

Joseph Misdraji

What do you do with serrated changes
in the setting of IBD?

Serrated polyps in IBD

- Patients with IBD can get serrated polyps. However, several studies indicate that the prevalence is low. Most of them are hyperplastic polyps.
- Serrated polyps without dysplasia occur in women, favor the right colon and often have BRAF mutations, whereas those with dysplasia occur in men, favor the left colon and are more likely to have KRAS mutations.
- Patients with IBD and serrated polyps *without* dysplasia may not have a significantly elevated cancer risk, whereas those with serrated polyps *with* dysplasia may have a cancer risk similar to patients with baseline dysplasia.
- Confounding the matter, however, is that adenomatous growths bordering IBD-related cancers are commonly villous or serrated, and some authors report that IBD-related dysplasia is often serrated.

Villous, hypermucinous mucosa in long standing ulcerative colitis shows high frequency of *K-ras* mutations

S N Andersen, T Løvig, O P F Clausen, et al.

Gut 1999;45:686–692

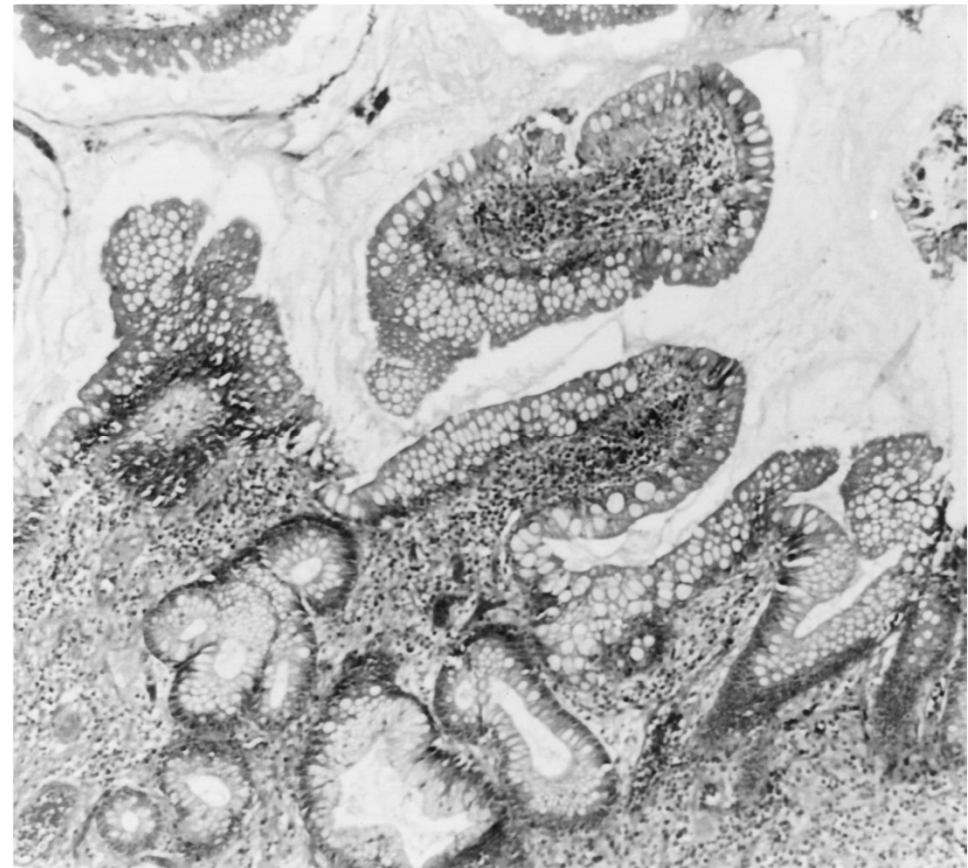
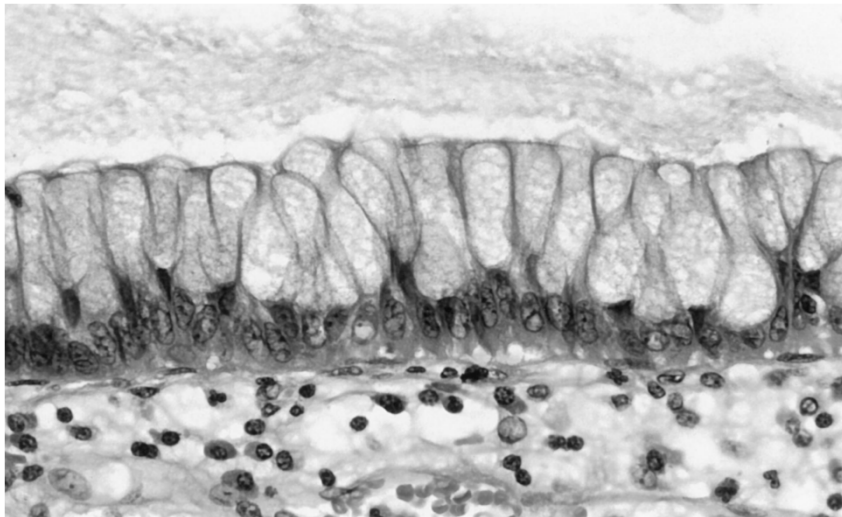
- 13 colectomies from patients with long-standing UC.
- Various mucosal lesions were tested for KRAS mutation.
 - Regenerating mucosa
 - Non-villous hypermucinous mucosa
 - Villous hypermucinous mucosa (indefinite for dysplasia)
 - Flat mucosa, indefinite for dysplasia
 - LGD
 - HGD
 - Carcinoma
- KRAS mutations were most frequent in villous hypermucinous mucosa (8/13 [61%])
- Cancer 20%; HGD 28%; LGD 4%; non-villous hypermucinous 14%

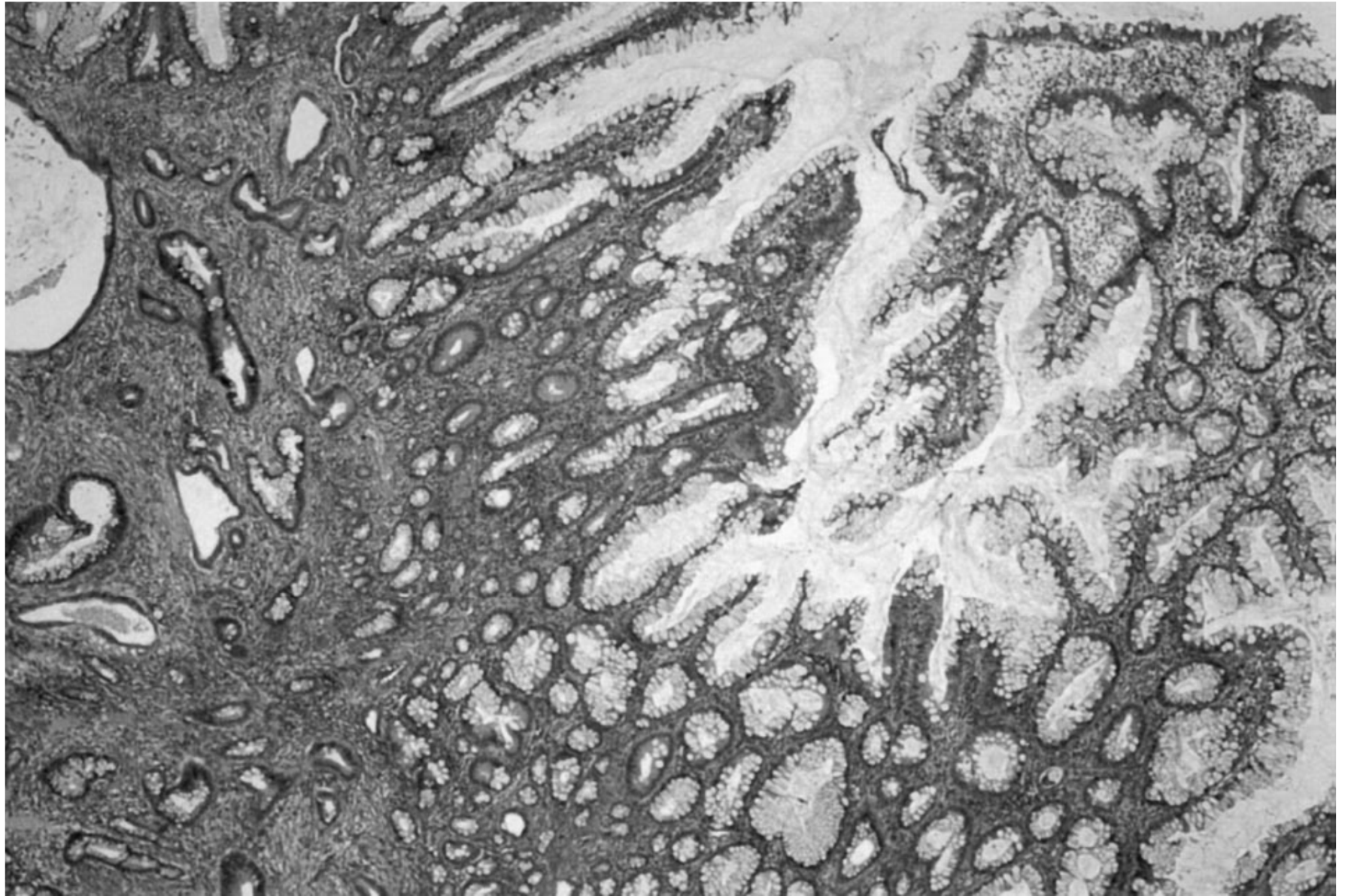


Hyperplastic-Like Mucosal Change in Crohn's Disease: An Unusual Form of Dysplasia?

