MOUNT SINAI HOSPITAL
Joseph and Wolf Lebovic Health Complex

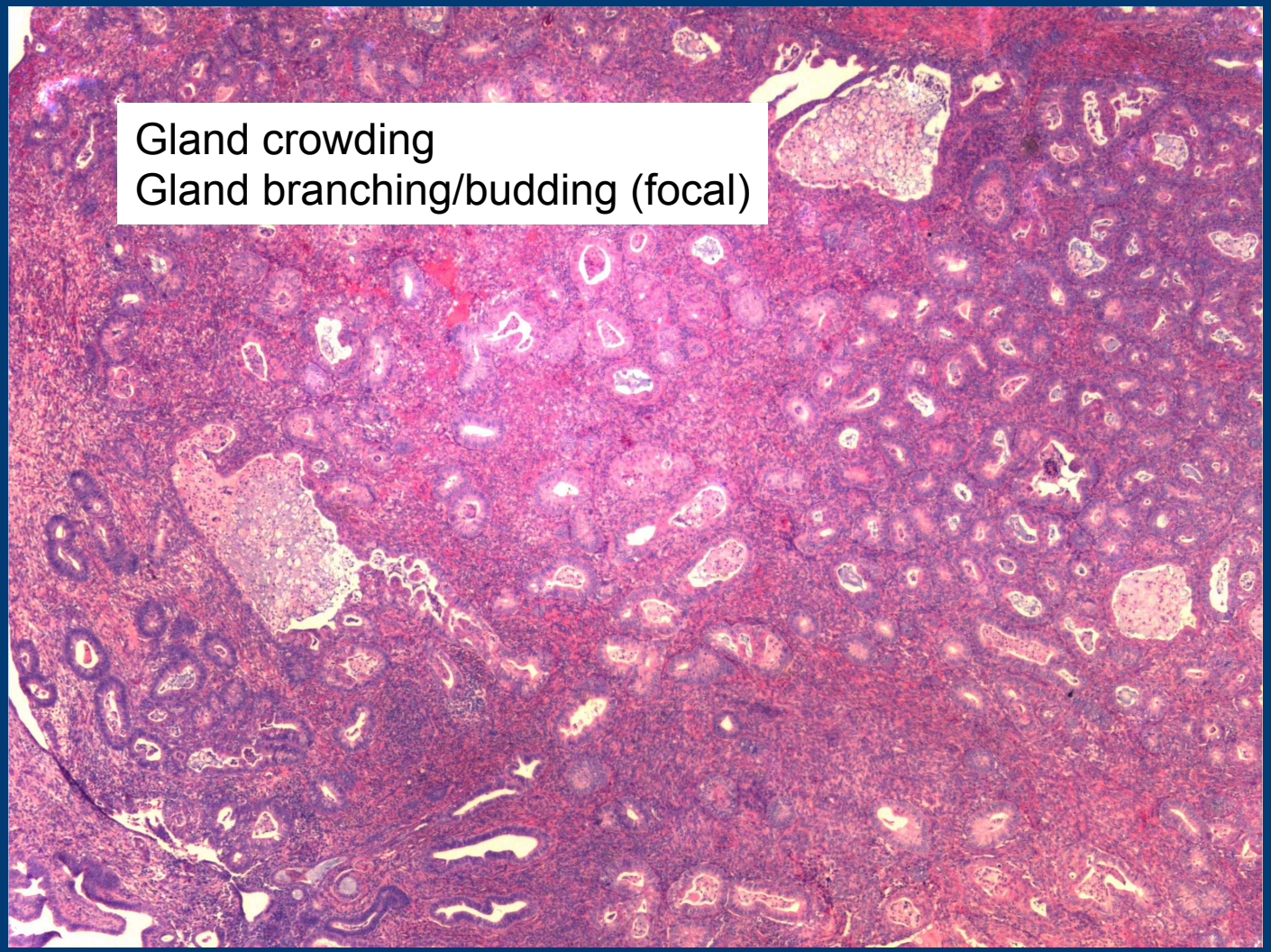
"Endometrial hyperplasia vs. Intraepithelial neoplasia"

Martin Chang, MD PhD FRCPC
Pathology Update
Friday November 9, 2012

Disclosure

No relevant financial conflicts to declare.

Case 1



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58F with uterine bleeding
Endometrial biopsy/polypectomy

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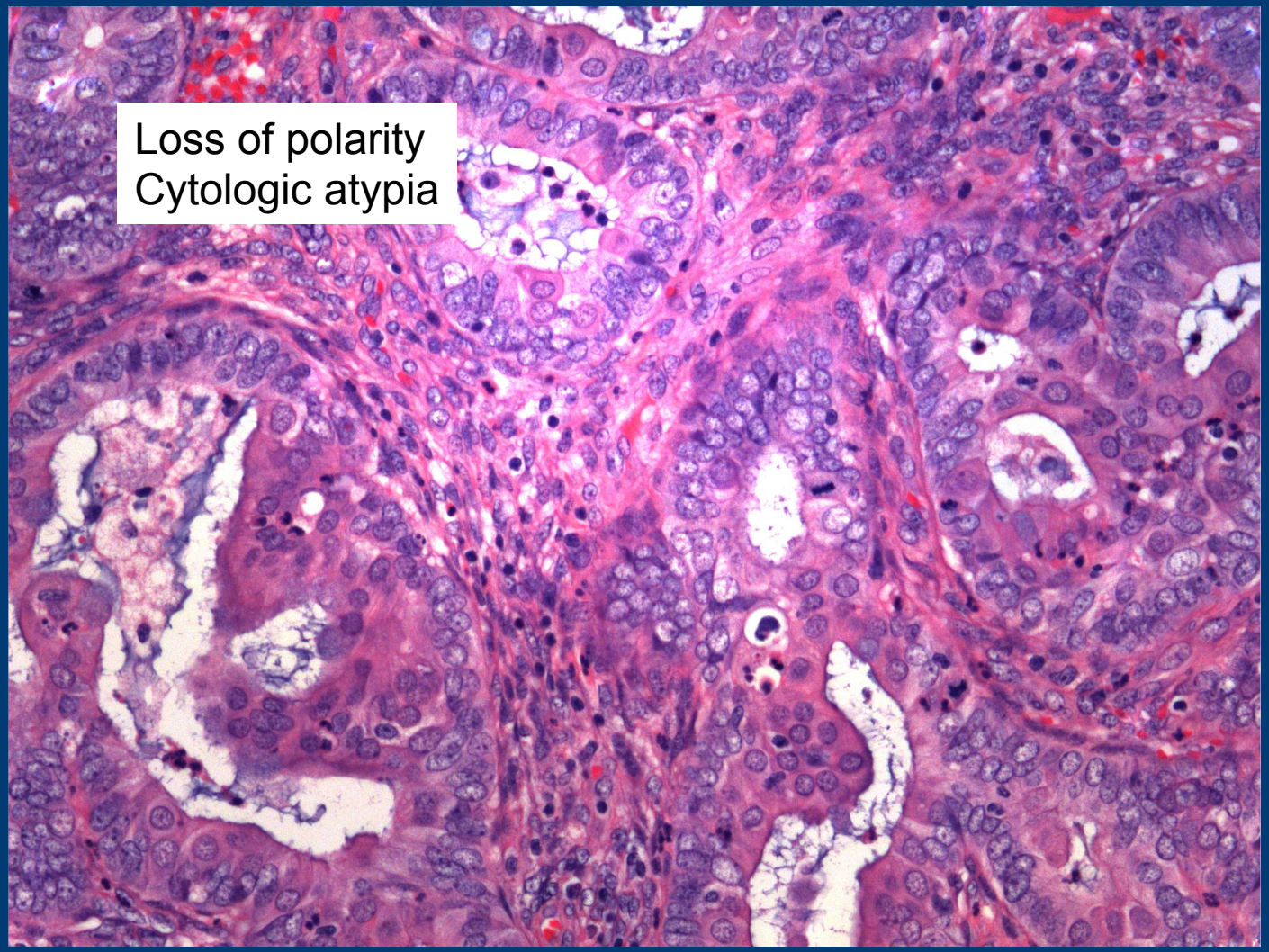

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58F with uterine bleeding
Endometrial biopsy/polypectomy

Multiple Choice

How would you classify this biopsy?

