

## Endometrial Metaplasia – Benign vs High Risk

Marisa R. Nucci, M.D.  
Division of Women's and Perinatal Pathology  
Brigham and Women's Hospital

## Disclosure

- None

2

## Introduction

- Definition: Epithelial differentiation that differs from conventional endometrioid epithelium
- Associated with range of lesions
- Best to consider “altered differentiation”

## Endometrial Metaplasia

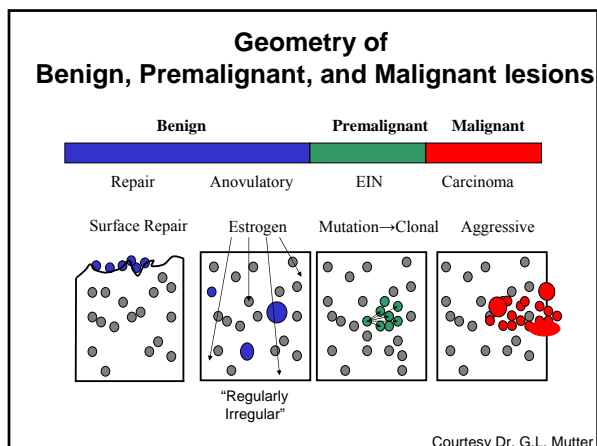
Squamous  
Tubal  
Mucinous  
Eosinophilic  
Papillary proliferations

## Topography and Mechanism

- Different mechanisms can incite different types of differentiation
- Determine underlying mechanism
- Use appropriate diagnostic terminology that reflects clinical significance

## Major Pathogenetic Mechanisms

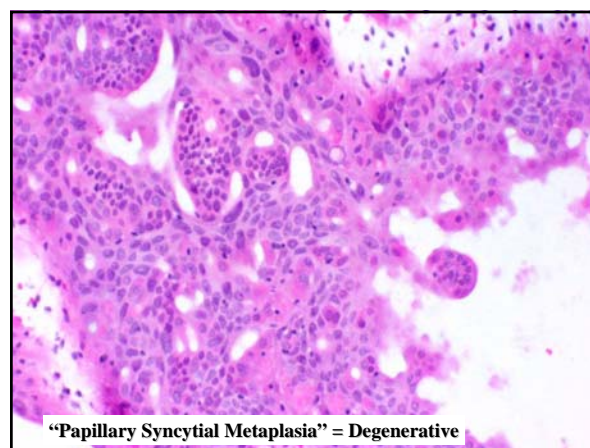
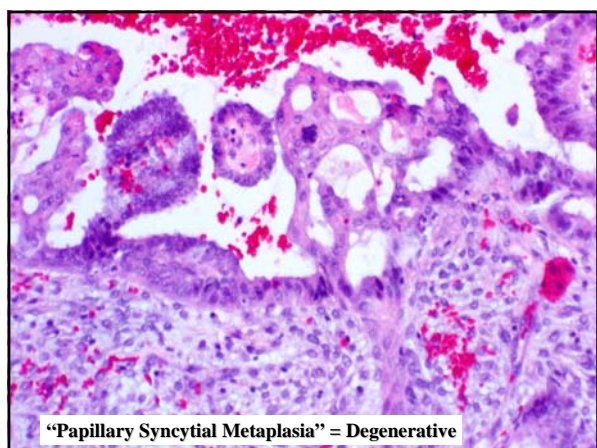
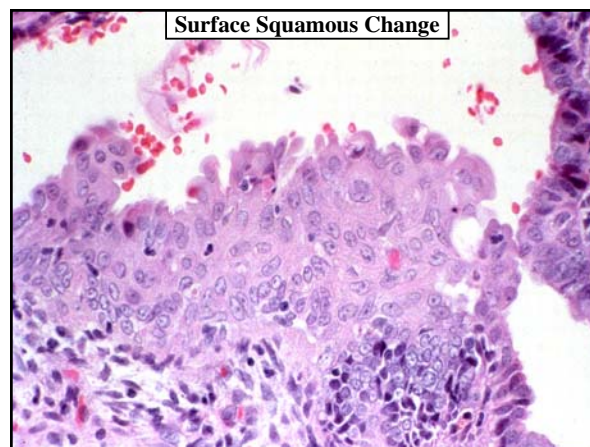
- Degenerative/reparative
- Hormonal
- Neoplastic

