

Benign mimics of endometrial carcinoma

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Benign vs malignant

- 1. Epithelial cytoplasmic change
- 2. Hyperplasia with atypia vs EIN
- 3. Diagnosis of grade 1 carcinoma
- 4. EIC
- 5. Endometrial polyps

Epithelial cytoplasmic change

- Syn = metaplasia
- Common in hyperplasia
- DD : atypia
- ECC by themselves have no neoplastic potential

Types of cytoplasmic change

- Squamous
- Ciliated cell
- Eosinophilic
- Mucinous
- Secretory:
 - Clear cell
 - Hobnail cell

Squamous differentiation

- Sign of estrogenic stimulation
- Often in hyperplasia
- Can be found in all grades of carcinoma

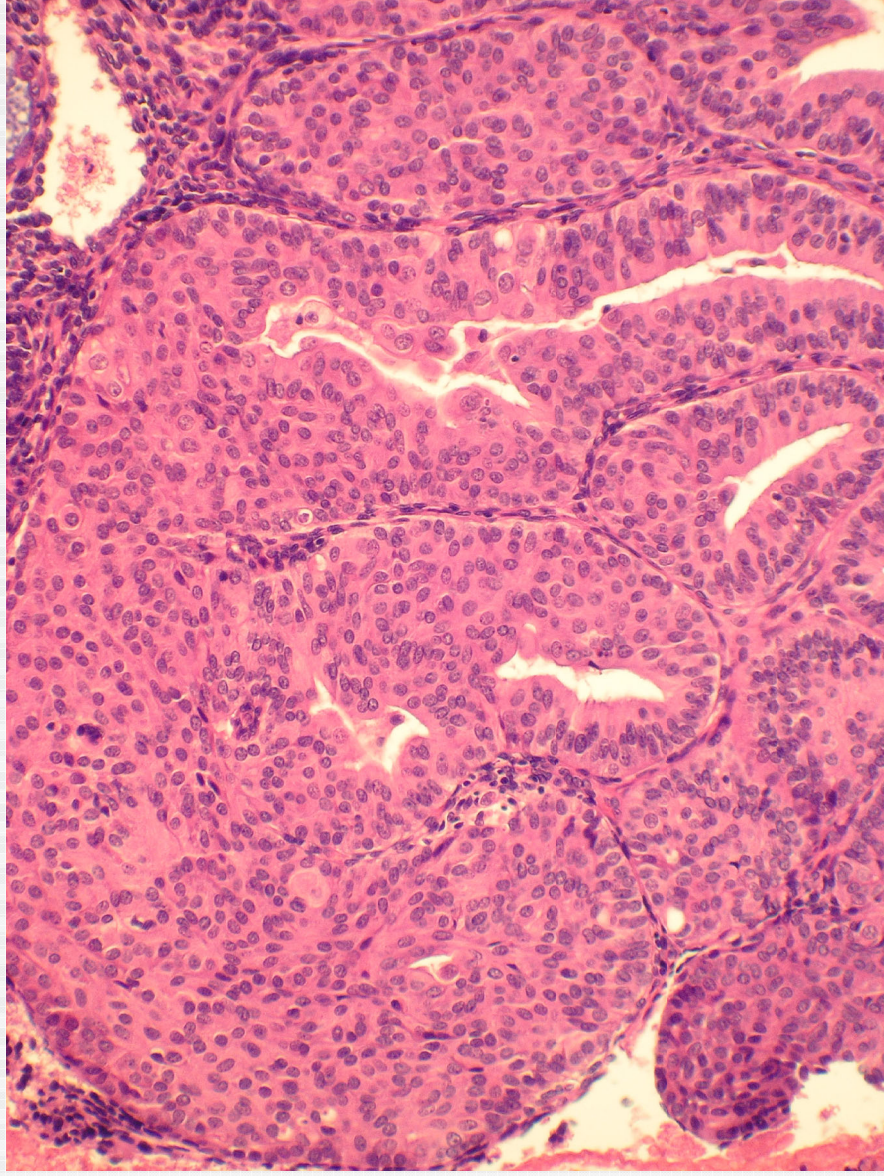
Squamous differentiation: histology

- Often nonkeratinizing
 - Keratinizing: more often in carcinoma
- Morules
 - Solid nests of uniform eosinophilic cells
 - Indistinct cell borders
 - Often intraluminal
 - Central necrosis can occur

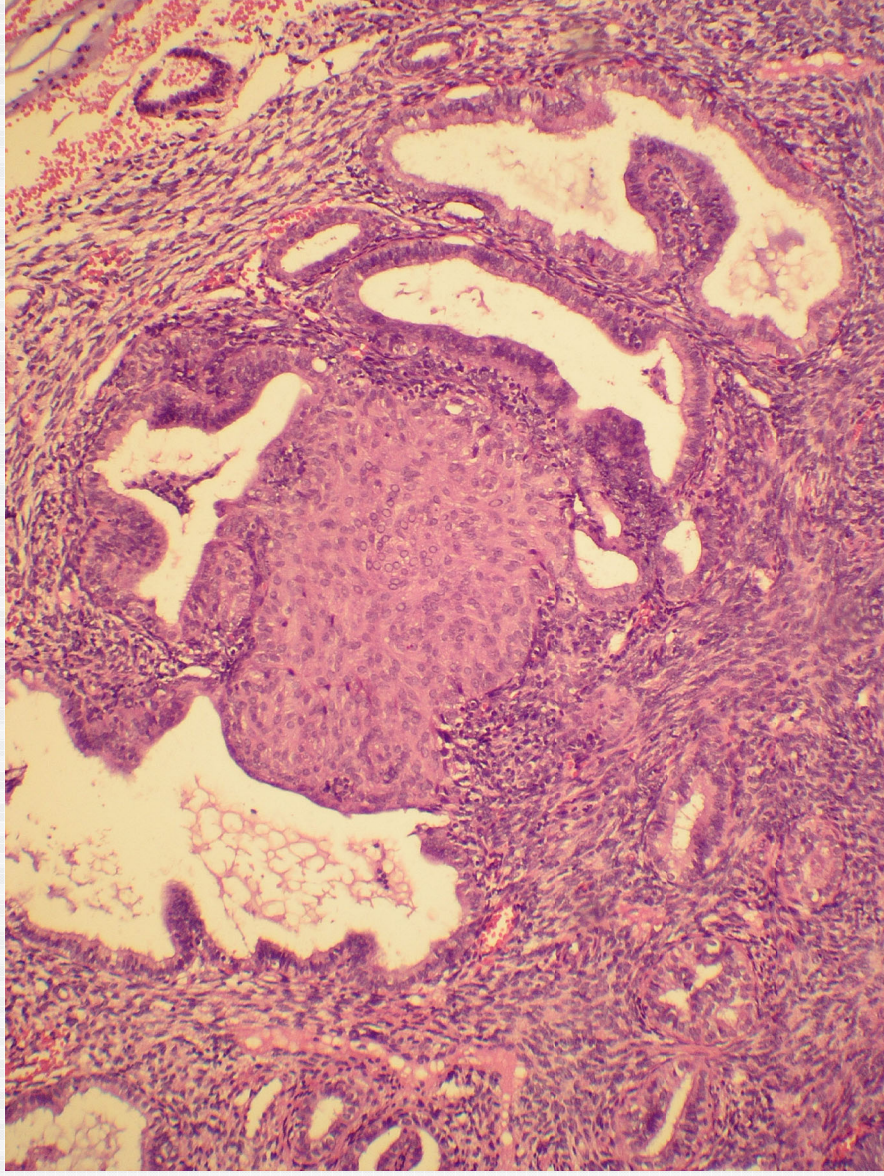
Squamous differentiation: cytology

- Bland cytology
- Nuclei: uniform, round to oval
centrally placed
- Rare mitosis
- Small nucleoli
- Cytoplasm: dense eosinophilic

Morulae



Morulae



Morulae ≠ squamous !!!

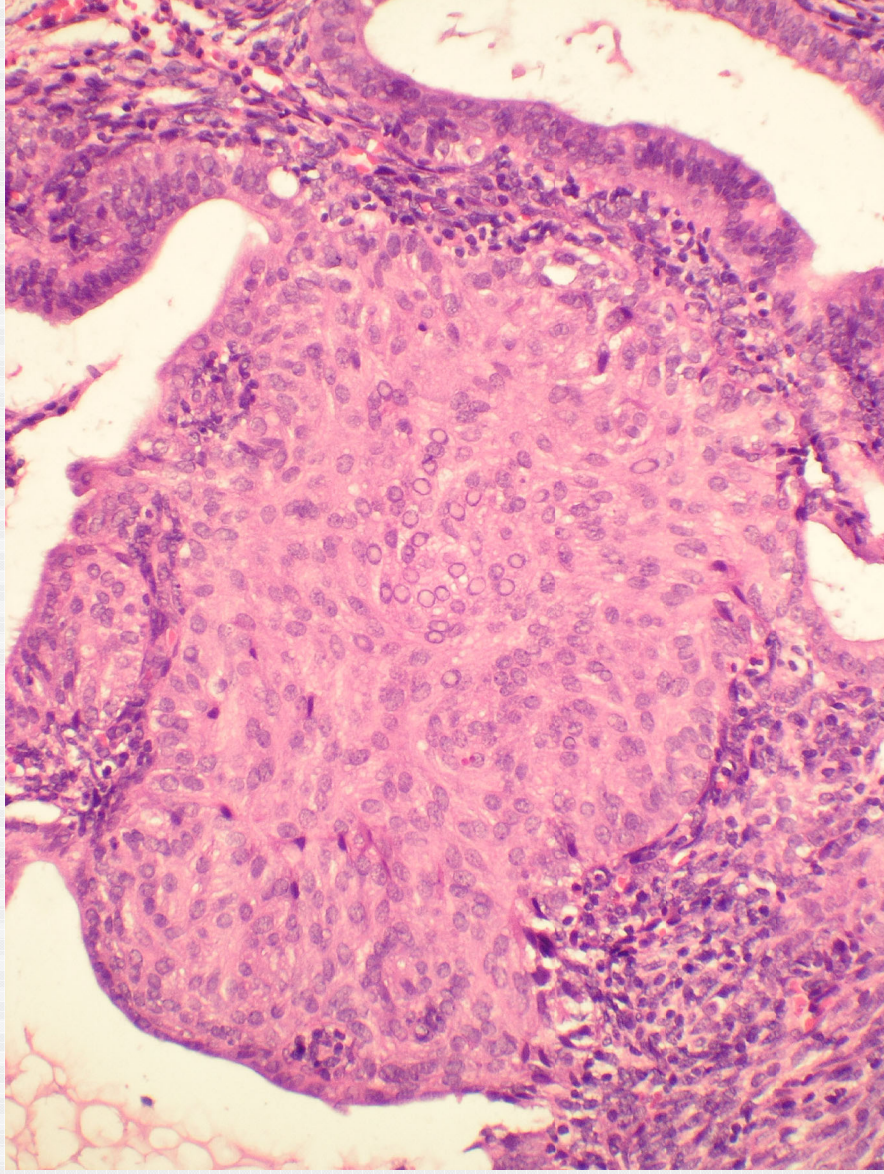
- Morulae are often CK -
S100 +

Probably neurogenic differentiation

Makishi: Morules and morule-like features associated with carcinomas in various organs: report with immunohistochemical and molecular studies

JCP 59 (2006): 95-100

Morulae



Ciliated cell change

- Syn = tubal metaplasia
- Ciliated cells can normally occur along surface epithelium
- **Glands** lined by ciliated cells are **not** normal !