Multiple Choice

How would you classify this biopsy?

1. Complex hyperplasia without atypia
2. Complex atypical hyperplasia
3. Endometrial intraepithelial neoplasia
4. Endometrial adenocarcinoma
5. Both 2) and 3)

Multiple Choice

Which of the following do you consider most correct?

Multiple Choice

Which of the following do you consider most correct?

1. Hyperplasia is an important precursor for adenocarcinoma.
2. Hyperplasia reflects benign estrogen-driven proliferation.
3. Intraepithelial neoplasia is the same as atypical hyperplasia.
4. Intraepithelial neoplasia is a more reproducible determinant of high-risk than atypical hyperplasia.

"Endometrial Hyperplasia" (According to WHO)

- "Simple vs. Complex"
  Based on degree of architectural complexity (crowding, budding).

- "Without atypia vs Atypical"
  Atypical cytology; loss of polarity.

Simple w/o atypia	Simple atypical
Complex w/o atypia	Complex atypical

Multiple Choice

Of all "endometrial hyperplasias" that you sign out, what percentage are "simple atypical hyperplasia"?

1. 0%
2. 1-5%
3. 5-10%
4. 10-20%

Multiple Choice

Of all “endometrial hyperplasias” that you sign out, what percentage are “simple atypical hyperplasia”?

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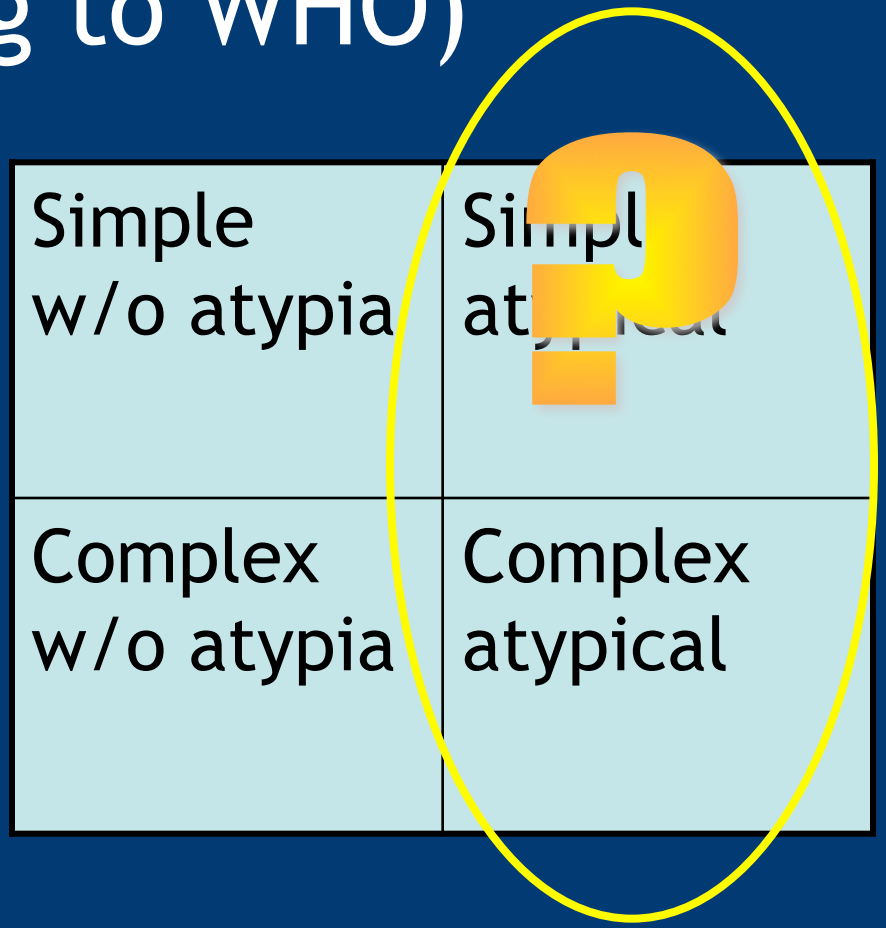
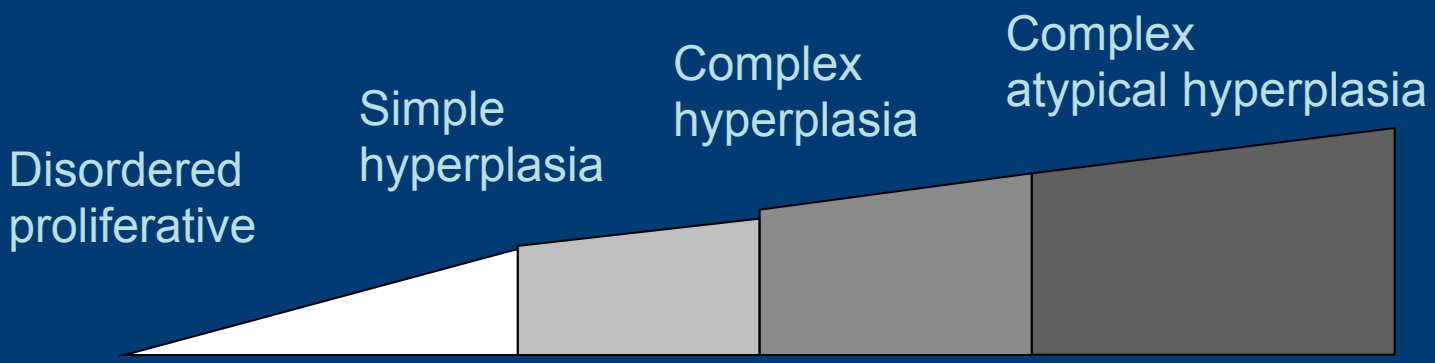


"Atypical Hyperplasia": ~10-fold risk to subsequently develop carcinoma.