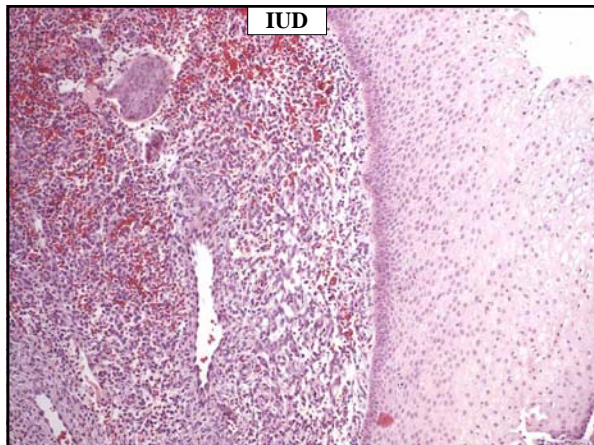
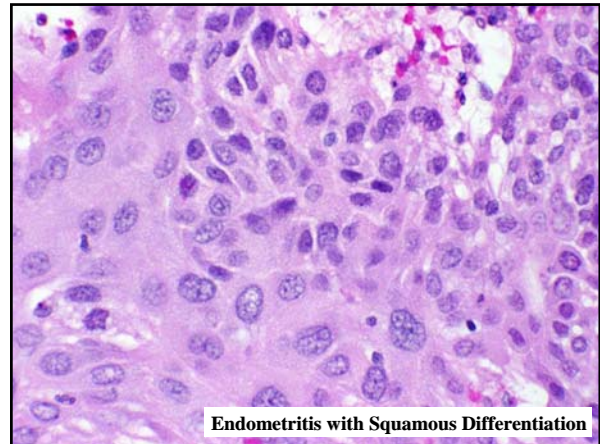
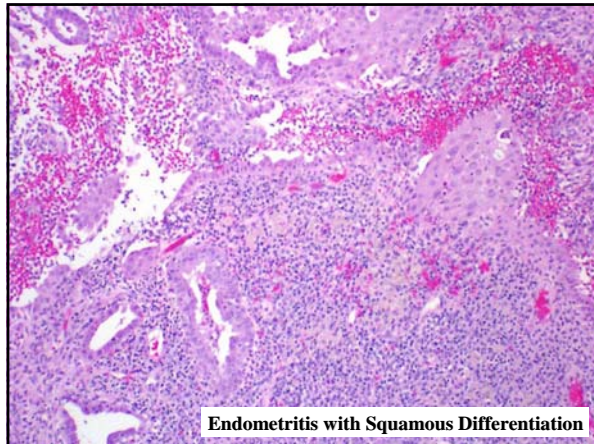


Differentiation to a Squamous Epithelium

Degenerative/Repair Category – No Risk

- Squamoid change associated with stromal breakdown/surface repair
  - Chronic endometritis
  - IUD
  - Infarcted Polyp
  - Trauma/prior procedure
- Typically focal change



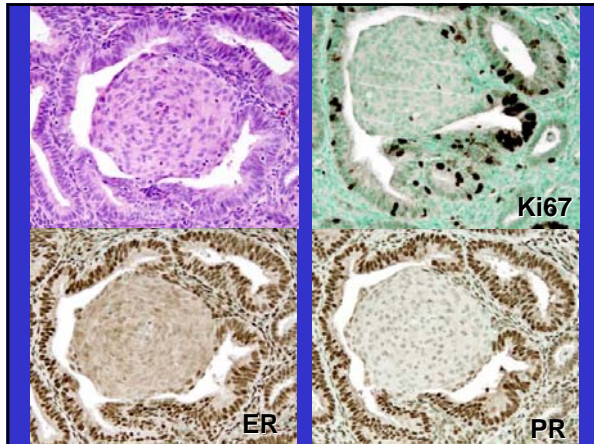


### Neoplastic Category – High Risk

- EIN with squamous morules
- Atypical polypoid adenomyoma (morules)
- Adenocarcinoma with squamous differentiation (morules or stratified squamous)

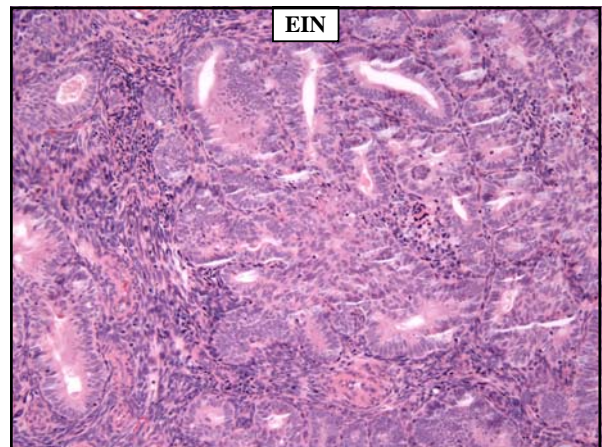
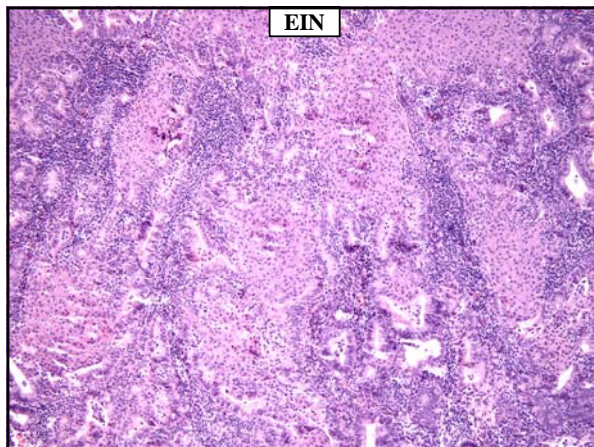
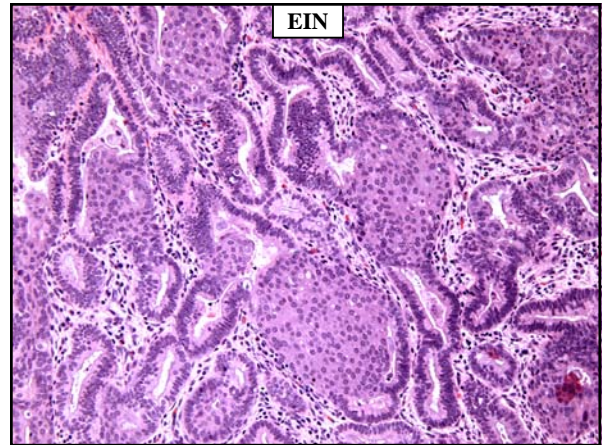
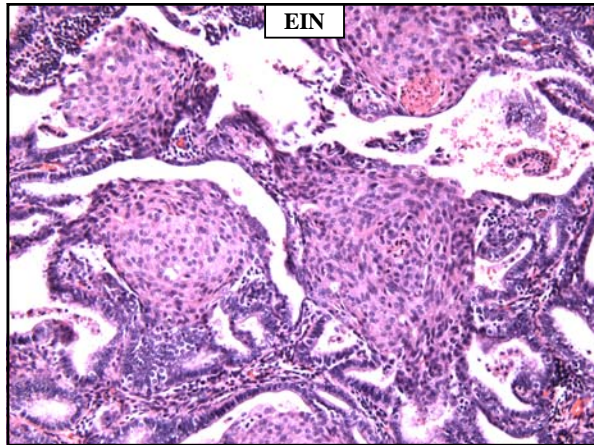
### Squamous Morular Metaplasia

