Gastric polyps and thickened folds

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KOPANA Seminar
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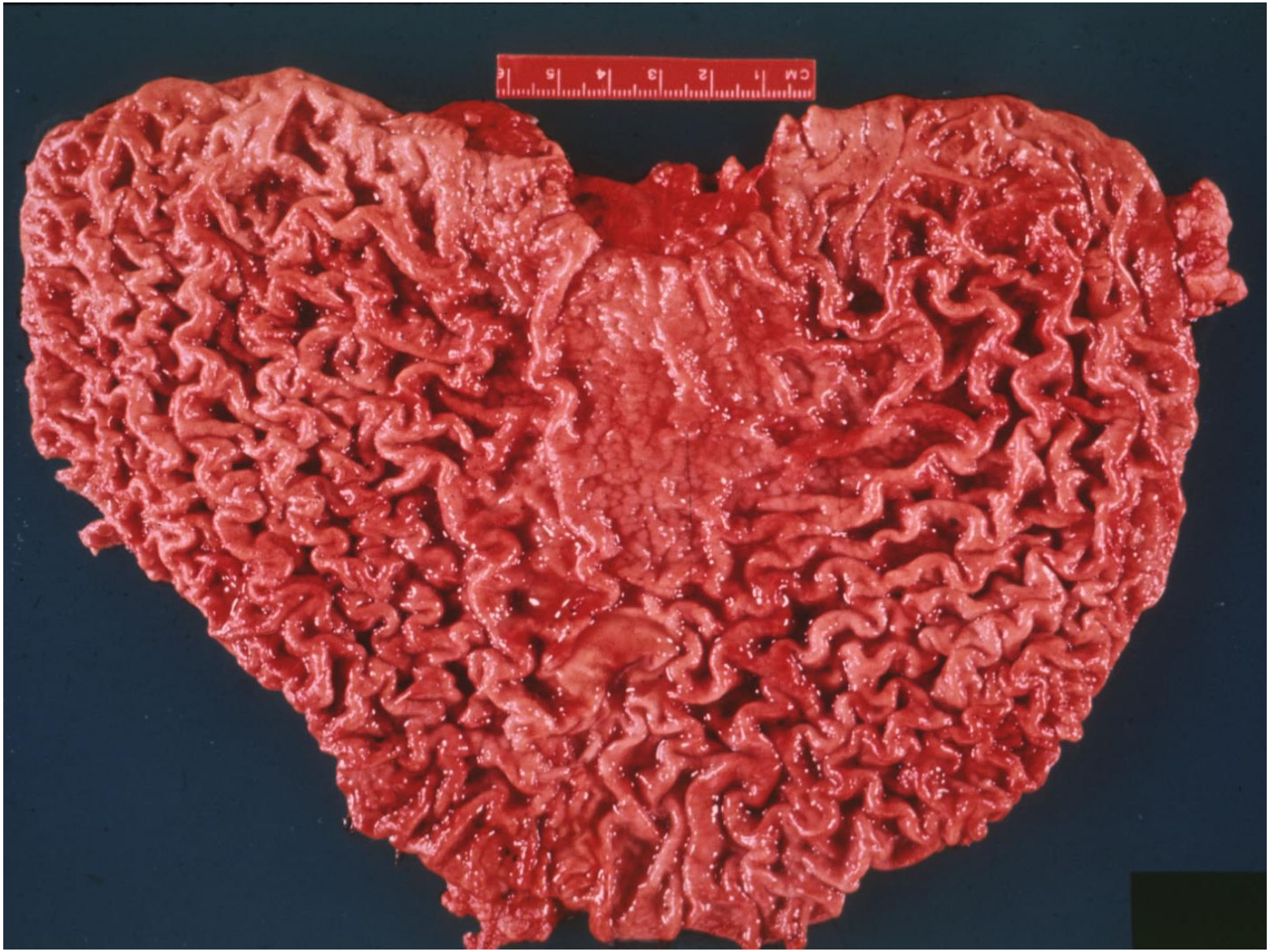
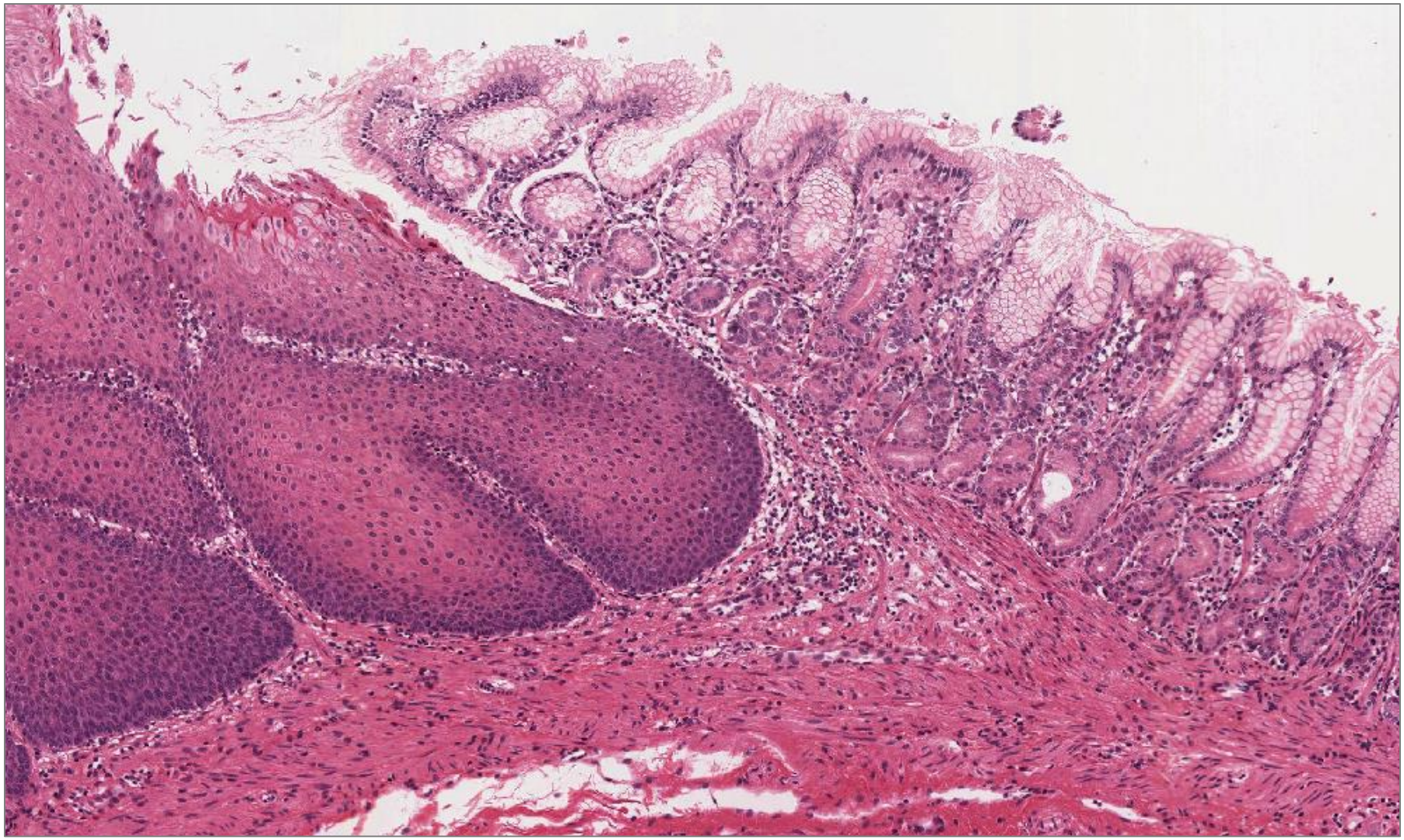
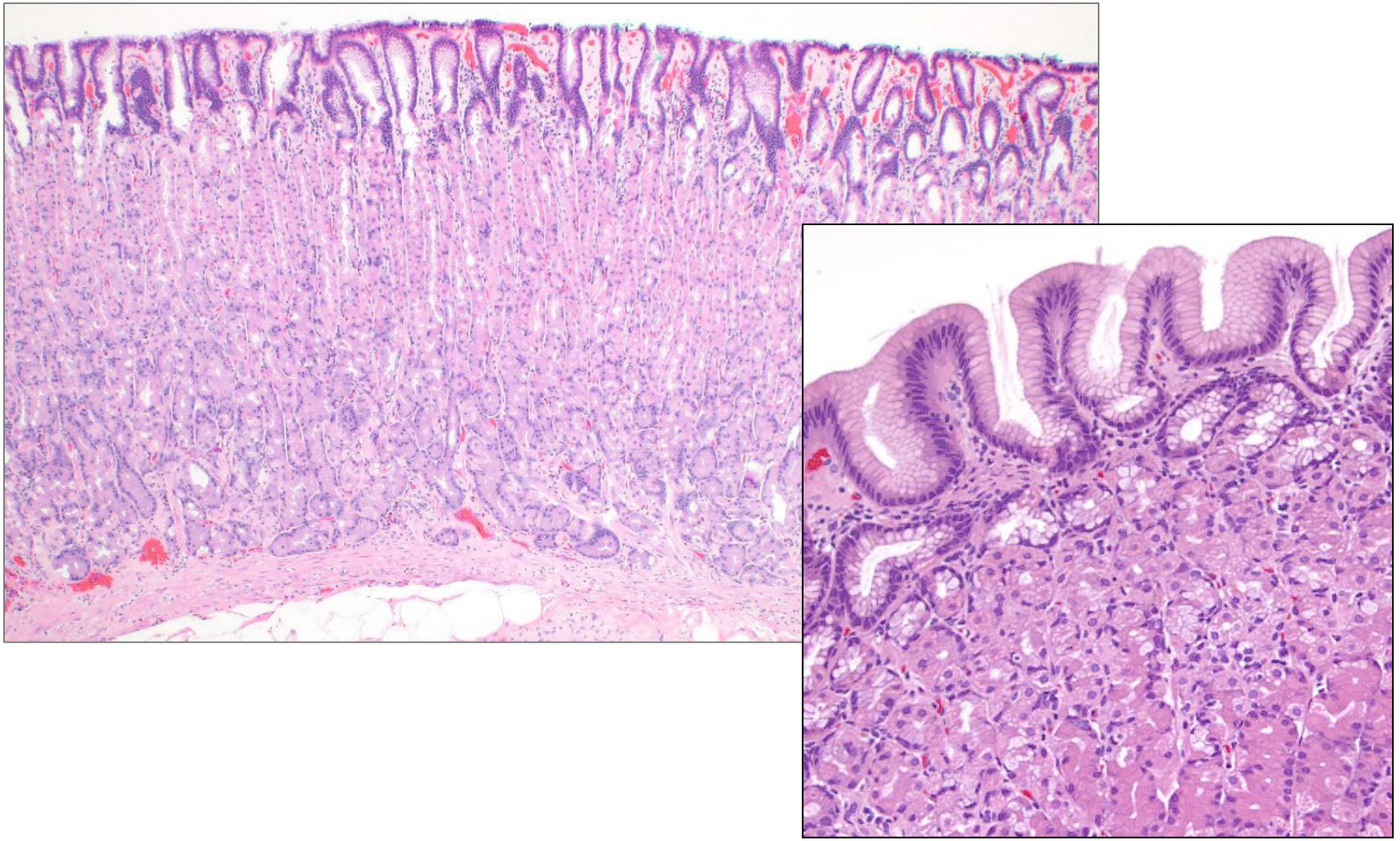
Normal stomach



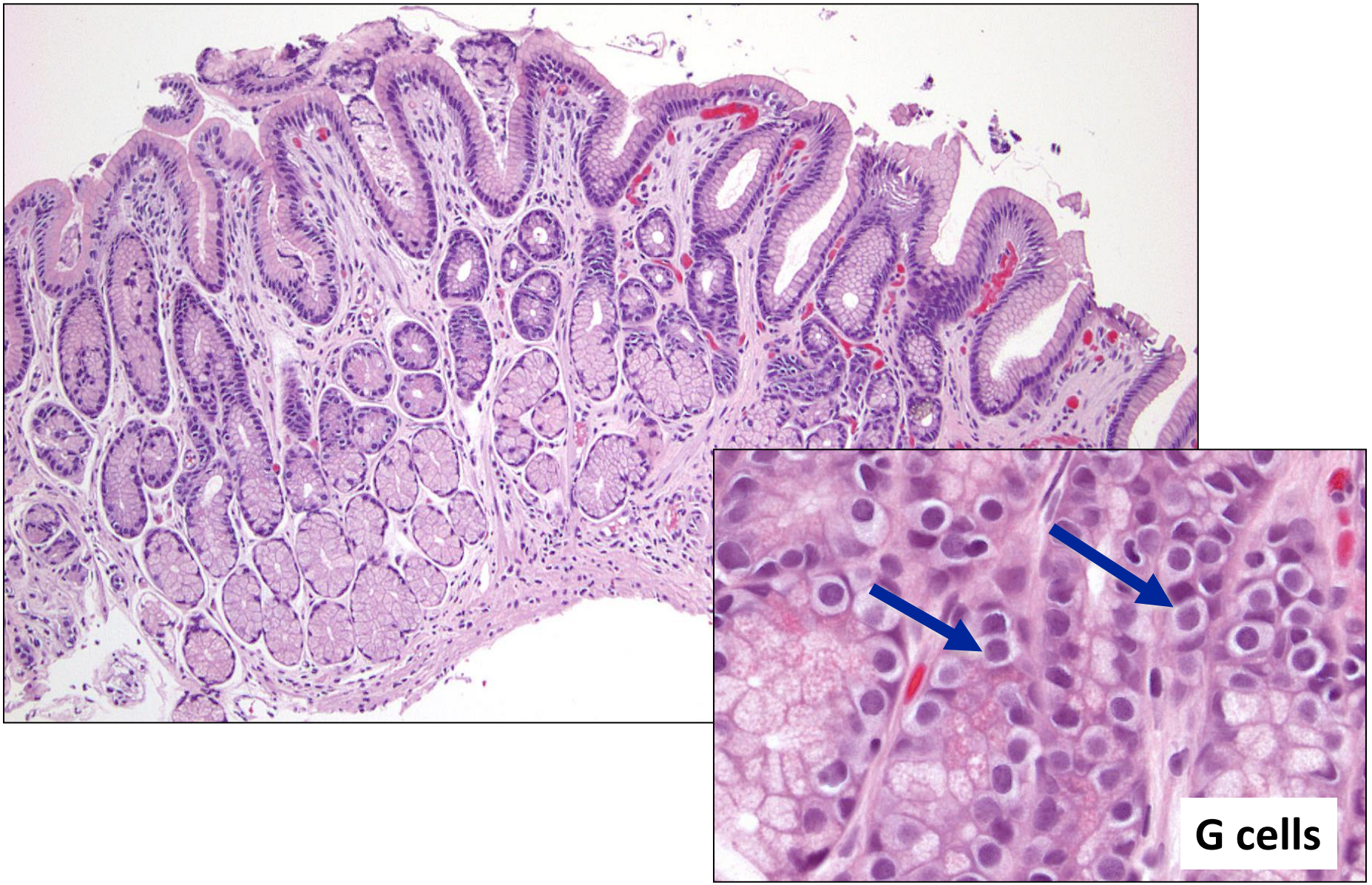
Squamocolumnar mucosa at the esophagogastric junction