Hyperplasia is a *morphologic* classification "assumed to evolve as a progressive spectrum"



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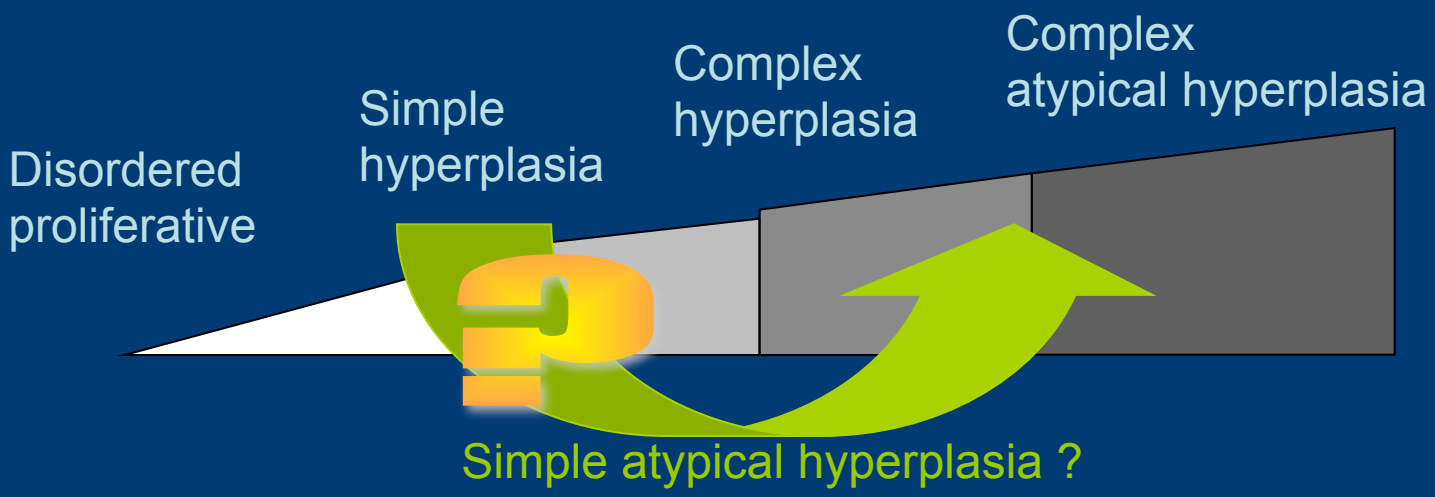

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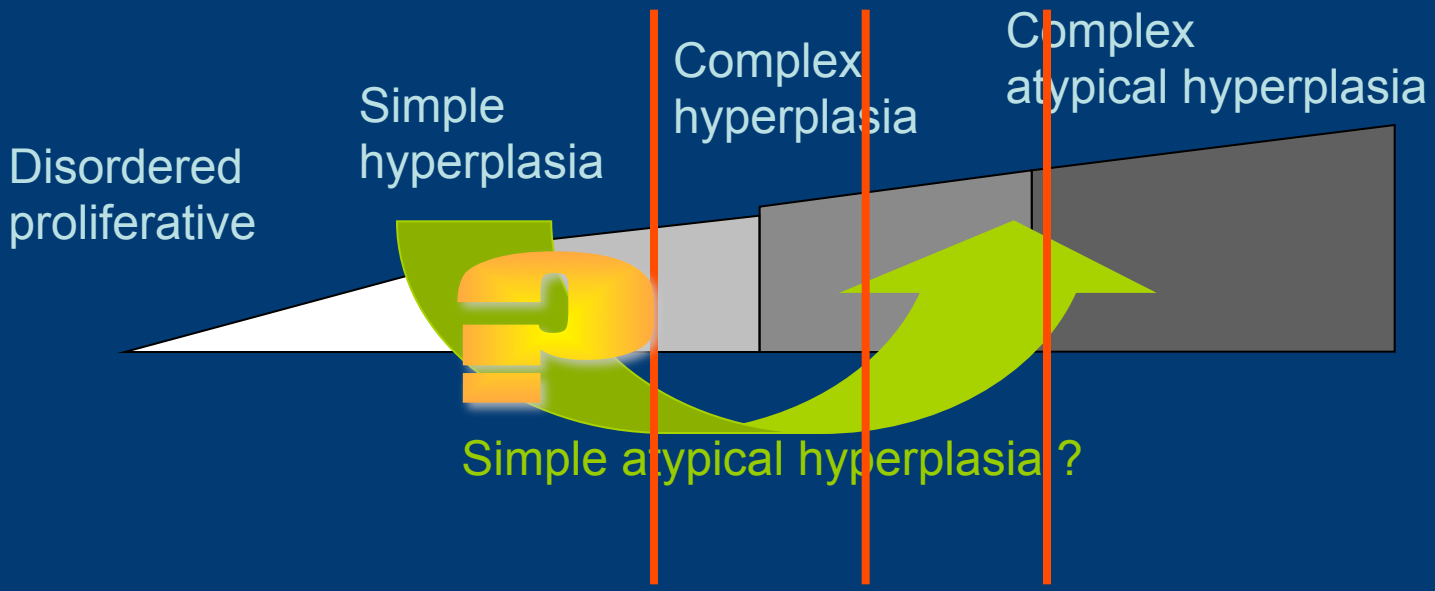

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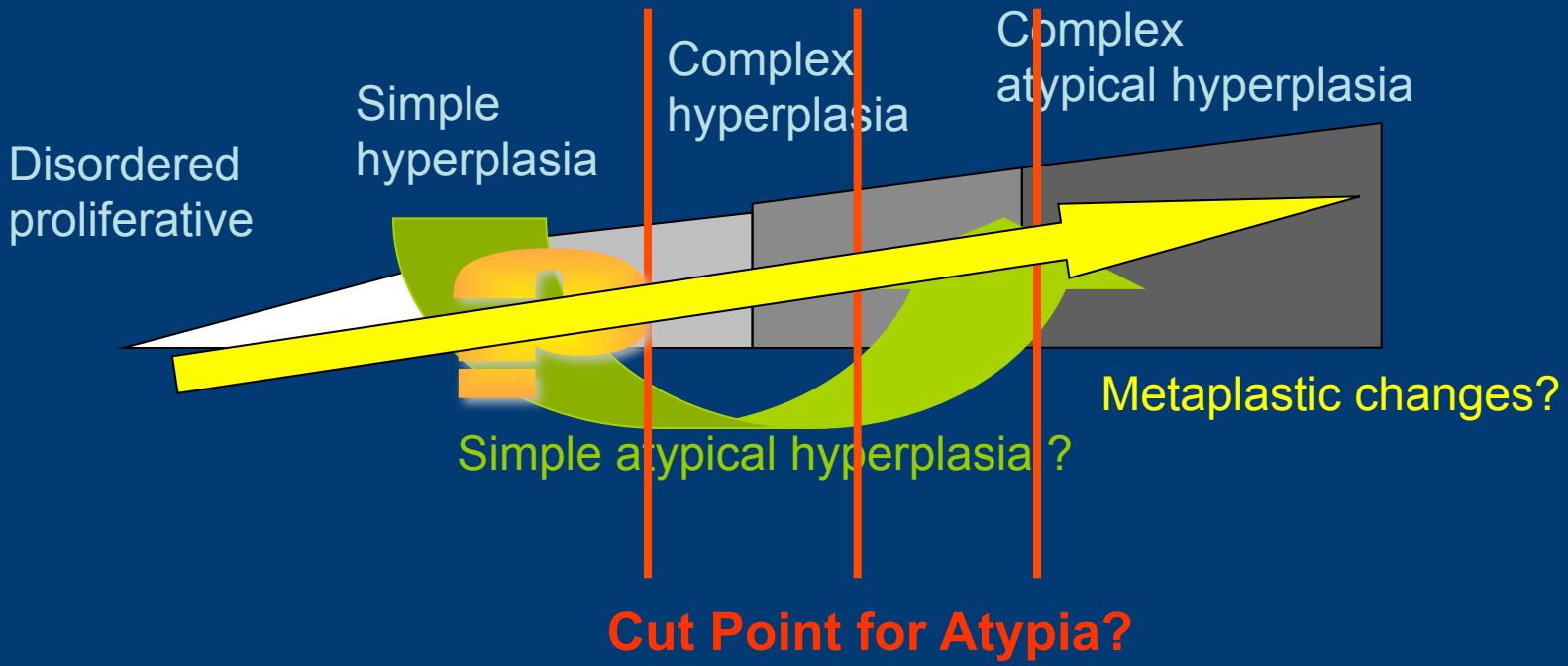