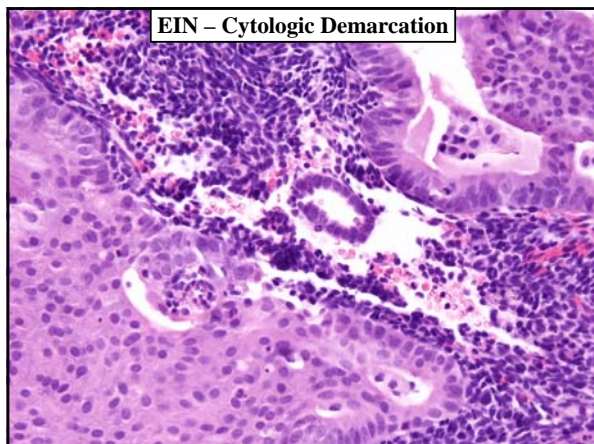
- Diagnosis and management depends on:
  - Degree/extent of glandular proliferation
  - Presence or absence of cytologic demarcation



### Endometrial Intraepithelial Neoplasia with Squamous Morular Metaplasia

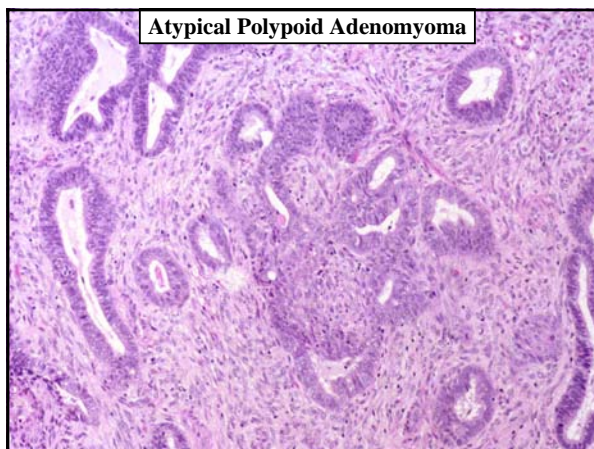
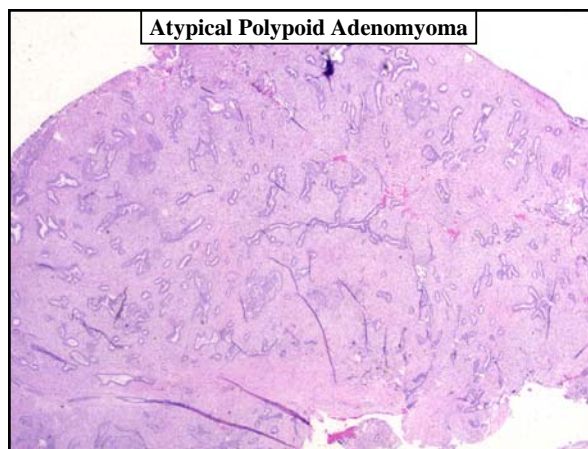
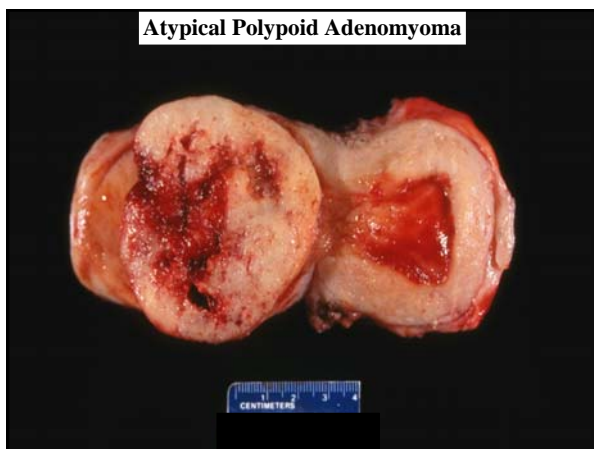
- Glandular crowding (VPS<55%)
- Cytologic demarcation
- Squamous morular metaplasia





### Atypical Polypoid Adenomyoma

- Polypoid, biphasic lesion
- Fourth and fifth decades (mean 39 years)
- Lower uterine segment
- Morular metaplasia in >90% of cases