Ciliated cell change: significance

- Sign of unexposed estrogens
- Can occur in hyperplasia

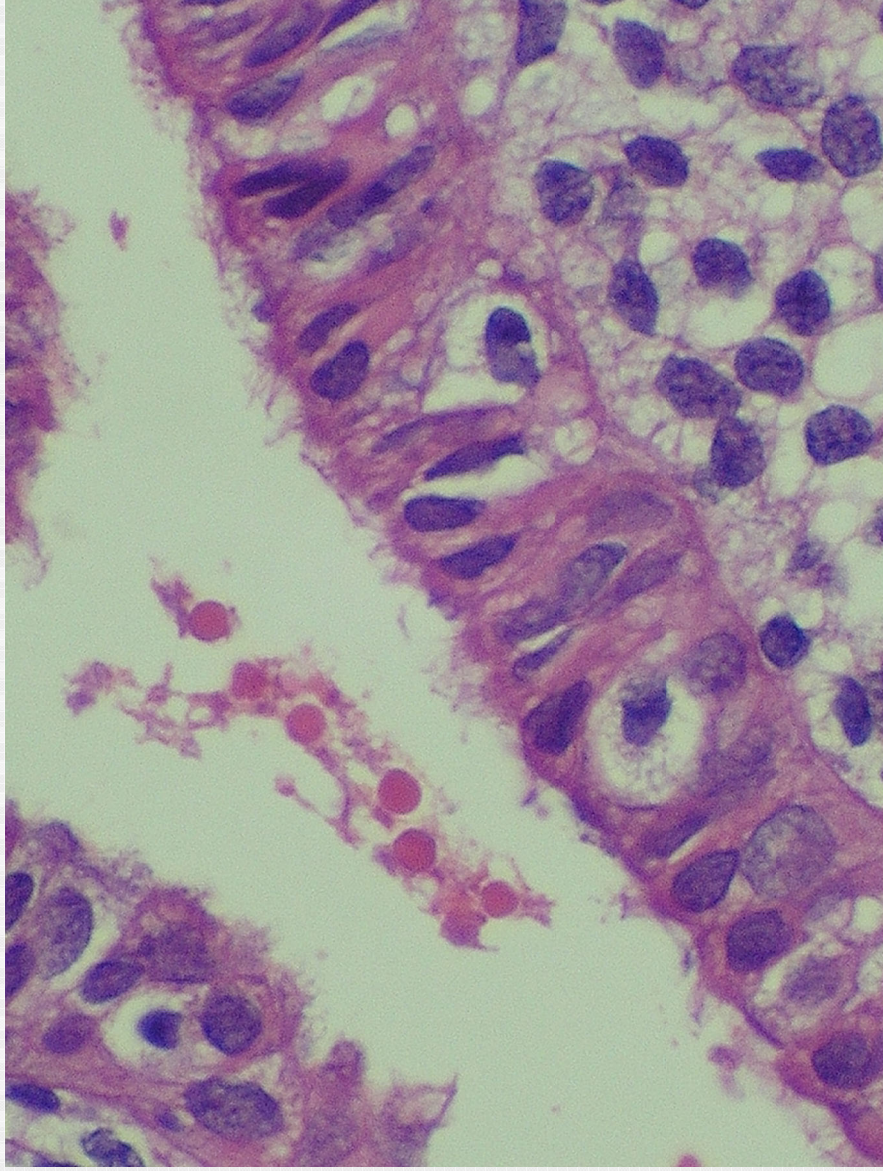
Ciliated cells: histology

- Small groups between nonciliated cells
- Cytoplasm: pale to eosinophilic
- Luminal border:
 - Cilia
 - Cuticle of dense cytoplasm

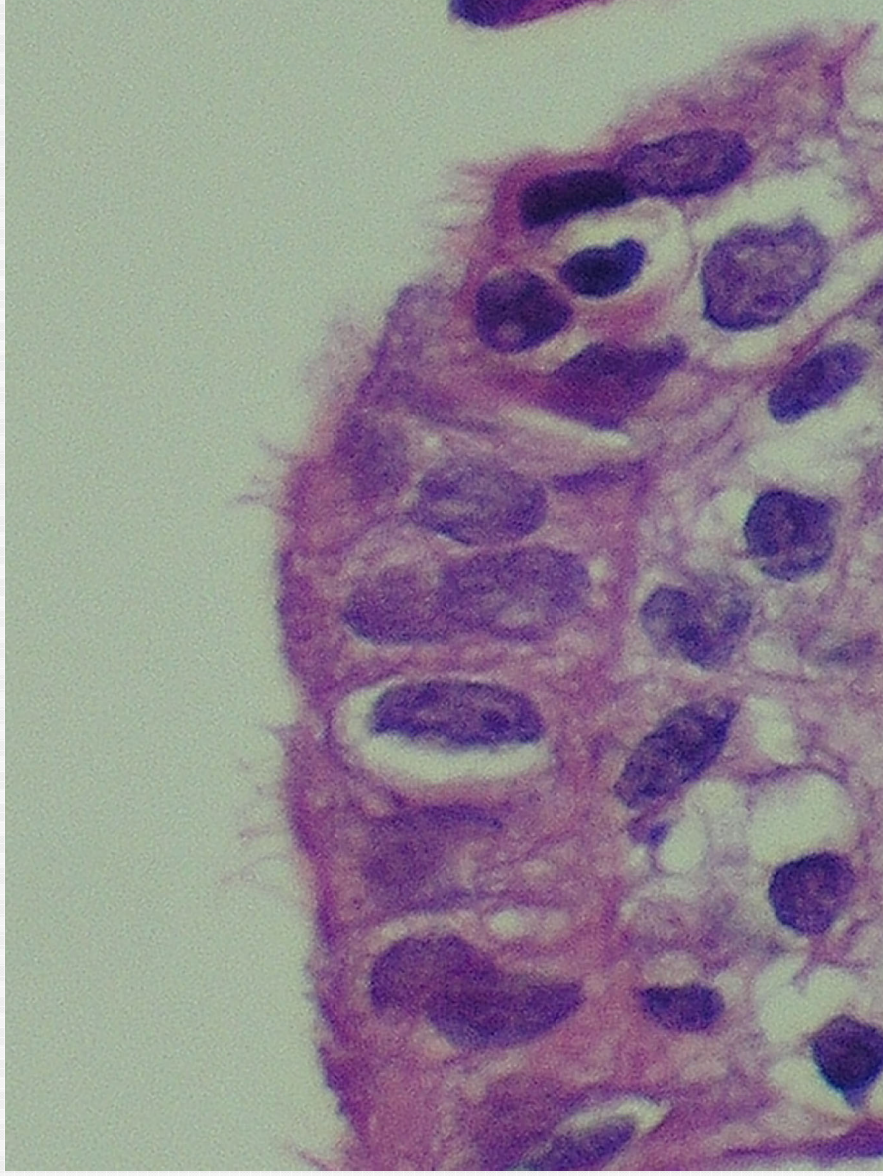
Ciliated cells: cytology

- Nuclei: mildly stratified
round to oval
slightly enlarged
even chromatin distribution
- Small nucleoli
- No mitosis

Ciliated cell change



Ciliated cell change



Ciliated cells: DD

- Nuclear features of enlargement and more rounded appearance

→ DD atypical hyperplasia

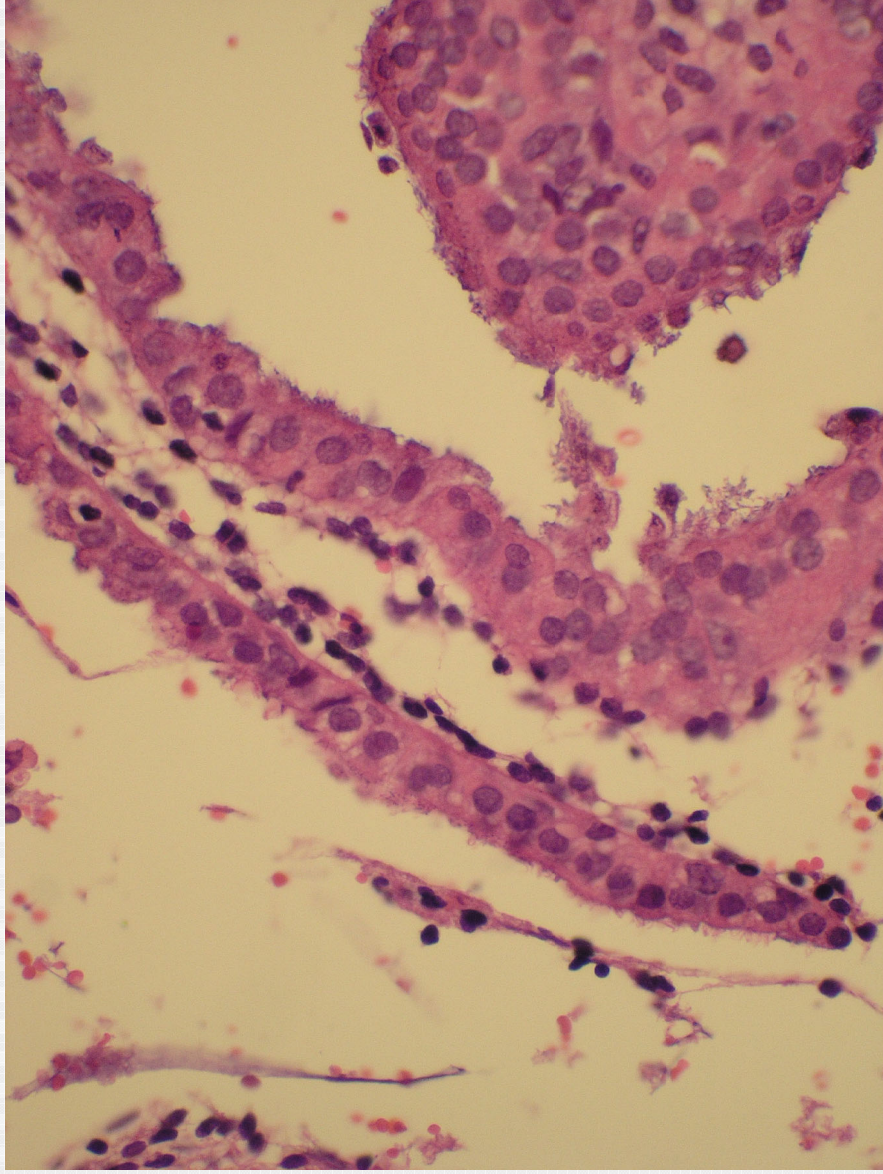
Eosinophilic cell change

- Can be variant of :
 - Ciliated cells
 - Squamous cells
 - Oncocytes
 - Eosinophilic syncytial change

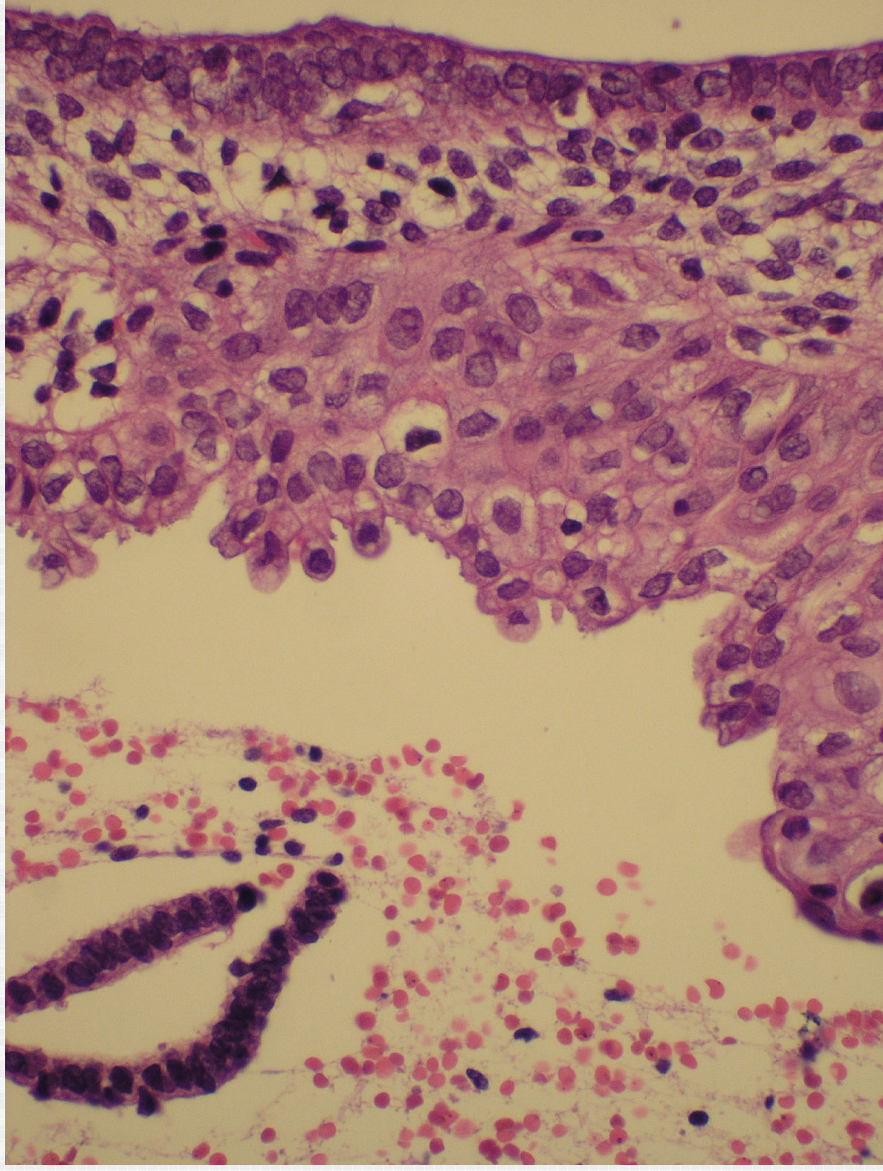
Eosinophilic cell change

- Can occur in
 - Atypical hyperplasia
 - Low-grade adenocarcinoma
- Important not to overlook a (pre)malignant process

