Peritoneal Malignancy Institute Basingstoke

Located at
Basingstoke and North Hampshire Hospital

Part of
Hampshire Hospital NHS Foundation Trust

University Hospital Southampton NHS
NHS Foundation Trust

Appendiceal neoplasia and pseudomyxoma peritonei

Norman Carr

RCPath Update 2017

Appendiceal mucinous neoplasms are unusual

- … but all of us see them from time to time
- Other conditions can mimic them, e.g. ruptured diverticula
- Correct diagnosis is important
  - prolonged follow-up
  - pseudomyxoma peritonei is now treated radically
- Contentious terminology addressed by recently published international consensus

A Consensus for Classification and Pathologic Reporting of Pseudomyxoma Peritonei and Associated Appendiceal Neoplasia

The Results of the Peritoneal Surface Oncology Group International (PSOGI) Modified Delphi Process

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Abstract: Pseudomyxoma peritonei (PMP) is a complex disease with unique biological behavior that usually arises from appendiceal mucinous neoplasia. The classification of PMP and its primary appendiceal neoplasia is contentious, and an international modified Delphi consensus process was instigated to address terminology and definitions. A classification of mucinous appendiceal neoplasia was developed, and it was agreed that matosis, respectively. A checklist for the pathologic reporting of PMP and appendiceal mucinous neoplasms was also developed. By adopting the classifications and definitions that were agreed, different centers will be able to use uniform terminology that will allow meaningful comparison of their results.

Key Words: appendiceal neoplasms, pseudomyxoma peritonei, appendix, peritoneum, Delphi technique

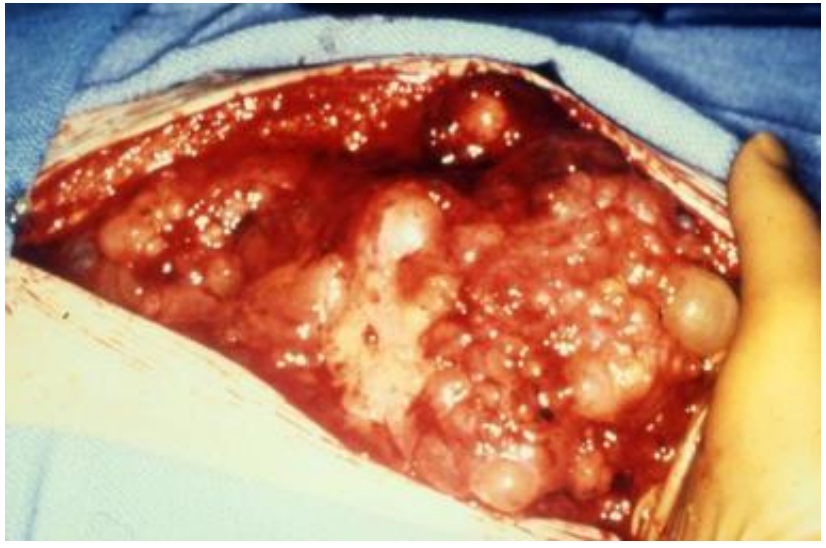
Am J Surg Pathol 2016; 40:14-26

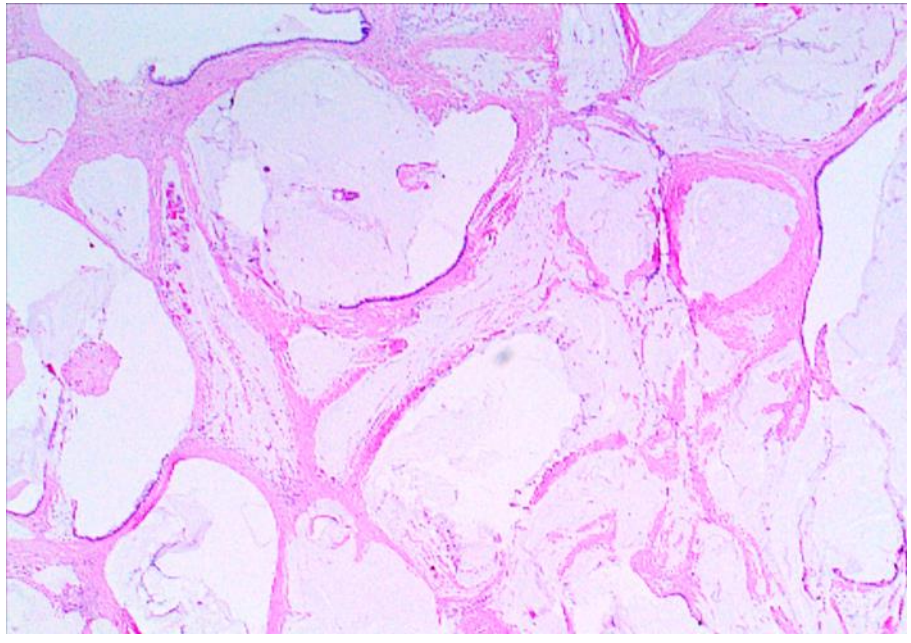
Scope of presentation

- Pseudomyxoma peritonei
- Appendiceal mucinous neoplasia

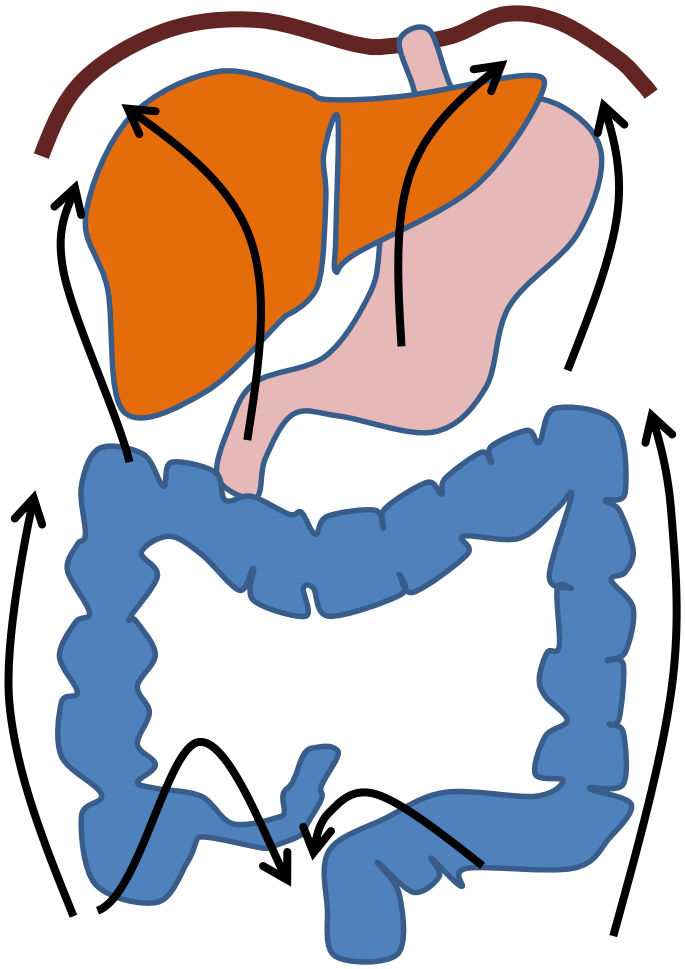
What is pseudomyxoma peritonei?

- A syndrome of mucinous tumour within the abdomen
  - tends not to invade/metastasise
  - grows relentlessly
  - death is usually by intestinal obstruction

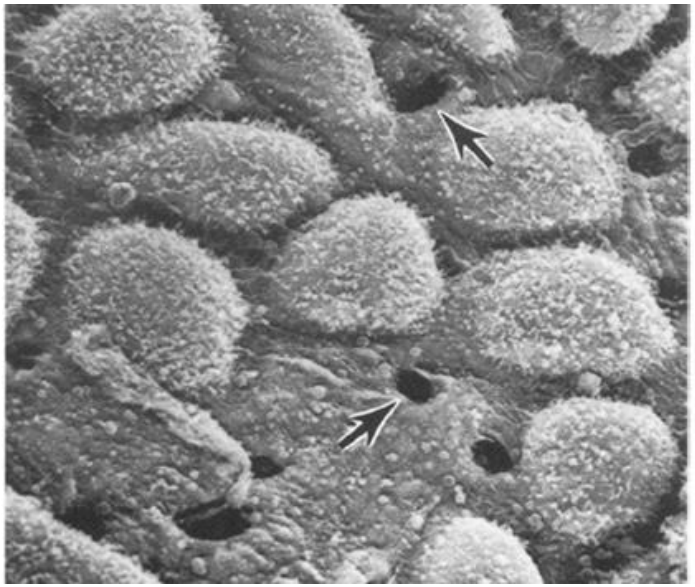




Pseudomyxoma peritonei is characterised by the redistribution phenomenon



- Omentum
- Paracolic gutters
- Pouch of Douglas
- Falciform ligament
- Subphrenic spaces



stomata

Most PMP arises from an appendiceal mucinous neoplasm

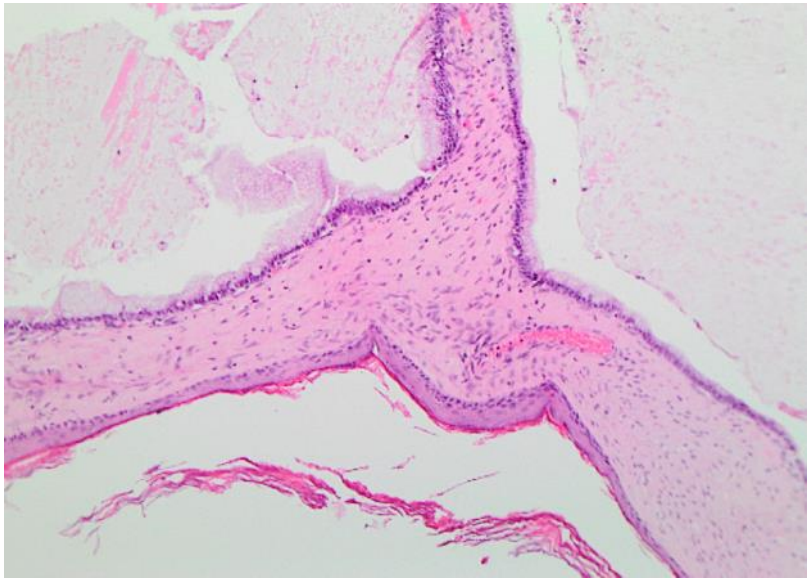
- Other primary sites include:
  - colon
  - urachus
  - IPMN

