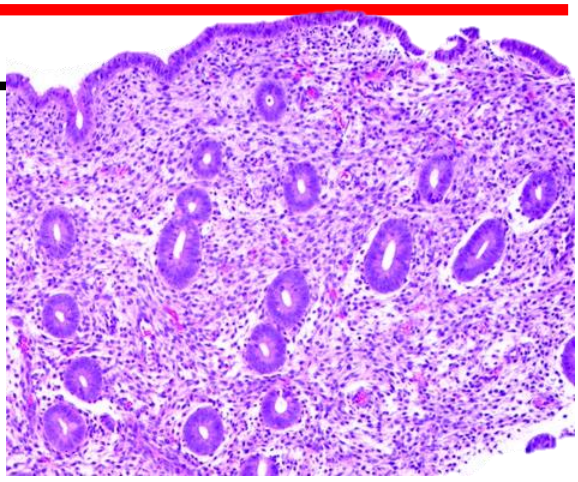
Benign Endometrium

Endometrial Cycle & Dating

Proliferative Phase



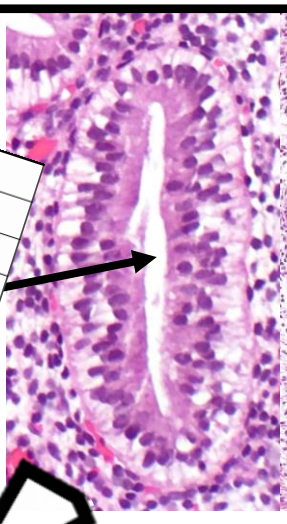
Cycle **days 4→14**, usually not subdivided

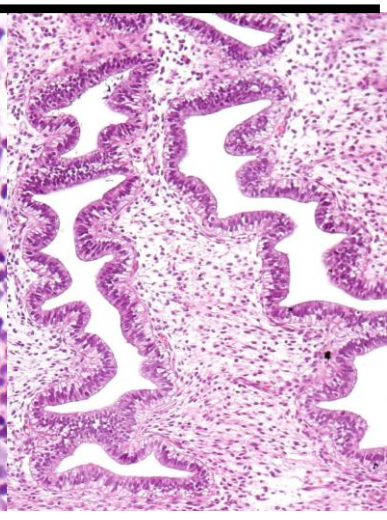
Dark blue tubular glands
Abundant stroma
Low columnar cells
Pseudostratified nuclei
Mitotic activity

Glands get a little convoluted late

Secretory Phase

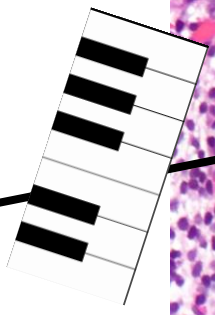
*Think: "**Serrations**"*





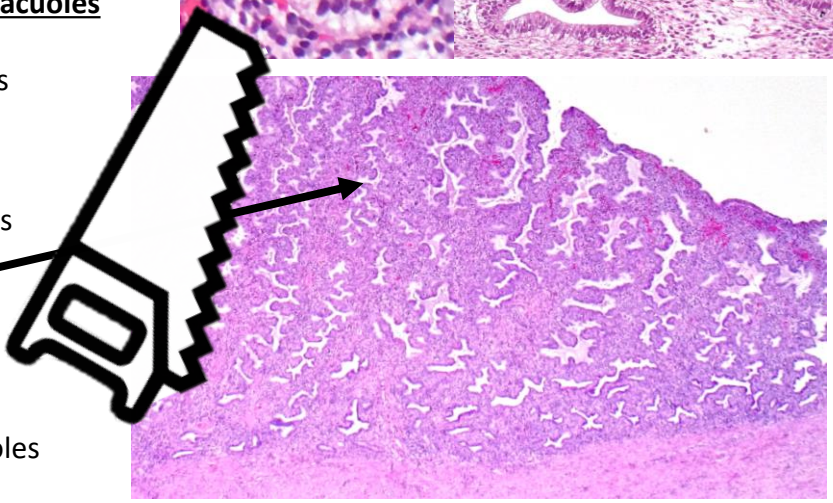
Not necessary to specifically date unless part of an infertility work-up