Sony P. Kilgore, M.D., Jessica E. Sigel, M.D., John R. Goldblum, M.D.
Mod Pathol 2000;13(7):797-801

Hyperplastic-like mucosal change: a diffuse
expanse of flat mucosa with an architecture
resembling that seen in hyperplastic polyps and
composed of cells with cytologically bland basal
nuclei and apical cytoplasmic mucin distension.





Hyperplastic-like mucosal change and cancer risk in Crohn's patients

- 30 Crohn's resections and 30 matched controls.
- HPC was identified in 10 (33%) cases of Crohn's related adenocarcinoma compared with 3 (10%) of resected Crohn's without cancer.
 - 5 cases distant to the cancer
 - 3 cases adjacent to the cancer
 - 2 cases both adjacent and distant
- 2/6 distant foci and 3/4 adjacent foci showed strong p53 expression, whereas non-HPC mucosa was p53 negative.
- 0/3 HPC in Crohn's cases without cancer stained for p53.

Detection rate and outcome of colonic serrated epithelial changes in patients with ulcerative colitis or Crohn's colitis

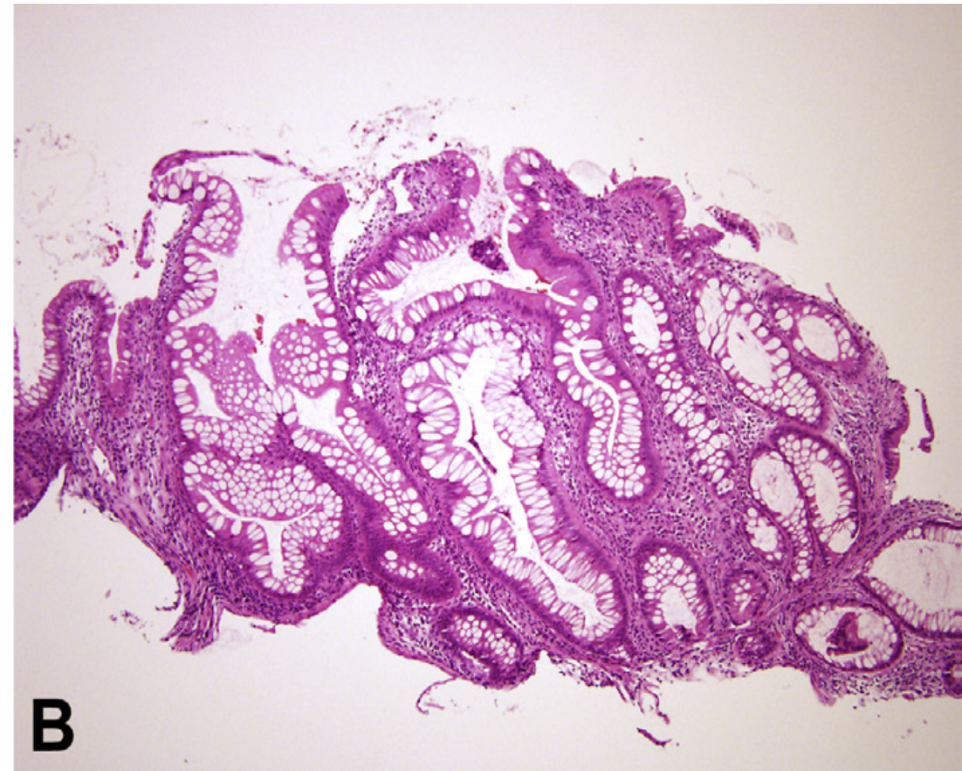
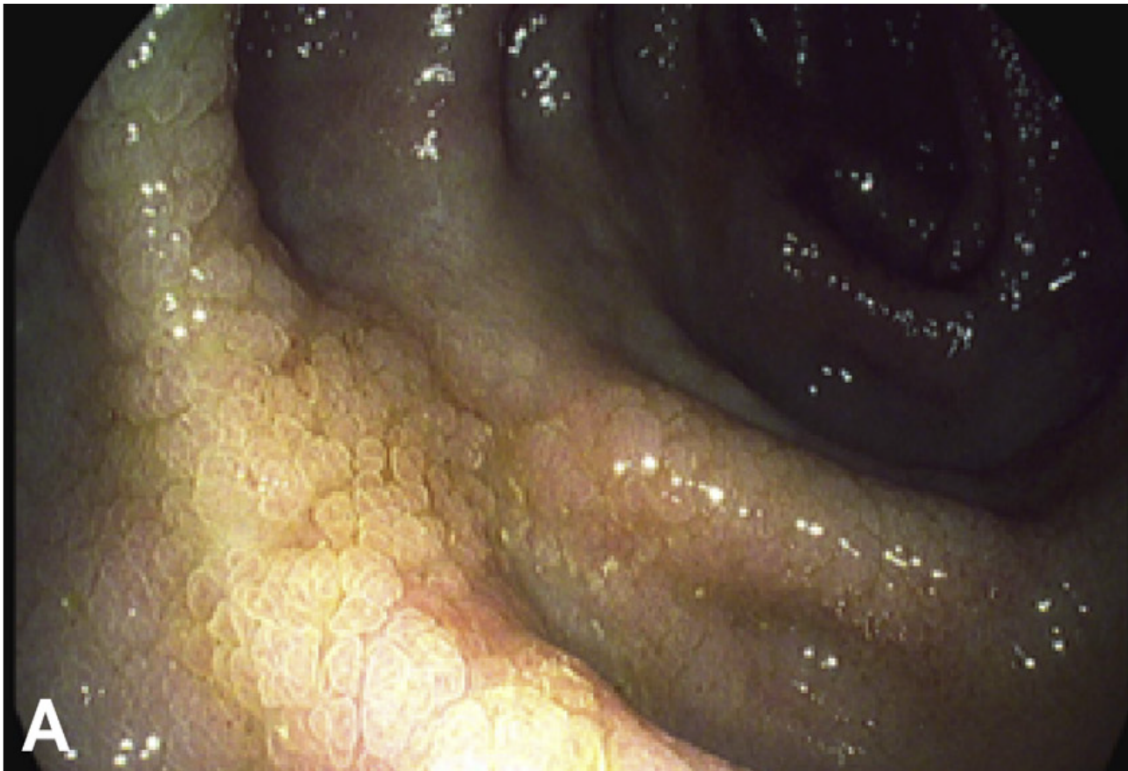
D. H. Johnson, S. Khanna, T. C. Smyrk, et al.

Aliment Pharmacol Ther 2014; 39: 1408–1417

- Introduction: SEC is a histological finding in which epithelial serrations are characteristically seen in the upper half of the crypt, as is typical of benign hyperplastic polyps.
- From 2006-2012, 79 patients with SEC identified.
 - 38% of lesions visible by endoscopy (as opposed to serrated polyps)
 - SEC occurred in the same side as prior dysplasia in 8 of 19 (42%) and in 11 of 14 (79%) of those with synchronous lesions.
- Compared to 50 controls, SEC patients were more likely to have known risk factors of colorectal neoplasia in IBD (older age and longer disease duration). PSC was also more common in this group.
- Of the 52 SEC patients without prior dysplasia, 28% (vs. 11% of controls) developed CRN (mostly LGD and no CRC). Dysplasia localized to same segment as SEC in only 5/11 cases.
- Conclusions
 - SEC occurred in patients with known risk factors for CRN: possibly mucosal injury response that identifies patients with significant cumulative inflammatory burden, at risk for future dysplasia.
 - After stratifying based on prior CRN history, SEC had no significant impact on risk of CRN.

Association between serrated epithelial changes and colorectal dysplasia in inflammatory bowel disease

Alyssa Parian, Joyce Koh, Berkeley N. Limketkai, et al.
Gastrointest Endosc 2016;84:87-95.



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- 247 index SEC lesions in 187 patients (10% ascending, 8% transverse, 37% descending, 38% rectum) without *prior* dysplasia. 15/187 (8%) had synchronous dysplasia.
- Only 22% were endoscopically visible.
- 24/112 (21%) of patients without index dysplasia (and follow up) developed dysplasia in the follow up interval (6 HGD/CA and 18 LGD) (median 34 m; range 4-101 m). But no control group.
- Concordance of location between SEC and dysplasia in 27/40 (68%) of cases.
- Significant risk factors for developing dysplasia were older age at IBD diagnosis, male, family hx of CRC, and follow up biopsy with SEC.

Serrated Colorectal Lesions in Patients With Inflammatory Bowel Disease

Alyssa M. Parian, MD, and Mark G. Lazarev, MD

Gastroenterology & Hepatology Volume 14, January 2018

Table 1. Histopathologic Characteristics of Serrated Lesions of the Colon

	Hyperplastic Polyps	Sessile Serrated Adenomas/Polyps	Traditional Serrated Adenomas	Serrated Epithelial Change^a
Serrations	Limited to top half of crypt	Top and bottom of crypt	Limited to top half of crypt	Top and bottom of crypt
Basal Crypt Architecture	Narrow, straight, tubular	Distorted, branching crypts dilated at base; inverted L or T shape	Ectopic crypts that are narrow, straight, and tubular with protuberant villiform architecture	Distorted; some crypts do not reach muscularis mucosae
Nuclear Features	Unremarkable	Small foci of pseudostratification, occasional mitosis in the upper crypt	Elongated nuclei, mild pseudostratification, occasional mitosis in the upper crypt	Unremarkable
Epithelium	Hypermaturation, microvesicular	Gastric-like mucin prominent	Eosinophilic	Goblet cell-rich

^aSerrated epithelial change is not a widely recognized histopathologic finding and does not have sanctioned World Health Organization criteria; in contrast, hyperplastic polyps, sessile serrated adenomas/polyps, and traditional serrated adenomas have criteria sanctioned by the World Health Organization.

Serrated epithelial change in ulcerative colitis patients is associated with high rate of colonic dysplasia.