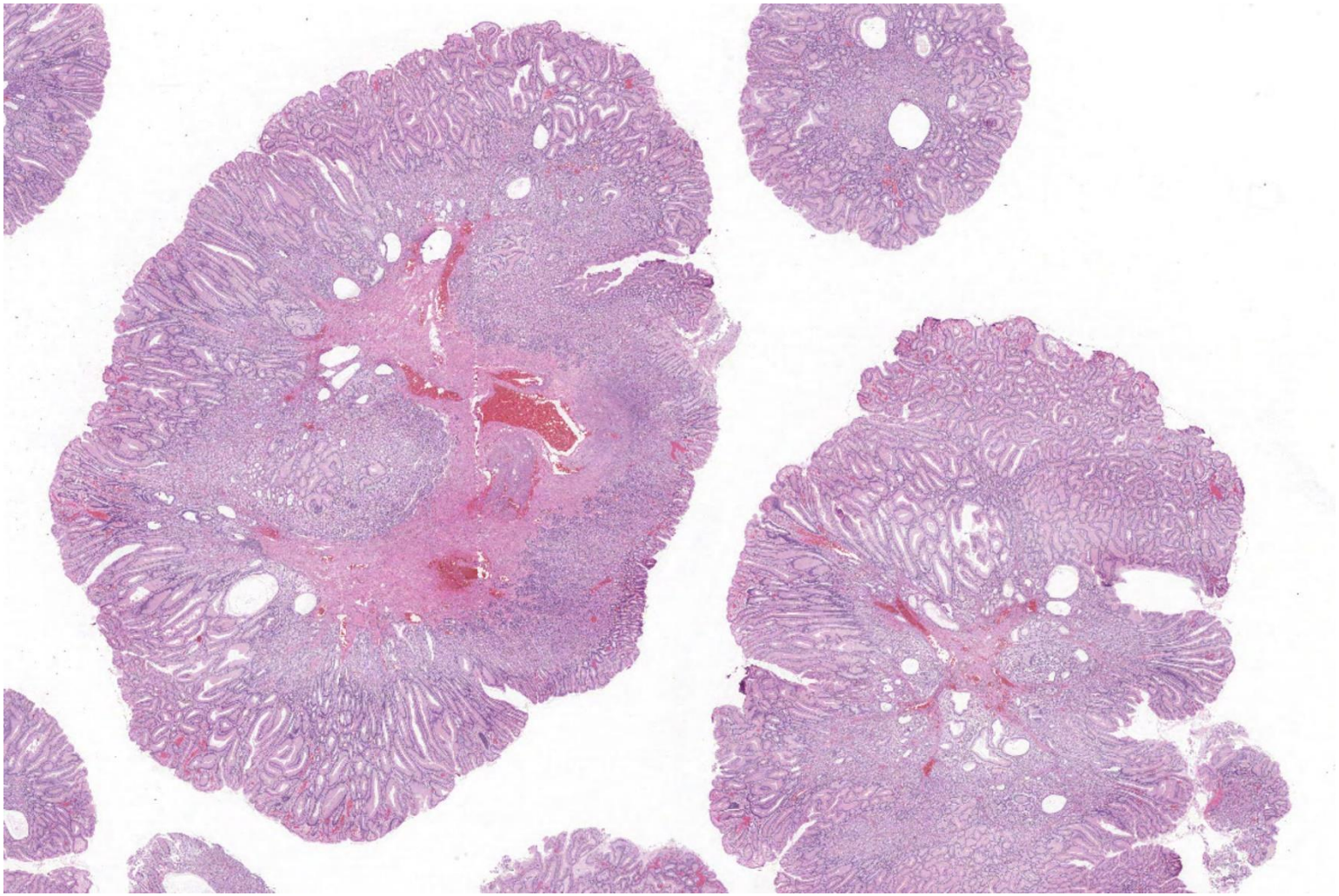
Oxyntic mucosa in gastric body & fundus

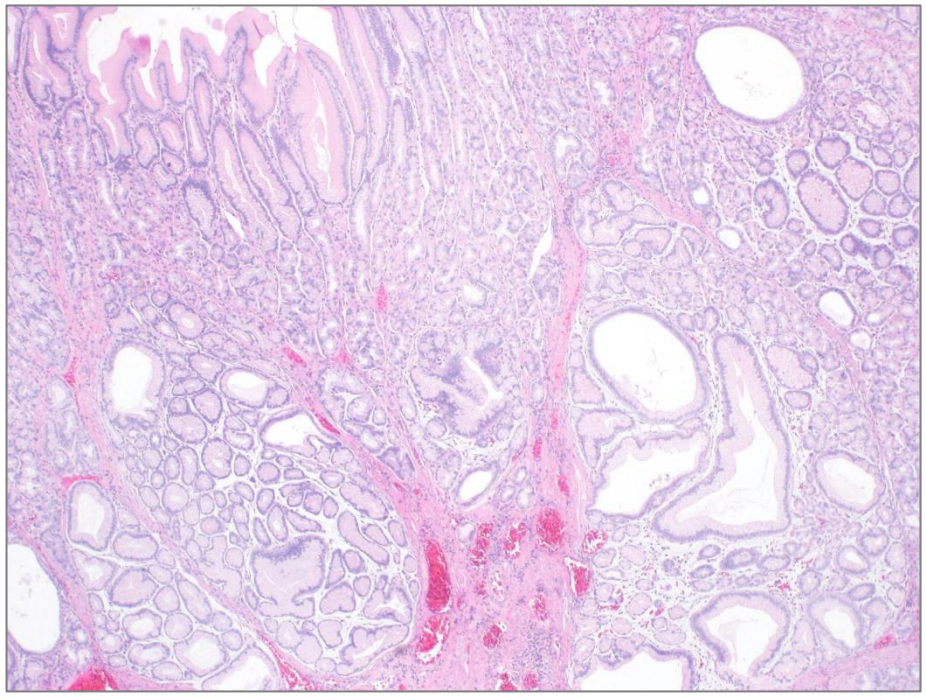


Gastric antrum

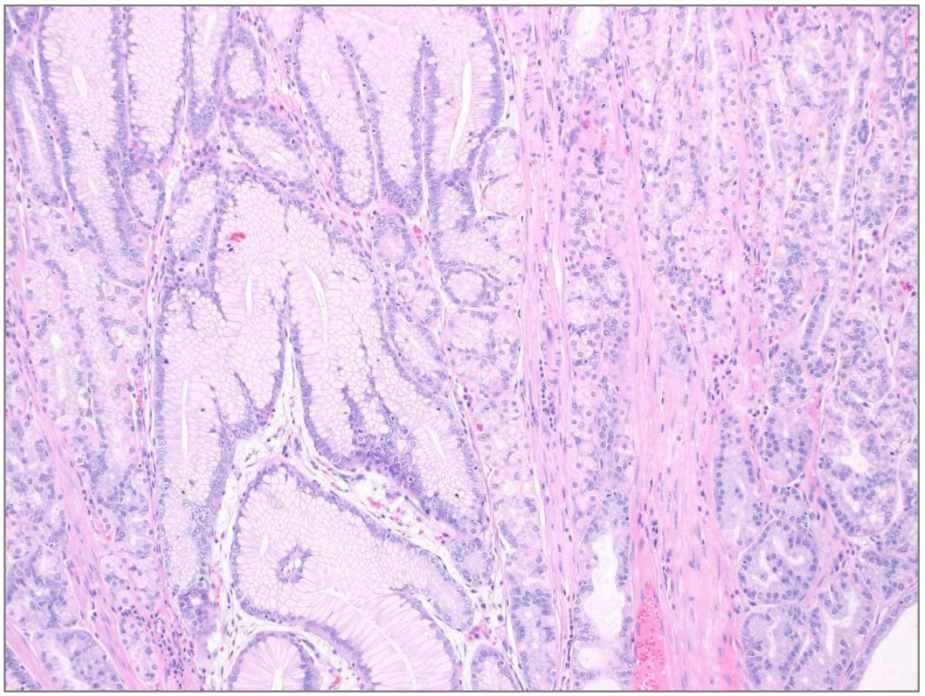


Case: 20 year-old man with multiple (>50) 0.3 - 2.0 cm gastric polyps. Several of the largest were removed





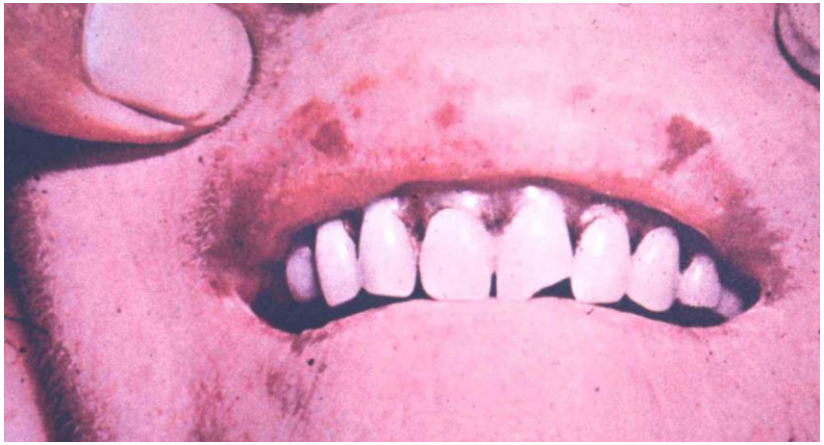
Branching smooth muscle



Disorganized gastric mucosal elements

Peutz-Jeghers syndrome

- ✓ Mucocutaneous pigmentation (lips, perioral, oral, palms, soles of feet)
- ✓ Hamartomatous gastrointestinal polyposis
- ✓ Increased risk cancer (e.g. GI tract, pancreas, lung, gynecologic, breast carcinoma, other neoplasms)



Peutz-Jeghers syndrome

Clinical diagnostic criteria (WHO 2010)

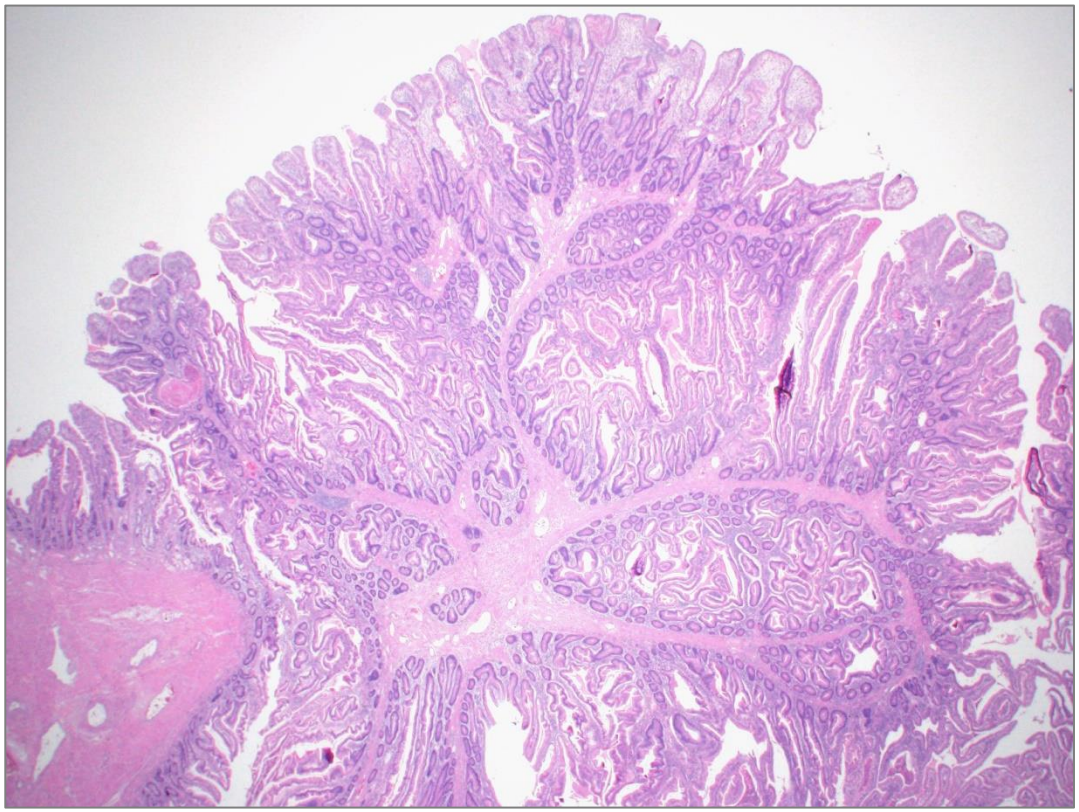
- ✓ 3 or more histologically confirmed PJP
- ✓ Any # PJP in an individual with family history of PJS
- ✓ Any # PJP in an individual who also has characteristic, prominent mucocutaneous pigmentation
- Characteristic, prominent mucocutaneous pigmentation in an individual with family history of PJS

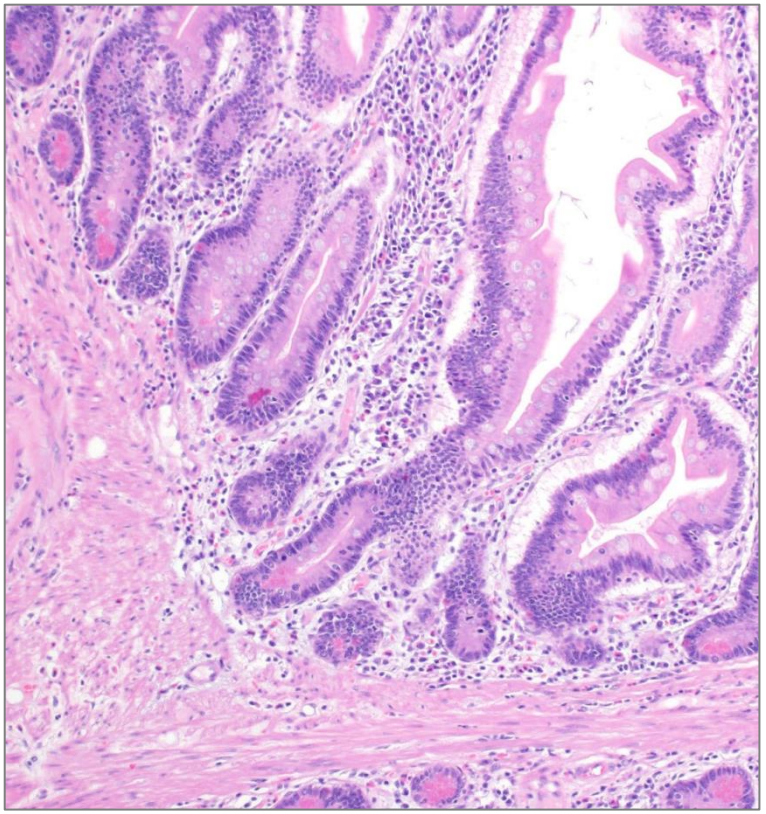
Genetics

- ***STK11*** / ***LKB1*** tumor suppressor gene mutation in most cases
- Autosomal dominant inheritance pattern

Peutz-Jeghers polyps

<u>Microscopic</u>: Arborizing bands of smooth muscle covered by native mucosa (hamartomatous polyps)



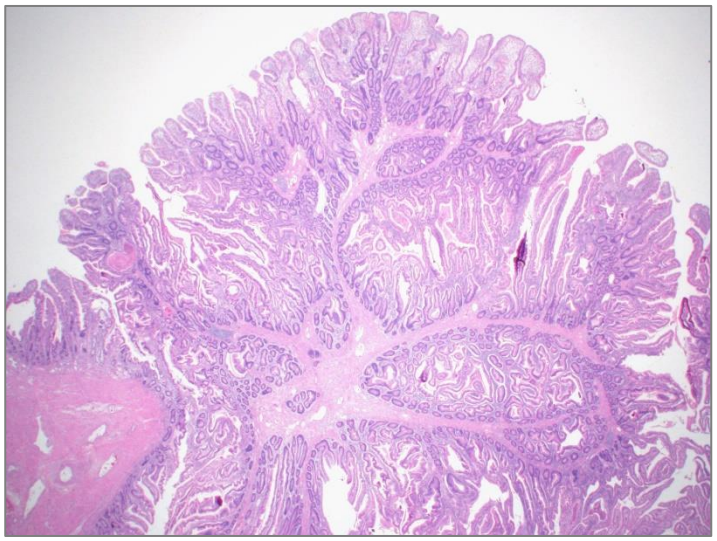


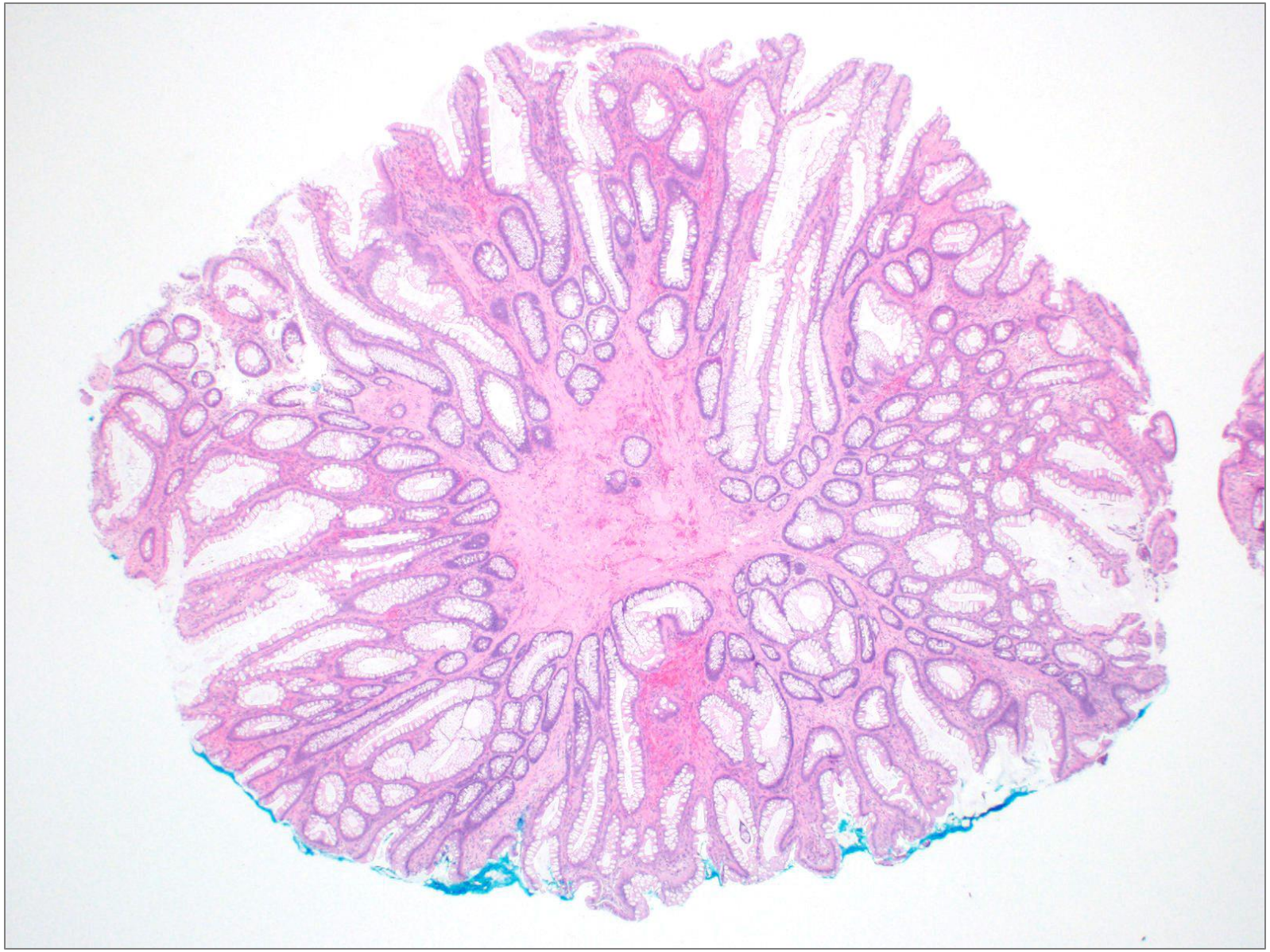
Small intestine Peutz-Jeghers polyp

Peutz-Jeghers polyps

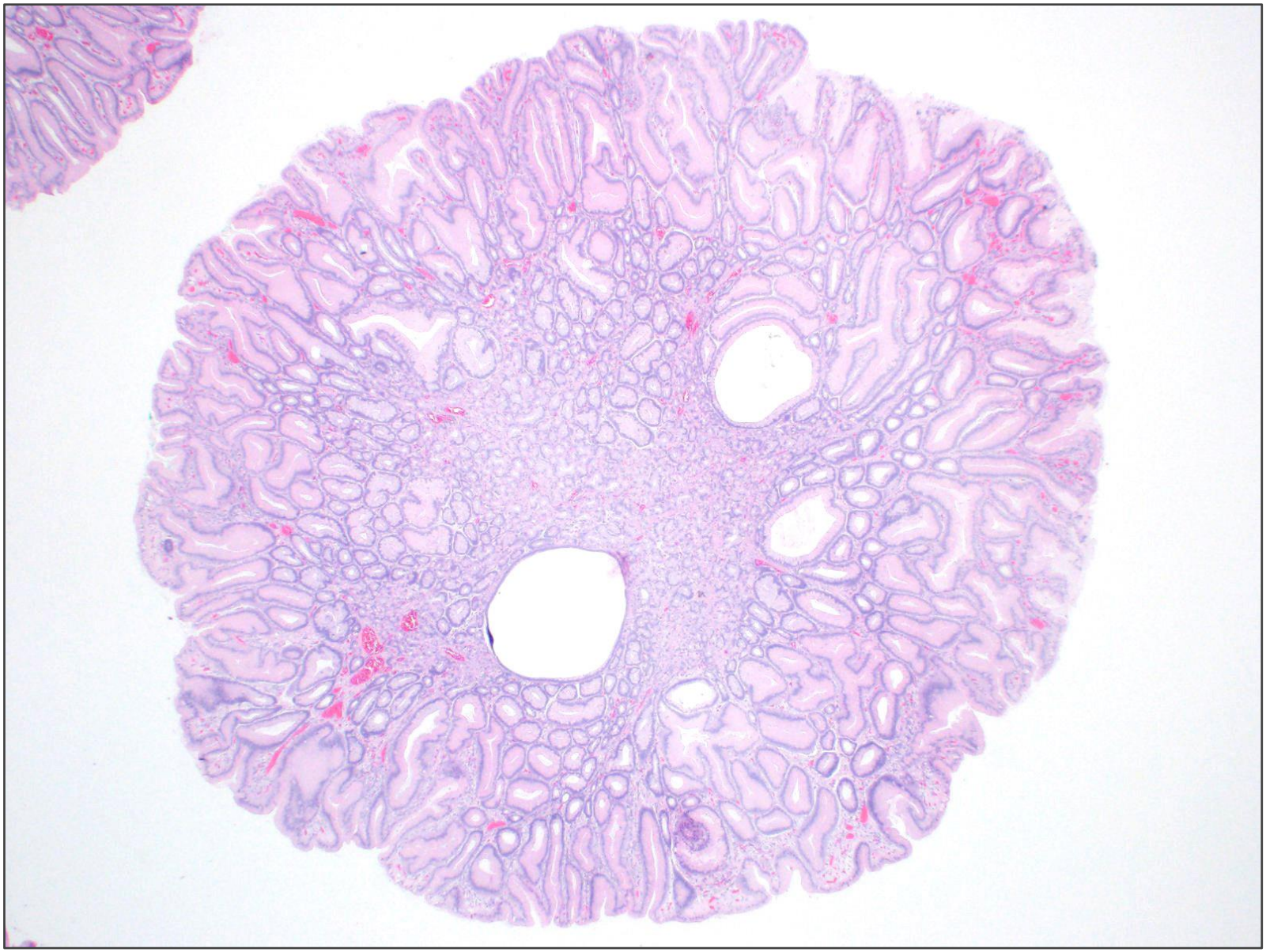
<u>Microscopic</u>: Hamartomatous polyps with arborizing bands of smooth muscle covered by native mucosa

- Features best seen in small bowel polyps
- Gastric and colonic polyps may not have typical morphology, but presumed to be PJPs when patient has known PJS
- Dysplasia is rare





Colonic Peutz-Jeghers polyp



Stomach: Peutz-Jeghers polyp lacking arborizing smooth muscle

Am J Surg Pathol. 2010 Nov;34(11):1656-62.