The ovary and pseudomyxoma

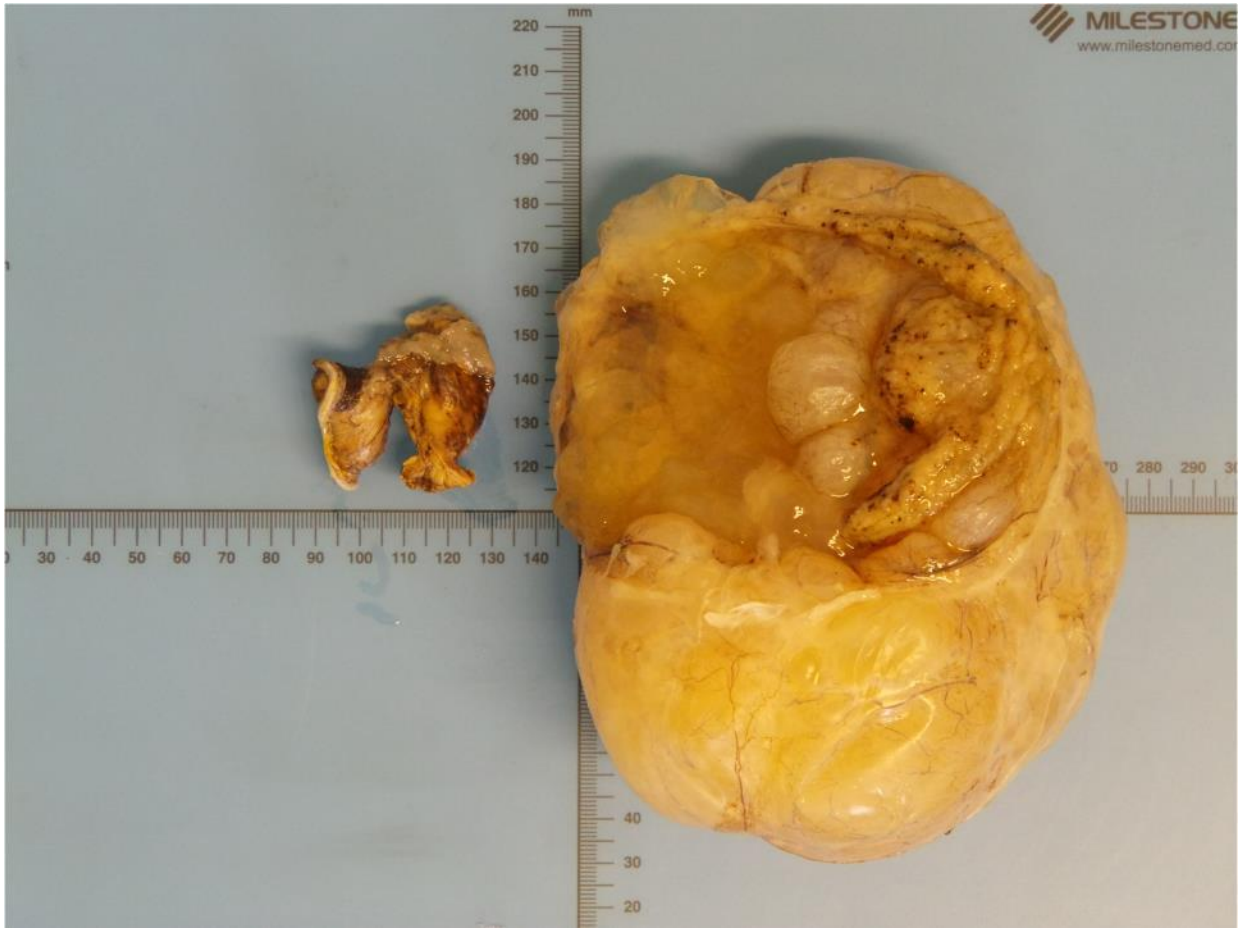
Primary ovarian mucinous neoplasms rarely produce pseudomyxoma:

- cystadenomas -> acellular mucin
- mucinous adenocarcinomas -> conventional cancer

Exception: low grade mucinous neoplasia arising in a teratoma



A case of pseudomyxoma thought to be an ovarian primary…



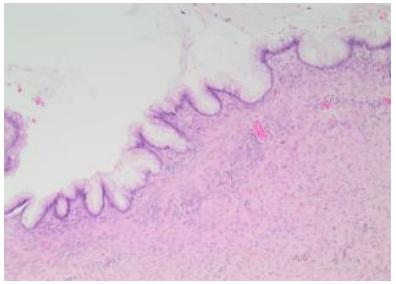
Useful features in practice when there are enteric features

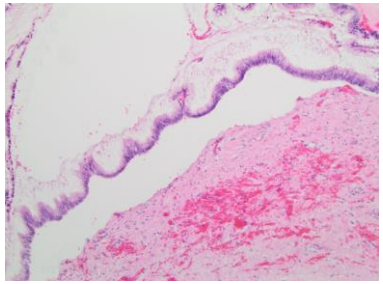
Favouring appendix or colorectum:

- Scalloping and retraction
- Infiltrative invasion
- Vascular invasion
- Dissecting mucin (pseudomyxoma ovarii)
- Signet ring cells
- SATB2+

Favouring ovary:

- Back-to-back neoplastic glands with no intervening stroma
- Associated primary teratoma
- CK7+ CK20- CDX2-

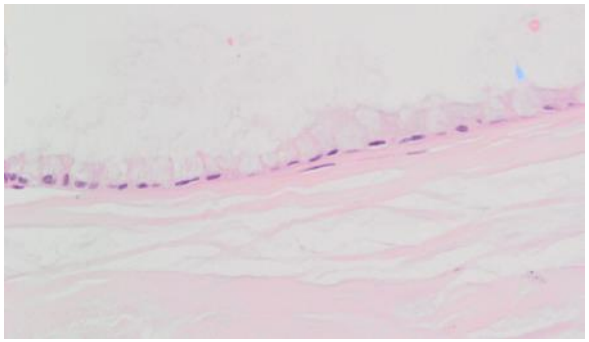


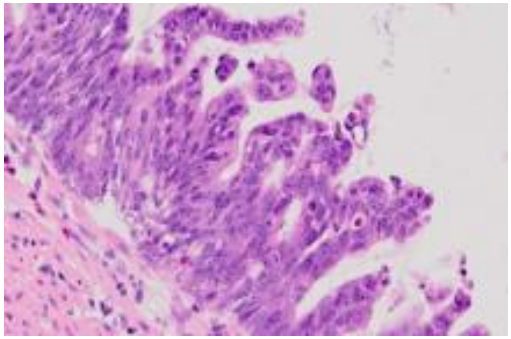


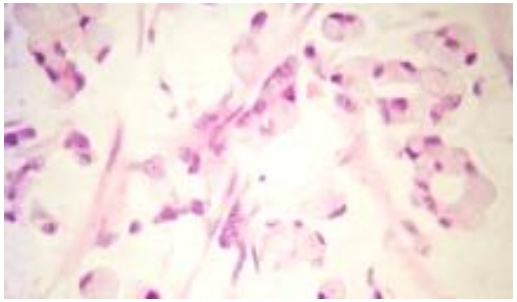
Li Z et al 2017
Stewart CJ et al 2014

Pseudomyxoma peritonei: classification

1. Low grade mucinous carcinoma peritonei (disseminated peritoneal adenomucinosis – DPAM)
2. High grade mucinous carcinoma peritonei (peritoneal mucinous carcinomatosis – PMCA)
3. High grade mucinous carcinoma peritonei with signet ring cells (PMCA-S)



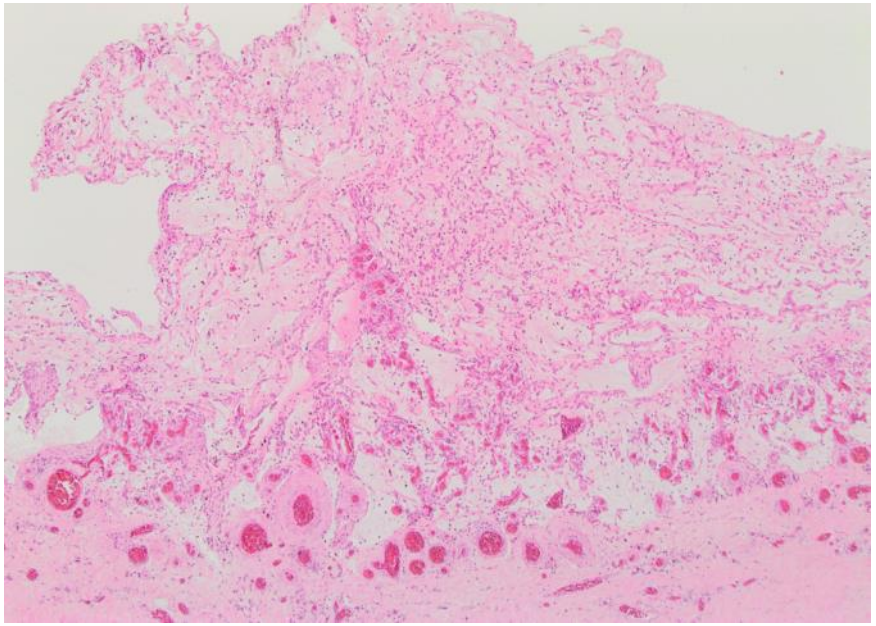




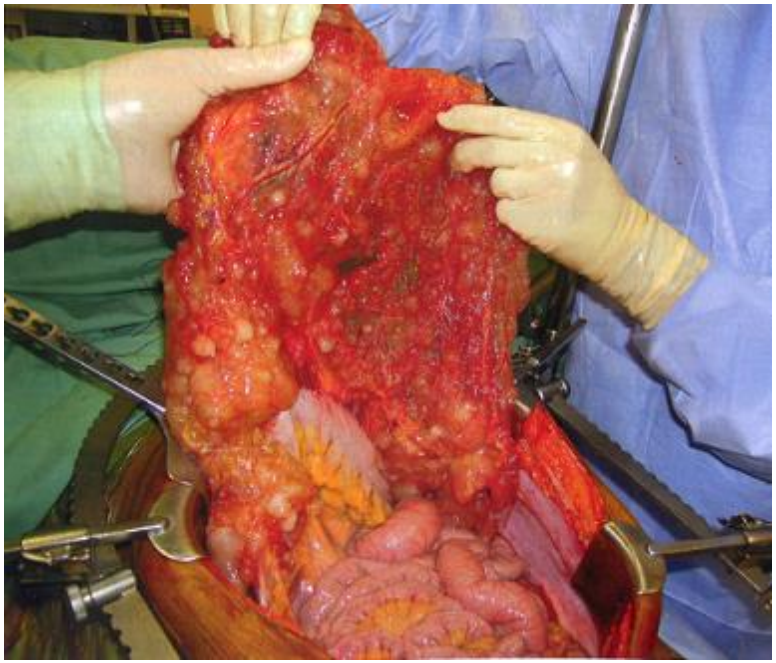
Davison JM et al 2014, Shetty S et al 2013, Sirintrapun SJ et al 2014