Parian AM, Chowdhury R, Rubin DT et al.

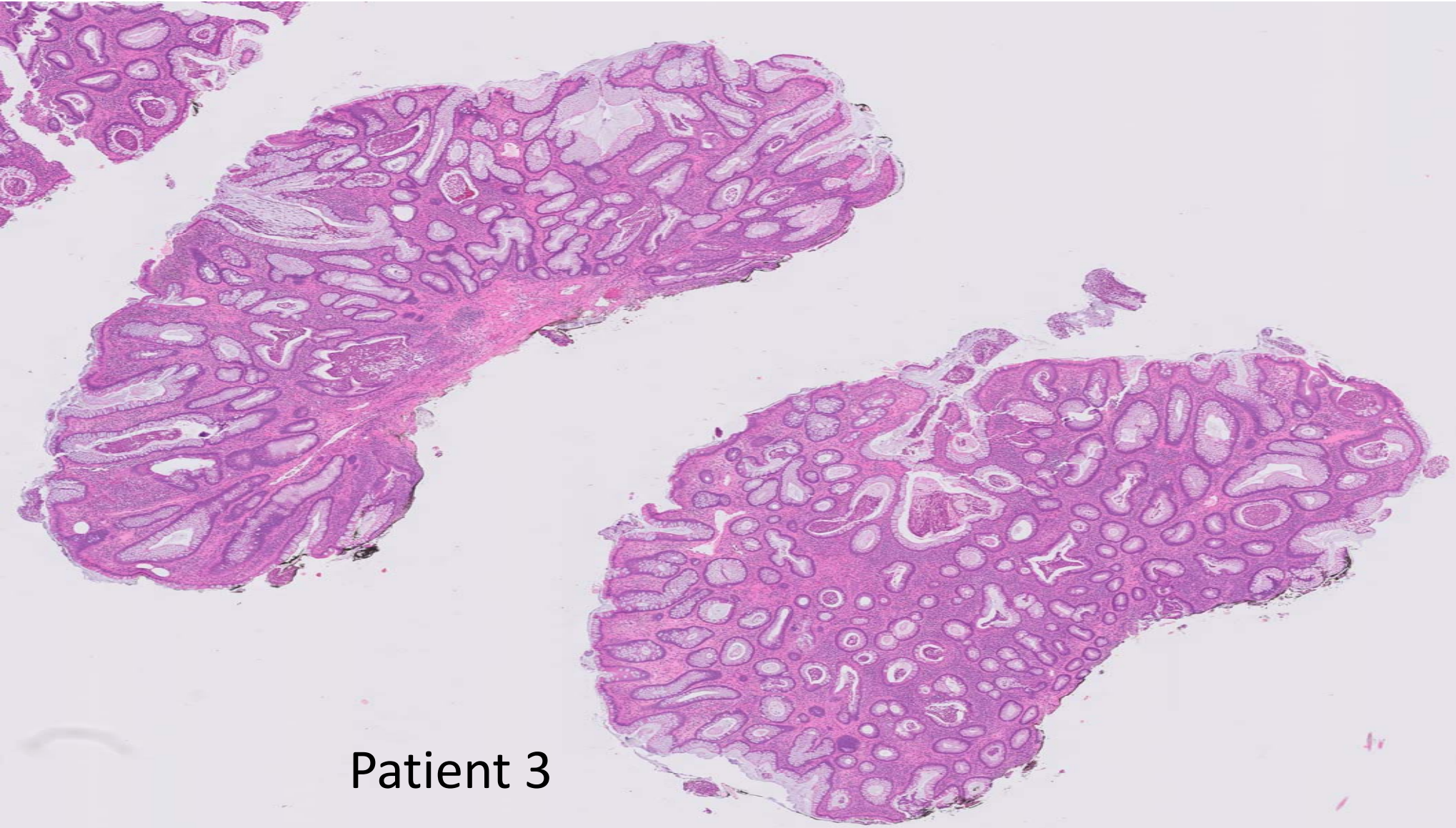
Gastroenterology 2017;152(5)Suppl 1:S76 *Abstract*

- 64 UC patients with SEC matched to 113 UC patients without SEC (by age, disease duration, disease extent). No prior dysplasia.
- UC with SEC had a higher rate of any dysplasia compared to UC without SEC (23.4% vs. 5.3%; $p < .001$)
- HGD/CRC was higher among UC with SEC (9.4% vs. 1.8%; $p = .03$)
- Time to dysplasia was shorter among UC with SEC (22.2m vs 116.3m; $p < .001$)

DNA Methylation and Mutation of Small Colonic Neoplasms in Ulcerative Colitis and Crohn's Colitis: Implications for Surveillance

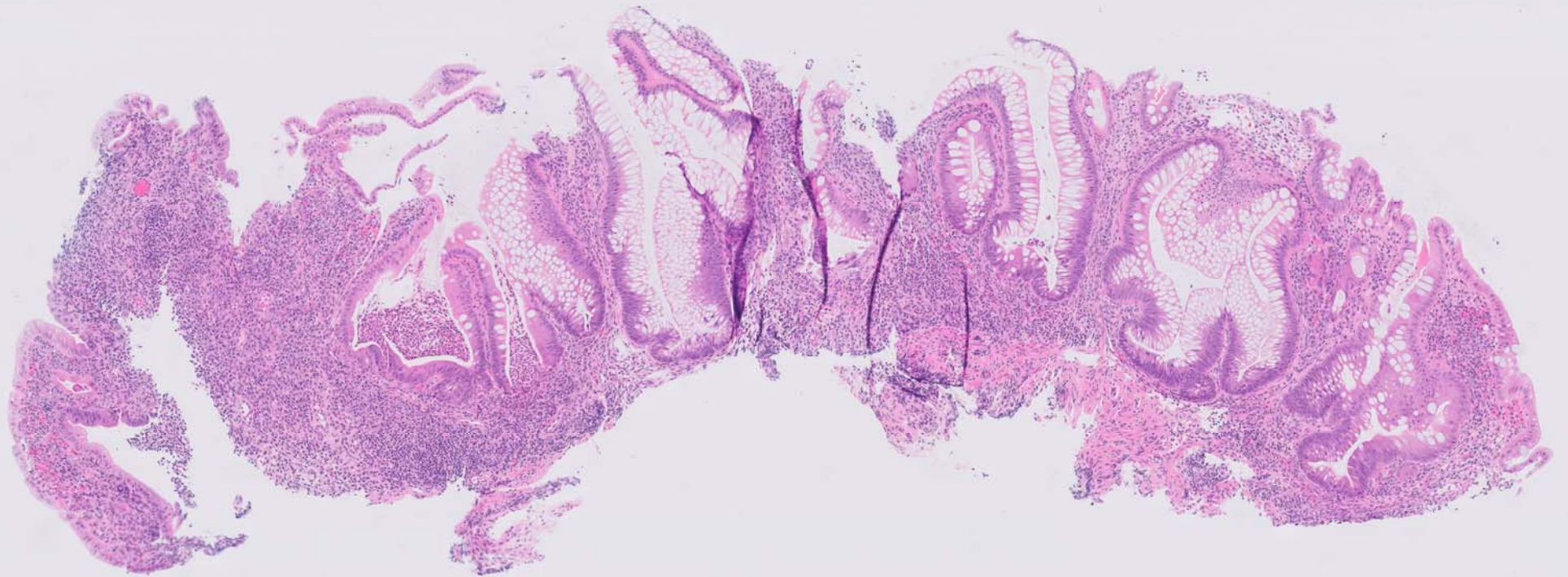
Johnson DH, Taylor WR, Aboelsoud MM, et al.
Inflamm Bowel Dis 2016;22:1559-1567.

