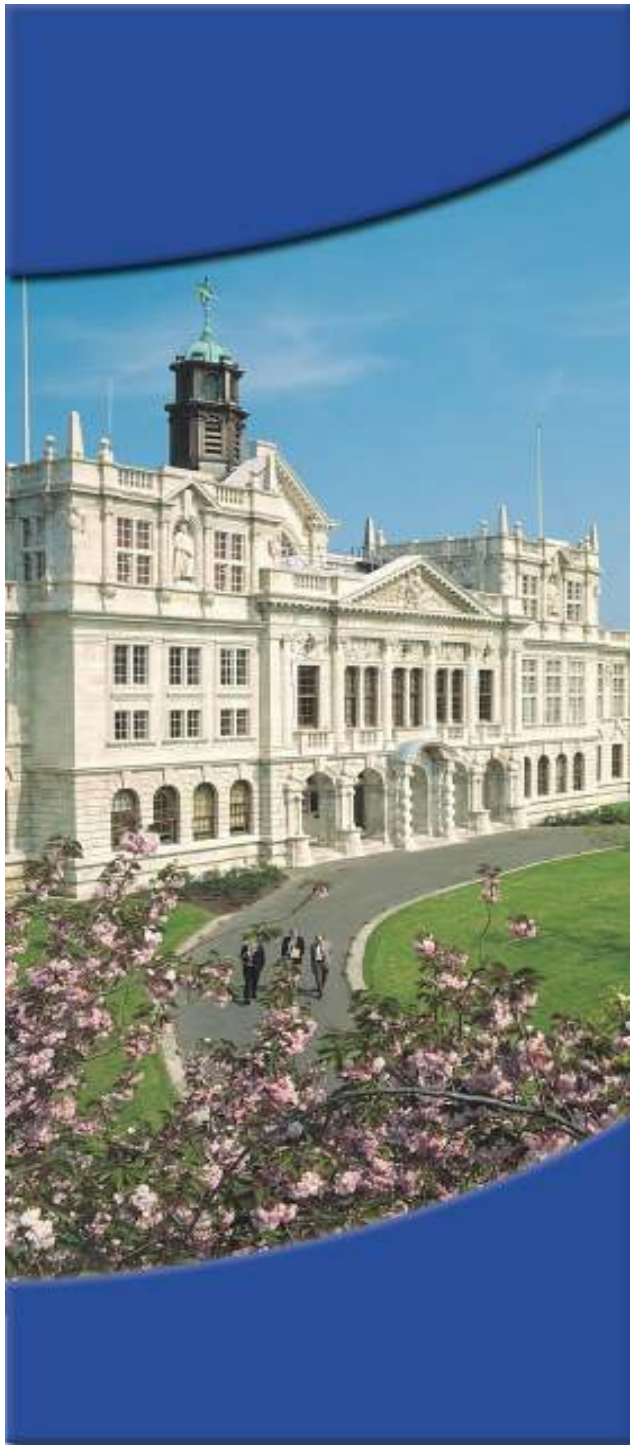


Serrated Lesions

Geraint Williams
Pathology Department
Cardiff University

CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

Serrated Lesions

Hyperplastic polyp

Serrated adenoma

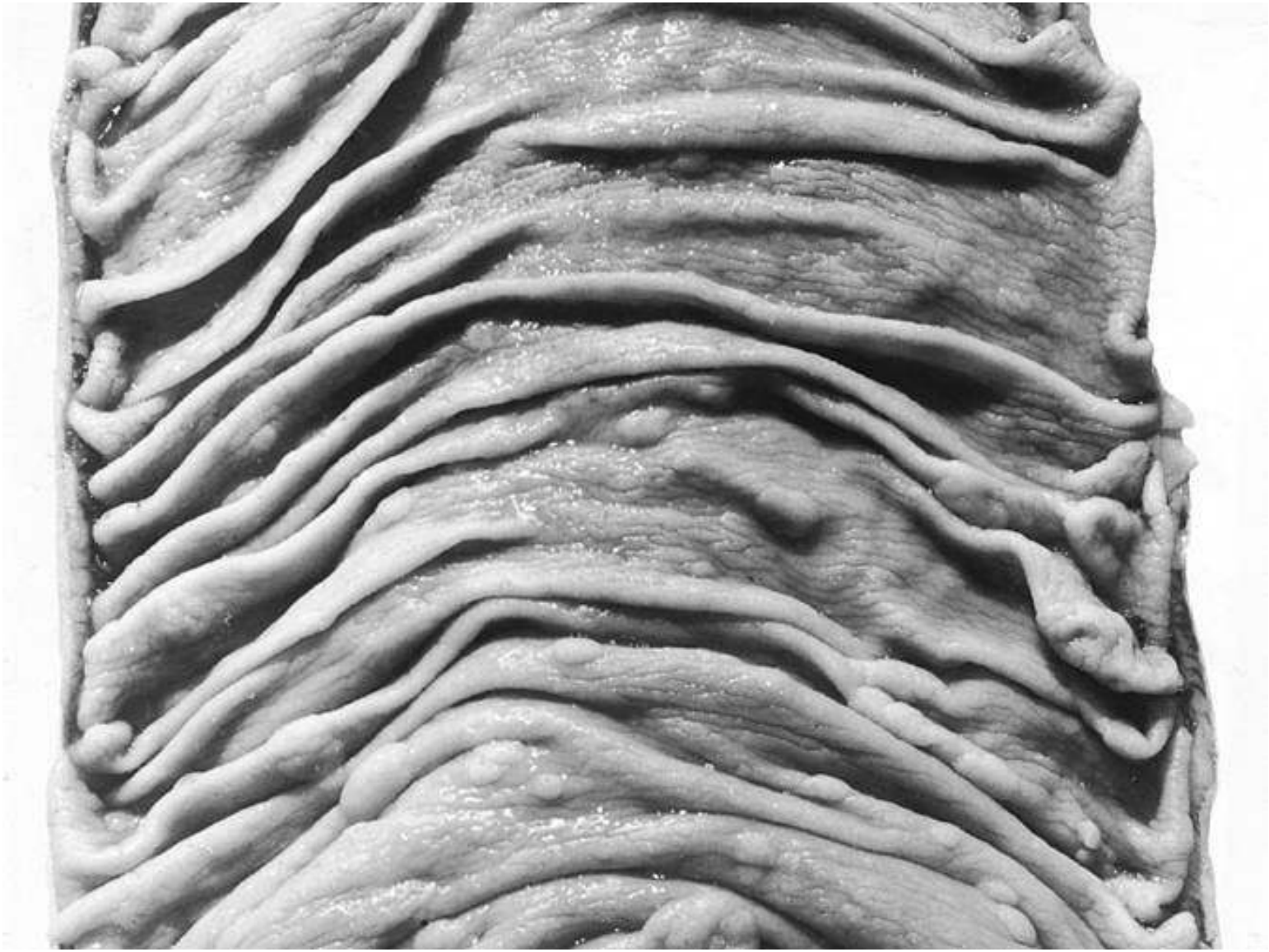
Mixed polyp

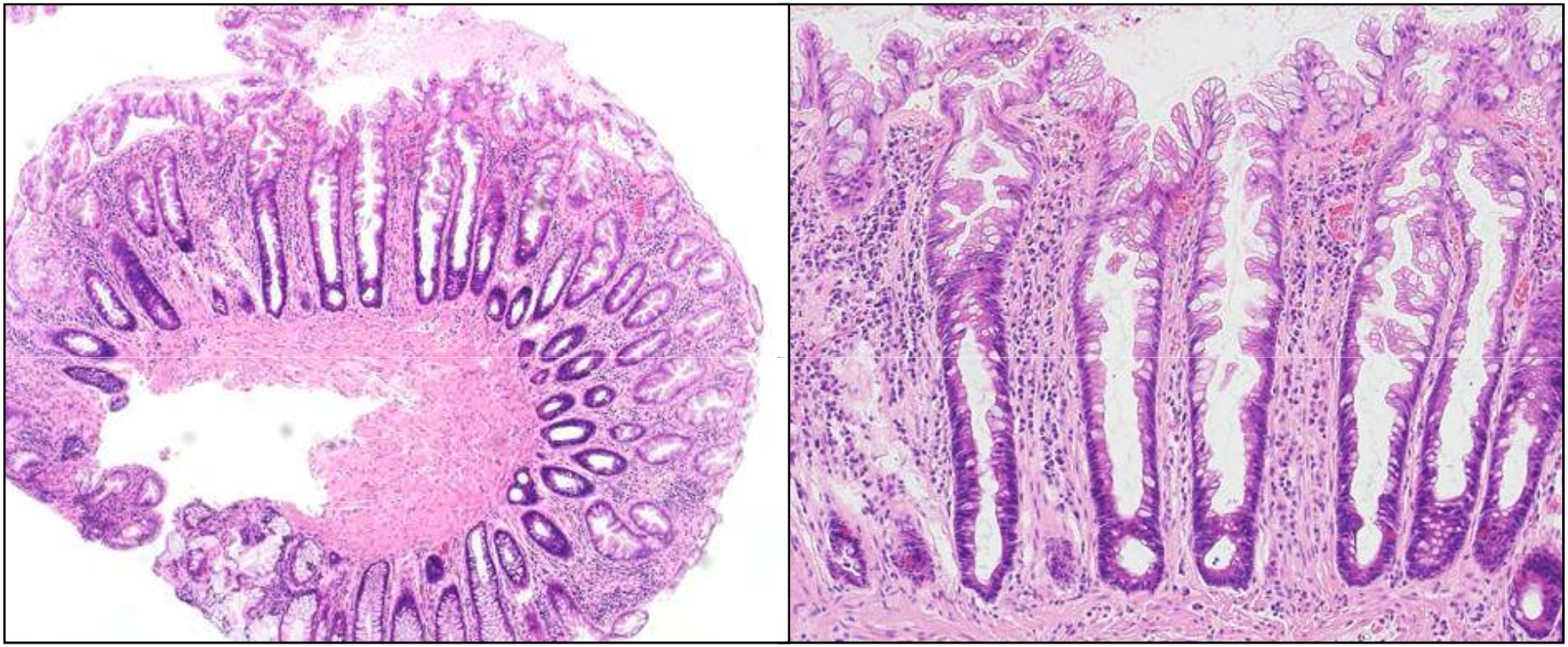
Sessile serrated polyp

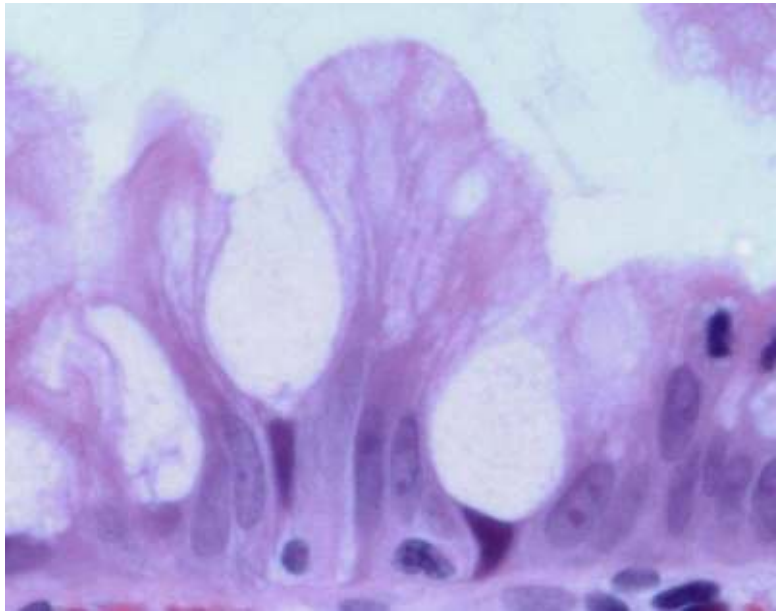
Serrated carcinoma

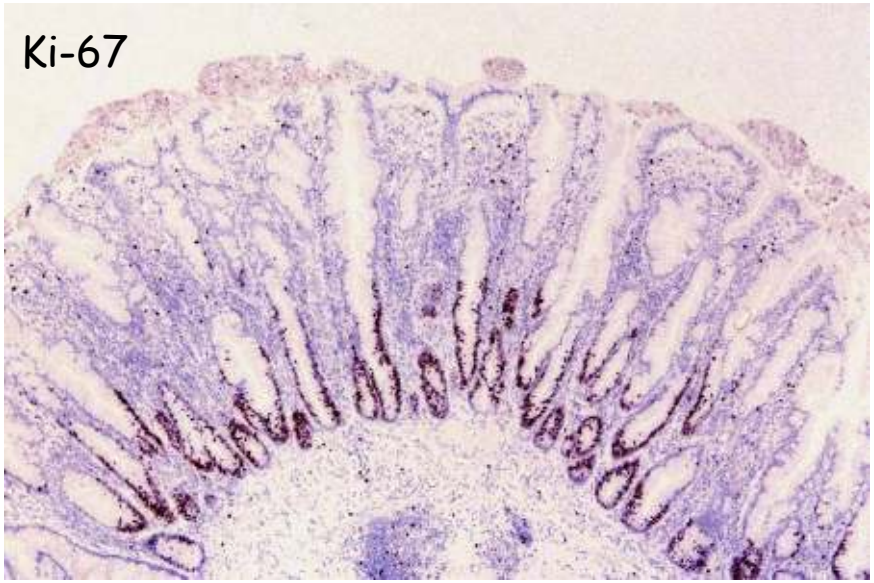
Hyperplastic Polyps

- Formerly metaplastic polyps
- Left > right, Male > female
- Infolded epithelial tufts, microvesicular cells, infrequent enlarged goblet cells in upper crypts
- May be prominent endocrine cells
- May be thickened subepithelial collagen plate
- No dysplasia
- Failure of anoikis (shedding of mature cells)



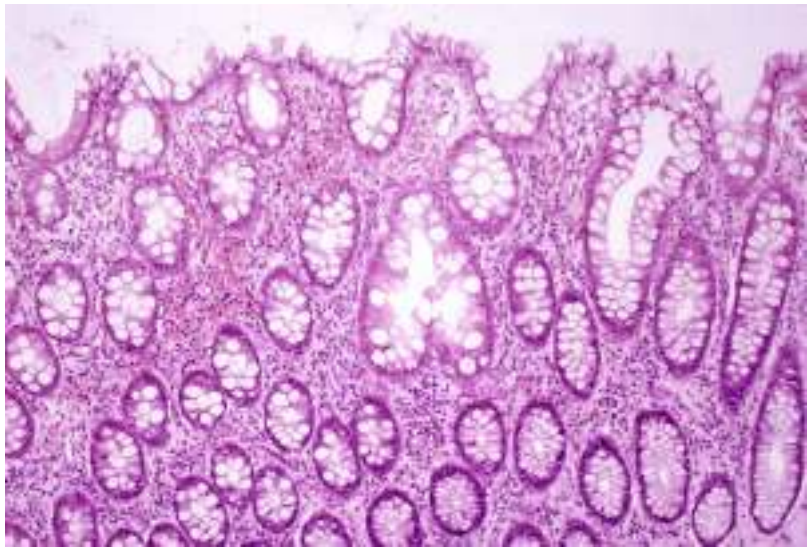





Ki-67

Hyperplastic Polyp

- Increase in frequency with age
- 17 times commoner in colons with carcinoma
- Similar dietary and lifestyle risk factors to CRC
- K-ras mutation common
- Clonal
- Monocryptal?



