Adenocarcinoma of the Cervix: In Situ vs Invasive Including Subtypes

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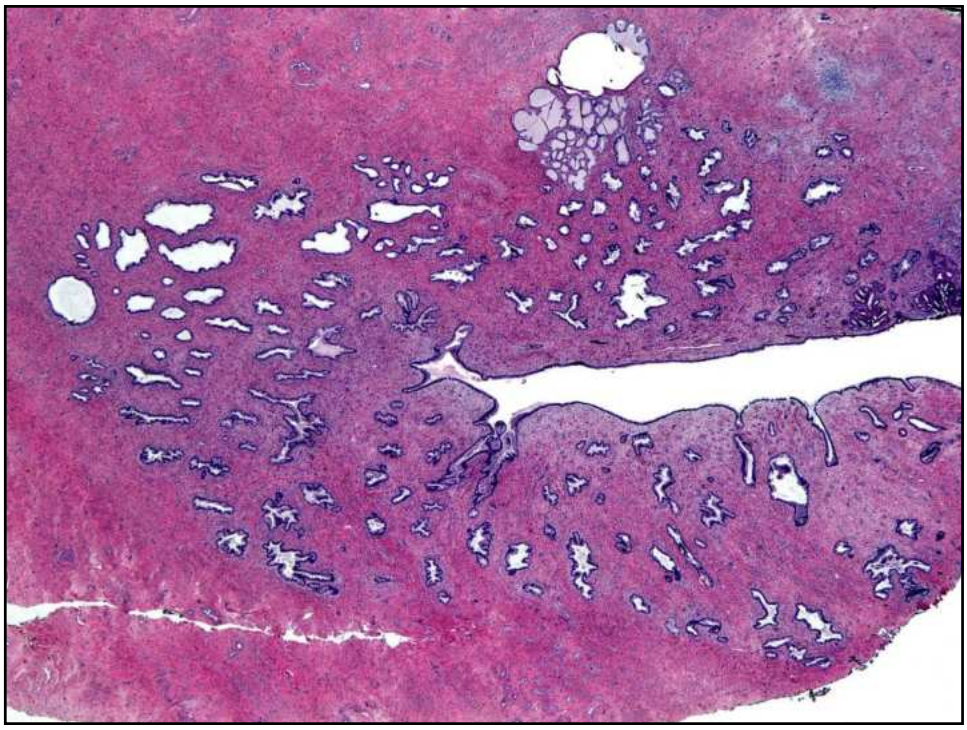
Cervical Adenocarcinoma

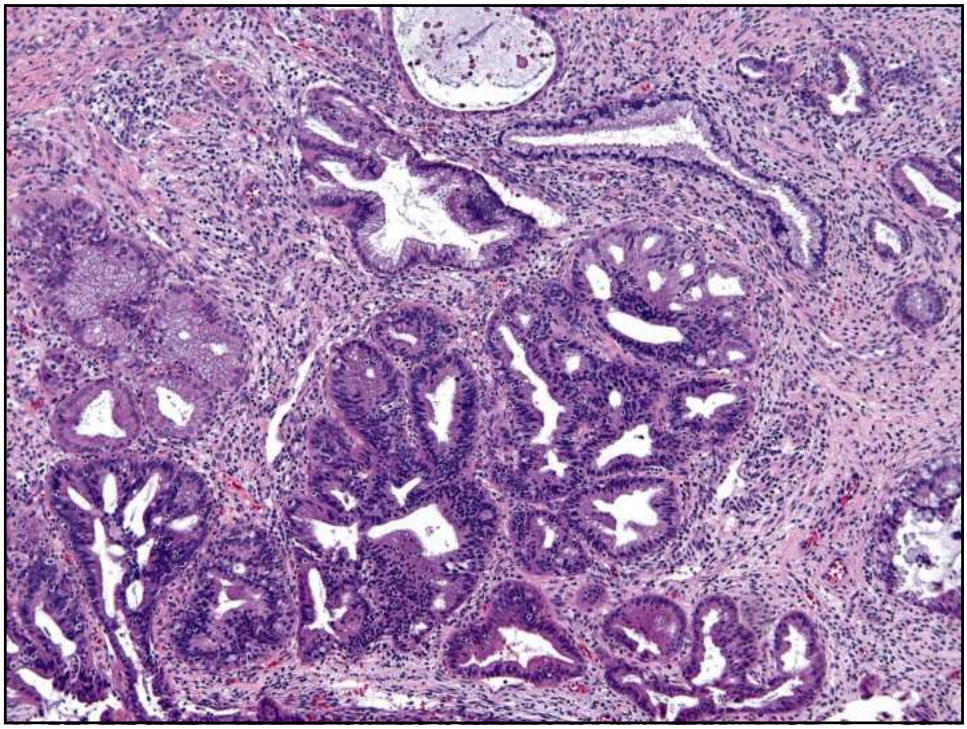
- Is it invasive?
- Size of tumor (vs in situ)
- Subtypes
- The pathology report