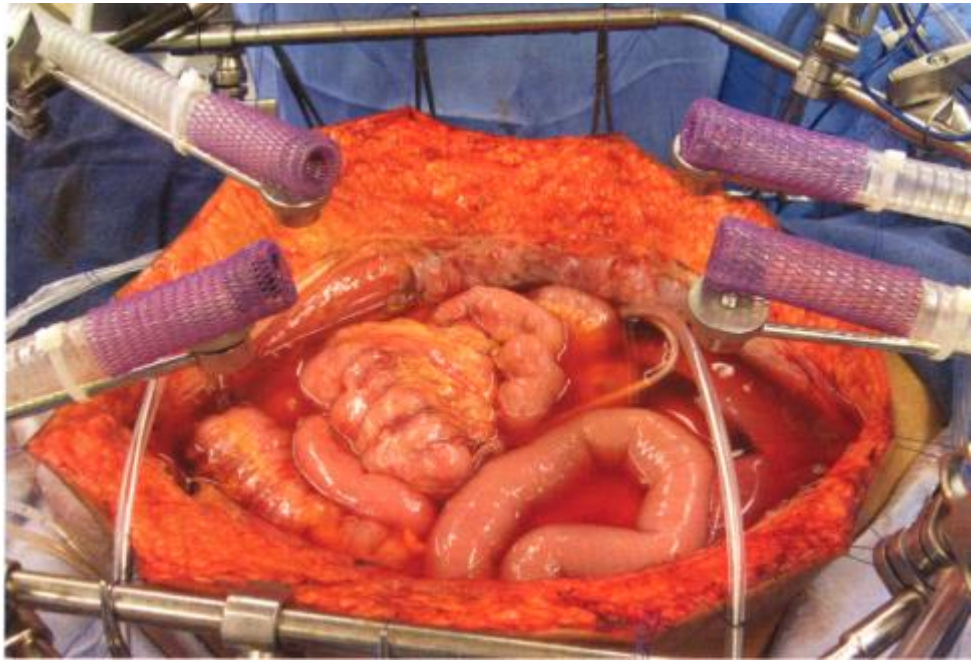
Acellular intra-abdominal mucin

- Can be a feature of PMP, but other causes exist (e.g. ruptured cystadenoma of ovary)
- In TNM8 for the appendix, acellular mucin within the abdominal cavity is classified pM1a

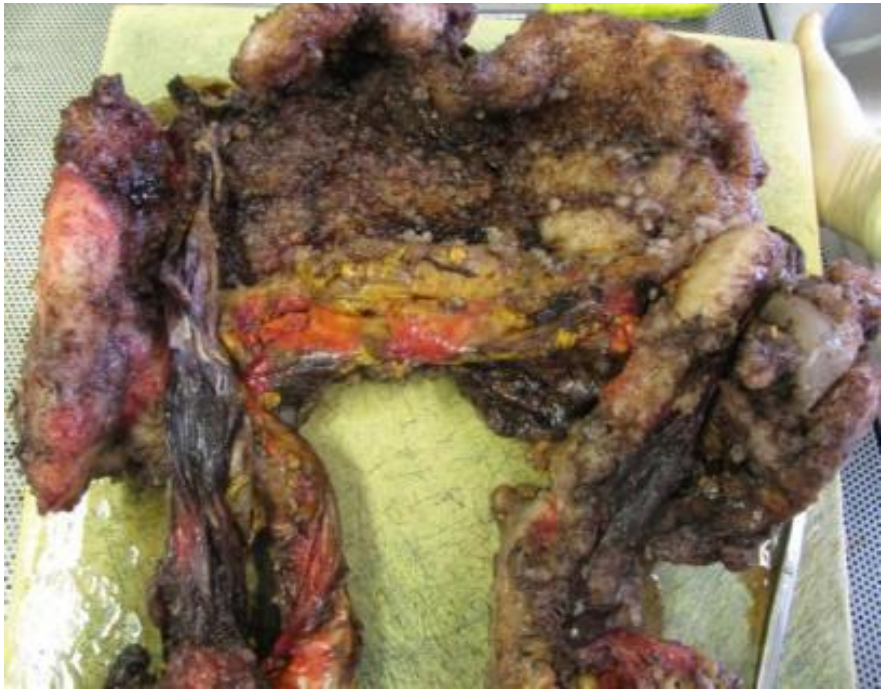


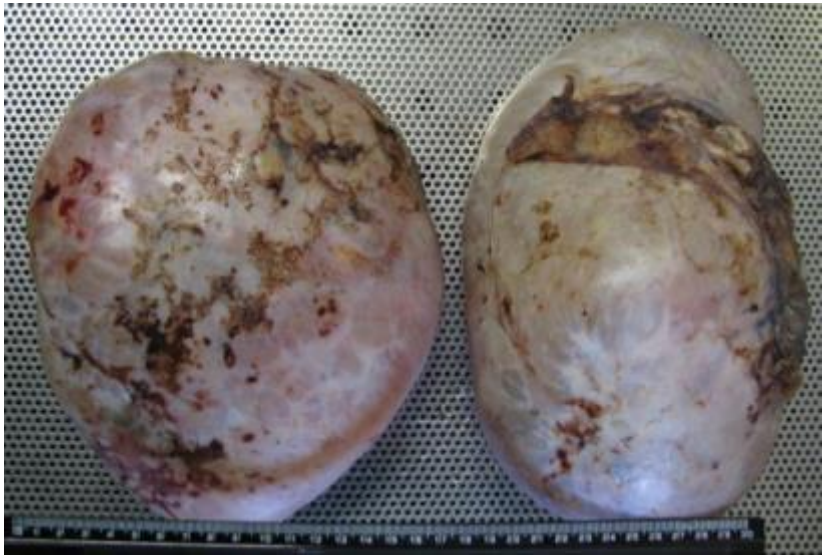
Cytoreductive surgery with heated intraperitoneal chemotherapy (HIPEC)



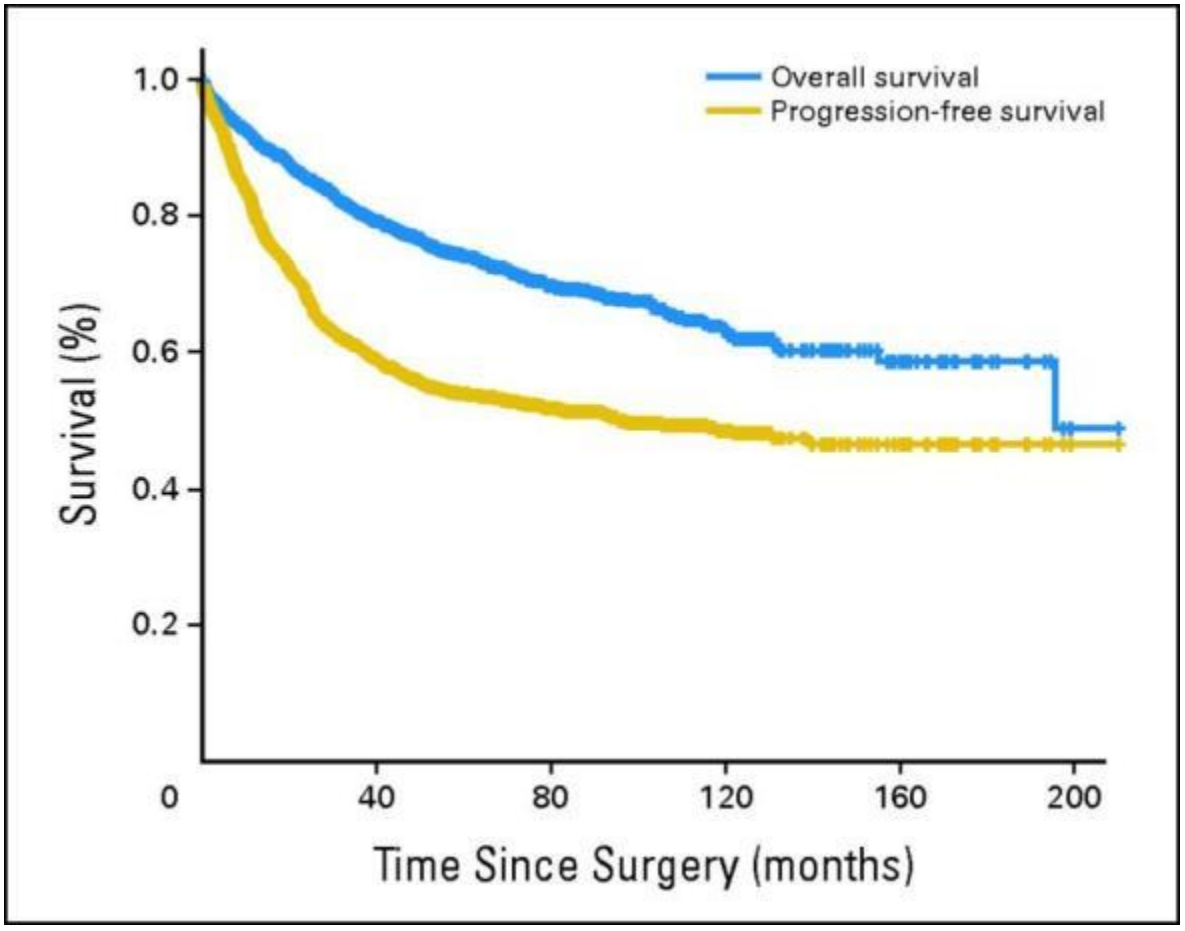


Surgical specimens





Survival of 2,298 patients with appendiceal PMP treated with cytoreductive surgery and HIPEC