Serrated Adenoma

Dysplasia by definition, usually low grade

Eosinophilic cytoplasm

Pseudostratified, 'pencillate' nuclei

May be tubular, tubulovillous or villous

Invade to give serrated carcinoma

Longacre & Fenoglio-Preiser 1990

Traditional Serrated Adenoma

1-15% of all adenomas

Often left sided

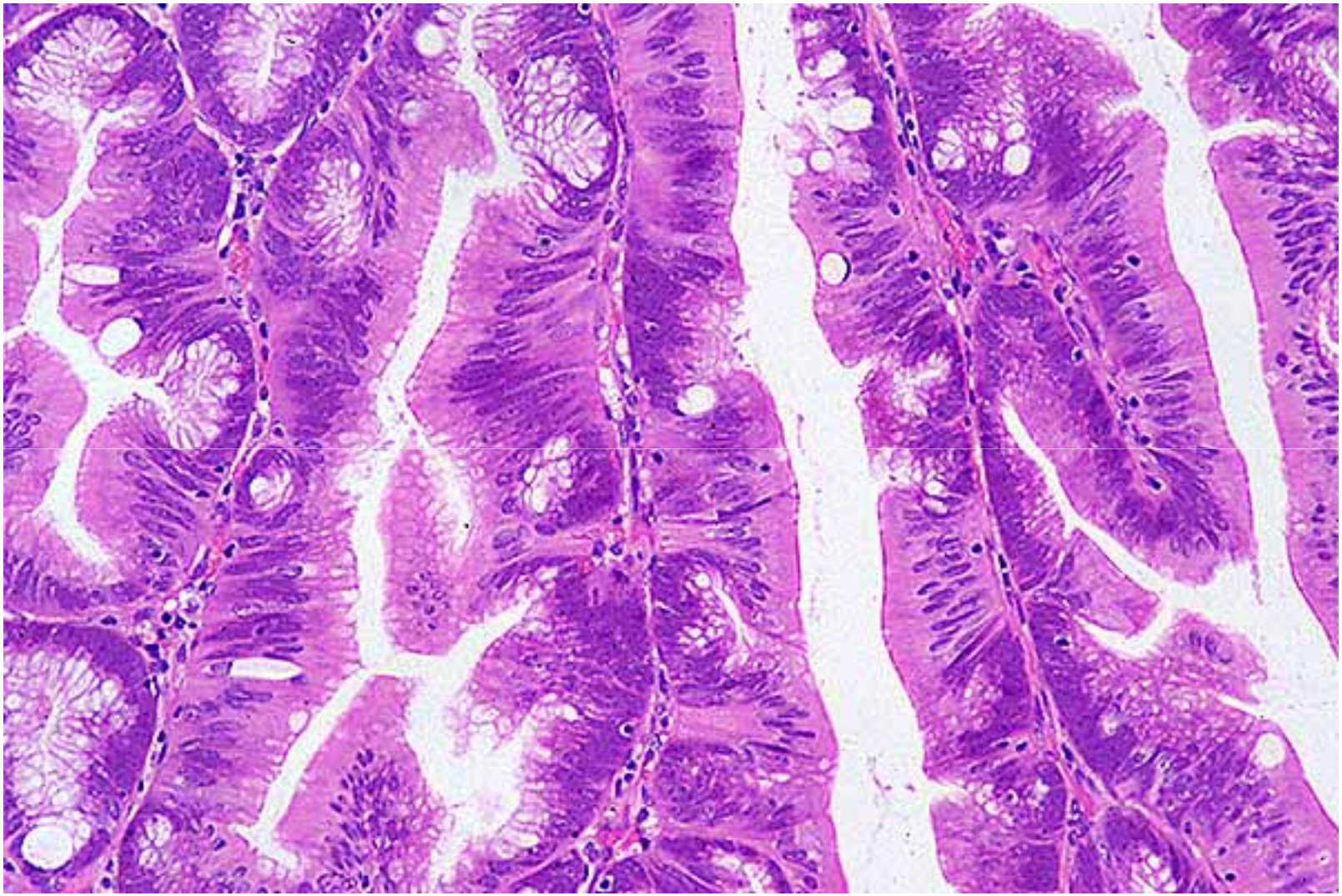
Frequently pedunculated, villiform

Short, budding, 'ectopic' crypts

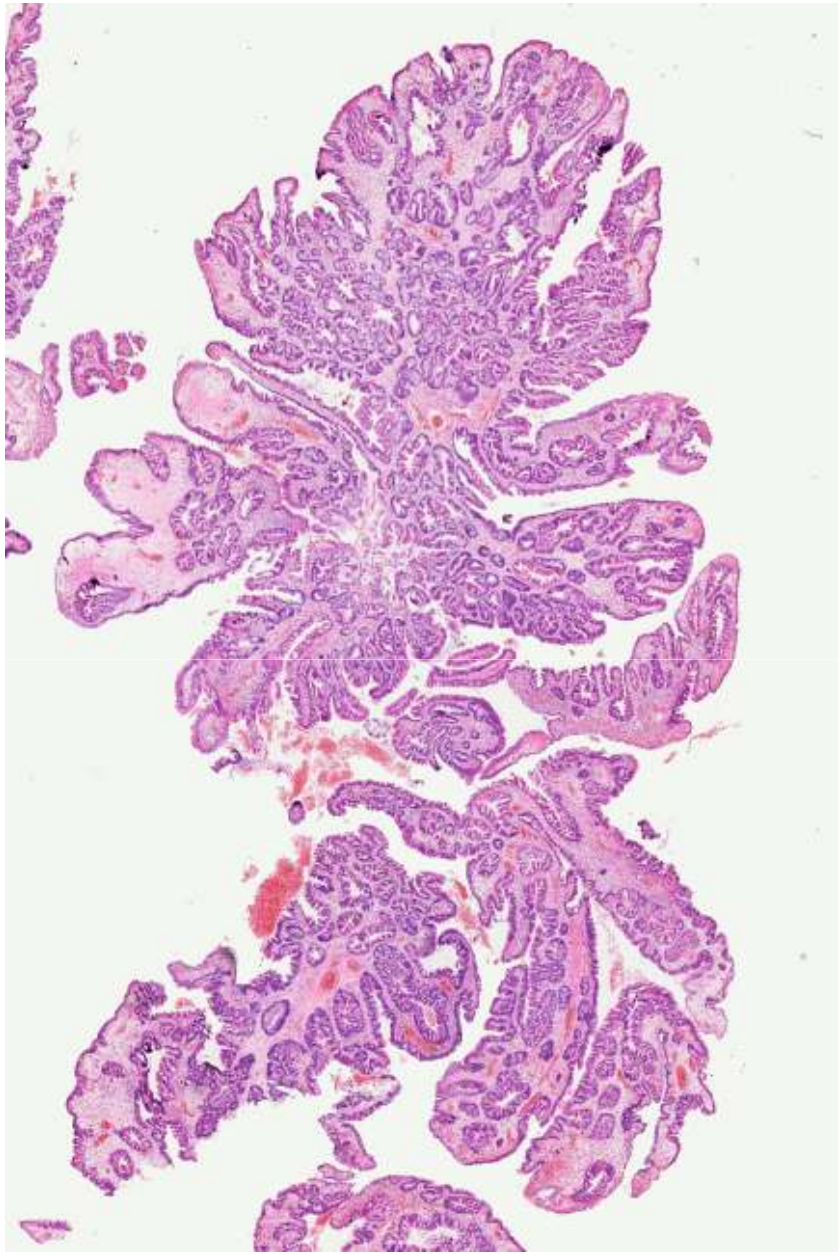
'Filiform' variants

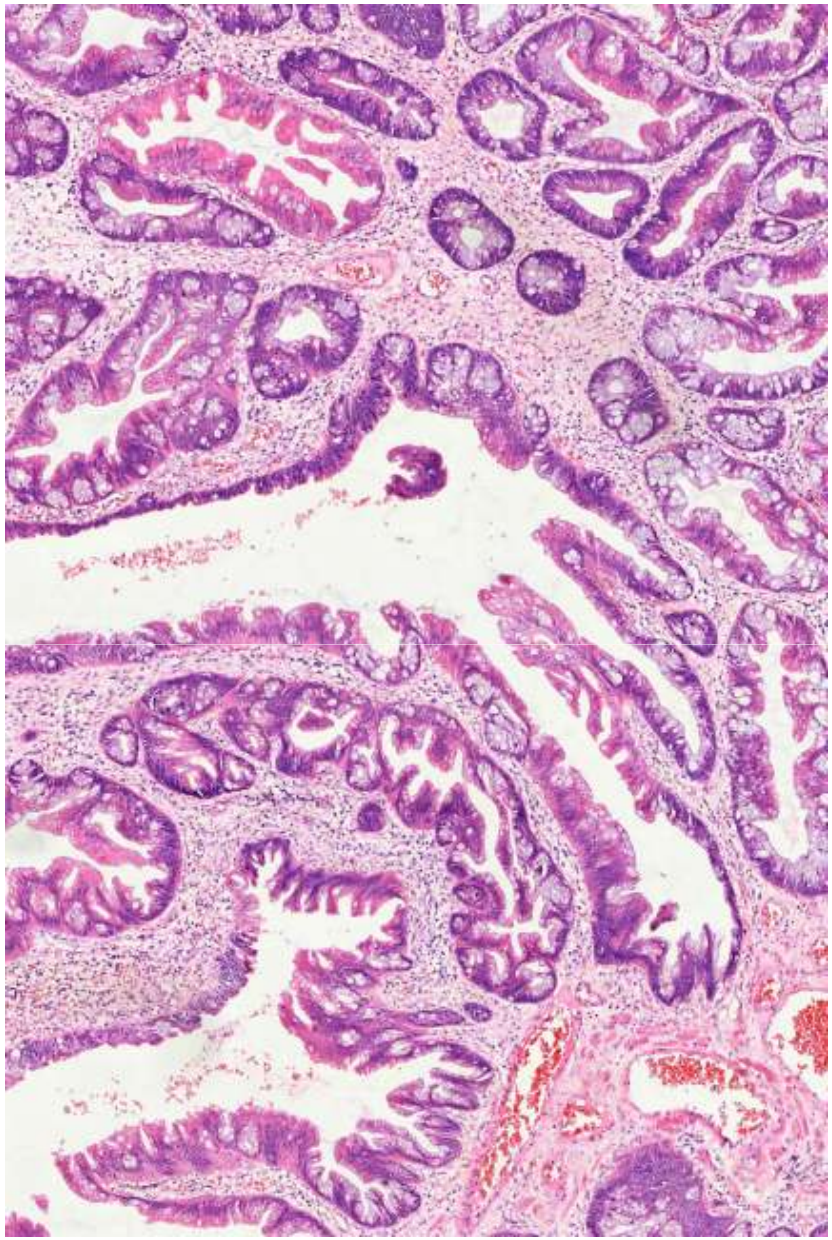
Torlakovic et al 2003, 2008

Yantiss et al 2007



'Traditional' Serrated adenoma (TSA)