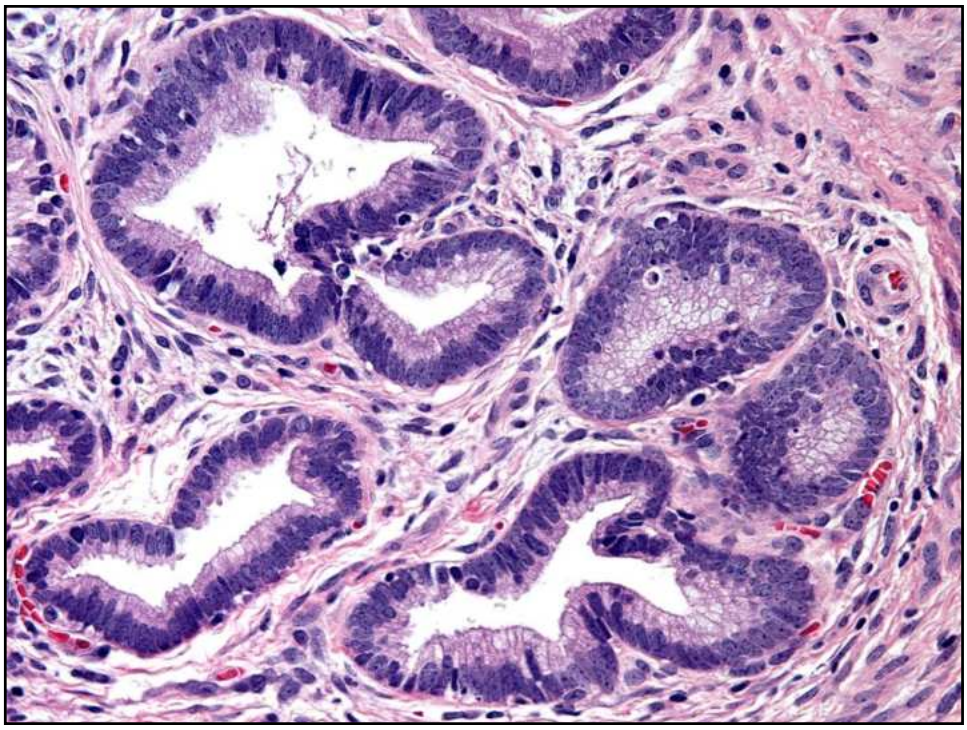
Is It Invasive?

- AIS
- Invasive adenocarcinoma (Silva)

50- year- old postmenopausal female undergoes cold knife cone for abnormal Pap test. No lesions are visible on colposcopy at time of cone. (photomicrographs of cone)