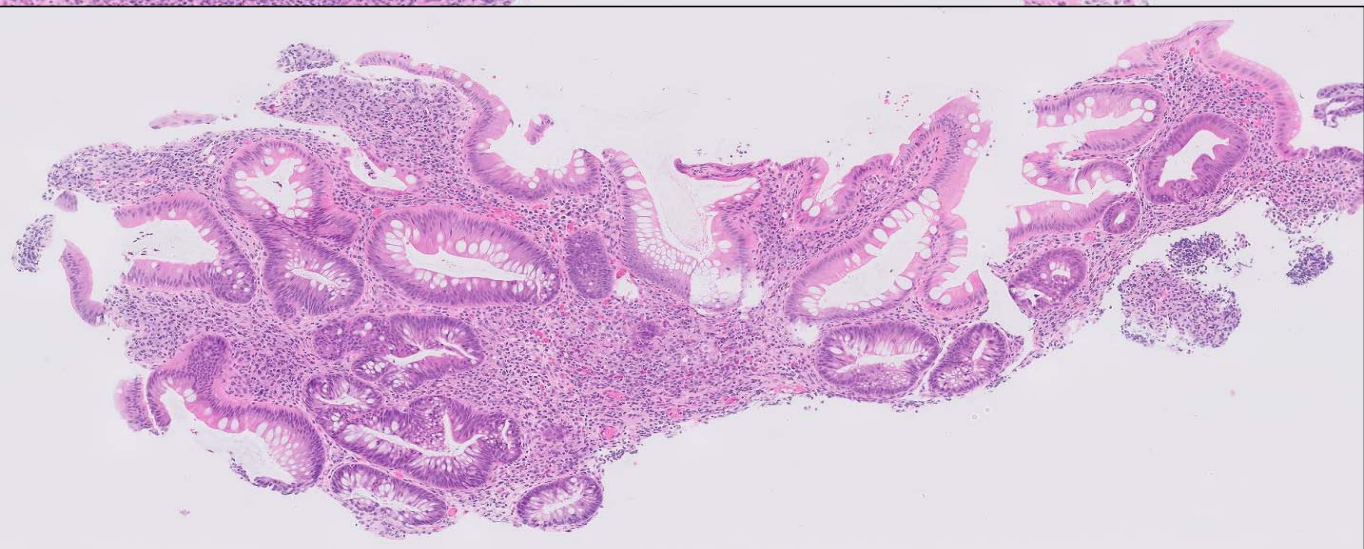
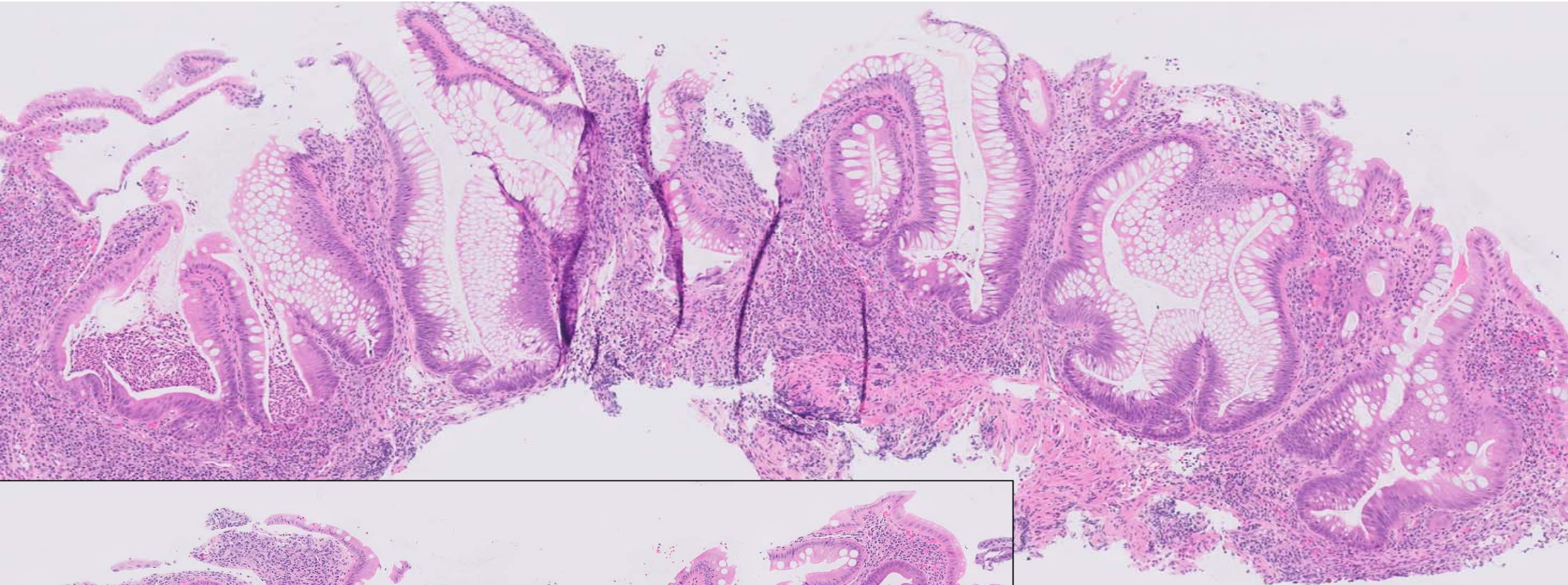
- 102 patients: 44 controls; 29 LGD; 19 SEC; 10 SSA
- Increasing levels of methylation of BMP3 and NDRG4 from control -> LGD -> SEC -> SSA.
- *BRAF V600E* mutation was found in 3/13 SEC (9%) and 4/10 SSA (40%).
- Mutant KRAS in 6/12 (50%) of SEC, which was higher than other groups and significantly higher than controls (14%).
- 23 patients went on to develop CRN; 6/44 IBD controls (14%), 14/27 LGD-IBD (52%), 1/11 SEC (9%), and 2/7 SSA/P (29%).
- Concluded that KRAS was often mutated in SEC but this did not predict subsequent neoplasia and SEC likely represents a hyperplastic phenomenon.