- Reproducibility "somewhat disappointing" (WHO 2003)
- "remains the best available classification" (WHO 2003)

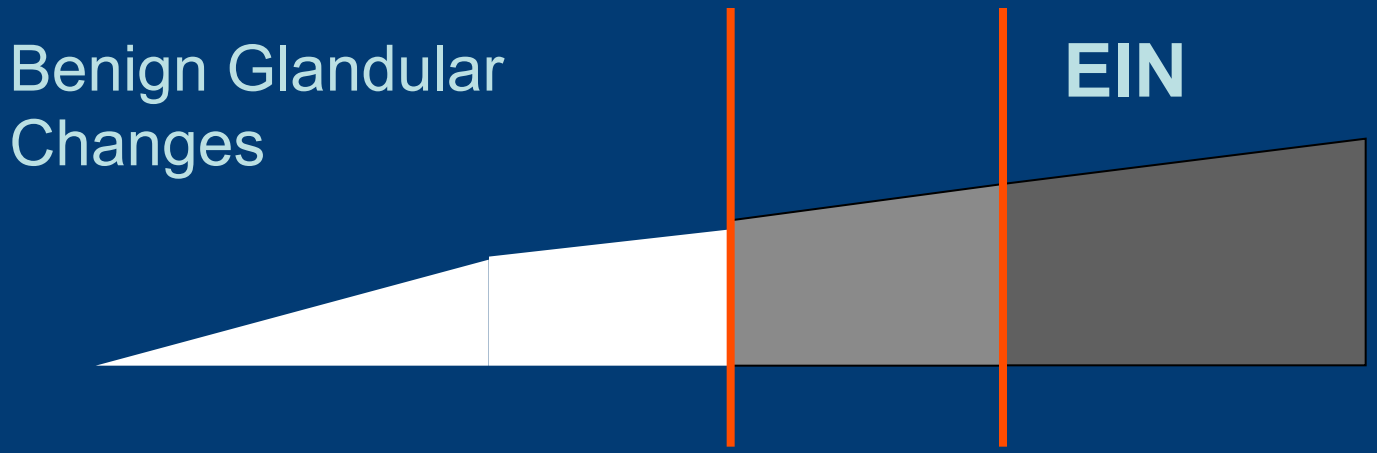
Endometrial Intraepithelial Neoplasia (EIN)

- A premalignant endometrial lesion meeting a set of reproducible diagnostic criteria

- Gland area greater than stromal area
- Cytologic difference relative to background
- Size > 1 mm
- Exclude benign and malignant mimics

See also: Mutter GL, Baak JA, Crum CP et al., J Pathol 2000
And also: www.endometrium.org

EIN is a *biological* classification with a distinct morphologic cut-point



- Criteria based on correlation studies using morphometric image analysis and PTEN evaluation

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(See also www.endometrium.org)

Predictive Power
Atypical Hyperplasia vs. EIN

- Both EIN and atypical hyperplasia are predictive of cancer on subsequent follow-up

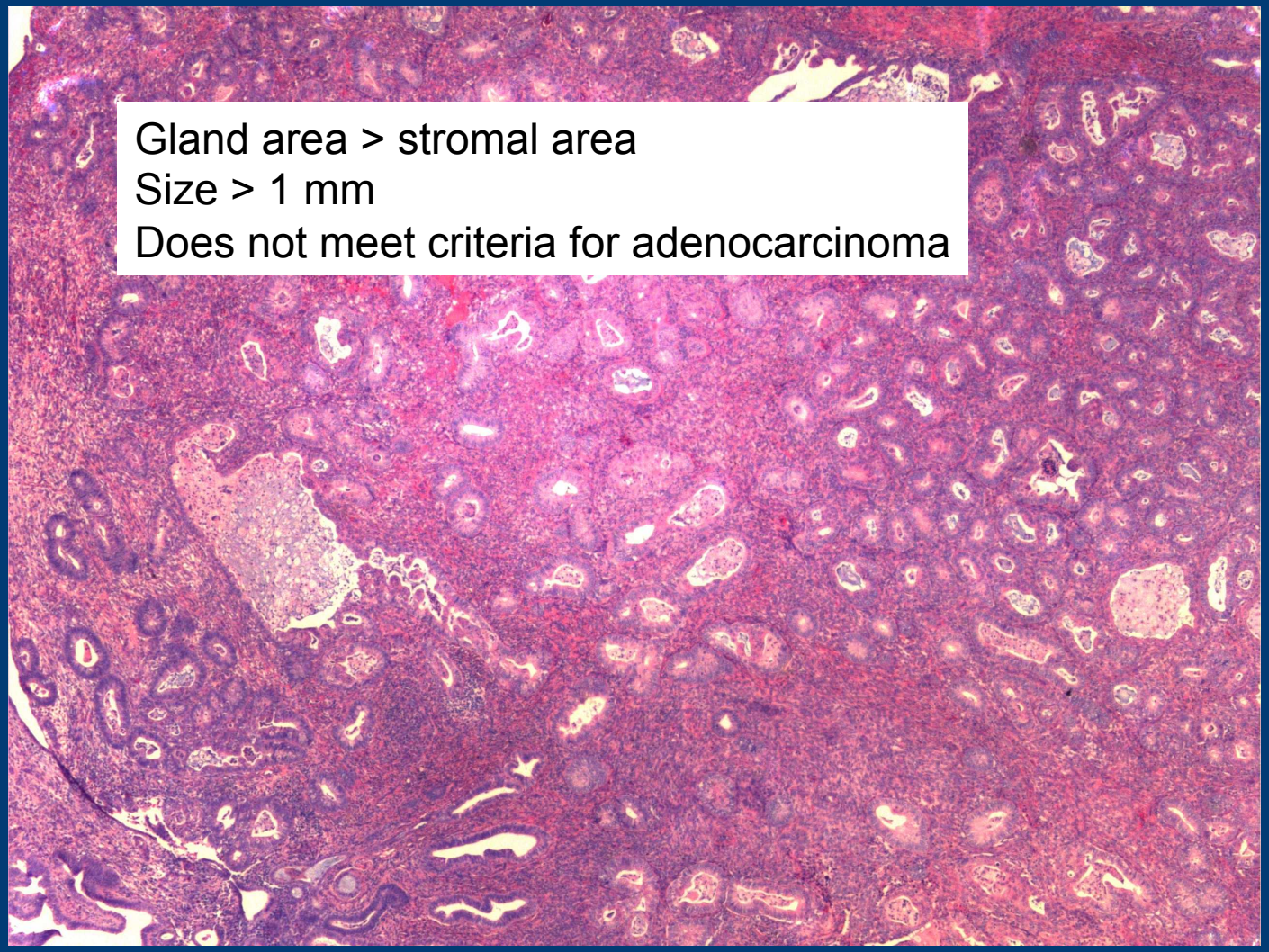
Baak et al., Cancer 2005	AH: RR = 7 EIN: RR= 45
Lacey et al., Cancer 2008	AH: RR = 9.2 EIN/Ca: RR = 9.0