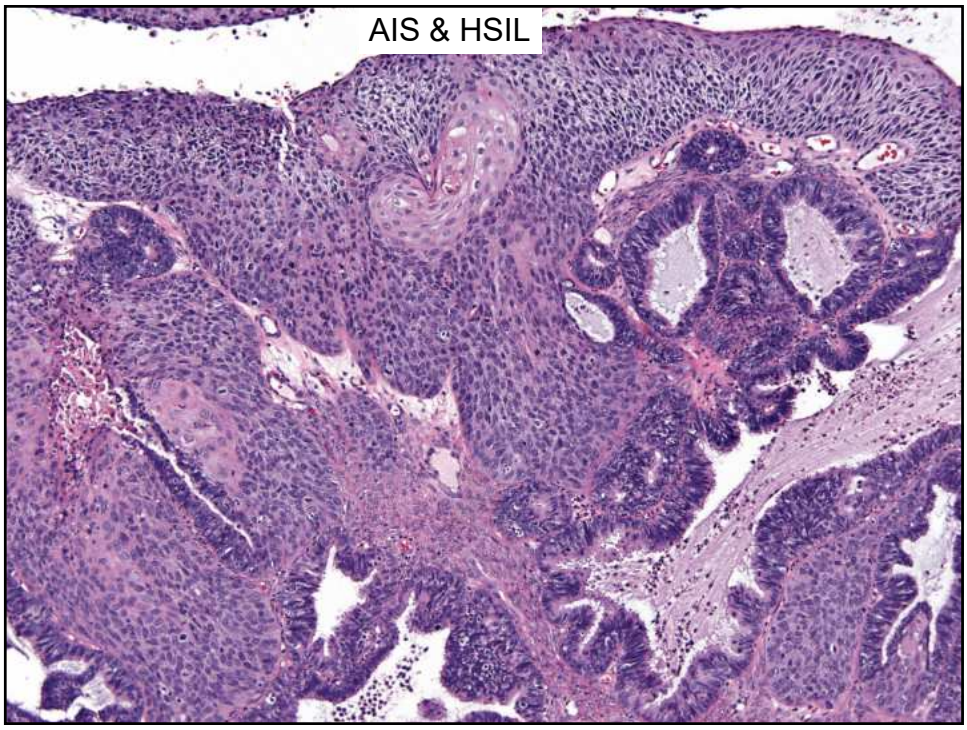
ADENOCARCINOMA IN SITU

Adenocarcinoma In Situ (AIS)

- Wide age range, but most common during the reproductive years (mean age, 37 years)
- Diagnosed in women 10-15 years younger than those with invasive CA
- Risk factors similar to those for squamous intraepithelial lesions (SIL)

Adenocarcinoma In Situ (AIS)

- Most women are asymptomatic.
- AIS is often identified during evaluation for an abnormal cervical cytology or biopsy performed for SIL.
- Most have no colposcopic abnormality
- Approximately 50% not visualized due to presence high in the endocervical canal



Adenocarcinoma In Situ (AIS)

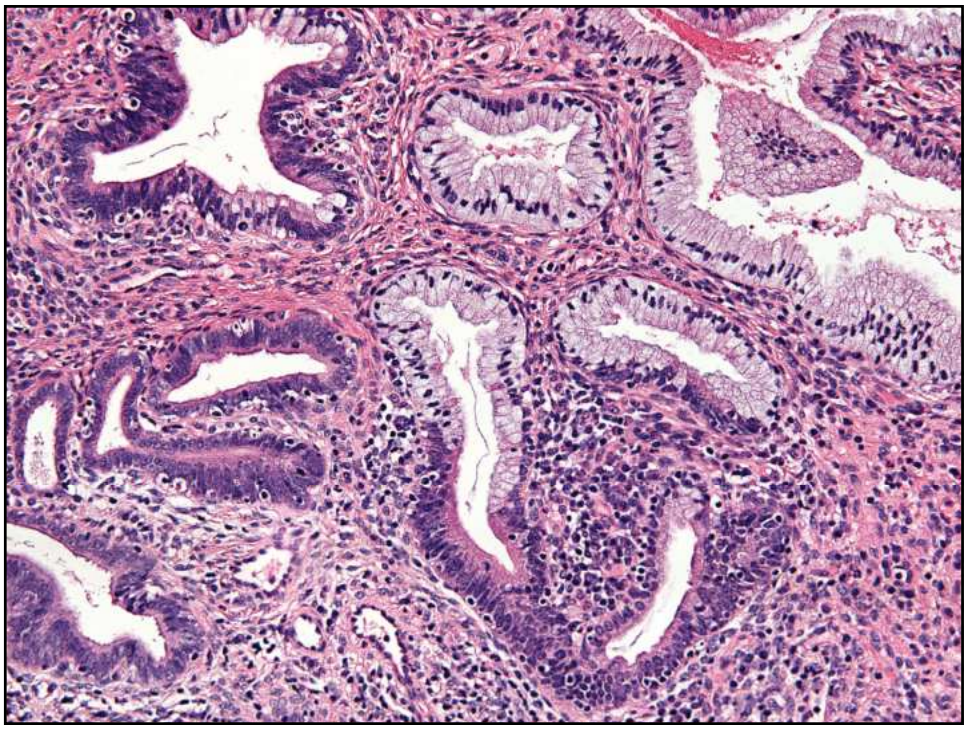
- Associated with SIL ~50% AIS
- Arises in transformation zone, extends contiguously, but irregularly – but rarely more than 2.5 cm in extent
- Multifocality can be seen, but has been over-emphasized