Patient 3

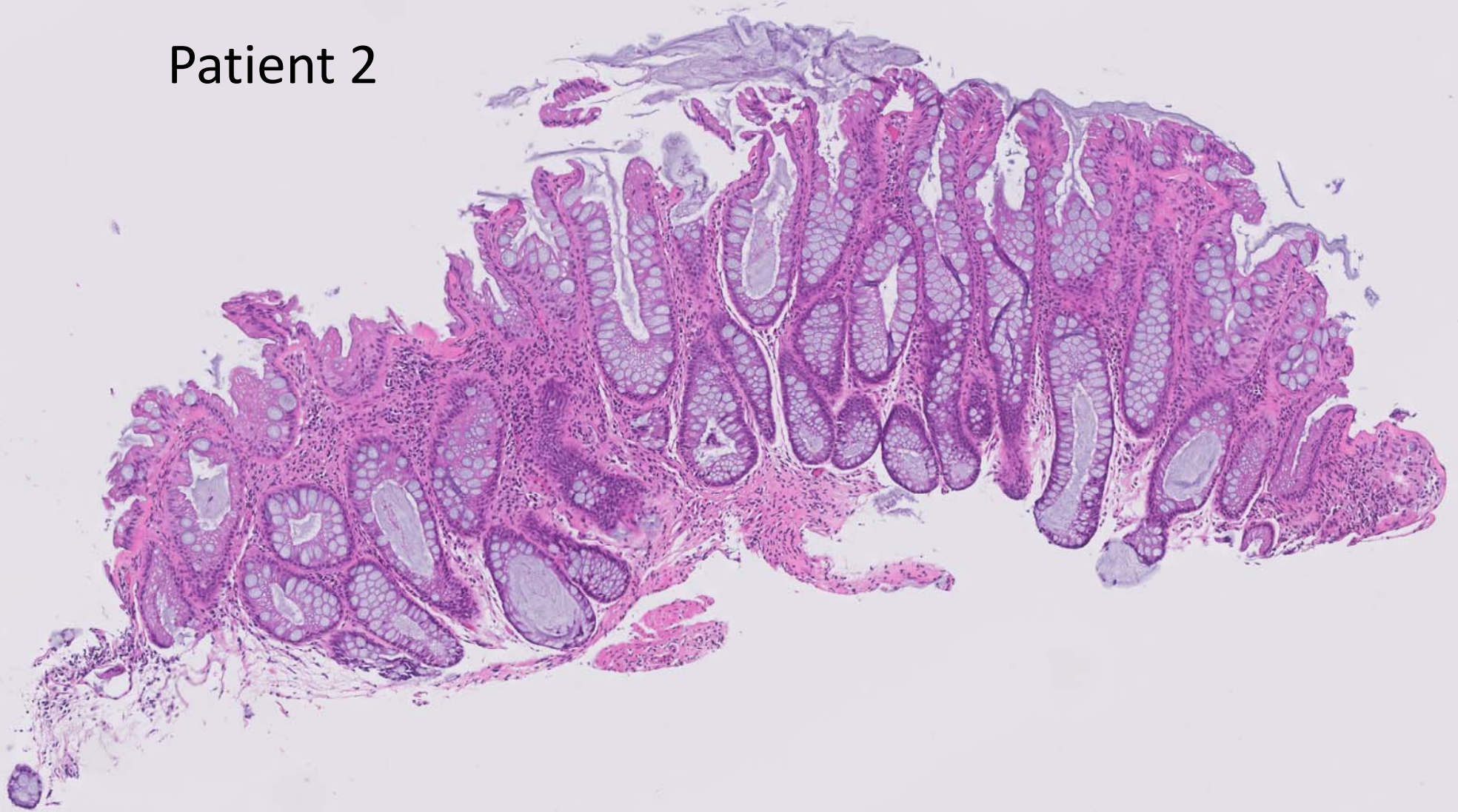
Patient 1



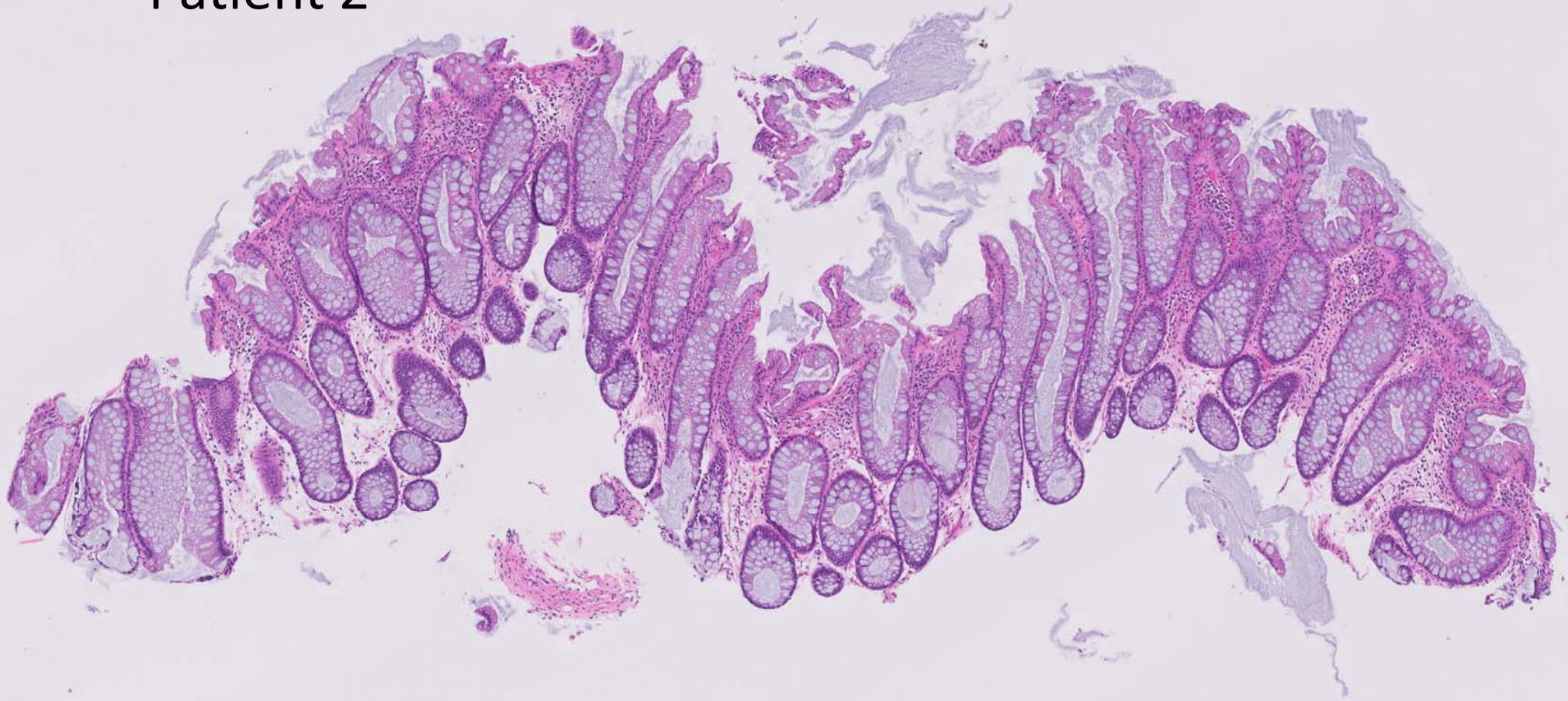


Patient 1

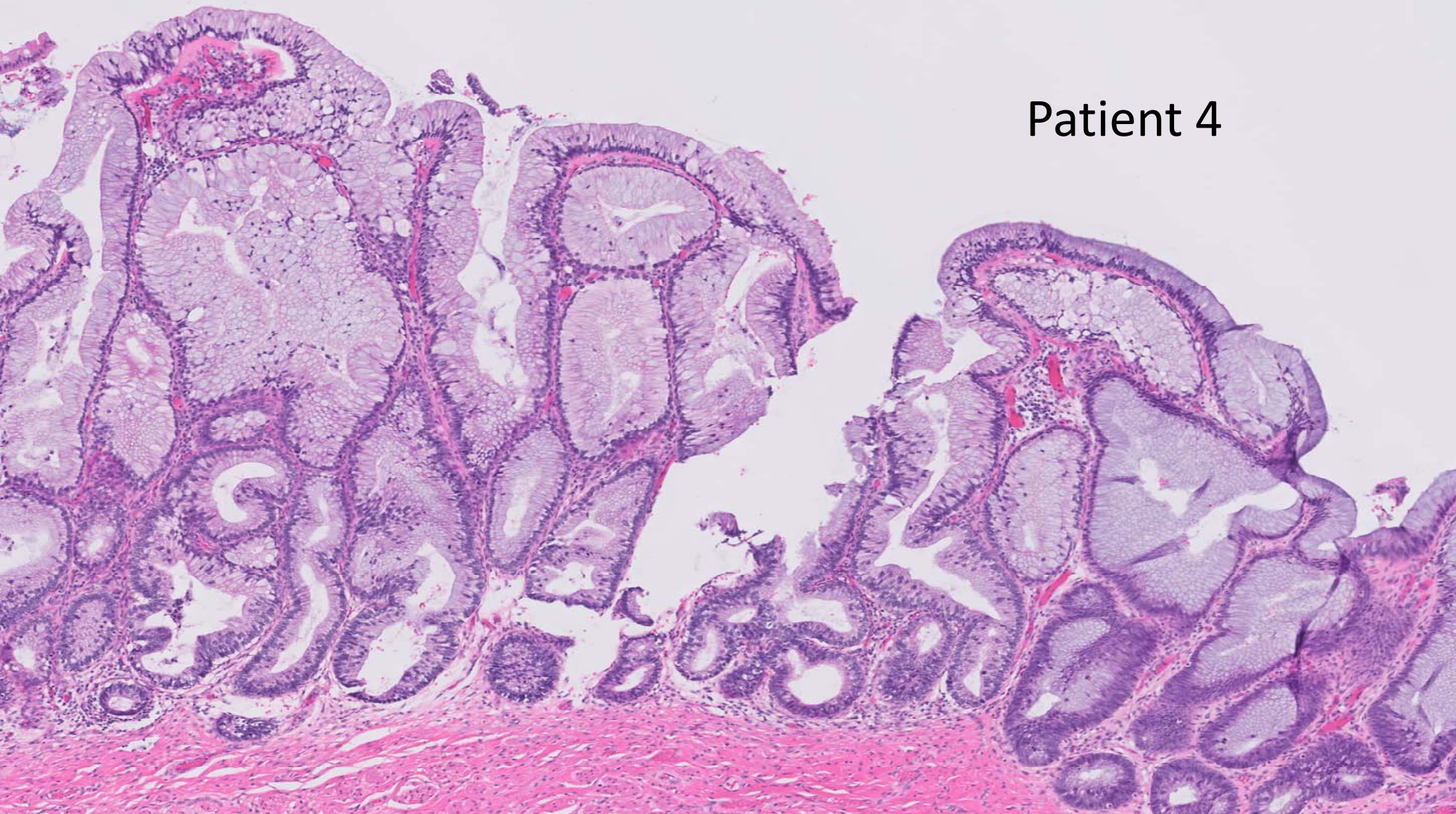