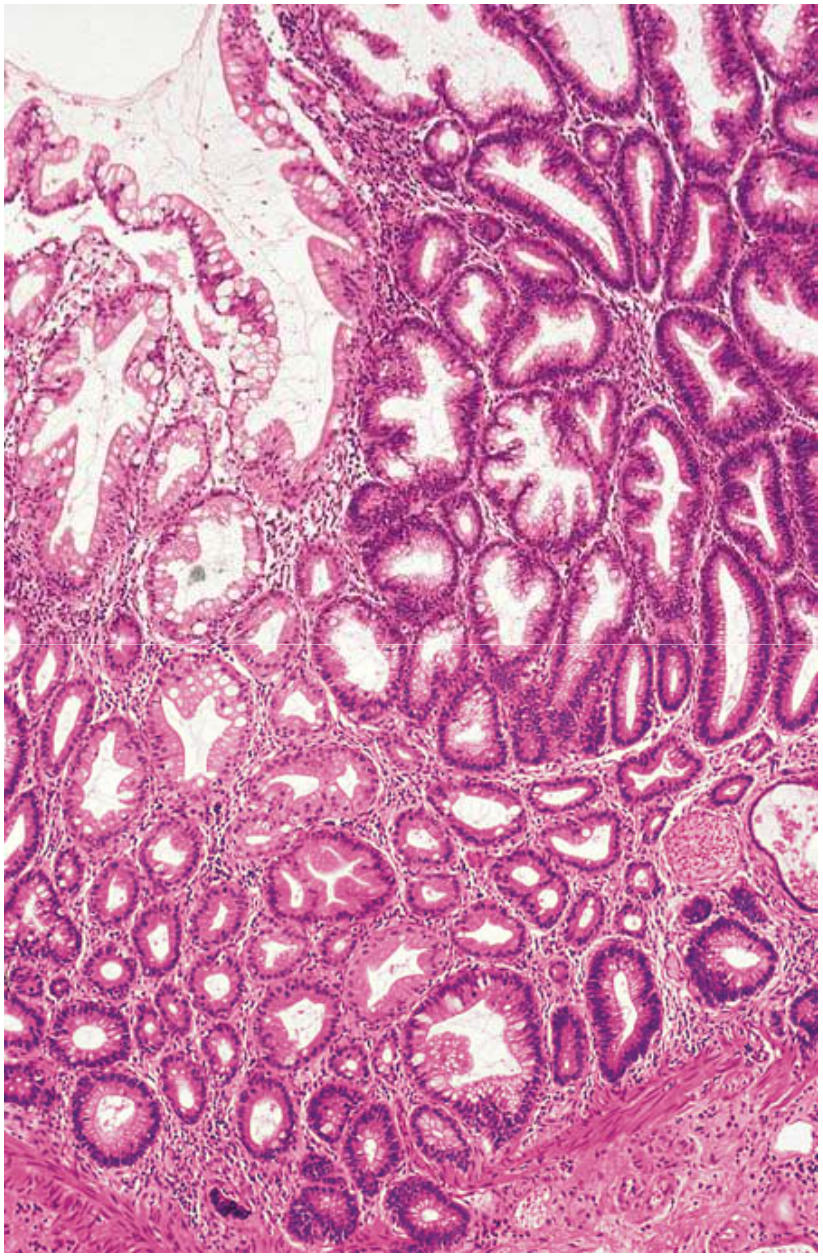
Filiform Serrated Adenoma

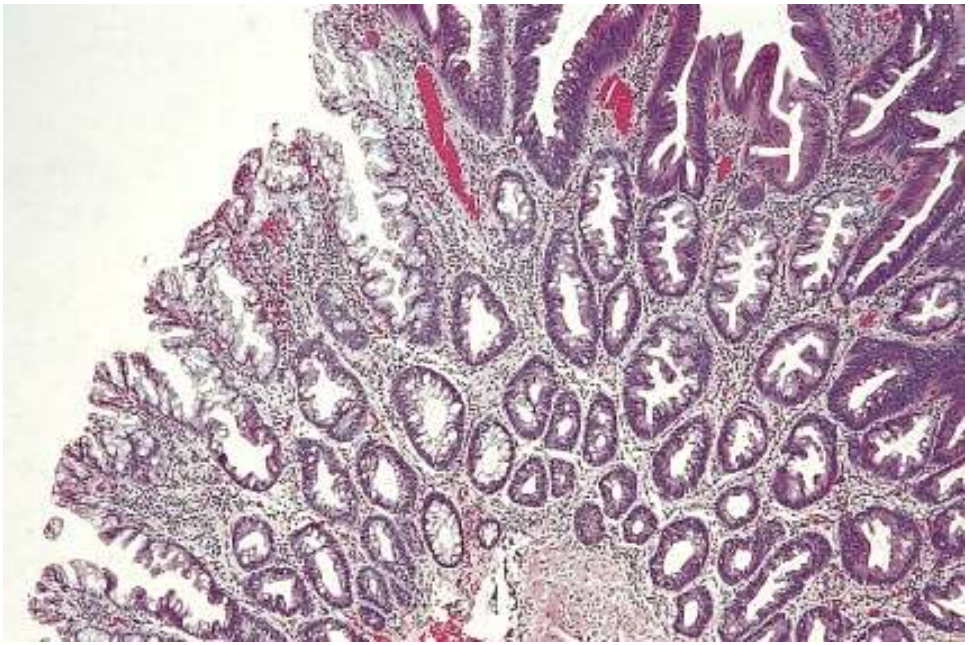
Mixed Polyps

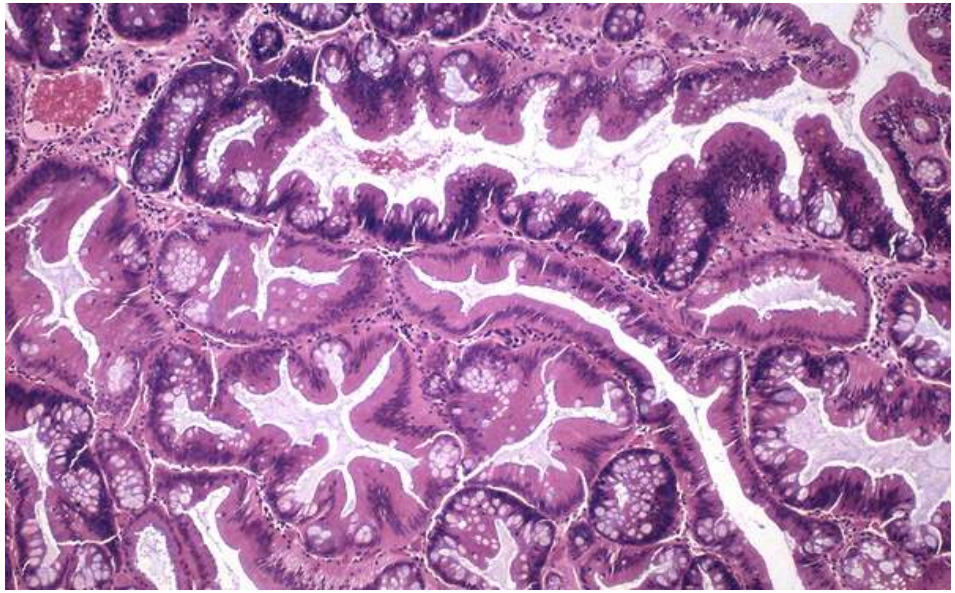
Collision between hyperplastic polyp and adenoma

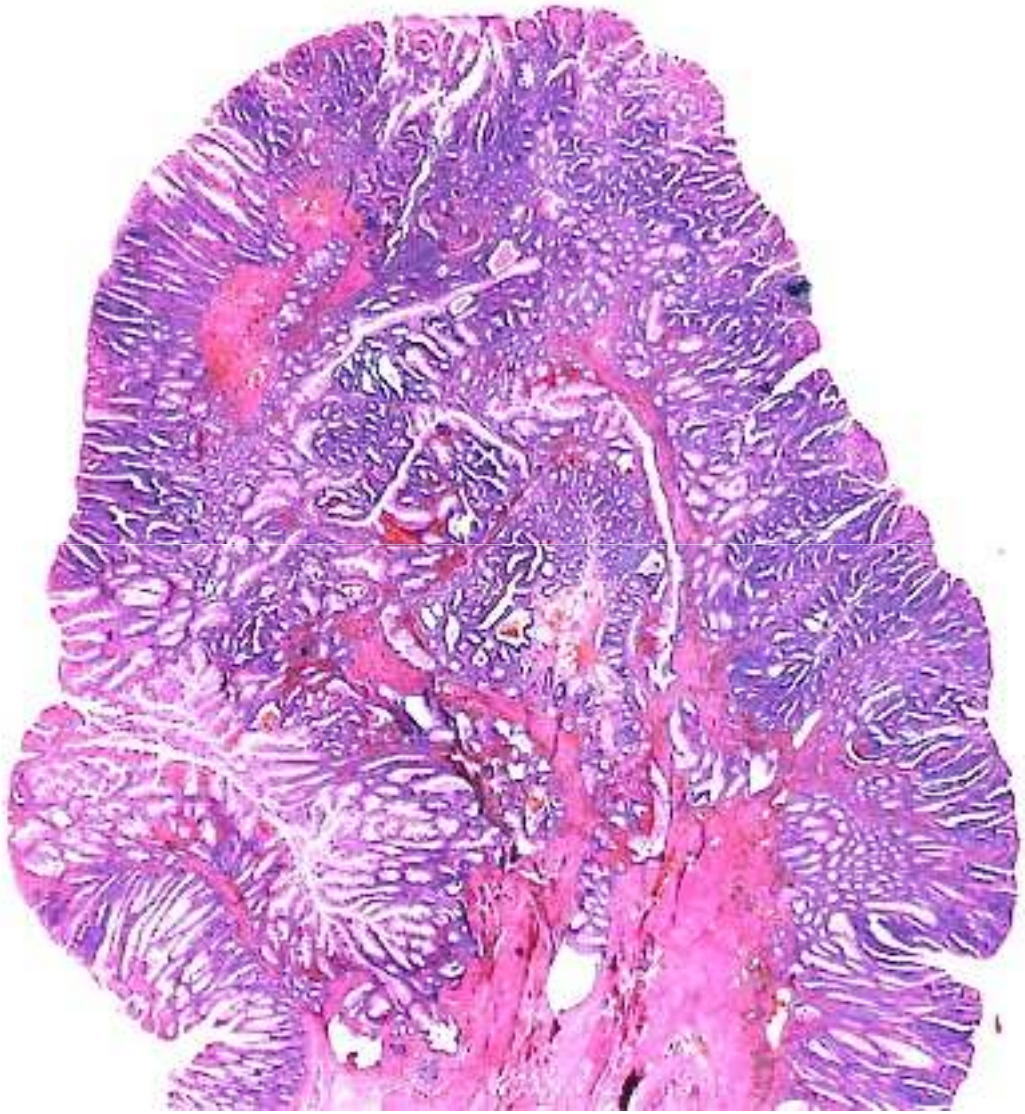
Dysplasia in Hyperplastic Polyp

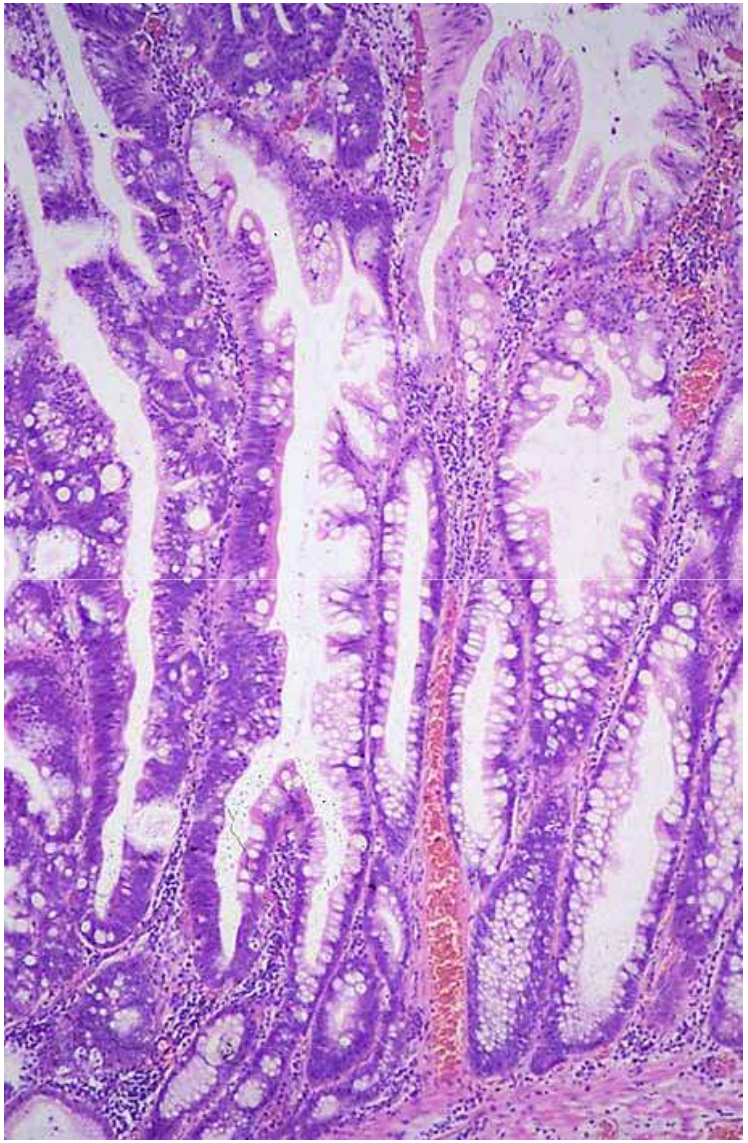
Longacre & Fenoglio-Preiser 1990











Sessile Serrated Lesion (Polyp, Adenoma)

- Serrated polyps with unusual architectural features
  - Horizontal orientation of deep crypts
  - Serration down to crypt base
- No conventional dysplasia but may have 'nuclear atypia' or 'hypermucinous' change
- Right colon
- Females > males
- Large sessile, poorly defined

