Appendix Lesions

Fibrous Obliteration
Non-neoplastic, benign process. Often incidental. Replacement of lumen by fibrous tissue with varying neural proliferation and adipocytes (so may stain with S100).

Serrated Lesions and Polyps
Identical to those in the colon. May be incidental or cause acute appendicitis. Associated with KRAS mutations.

Hyperplastic polyp: Polyp with serrations of superficial crypts only
More common

Sessile Serrated Lesion (formerly Sessile serrated adenoma/polyp):
Serrated polyp with distortion extending to crypt bases, often circumferential.
→ Can develop (adenoma-like) dysplasia (high-grade or low-grade)
→ villous growth → eventual possible adenocarcinoma

Adenocarcinoma
Looks just like adenocarcinoma of the colon.
Can be NOS, mucinous, signet-ring, etc...
Frequent KRAS and GNAS mutations.
Staging very similar to colonic adenocarcinoma.
Irregular malignant glands infiltrating the stroma (often with a desmoplastic response)

Neuroendocrine tumors
Most common appendiceal tumor by far.
Incidence of ~1% of all appendectomies.
Majority in appendiceal tip (so be sure to sample this!)
Occur at younger age than NETs elsewhere in GI tract.
May present incidentally or with acute appendicitis.
Good prognosis (>95% survival) if confined to appendix.
Looks and is graded like other GI NETs (see separate guide for details)
Nests and cords of cells with monotonous nuclei with “salt and pepper” chromatin
Appendiceal Mucinous Neoplasms

### Low-grade Appendiceal Mucinous Neoplasm (LAMN):
- Villous mucinous epithelium with tall cytoplasmic mucin vacuoles
- Low-grade cytology (nuclei compressed to pseudostratified)
- Broad, pushing border with compression of lamina propria and fibrosis
- Mucin may dissect through wall (with or without epithelium)
- Prognosis is very stage-dependent (earlier is much better)

### High-grade Appendiceal Mucinous Neoplasm (HAMN):
- Similar to LAMN, with additional complex architecture (micropapillary or cribriform) and/or cytologic atypia
- Infiltrative growth?!. → Adenocarcinoma!

Both have frequent KRAS mutations.
- Both are considered in situ [“pTis(LAMN)"], if confined by the muscularis propria. If through muscle into subserosa → pT3.
- If serosa involved → pT4a
- Acellular peritoneal deposits → pM1a
- Cellular peritoneal deposits → pM1b (higher risk for spread/recurrence → pseudomyxoma peritonei)

### Goblet Cell Adenocarcinoma

Amphicrine (having both endocrine and exocrine features) tumor with goblet-like mucinous cells, endocrine cells, and Paneth-like cells.
- Must have at least some low-grade pattern for Dx.
- Usually located at appendiceal tip.
- Stage as an Adenocarcinoma.

#### Low-grade pattern:
- Tubules and clusters of goblet-like mucinous cells; endocrine and Paneth-like cells with granular eosinophilic cytoplasm, mild nuclear atypia, and no stromal reaction.

#### High-grade pattern:
- Tumor cells infiltrating as single cells, complex anastomosing tubules, cribriform masses, or sheets. Signet-ring cells.
- High-grade cytologic features.
- Desmoplastic response.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Tubular/Clustered (Low-grade Pattern)</th>
<th>Loss of tubular/clustered growth (High-grade pattern)</th>
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<tbody>
<tr>
<td>1</td>
<td>&gt;75%</td>
<td>&lt;25%</td>
</tr>
<tr>
<td>2</td>
<td>50-75%</td>
<td>25-50%</td>
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<tr>
<td>3</td>
<td>&lt;50%</td>
<td>&gt;50%</td>
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