

Course AP104

Hyperplasias

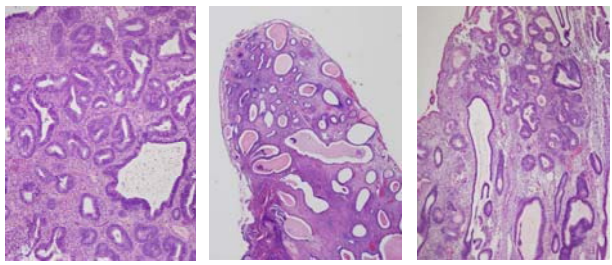
Hormonal Effect or Precancer?

George L. Mutter, MD
 Harvard Medical School and
 Brigham and Women's Hospital
 Boston, MA



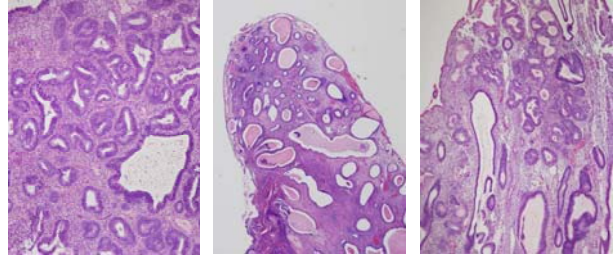
“Endometrial Hyperplasia”

A morphologic Definition

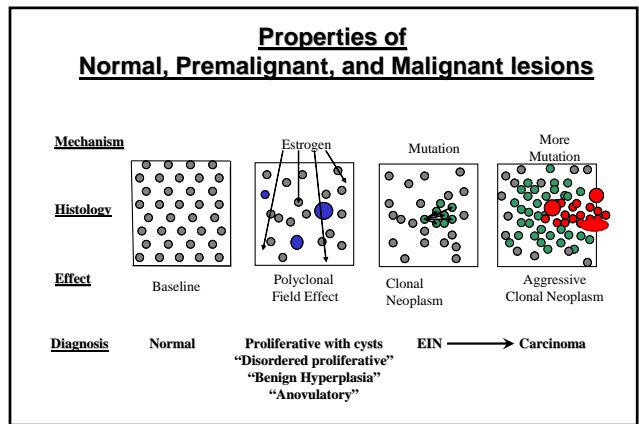


“Endometrial Hyperplasia”

A morphologic Definition

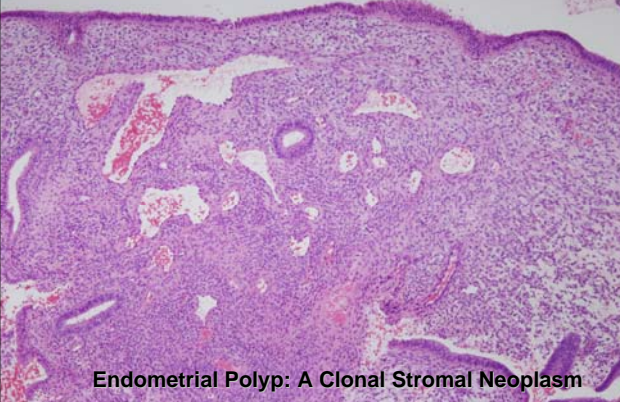


Anovulatory	Polyp	EIN (intraepithelial neoplasia)
E2 Effect (EM=Normal)	Stromal Neoplasm	Premalignant neoplasm
HR=2-4	HR=1-1.5	HR=45