### Atypical Polypoid Adenomyoma

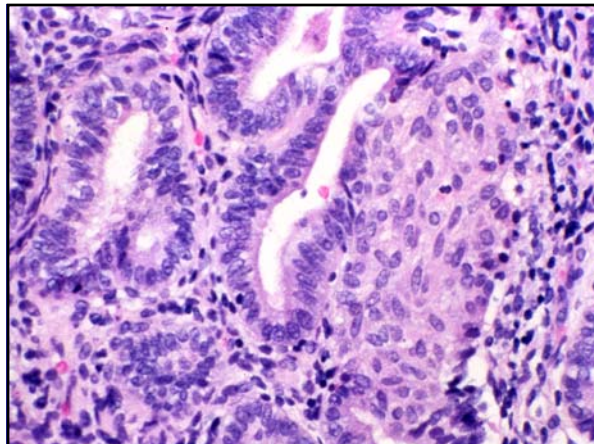
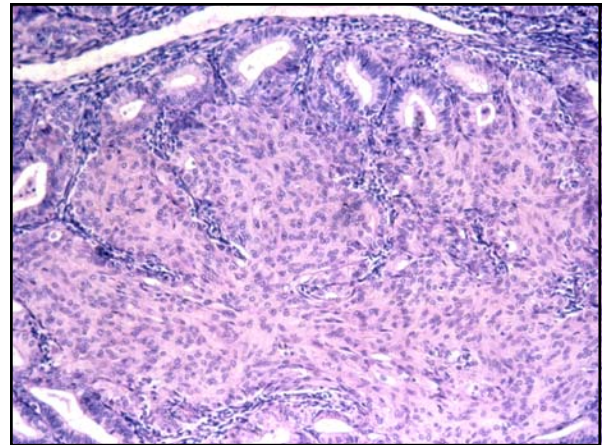
- Persistent, recurrent disease
- Local excision, hormonal therapy and close clinical follow-up vs. hysterectomy

### Atypical Polypoid Adenomyoma

- Distinguish from EIN by:
  - Polypoid fragments
  - Distinctive stroma
- Distinguish from myoinvasive adenocarcinoma by:
  - Less architecturally complex
  - Lack of separate fragments of typical adenocarcinoma

### Uncertain Diagnostic Category – but with risk of subsequent neoplasia

- Isolated squamous morules
  - Primary abnormality
  - Following treatment of EIN with morules
- Endometrial glandular proliferations, difficult to classify, but associated with morules



### Squamous Morular Metaplasia

Risk of subsequent endometrial neoplasia

Pattern	N	Morphology	Followup (%) mean 25 mo.		
			NL	EIN	CA
Grade 1	29	Isolated/No gland crowding	89.7	6.7	3.4
Grade 2	28	Gland crowding No cytologic change	57.1	28.6	14.3
Grade 3	19	Gland crowding/ Cytologic change	42.1	42.1	15.7

Lomo et al, 2004

### Isolated Squamous Morular Metaplasia

Descriptive diagnosis and follow-up sampling

- e.g. Proliferative/secretory endometrium with focal squamous morular metaplasia.
- Follow-up sampling in 9-12 months is recommended (if a curetting); earlier if biopsy

### Endometrial Alteration with Squamous Morular Metaplasia

Descriptive diagnosis and follow-up sampling

- e.g. Endometrial glandular crowding and complexity associated with squamous morular metaplasia
- Note: Diagnostic features of EIN are not present, nevertheless, close clinical followup with repeat sampling in 6 months is recommended due to the area of glandular crowding.

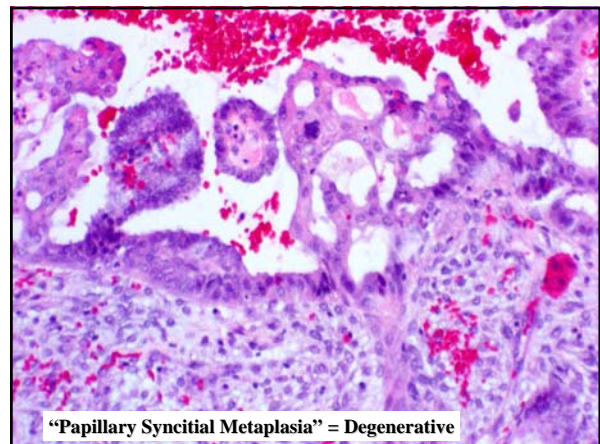
### Differentiation to a Mucinous Epithelium

### Mucinous Differentiation in Endometrial Epithelium

- Intracytoplasmic mucin droplets
- Well formed mucinous epithelium
  - Most commonly endocervical
  - Rarely, intestinal (gastric, colonic)