Interval Phase
Cycle days 15→16 (post-ovulation)
Scattered subnuclear vacuoles
Otherwise, resembles proliferative phase



Early Secretory
Cycle days 17→19
Most cells have uniform **subnuclear clear vacuoles**
*think: "**piano keys**"*
Decreased pseudostratification and mitoses

Mid Secretory
Cycle days 20→22
Dilated glands with secretions; Apical blebs
Single layer of basally oriented cells

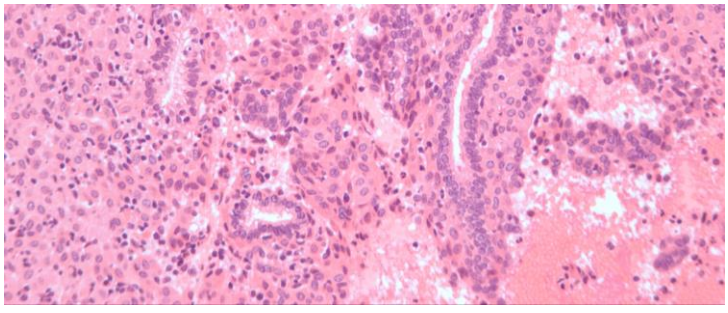


Late Secretory
Cycle days 23→29
Serrated, "**saw toothed**" glands
Condensation of predecidua around arterioles

Menstrual Phase

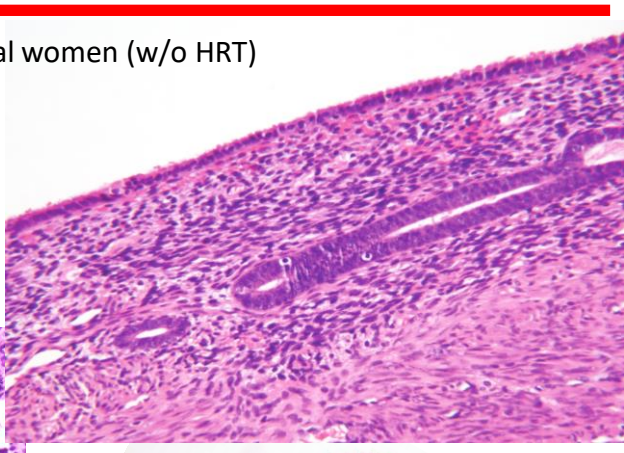
Cycle days 1→4

Stromal **hemorrhage**→ very **red** appearing
Neutrophils, fibrin thrombi
Fragmented glands with secretory exhaustion



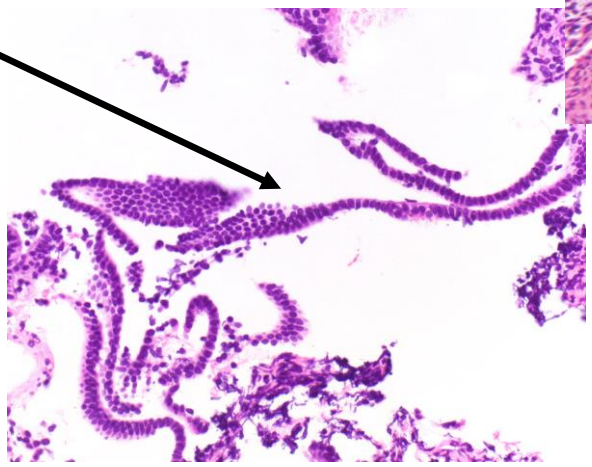
Atrophy

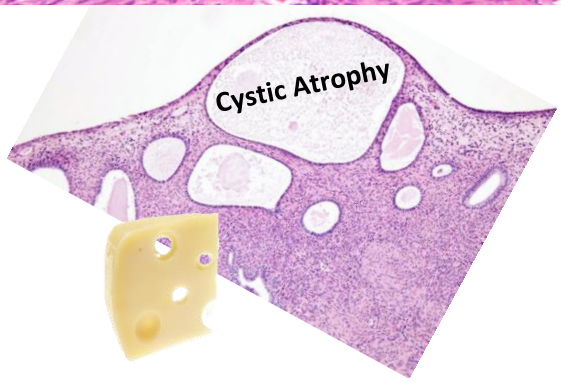
Normal/expected in post-menopausal women (w/o HRT)