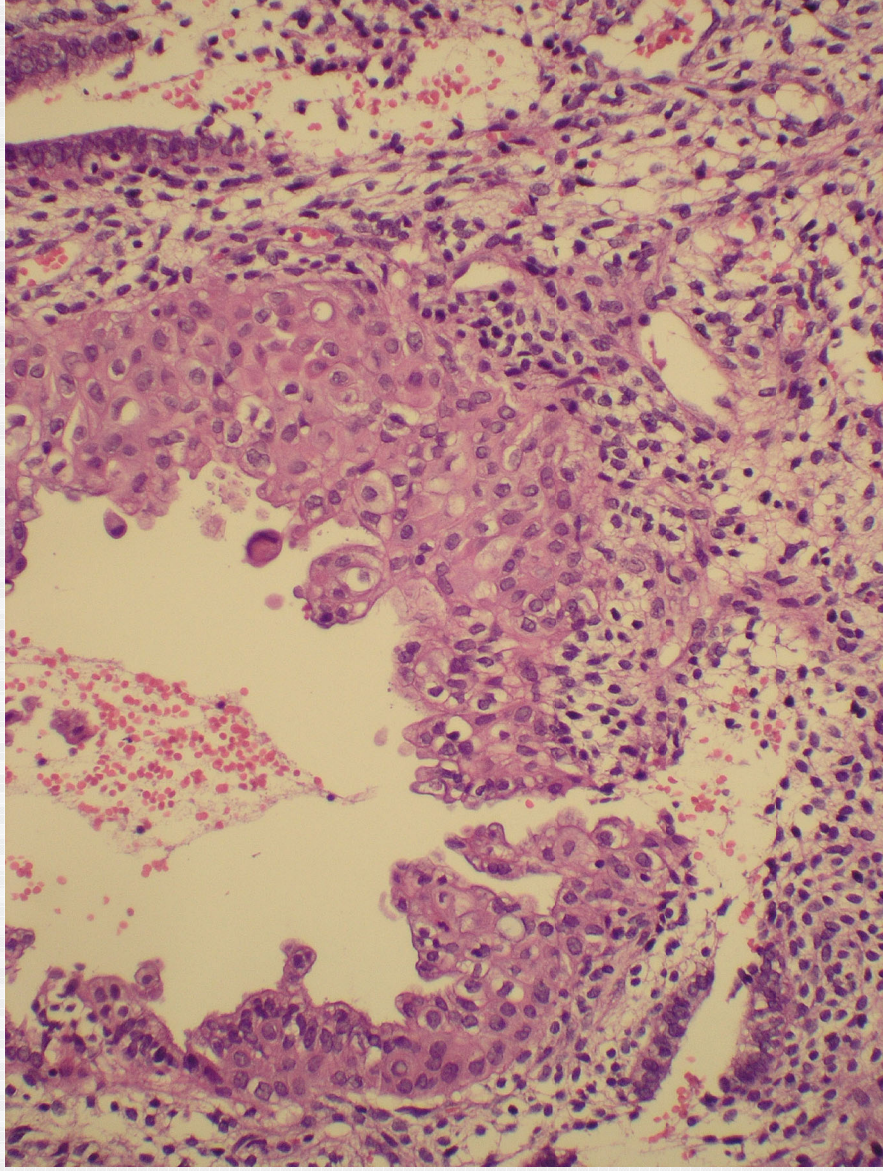
Eosinophilic cell change



Eosinophilic cell change



Eosinophilic syncytial cell change



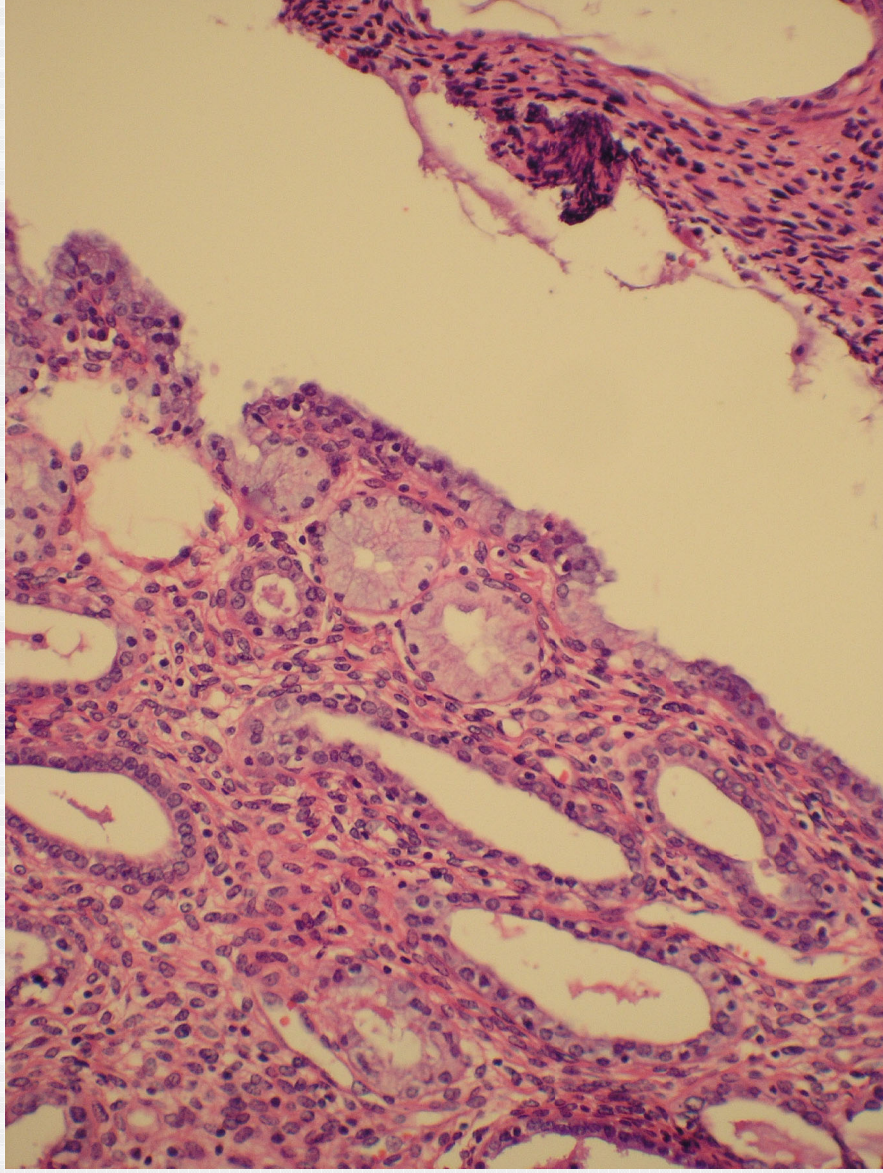
Mucinous change: histology

- Abundant mucinous cytoplasm
 - Resembles normal endocervix
- Often small papillary projections

Mucinous change: cytology

- Columnar cells
- Basal nuclei, small and uniform
- Abundant pale supranuclear cytoplasm
- Rarely goblet cells: “intestinal metaplasia”

Mucinous cell change



Mucinous change: importance

- Most often in association with carcinoma or atypical hyperplasia
- Careful examination of the rest of the endometrium is necessary

Secretory cell change

- Exclude progestin-related effects
- If excluded: very rare
- Usually focal: limited to scattered glands

Secretory cell change: cytology

- Clear cytoplasm: glycogen
- Resembles secretory or gestational endometrium
- Hobnail cells can occur
 - Resembles Arrias-Stella

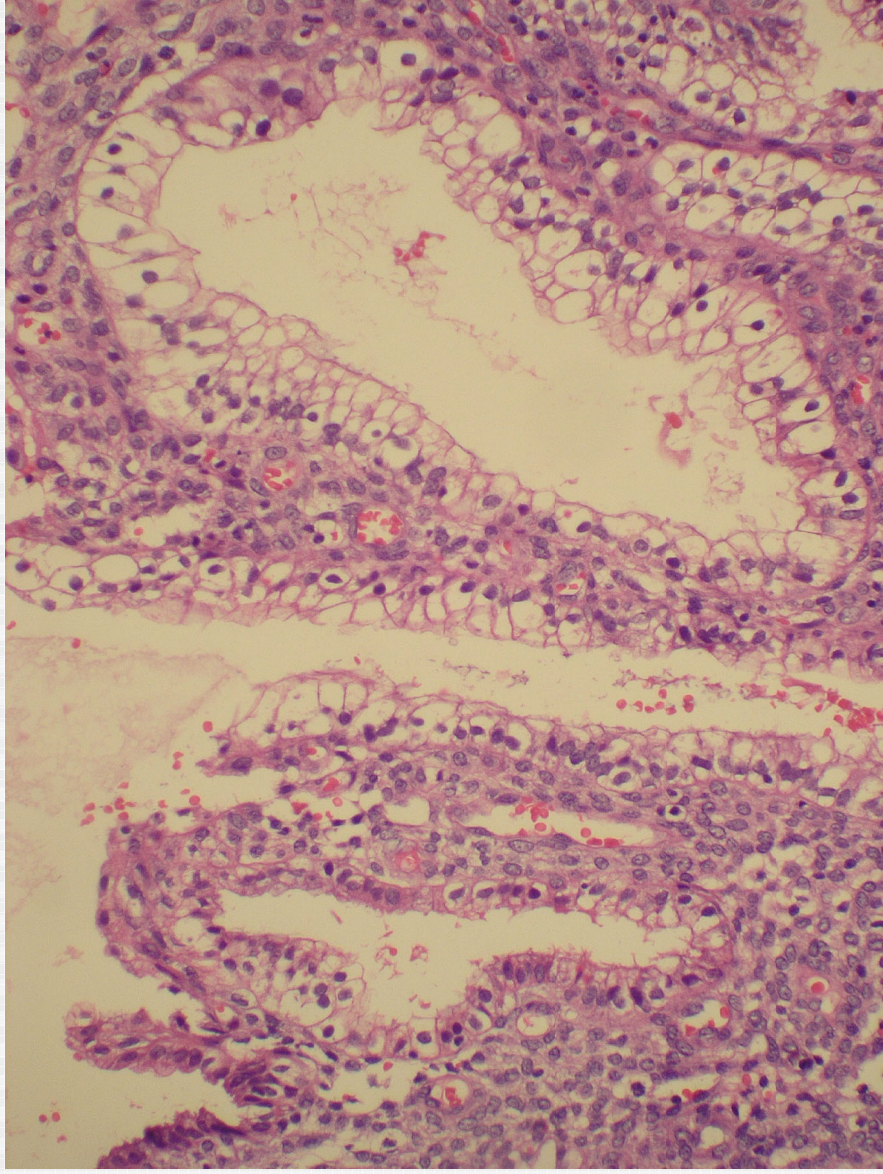
Secretory cell change

- In endometrium with estrogenic effects:
hyperplasia to carcinoma

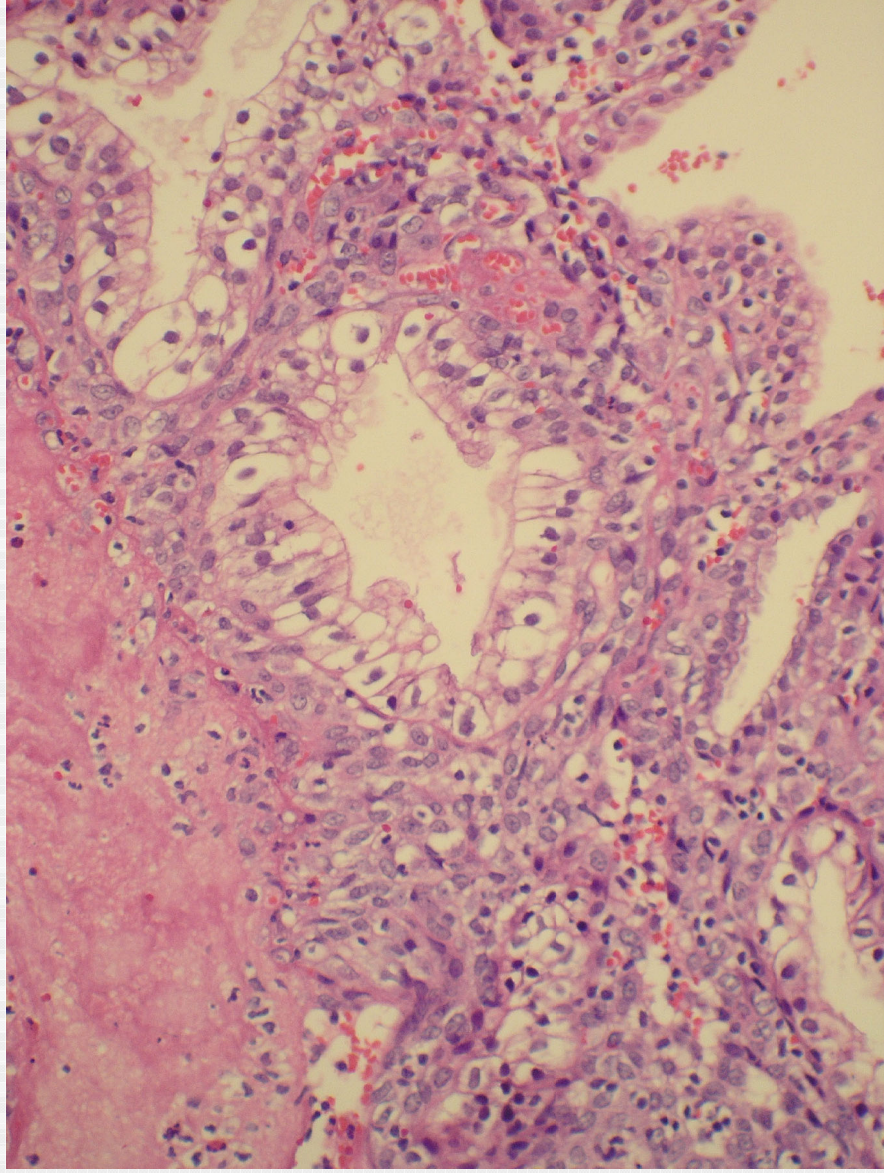
Secretory cell change

- Diffuse secretory change in hyperplasia:
“ secretory hyperplasia “
- In pre- or perimenopausal women with hyperplasia and sporadic ovulation or treatment with progestins

Secretory cell change



Secretory cell change



Epithelial cytoplasmic change: DD with atypia

- Atypia
 - Nuclei enlarged
 - Nuclei rounded
 - Vesicular chromatin
 - Irregular nuclear membrane
 - Nuclei stratified
- ECC
 - Relative bland features

EIN or atypical hyperplasia?