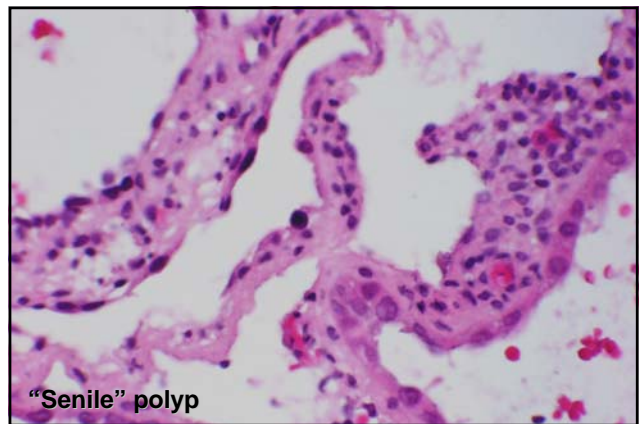
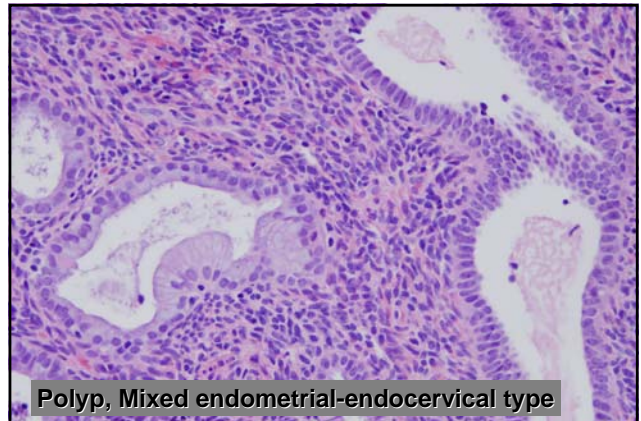
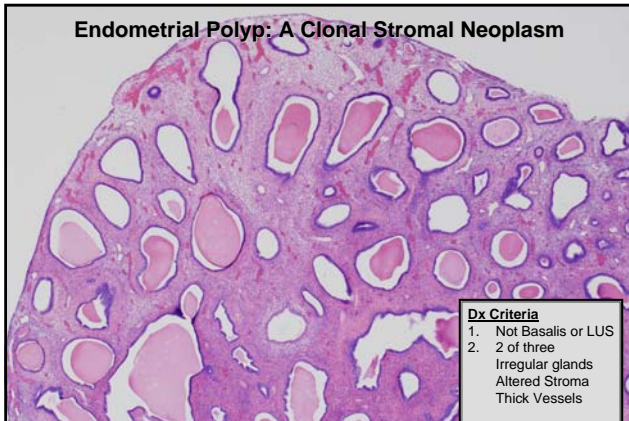


Polyps

- Dx background separately
- May contain other lesions (EIN)
- Do not cycle normally. (Do not date).
- Not a gross (or hysteroscopic) Dx



Endometrial Polyp: A Clonal Stromal Neoplasm

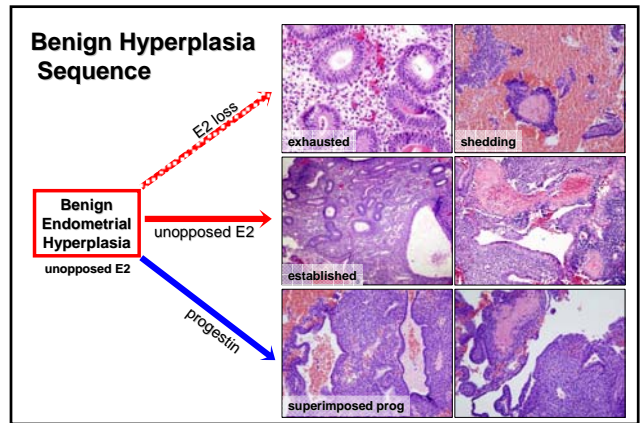
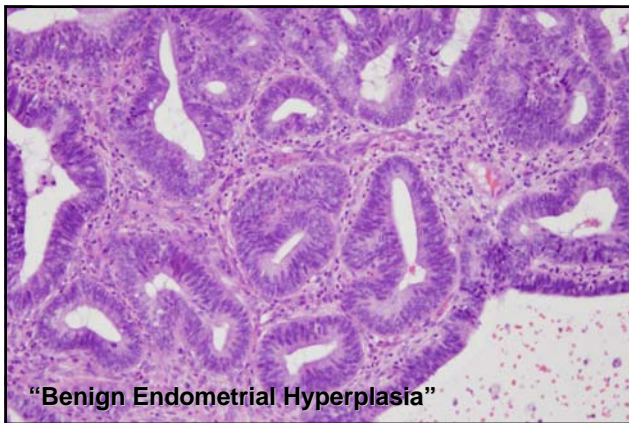
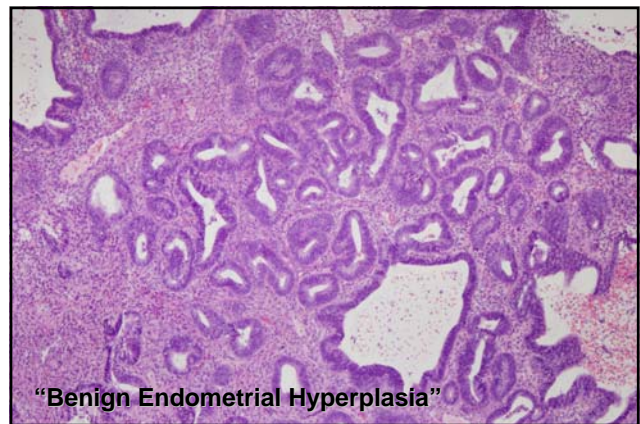
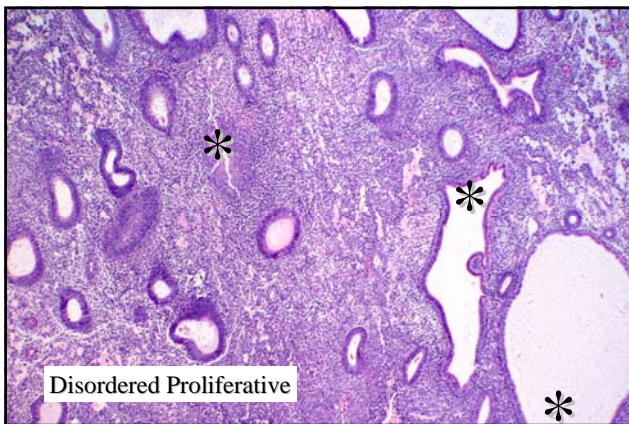
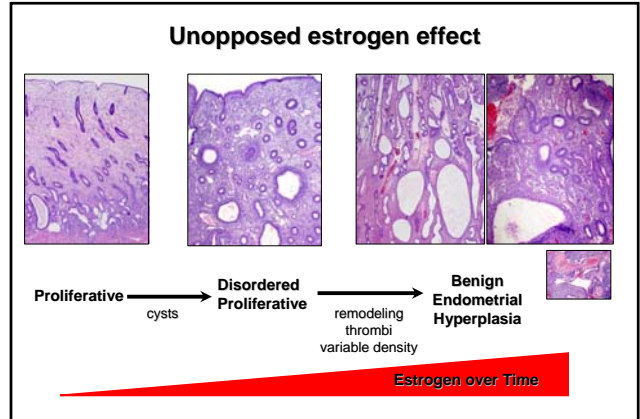
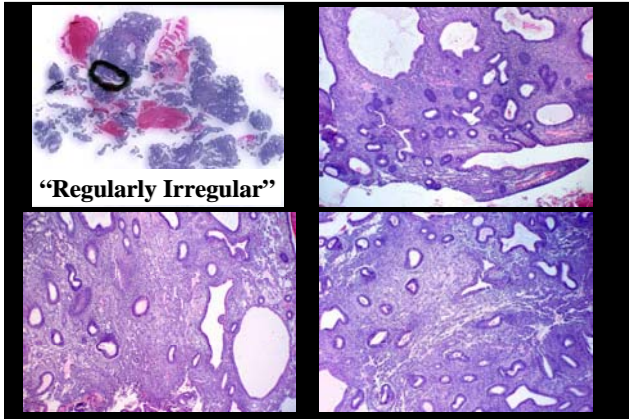


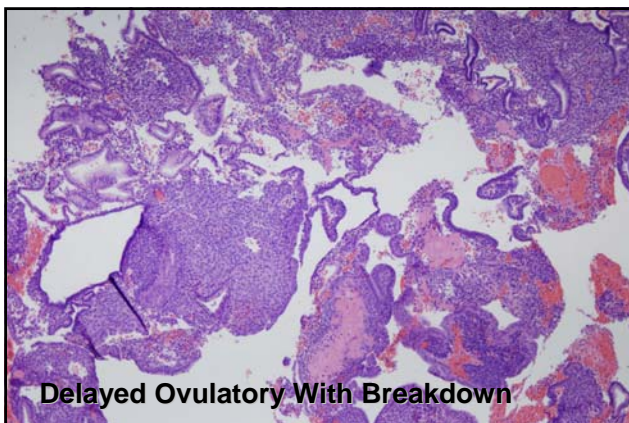
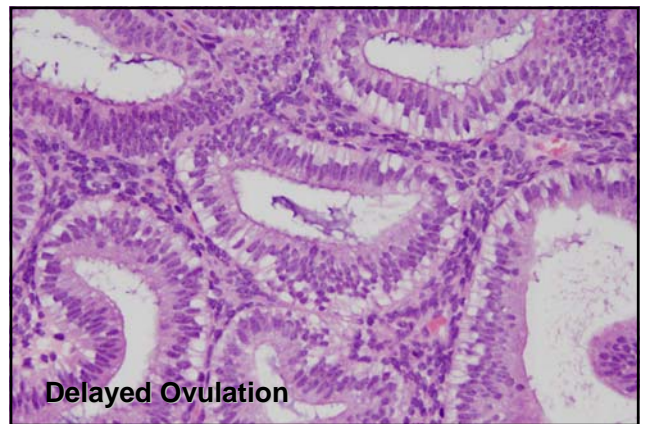
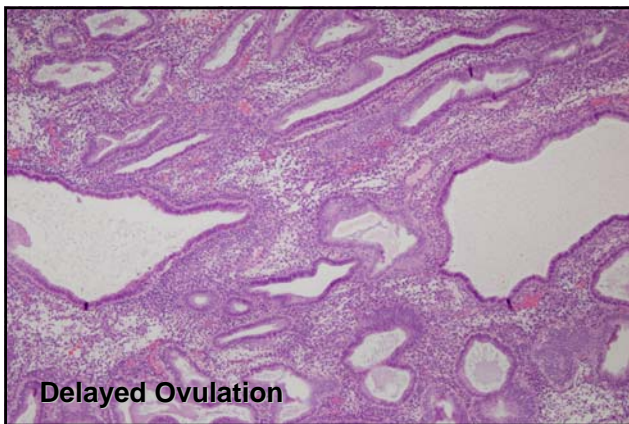
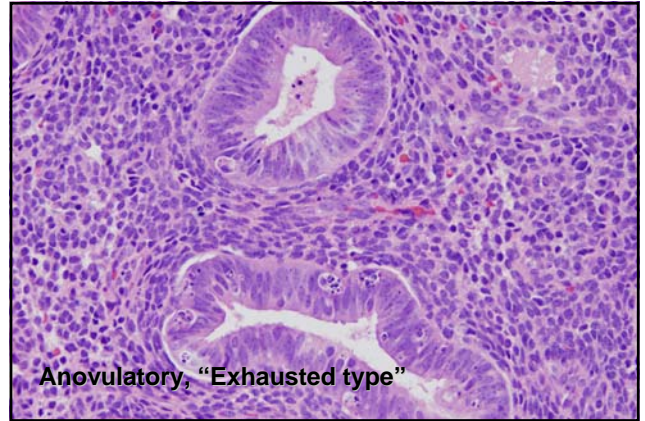
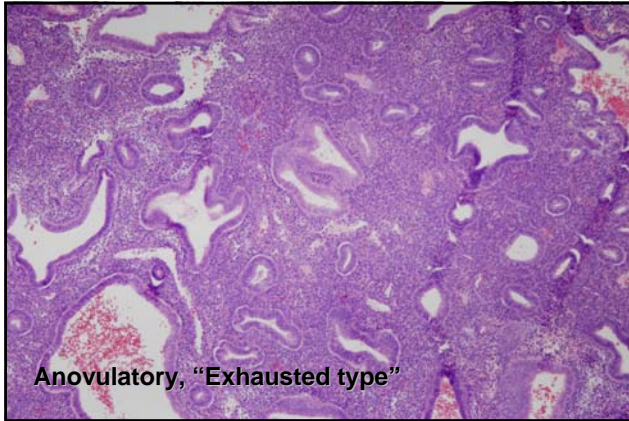
EIN Diagnostic Classes

EIN Nomenclature	Topography	Functional Category	Treatment	ICD9
Benign endometrial hyperplasia (Unopposed Estrogen effect)	Diffuse	Estrogen Effect	Hormonal therapy	621.34
EIN Endometrial Intraepithelial Neoplasia	Focal progressing to diffuse	Precancer	Hormonal or surgical	621.35
Carcinoma	Focal progressing to diffuse	Cancer	Surgical stage-based	182.0

Diffuse (Field) Lesions

- Hormonal Changes
- Neoplasm that replaces Compartment





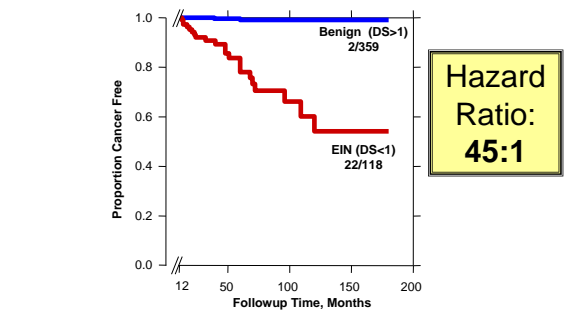
- Localized Lesions**
- Neoplasm
 - Cancer
 - Precancer (EIN)
 - Polyp (stromal tumor)
 - Sampling (LUS, Cervix, basalis)
 - Secondary effect (fibroid)



EIN Concurrent Cancer

- **39%** (43/110) Carcinoma <1 year
(Retrospective, Baak 2005)
- **37%** (56/153) Carcinoma at hysterectomy
(Prospective Clinical Trial: GOG167, Trimble 2006)
- **32%** (18/56) of concurrent CA myoinvasive
(Prospective Clinical Trial: GOG167, Mutter 2008)

>1-Year Cancer Progression Following Biopsy EIN Diagnosis



n=477 FU 13-180 months
HR 45.4

Baak, Mutter, et al, 2005 (Cancer)

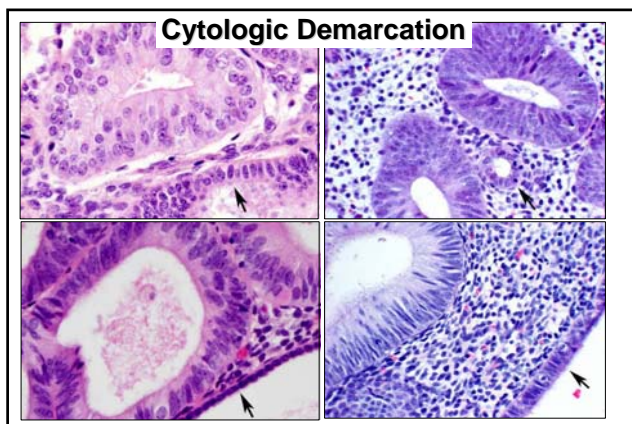
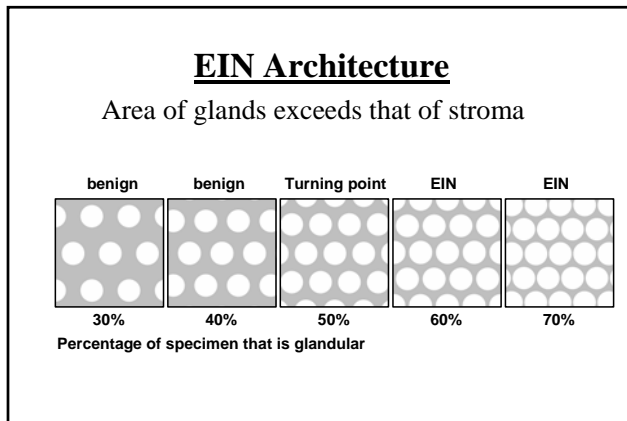
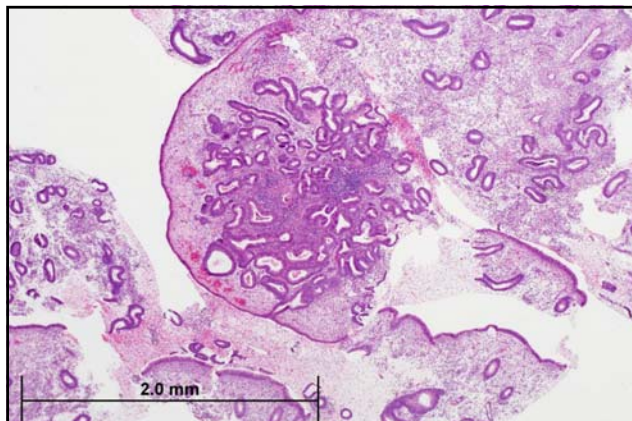
BWH EIN Experience 2002-2007

- 177 new cases on Bx
- Dx by clinical pool of 8 pathologists, 1 hospital.
- 88% had some followup (median 74 days)
- Overall Cancer incidence 35.7% (56/157)
 - 26 initial Bx, 30 during f/u

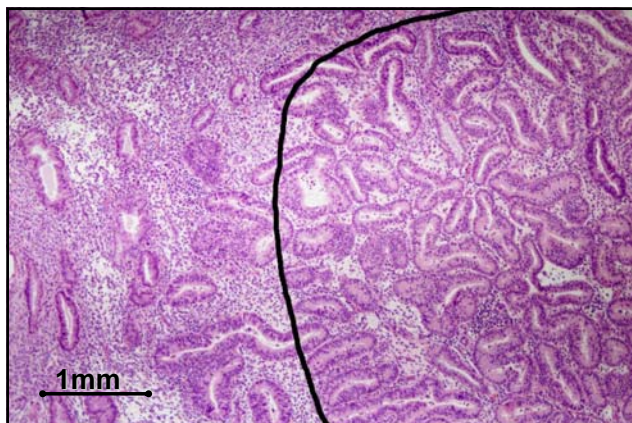
Semere et al, 2011

EIN Diagnostic Criteria

EIN Criterion	Comments
Architecture	Area of Glands>Stroma (VPS<55%)
Cytology	Cytology differs between architecturally crowded focus and background.
Size >1 mm	Maximum linear dimension exceeds 1mm.
Exclude mimics	Benign conditions with overlapping criteria: Basalis, secretory, polyps, repair, etc..
Exclude Cancer	Carcinoma if mazelike glands, solid areas, or significant cribriforming