Morphologic Characterization of Syndromic Gastric Polyps

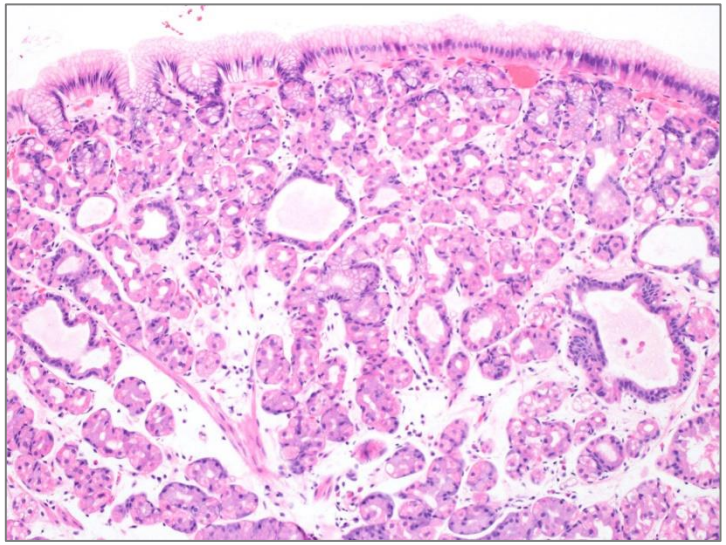
Dora Lam-Himlin, MD, Jason Y. Park, MD, PhD, Toby C. Cornish, MD, PhD, Chanjuan Shi, MD, PhD, and Elizabeth Montgomery, MD

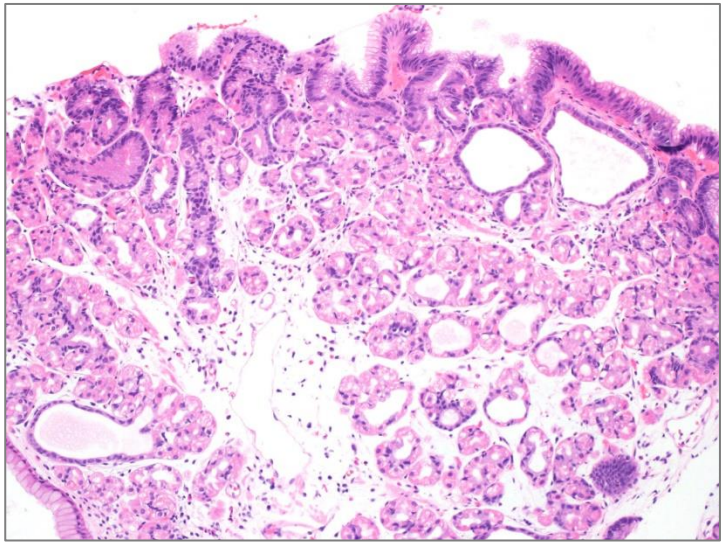
- Polyps included in study:
  - Gastric polyps from patients with Peutz-Jeghers syndrome and Juvenile polyposis
  - Hyperplastic polyps from non-syndromic patients

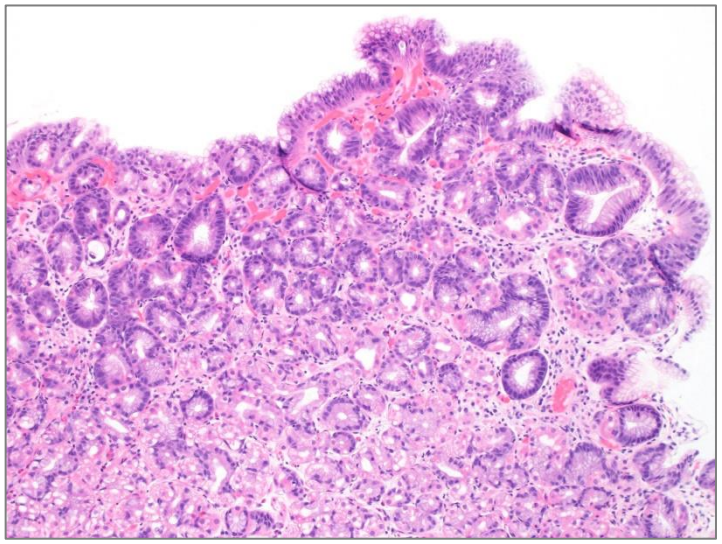
- Adhering to histologic criteria, accuracy was better for PJP (54%) but was worse for JP (41%) and HP (73%). Accuracy better if polyp >1cm.

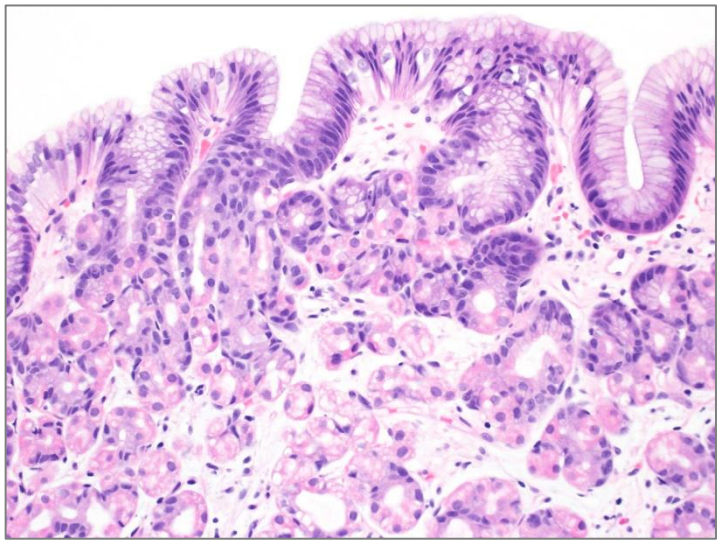
- **Conclusion: Histologic features to distinguish gastric JPs and PJPs from HPs are unreliable**

Case: 35 year-old woman with innumerable gastric polyps









Familial adenomatous polyposis

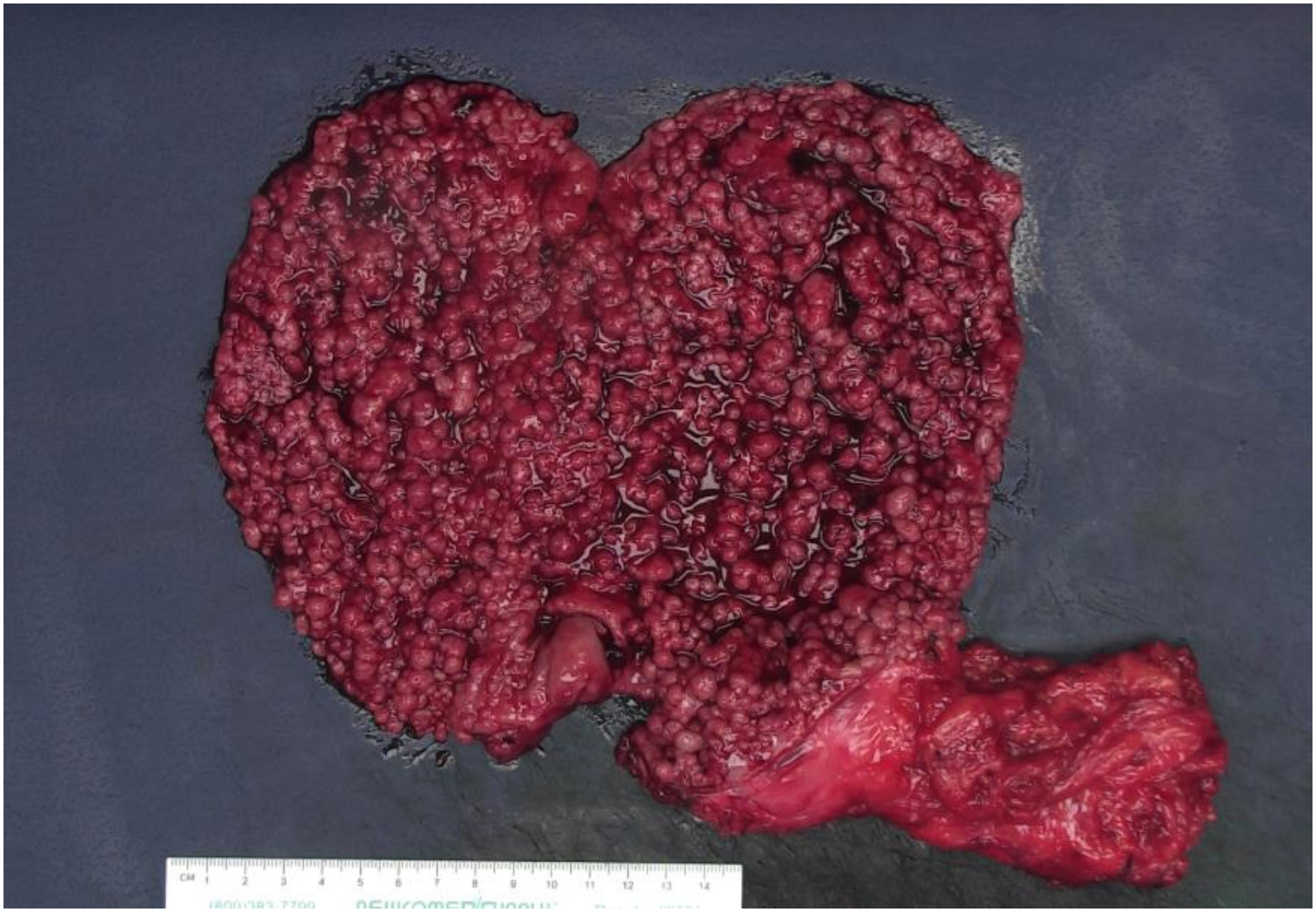
- *APC* tumor suppressor gene mutation
- Autosomal dominant pattern of inheritance

- Gastrointestinal manifestations
  - Numerous colonic adenomas
  - Small intestine adenomas
  - Stomach polyps:
    - Mostly FGPs +/- LGD dysplasia in Western populations
    - Adenomas (foveolar-type, pyloric gland adenomas)

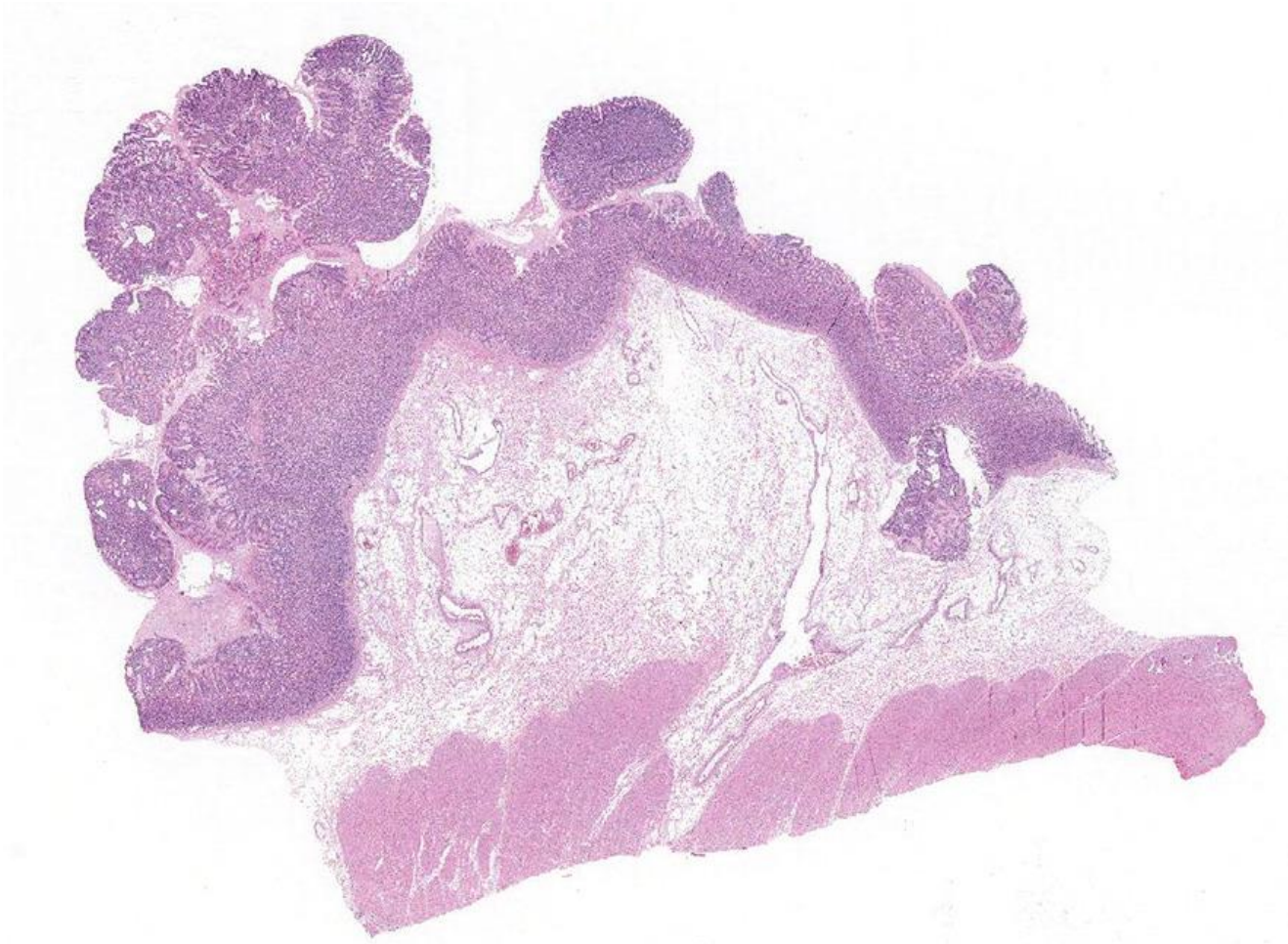
Dysplastic fundic gland polyps

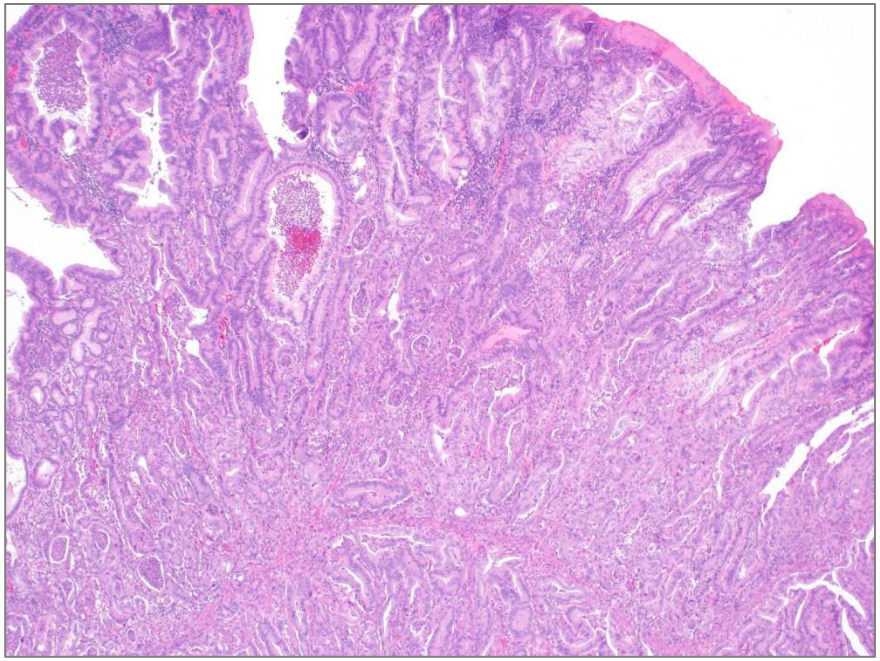
- FGPs with LGD
  - FAP, other syndromes (MUTYH-associated polyposis)
  - Sporadic
- Risk of malignant transformation of FGP with dysplasia very low in Western populations
- Conservative management

Stomach resected from patient with FAP

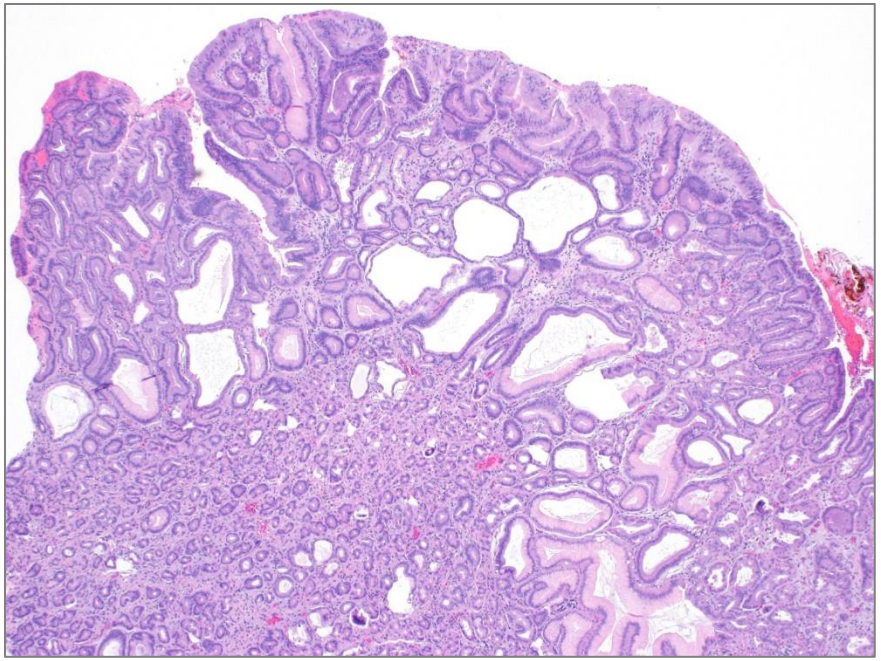


Numerous FGPs with LGD



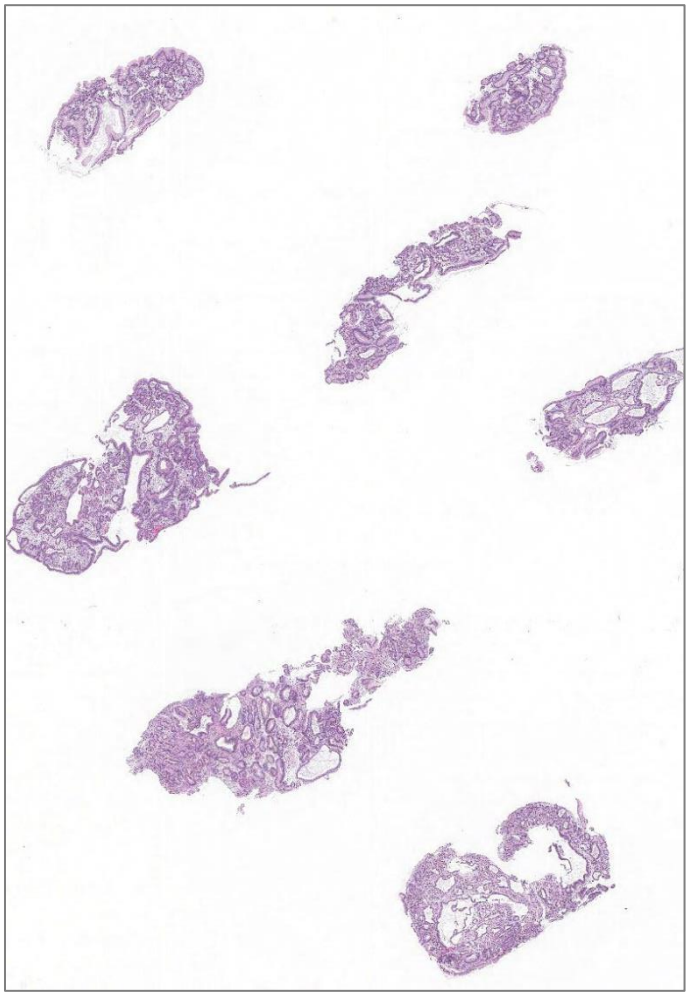


Adenocarcinoma arising in an adenoma

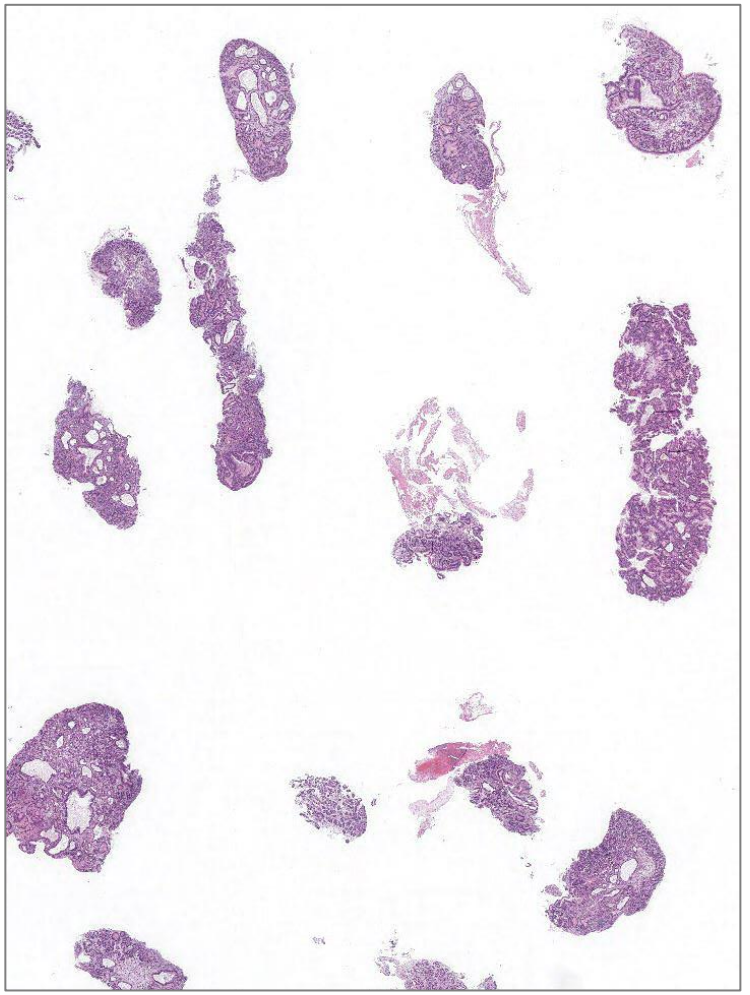


Dysplastic FGP

Case: 55 year-old woman with numerous polyps in the gastric body and fundus. Polyps and intervening mucosa biopsied:



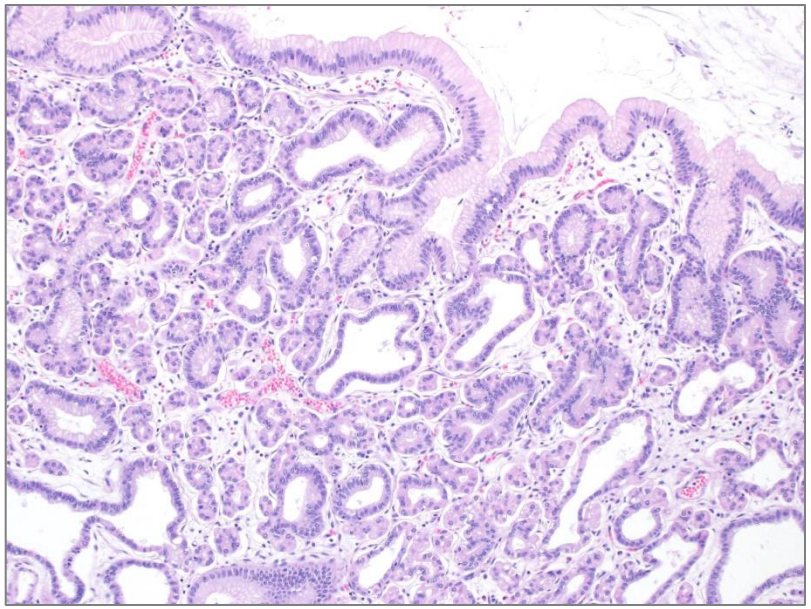
Polyps



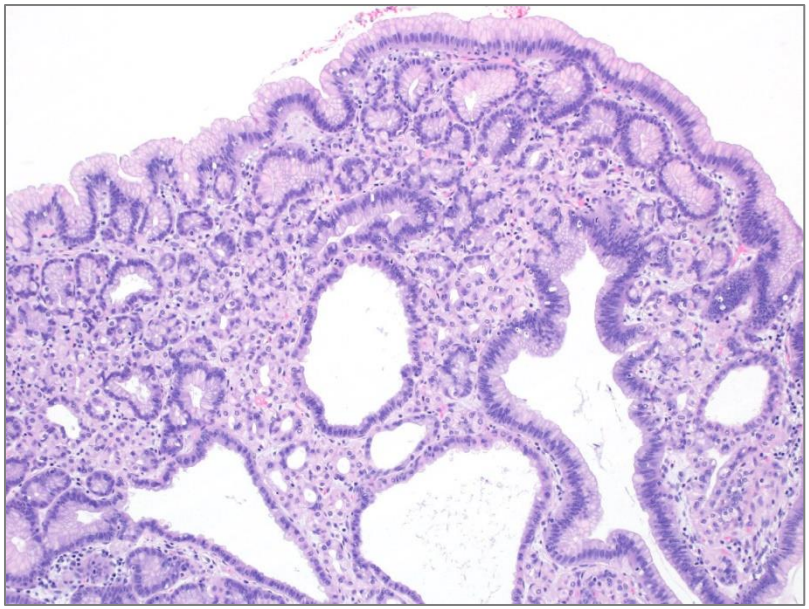
Intervening flat mucosa

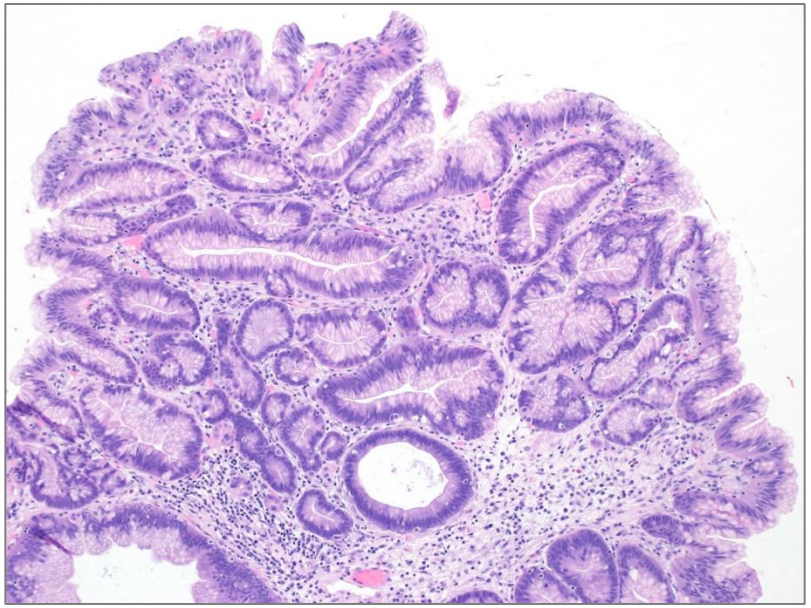
Polyp biopsies

Mostly fundic gland polyps



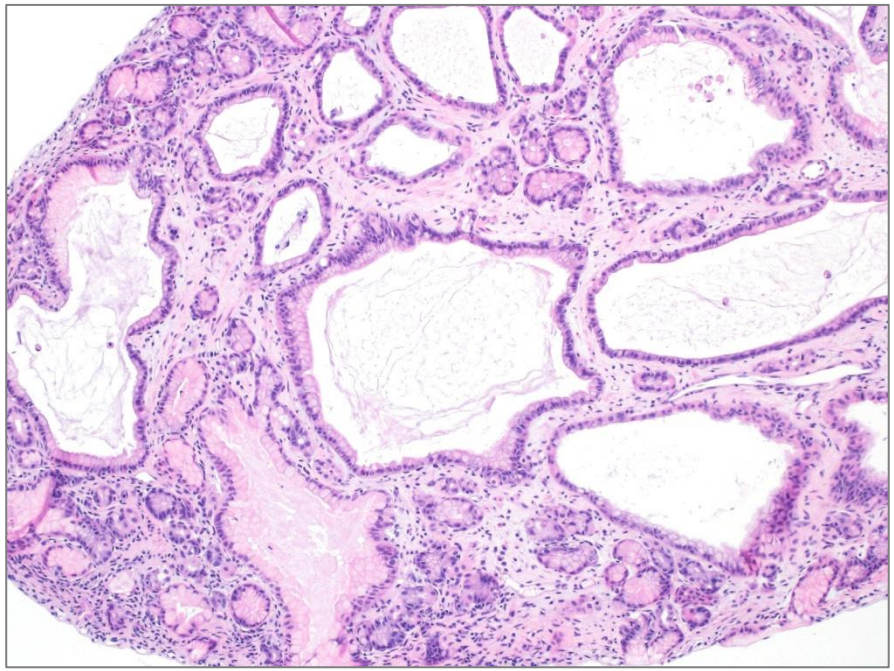
Some FGPs dysplastic



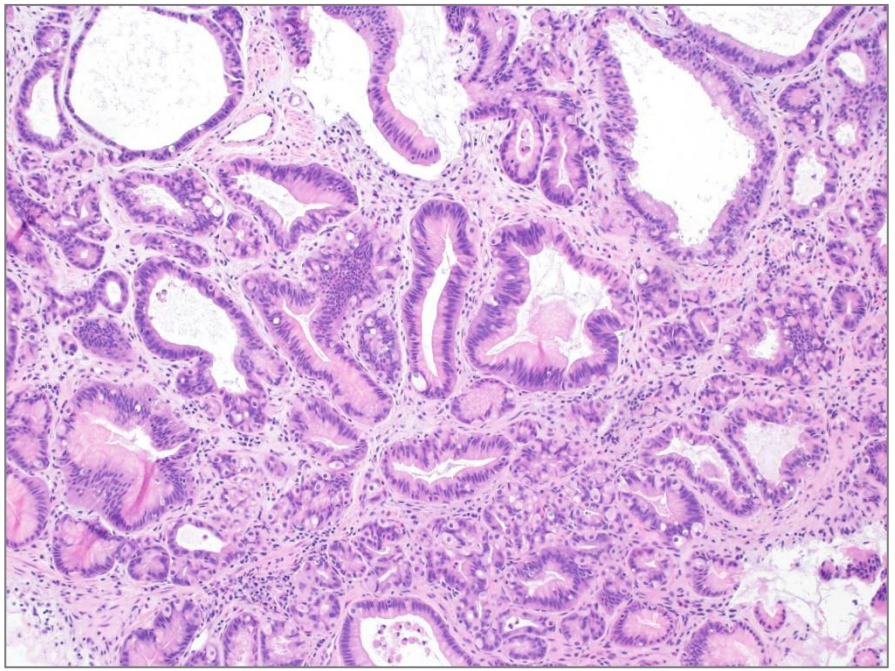


Few adenomas (foveolar)

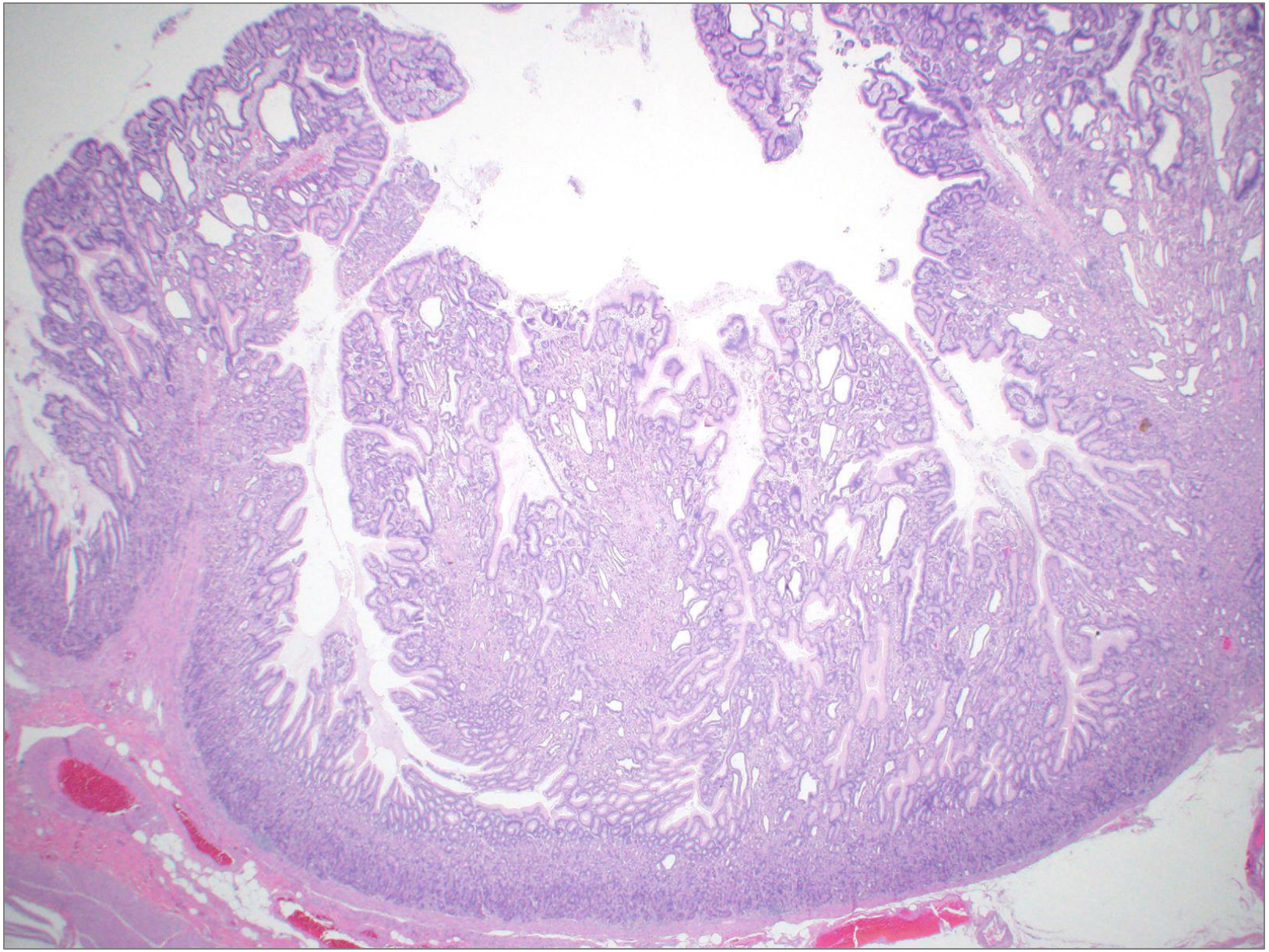
Intervening flat mucosa not normal



Fundic gland polyp



Fundic gland polyp with LGD

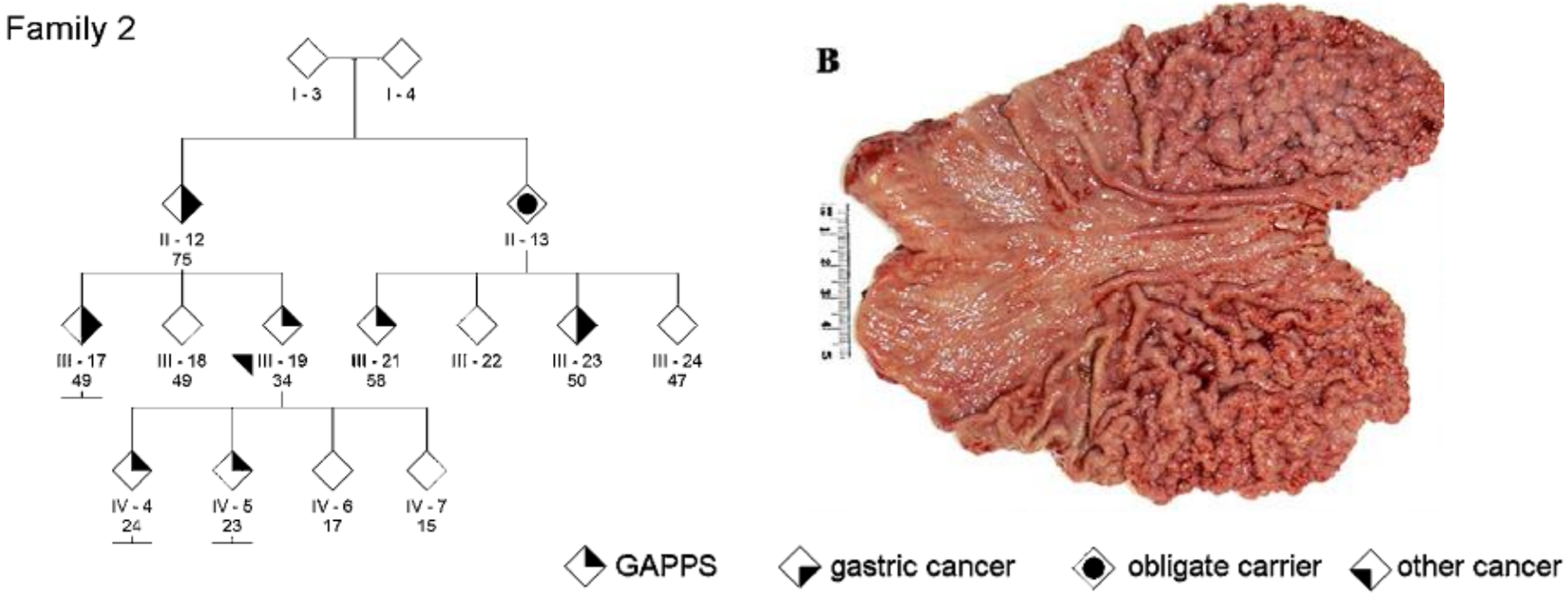


Section of gastric body: Numerous polyps with foci of dysplasia

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] A Shulkes,[6] F Grimpen,[7] A Clouston,[7] D Moore,[8] D Cullen,[9] D Ormonde,[9] D Mounkley,[10] X Wen,[11] N Lindor,[12] F Carneiro,[11] D G Huntsman,[4] G Chenevix-Trench,[5] G K Suthers[2,13]

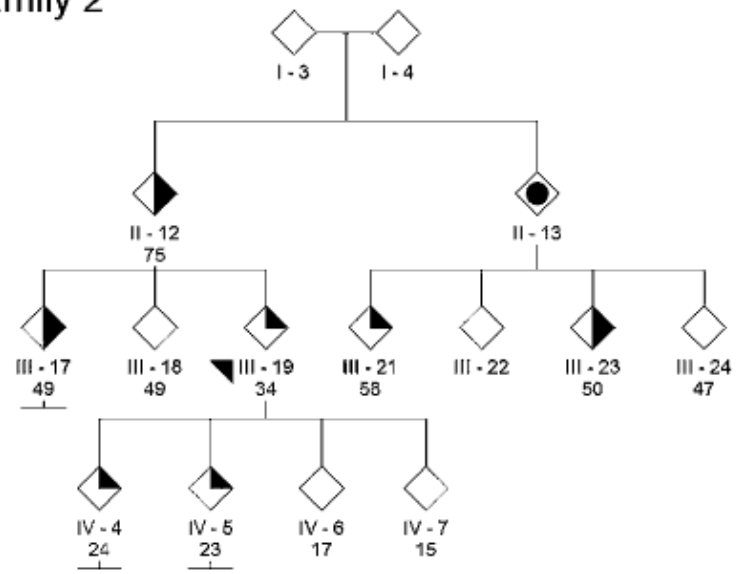
Gut 2012;61:774-779



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

Gut 2012;61:774-779

Family 2

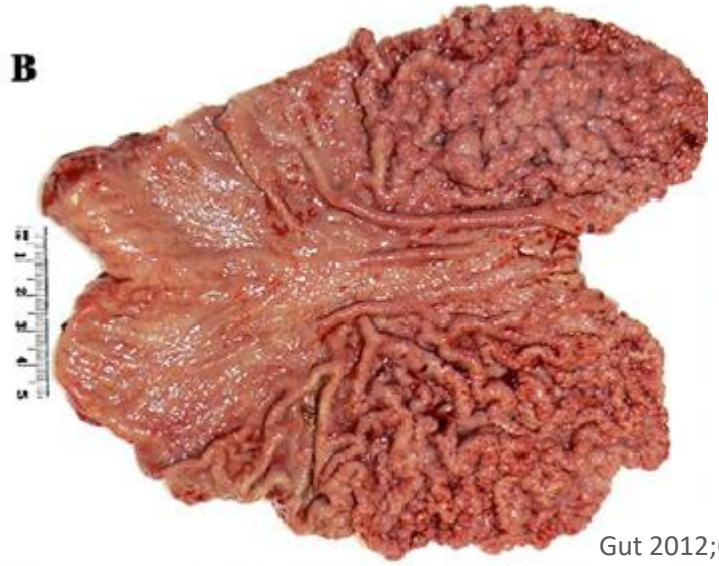


- Described 3 families with GAPPS (Australian, American, Canadian)
- Autosomal dominant
- Incomplete penetrance
- Numerous gastric polyps
- Increased risk gastric adenocarcinoma

GAPPS gastric cancer obligate carrier other cancer

Gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS) syndrome

- Polyposis in proximal stomach
  - Majority of polyps fundic glands polyps +/- dysplasia
  - Few adenomas and hyperplastic polyps
- Relative sparing of antrum and lesser curvature



Gut 2012;61:774-779

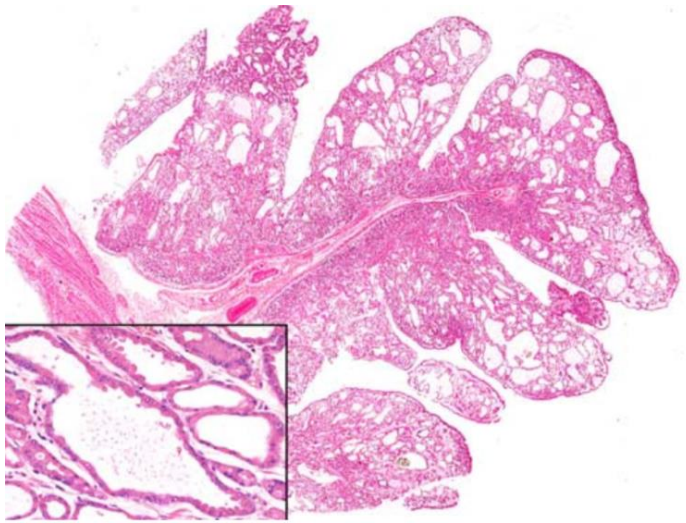


Fig. 2. Am J Surg Pathol. 2018;42(1):1-8

Gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS) syndrome

Propose criteria (Gut 2012;61:774-779)

1. Gastric polyps restricted to body and fundus with no evidence colorectal or duodenal polyposis
2. >100 polyps carpeting proximal stomach in index case or >30 polyps in 1st degree relative of another case
3. Predominantly FGPs, some with dysplasia (or a family member with either dysplastic FGPs or gastric adenocarcinoma)
4. Autosomal dominant pattern of inheritance
5. Exclusions of other heritable gastric polyposis syndromes and use of PPIs (repeat endoscopy off therapy)

ARTICLE

Am J Hum Genet. 2016;98(5):830-842

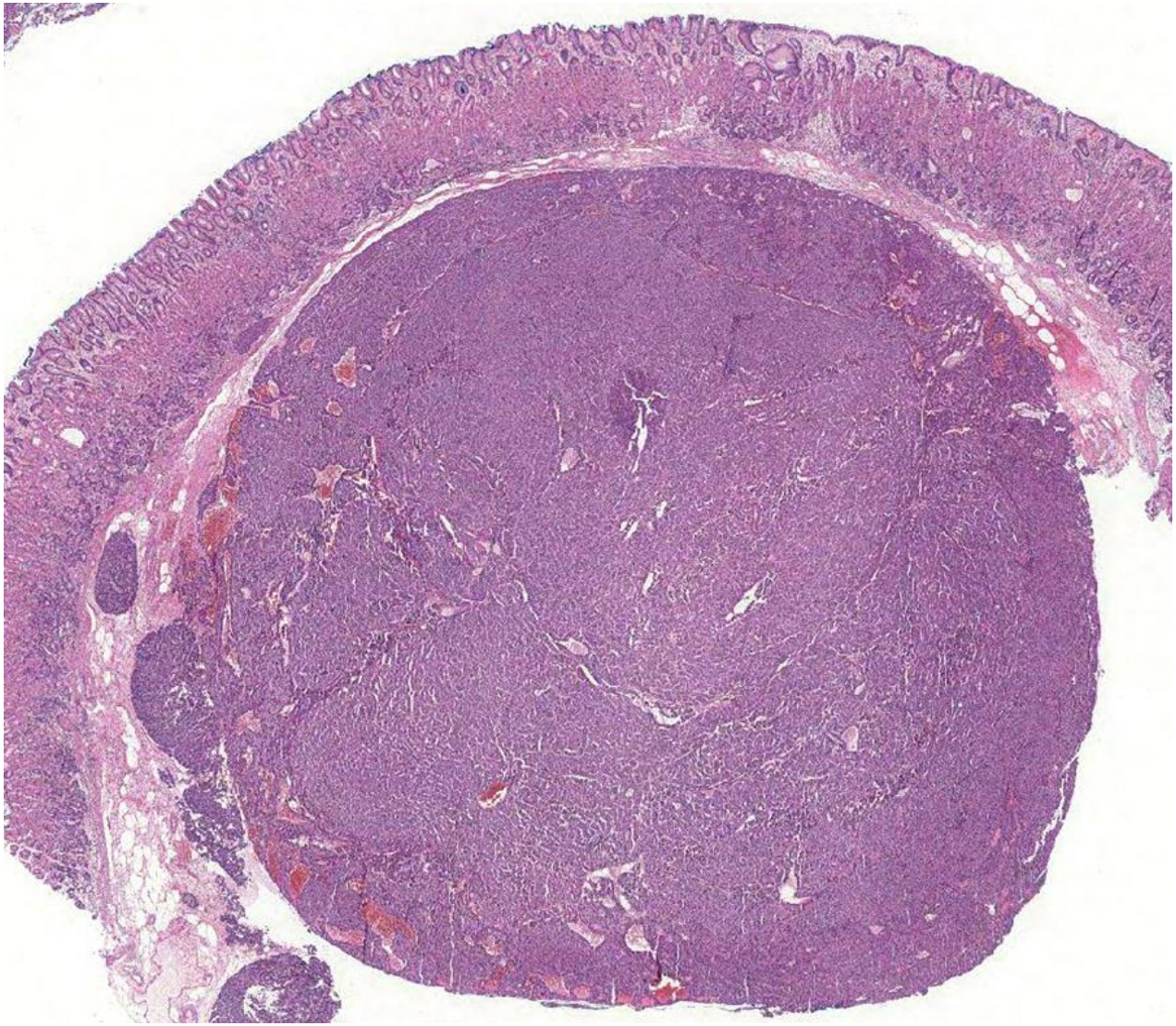
Point Mutations in Exon 1B of *APC* Reveal Gastric Adenocarcinoma and Proximal Polyposis of the Stomach as a Familial Adenomatous Polyposis Variant

Jun Li,[1] Susan L. Woods,[2] Sue Healey,[1] Jonathan Beesley,[1] Xiaoqing Chen,[1] Jason S. Lee,[1] Haran Sivakumaran,[1] Nicci Wayte,[1] Katia Nones,[1] Joshua J. Waterfall,[3] John Pearson,[1,4] et al.

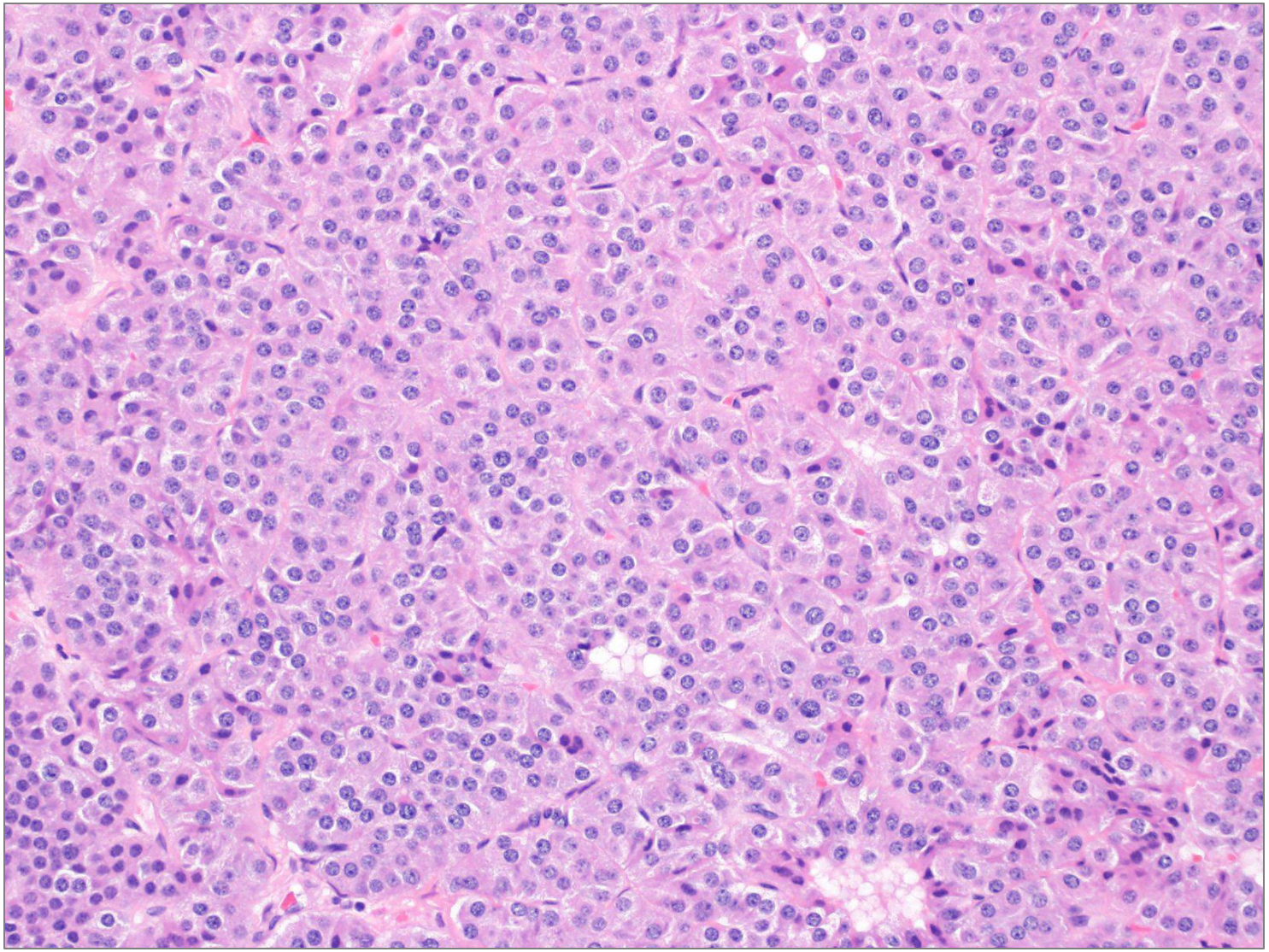
Identified mutation in GAPPS

- 3 previously reported families + 3 new North American families
- **Point mutations in APC promoter 1B** in all 6 families
- Similar mutations in *rare* families with FAP → GAPPS a variant of FAP?

Case: A 60 year-old woman with two gastric nodules, 1.5 cm and 2.5 cm.



Well-differentiated neuroendocrine tumor



Well-differentiated neuroendocrine tumor

Classification (WHO 2010):

- **Type I**: **Arise in autoimmune atrophic gastritis (~75%)**
  - Hypergastrinemia
  - Typically multiple, small (< 1cm) indolent NET
  - Conservative management (Endoscopic resection)

- **Type II**: **Associated with multiple endocrine neoplasia type 1 (MEN1) and Zollinger-Ellison syndrome (~5%)**
  - Hypergastrinemia (duodenal or pancreatic gastrinoma)
  - Multiple NET, most <1.5 cm
  - Conservative management if small

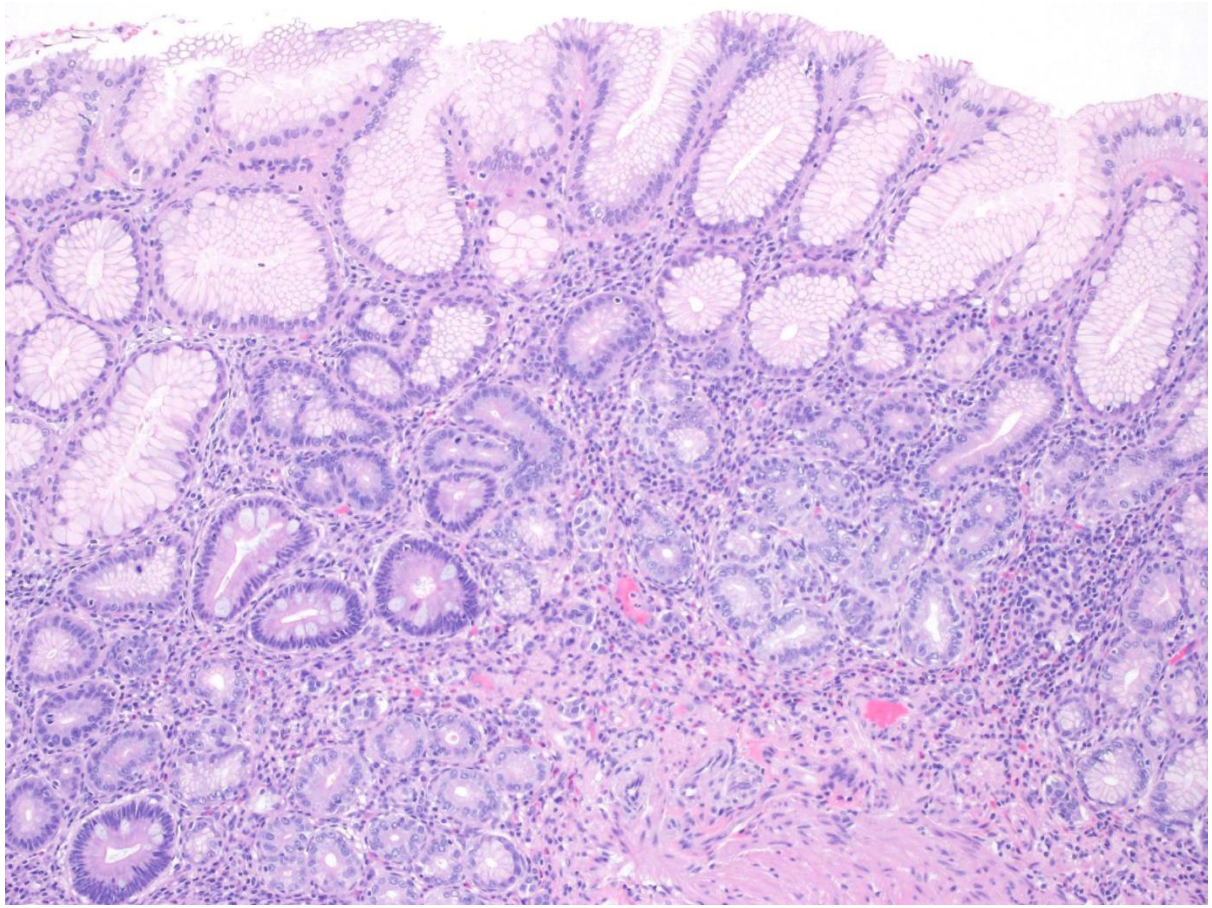
- **Type III**: **Sporadic (~20%)**
  - Typically solitary
  - Normal gastrin level
  - More aggressive, surgical resection for larger tumors

Well-differentiated neuroendocrine tumor

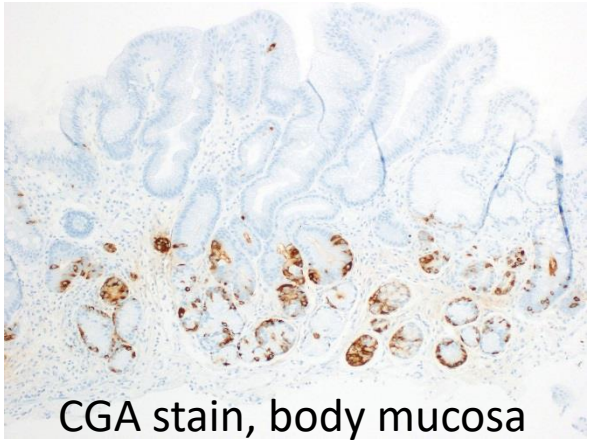
- Classification WHO 2010:
  - Type I: Autoimmune atrophic gastritis
  - Type II: MEN1 - Zollinger-Ellison syndrome
  - Type III: Sporadic

- **Flat mucosal biopsies** are important to consider as they can provide information about the setting in which the NET is arising

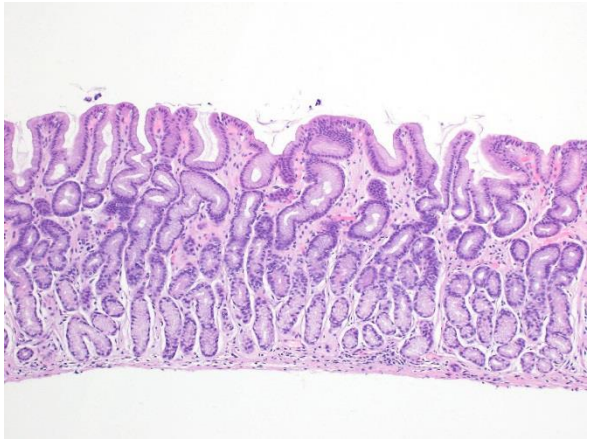
Autoimmune atrophic gastritis



Body mucosa



CGA stain, body mucosa



Antral mucosa

Autoimmune atrophic gastritis

- Chronic atrophic gastritis , corpus-restricted

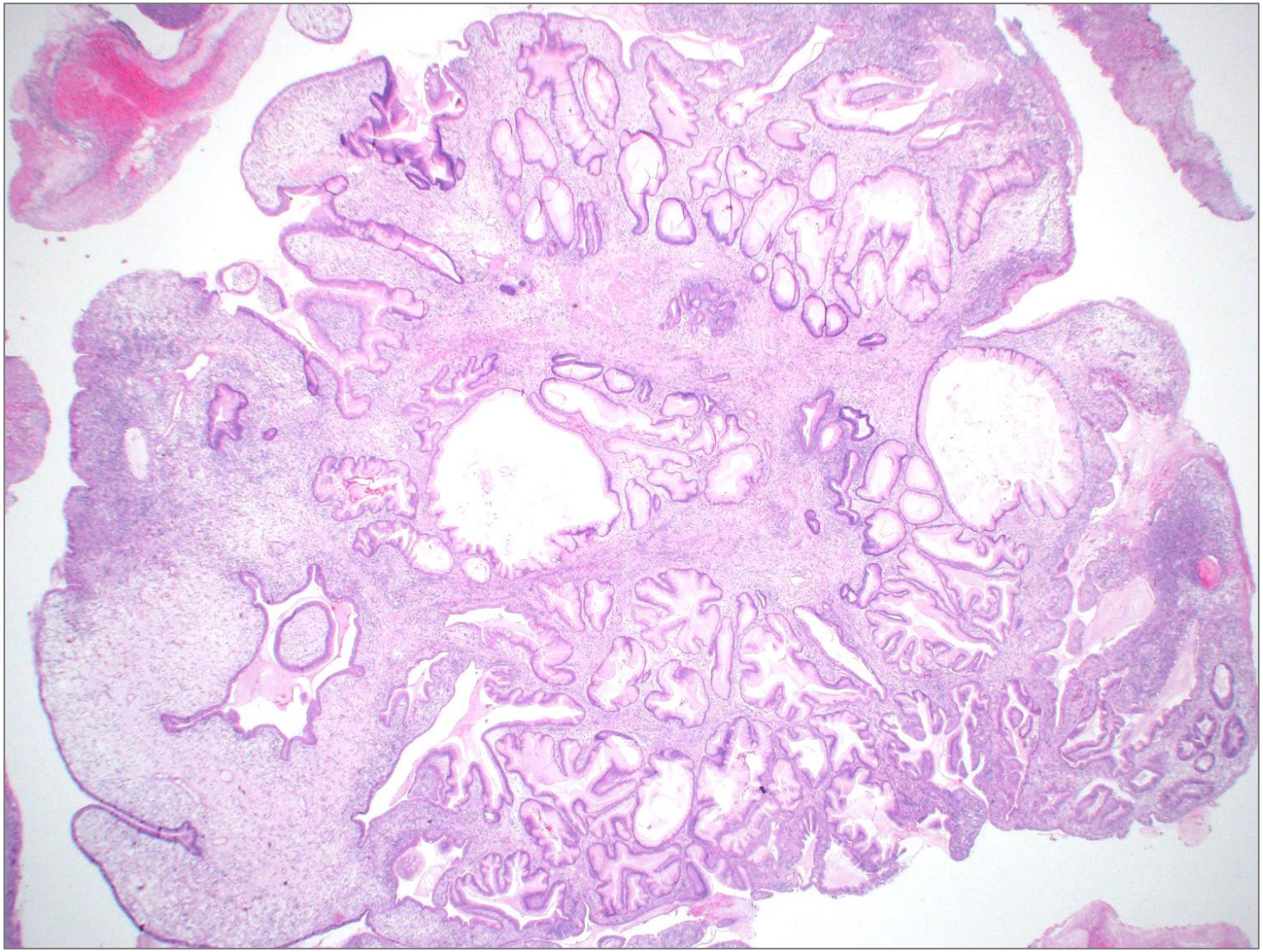
- Serum anti-parietal cell & anti-intrinsic factor antibodies
- Many patients have iron deficiency anemia or pernicious anemia
- Hypochlorhydria, achlorhydria, hypergastrinemia, low pepsinogen levels

- 3 stages (early phase, florid phase, end stage)
- ECL cell hyperplasia, neuroendocrine tumors
- Hyperplastic polyps, dysplastic polyps, carcinoma

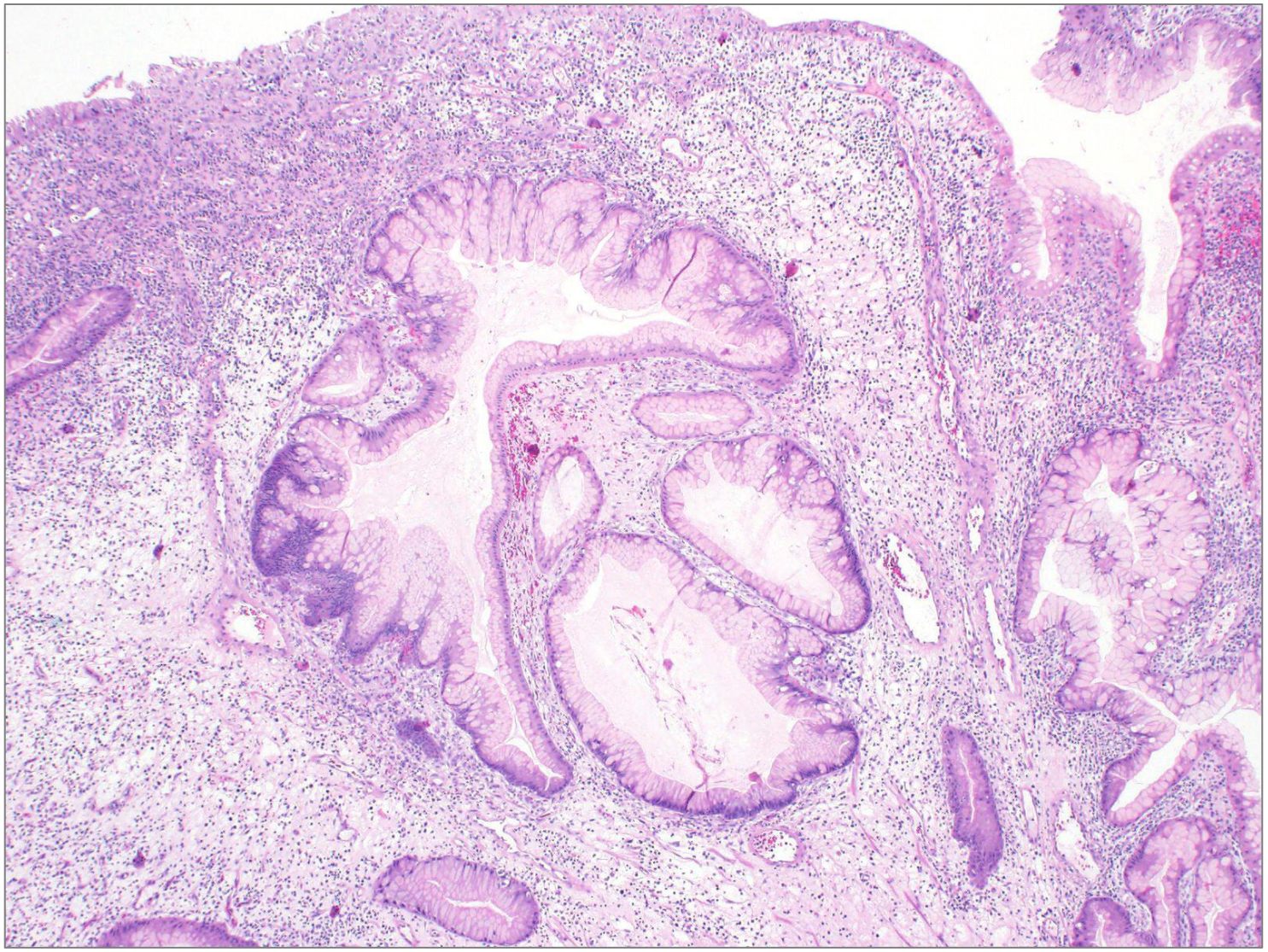
Gastric hyperplastic polyp

- Ill-defined term
- Microscopic: Elongated, branching, cystically dilated foveolae, and edematous, expanded, inflamed lamina propria
- Occurs in various settings including autoimmune atrophic gastritis and H. pylori gastritis
- When large, ulceration is common and reactive epithelial changes can mimic dysplasia

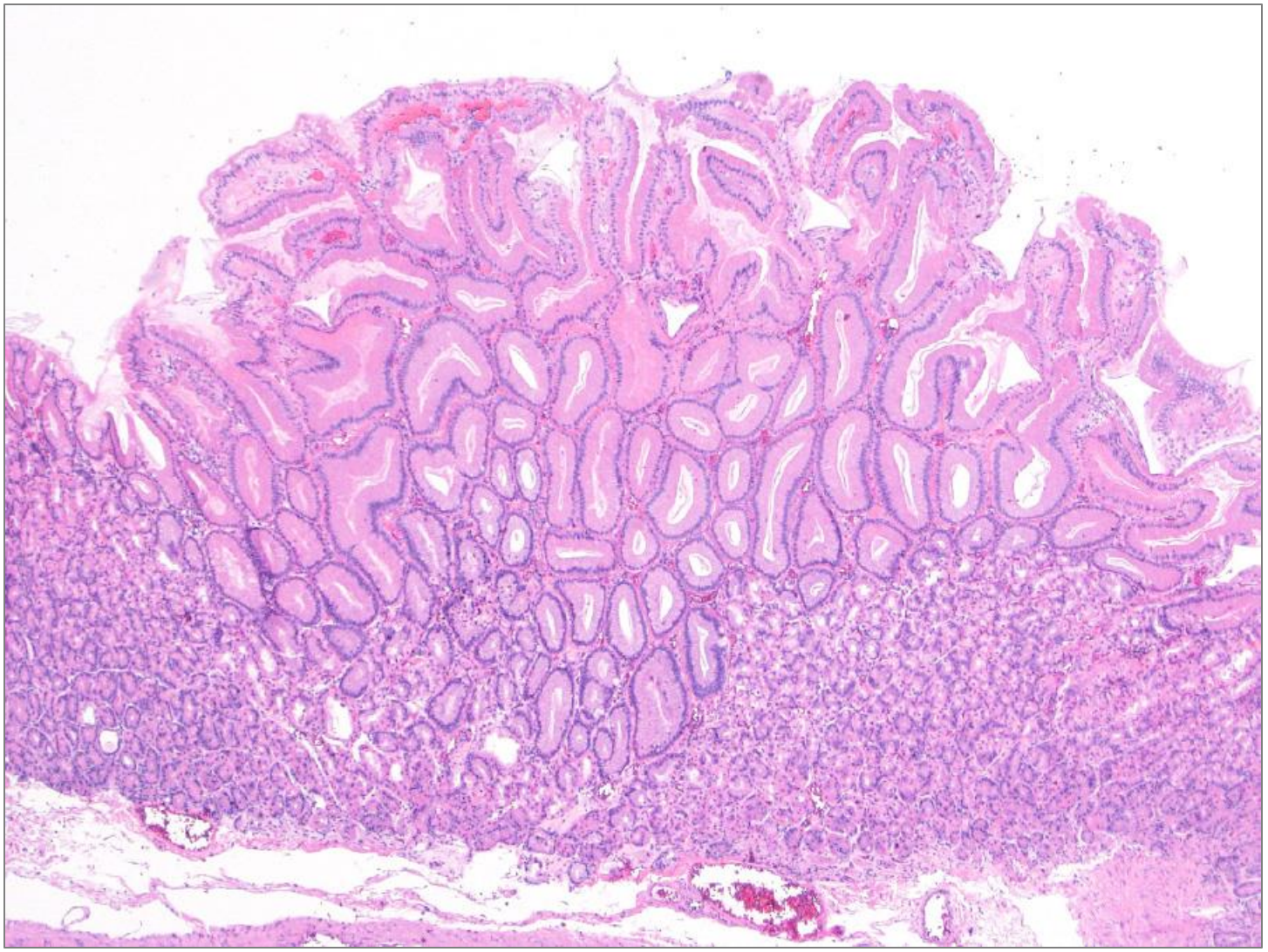
Hyperplastic polyp



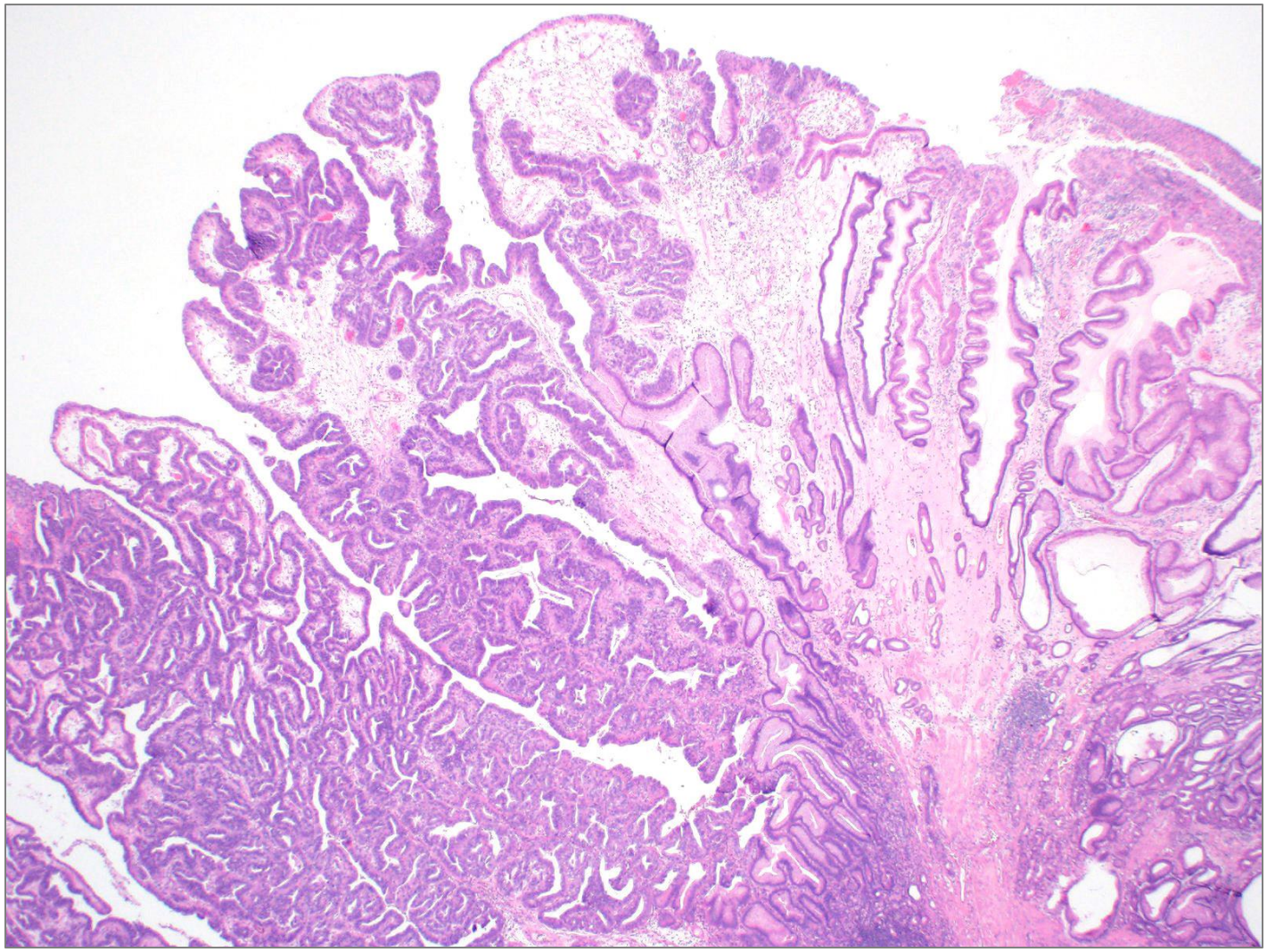
Hyperplastic polyp

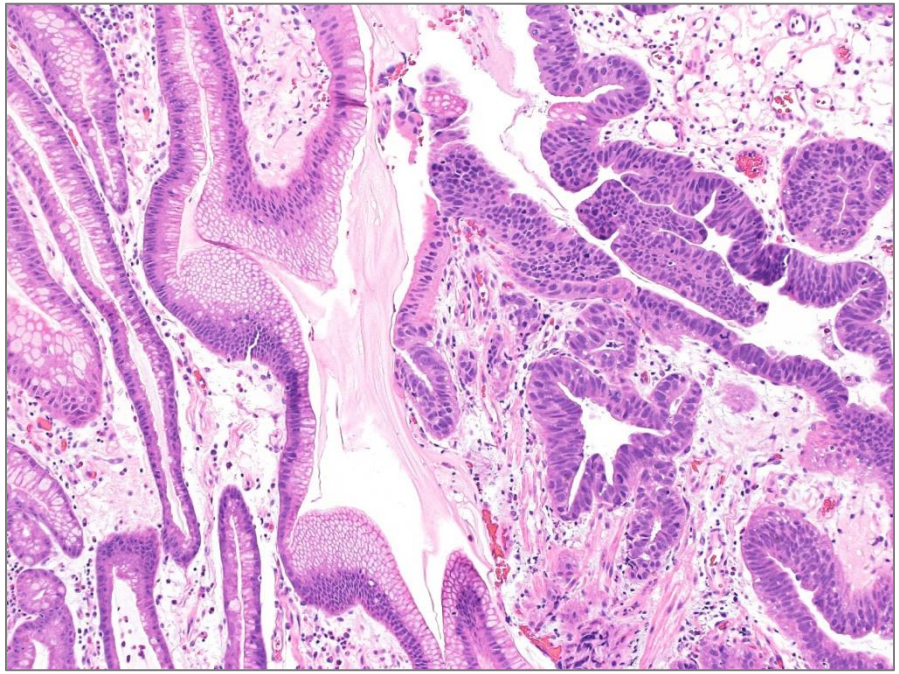


Focal foveolar hyperplasia

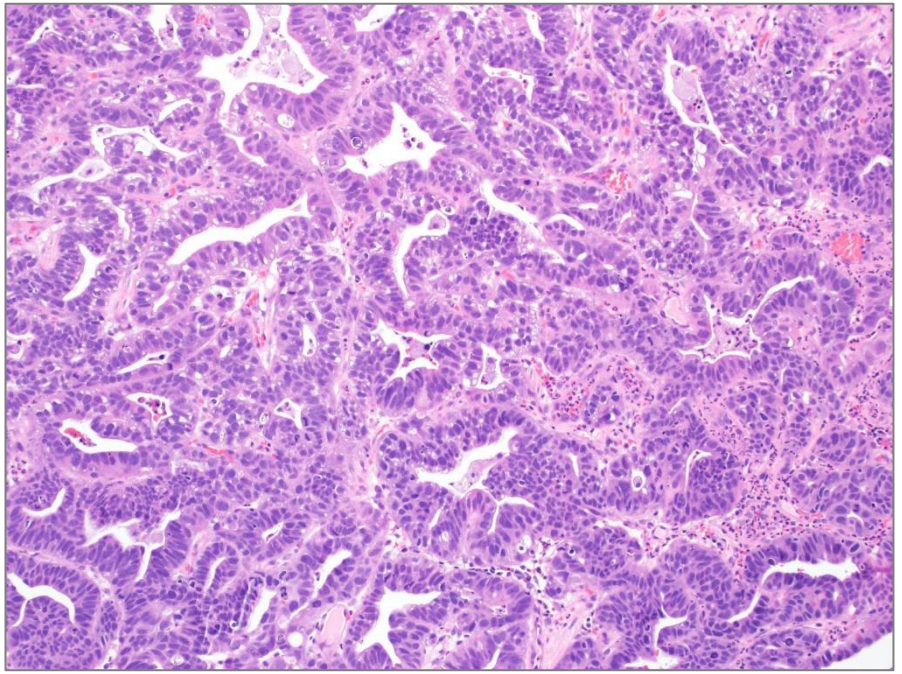


Is this an adenoma with adjacent HP like changes, or a hyperplastic polyp with dysplasia?