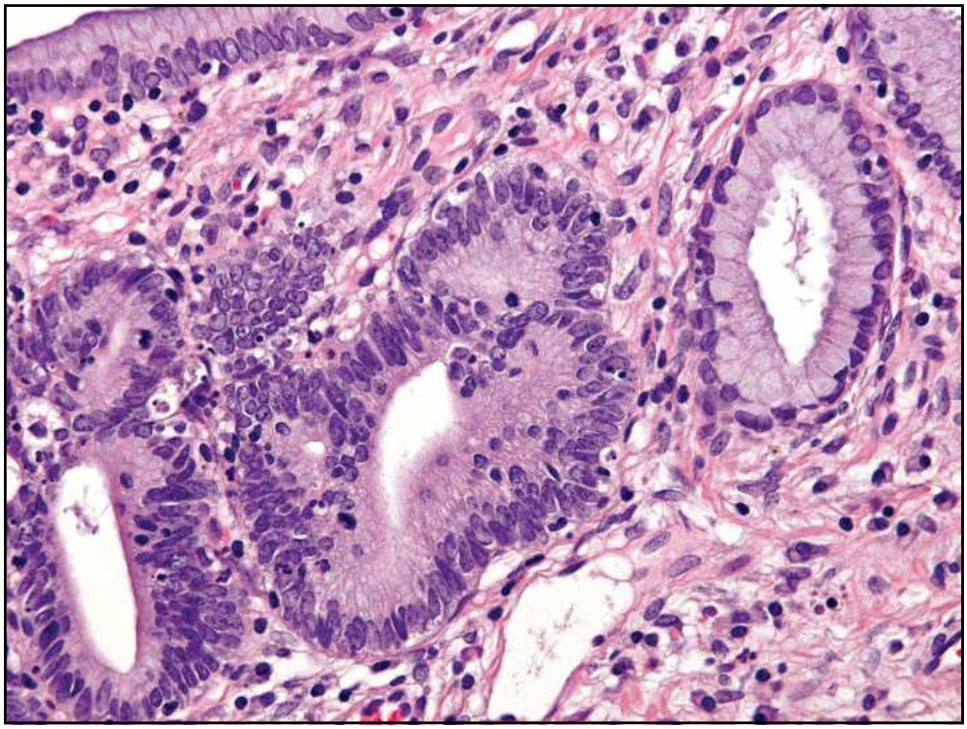
Adenocarcinoma In Situ (AIS)

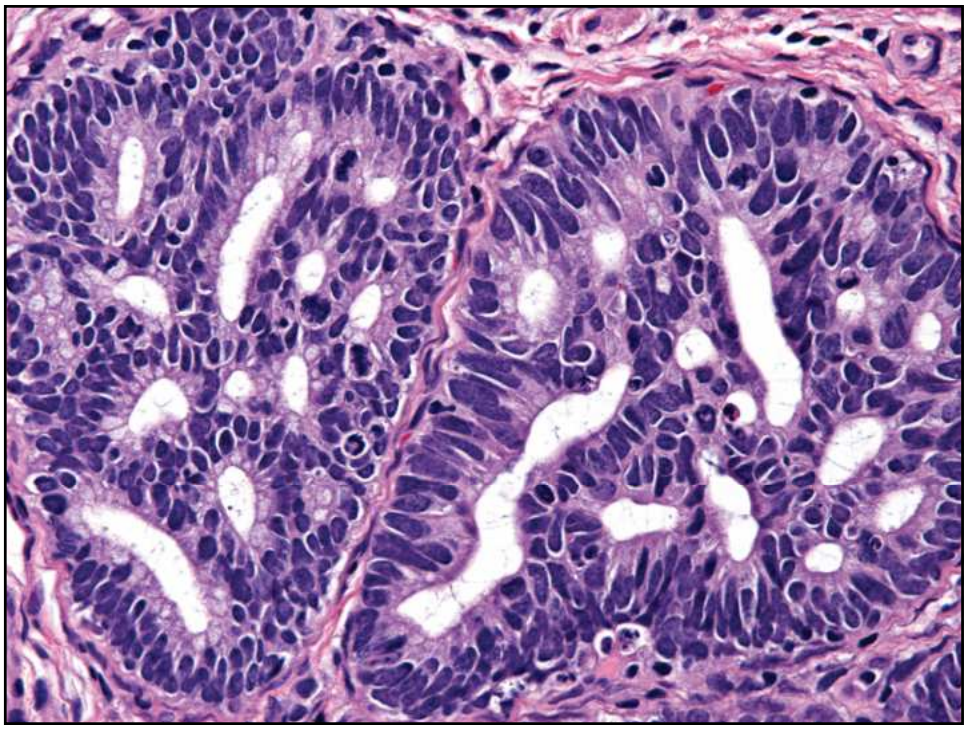
- Look for darker, more basophilic glands with abrupt transition from normal mucinous epithelium
- High power
  - Floating (luminal) mitoses; apoptotic bodies
  - Enlarged and elongate nuclei; irregular
  - Crowding and stratification; loss of polarity
  - Nuclear hyperchromasia - fine or coarsely granular chromatin