Thin→ 1 layer of flattened epithelium
NO mitoses
Simple, widely spaced glands, often running parallel to surface, in **collagenized stroma**

On Biopsy: Often **scant strips** of surface epithelium shaped like **paperclips** with scant stroma





If features are between proliferative and atrophic→ "**Weakly Proliferative**" or "**Inactive**" **endometrium**

Pregnancy/Hormone-related Changes

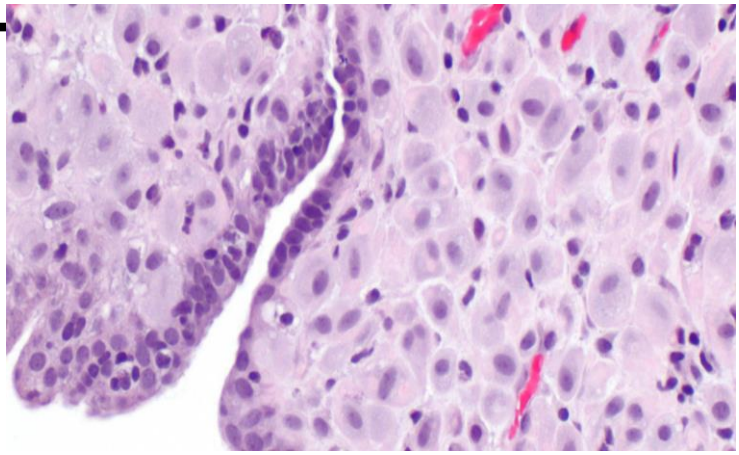
Decidualization

Caused by **progestin** (Seen in pregnancy and also with progestin drugs)

Sheets of **large, epithelioid cells** with pink cytoplasm, distinct cell membranes, and round/oval central nuclei.

Associated glands are widely spaced and atrophic

(In early pregnancy, before decidualization, endometrium is hypersecretory)



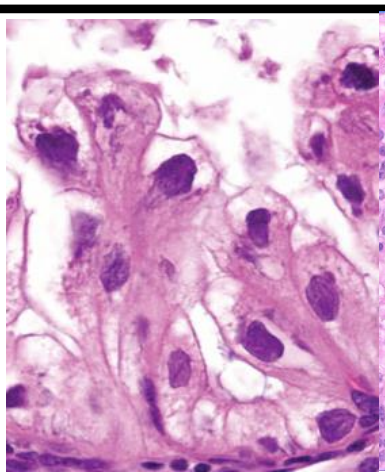
Arias-Stella Reaction

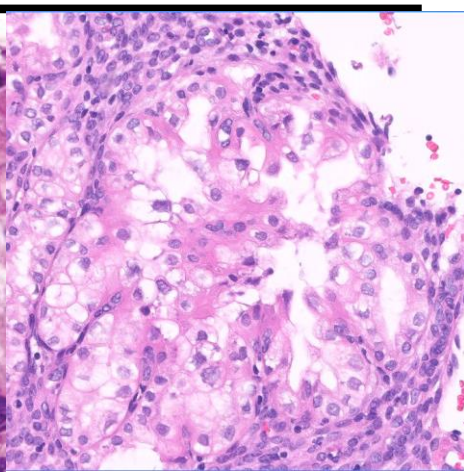
Seen in **pregnancy** and gestational trophoblastic disease. Incidental finding.

Tufted proliferation within glands lined by cells with **enlarged, pleomorphic, hyperchromatic nuclei** and abundant clear to pink cytoplasm.

Can ***mimic*** **malignancy, but** ***benign***

Unlike clear cell carcinoma: See other pregnancy changes, Few mitoses, No invasion, Only focal, Low Ki67.