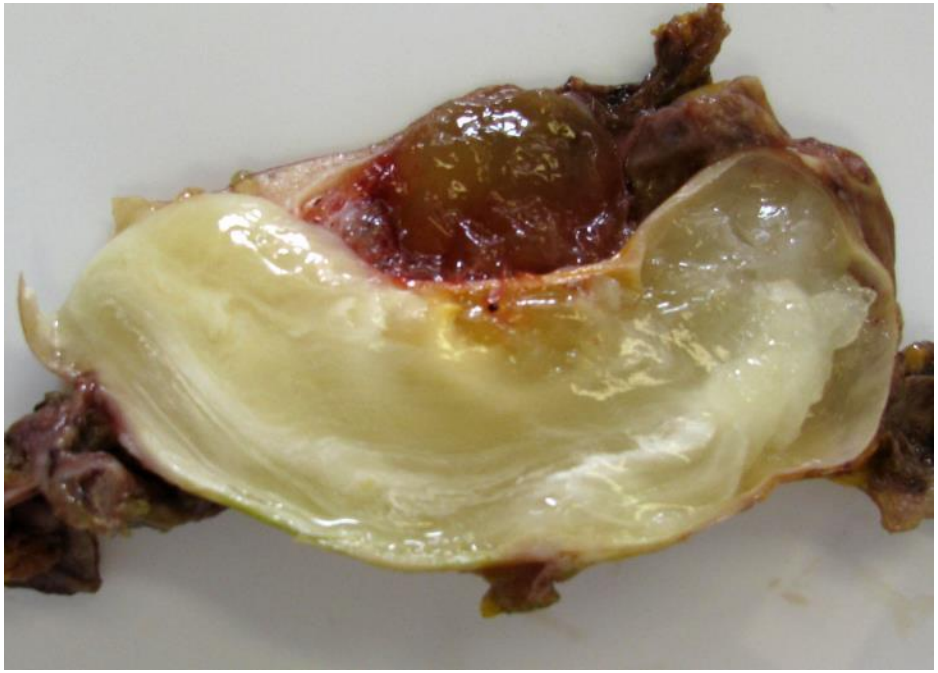


Chua TC et al 2012

C.f. Mayo results of <25% overall survival at 17 years

(Gough DB et al 1994)

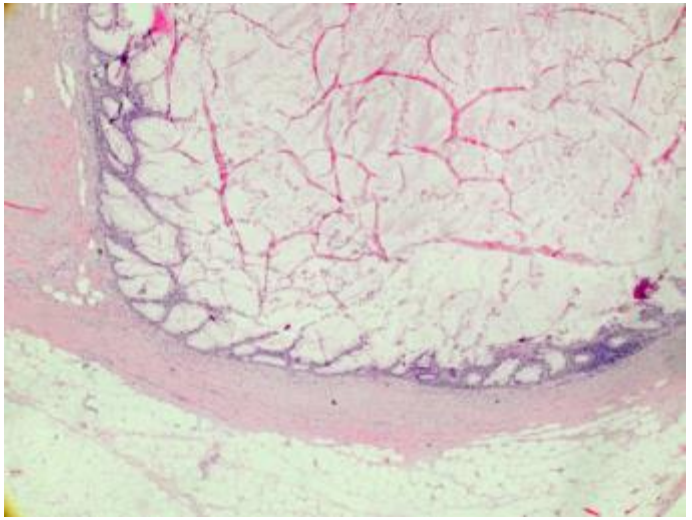
Appendiceal mucinous neoplasms

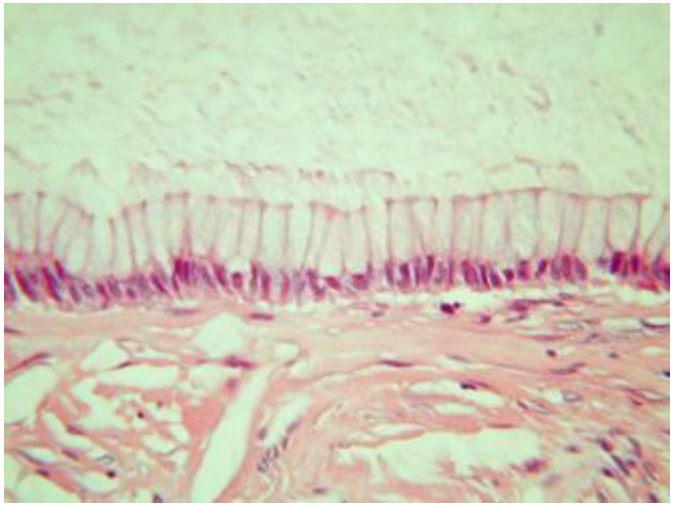


Low grade appendiceal mucinous neoplasm (LAMN)

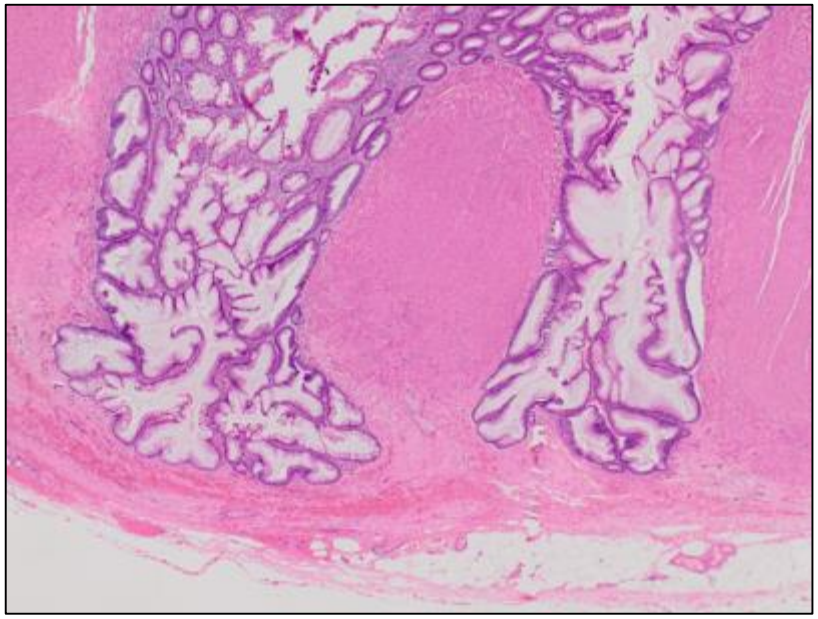
Mucinous neoplasm with low grade cytological atypia and any of:

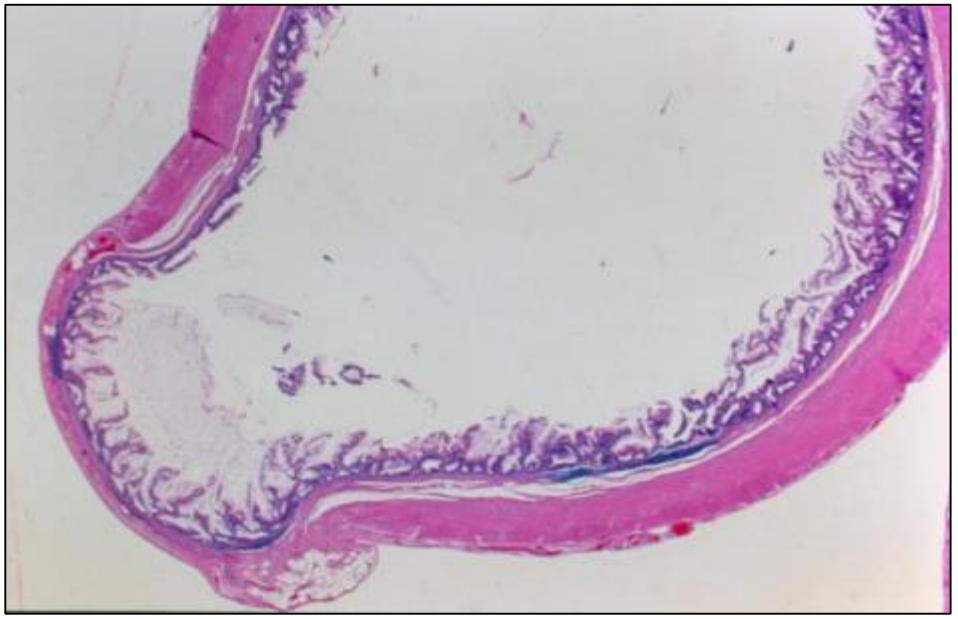
- loss of muscularis mucosae
- fibrosis of submucosa
- ‘pushing invasion’ (expansile or diverticulum-like growth)
- dissection of acellular mucin in wall
- undulating or flattened epithelial growth
- rupture of appendix
- mucin and/or cells outside appendix