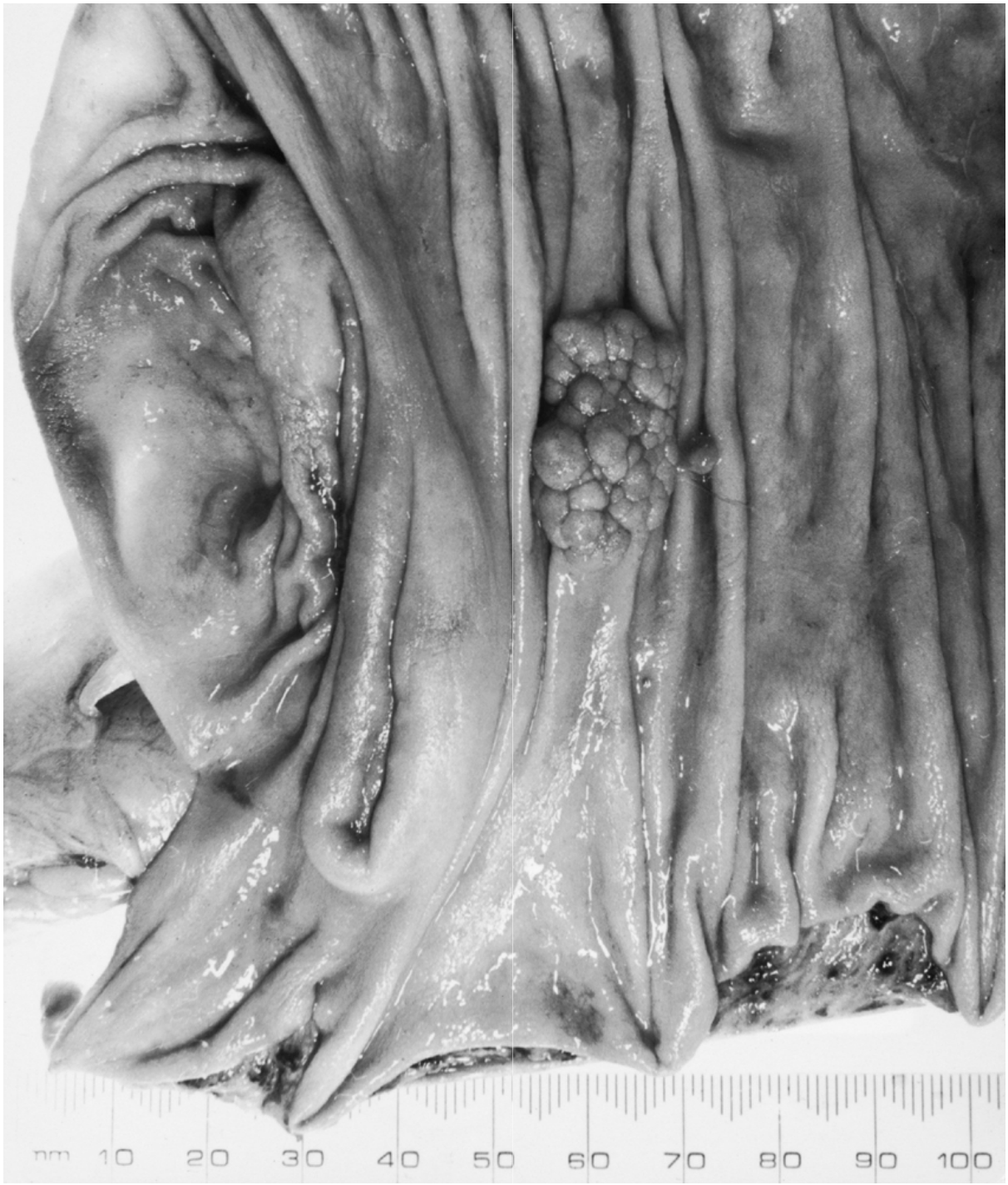
Torlakovic & Snover 1996

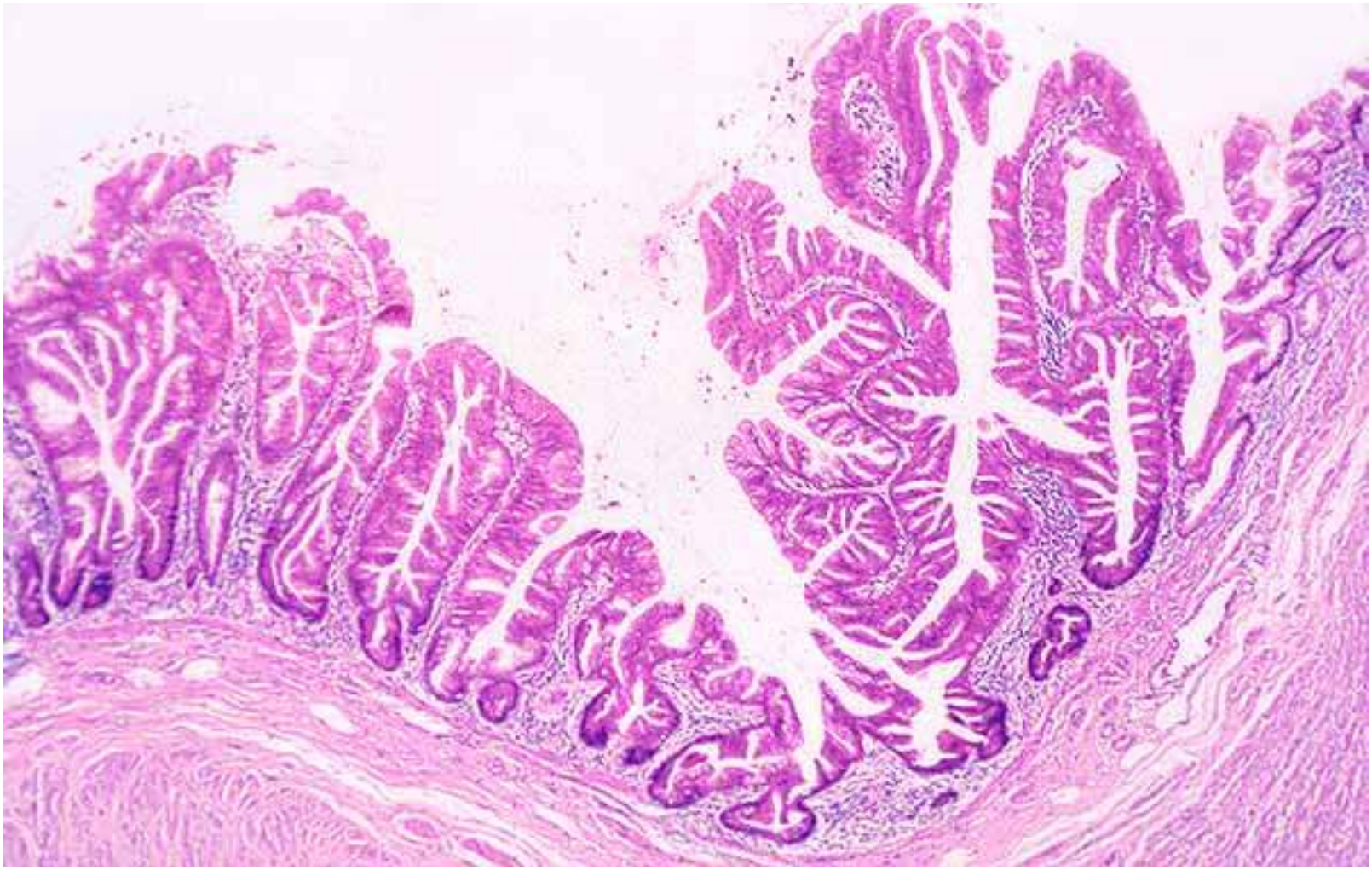
Sessile Serrated Lesion (Polyp, Adenoma)

- Crypt dilatation
- Abnormal proliferation
- Normal subepithelial collagen plate
- Loss of MLH1
- Sometimes found in hyperplastic polyposis
- Often express MUC5AC or MUC6