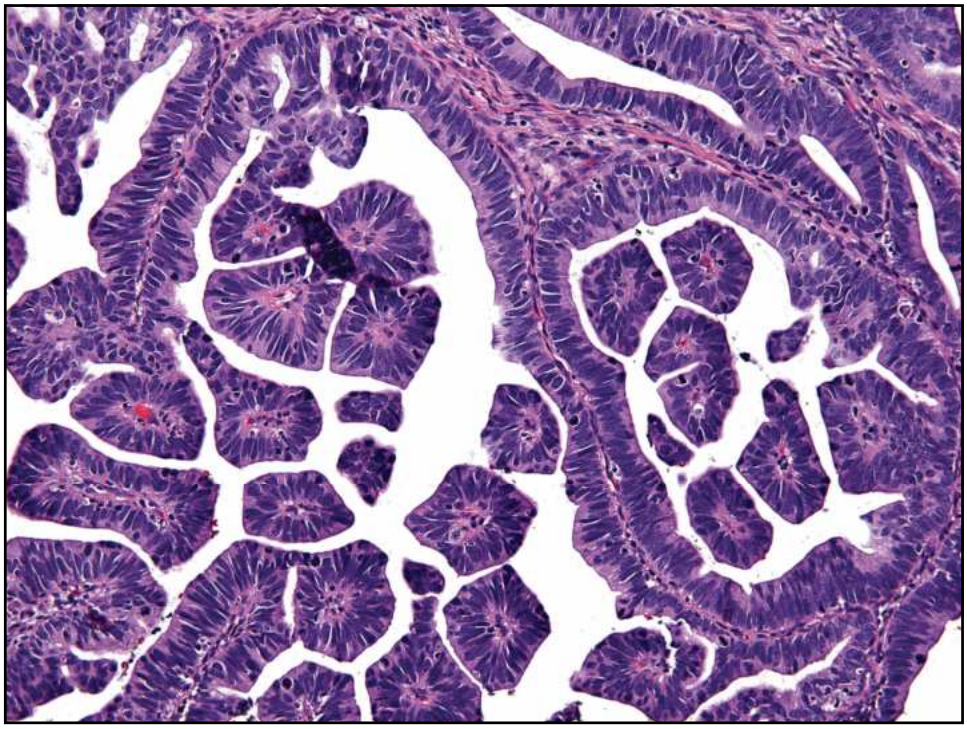
Adenocarcinoma In Situ (AIS)

- Preservation of lobular architecture, but
- Glands may be larger, more numerous and generally more pronounced than adjacent normal glandular lobular units
- Jagged infiltration is not present
- Cytoplasm may be pale, mucinous (small droplets or full blown goblet cells), or eosinophilic