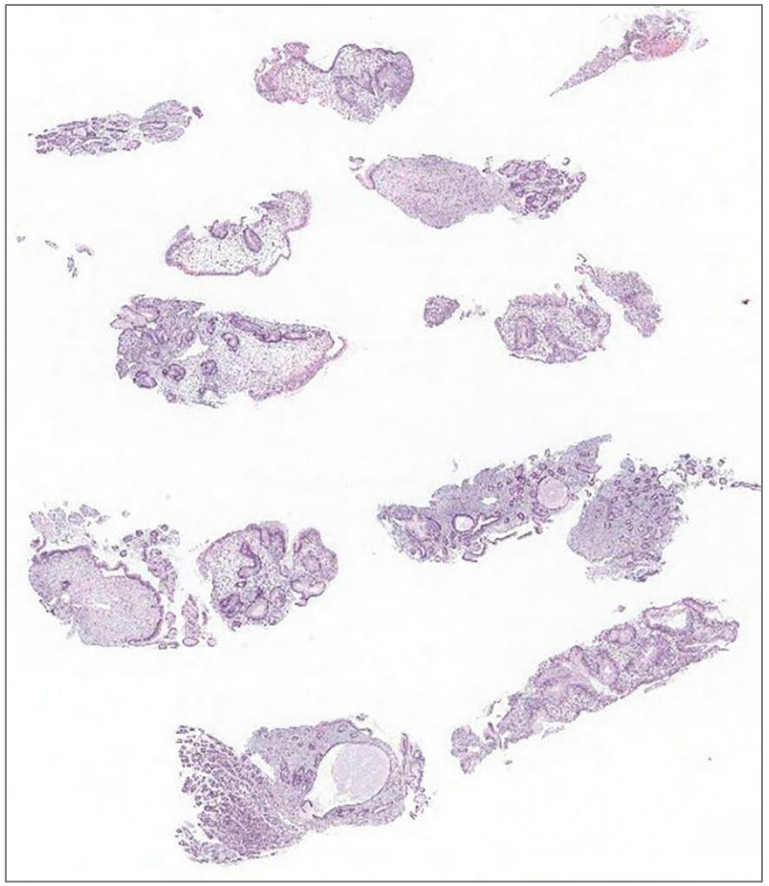


Dysplastic columnar epithelium

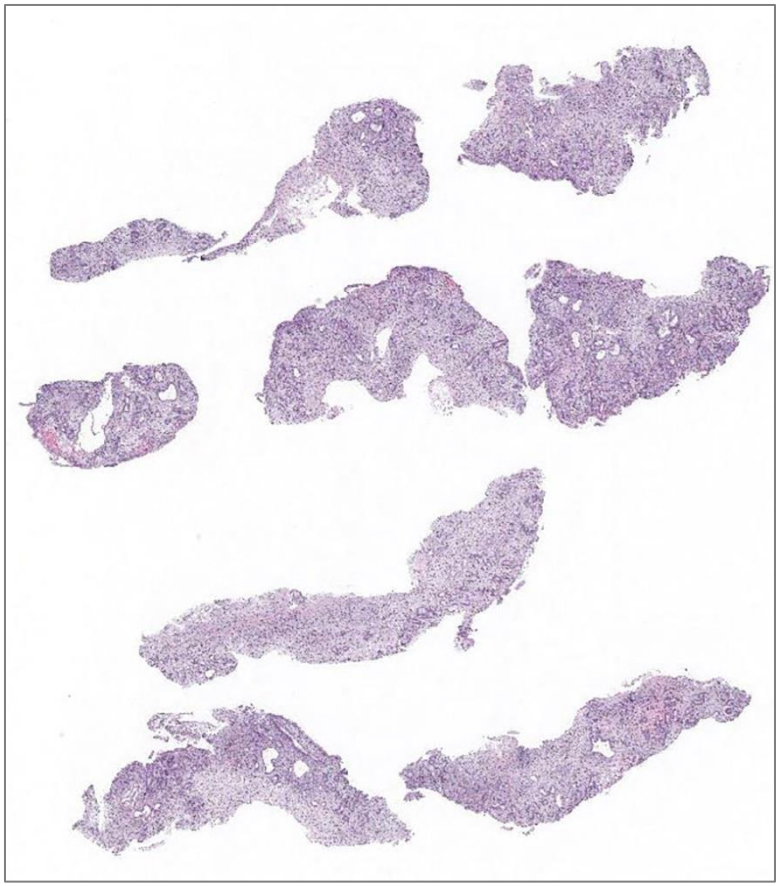


Adenocarcinoma invading LP

Case: A 59 year-old man with diarrhea and significant weight loss in the past year. Diffusely nodular and polypoid gastric and duodenal mucosal

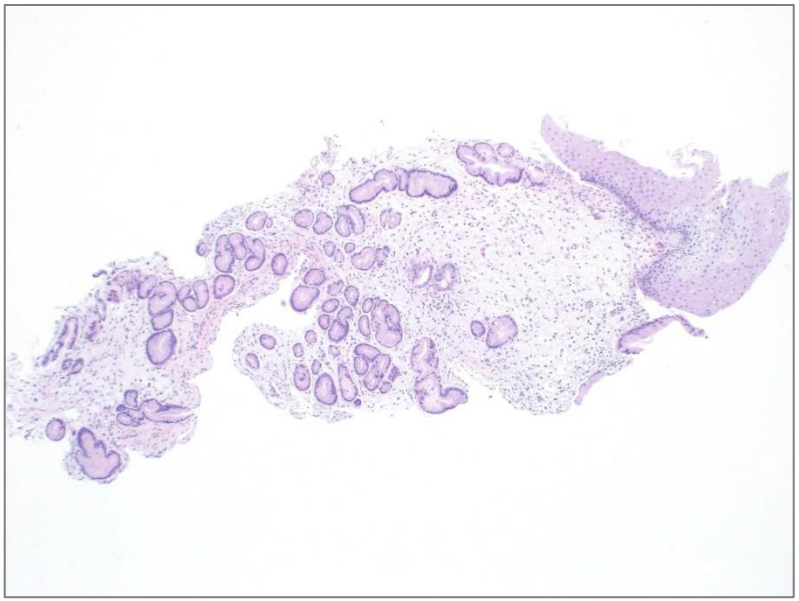


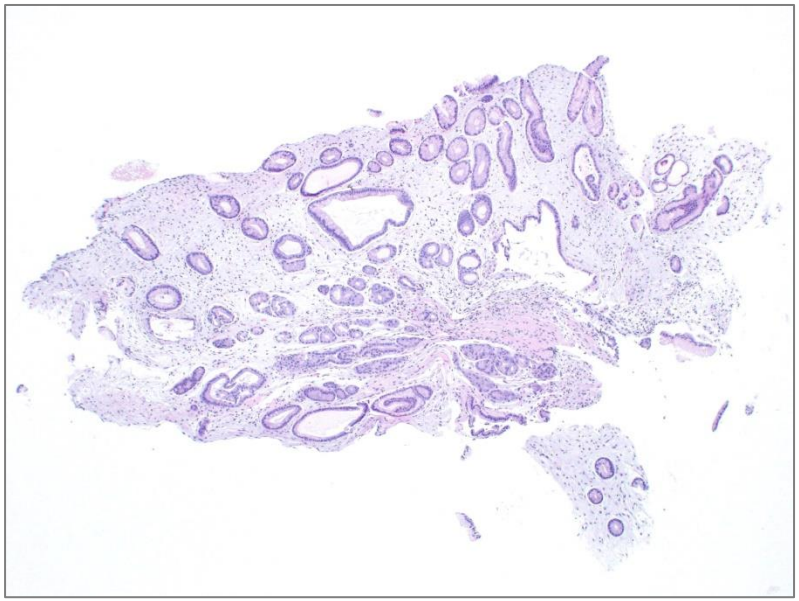
stomach

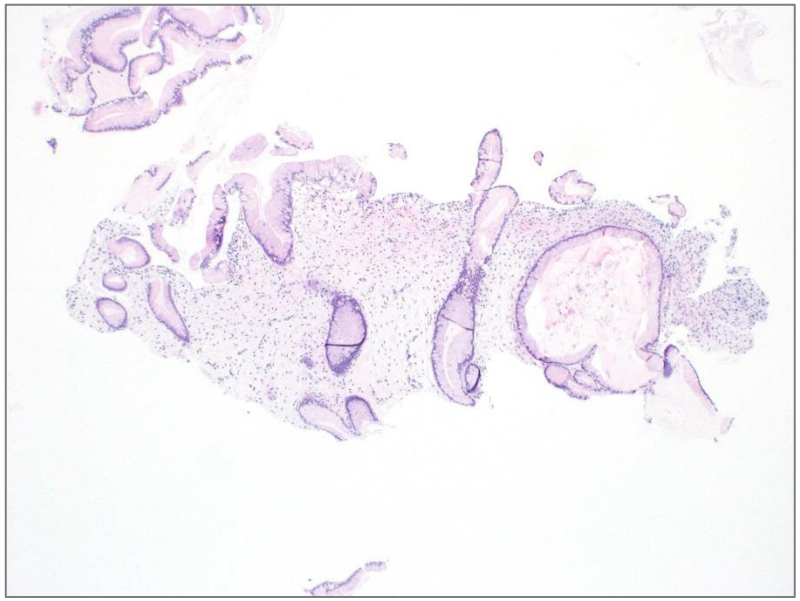


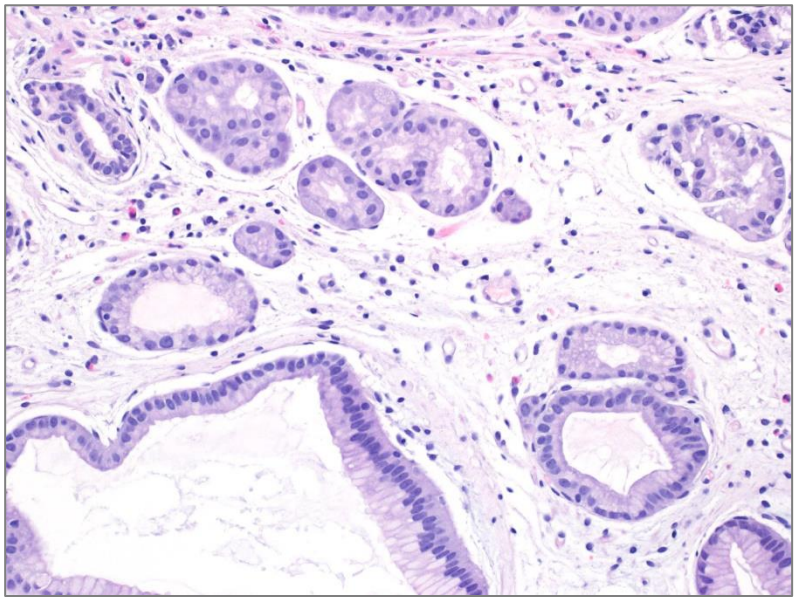
duodenum

Stomach biopsies

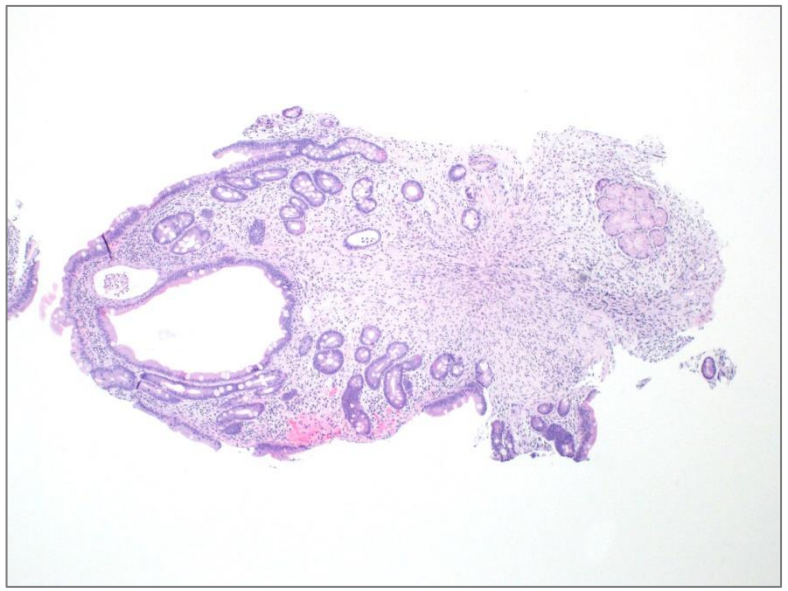


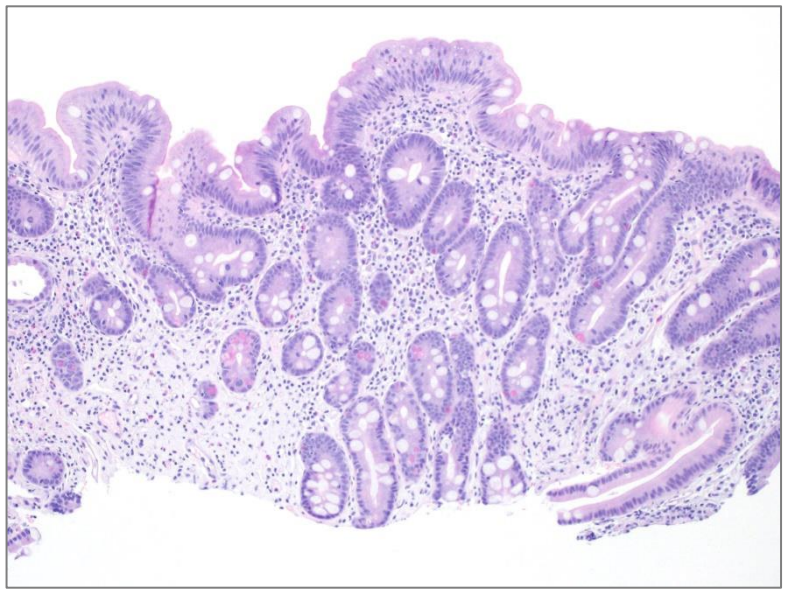




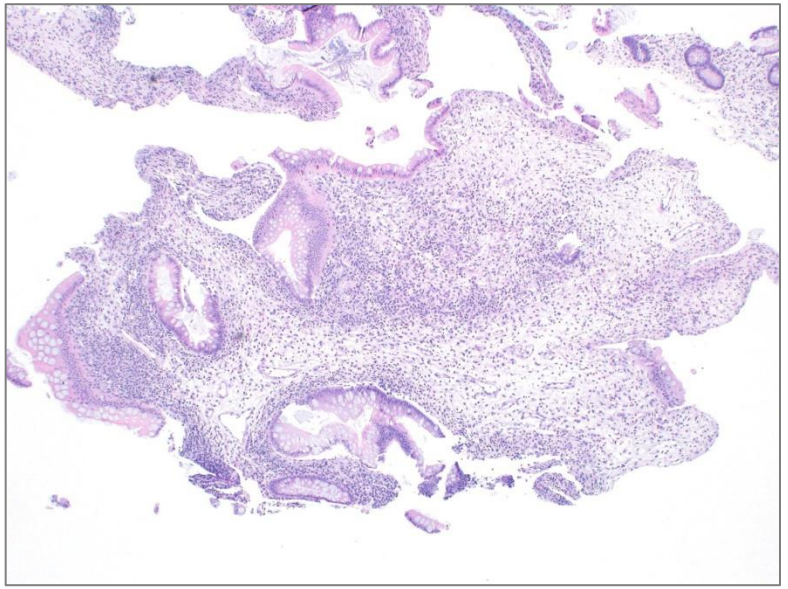


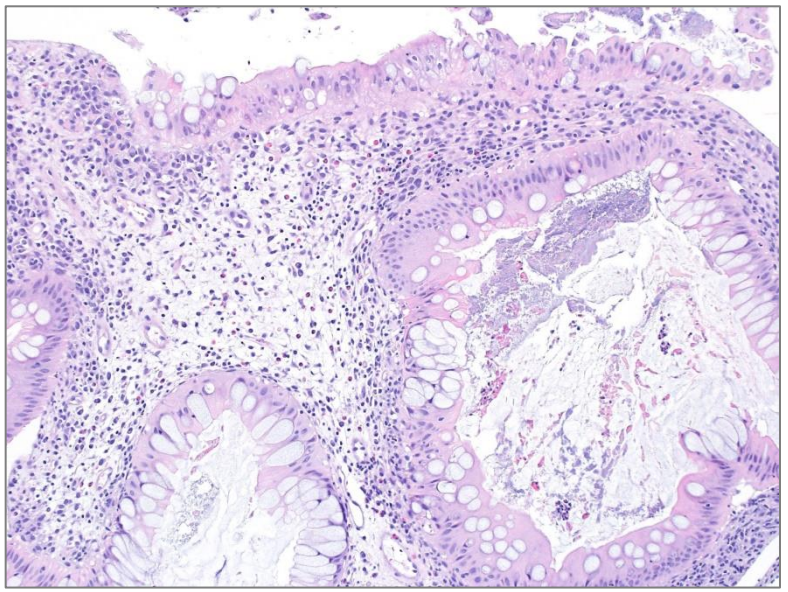
Duodenum





Colon





Cronkhite-Canada syndrome

Rare acquired disorder first reported by Drs. Leonard Cronhkhite Jr. & Wilma Canada in 1955

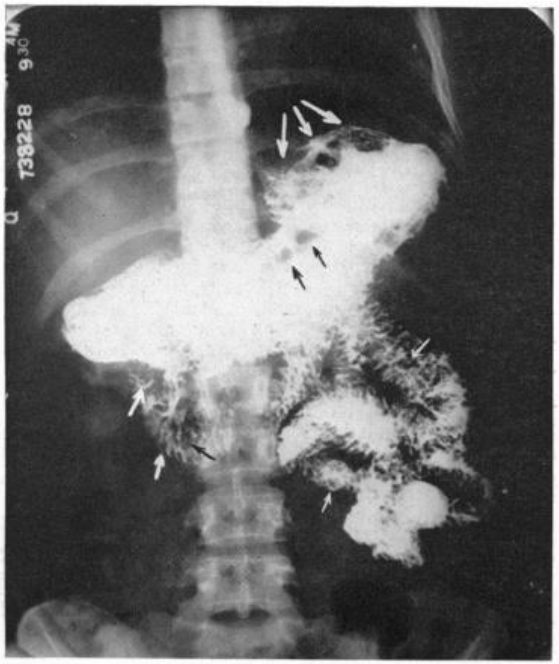


FIGURE 1. *Roentgenogram in Case 1, Showing a Large Polypoid Filling Defect in the Fundus and Similar Smaller Defects in the Body of the Stomach.*
The visualized loops of small intestine show many scattered, rounded filling defects and generalized coarsening of the mucosal pattern.

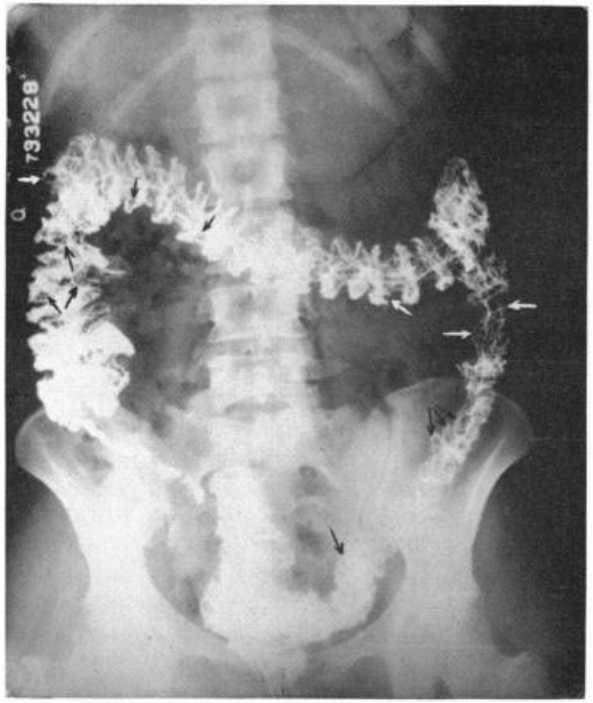


FIGURE 3. *Film Taken after Evacuation in Case 1, Showing Replacement of the Normal Mucosal Pattern by Varying-Sized, Separate and Confluent, Rounded Filling Defects.*
No normal mucosa is visible.

Cronkhite LW Jr, Canada WJ. NJEM 1955;252(24):1011-5

Cronkhite-Canada syndrome

GI tract polyposis

- Typically diffuse with esophageal sparing

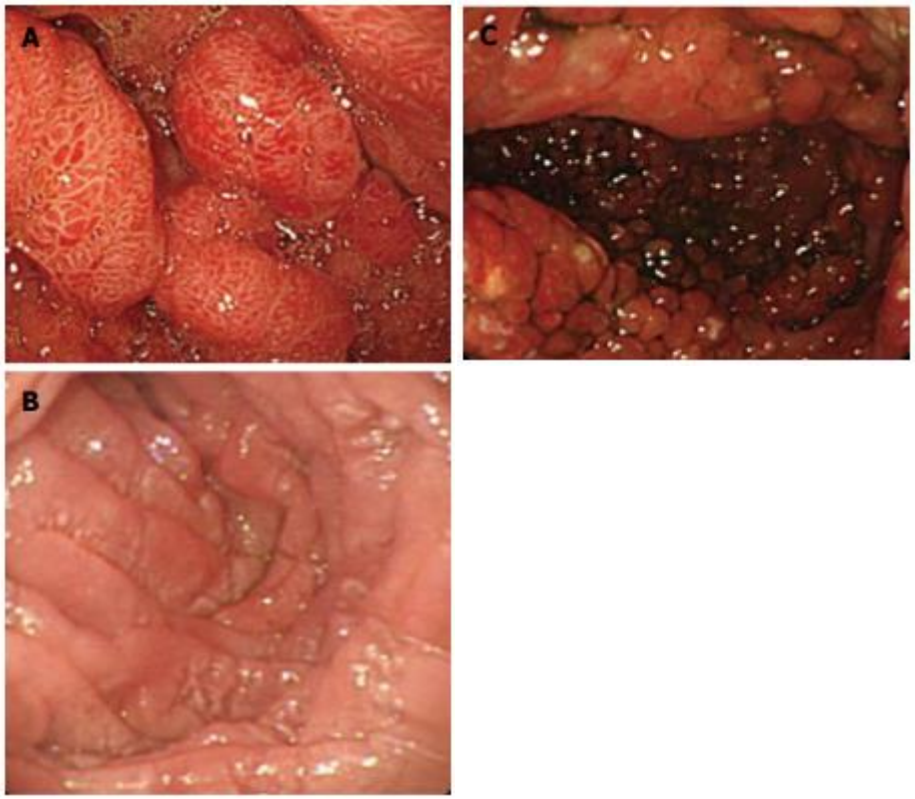


Figure 2 Endoscopy results. A: Numerous polyps in the stomach; B: Mucosal edema in the descendant duodenum; C: Multiple polyps in the colon.