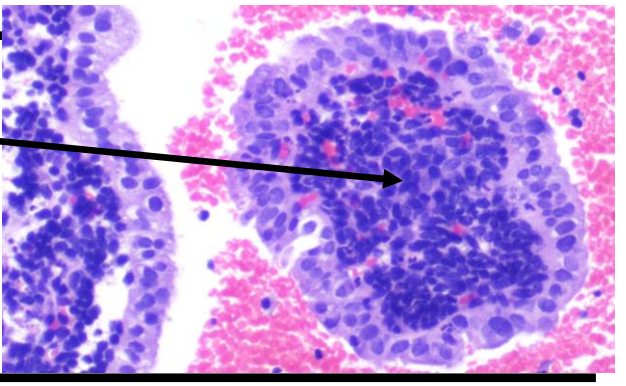
Dysfunctional Endometrium

Often due to **Anovulatory cycles.** Normal in perimenopausal period. Also see with PCOS.
(No ovulation → No corpus luteum → No progesterone while follicles make estrogen → stimulation of proliferative endometrium → Either outgrows estrogen or follicles can't make enough estrogen → breakdown)

Glandular and Stromal Breakdown

Tight aggregates of collapsed and condense stroma
Appear very dark. Hyperchromatic nuclei with scant cytoplasm
Think: ***"Blue cannon balls"***

± Epithelial cell rim
May see associated metaplastic changes



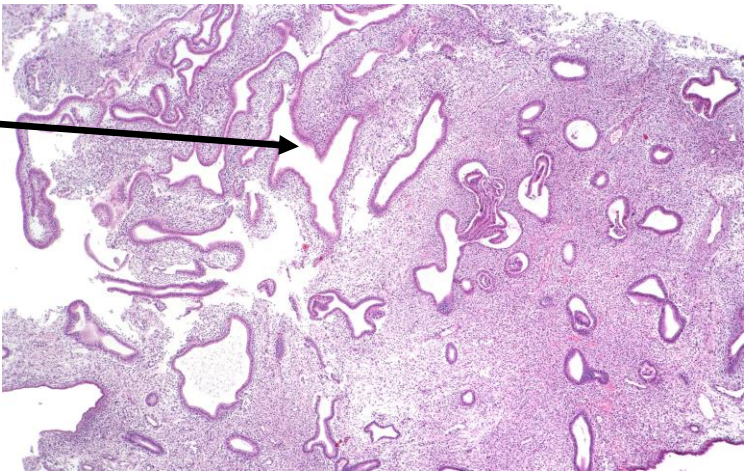
Disordered Proliferation

Variably/haphazardly shaped glands
(e.g, branching), including **cystically dilated**

Glands/cells identical to proliferative endometrium

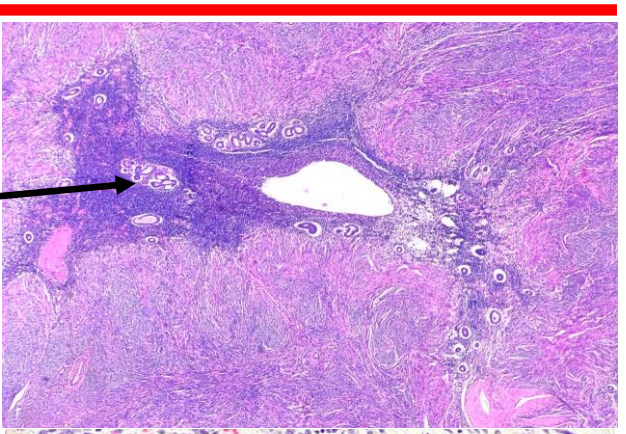
Abundant stroma
Gland:Stroma ratio often 1:1, if becomes >2:1, then consider *hyperplasia* (see endometrial tumor notes)

Often coinciding breakdown



Adenomyosis/Endometriosis

Endometrial glands *and* stroma outside of their usual endometrial cavity location → cause **dysmenorrhea** and/or menorrhagia

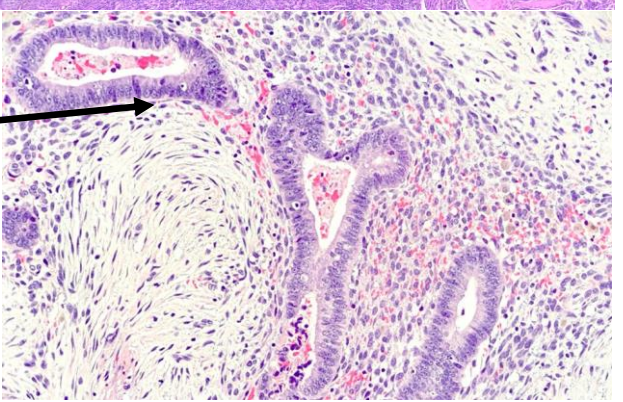


Adenomyosis

Endometrial glands and stroma in the myometrium. Distance from normal junction not standardized, so consider using the rough guideline of a 4x field.