Reproducibility: Atypical Hyperplasia vs. EIN

- EIN Criteria are more reproducible than "atypical hyperplasia"

Kendall et al., Am J Surg Pathol 1998	AH: kappa = 0.47
Zaino et al., Cancer 2006	AH: kappa = 0.34-0.43
Hecht et al., Mod Pathol 2005	EIN: kappa = 0.73-0.90
Usubutun et al., Mod Pathol 2008	EIN: kappa = 0.45-0.84

Case 1



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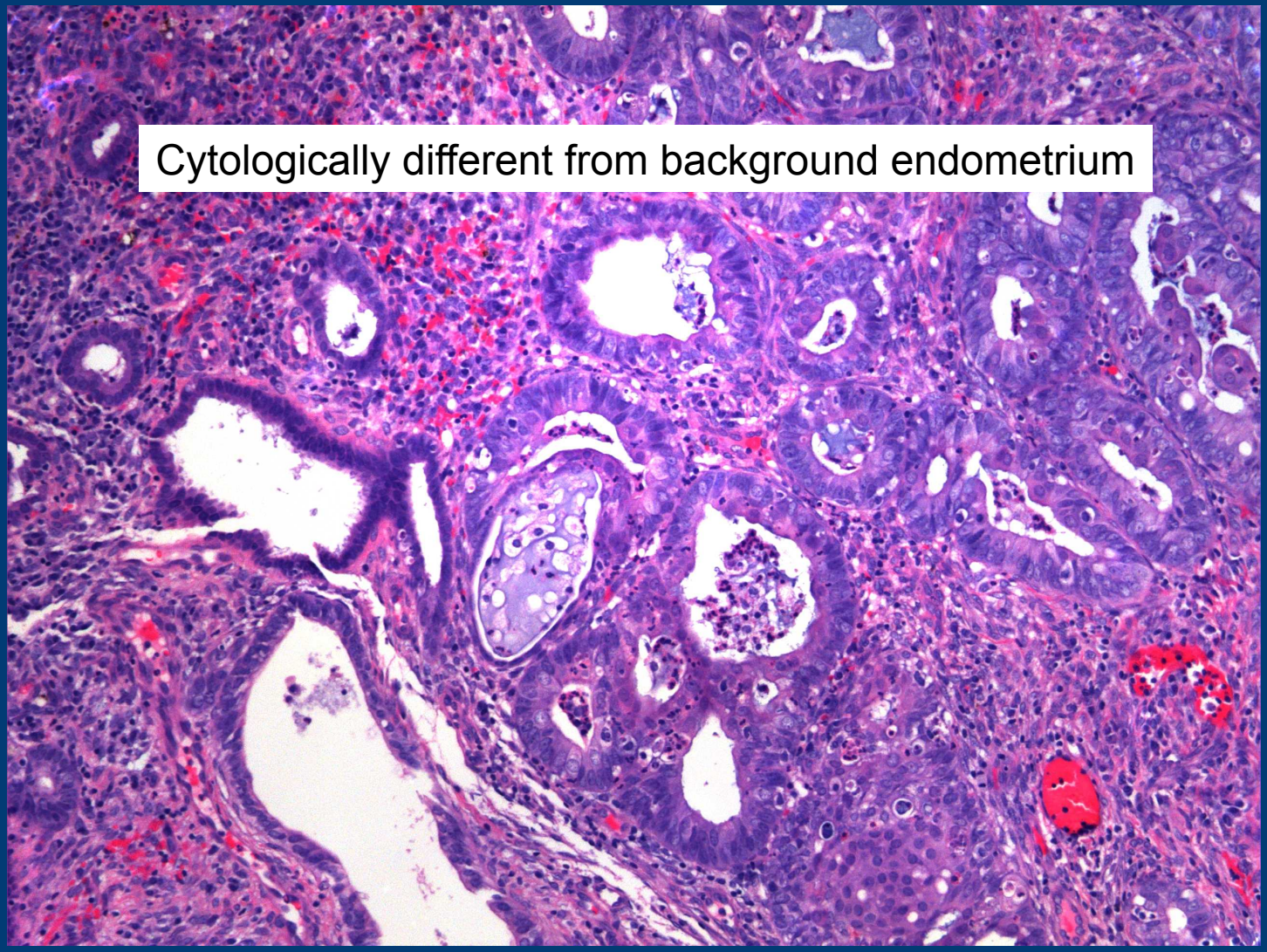