- EIN ≠ EIC !!!!!
- Clonal proliferation of mutated cells

PTEN suppressor gen deficient

EIN: diagnostic criteria

- Area of glands greater than stroma
 - VPS < 50 %
 - Morphometry
- In this focus: abnormal cytology
- Size > 1 mm
- IHC: PTEN -

Hyperplasia: WHO classification

- Simple hyperplasia without atypia
- Complex hyperplasia without atypia
- Simple hyperplasia with atypia
- Complex hyperplasia with atypia

Simple or complex ?

- Complex = adenomatous
- Degree of glandular crowding and structural complexity
- Often coexistence
- No clinical importance

Atypical or not ?

- Specific nuclear features
 - Nuclei round and enlarged, not oval
 - Loss of polarity, stratification
 - Vesicular coarse chromatine
 - Prominent nucleoli

EIN or atypical hyperplasia ?

- Still debate !! Future will tell
- EIN offers pathogenetic model, PTEN and morphometry not always available
- Use of WHO (atypical hyperplasia) is standard, reproducible, well known by pathologists and clinicians

Criteria for the diagnosis of grade 1 carcinoma

= criteria for identification of stromal invasion

3 features, 1 is sufficient

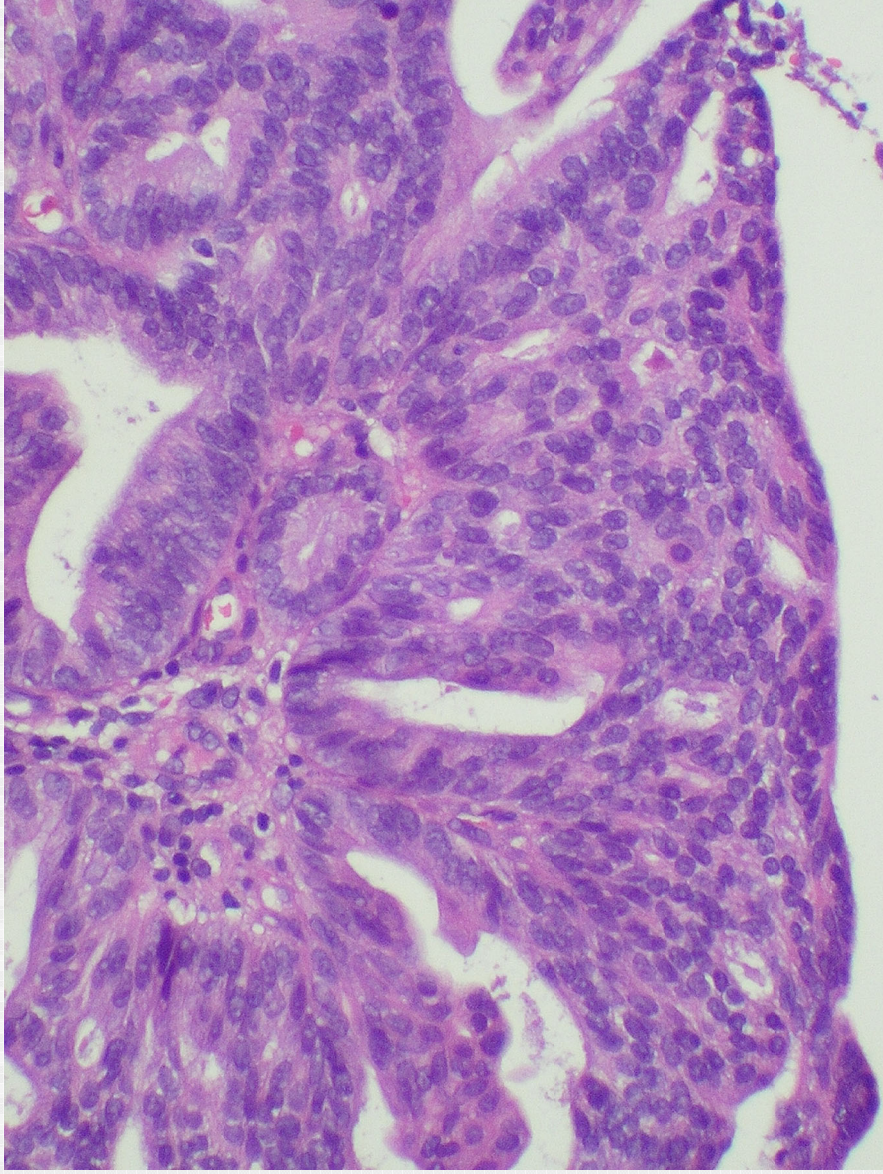
Criteria for stromal invasion

- Confluent glandular pattern
- Desmoplastic reaction of stroma
- Extensive papillary pattern

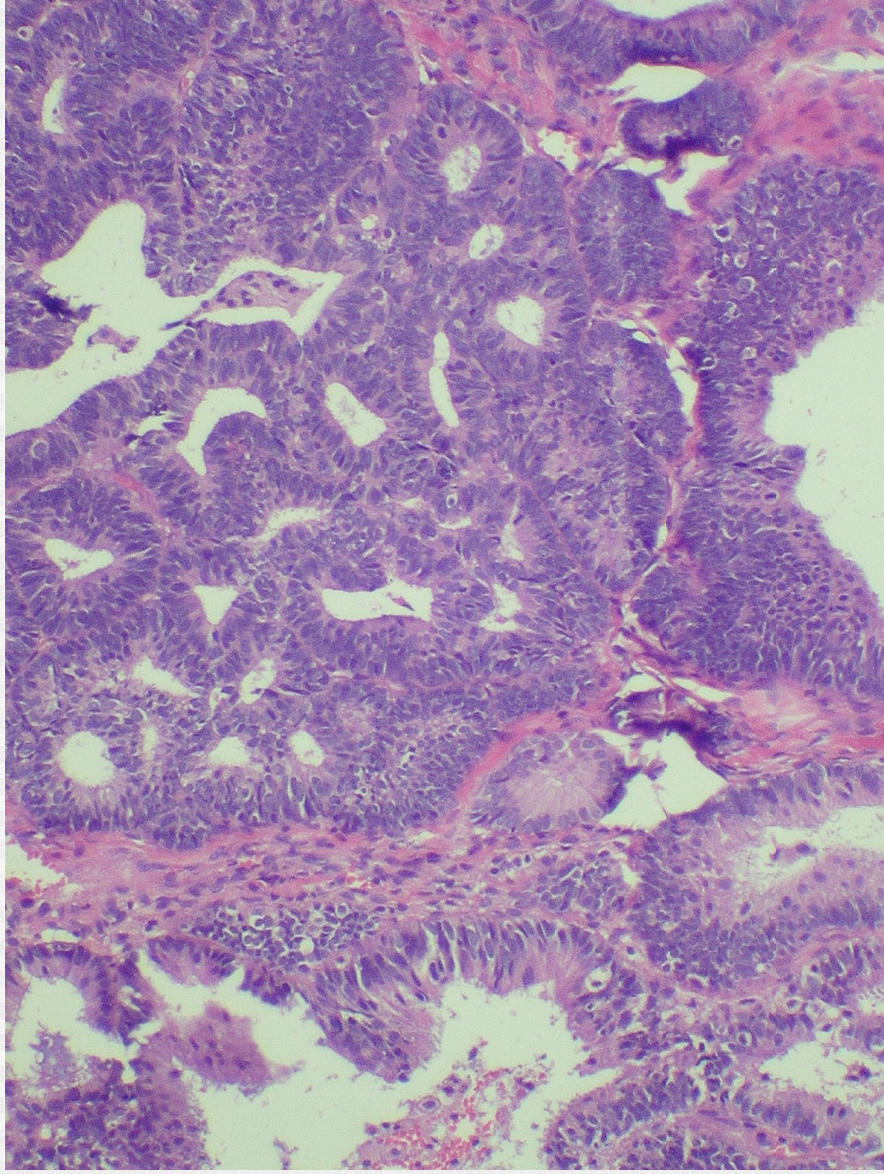
Confluent glandular pattern

- Individual glands merge
- **No** intervening stroma
- Cribriform pattern

Confluent glandular pattern



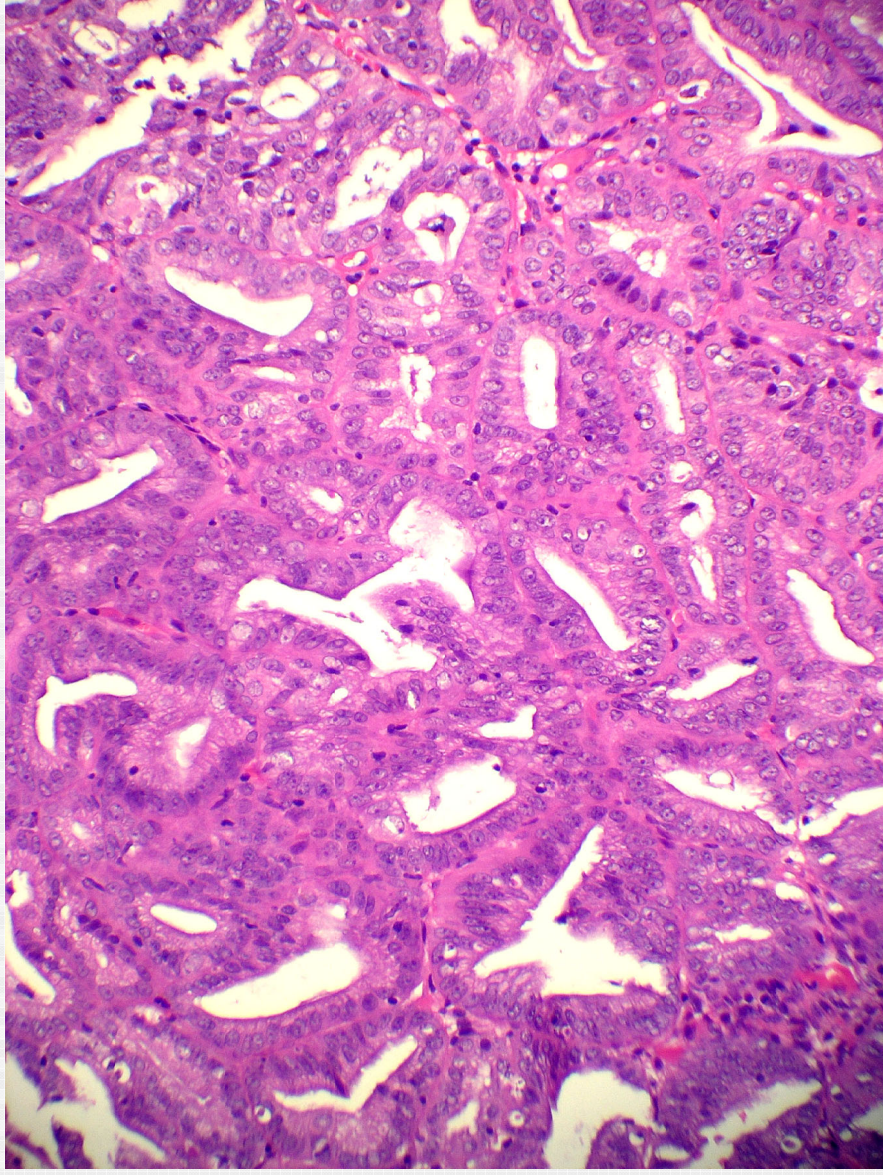
Confluent glandular pattern



Desmoplastic reaction

- Stromal cells that are more spindle-shaped
- Nuclei elongated
- Eosinophilic appearance