Patient 2

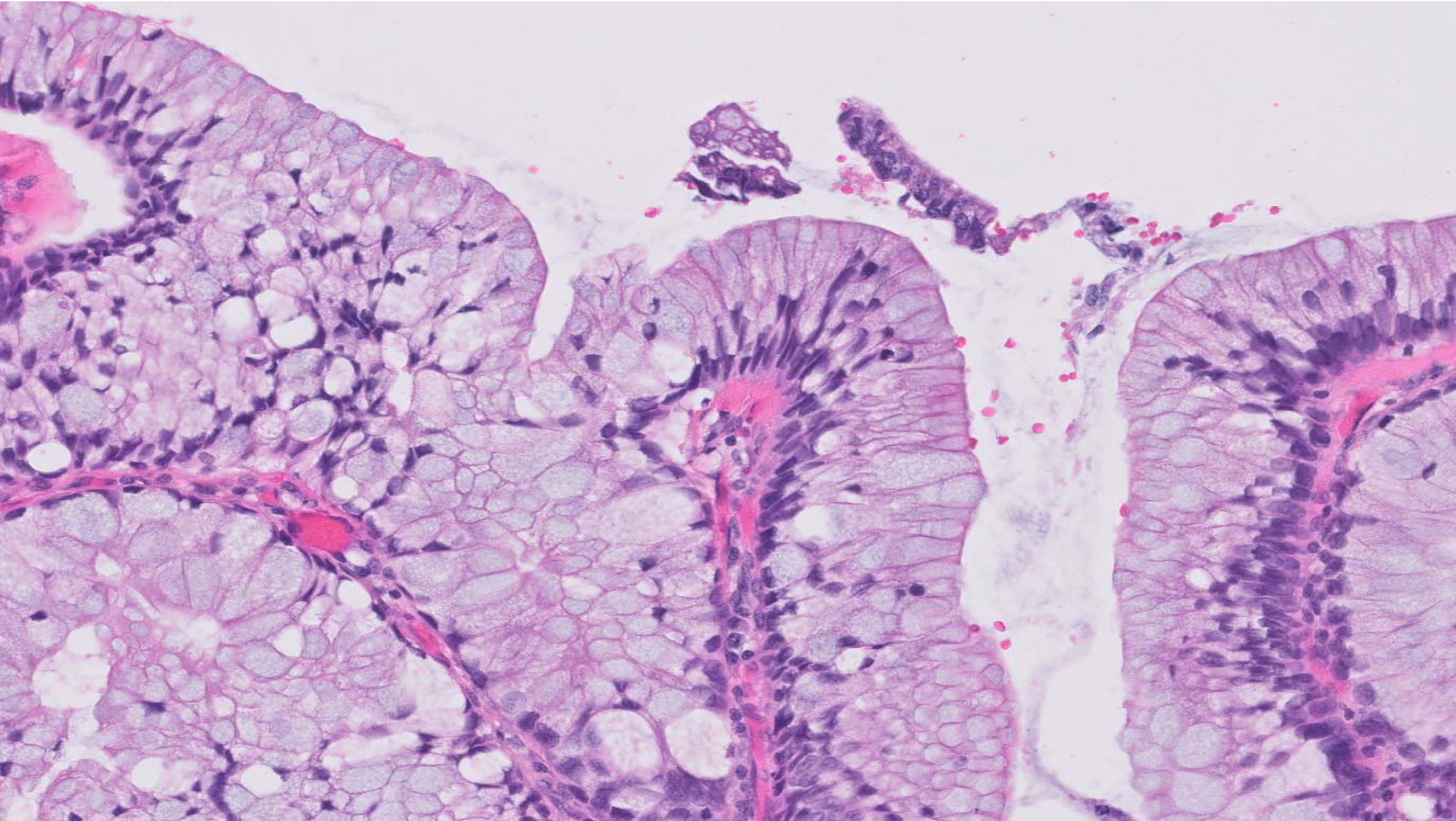


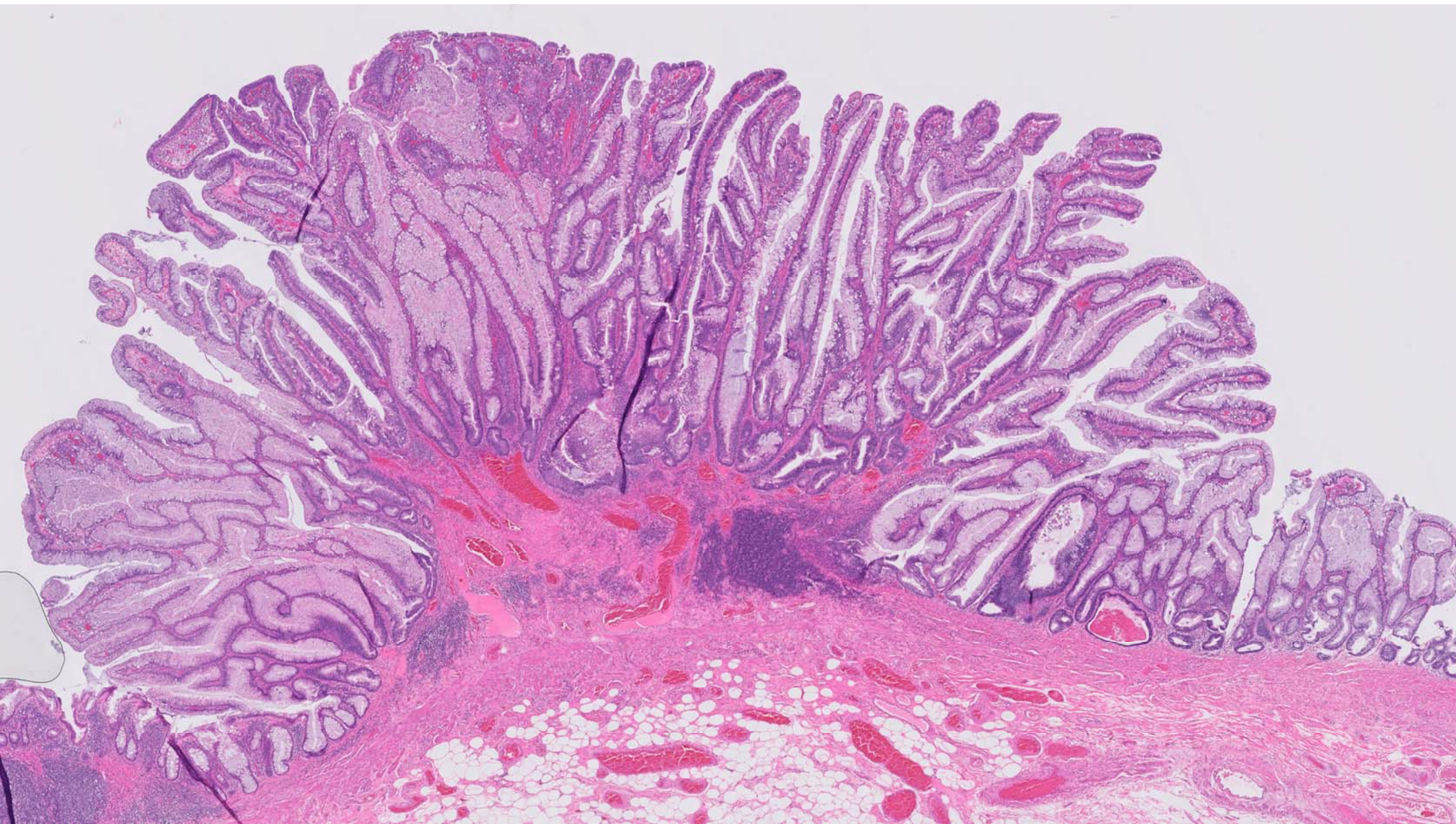
Patient 2

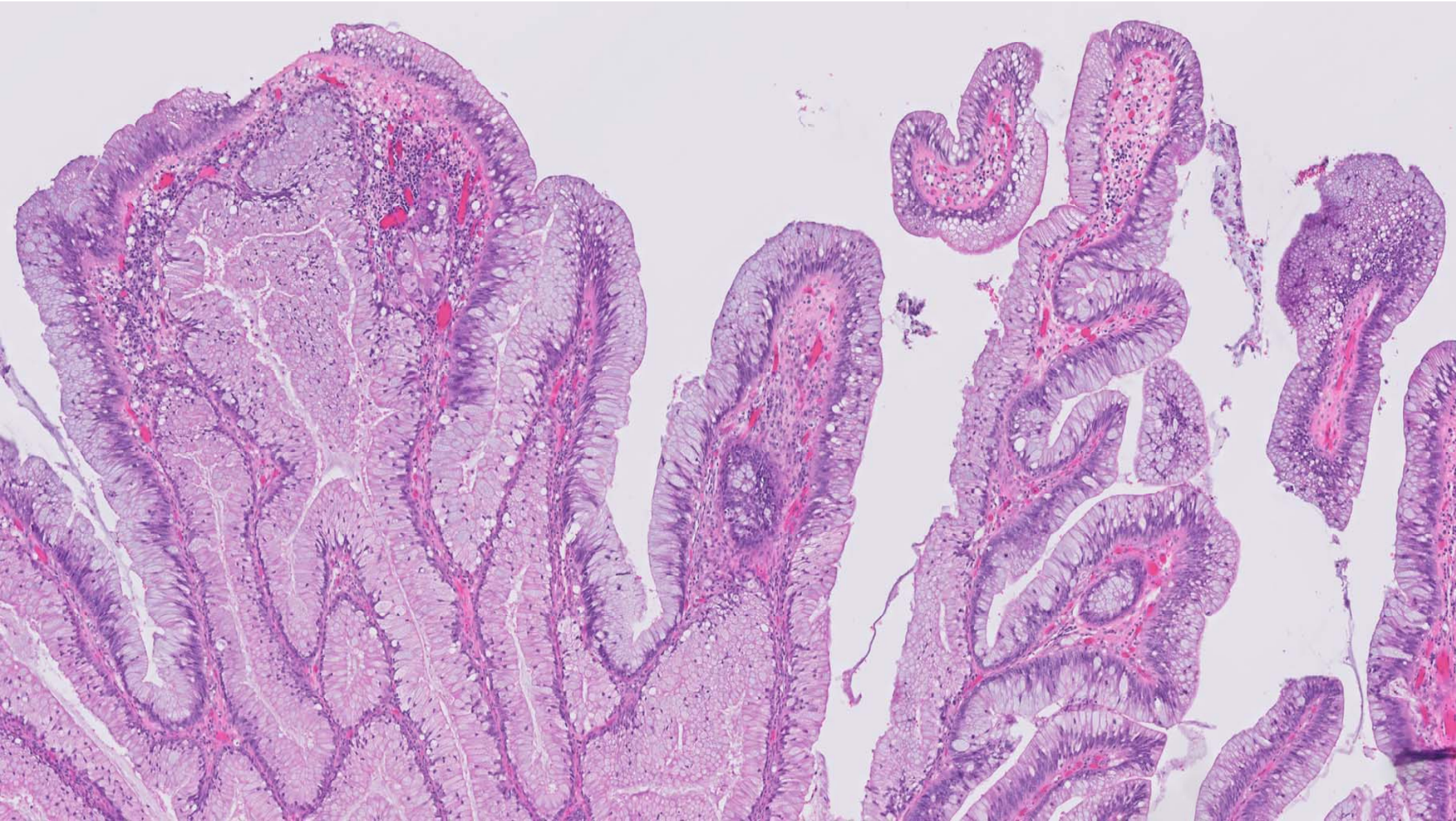


