

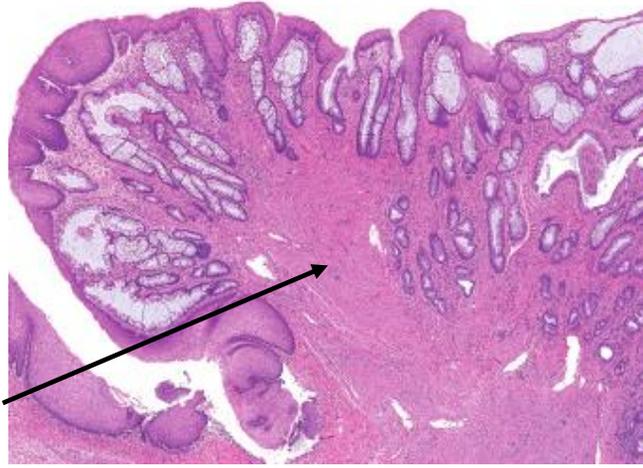
# Tumors of the Anus

## Benign Tumors

### Inflammatory Cloacogenic Polyp

Non-neoplastic polyp arising at the anal transition zone  
May involve lower rectum, often anterior.  
Thought to be due to **prolapse** (on a spectrum with solitary rectal ulcer syndrome and rectal prolapse)

Surface may include squamous, glandular, or transitional epithelium, which is often hyperplastic, without dysplasia  
**Stromal inflammation**, surface ulceration, and granulation tissue are often present  
Classic feature: **Fibromuscular proliferation around glands**



### Squamous Intraepithelial Lesions (SIL)

Non-invasive cytologic and architectural abnormalities of squamous epithelium, associated with HPV infection

*See separate "Lower Anogenital Squamous Tract" (LAST) guide for additional information*

#### Low-grade Squamous Intraepithelial Lesion (LSIL)

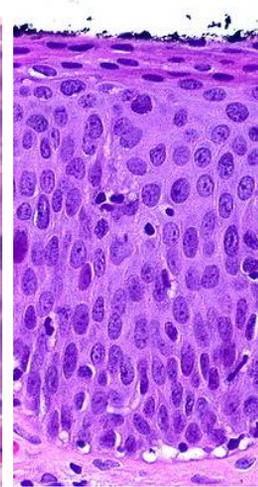
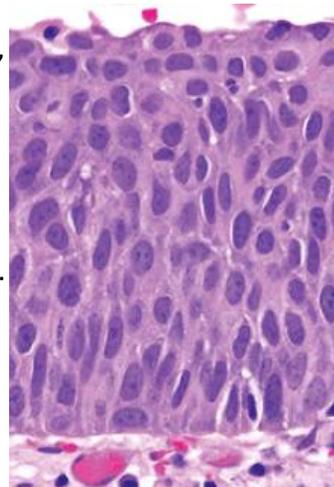
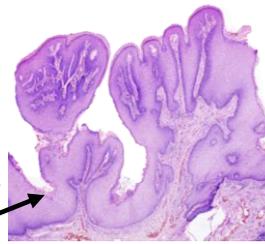
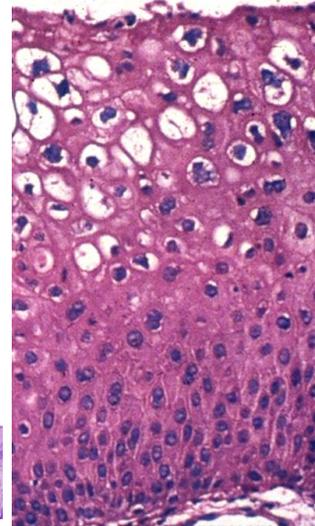
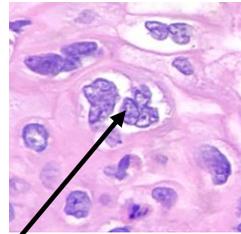
(AIN1, Condyloma)

Cytologic atypia and mitotic figures in the lower 1/3 of epithelium with associated **superficial Koilocytic atypia**.

"Atypia" = hyperchromatic nuclei with irregular nuclear contours.

Koilocytes = large superficial cells with large, hyperchromatic, "raisinoid" nuclei and perinuclear halos. Sometimes multinucleated

If papillomatous exophytic growth → **Condyloma**, often has marked epithelial thickening, parakeratosis, broad rete pegs, and koilocytic atypia.