Ectodermal changes

- Onychodystrophy
- Alopecia
- Cutaneous hyperpigmentation

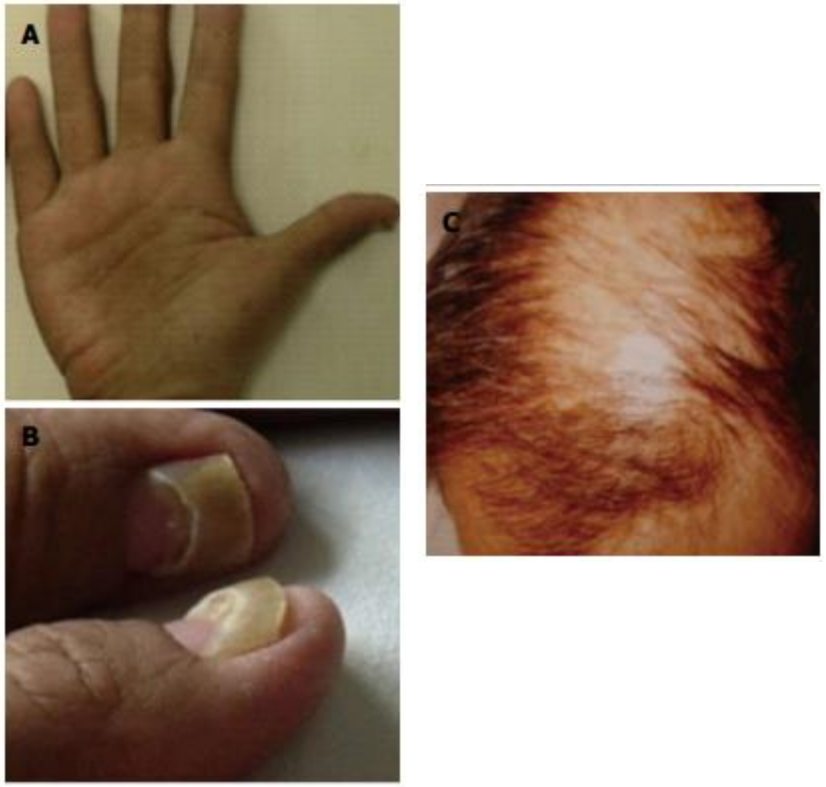


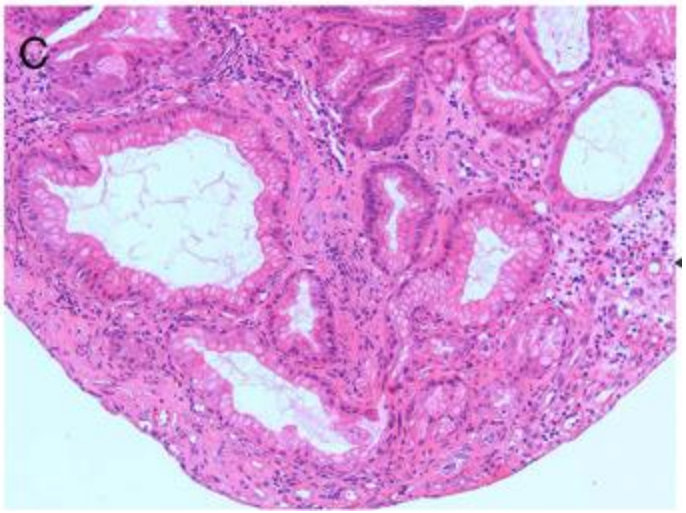
Figure 1 Clinical presence, cutaneous symptoms. A: Hyperpigmentation of palm; B: Onychodystrophy; C: Alopecia.

Wen XH, et al. World J Gastroenterol. 2014;20(23):7518-22

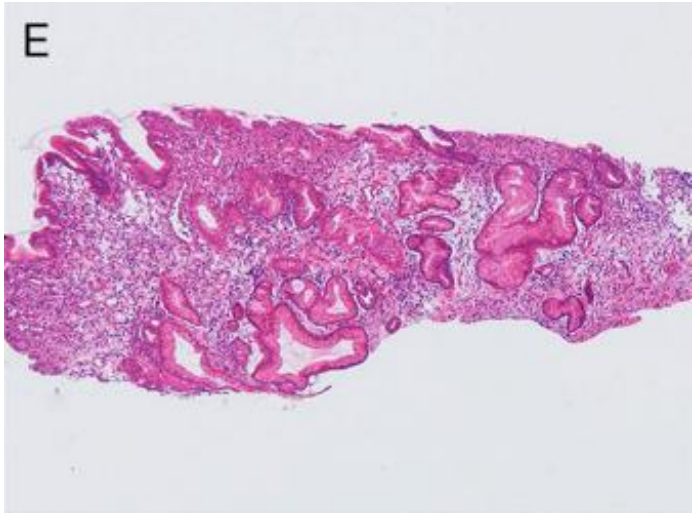
Cronkhite-Canada syndrome

Microscopic

- Broad based polyps
- Hamartomatous polyps with expanded, edematous, and inflamed lamina propria with cystically dilated foveolae or crypts.
- Similar changes in endoscopically flat mucosa



Gastric polyp



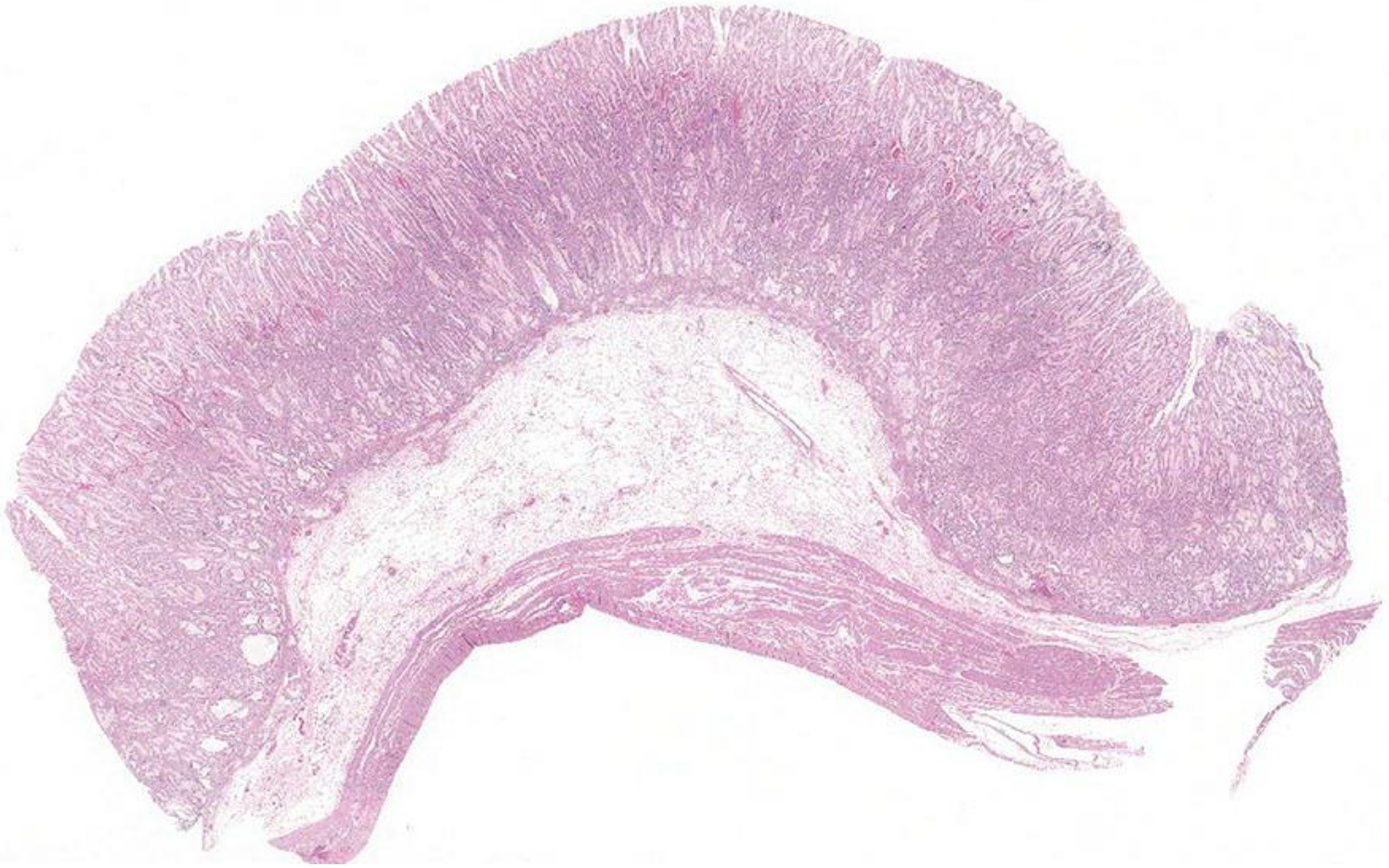
Flat gastric mucosa

Slavik T, Montgomery EA. J Clin Pathol 2014;67:891-897.

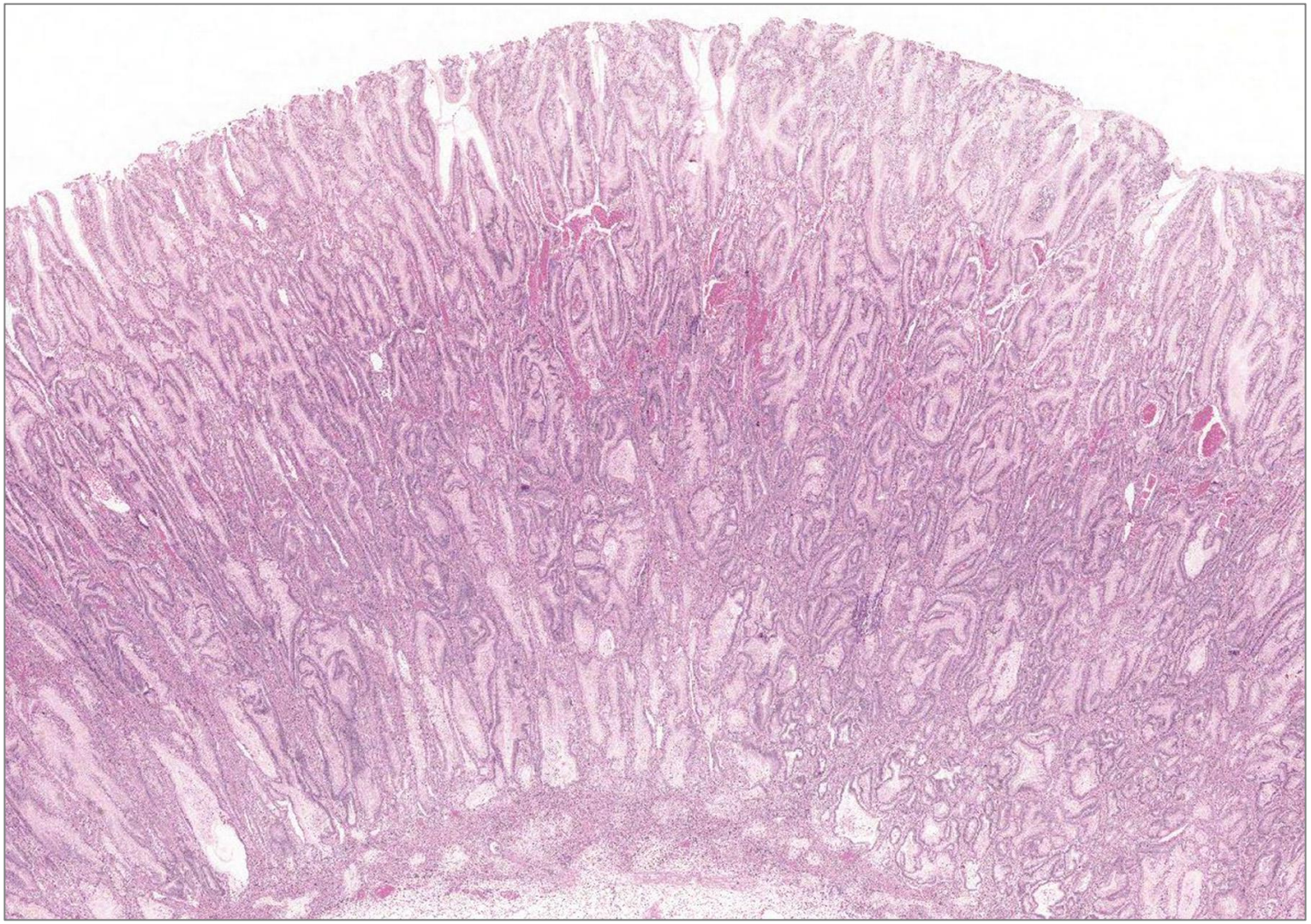
Cronkhite-Canada syndrome

- Various symptoms
  - Diarrhea, weight loss, abdominal pain, malnutrition, peripheral edema
- Most patients >50 years (avg. ~60 years)
- Uncertain etiology, possibly autoimmune
  - Response to immunosuppressants (e.g. corticosteroids)
  - Increased IgG4+ cells
- Progressive malnutrition and poor prognosis
  - Complete remission in <5% patients
  - 5 year mortality rate ~50% (GI bleeding, sepsis, other)

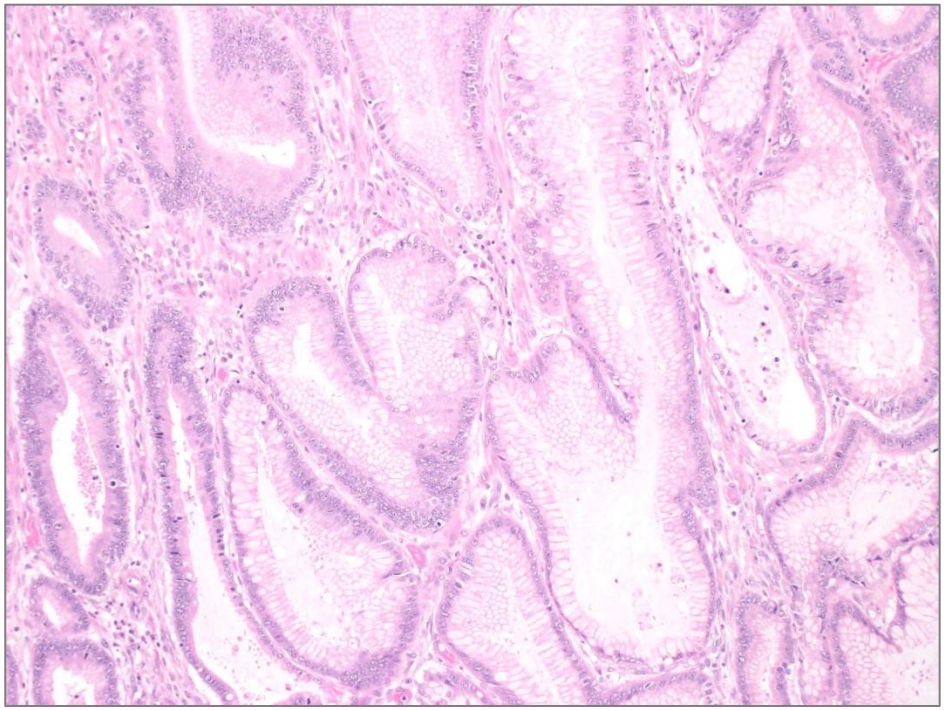
Case: 50 year-old man with abdominal pain found to have enlarged gastric folds in the gastric fundus and body.



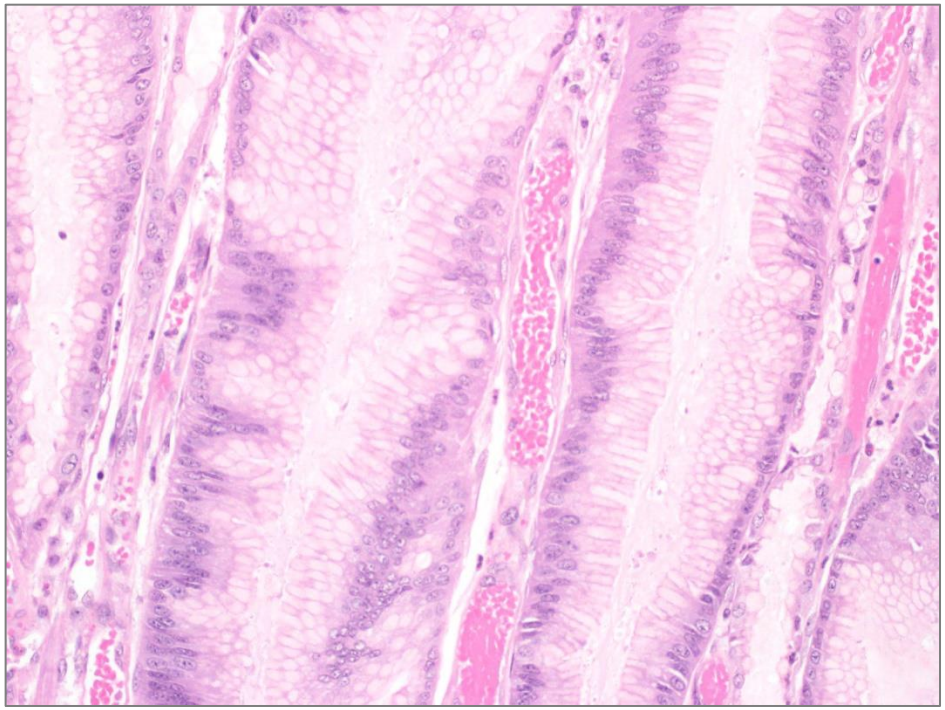
Gastric body



Gastric body: Oxyntic gland atrophy, diffuse foveolar hyperplasia, inflammation



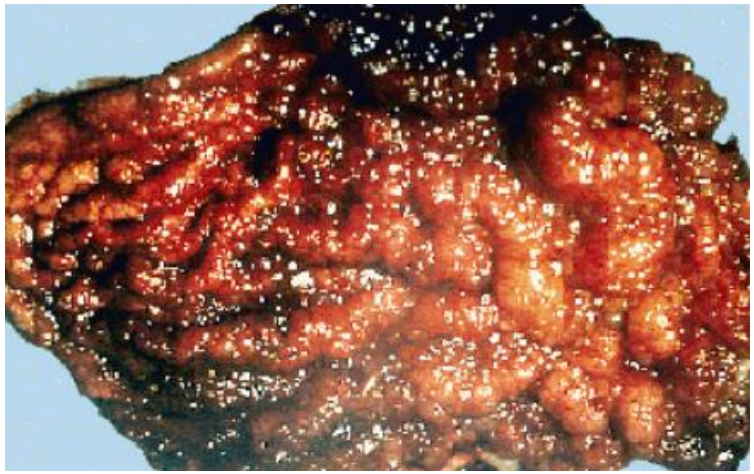
Cystic dilation



Non-dysplastic foveolar epithelium

Ménétrier's disease

- Rare acquired condition
  - Most common in middle aged men
  - Unknown etiology. ?infection
  - ? Increased cancer risk



Lewin KJ, Appelman HD. Tumors of the esophagus and stomach. AFIP third series, fascicle 18, 1996.

- Clinical features
  - Giant gastric folds in body & fundus
  - Low acid production
  - Protein loss with hypoalbuminemia
  - Possible presentations include weight loss, vomiting, epigastric abdominal pain, anorexia, peripheral edema

Ménétrier's disease

Microscopic

- Diffuse foveolar hyperplasia, cystic dilation
- Oxyntic gland atrophy
- Variable inflammation
- Mucosal edema

Differential

- Cronkhite-Canada syndrome
  - Distribution – antral involvement and intestinal polyposis
  - Clinical manifestations
- Zollinger-Ellison Syndrome
  - Fundic gland and parietal cell hyperplasia

Features to consider when evaluating gastric mucosal polyps and thickened folds:

- Histology
- Number of gastric polyps
- Distribution of polyps within stomach
- Background gastric mucosal changes

- Intestinal polyposis
- Clinical signs and symptoms
- Clinical history (e.g. known syndrome, family history, demographics)