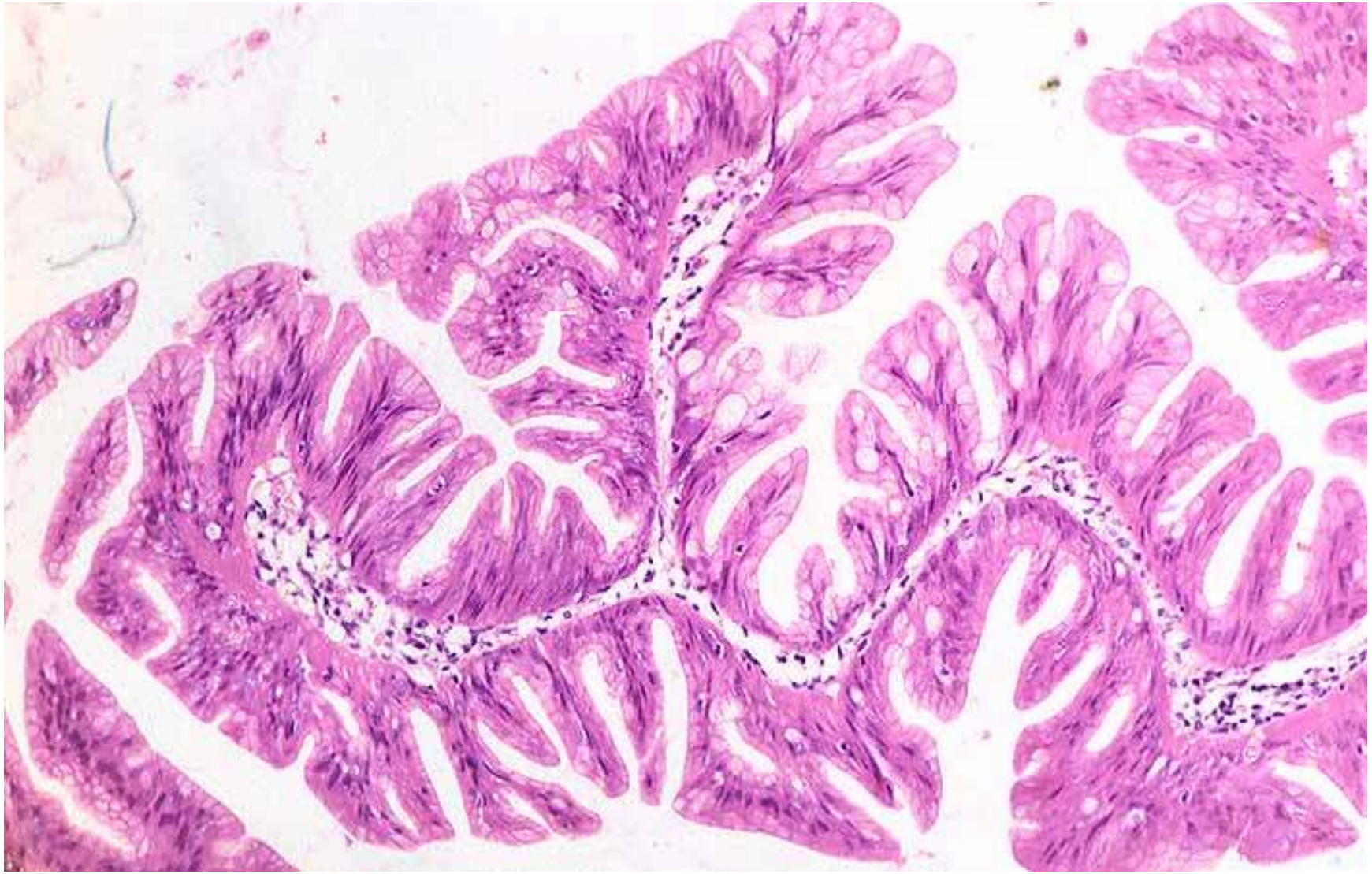
Torlakovic et al 2003 AJSP 27: 65-81

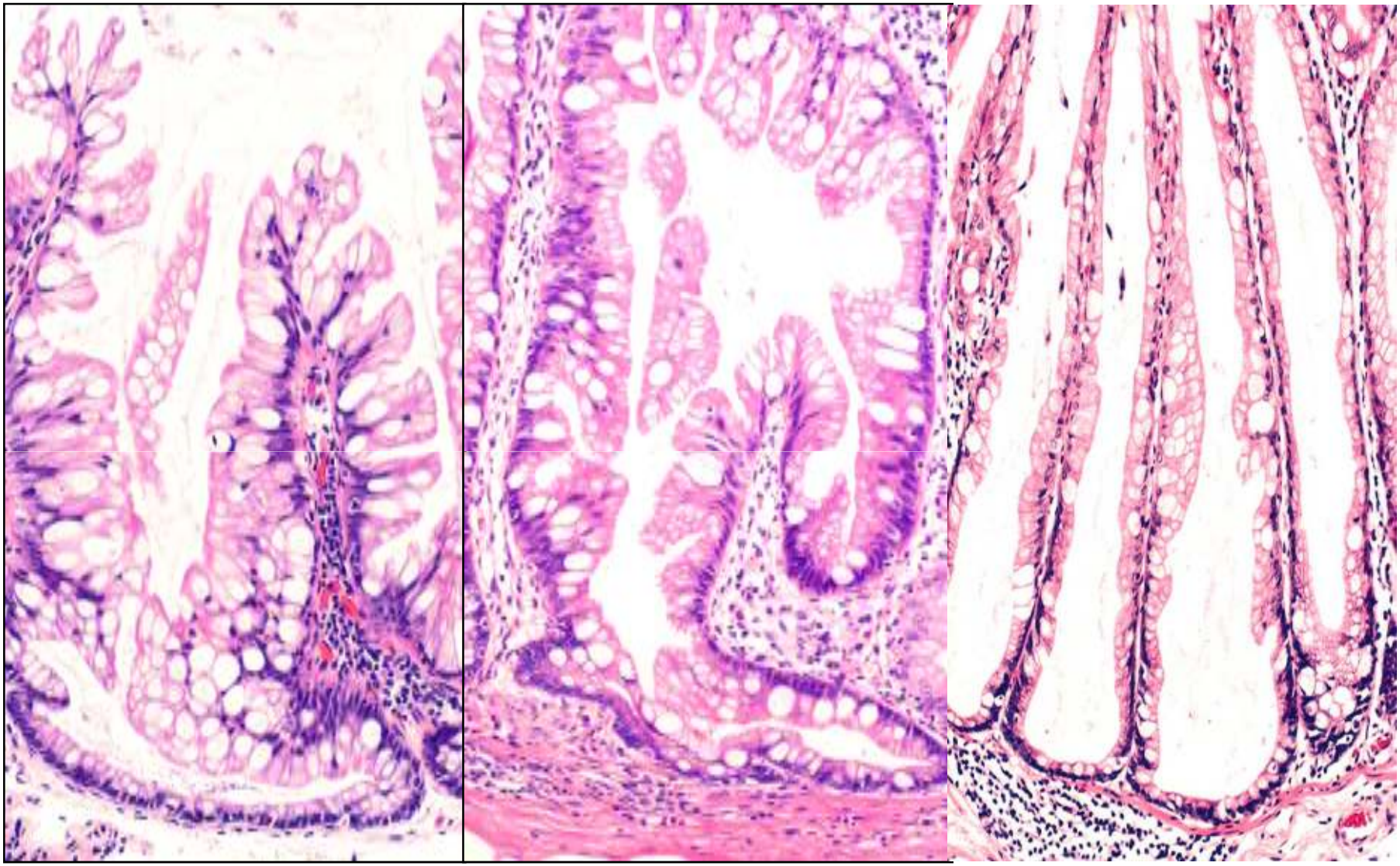

cm


mm 10 20 30 40 50 60 70 80 90 100



Sessile serrated lesion

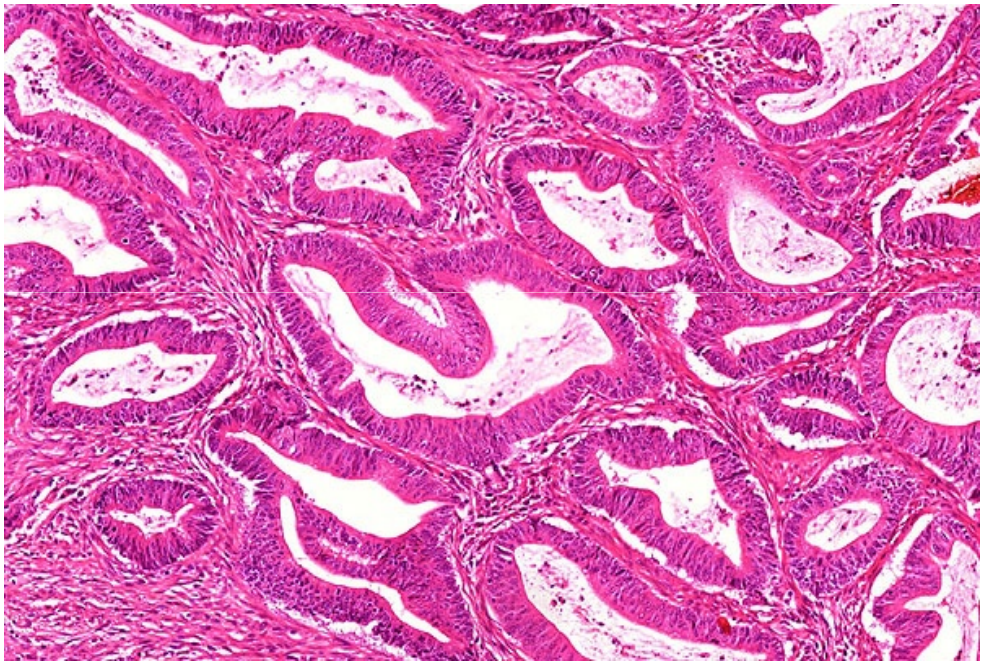


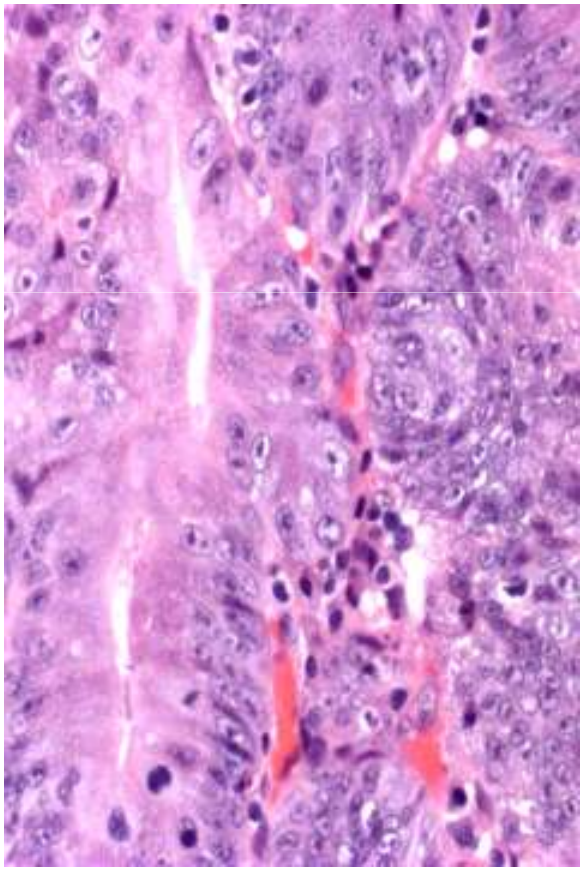