Associated myometrial hypertrophy → grossly thick and trabeculated with cysts.

Adenomyoma—leiomyoma-like smooth muscle nodule with associated adenomyosis



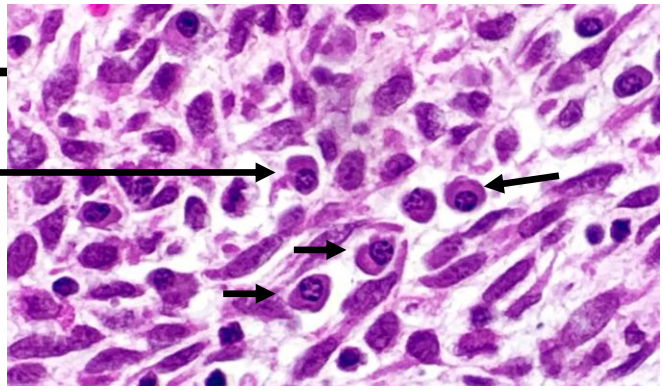
Endometriosis

Endometrial glands and stroma outside of the uterus (e.g., uterine serosa, pelvis, etc…). Often see **hemosiderin-laden macrophages.**

Grossly, looks like brown adhesions or "powder burns"

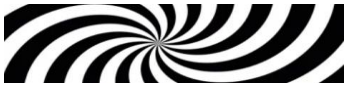
Endometritis

Chronic Endometritis

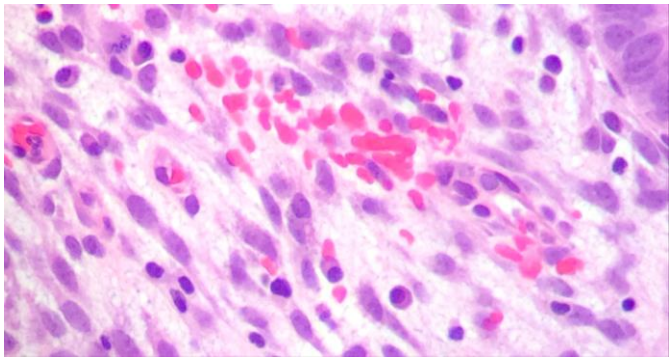


Defined by the presence of <u>plasma cells</u>.

Often associated **lymphocytic infiltrate** and **<u>reactive spindled stromal changes</u>** with elongated, fibroblast-like stromal cells swirling around glands and forming pinwheels (seeing these other features should prompt a plasma cell hunt).



Of note, some lymphocytes and follicles are <u>normal</u>.

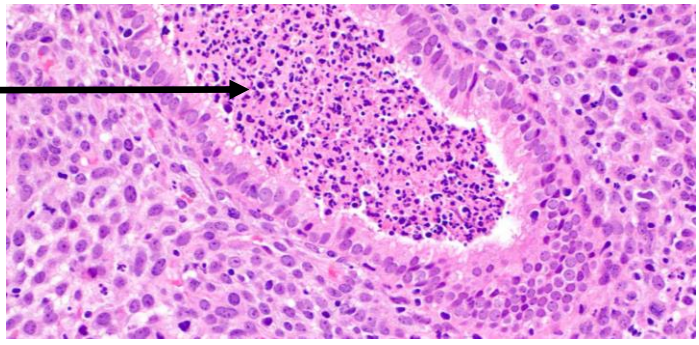


May be asymptomatic, or present with pain, bleeding, or infertility.
Risk factors: recent pregnancy/abortion, IUD, salpingitis

Using CD138 to diagnose is controversial and may lead to over diagnosis, so try to rely on morphology.

Treat with antibiotics.