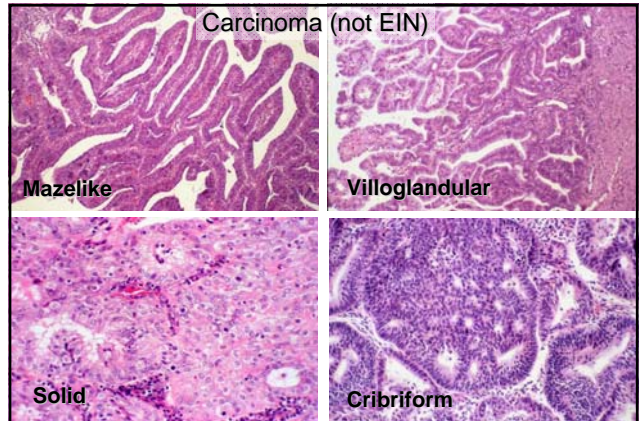
- Minimum Size**
- Region with glands > stroma and altered cytology
 - 1mm minimum diameter
 - Correlates with outcome



- Exclusions**
- Normal Tissue
LUS/Basalis
Secretory endometrium
 - Artifact
 - Polyp
 - Reactive
 - Cancer

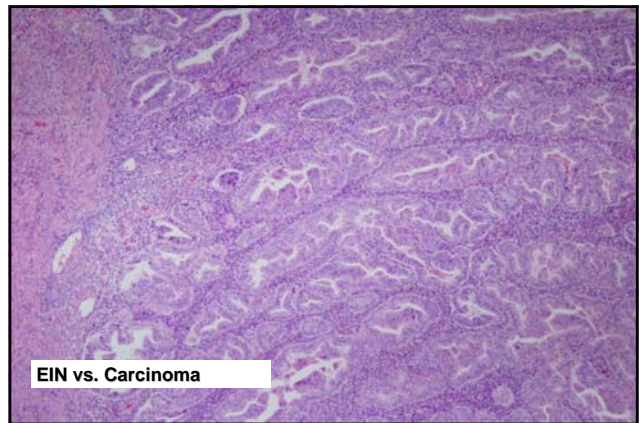
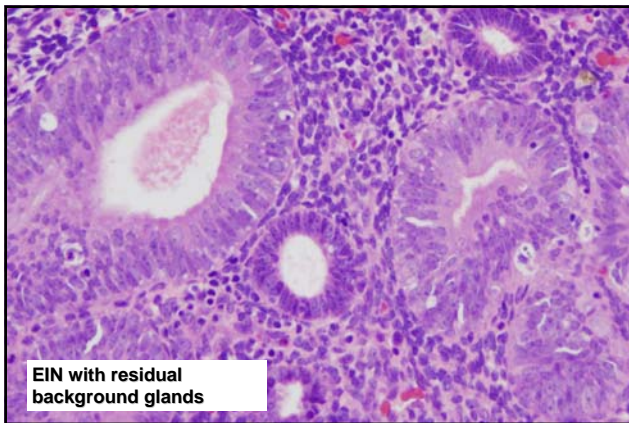
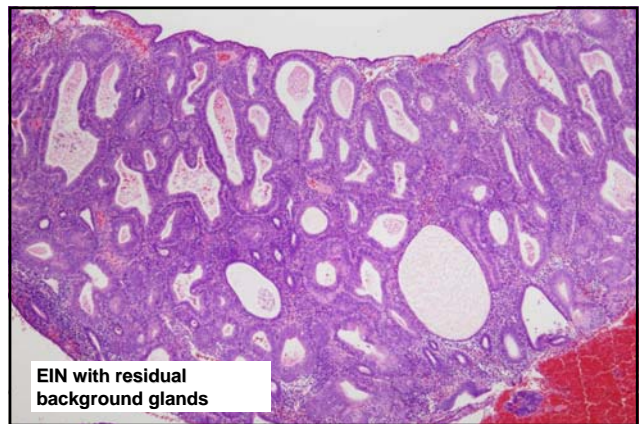
Carcinoma vs. EIN

- Rambling Glands
- Extensive Cribriforming
- Large Solid Areas
- Myometrial Invasion