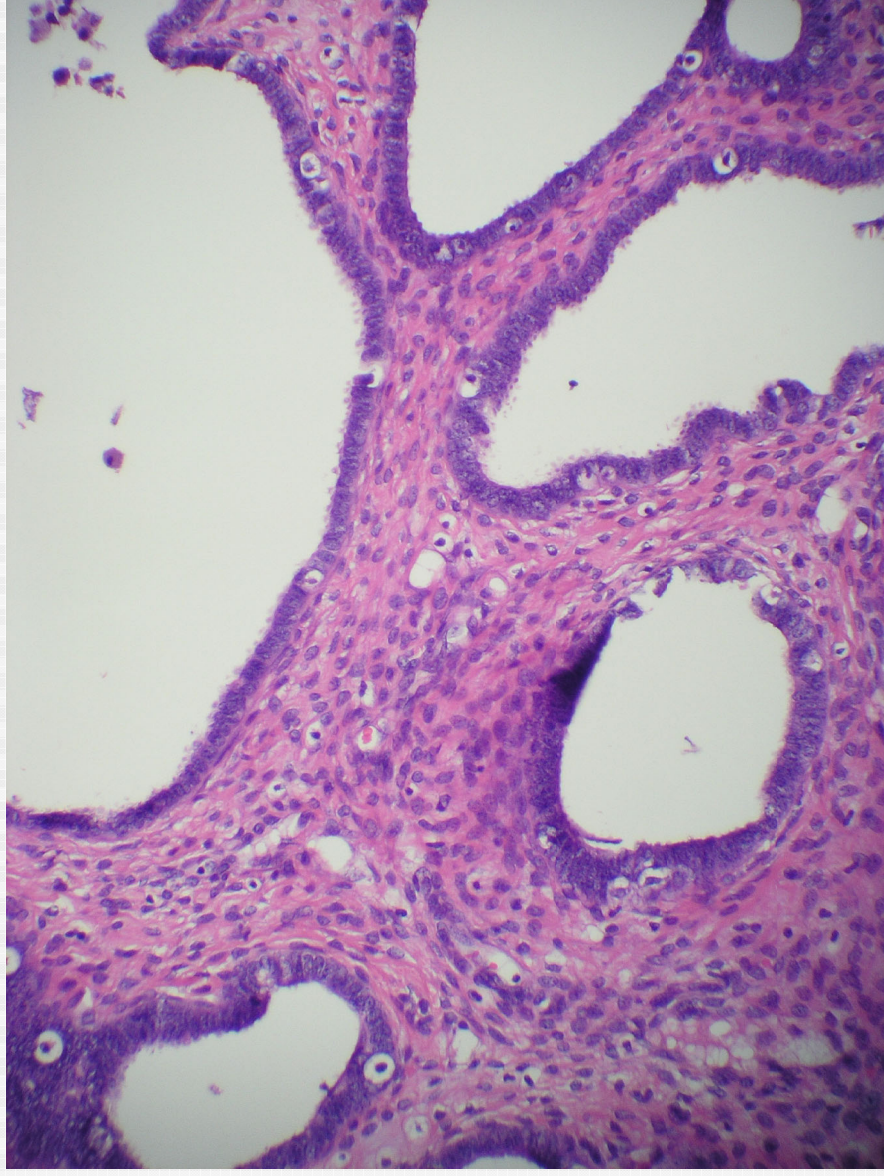
Desmoplastic stroma



Desmoplastic stroma: DD

- Dense stroma in polyps
- Stromal alteration due to marked inflammation
- Stroma of lower uterine segment
- Stroma of atypical polypoid adenomyoma

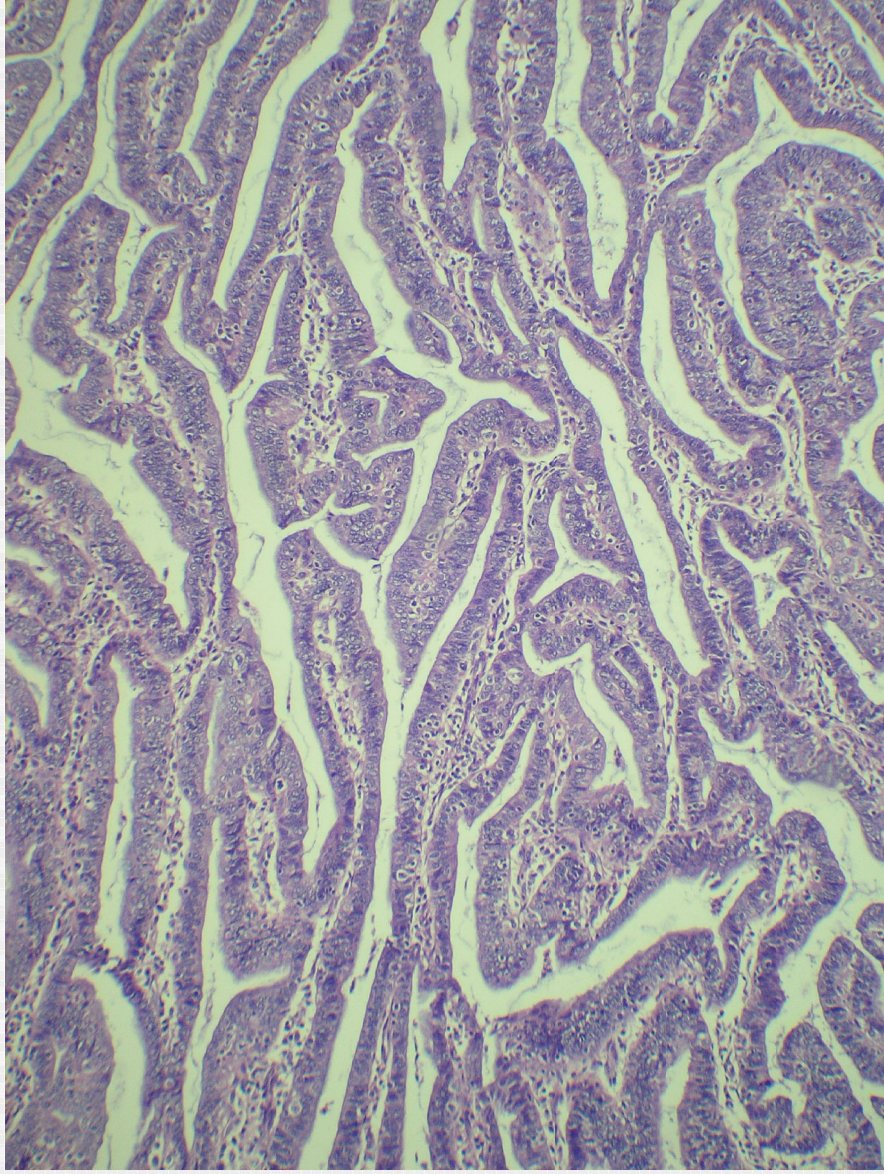
Fibrous stroma in polyp



Extensive papillary pattern

- Feature of villoglandular carcinoma
- Stroma is **not** desmoplastic

Villoglandular Ca



Identification of stromal invasion

- Features should be **quantitatively significant**
- At least half of a low-power field (x4)
= 2 mm

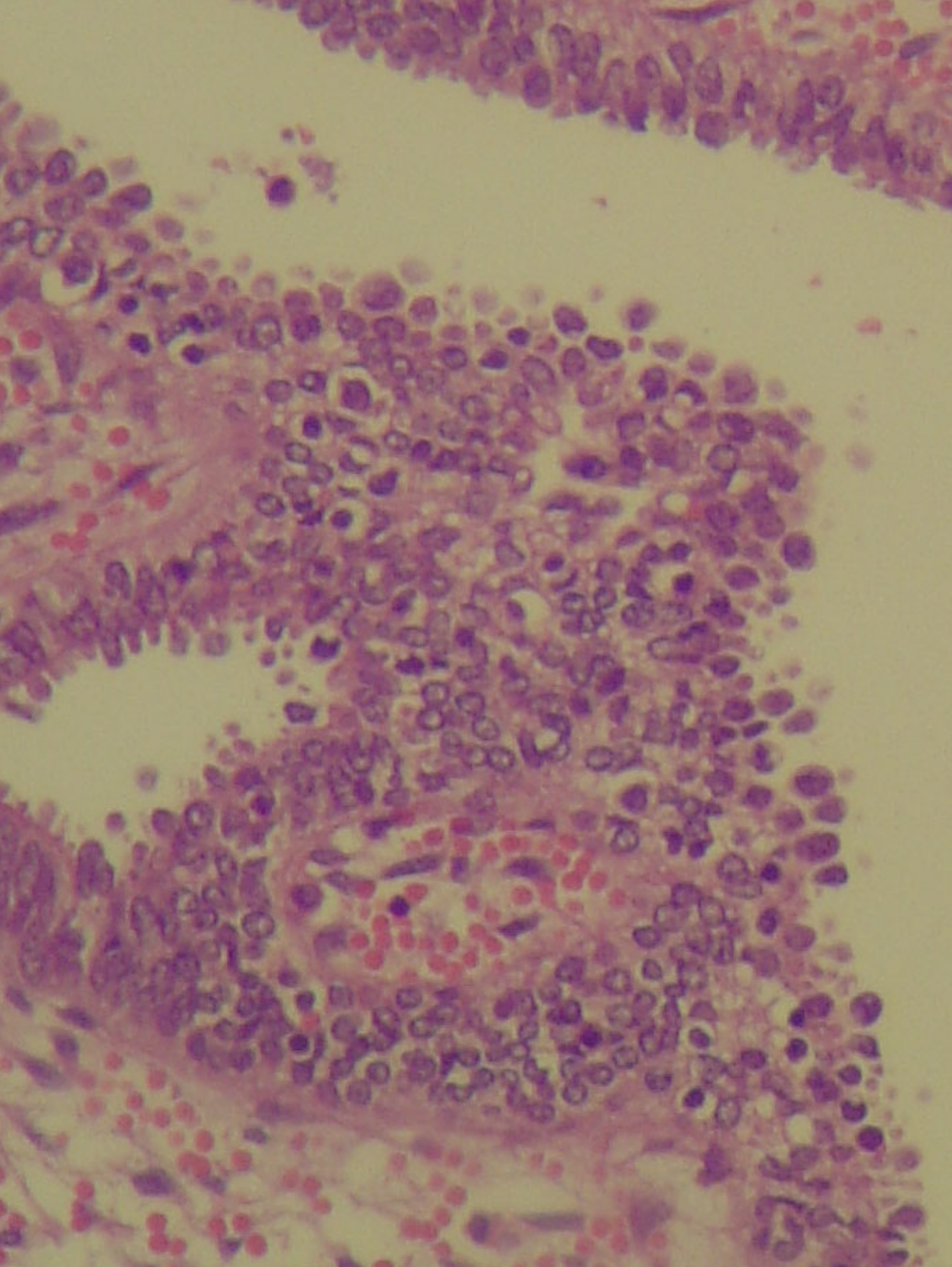
Don't use this too rigid !!

Endometrial intraepithelial carcinoma

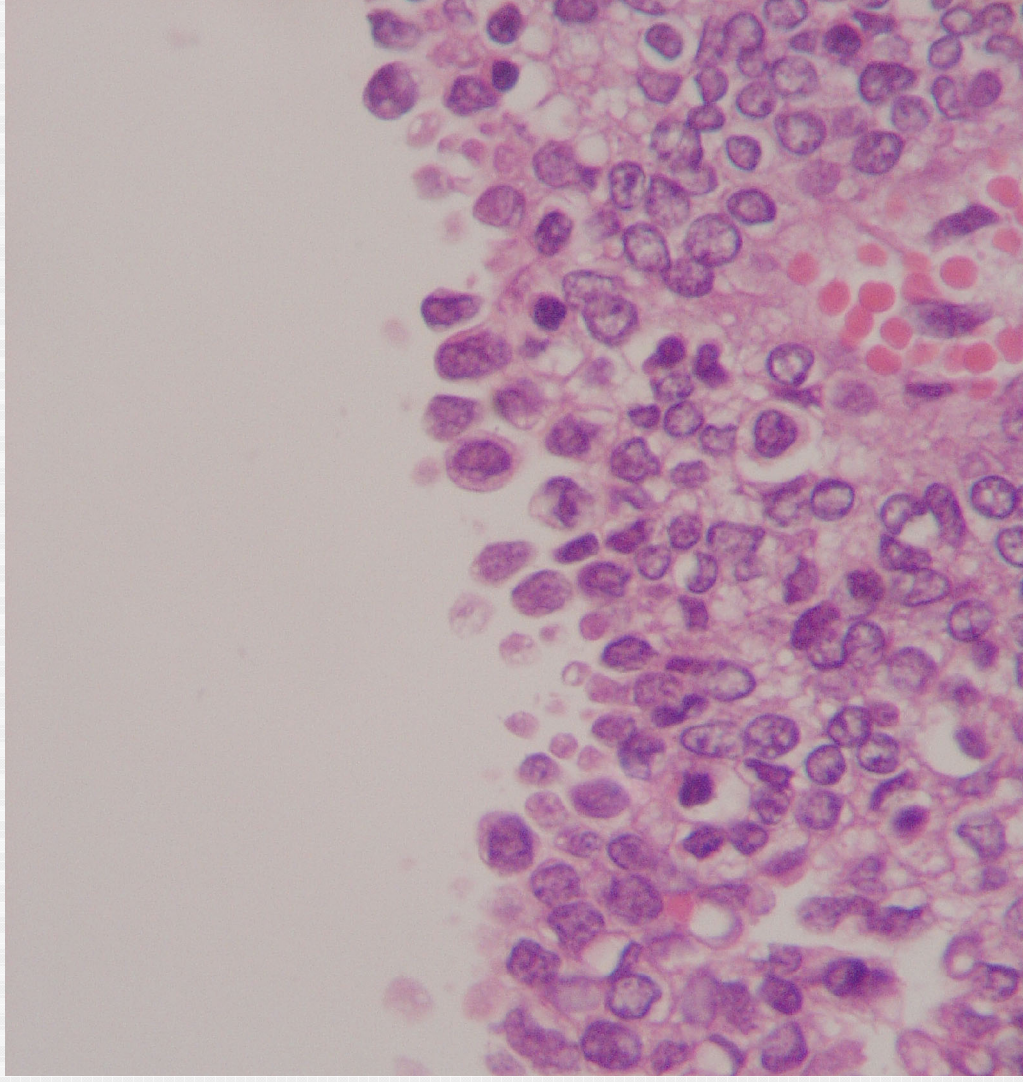
- Precursor of type 2 carcinoma
- Do NOT confuse with EIN
(precursor of type 1)