Acute Endometritis

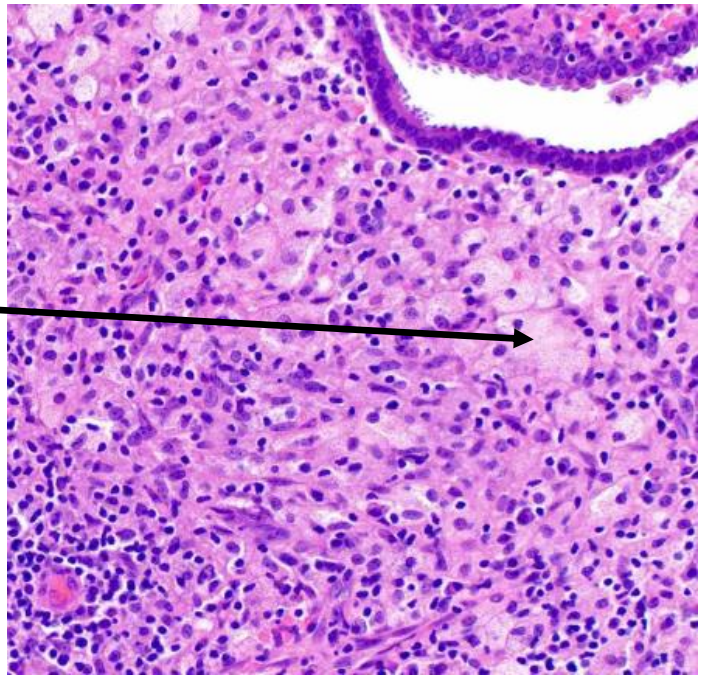


<u>Acute inflammation</u> with **Microabscesses**, intraepithelial neutrophils, and gland destruction

Usually a <u>clinical diagnosis</u> (no biopsy)
Often **<u>postpartum</u>** or postabortion.

Of note, menstrual endometrium has abundant acute inflammation *normally*, so use clinical information to not over diagnose.

Other Endometritis



Granulomatous Endometritis

Rare in US. Always stain to rule out infection, particularly TB (do mycobacterial and fungal stains). Giant cells may be seen with prior instrumentation and ≠ granulomas.

Xanthogranulomatous Endometritis

Usually post-menopausal women with cervical stenosis. Sheets of macrophages with foamy cytoplasm, lymphocytes, plasma cells, neutrophils, cholesterol clefts, and hemosiderin.

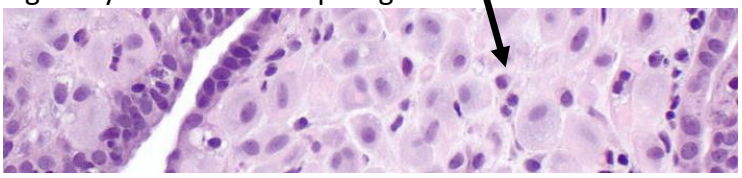
Malakoplakia

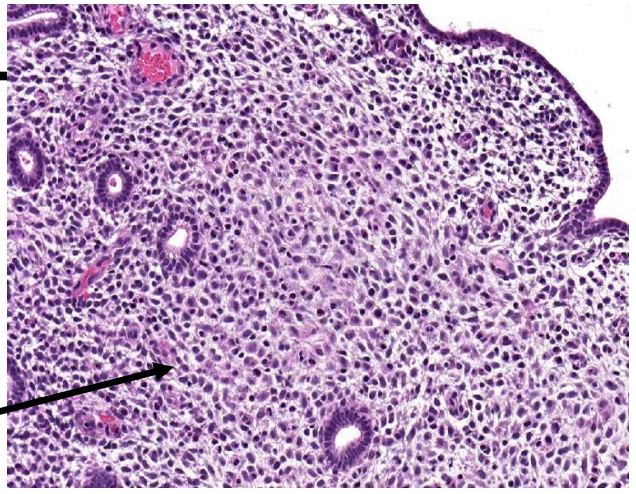
Like in the GU tract.
Sheets of histiocytes with Michaelis-Guttmann bodies, which stain with Calcium stains.