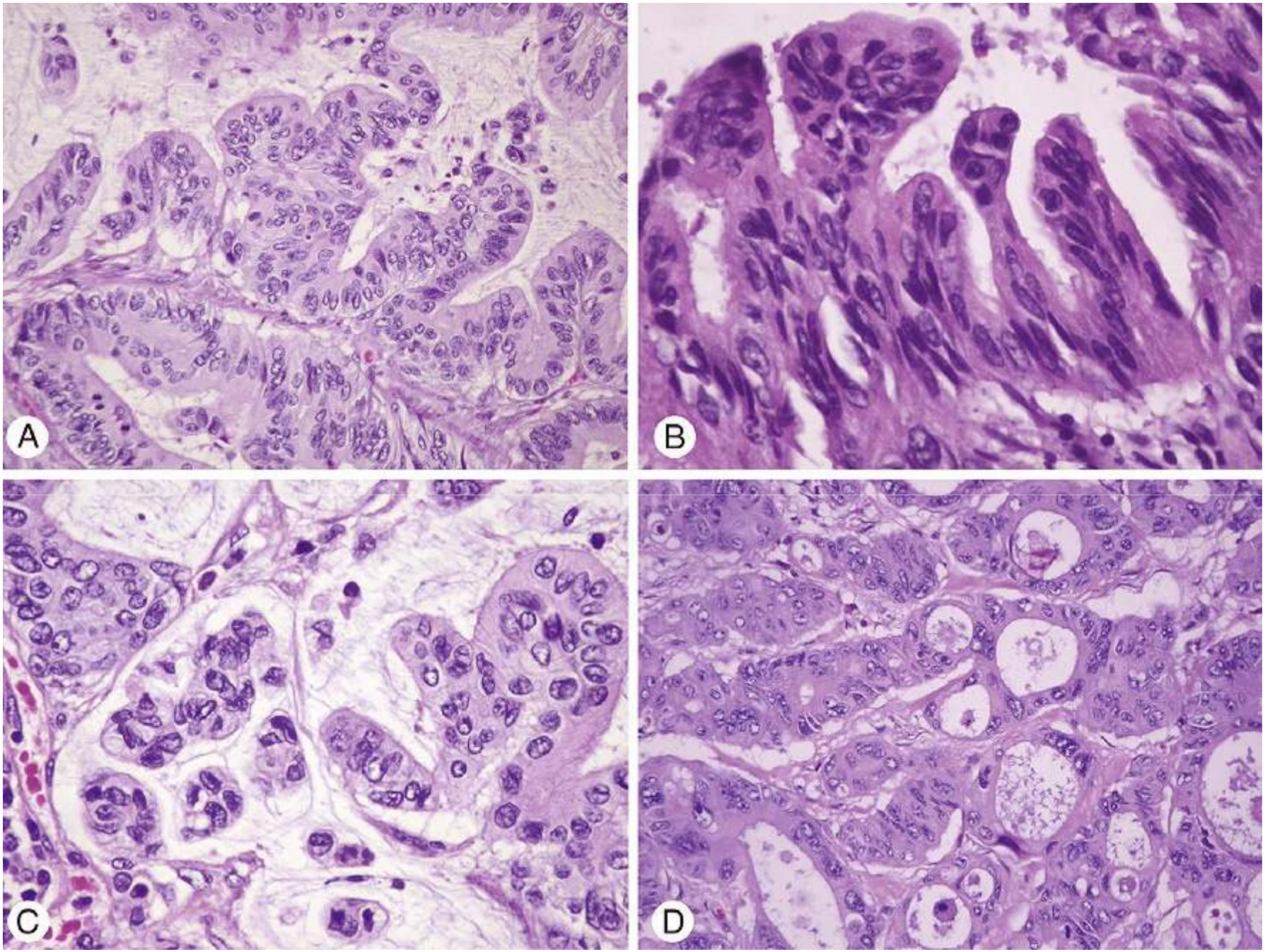
Serrated Adenocarcinoma

- 5-10% colorectal cancer
- Right colon and rectum
- Serrated, mucinous or trabecular growth pattern
- Abundant eosinophilic cytoplasm
- Chromatin condensation
- Preserved polarity
- No 'dirty' necrosis