#### High-grade Squamous Intraepithelial Lesion (HSIL)

Marked cytologic atypia and superficial mitotic figures involving full thickness (for CIS/AIN3) or up to 2/3 (for AIN2).

**Nuclei are hyperchromatic with irregular nuclear contours.**

Loss of architectural polarity (Top looks like bottom)

**Diffuse "Block positive" P16 staining**

Can screen for Anal SIL in high risk populations (e.g., HIV+) with anal Pap smears.

## Fibroepithelial Polyp

Aka “Hypertrophic anal papillae” or “Skin tag”

**Non-neoplastic, benign polypoid projections of anal squamous epithelium with underlying subepithelial connective tissue.**

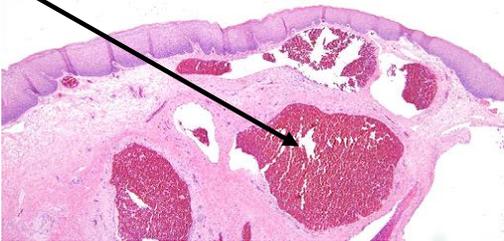
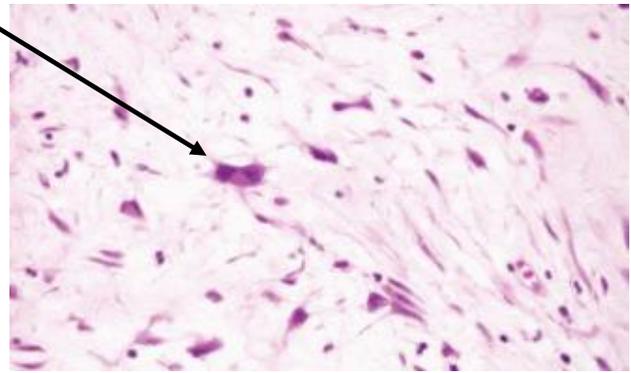
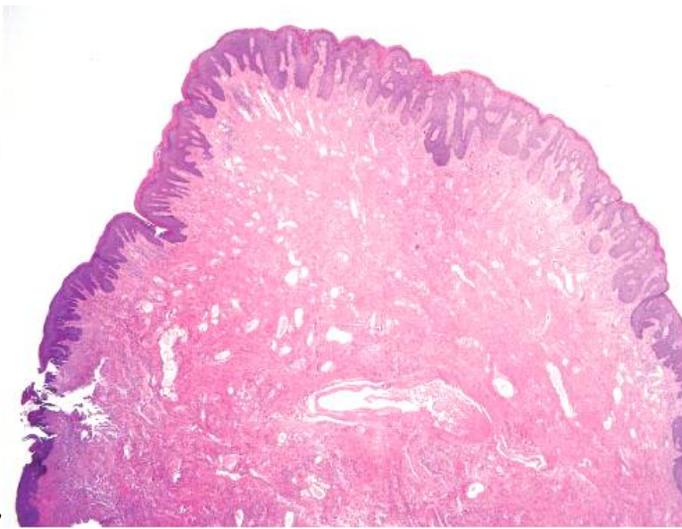
Very common! May resemble hemorrhoids clinically.

**Surface:** Squamous epithelium usually.

**Core:** Loose fibrovascular connective tissue.

May have multinucleated giant cells or fibroblasts with bizarre nuclei (large, smudged, hyperchromatic), which are thought to be degenerative (like “ancient change” in a schwannoma), often CD34+.

If contain large dilated vascular spaces consider: a **Hemorrhoid.**



## Paget's Disease

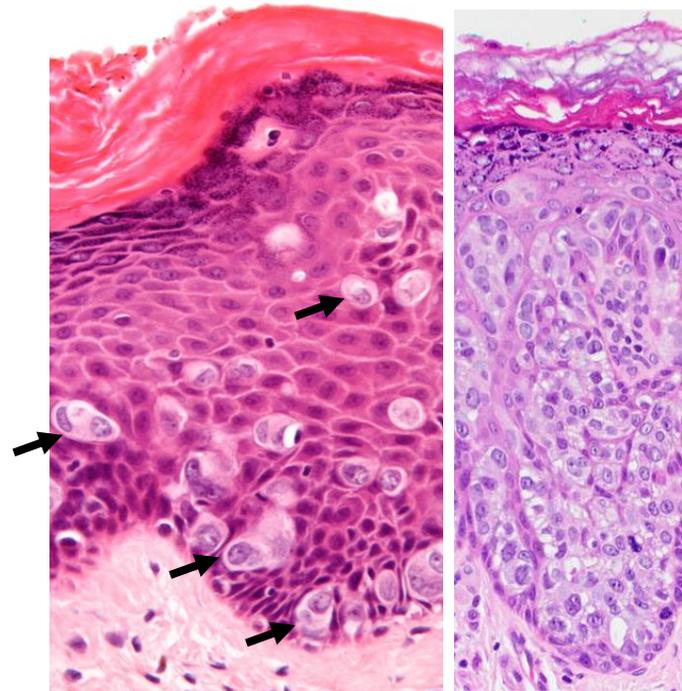
Pagetoid spread of **malignant glandular cells** within the squamous epithelium (an in situ lesion) Large pleomorphic cells with abundant pale cytoplasm. May infiltrate singly or form glandular structures in squamous epithelium.

Clinically, skin is erythematous and itchy.

May be Primary or Secondary:

**Primary** → Likely derived from adnexal structures, has an apocrine phenotype (IHC: CK7+, CK20/CDX2-, GCDFP-15/GATA-3 +), Not associated with an underlying neoplasm

**Secondary** → Derived from an underlying rectal or anal neoplasm (often rectal adenocarcinoma). Phenotype depends on underlying malignancy (often CK20 & CDX2 +)



Management: Must clinically (and with IHC) evaluate if this is primary or secondary and exclude rectal origin. If primary, has a strong tendency to recur, and can become invasive.

**DDX:** **Melanoma** (S100, HMB45, SOX10, Melan-A +) and **SCCIS** (CK5/6+, often block positive P16)

## Other Benign Tumors

### *Developmental and Acquired cysts:*

**Duplication cyst**—Lined by columnar, organized GI epithelium with a well-formed, double muscle layer and nerve plexus

**Tailgut Cyst**—(Retrorectal cystic hamartoma) Cystic mass near sacrum lined by any type of GI tract epithelium, including squamous, with disorganized smooth muscle bundles

**Also: Epidermoid cyst, Anal duct cyst, Median raphe cyst, Mature cystic teratomas, etc...**

**Ectopic breast tissue**—the “milk line” extends to the perianal area, so you can have ectopic breast tissue and even breast tumors (e.g., phyllodes tumors)

**Hidradenoma Papilliferum**—well-circumscribed nodule with papillary architecture of ducts lined by a double layer of epithelial cells with decapitation secretion (essentially the cutaneous counterpart of a breast intraductal papilloma). Almost exclusively in middle-aged women.

## Malignant Tumors

### General Considerations

If a lesion can be completely visualized with gentle traction of the buttocks, it is considered a Perianal lesion (not anal), which is similar to skin lesions on other parts of the body.

Carcinomas above the dentate line → metastasize to perirectal and internal iliac nodes

Carcinomas below the dentate line → metastasize to inguinal and femoral lymph nodes

### Squamous Cell Carcinoma

Malignant epithelial tumor derived from the anal squamous mucosa with **keratin production, intercellular bridges, and frequent HPV infection.**

Infiltrating squamous cell clusters and strands with malignant nuclei and eosinophilic cytoplasm.

Most common in older patients and women.

**HPV infection in ~90% of cases** (most commonly type 16).

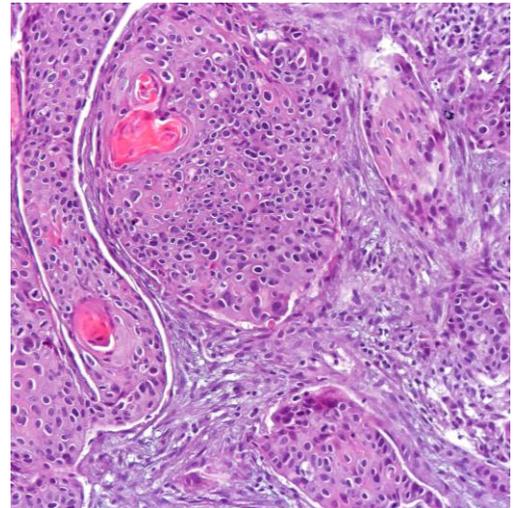
Risk factors: Immunodeficiency (particularly HIV), anal receptive intercourse, and smoking

#### ***Histologically heterogeneous***

**Basaloid pattern**—marked hyperchromasia, scant cytoplasm, and peripheral palisading (reminiscent of BCC), formerly called cloacogenic carcinoma

Admixed mucin-containing cells (try to avoid using term mucoepidermoid carcinoma to avoid confusion)

**Verrucous carcinoma**—Bland, well-differentiated thickened epithelium with bulbous exophytic fronds and endophytic “pushing” invasion. Lacks HPV cytopathic effect or significant atypia. Cannot Dx on biopsy. Often associated inflammatory infiltrate. Locally destructive but does not metastasize.



# Anal Adenocarcinoma

Adenocarcinoma that arises in the anal canal.

Can be extra or intramucosal:

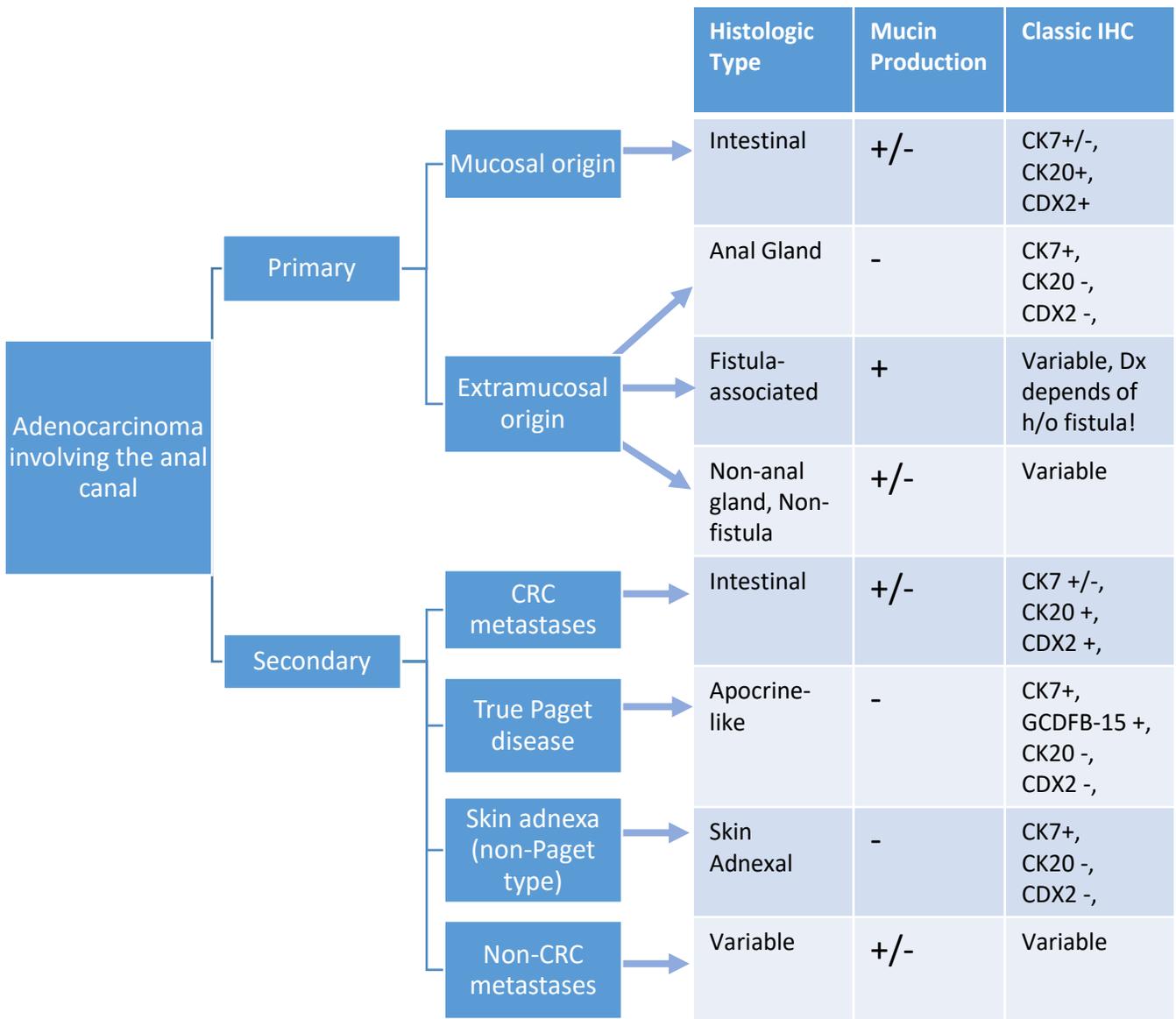
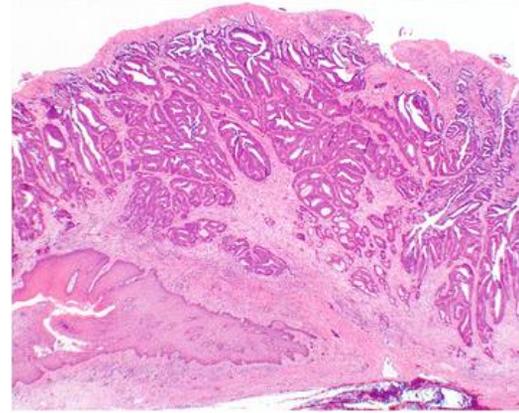
**Intramucosal** → Arises from luminal mucosa and is intestinal-type