Other Changes/Metaplasia

Oral Contraceptive Effect

If **Progestin-only**: See **decidualization** like during late pregnancy with small atrophic glands

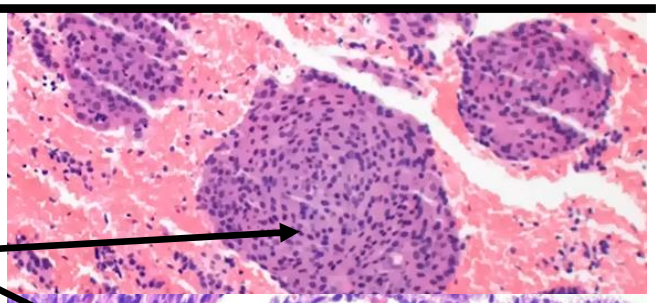




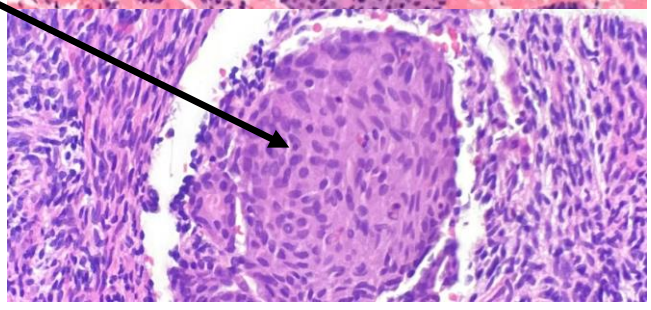
If **Estrogen & Progestin**: Small, inactive, tubular glands with abundant stroma of plump spindled cells

Squamous Morular Metaplasia

Solid nests of bland immature epithelium within endometrioid glands.
Epithelioid to spindled. May have central necrosis.
Can be "free floating" without adjacent endometrium.



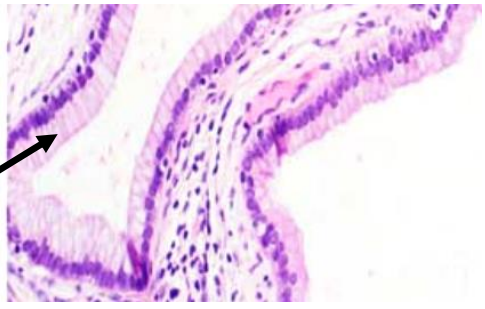
Immunophenotype is actually *not* squamous!
IHC: (+)CDX2/SATB2, Nuclear β-catenin, (-)p63, ER, EMA



Associated with concurrent or subsequent risk lesions/cancer (CAH/EIN, APA, Endometrioid carcinoma), so further clinical follow-up should be recommended if more than focal.

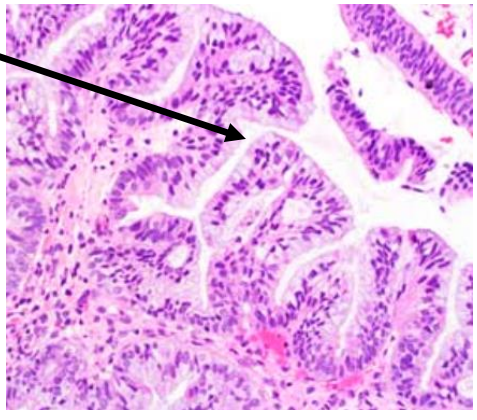
Mucinous Metaplasia/Change

Replacement **by columnar, mucin-rich, endocervical-like epithelium.**
(GI-type mucinous metaplasia with goblet cells is rare)

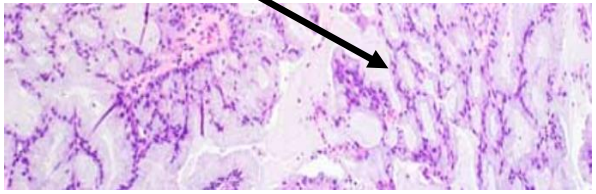


Usually focal and cytologically bland. Simple architecture (tubes, with rare tufting)→ Benign and can just classify as "**mucinous metaplasia**"

However, it gets increasingly complex → associated with carcinoma (endometrioid/mucinous) on hysterectomy → "**Atypical Mucinous Glandular Proliferation**" (should prompt additional sampling at least)