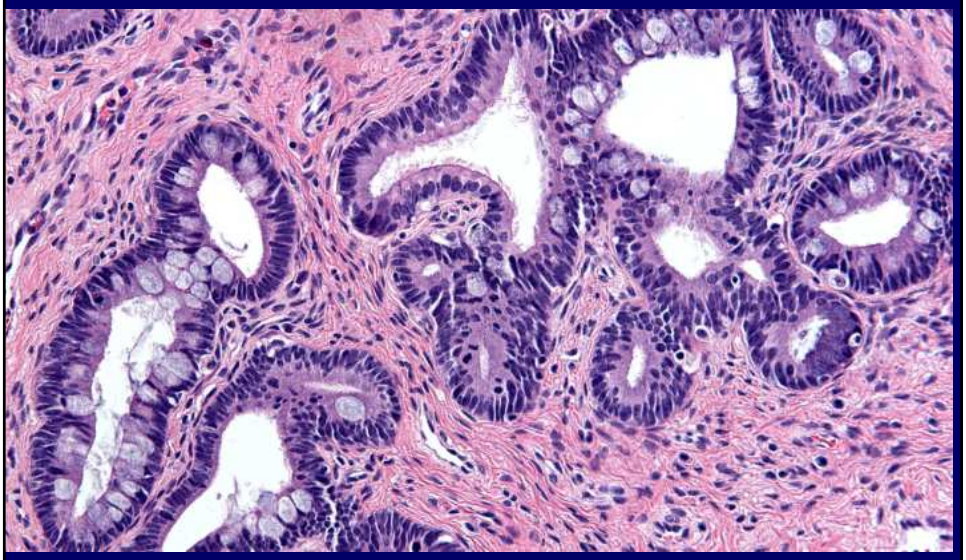




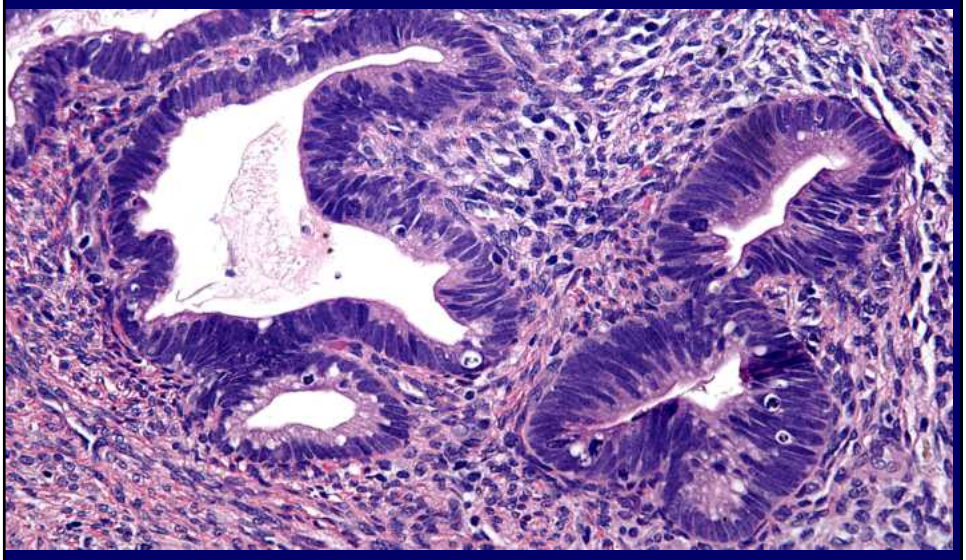
AIS Types

- Usual (mucinous) type: majority
- Intestinal (goblet cell) type
- Mucin-depleted (endometrioid) type
- Tubal or ciliated type
- Poorly differentiated or stratified type
- Superficial or early

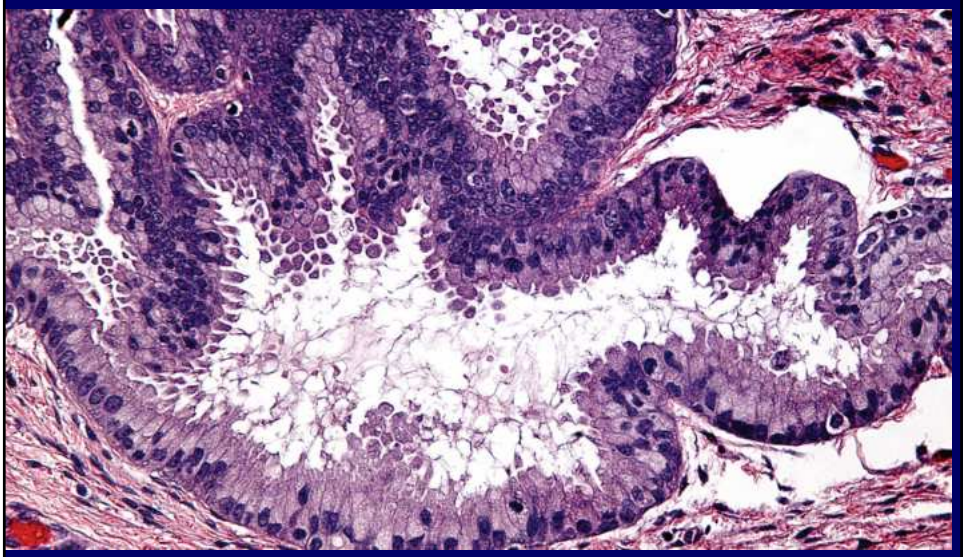
Goblet cell (intestinal differentiation)



Mucin-depleted (“endometrioid”)



Tubal or ciliated



Superficial ('Early') AIS

- May appear 'stuck-on' or patch-like
- Similar cytologic features of usual AIS
- May be more common in younger age group (mean, 26 years)
- Significance not established, but may be very focal; possible relationship to unexplained AGUS

Borderline Lesions: A Case for Dysplasia?

- There are glandular lesions that exhibit some but not all the features of AIS
- