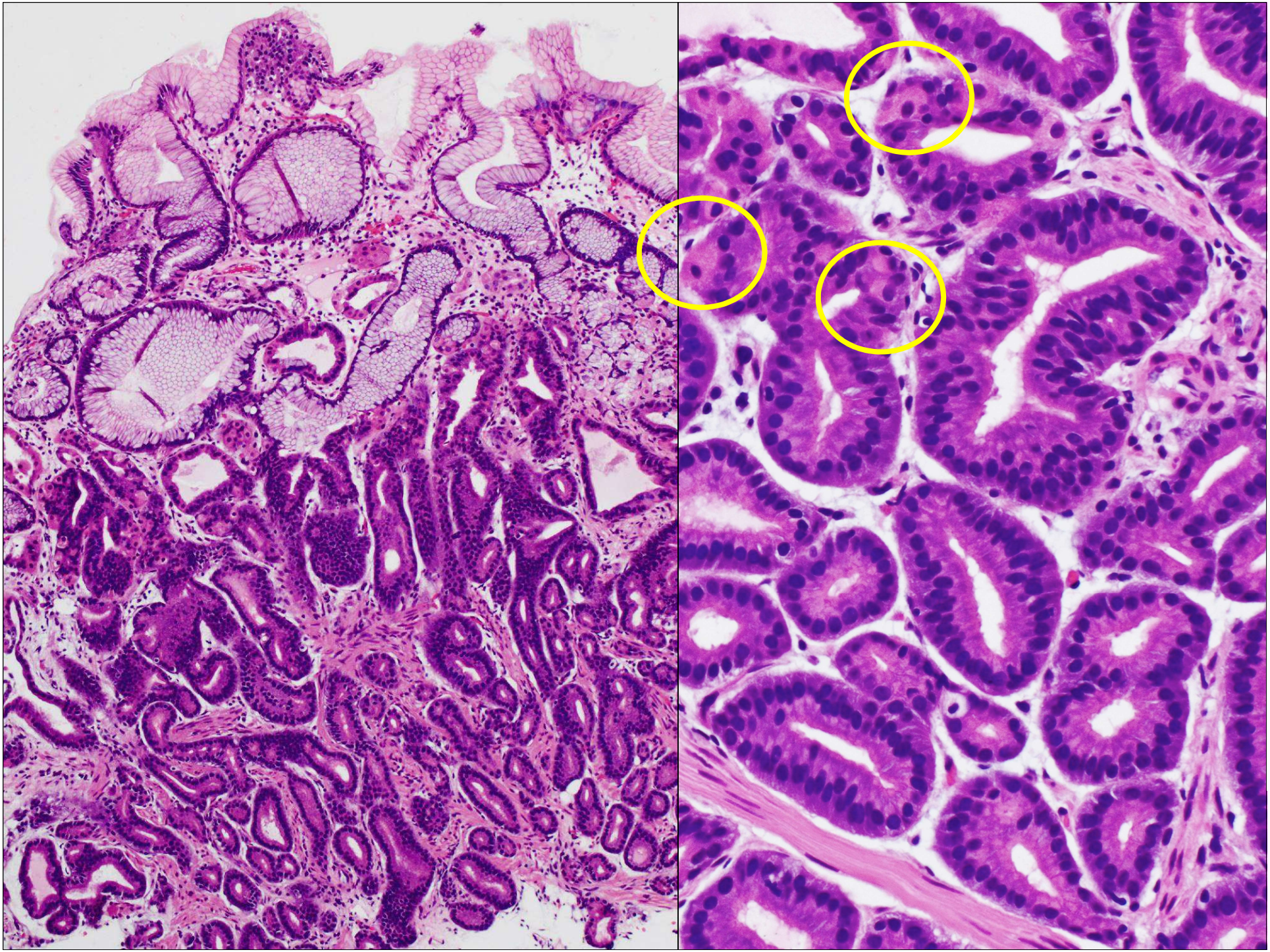
A Proposal for Reclassification as Oxyntic Gland Polyp/Adenoma

Singhi A AJSP. 2012;1030-1035.



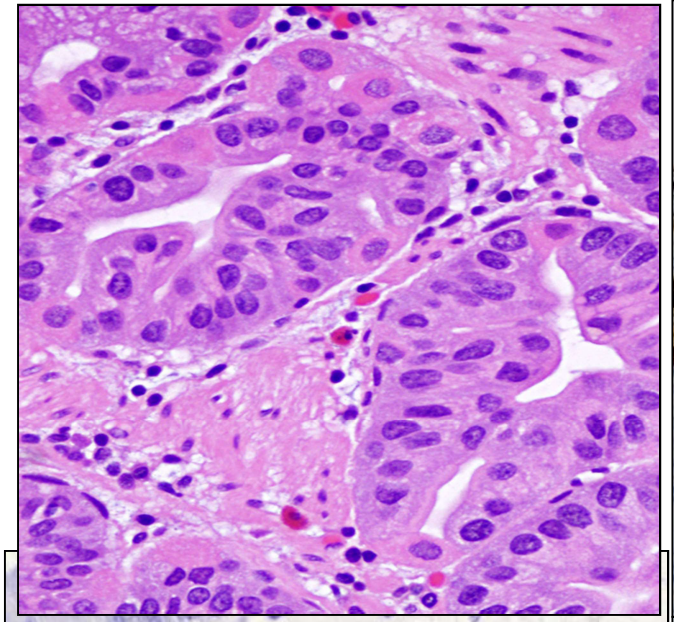


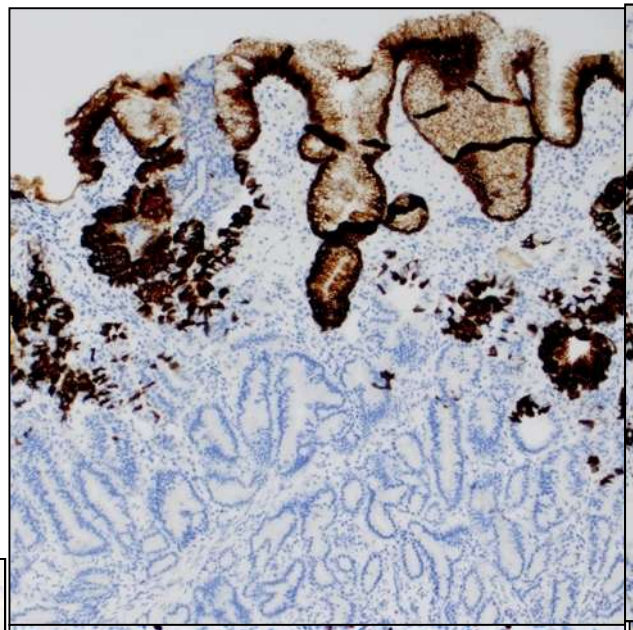

Chief cells
Parietal cells

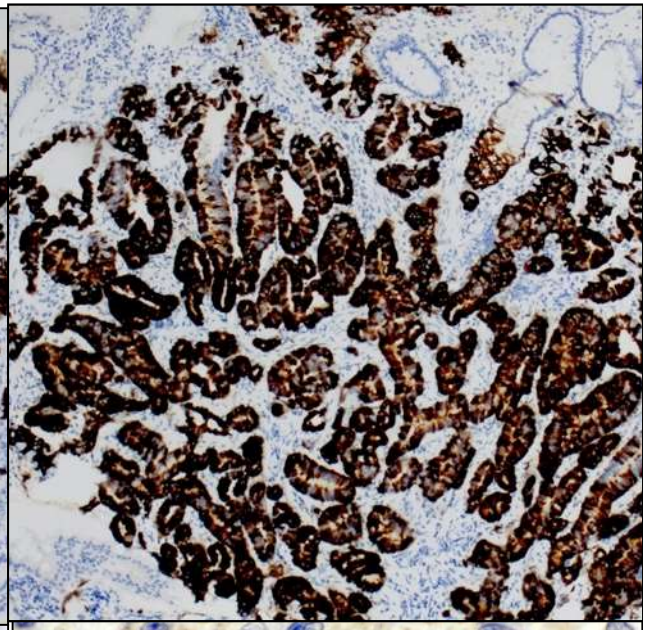


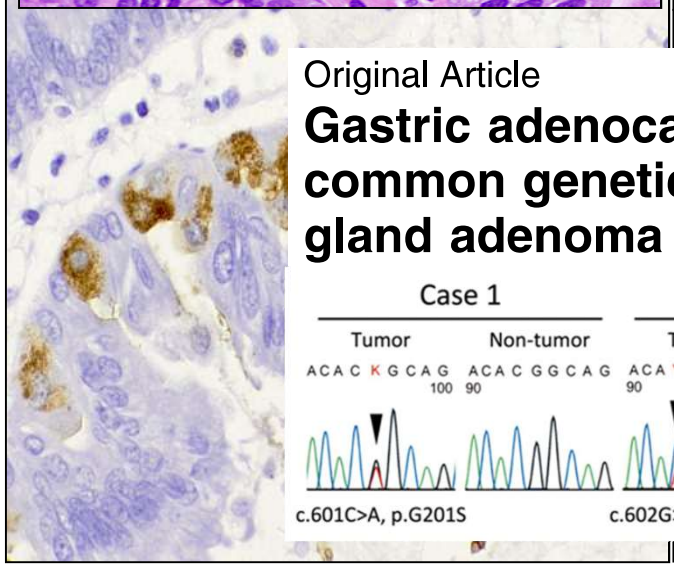
MUC5AC

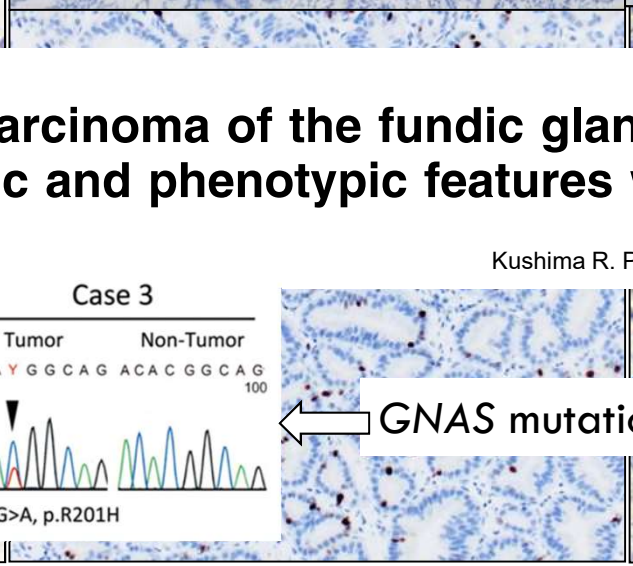
MUC6

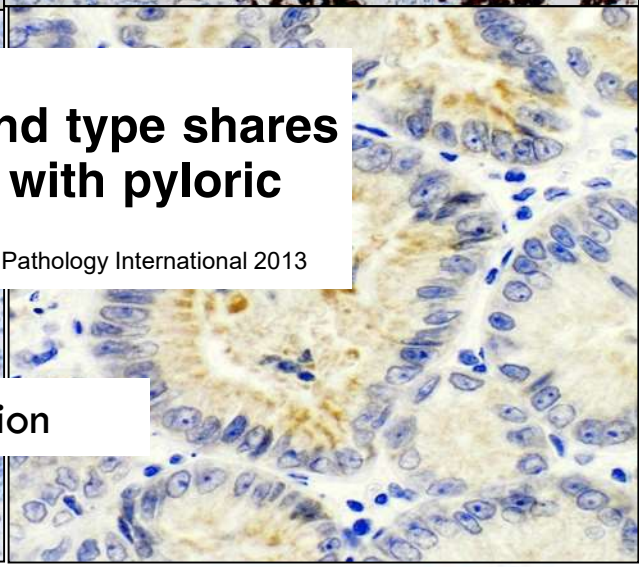












Original Article

Gastric adenocarcinoma of the fundic gland type shares common genetic and phenotypic features with pyloric gland adenoma

Kushima R. Pathology International 2013

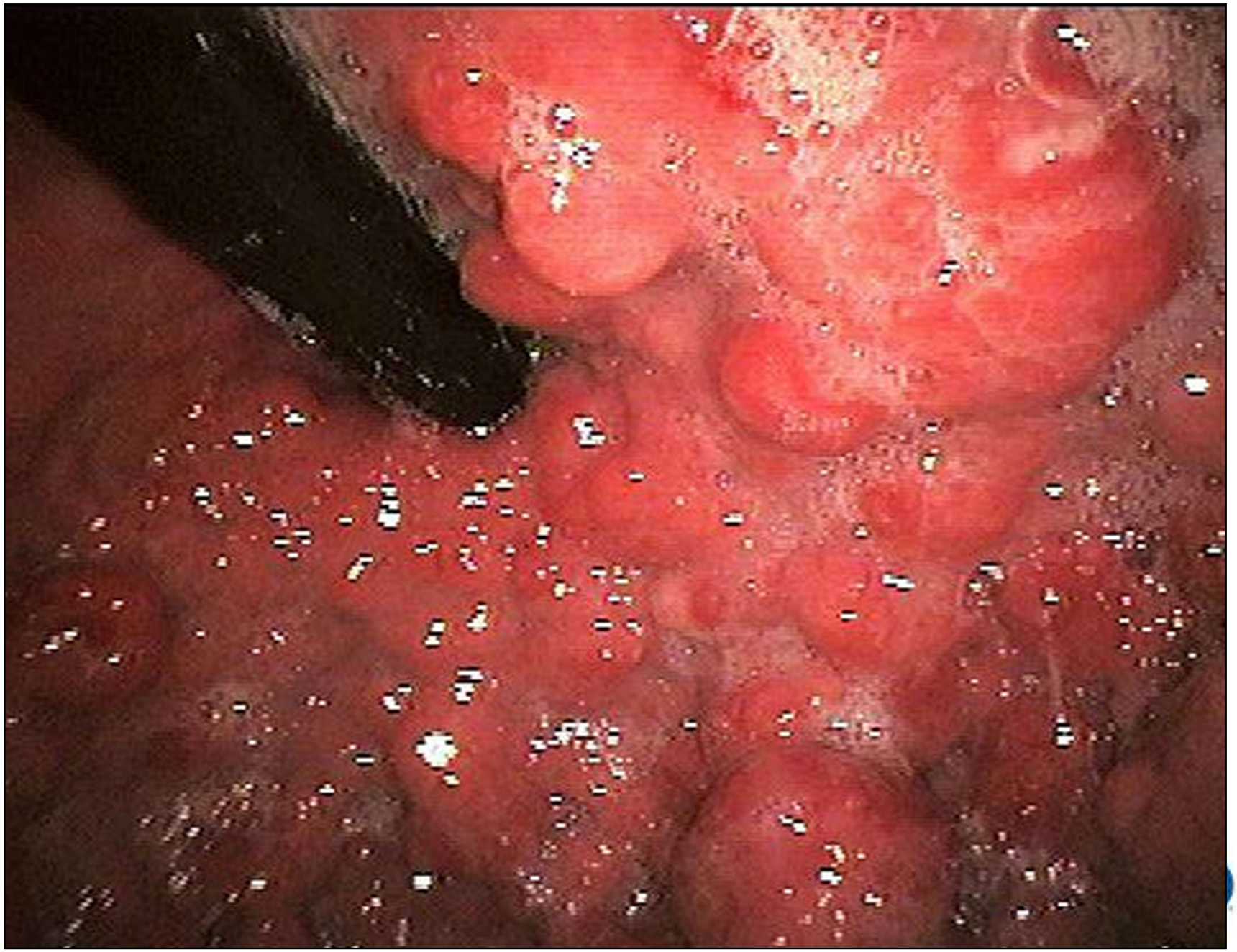
⇦ *GNAS* mutation

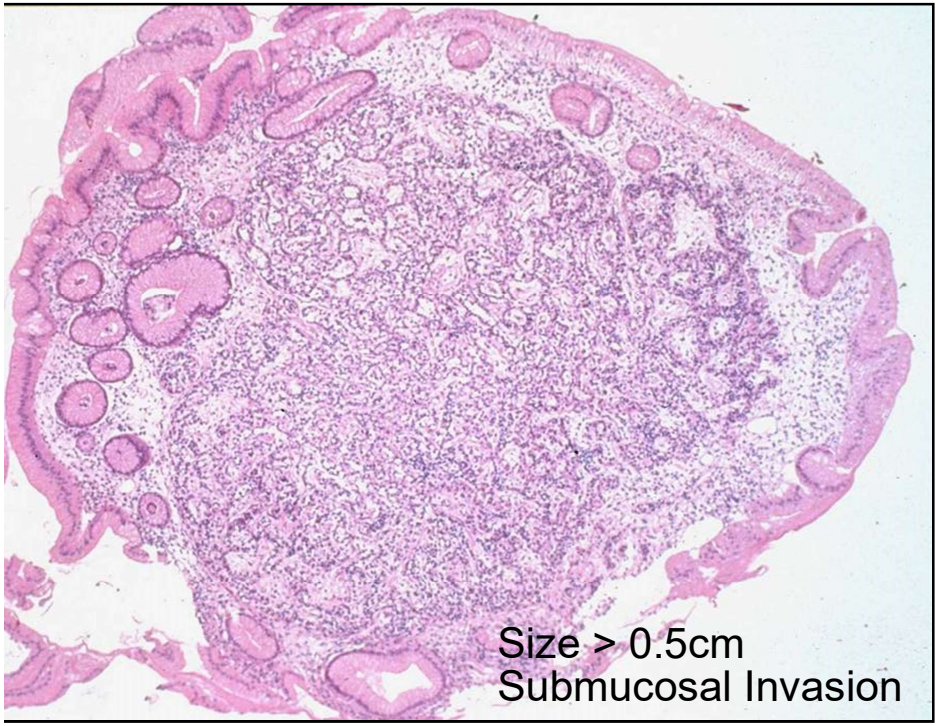
H^+/K^+ ATP ase

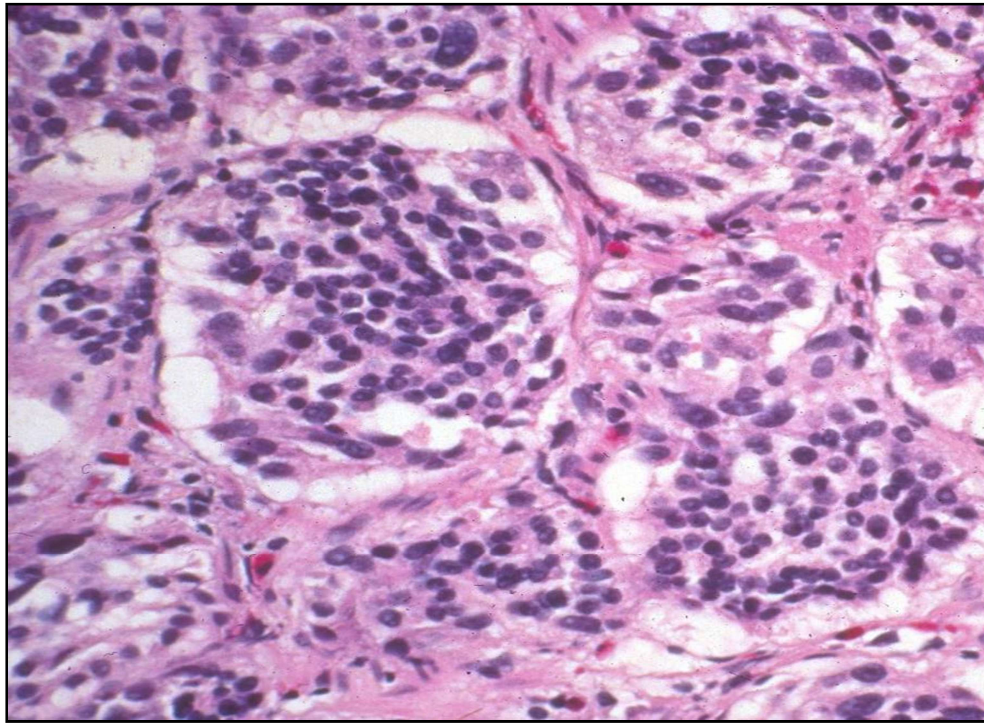
Ki-67

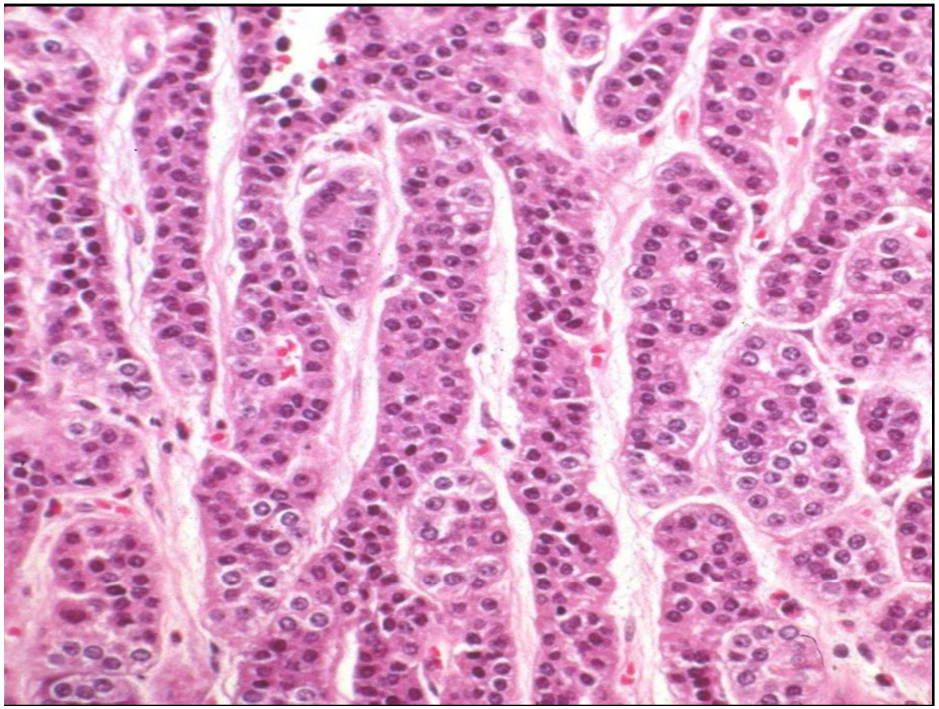
Pepsinogen I

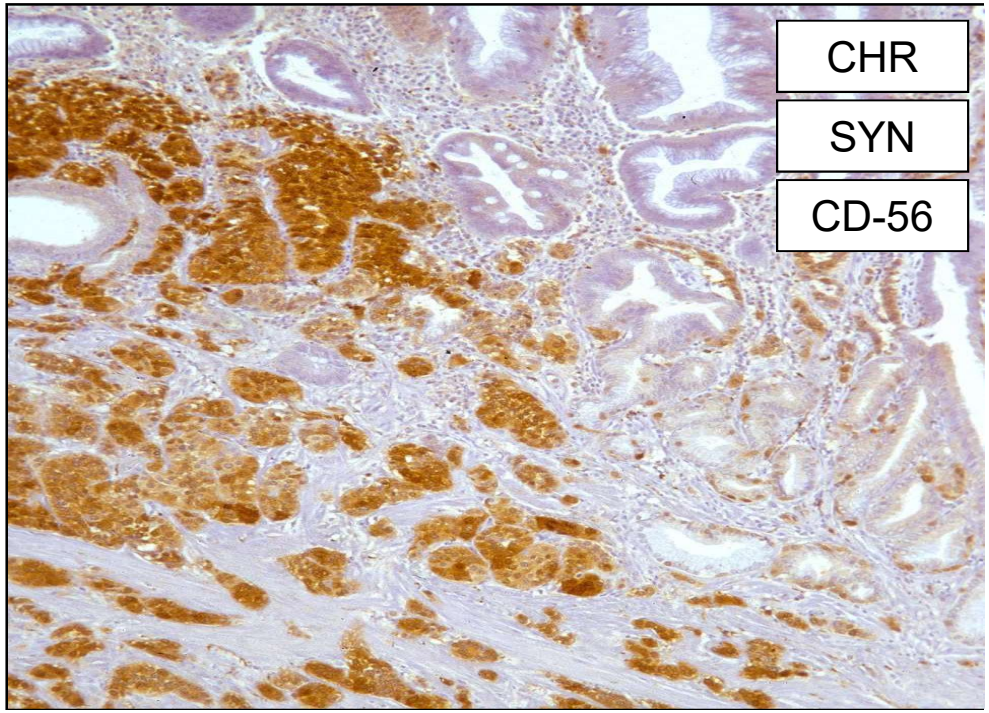
NET (Neuroendocrine Tumors) in Autoimmune Gastritis




Size > 0.5cm
Submucosal Invasion






CHR
SYN
CD-56

Gastric Neuroendocrine Tumors

Types 1,2, 3 are ECL cells tumors

- Increasing prevalence (?increase in endoscopic examination):
  - 2% of gastric malignancies (0.5% in '50)
  - 9% of intestinal neuroendocrine neoplasia (2.4% in '50)

Type	Background	%	Sex	# of tumors	Size	Invasion	Mets/ Prognosis
1	Autoimmune Gastritis ECL-cell hyperplasia	70	F (65%)	Multiple (70%)	Most are small	superficial	<10% Good
2	MEN-I,ZES, Hyperparathyroidism ECL-cell hyperplasia Non atrophic or hypertrophic mucosa	5-8	M=F	Multiple (100%)	Small (<1cm)	superficial	10% Good
3	Sporadic Normal or chronic gastritis but no atrophy	20	M (80%)	Single (100%)	Variable	deep	65% Mod/Poor

Grade 1 *(<2 mitoses x 10 HPF; <2% Ki67 index)*

Grade 2 *(<20 mitoses x 10 HPF; 3-20% Ki67 index)*

Type I Gastric NET
(most common)

- **Most common type (~70%)**
- **Predilection for older females**
- **Associated w/ autoimmune gastritis**
  - Hypo/achlorhydria
  - Hypergastrinemia & antral G-cell hyperplasia
  - Pernicious anemia (subset)
- **ECL cell proliferation**
- **Small and multicentric**
- **Rare angioinvasion**
- **Metastases are exceptional**
  - ***LN (5%); Liver mets (2.5%)***

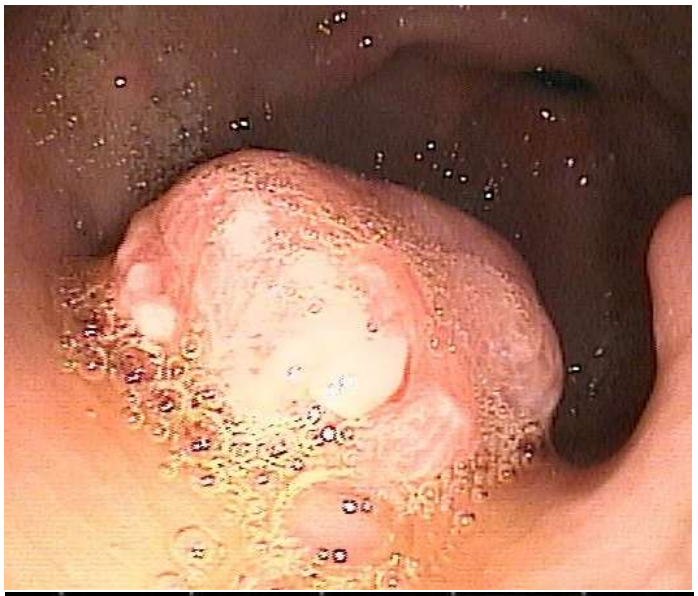
Type II Gastric NET
(least common)

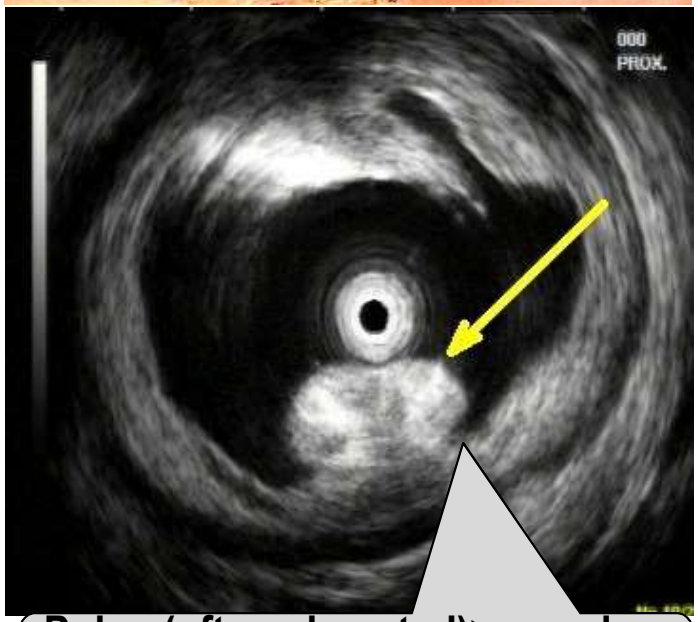
- **Associated w/ ZES/MEN-1 (13-30%)**
- **Hypertrophic hypersecretory gastropathy**
- Hypergastrinemia (gastrinoma associated)
- **ECL cell hyperplasia may be present**
- **Small and multicentric**
- **Metastases are rare**
  - ***LN (30%); Liver mets (10%)***

Management type I:

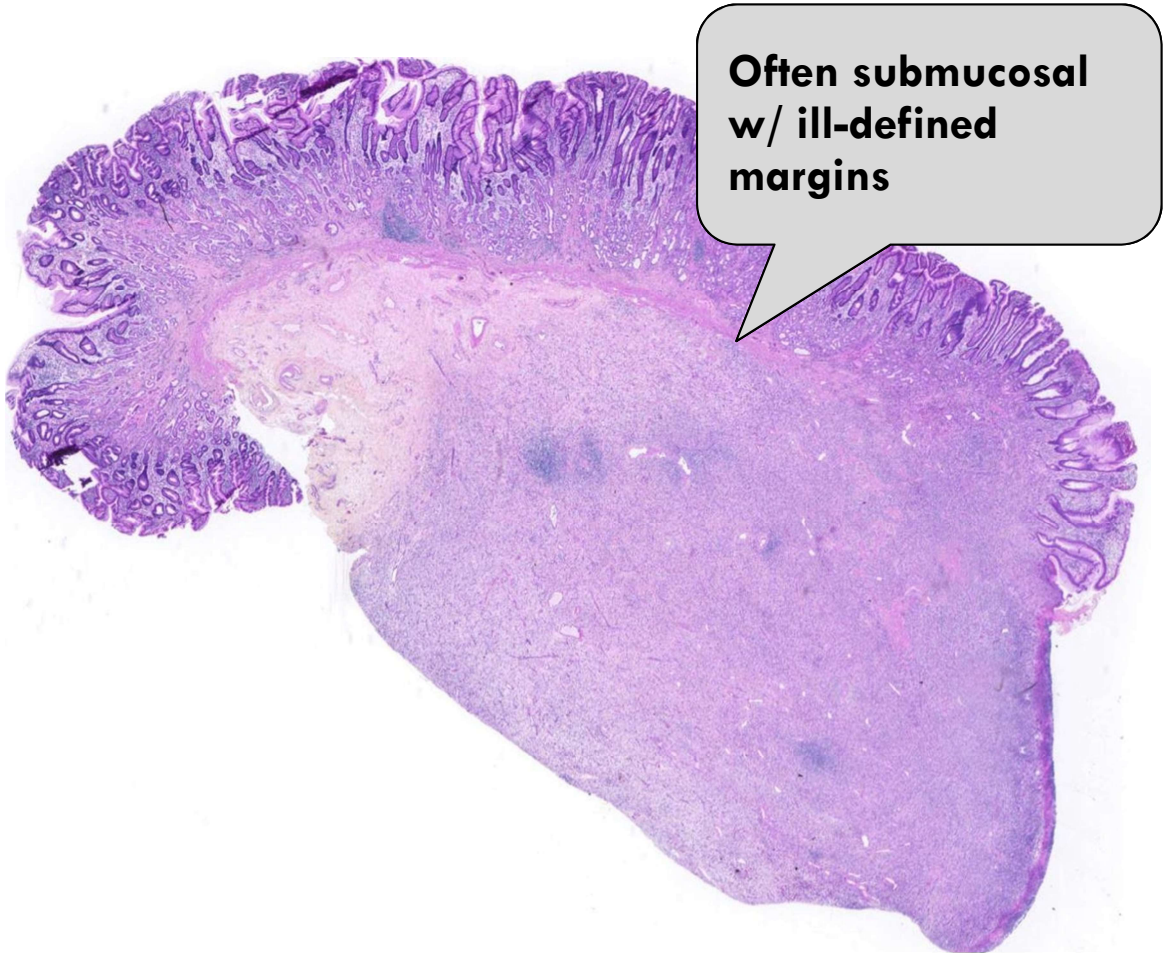
- > 2cm: high risk of metastases (resection either of the lesion or antrectomy)
- <1cm may remain stable in most cases
- 1-2 cm: ESD (or resection or antrectomy for numerous lesions)

Inflammatory Fibroid Polyp



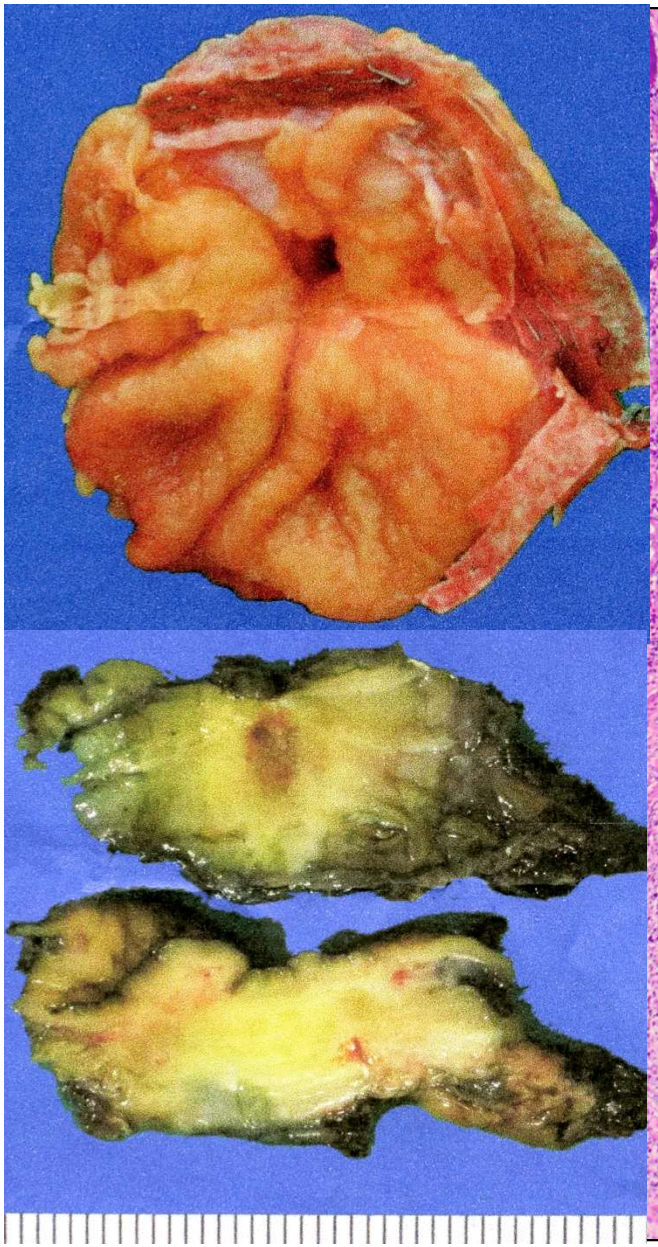


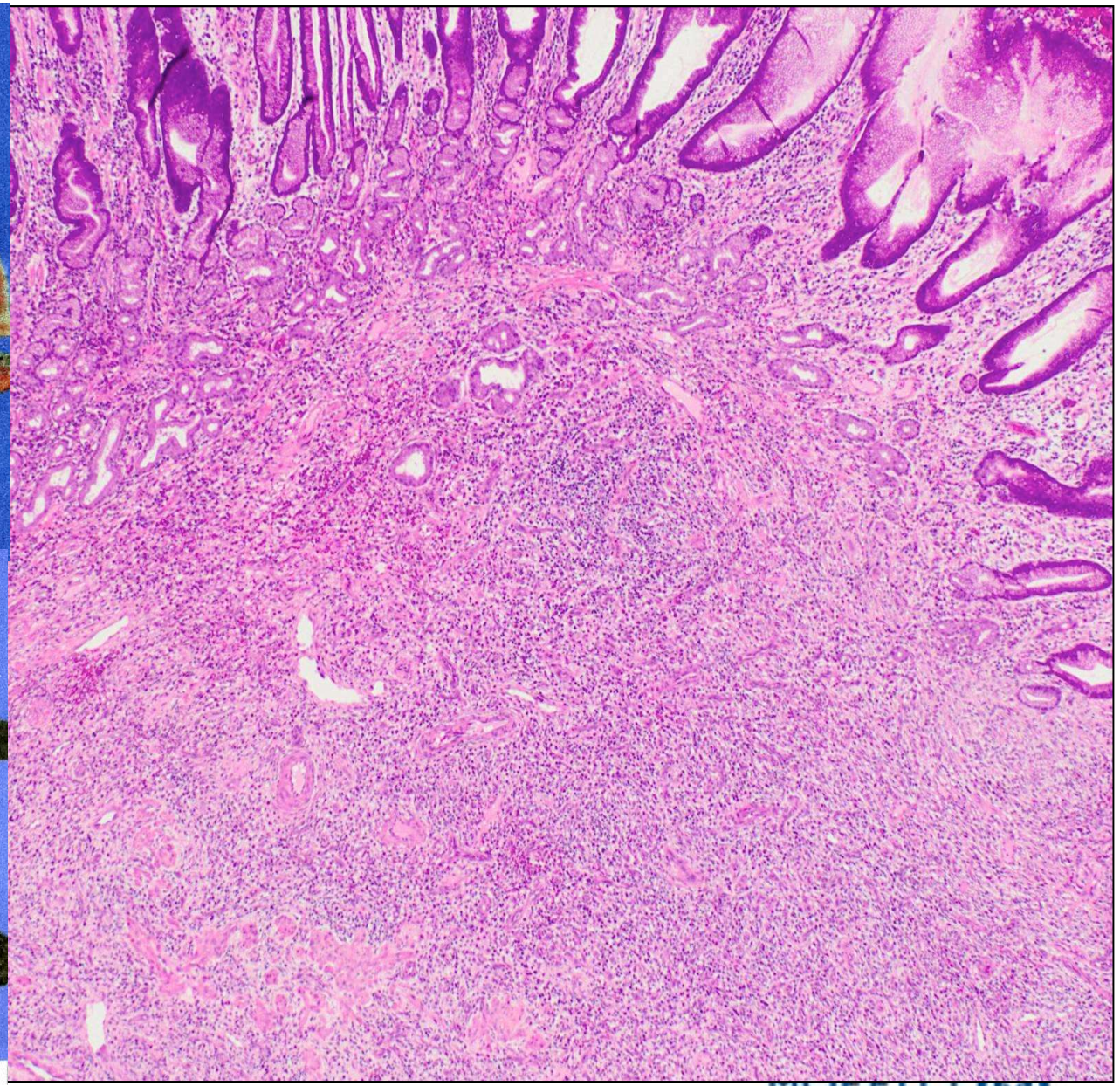
Polyp (often ulcerated)> mural mass

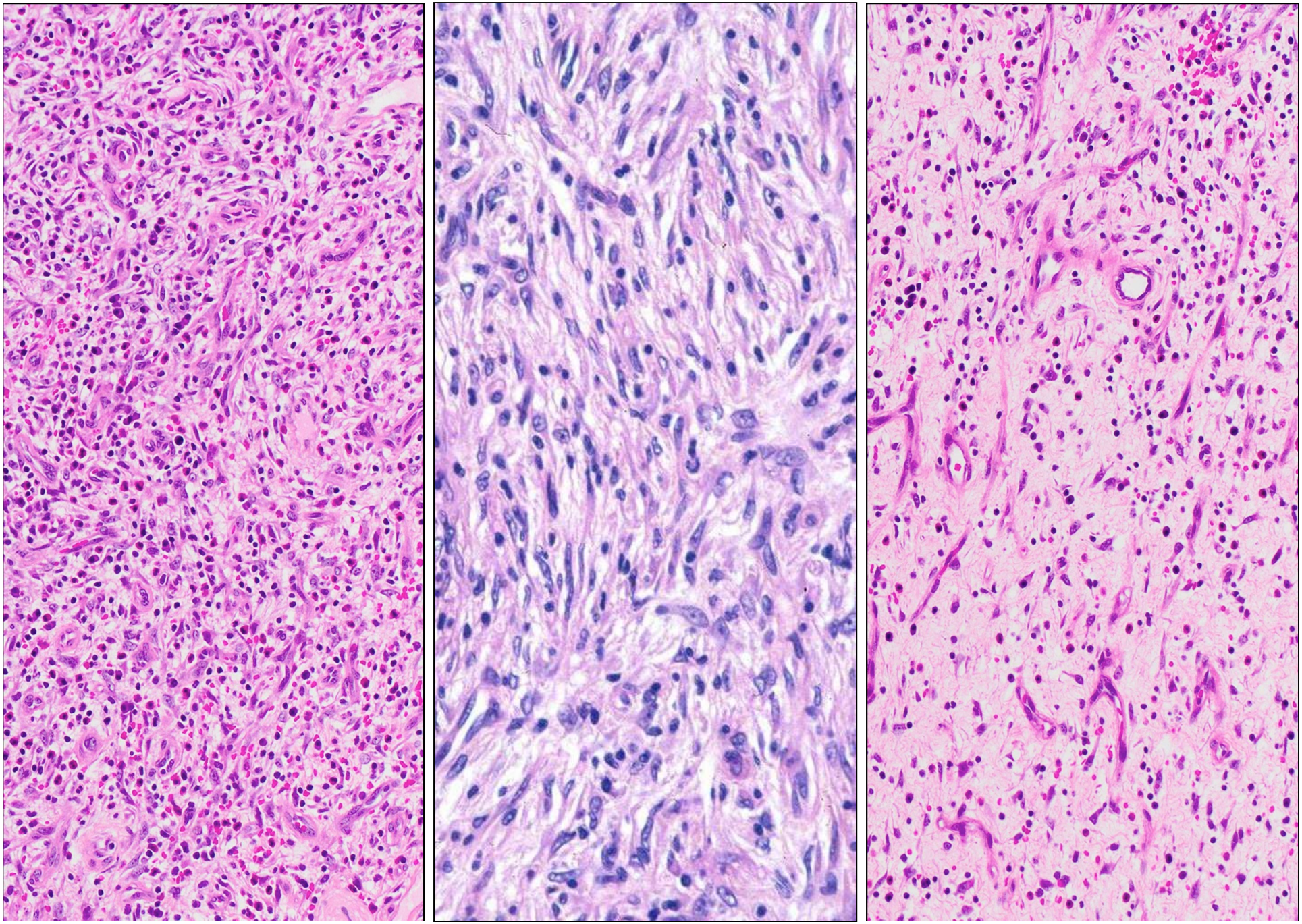


Often submucosal w/ ill-defined margins

- Benign- Antrum (70%) & ileum (20%)
- Wide age range (mean age 60)
- Intussusception (small bowel)



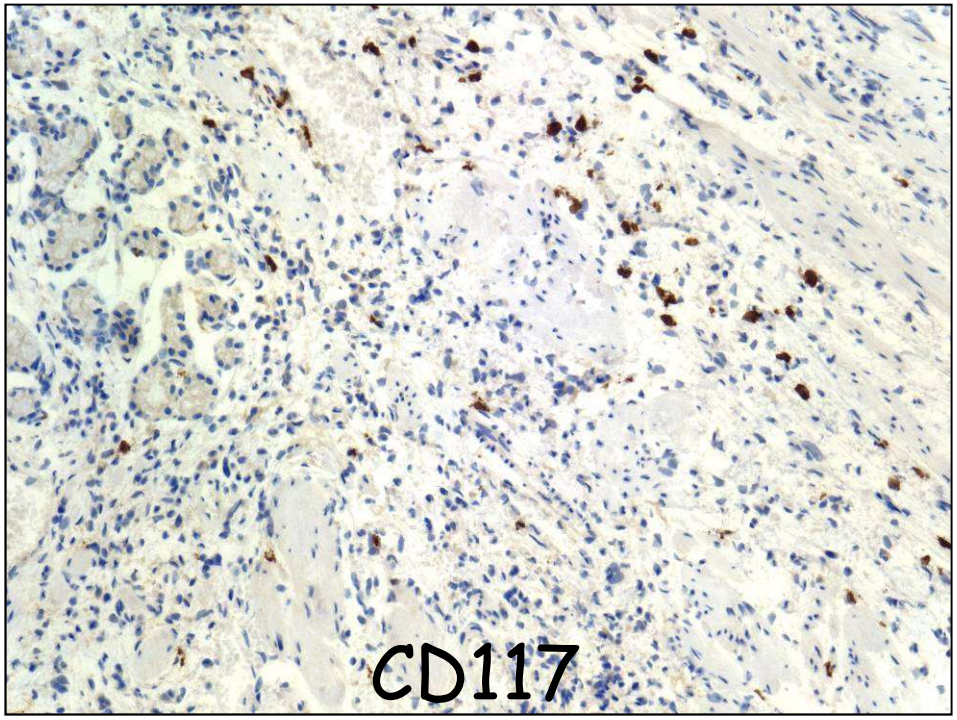


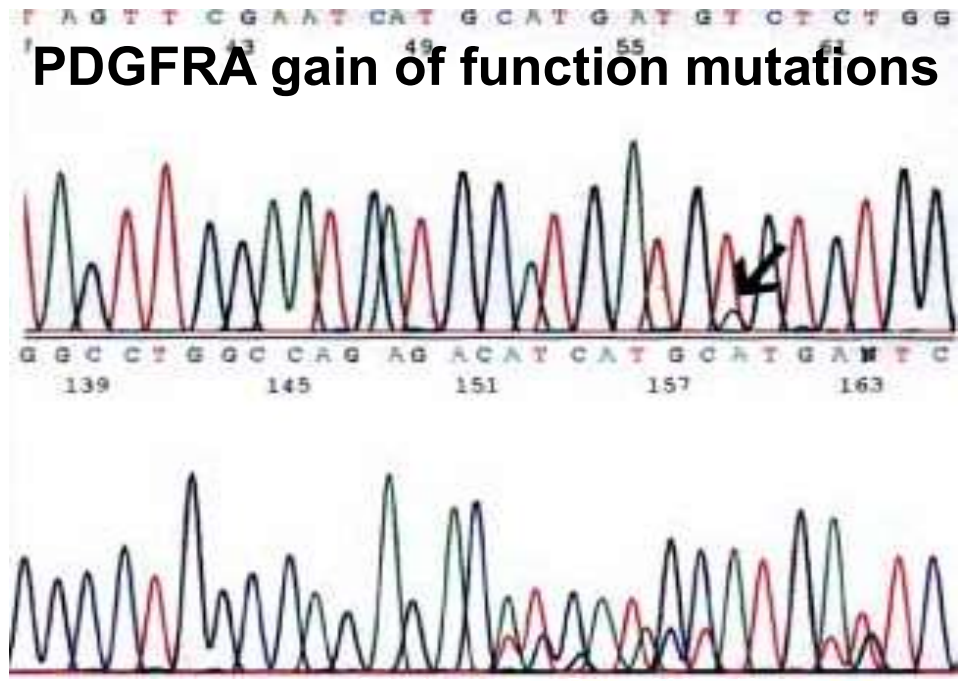


- Cell of origin: *fibroblastic? Myofibroblastic?, histiocytic or dendritic cells?*

- *cells are (+) for CD34, fascin and calponin, [SMA can be seen].*

- *c-kit, S100, desmin: negative.*





Gastric polyps: characteristics and management strategies

Table 2 Gastric polyp characteristics and malignant potential

Polyp type	Usual number and size	Usual site	Malignant potential of polyp	Malignant potential of background mucosa	Management
Sporadic fundic gland polyp					
Familial adenomatous polyposis-associated fundic gland polyp					
Hyperplastic					
Adenoma					

Goddard AF. Gut 2010;59:1270-1276

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Thank You!

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