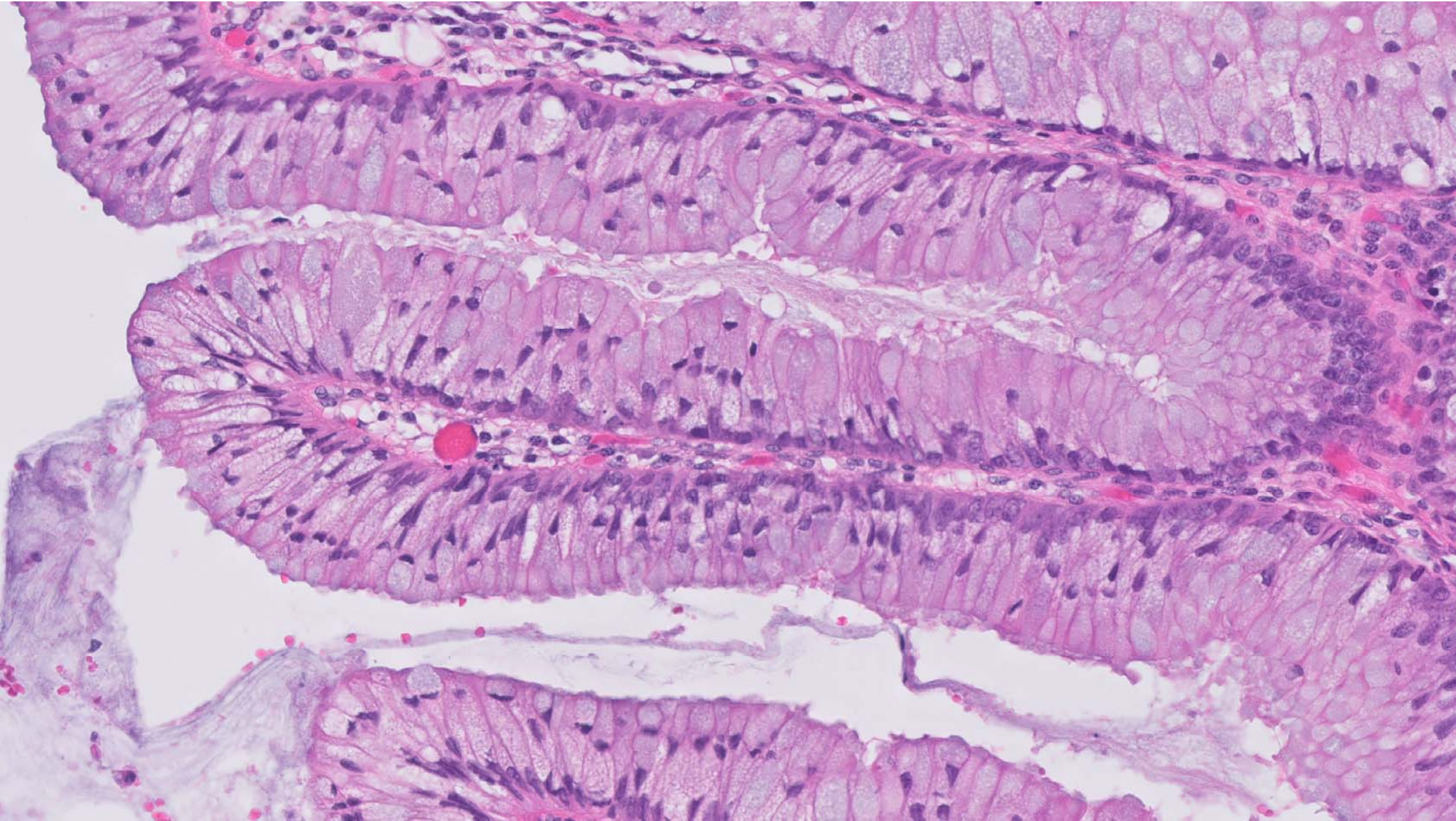
Patient 4

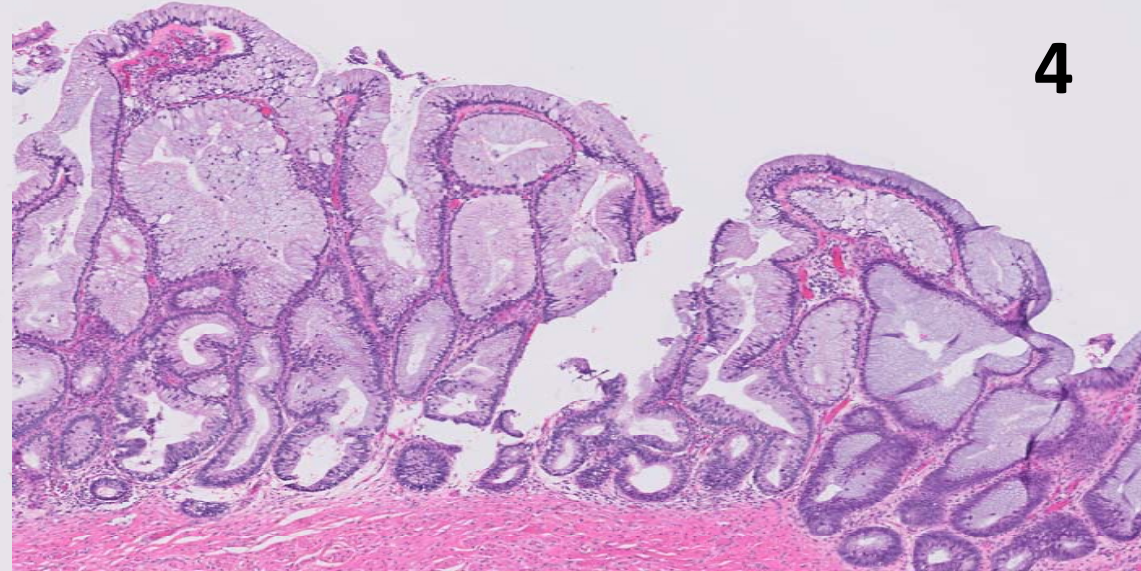
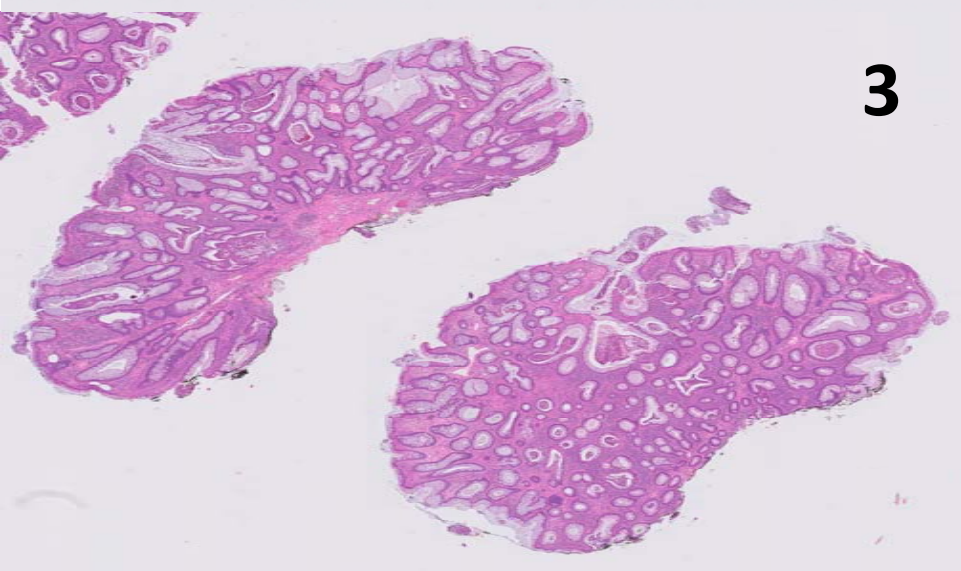
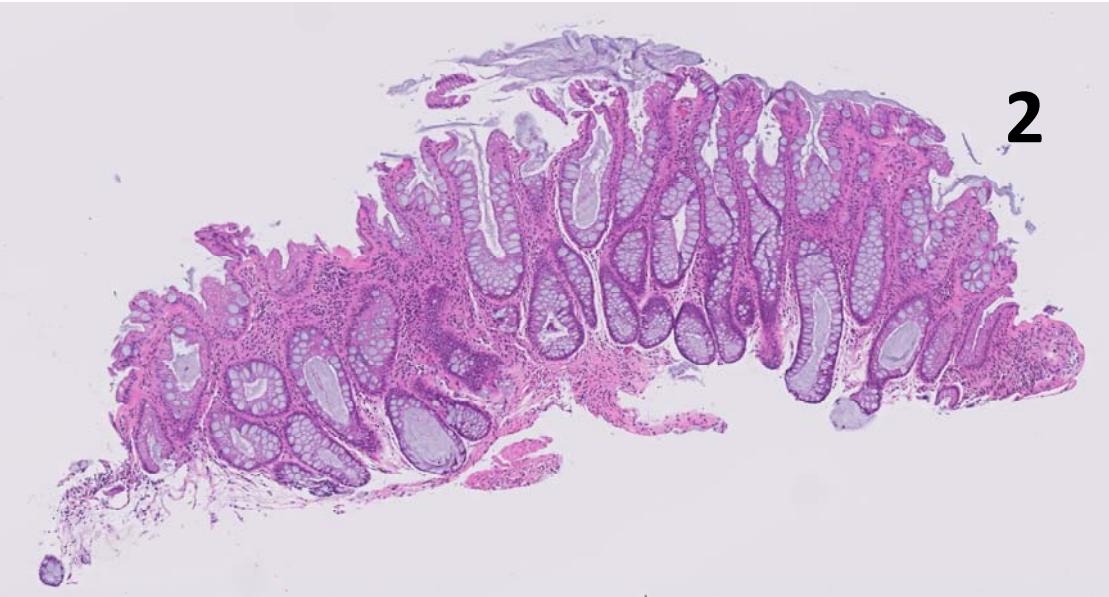