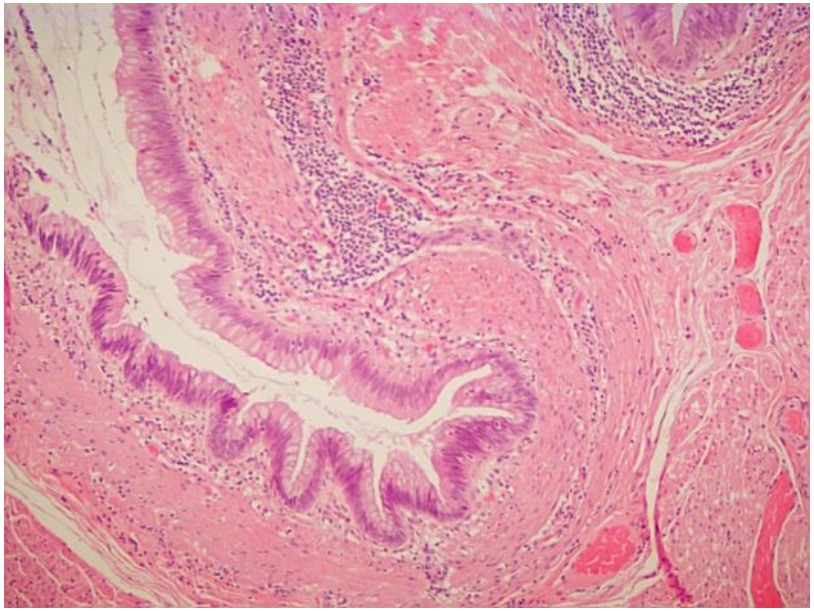


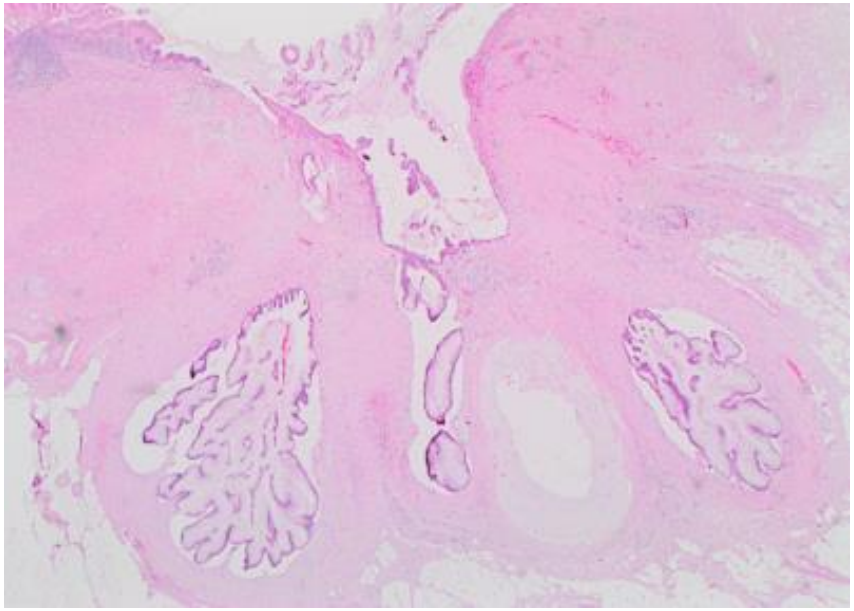


LAMN: Pushing invasion

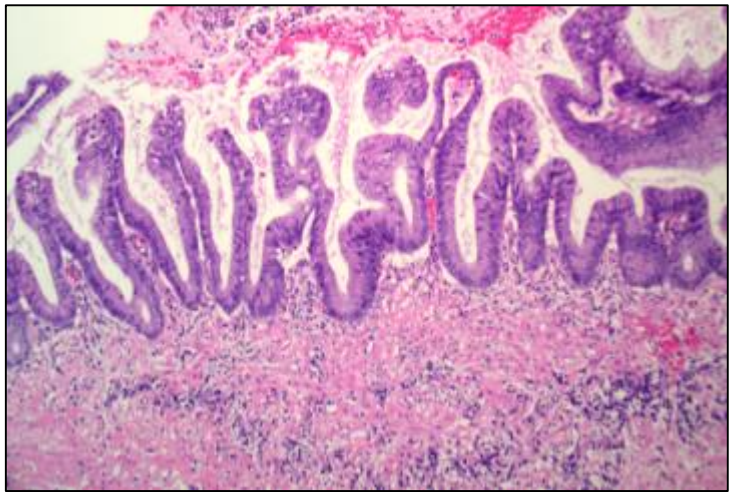


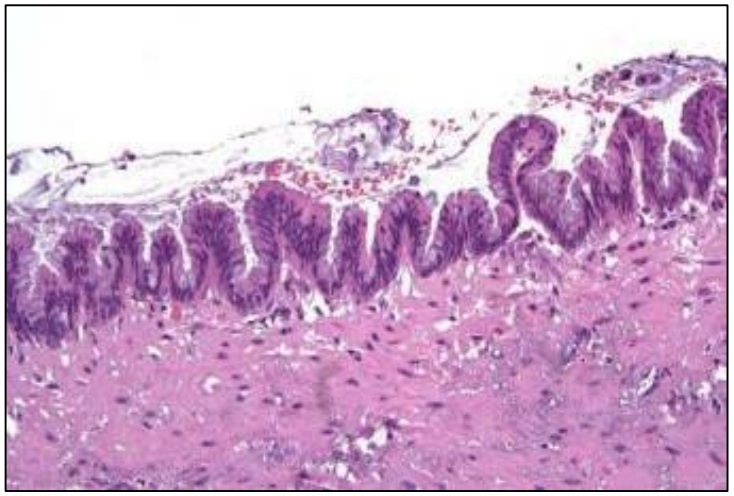


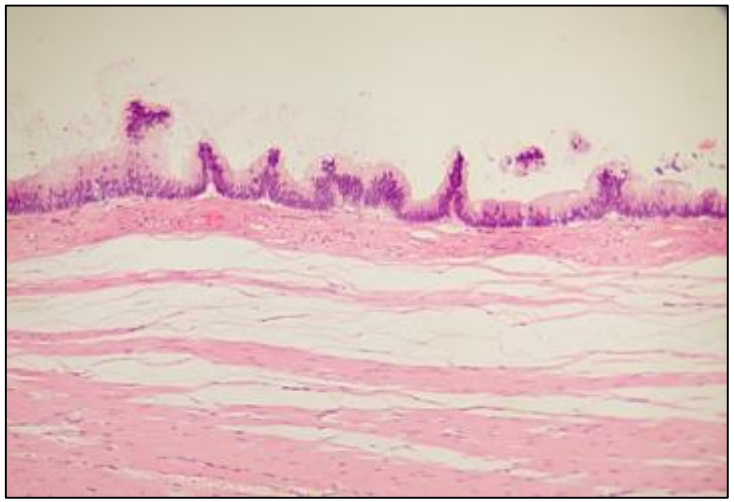


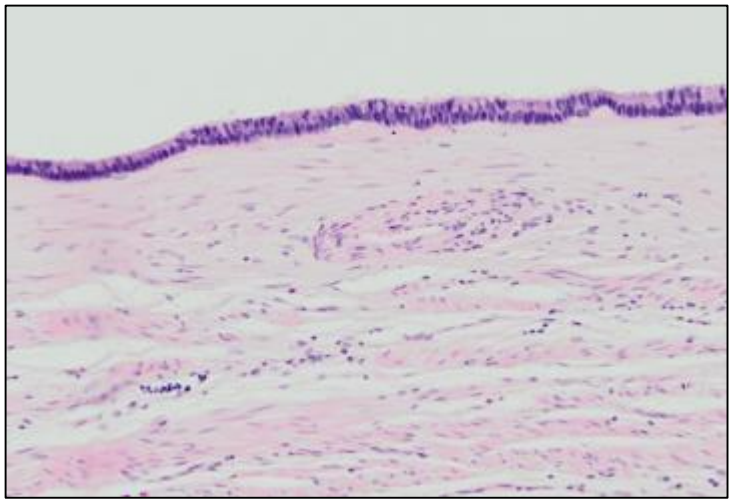


LAMN: Patterns of growth

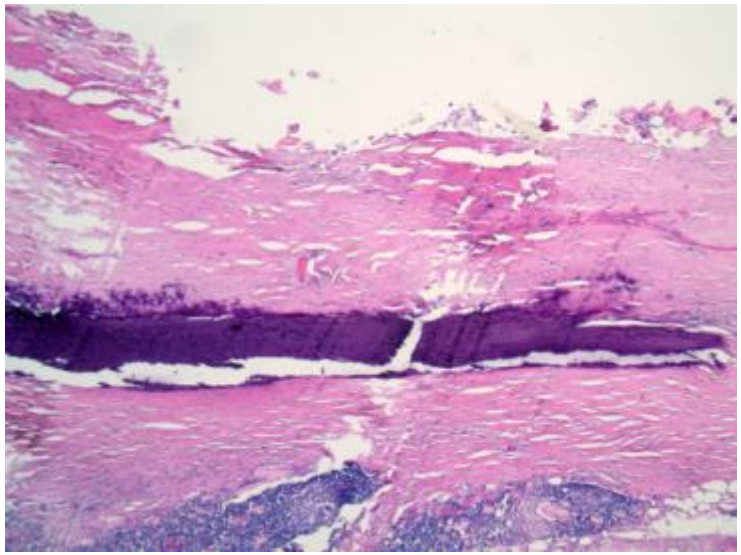


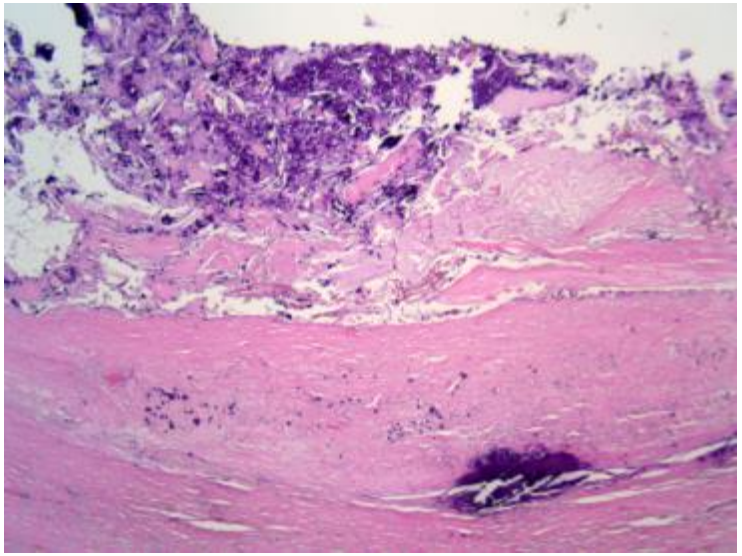






LAMN: denuded epithelium





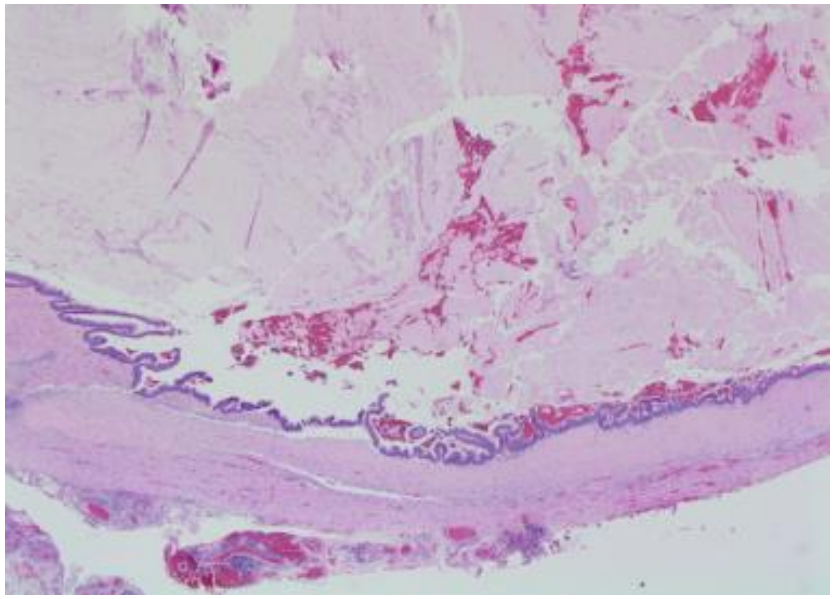
Sample adequately – submitting entire appendix is recommended