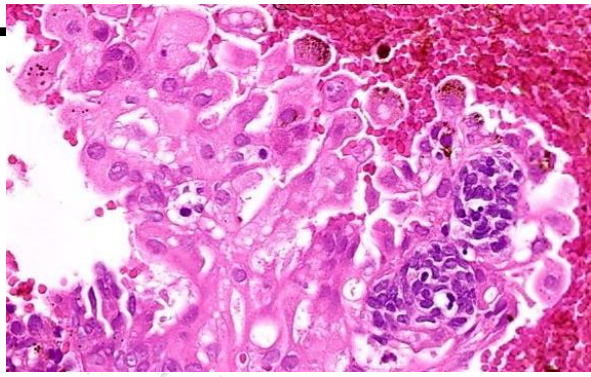
If confluent/cribriform architecture, severe pleomorphism, or invasion→ **Mucinous carcinoma**

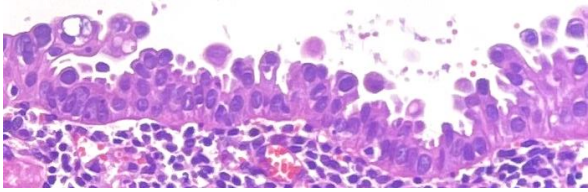


Papillary Syncytial Change/Metaplasia

Epithelium has **bright pink cytoplasm** and indistinct cell borders.
Small **papillary structures** (without fibrovascular cores).
Usually only at **surface**.
Most common with **breakdown**, atrophy, or infarcted polyps.
Generally bland nuclei, but may be reactive and "hobnail"

Can mimic Serous Carcinoma, but few mitoses, low Ki67 (~1%), increased (but still wild-type) p53.
Both usually have diffuse p16 often and decreased ER.

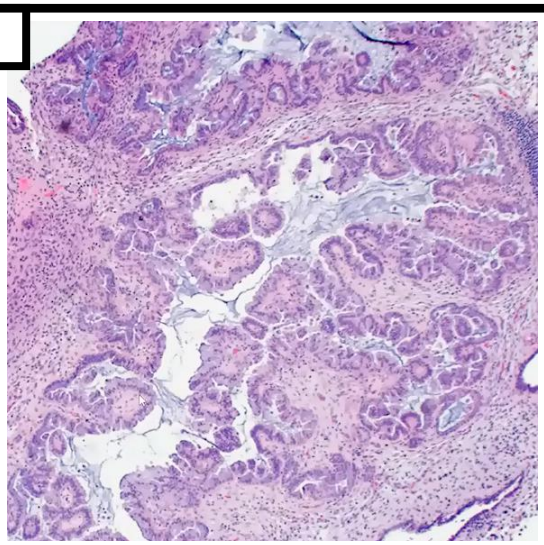


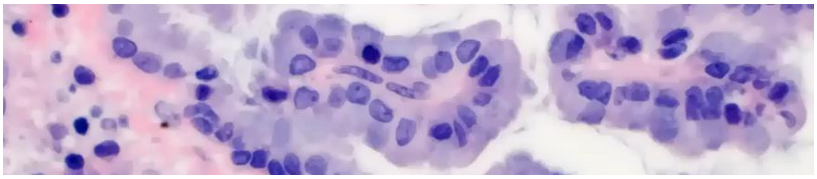


Papillary Proliferation of the Endometrium

Papillary proliferation. Mostly seen in polyps.
Simple or complex papillary branching.
Bland nuclei. No abnormal mitotic activity.
Mucinous or eosinophilic metaplasia.

Risk of concurrent/subsequent CAH/EIN or Endometrioid Carcinoma→ Recommend further clinical evaluation.





Tubal Metaplasia (Ciliated Cell Change)

Ciliated cells dominate epithelium
Resembles fallopian tube lining

(some ciliated cells are normal on surface and proliferative glands)

Cytologically bland.
Some cells have perinuclear halos.

Other Changes

Hobnail Cell Change: Most common as part of post-curettage atypia or ischemic polyp as reactive atypia.

Clear cell change: Abundant clear cytoplasm (glycogen). Cytologically bland. Often focal. Rare.

Eosinophilic cell change: Abundant pink cytoplasm. Round, bland nuclei.