### Degenerative/Repair Category – No Risk

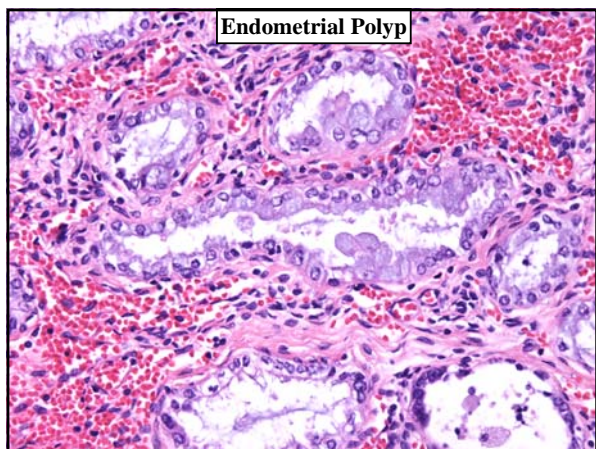
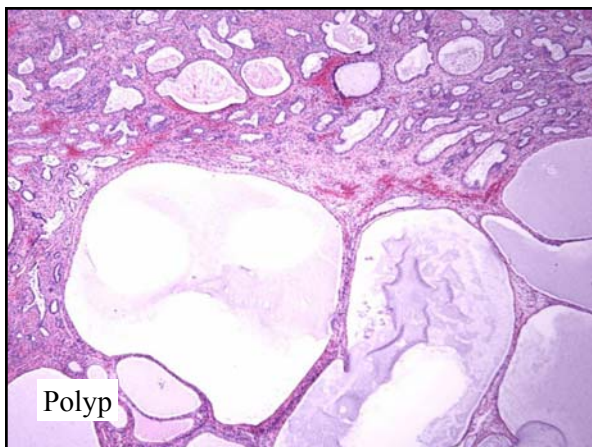
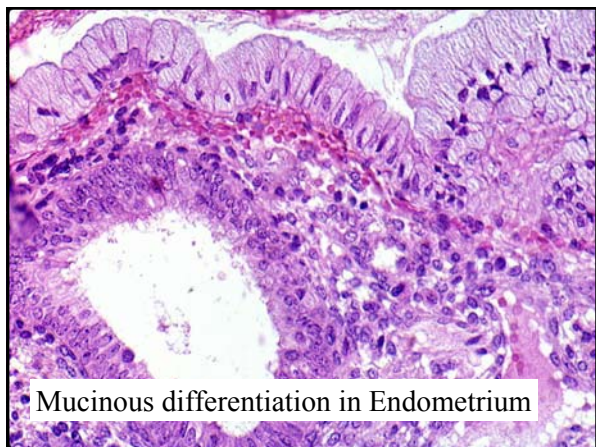
- Syncytial repair and stromal breakdown
- Hormonal therapy
- Endometrial polyp





**Mucinous Differentiation**

- Low – risk of subsequent neoplasia
  - Simple, typically endocervical type epithelium
  - Involving endometrial surface or glands as a single layer
  - Most commonly seen in samples from perimenopausal women

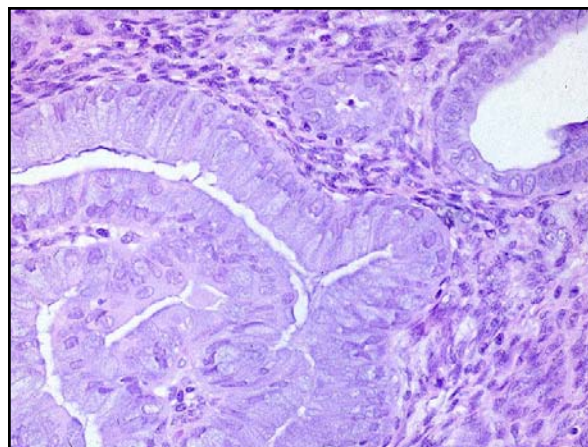
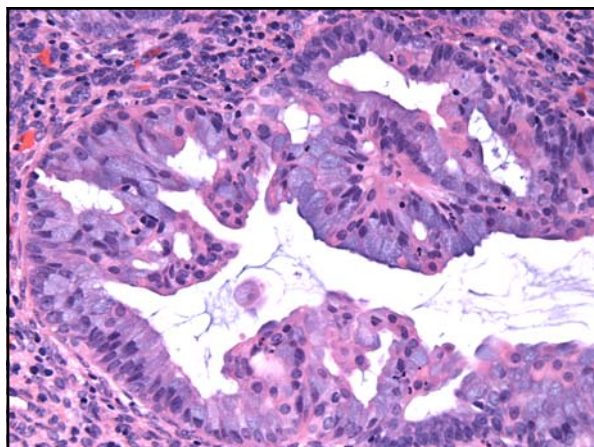
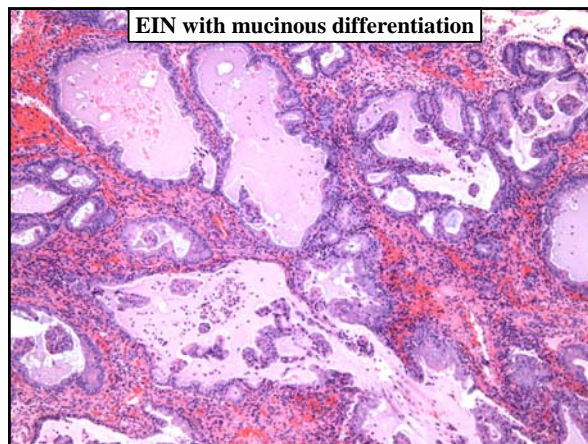


**Neoplastic Category – High Risk**

- EIN with mucinous differentiation
- Well differentiated mucinous adenocarcinoma (villoglandular, microglandular like)

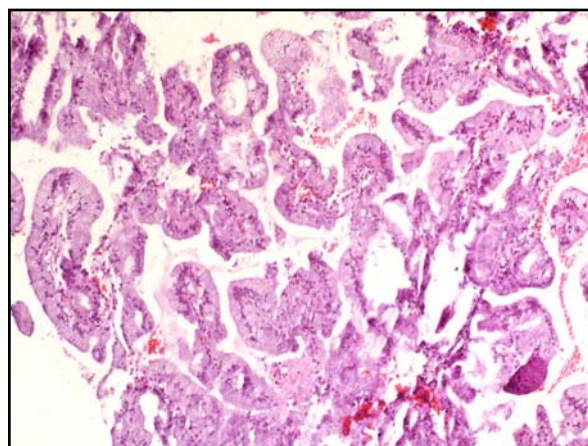
### EIN with Mucinous Differentiation

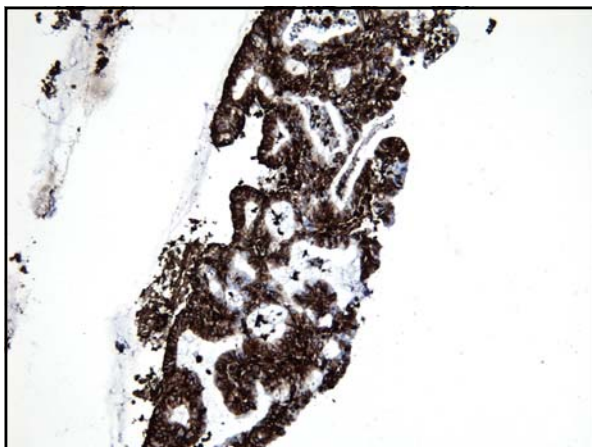
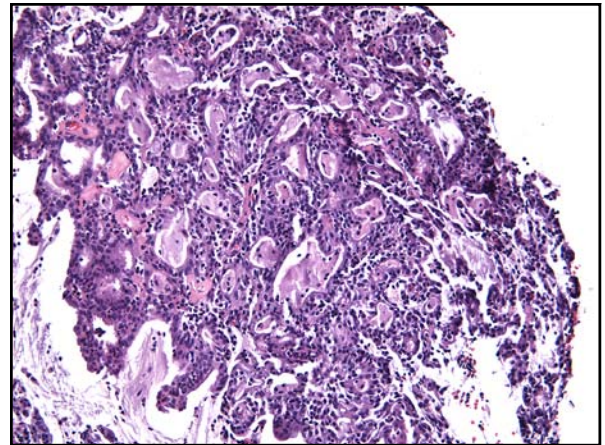
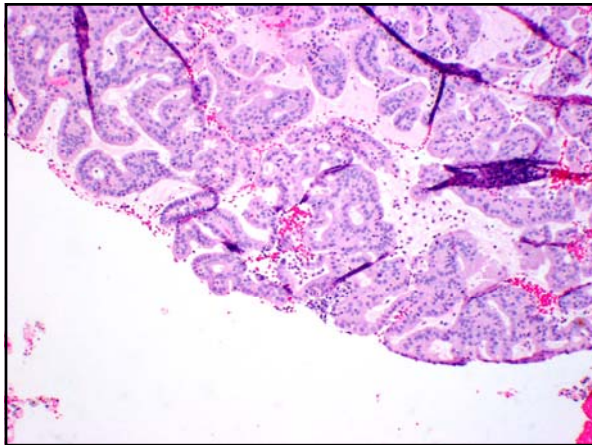
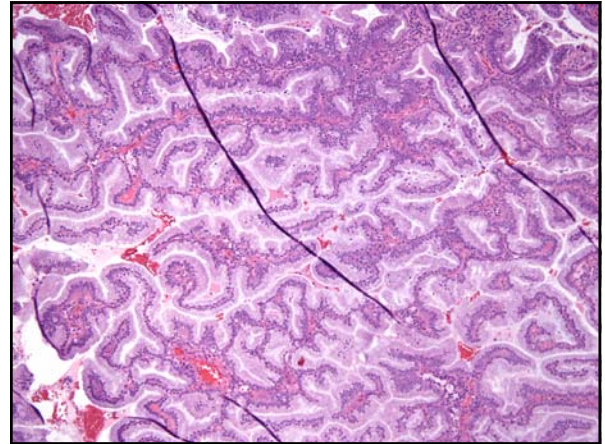
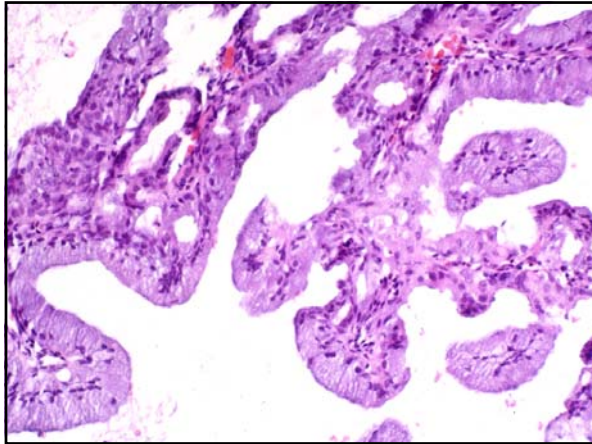
- Meets EIN VPS and size criteria
- Usually localizing lesion
- May blend into more endometrioid lesion



### Mucinous Differentiation

- Consider carcinoma if:
  - Complex, microglandular growth pattern
  - Villous architecture
  - Extensive papillary formation (with stromal cores)

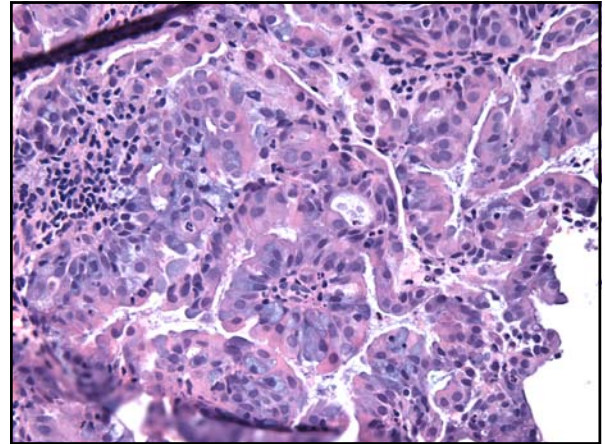
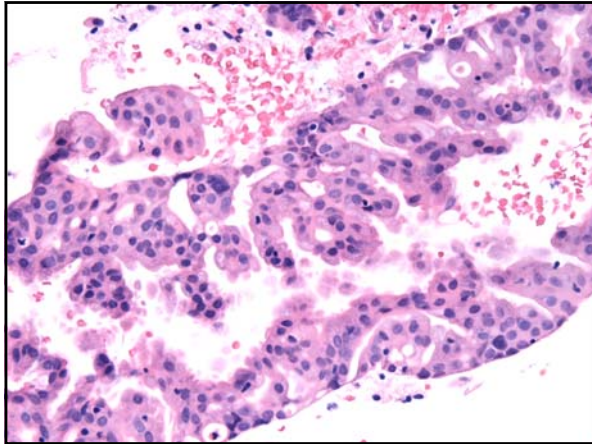




Uncertain Diagnostic Category – but with risk of subsequent neoplasia

Diagnosing Carcinoma in the biopsy/ curetting:

- Depends on amount and condition (fragmentation) of sample
- Pitfalls to keep in mind:
  - Mitoses rare, cytology bland
  - Exclusion of mimics critical



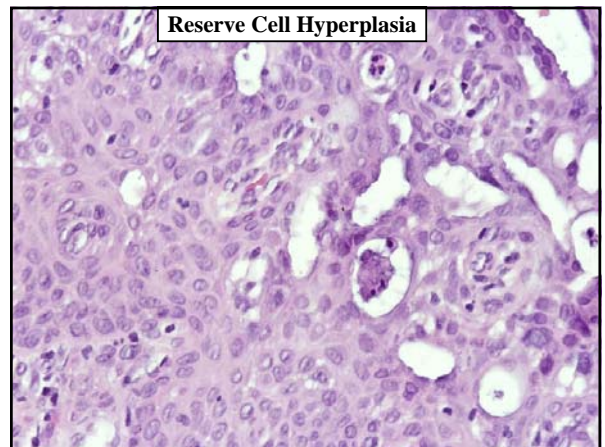
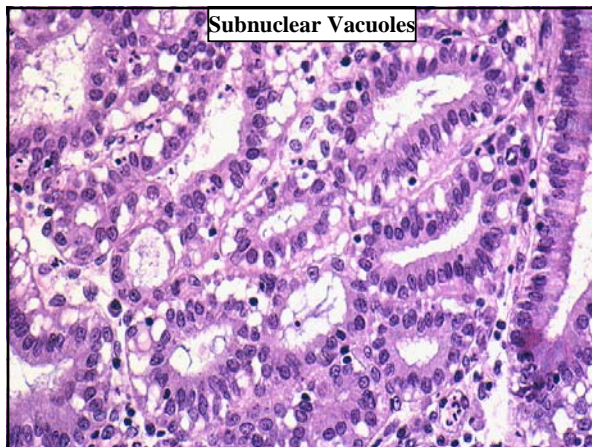
### Mucinous Metaplasia with Complex Architecture

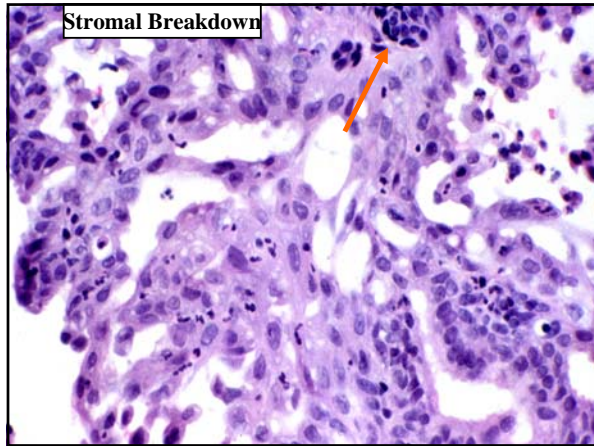
Diagnosis: Complex mucinous epithelial proliferation, see NOTE.

NOTE: Findings are worrisome for a neoplastic process; however the (scant amount/ fragmentation/preservation) precludes a more definitive diagnosis. Followup sampling is recommended.