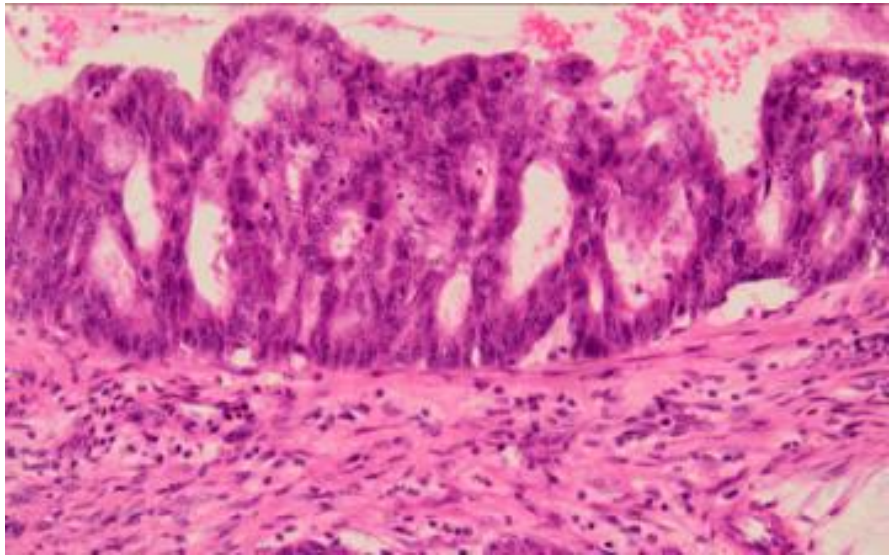
LAMN in TNM8

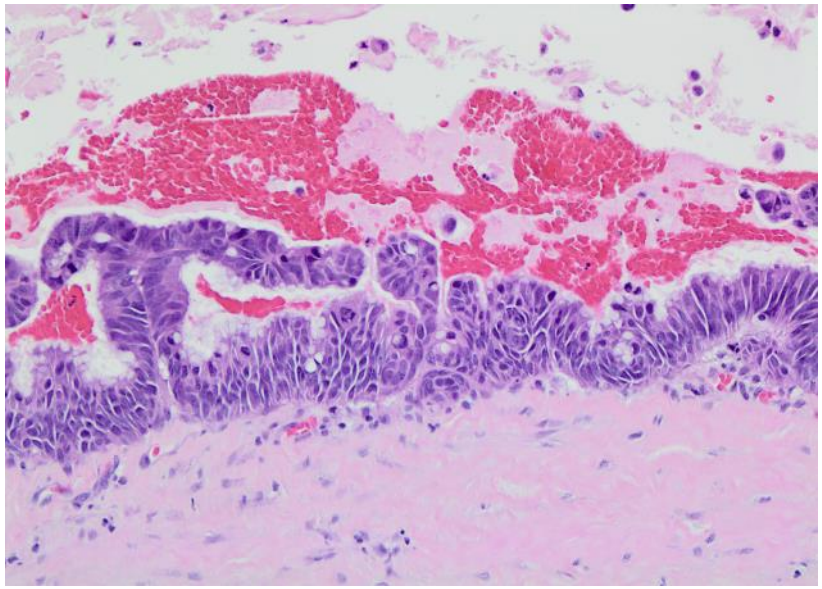
LAMN confined to appendix (acellular mucin or mucinous epithelium may extend into muscularis propria)	**Tis (LAMN)**
Tumour invades subserosa or mesoappendix	**T3**
Tumour perforates visceral peritoneum, including cells and/or mucin on the serosa	**T4a**

High grade appendiceal mucinous neoplasm (HAMN)

- No infiltrative invasion, but high grade cytology







Why distinguish HAMN from LAMN?

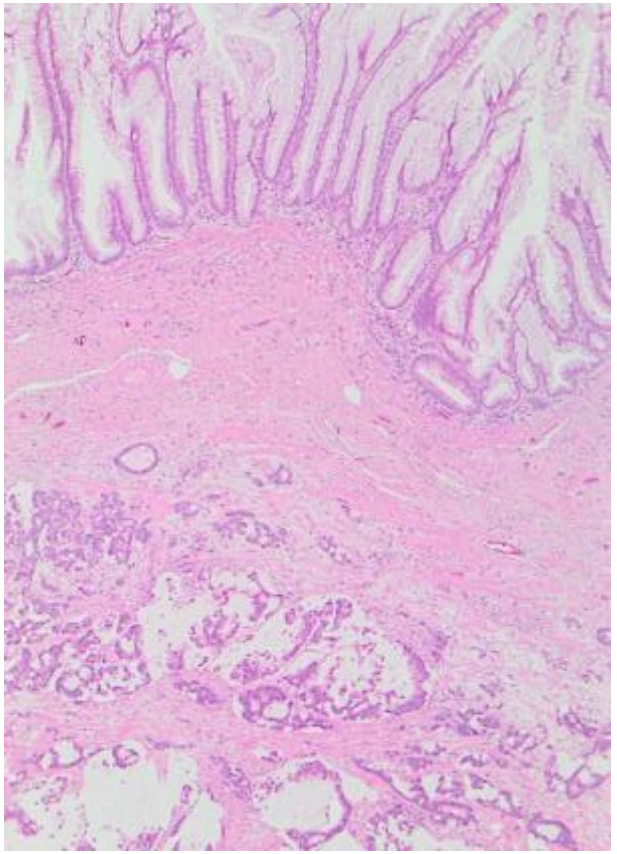
(1) In a series of 49 cases, subsequent PMP was more likely with high grade dysplasia (36%) than low-grade dysplasia (6%)

(2) patients with “noninvasive mucinous adenocarcinoma” (corresponding to HAMN) had decreased survival compared to LAMN ($p<0.01$)

1. Yantiss RK et al 2009
2. Misdraji J et al 2003

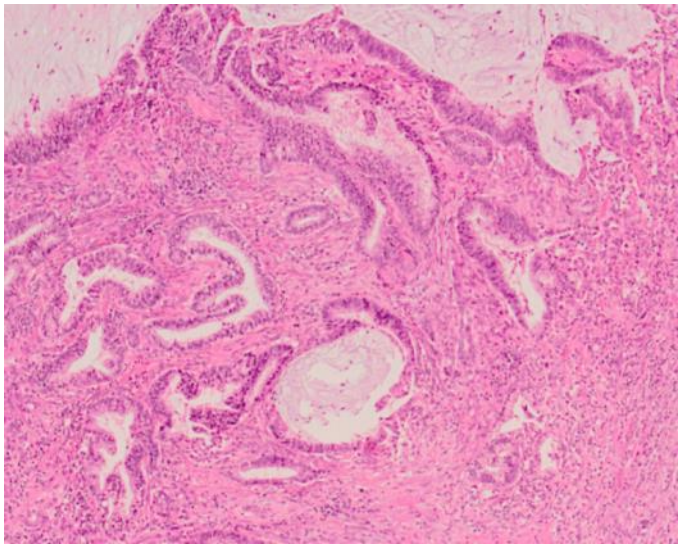
Mucinous appendiceal adenocarcinoma

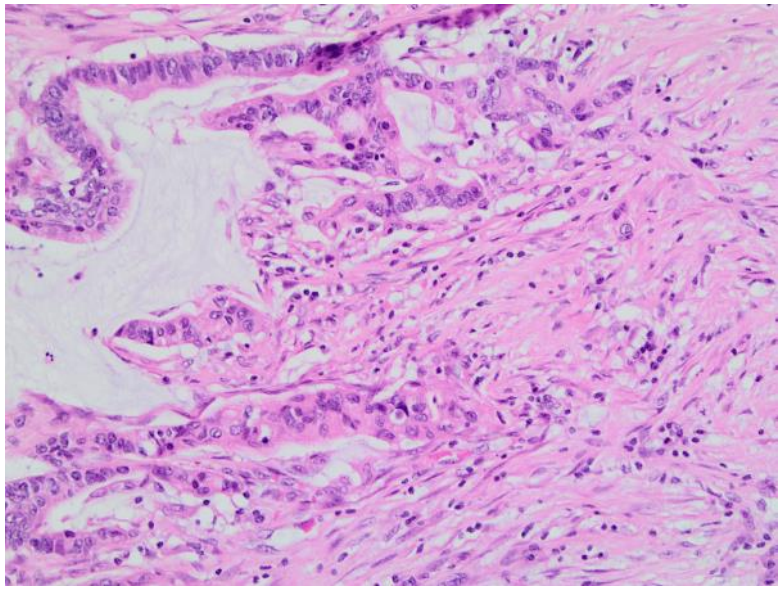
- Infiltrative invasion
  - Well differentiated
  - Moderately differentiated
  - Poorly differentiated
  - Poorly differentiated with signet ring cells