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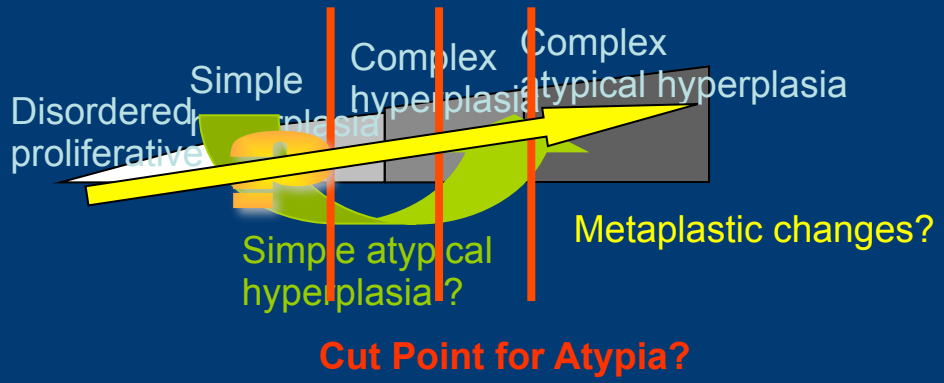
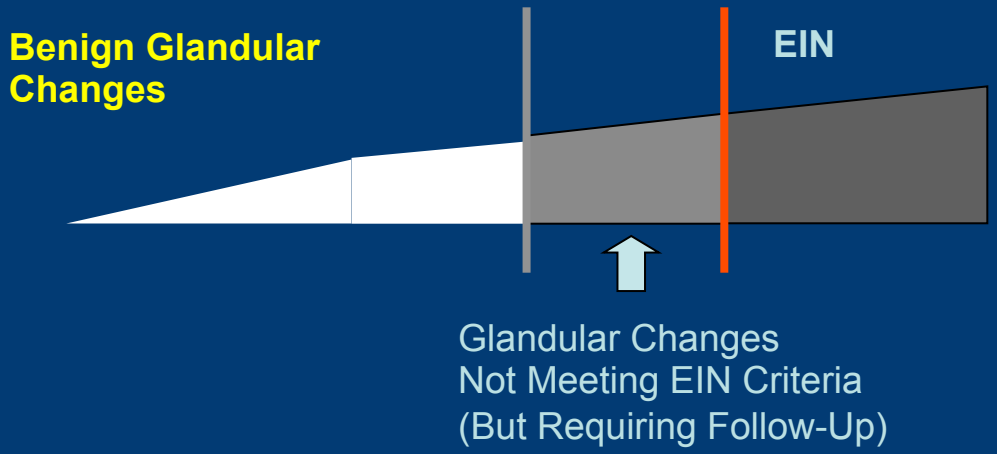
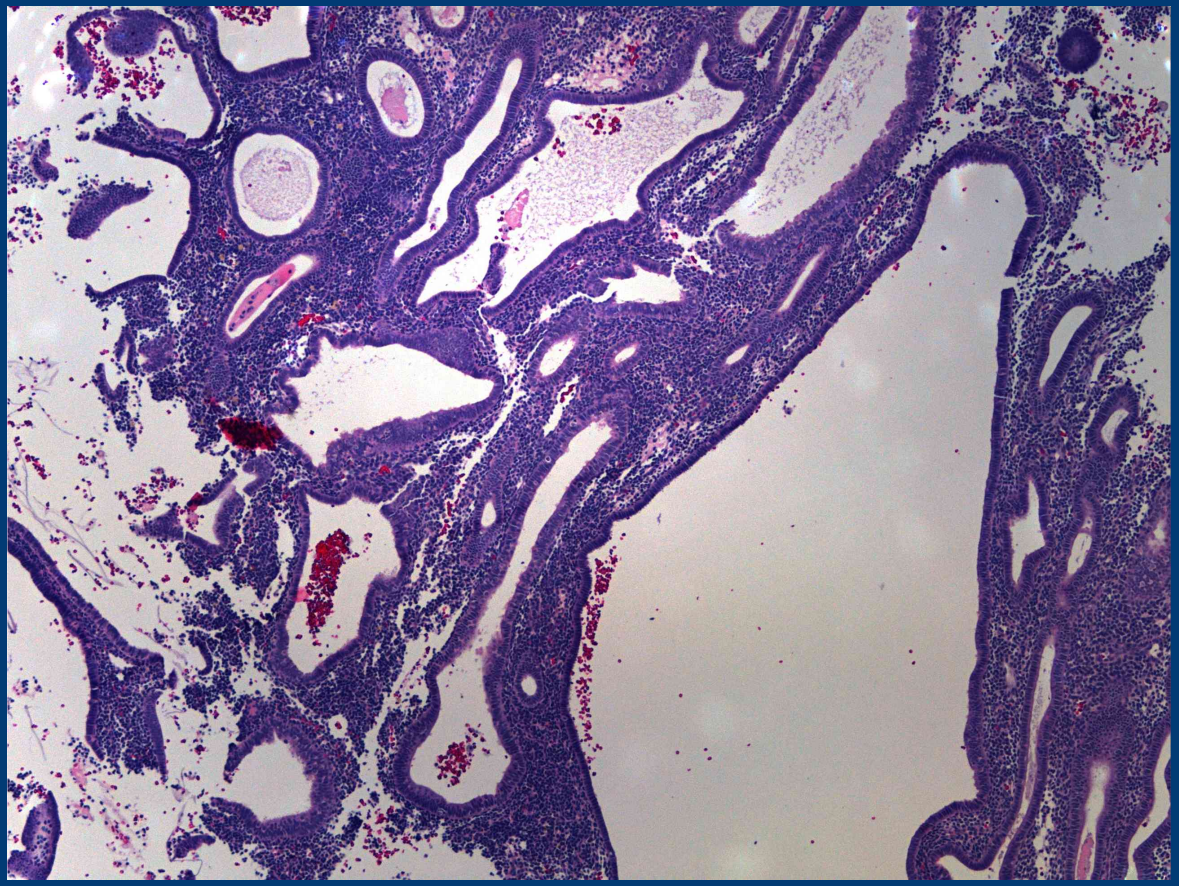
Recap: Hyperplasia vs. EIN





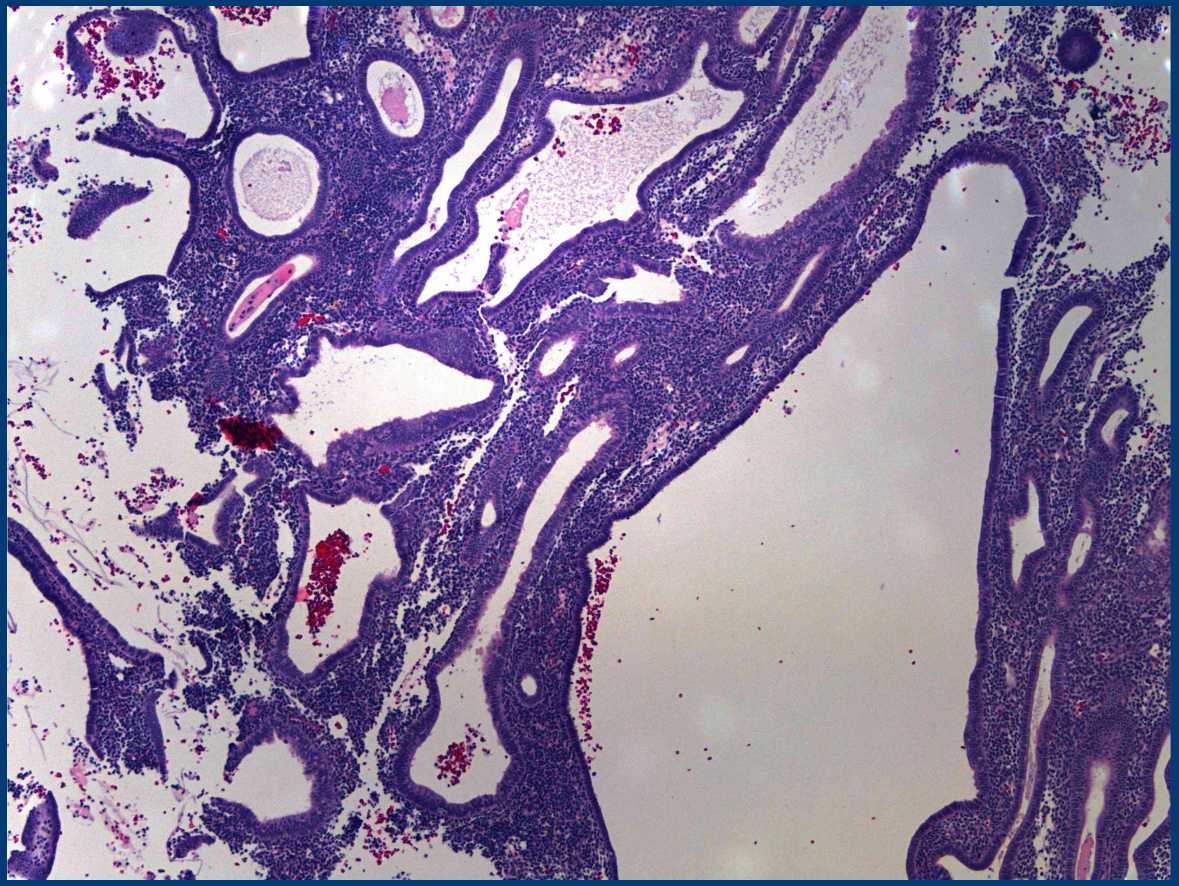
Example: Benign Change



WHO System:
-Simple Hyperplasia?
-Disordered proliferative?