### Exclusion of Mimics

- Exclude cervical MGH
  - Endometrial vs. endocervical stroma
  - Presence of reserve cell hyperplasia
  - Presence of sub/supranuclear vacuoles
- Epithelial complexity associated with repair
  - Associated stromal breakdown



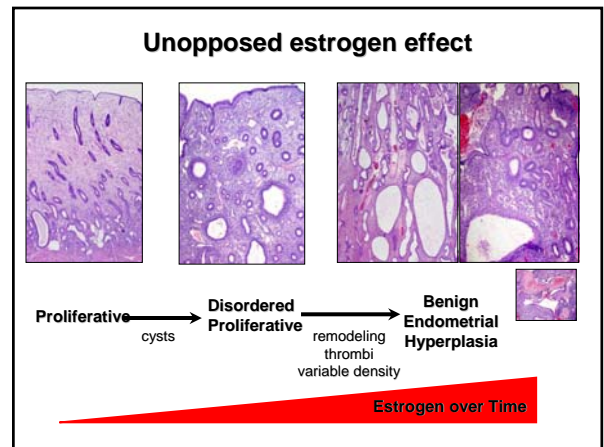
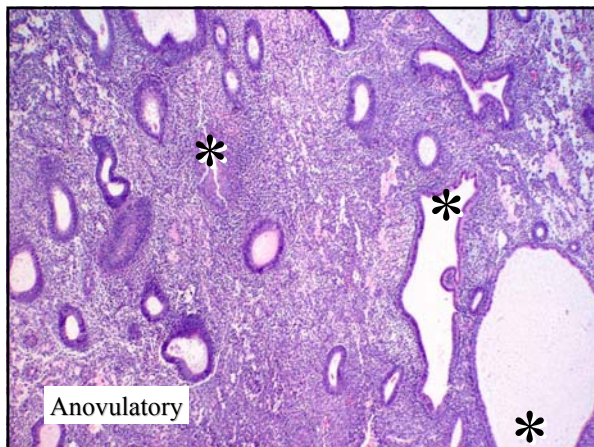
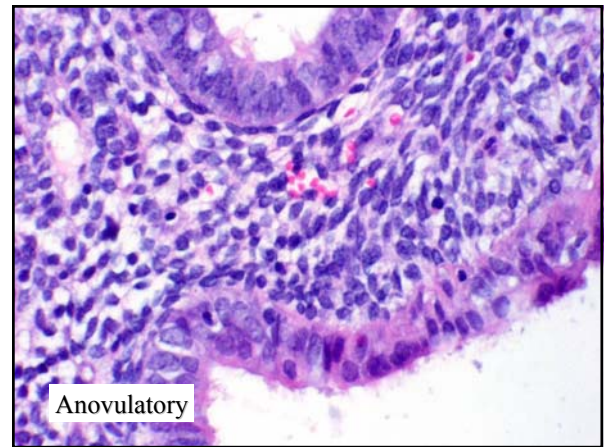


Differentiation to a Tubal Epithelium

**Hormonal Category – Low Risk**

- Disordered Proliferative Endometrium with cysts and tubal change (anovulatory type)
- Benign Endometrial Hyperplasia

All due to Unopposed estrogen effect



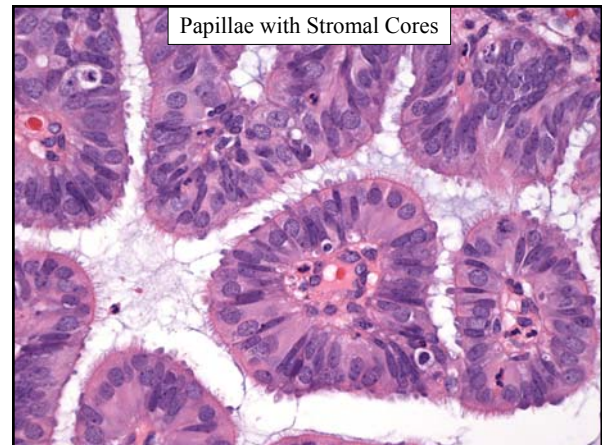
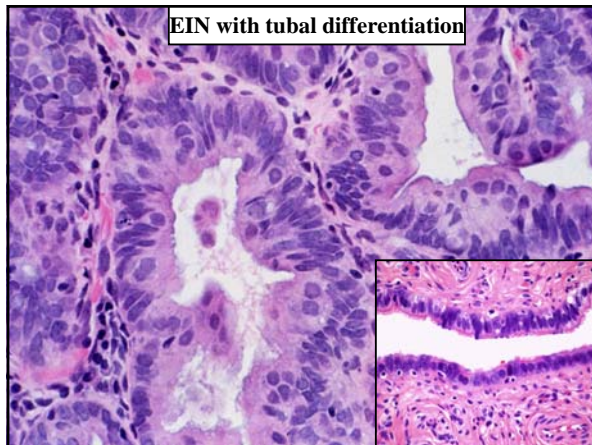
### Neoplastic Category – High Risk

- EIN with tubal differentiation

### EIN with tubal differentiation

- Glands have pink cytoplasm, interspersed round cells, +/- cilia
- Tubal glands geographic
- Usual EIN criteria met (VPS, size, mimic exclusion)

Diagnosis: EIN with tubal differentiation



### Endometrial Metaplasia – Diagnostic Pitfalls

- Squamous morular metaplasia
  - Adenocarcinoma with squamous differentiation
  - EIN with morular metaplasia
  - Squamous carcinoma
  - Atypical polypoid adenomyoma
- Mucinous metaplasia
  - MGH
  - Well differentiated mucinous carcinoma
- Tubal/eosinophilic metaplasia
  - Coexistent EIN or adenocarcinoma

### Endometrial Metaplasia – Diagnostic Pitfalls

- If there is a cribriform architecture, consider:
  - Pseudo-cribriform reparative processes
  - Papillary syncytial metaplasia
  - MGH of cervix
  - Adenocarcinoma (particularly mucinous)

### Endometrial Metaplasia

- Regard as alterations in differentiation
- Be aware of their association with both benign and malignant processes, i.e. conceptualize as a spectrum of changes
- Recommend follow-up when necessary