Serrated Adenocarcinoma





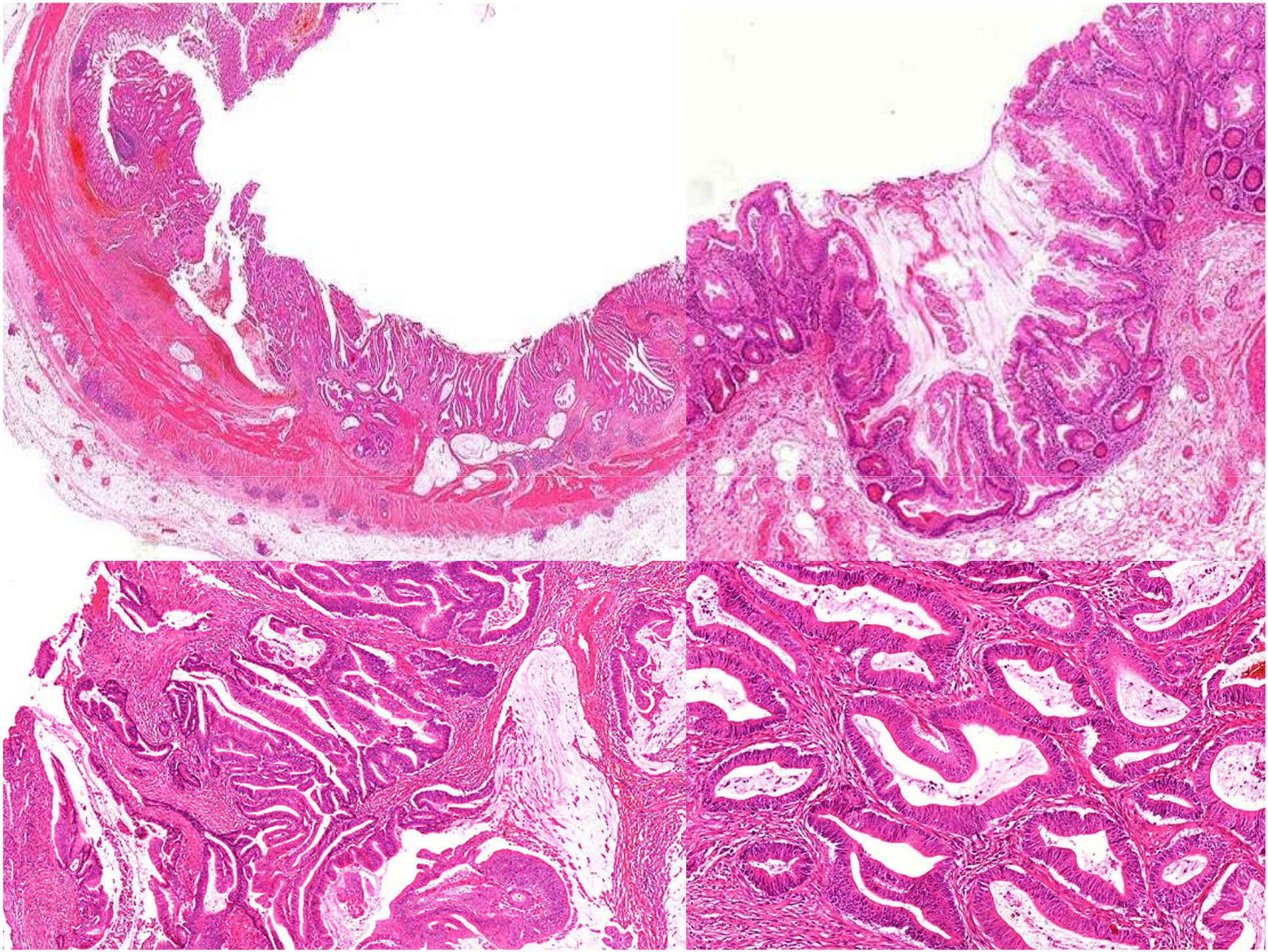


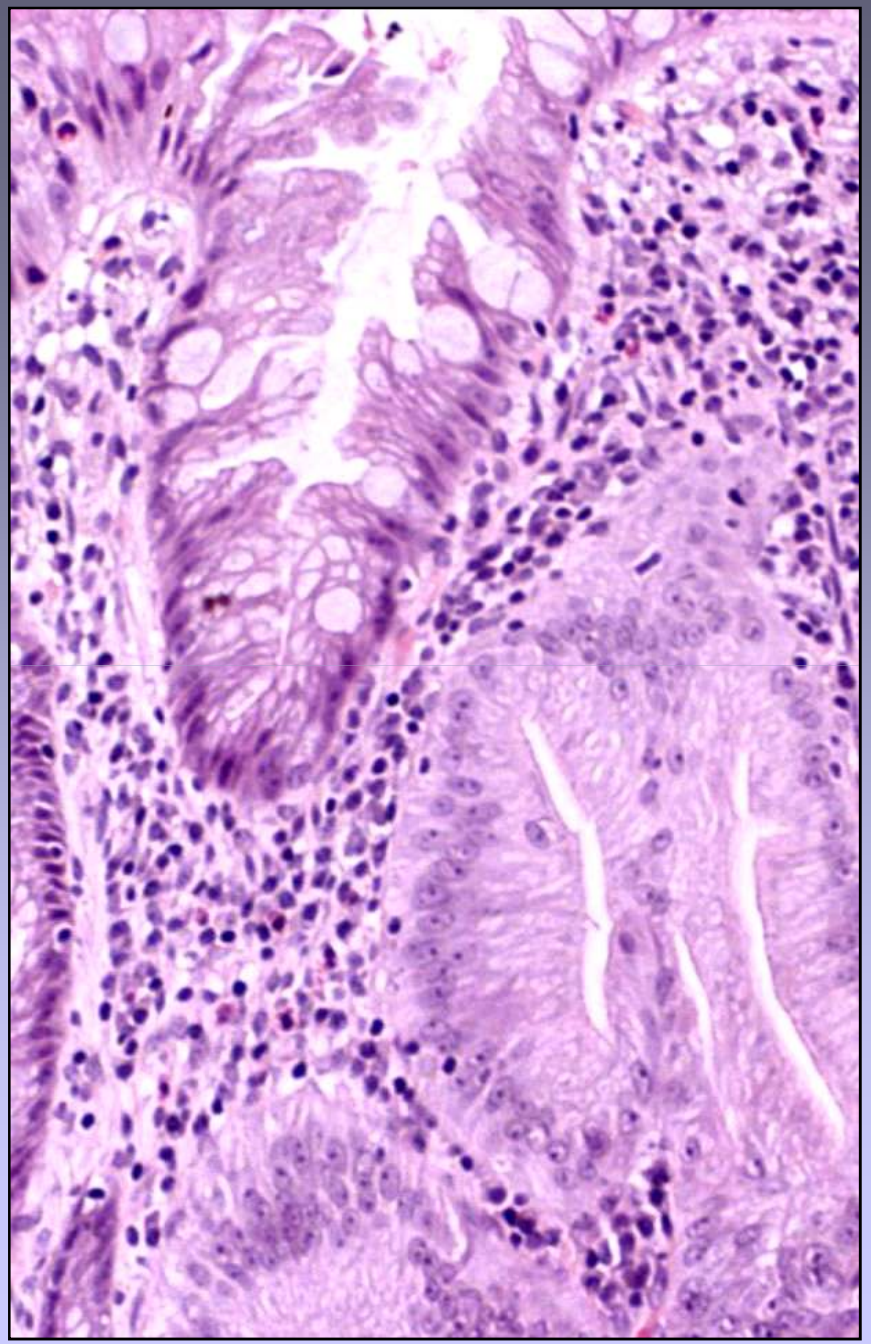
Garcia-Solano J *et al* 2010 *Hum Pathol* 41: 1359-68

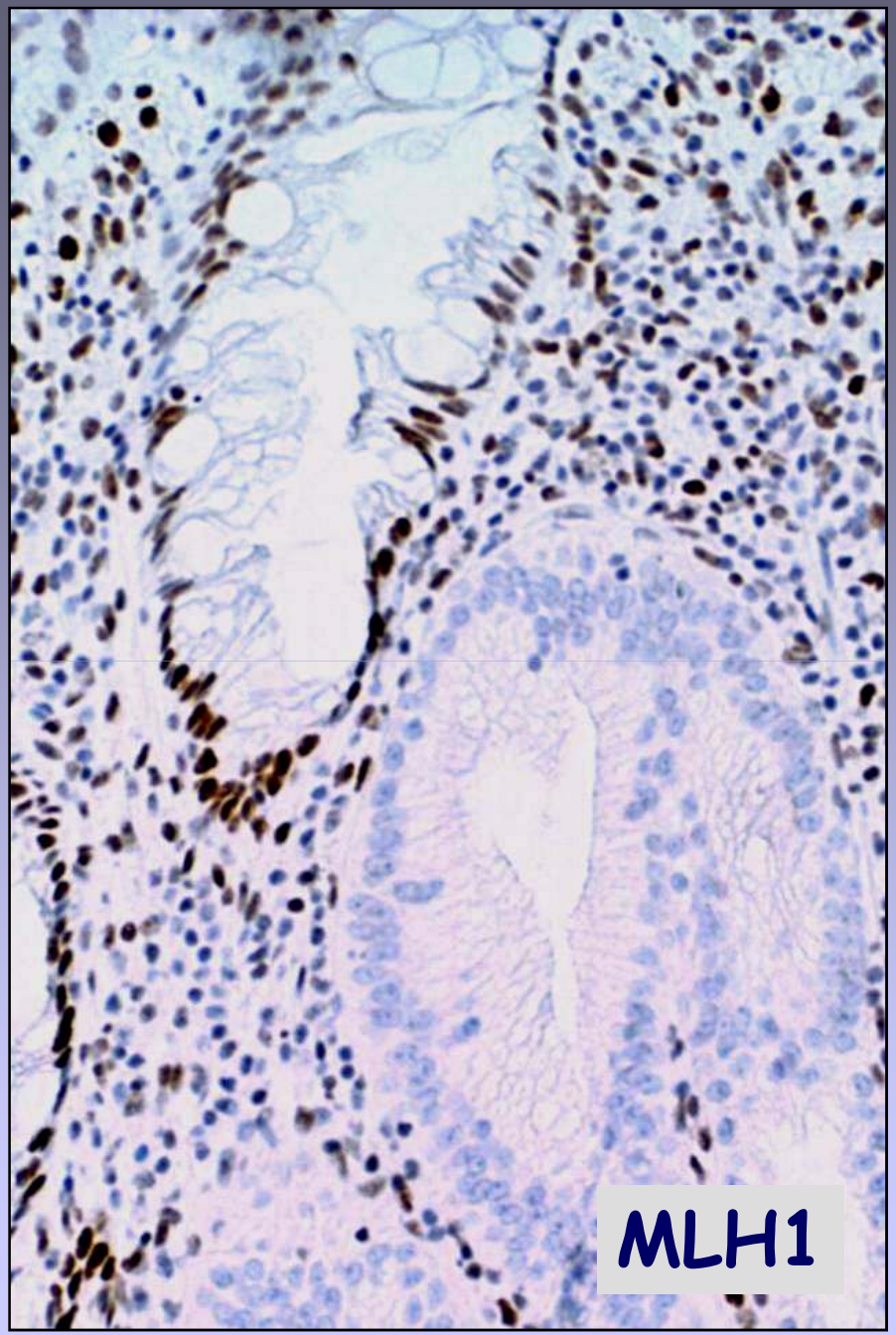
Serrated Adenocarcinoma

- Most arise in traditional serrated adenomas and are MSS
  - Distal tumours
  - Poor prognosis (30% 5-year survival)
- 20% arise in sessile serrated polyps and have MSI
  - Proximal tumours
  - Good prognosis (70% 5-year survival)