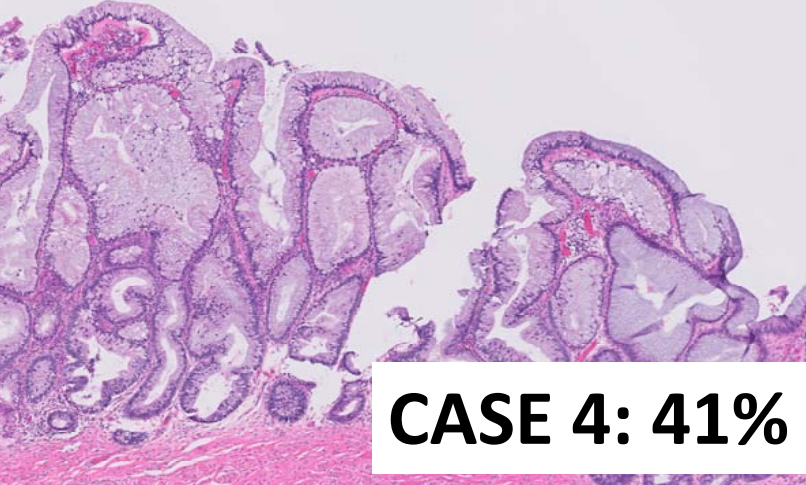
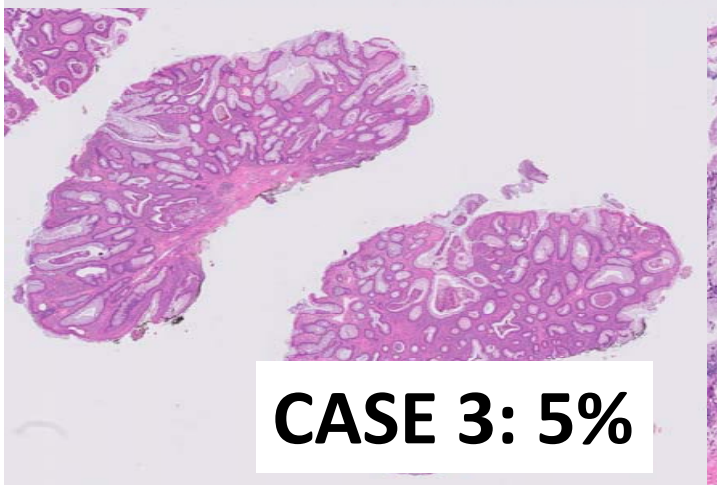
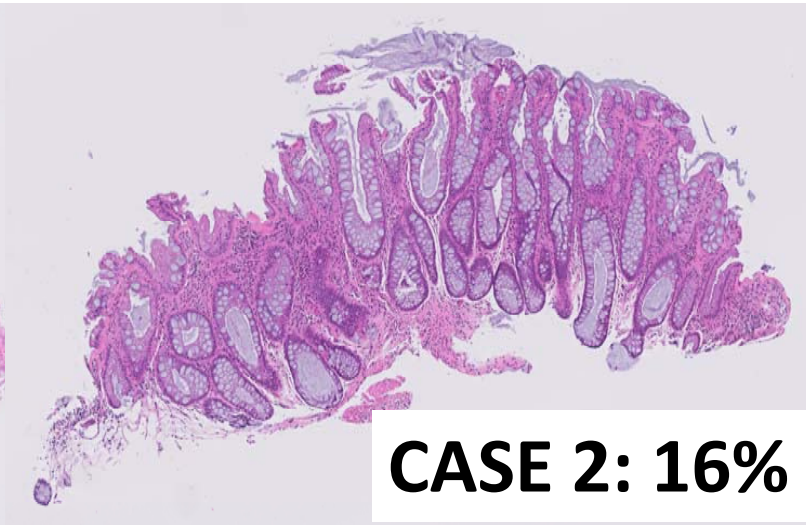
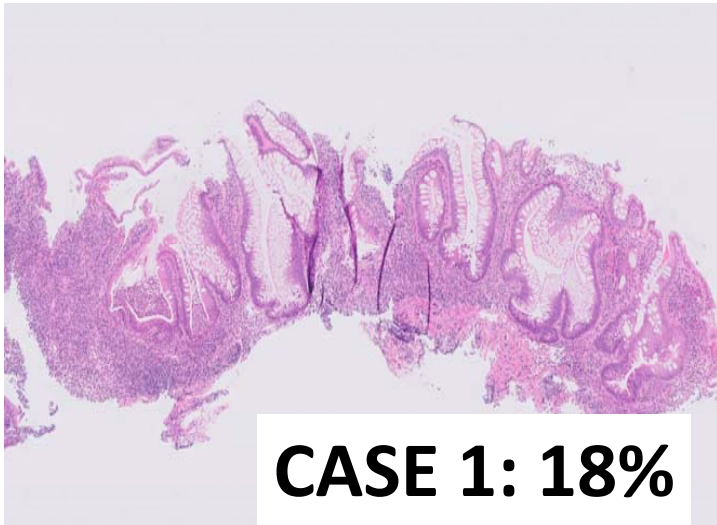








Q: All of these following photos are from patients with chronic idiopathic inflammatory bowel disease. Which of these 4 patients would you consider as having "serrated epithelial change"?



**NONE
OF
THESE:
20%**

MOU2

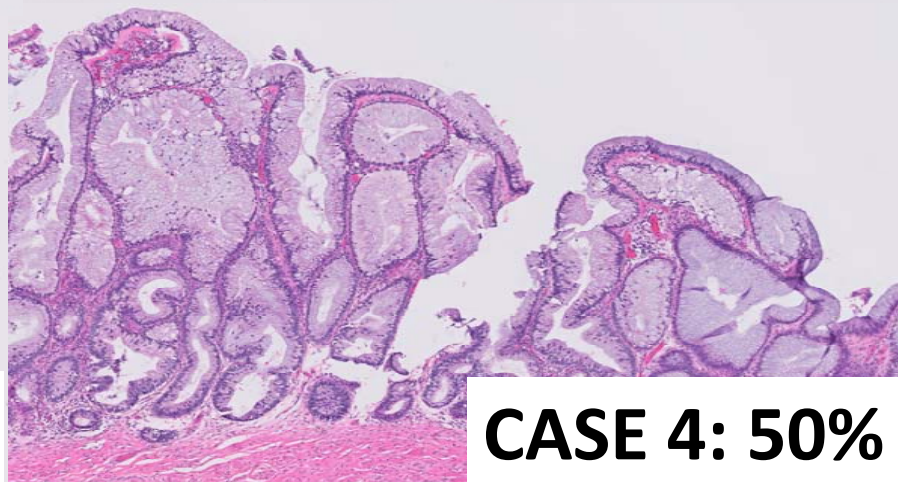
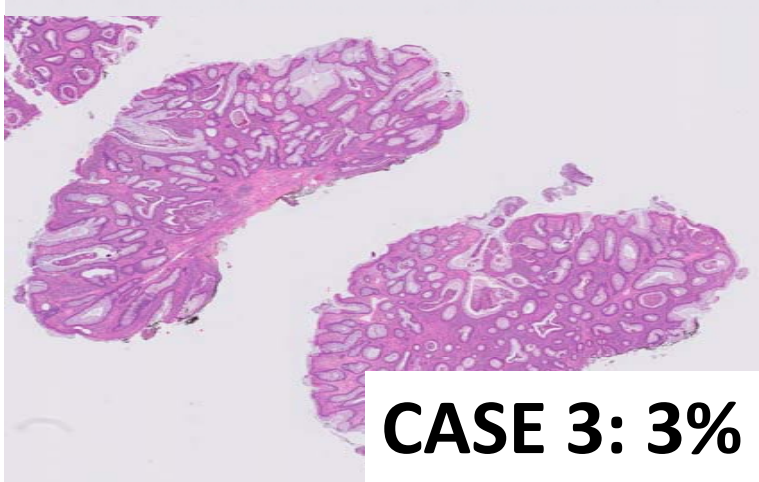
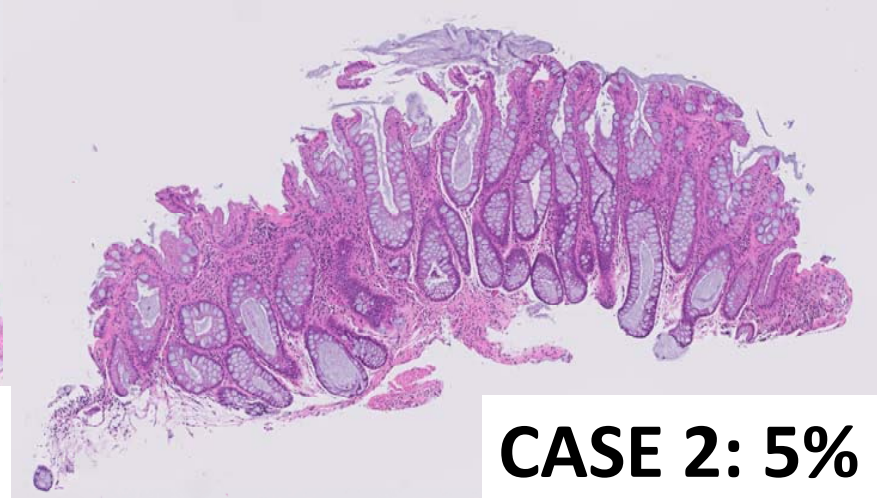
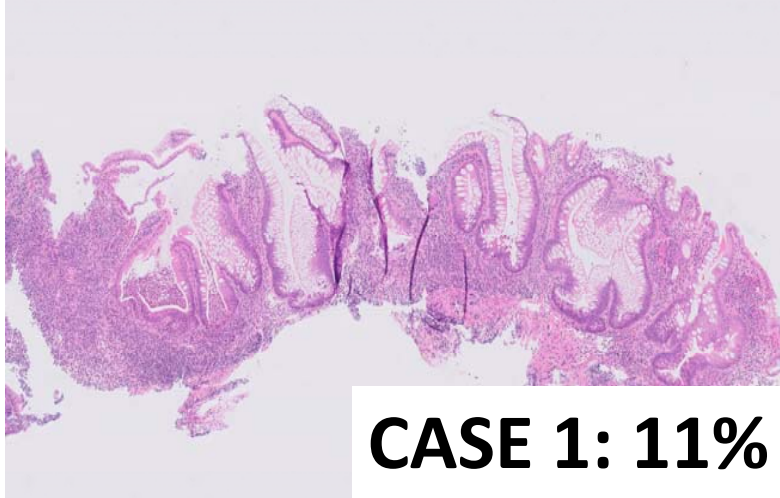
Q: All of these following photos are from patients with chronic idiopathic inflammatory bowel disease. Which of these 4 patients would you consider as having "serrated epithelial change"?

#	Answer	%	Count
1	1	17.57%	13
2	2	16.22%	12
3	3	5.41%	4
4	4	40.54%	30
5	none	20.27%	15
	Total	100%	74

MOU2 HERE IS THE RAW NUMBERS FOR Q1

Microsoft Office User, 2/10/2019

Question 2: Of the lesions presented in the previous question, which would you consider to have potential to progress to cancer?



**NONE:
19%**

**ALL:
12%**

MOU9

Question 2: Of the lesions presented in the previous question, which would you consider to have potential to progress to cancer?

#	Answer	%	Count
1	1	10.81%	8
2	2	5.41%	4
3	3	2.70%	2
4	4	50.00%	37
5	all	12.16%	9
6	none	18.92%	14
	Total	100%	74

Slide 27

MOU9 Here is the slide with the updated chart of numbers in case you need it
Microsoft Office User, 2/10/2019

What I do...

- I have almost never reported “serrated epithelial change” because I am not sure the diagnosis is reproducible and I am not sure that I can reliably identify a specific lesion that is clinically meaningful.