EIC

- severe atypical cells on surface and in glands
- hobnail cells
- p53 diffuse and intense + (not always)



EIC: cytology



EIC: importance

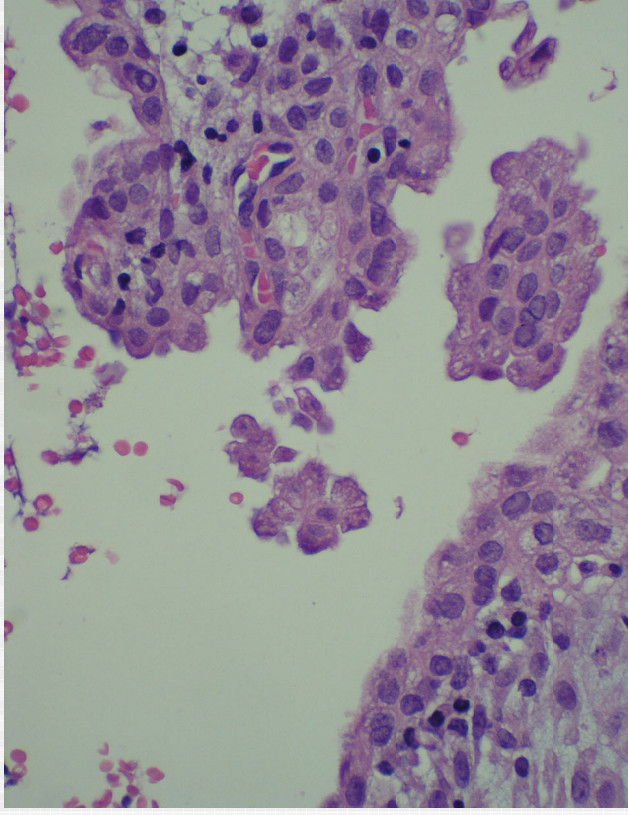
- Can be disseminated even in absence of invasive carcinoma
- Mimics metastatic serous carcinoma of ovary

EIC: DD

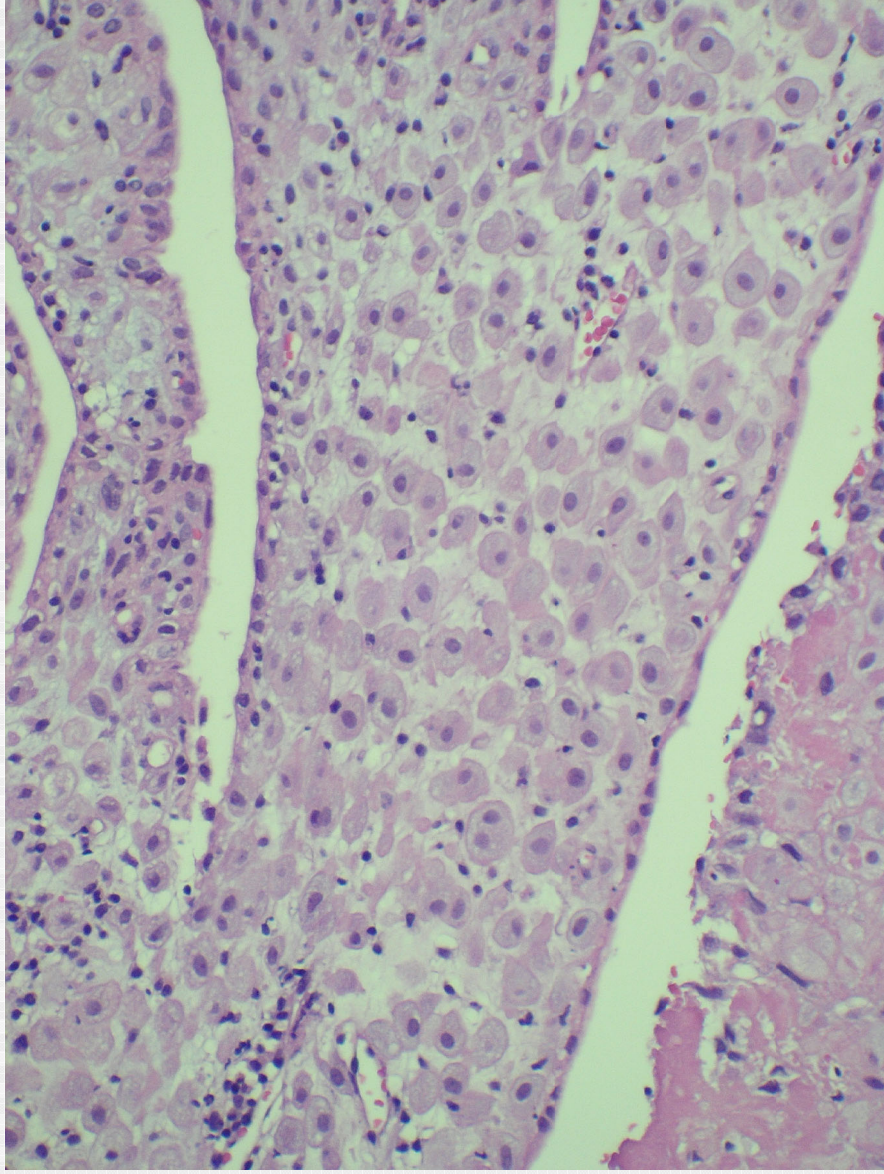
- Arias-Stella
- Reactive hobnail cells due to polyp, post biopsy, ...
- Metaplasia

EIC or not?

- Hobnailcells
- Less cohesion
- Atypia
- Age: 29
- Rest:

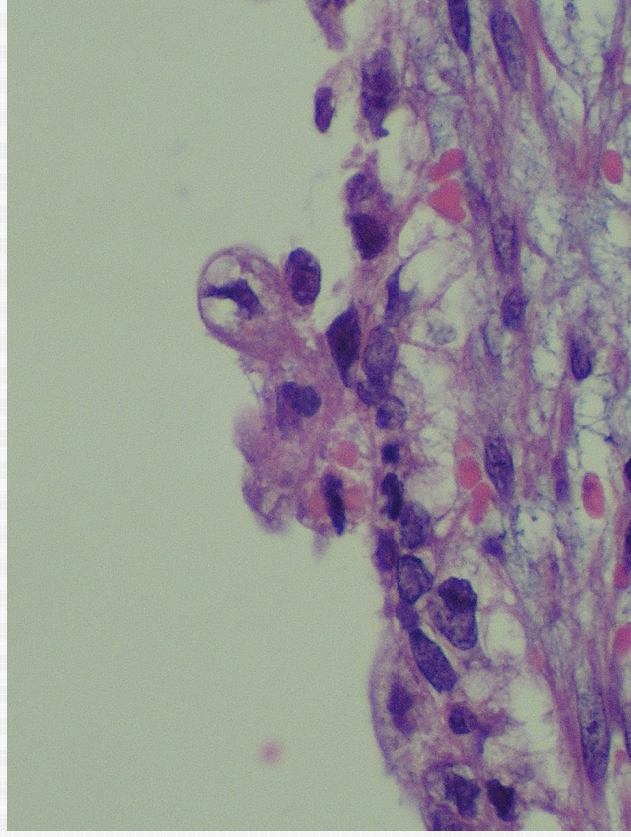


Arias-Stella



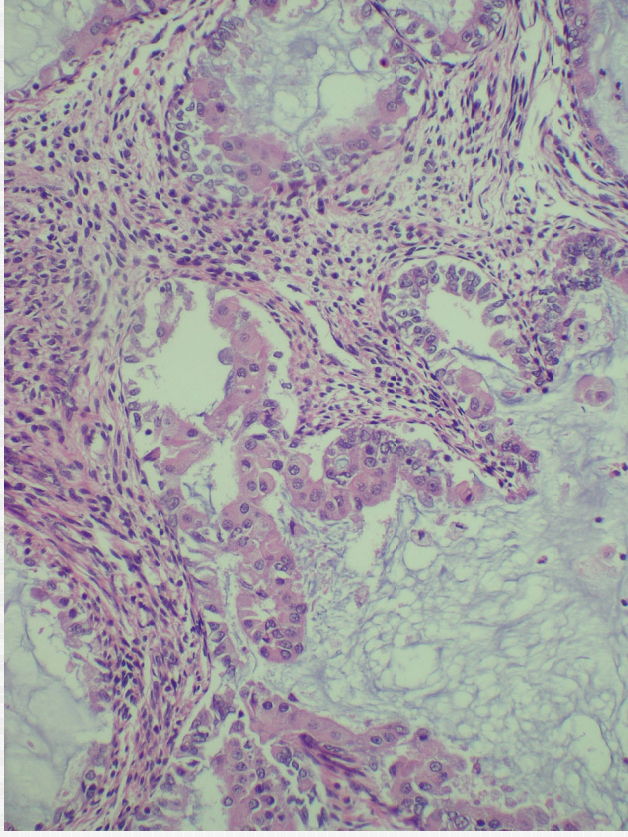
EIC or not?

- Large cells
- Atrophic endometrium
- Little atypia
- Post-curetting



EIC or not ?

- Large cells
- Eosinophilic cytoplasm
- No nuclear enlargement
- No atypia
- Metaplasia