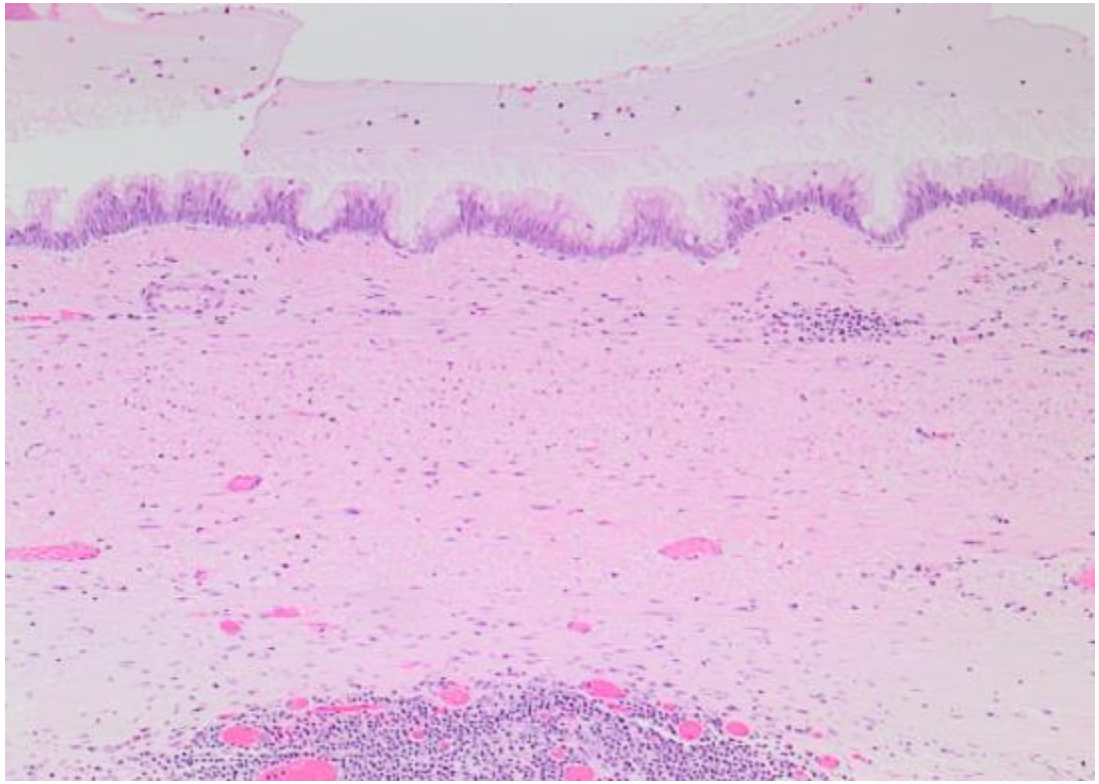
Features of infiltrative invasion

- Desmoplastic stroma
- Tumor budding (discohesive single cells or clusters of up to 5 cells)
- Small, irregular/angulated glands

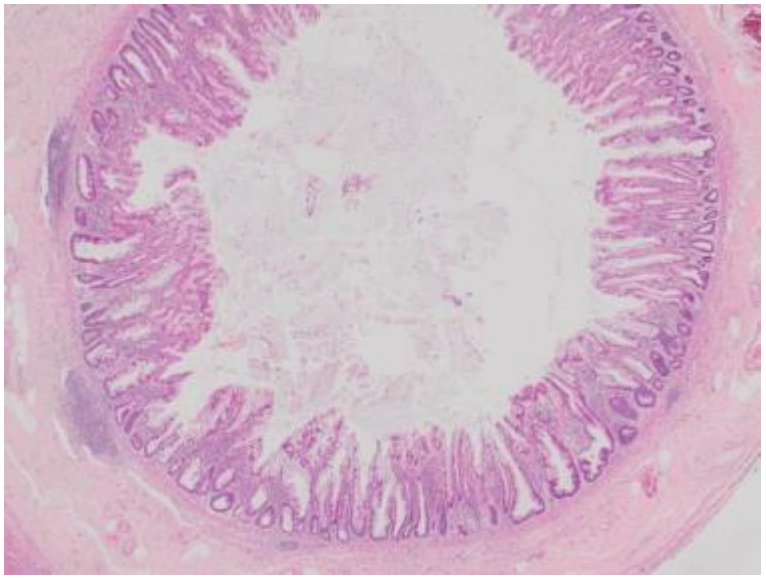




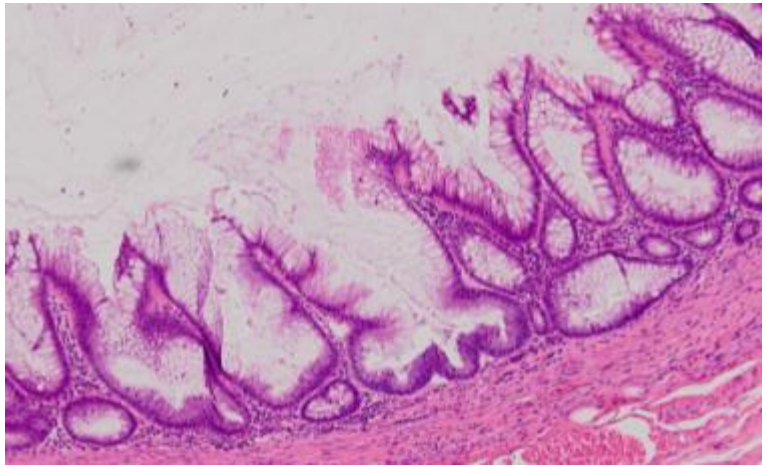
Fibrosis beneath LAMN

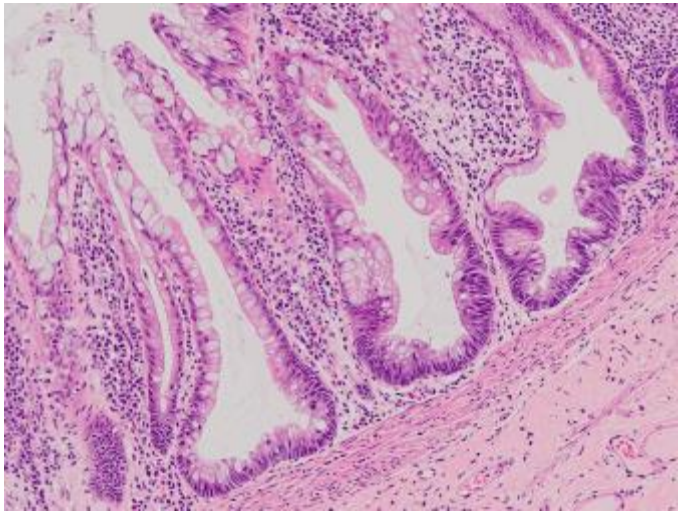


Serrated polyp



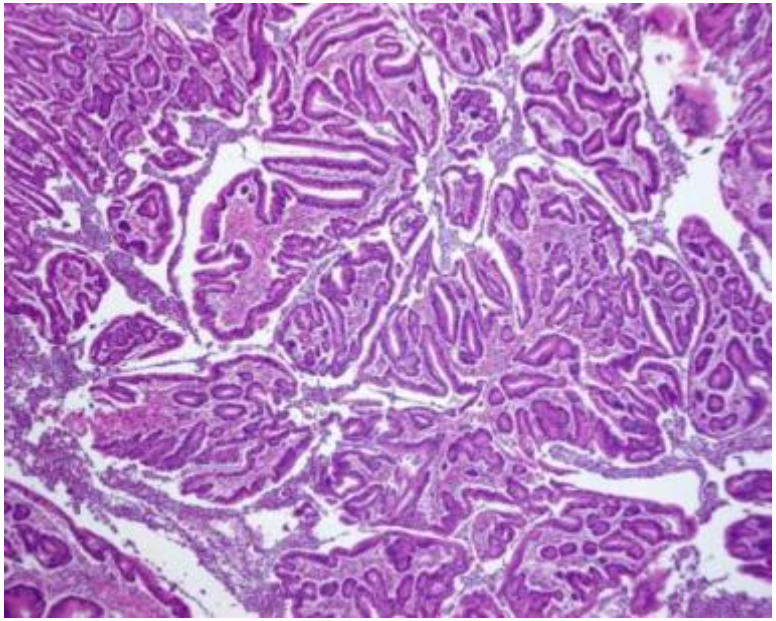
- Resemble colorectal sessile serrated lesion
- Muscularis intact
- Different genetics from colon (*KRAS* and *GNAS*, not *BRAF* or DNA MMR defects)
- With or without dysplasia