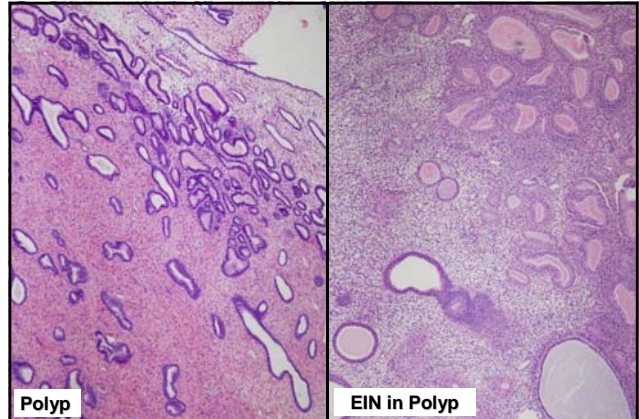
Non-Localizing EIN

- Involves entire compartment
- About 20% of all EIN
- Overrun background glands
- Cancer vs. EIN?



Endometrial Polyp

- Features can overlap with EIN
- Should be excluded as mimic
- 1/3 of EIN within Polyp
Usually localizing lesion
Need substantial cytologic change to Dx
?Clinical repercussions of location



Subdiagnostic EIN: "Gland Crowding"

n=143 (0.3% of 71,579 specimens)

- Altered cytology
- Size < 1mm
- Glands < stroma
- Secretory/Polyp
- Recommend 3-6 mo f/u
- Bx or EMC
- Outcomes (n=143)
77% Benign
19% EIN
4% Cancer

Nucci et al, 2010

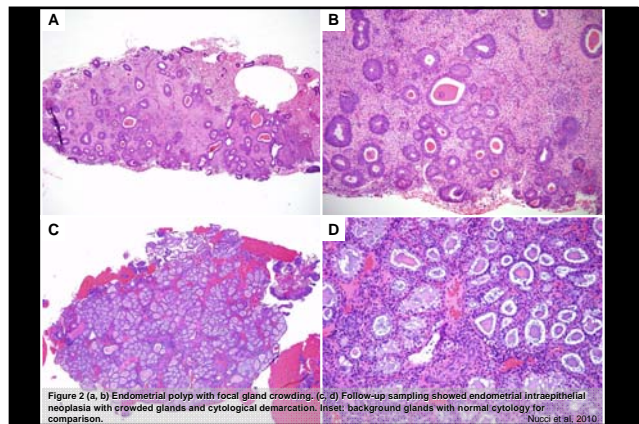
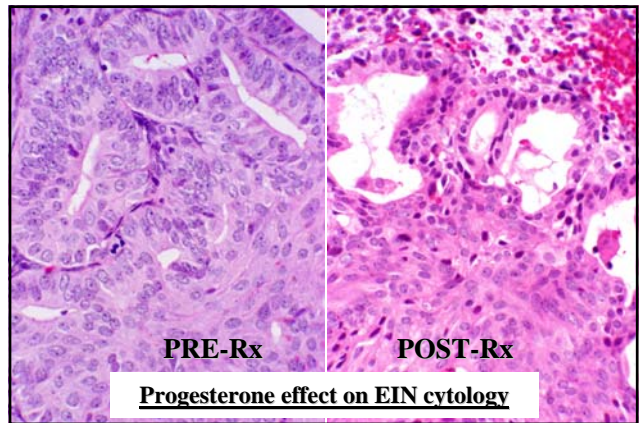


Figure 2 (a, b) Endometrial polyp with focal gland crowding. (c, d) Follow-up sampling showed endometrial intraepithelial neoplasia with crowded glands and cytological demarcation. Inset: background glands with normal cytology for comparison. Nucci et al, 2010.

Progesterone effect

- Stromal expansion decreases gland density
- Makes neoplastic cytology bland
- Nuclear enlargement and rounding in normal cells
- Withdrawal synchronizes shed



Progesterone effect on EIN cytology

Management

- **EIN:**
 - like atypical hyperplasia (roca, hyst, hormones)
- **Estrogen effect (non-EIN)**
 - Symptomatic and/or endocrine
- **Endometrial polyps**
 - Symptomatic. Resample if worried.
- **Uncertain Dx.**
 - Depends on the problem