Makinen et al 2001 J Pathol 193: 286-94






MLH1

Right Sided Serrated Neoplasia

Microsatellite instability

MLH1 inactivation

DNA methylation (CIMP)

BRAF mutation (80% in SSAs)

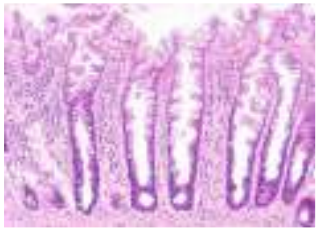
Baker K *et al* J Clin Pathol 2004; 57: 1089

BRAF mutation

• Typical adenomas	0%
• Typical hyperplastic polyps	19%
• Sessile serrated adenomas	75-82%
• Traditional serrated adenomas	20-30%
• Mixed Polyps	57-89%
• HNPCC cancers	0%
• All colorectal cancers	15%
• MSI-high non-HNPCC cancers	76%

Serrated Neoplasia Pathway

Proximal hyperplastic polyp



↓

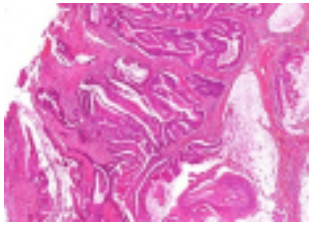
Sessile serrated polyp

↓

Sessile serrated adenoma

↓

MSI-high, methylation-rich
non-HNPCC "serrated" carcinoma



Higuchi T & Jass JR 2004 *J Clin Pathol* 57: 682

Left Sided Serrated Neoplasia

Microsatellite stable

MLH1 expression retained

DNA methylation (CIMP)

No *BRAF* mutation

K-ras mutation (80% in TSAs)

Traditional Serrated Neoplasia Pathway

Hyperplastic polyp
(Goblet cell type)

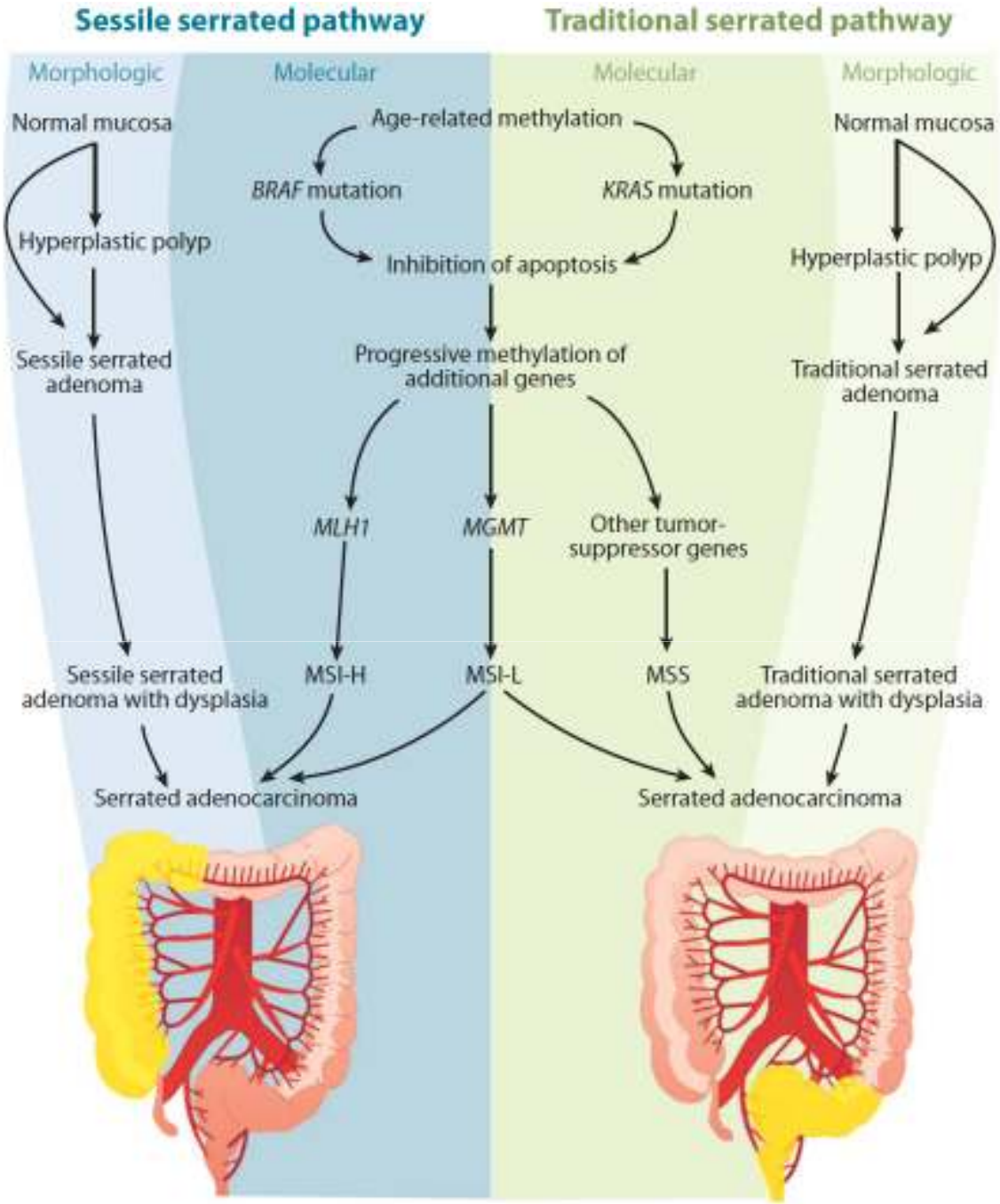
↓

Traditional serrated adenoma

↓

Distal MSS non-HNPCC serrated carcinoma

Higuchi T & Jass JR 2004 *J Clin Pathol* 57: 682



From: Noffsinger AE Ann Rev Pathol Mech Dis 2009; 4: 343-64

1250 Polyps at Colonoscopy

Polyp		Dysplasia	%
Adenoma	Tubular	+	55
	Tubulovillous	+	15
	Villous	+	1
Serrated polyps	Hyperplastic	-	24.5
	Sessile Serrated Polyp	-	2.5
	Mixed Polyp	+	0.8
	Serrated Adenoma (TSA)	+	1.2

Frequency of SSPs reaches 7% in some series;
observer reproducibility is an issue!

Risk of Malignancy in Sessile Serrated Lesions

- Unknown
- Up to 20% of cancers arise by the serrated pathways
- Microsatellite instability may speed up the evolution into carcinoma
- Patients with SSAs more likely to have additional serrated lesions and proximal hyperplastic polyps
- Case reports of rapid evolution of SSA to cancer
- Small series suggest further neoplasia occurs with similar (or greater) frequencies in SSA patients compared with adenoma patients

Natural History of Sessile Serrated Adenomas

- Asymptomatic population, 50-75 yrs, undergoing screening colonoscopy, N=3121
- 7.9% had Proximal large (>10mm) Non-dysplastic Serrated Polyps
- More likely than those without proximal NDSP to have advanced neoplasia (17.3% vs 10.0%) at baseline
- Large proximal NDSP and no neoplasia at baseline 3.14 times more likely to have subsequent neoplasia

Schreiner MA et al Gastroenterology 2010; 139: 1497-1502

Natural History of Sessile Serrated Adenomas

- 40 patients with SSAs and no history of colonic neoplasia
- 5 (12.5%) developed cancer, all in proximal colon
- 4/5 cancers had MSI

- 1.8% matched adenoma patients developed cancer

Lu FI et al AJSP 2010; 34: 927-34

Sessile Serrated Adenomas and 'Advanced' Histology

- Lieberman D et al
  Polyp Size and Advanced Histology in Patients Undergoing Colonoscopy Screening: Implications for CT Colonography
  Gastroenterology 2008; 135: 1100-5

- Van Dekken et al
  Screening for colorectal cancer: randomised trial comparing guaiac-based and immunochemical faecal occult blood testing and flexible sigmoidoscopy. Gut 2010; 59: 62-8

Management of Patients with Serrated Lesions

Typical Small Distal Hyperplastic Polyps

- No follow-up

Right sided Serrated Lesions

- Caution – depends on age, comorbidity, family history etc (but some recommend 3 yearly surveillance)

Sessile serrated polyps >1cm

- Excise and follow up for recurrence ~3 yearly

Dysplastic serrated lesions

- As adenomas

Reporting Serrated Lesions

Current requirements and proformas do not record serrated lesions per se (apart from hyperplastic polyps).

Serrated adenomas are recorded with conventional tubular, tubulovillous or villous adenomas – serration is not recognised.

SSPs are reported as right sided hyperplastic polyps – this may be harming people!

Reporting Serrated Lesions

Time for Change:

We need to agree a nomenclature for right sided sessile non dysplastic lesions – SSP or SSA (or SSA/P)

We must introduce categories for serrated adenomas and sessile serrated polyps in proformas, and modify diagnostic guidelines accordingly

We must review regularly the management implications for patients with serrated lesions.

- Serrated Lesions, once the Cinderellas of Colorectal Pathology, are assuming increased interest and clinical importance

- They probably contribute to the pathogenesis of up to 20% of Colorectal Cancers

- Serrated adenomas are biologically different in the left and right colons

- There is, as yet, insufficient data on which to make firm recommendations on surveillance of individuals with sessile serrated polyps without overt dysplasia

- We must modify our recording/reporting of serrated lesions within the BCSP

Acknowledgements

The late Jeremy Jass
Marco Novelli