**Extramucosal** → Does NOT arise from lumina (no in situ component) may be associated with an anal glands, fistula, or other structures

**Anal gland adenocarcinomas** arise from the anal gland/duct. They form infiltrative masses in the wall of the anus. IHC: CK7+, CK20/CDX2-. Be sure to exclude a metastasis (e.g., GYN)

**Most fistula-associated adenocarcinomas** most often arise in the setting of Crohn's disease and are mucinous.

All types can show Pagetoid spread → Secondary Paget's disease!



# Neuroendocrine Neoplasms

Neuroendocrine Carcinomas are much more common than well-differentiated neuroendocrine tumors.

## Neuroendocrine Carcinomas:

Often arise from non-neuroendocrine tumors (and subsequently develop neuroendocrine differentiation.

**Sheet-like growth**

Not Graded. Ki67/Mitotic index >20% (often much higher).

Malignant! Very metabolically active/**rapidly growing**

→ see on normal FDG-PET scan

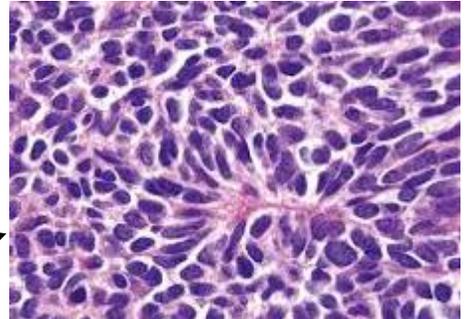
Molecular: p53, RB1 (and other carcinoma-associated mutations)

Treatment: Platinum-containing chemotherapy

## Small Cell Neuroendocrine Carcinoma

Morphology: Fusiform nuclei, **finely granular chromatin**, **scant cytoplasm**, and nuclear molding. Extensive necrosis.

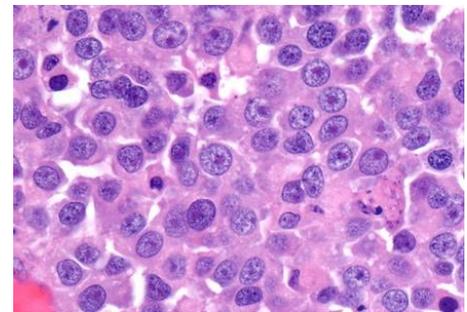
Tons of mitoses. Ki67 almost 100%.



## Large Cell Neuroendocrine Carcinoma

Morphology: Large, round nuclei, with **prominent nucleoli**, and moderate amounts of cytoplasm. Sheet-like to nested growth.

Ki67 often in 60-80% range.



# Melanoma

Malignant transformation of melanocytes present in the anal mucosa/transition zone.

Very rare.

Typically old/elderly patients. More common in women.

Typically polypoid masses near dentate line.

Typically epithelial morphology. Large, malignant cells with frequent Macronucleoli.

Dusky greyish cytoplasm with frequent pigmentation.

IHC: Typical melanocyte markers (S100, SOX10, HMB45, Melan-A)

Molecular/Therapeutics:

BRAF mutations → BRAF inhibitors (e.g., vemurafenib)

CKIT mutations → tyrosine kinase inhibitors (e.g., imatinib)

Poor prognosis.