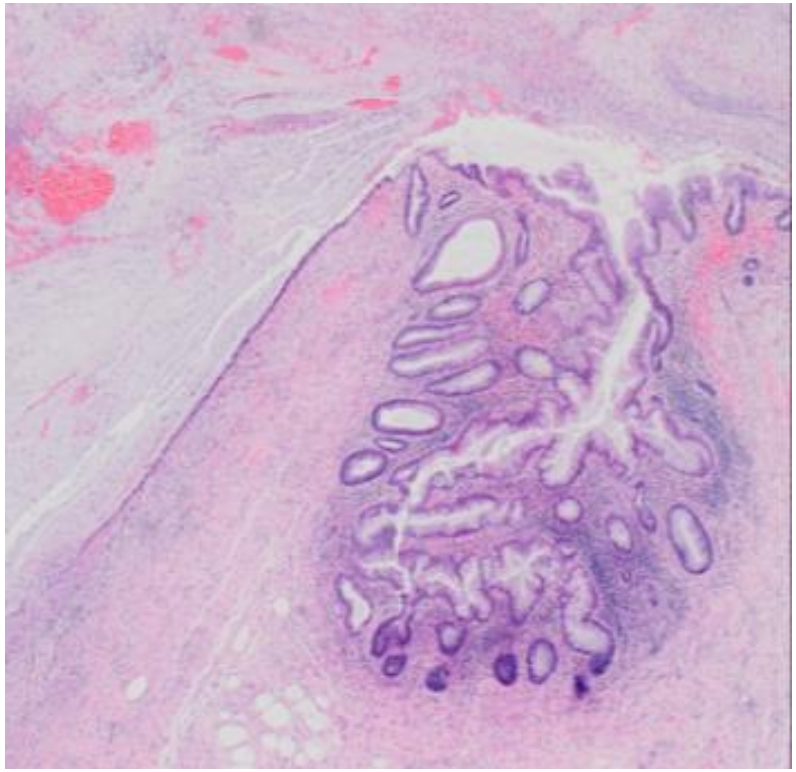


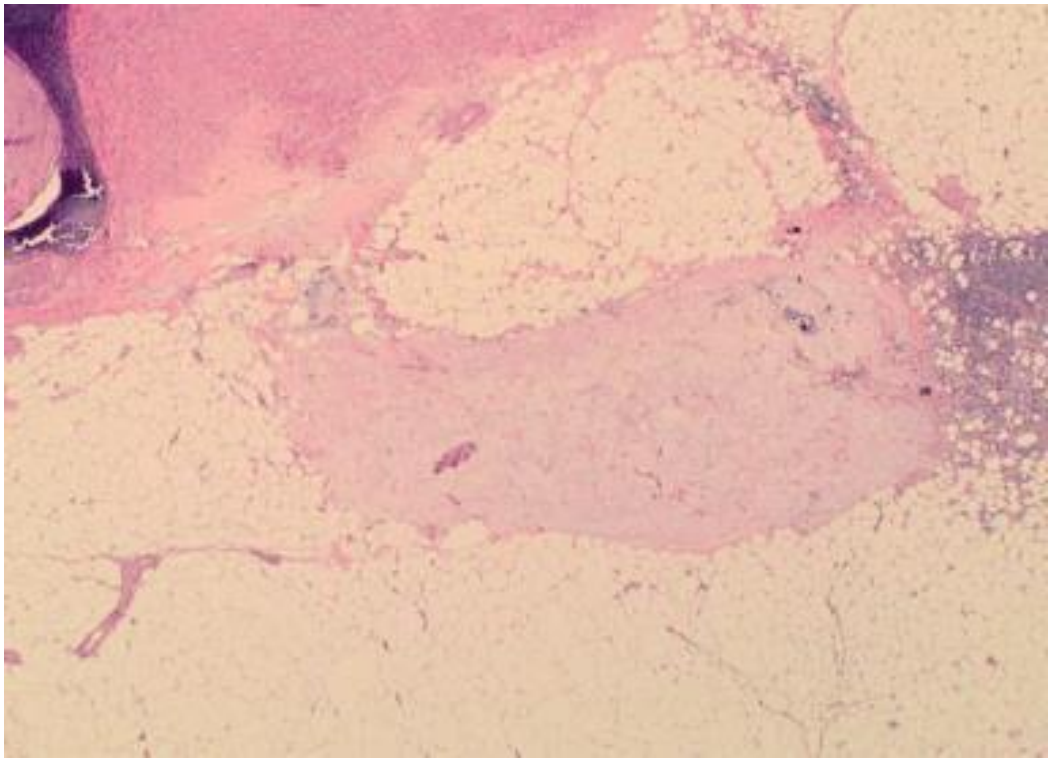
Tubular, tubulovillous or villous adenoma

- Rare
- Resemble typical colorectal type



Ruptured diverticulum

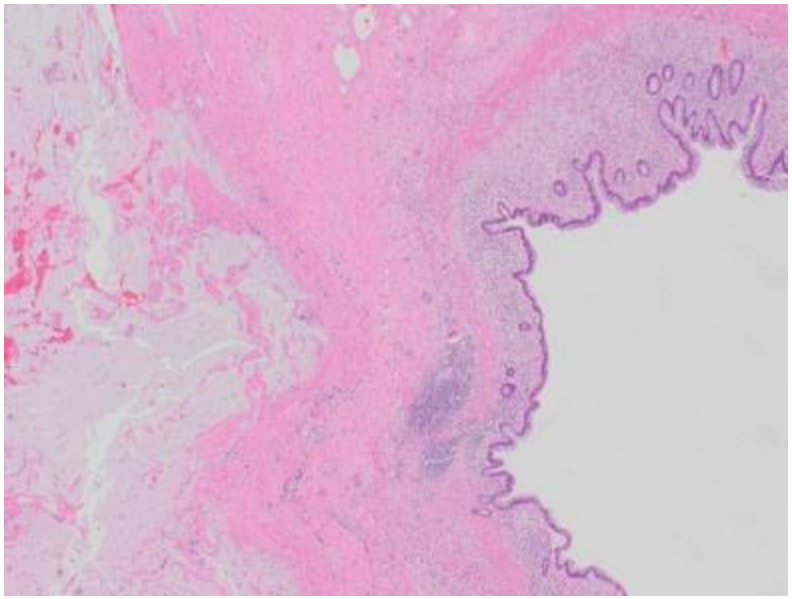


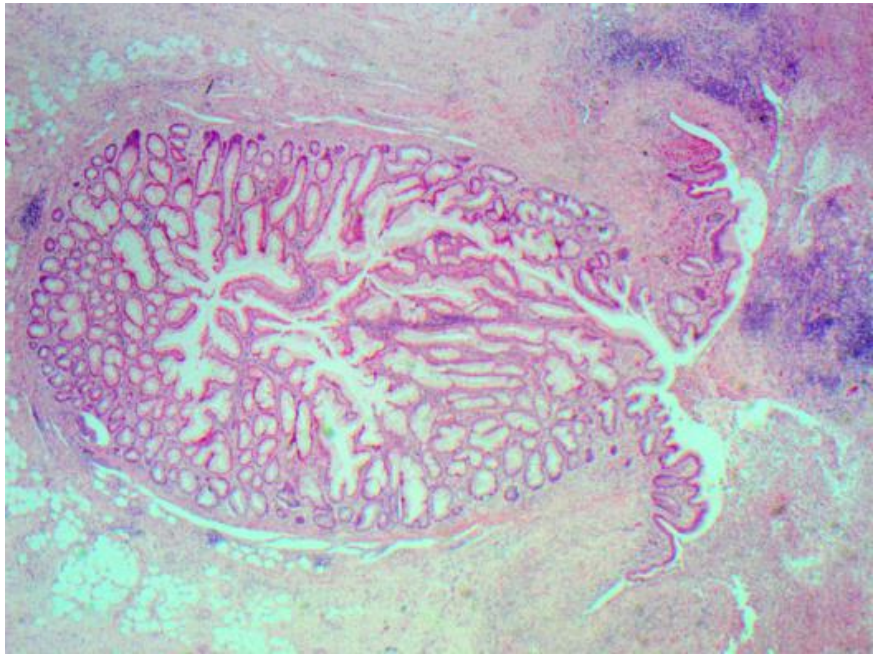


Favouring a diverticulum

1. Atrophy and crypt disarray, but preservation of essential mucosal architecture
2. Hyperplastic changes confined to the luminal portion of the mucosa

Hsu M et al 2009

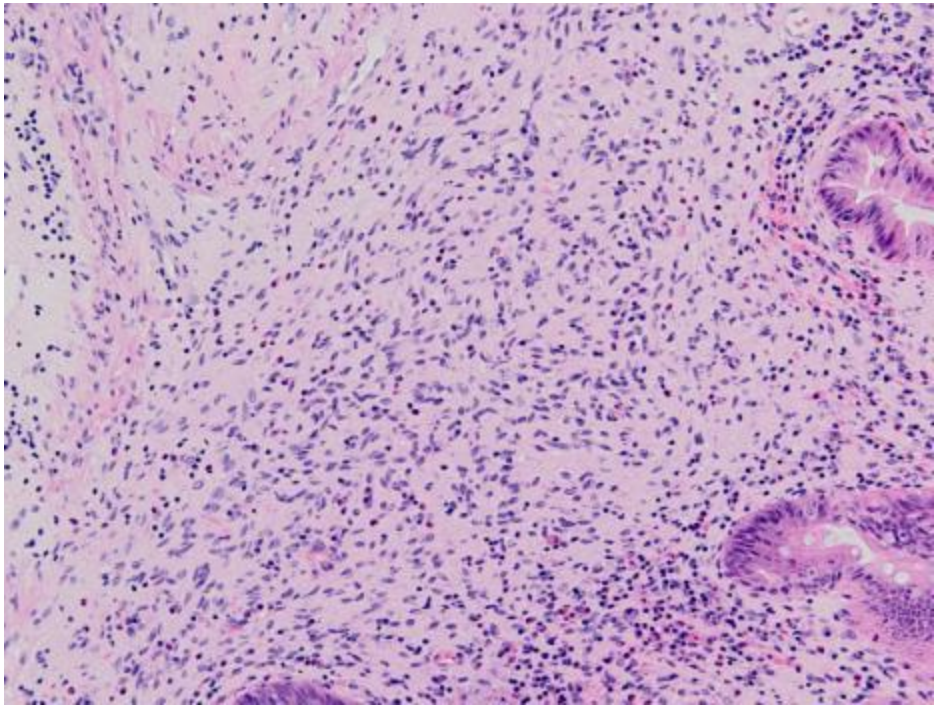


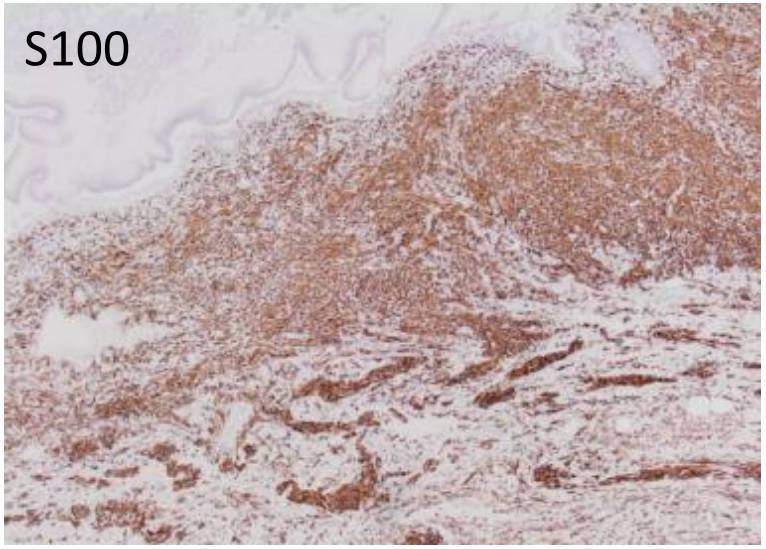


Favouring a diverticulum

3. Neuromatous mucosal proliferation

- S100 positive and EMA negative
  - related to axial neuromas
  - not perineuriomas





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