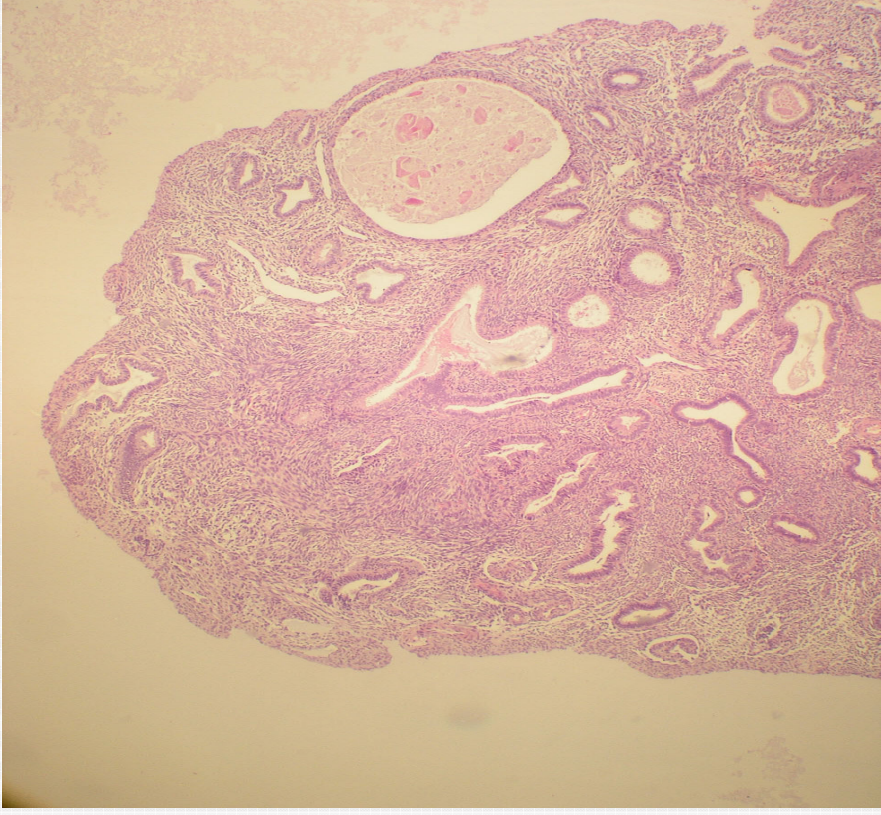


Endometrial polyps: diagnosis

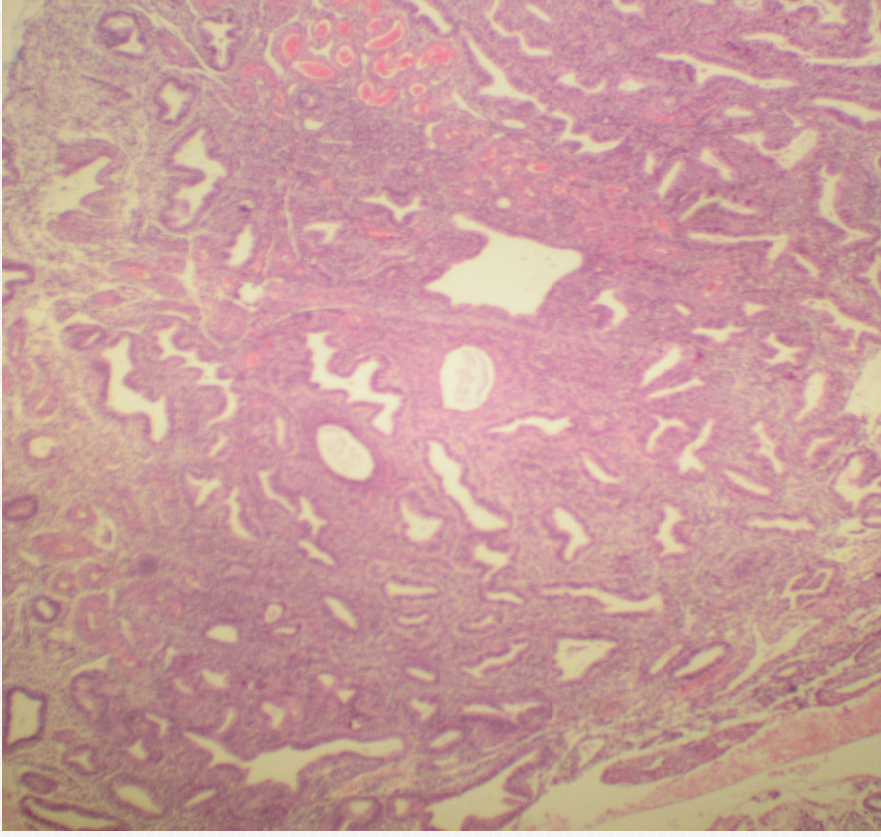
- Large tissue fragments
- Surface epithelium on 3 sides
- Dense stroma, sometimes fibrous
- Thick-walled vessels

Polyp

- Large fragment
- Surface epithelium on 3 sides
- Irregular and dilated glands
- Fibrous stroma

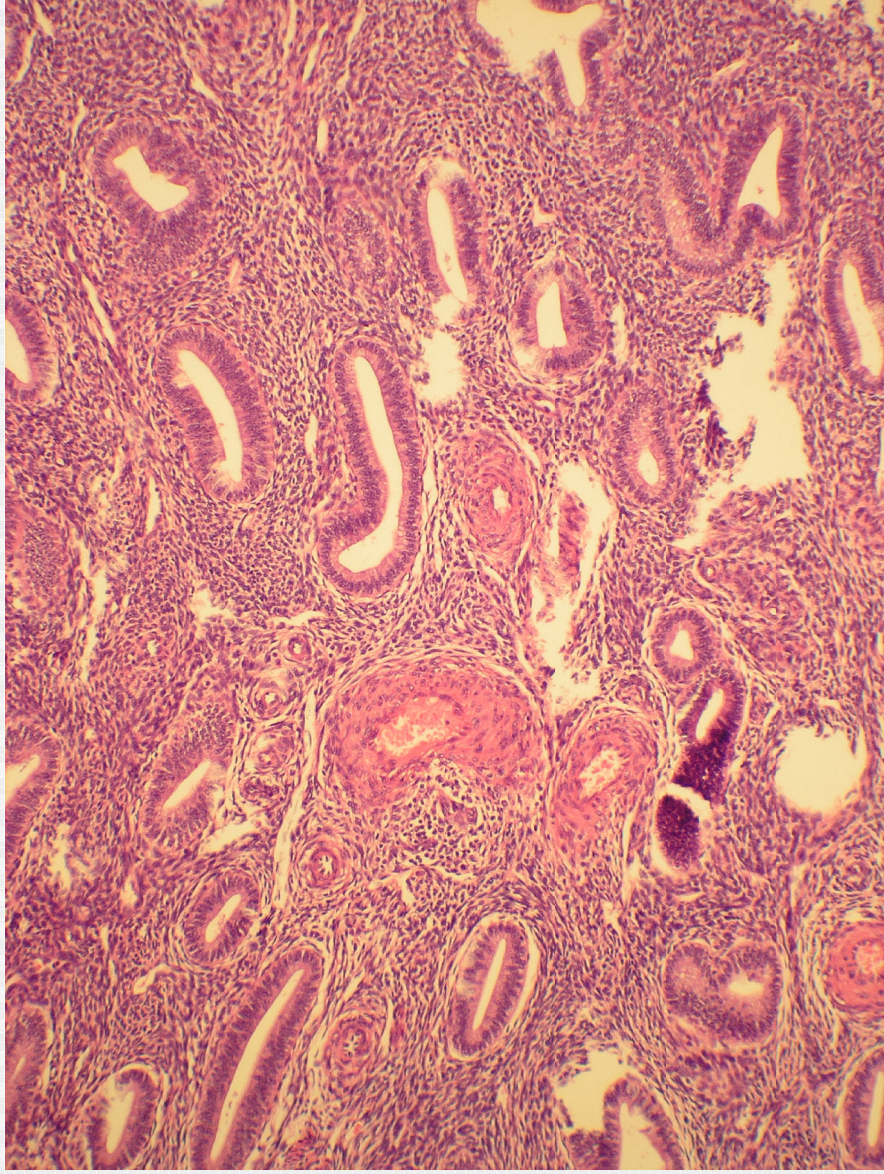


Polyp



- Large fragment
- Irregular glands
- Thick walled vessels
- Fibrous stroma

Thick walled vessels

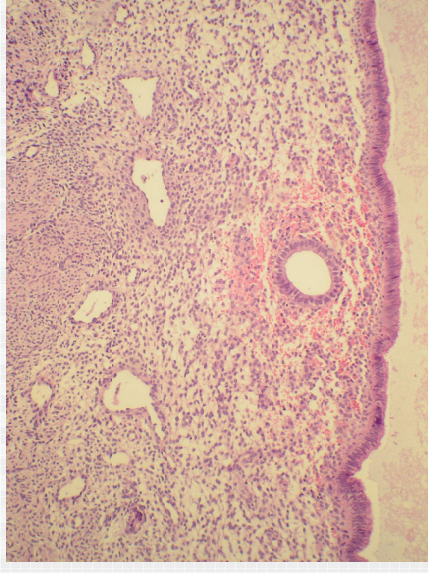
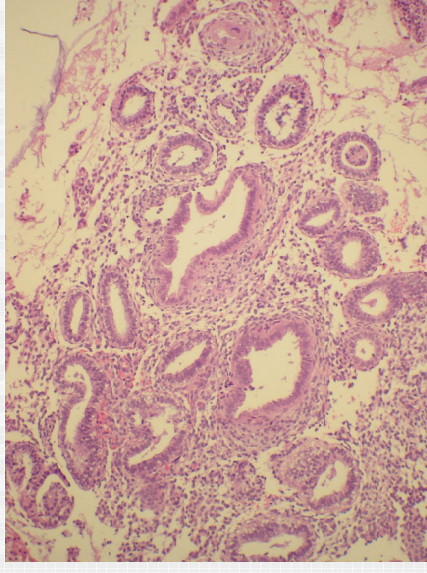


Endometrial polyps: glands

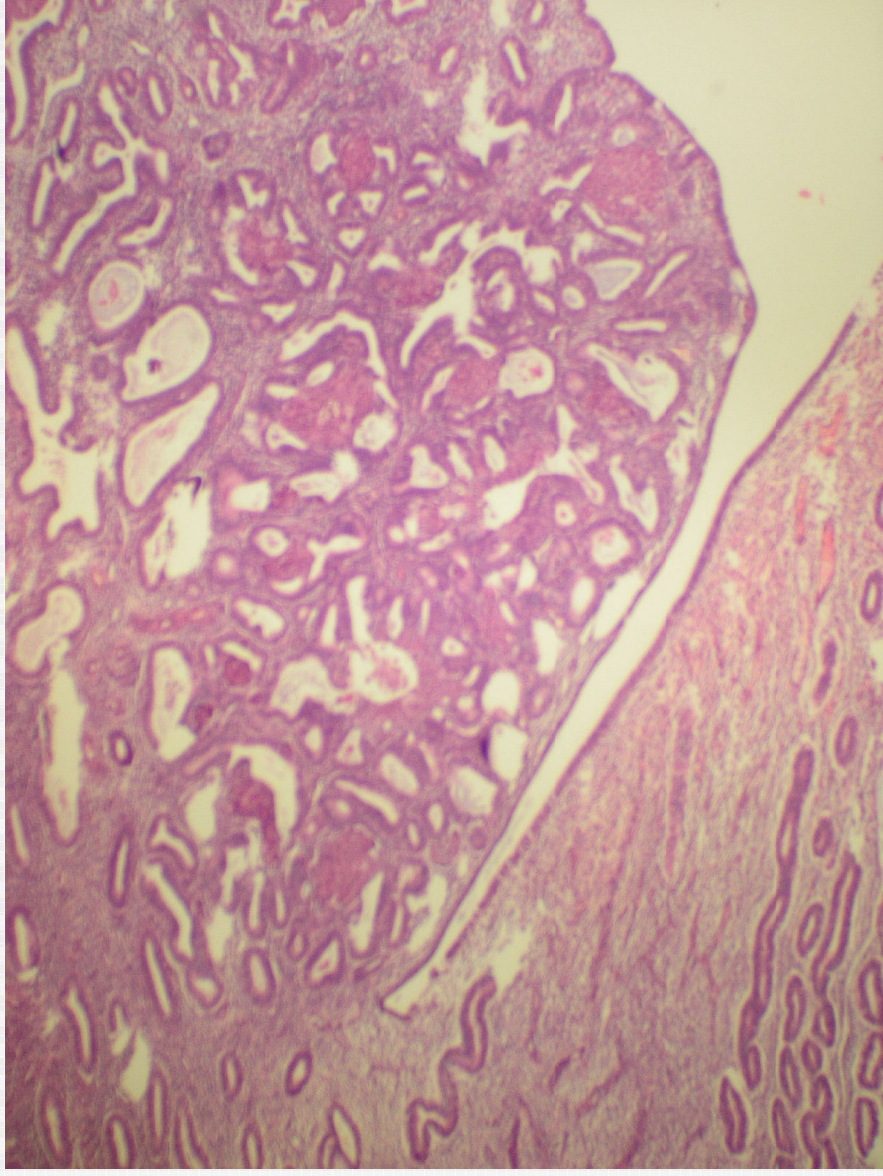
- Glands more irregular, tortuous and dilated than normal glands
- Glands appearing “out-of phase”
- Distinct fragments with different appearance than other fragments