EIN System:
-Classify as benign.
-“Proliferative endometrium with alterations in gland architecture consistent with anovulation”

Example: Benign Change

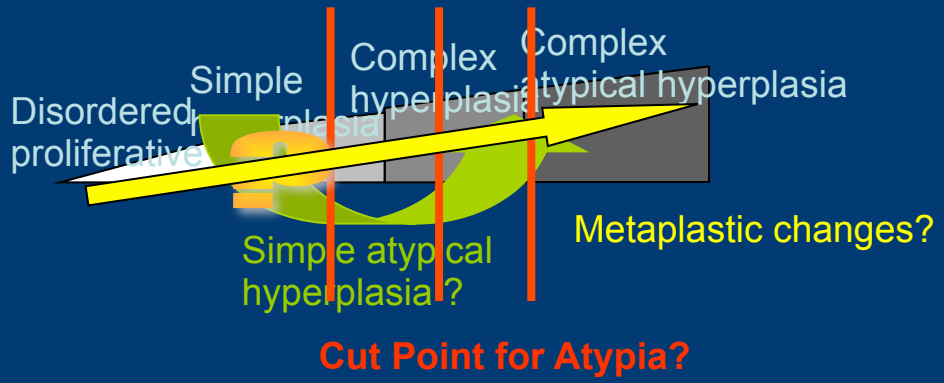


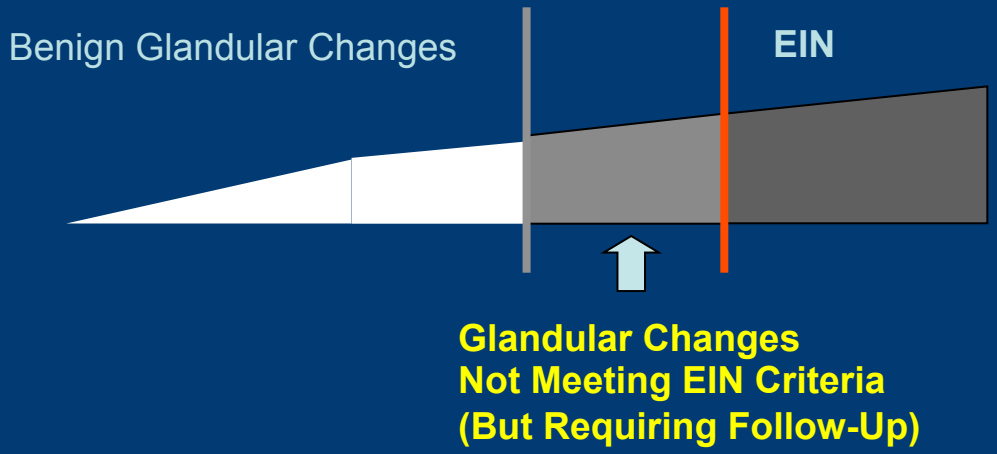
WHO System:
-Simple Hyperplasia?
-Disordered proliferative?

EIN System:
-Classify as benign.
-“Proliferative endometrium with alterations in gland architecture consistent with anovulation”

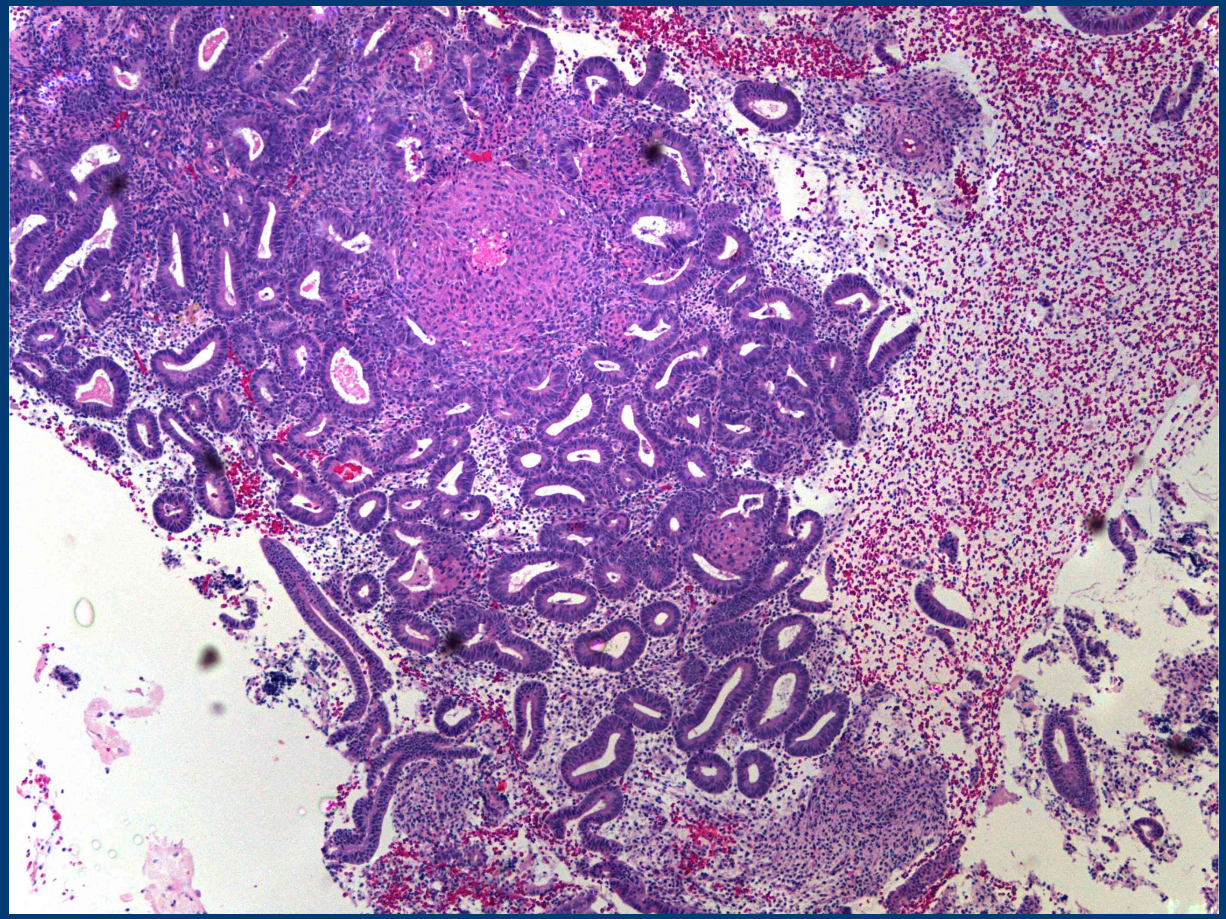
Suggestion:
Do what your clinicians understand, but do not use “concerning” terminology.

Recap: Hyperplasia vs. EIN





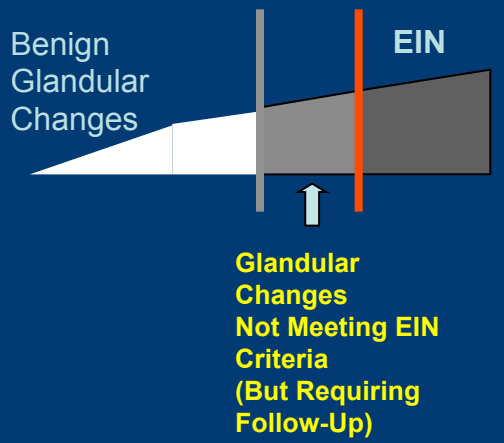
Example: “Complex Hyperplasia”



WHO System:
-Complex hyperplasia
(with squamous morules)

"Concerning" Lesions That do not meet EIN Criteria

Pattern	Risk	Recommend
Papillary synctitial metaplasia, simple metaplastic lesions	Low	Routine clinical
Atypical surface repair ("PSM with stratification")	Unclear	Rebiopsy (4-6 mo)
Squamous morular metaplasia (With or without crowding)	Mod	Rebiopsy (6 mo)
Complex tubal metaplasia	High	Treat as AH/EIN
Mucinous metaplasia with complex growth	High	Treat as AH/EIN



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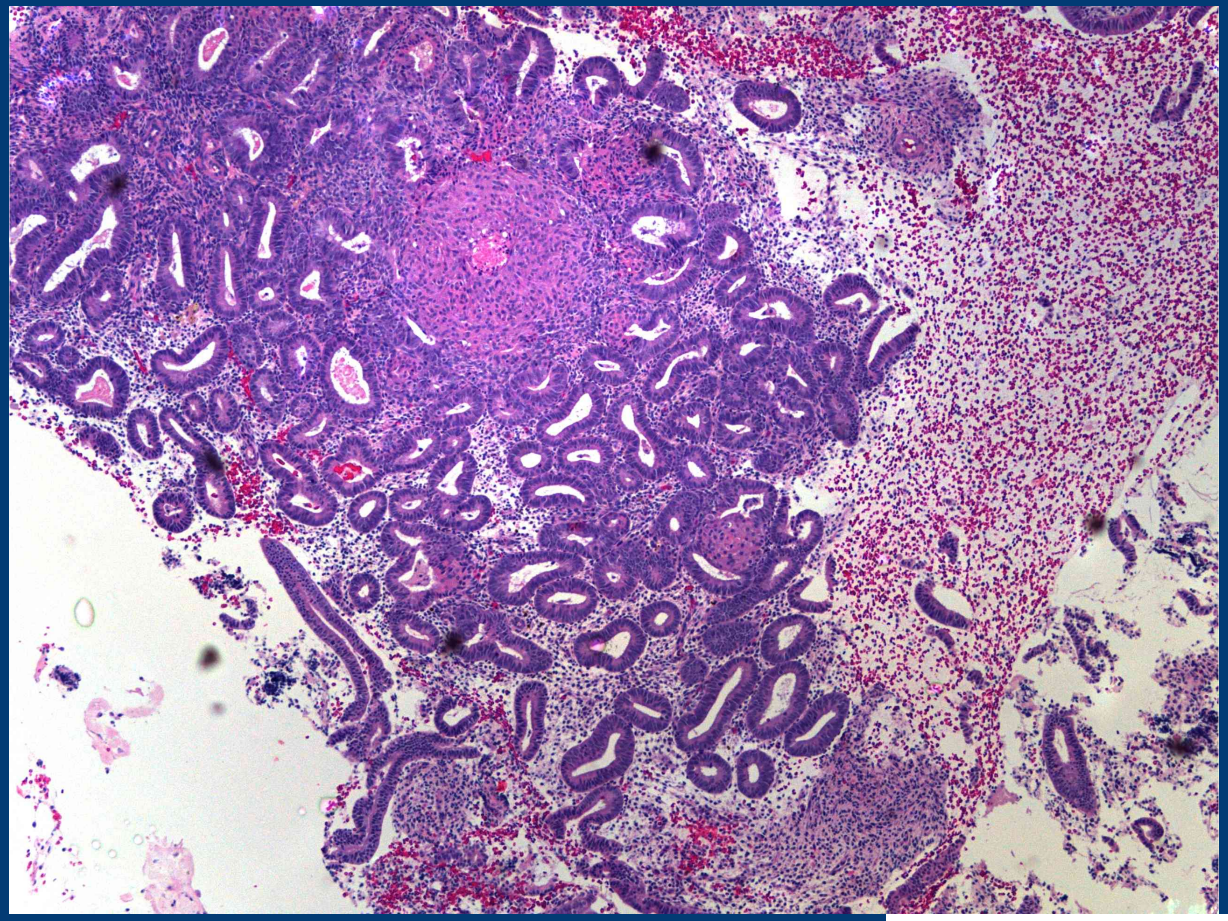
See also: Crum, Nucci, Mutter in:
Diagnostic Gynecologic and Obstetric Pathology

Example: “Complex Hyperplasia”

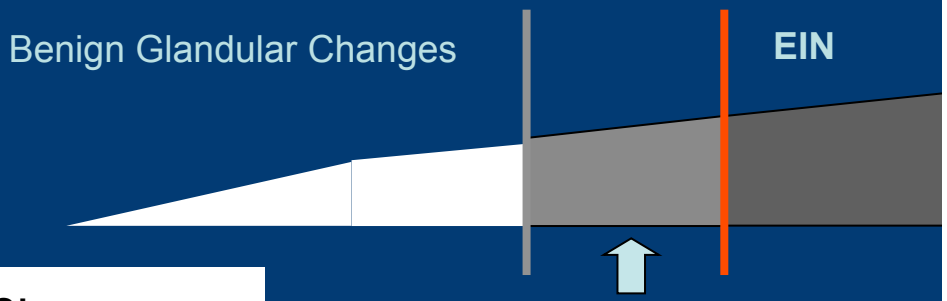


WHO System:
-Complex hyperplasia (with squamous morules)

EIN System:
- “Proliferative endometrium, with gland crowding and squamous morular metaplasia. Recommend repeat biopsy in 6 mo.”
-Does **not** meet EIN Criteria, but needs follow-up.

Not all “complex hyperplasias” are created equal. If EIN criteria are not met, evidence-based recommendation based on descriptive pattern is warranted.

A (Highly Simplified) EIN User's Guide



EIN:
Ensure criteria are met.
Call "atypical (complex) hyperplasia" or EIN (if clinicians understand).

Benign Changes:
Avoid calling "hyperplasia".
Use reassuring terminology and/or descriptors

Glandular Changes
Not Meeting EIN Criteria
(But Requiring Follow-Up)

Evidence-based recommendation based on descriptive pattern.
Usually involves rebiopsy.

These cases are relatively rare.
Consider sending for consultation.

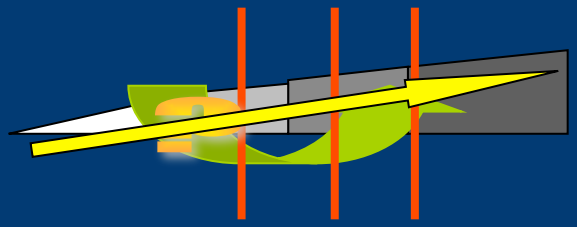
Multiple Choice

Which scheme of representing cancer risk do you prefer?

Multiple Choice

Which scheme of representing cancer risk do you prefer?

1.



2.

Multiple Choice

Which of the following do you consider most correct?

Multiple Choice

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Multiple Choice

Which of the following do you consider most correct?

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Atypical Hyperplasia vs EIN

- Both are H&E diagnoses
  (no role for IHC, except *rarely* to r/o serous ca)
- AH and EIN both predict cancer risk on follow-up
- EIN is more reproducible than AH
- AH is still more widely used and recognized.
- But EIN can be learned!!

Acknowledgements

- Dr. George Mutter
- Dr. Christopher Crum
- Dr. Marisa Nucci