Polypous and non-polypous fragments

- Distinct appearance
- Glands irregular, tortuous
- Epithelium out of phase



Polyp with non-polypous endometrium

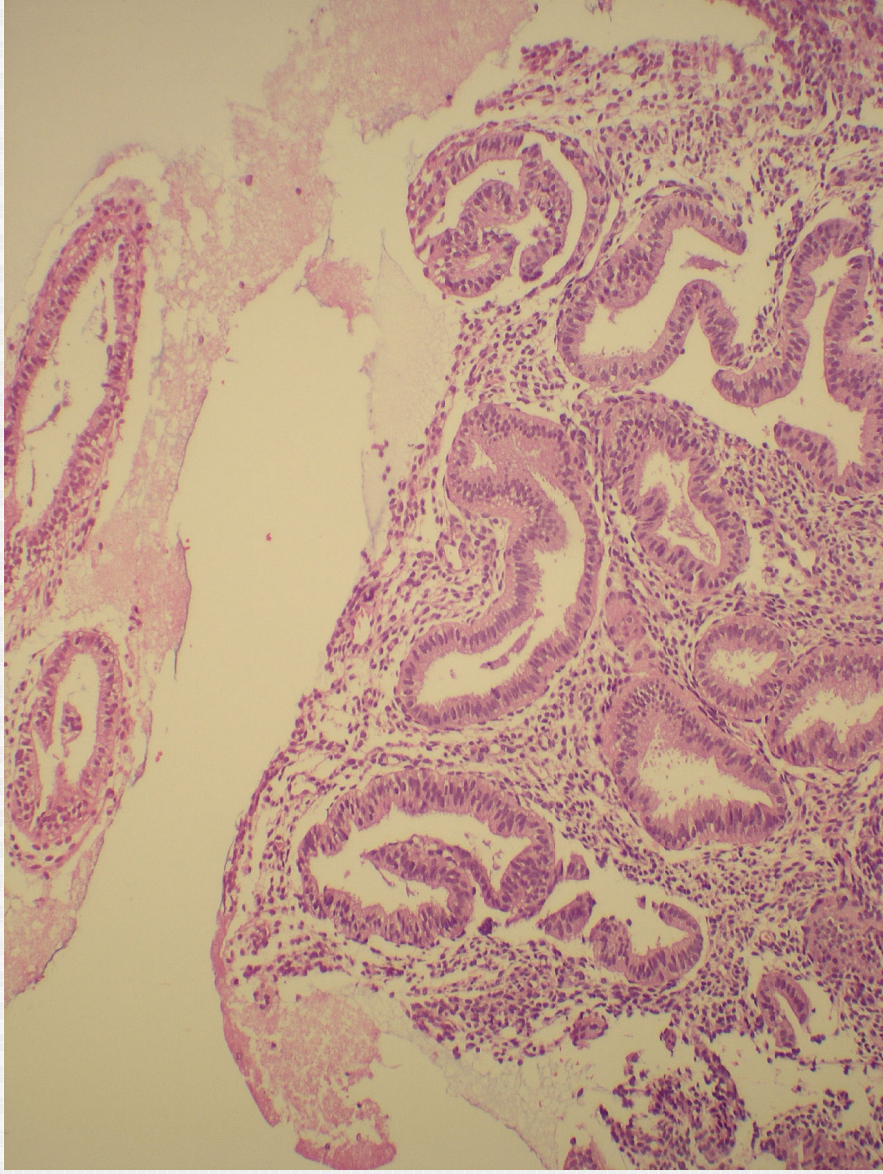


Endometrial polyps: helpful feature

- Normal glands have their axes perpendicular to the surface
- In polyps: glands lose their orientation
- Long axis parallel to surface
- Kim: A diagnostically useful histopathologic feature of endometrial polyp

Am J Surg Pathol (2004) 28: 1057-1062

Endometrial polyp: axis of gland



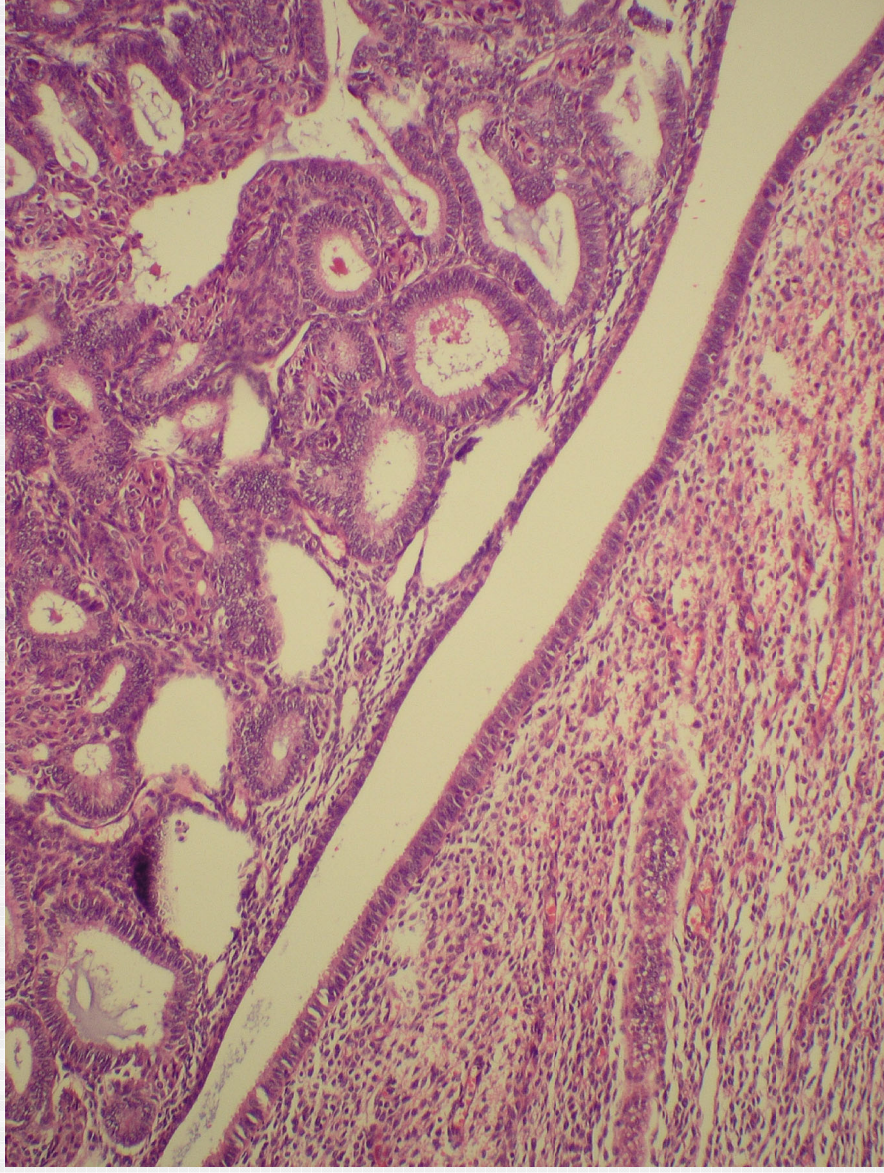
Endometrial polyps: patterns

- Proliferative/hyperplastic
- Atrophic
- Functional
- Mixed endometrial-endocervical
- Adenomyomatous
- Atypical polypoid adenomyoma

Proliferative/hyperplastic polyp

- Irregular proliferating glands
- Pseudostratification nuclei
- Mitosis
- Looks like disordered proliferation or hyperplasia without atypia
- Identifying **noninvolved** endometrium !!

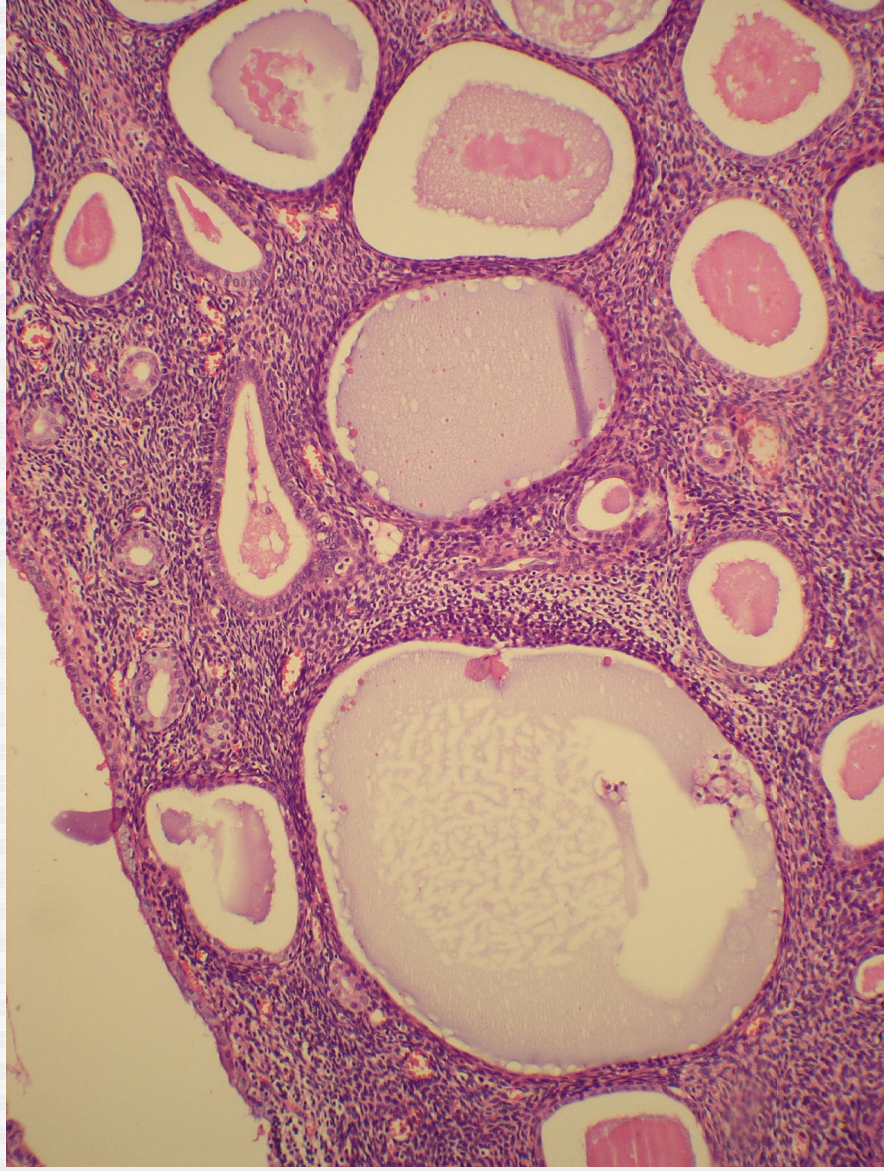
Endometrial polyp: hyperplastic type



Atrophic polyp

- Atrophic glands
- Low columnar epithelium
- Often dilated and cystic glands
- Dense fibrous stroma

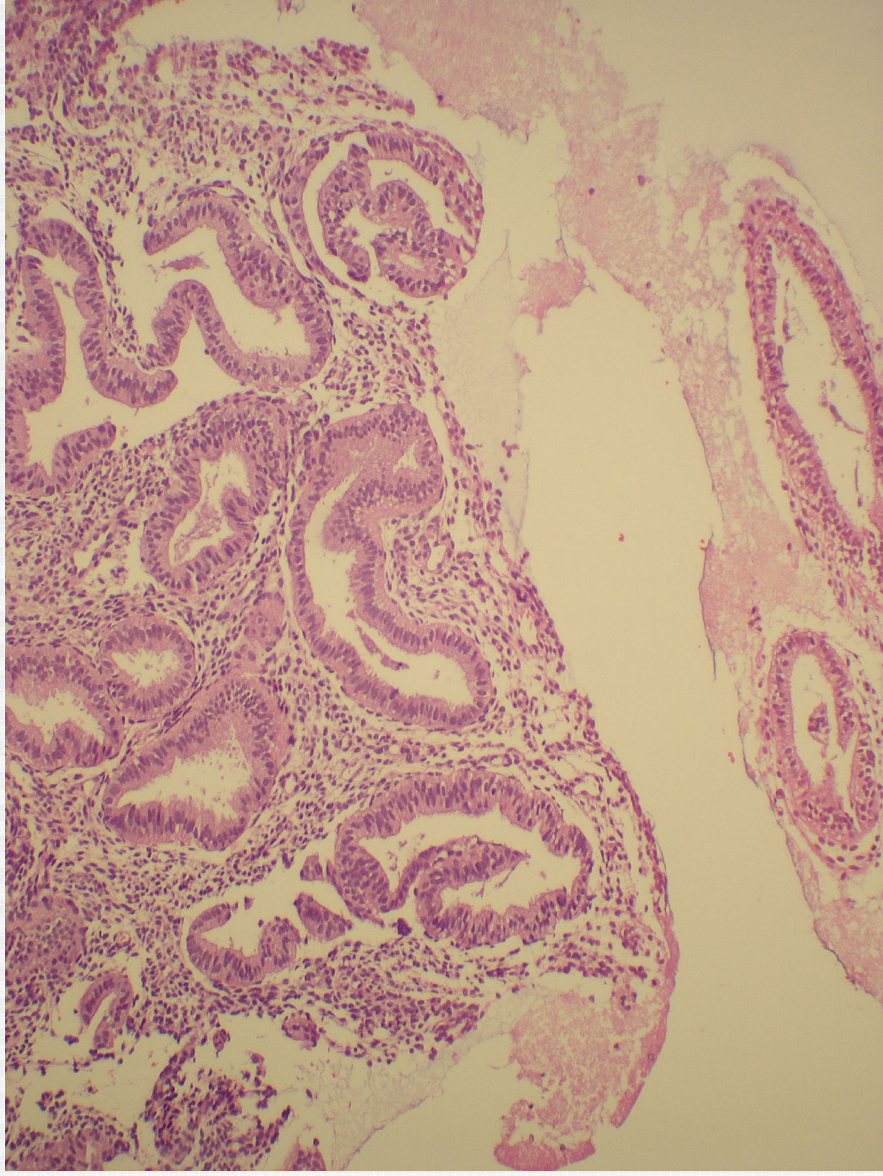
Endometrial polyp: atrophic type



Functional polyp

- Difficult to diagnose
- Haphazard distribution of glands
- Loss of orientation

Endometrial polyp: functional type



Mixed endometrial/endocervical pattern

- Originate in LUS or upper endocx
- Both endometrial and endocervical-type epithelium
- Fibrous stroma (like LUS)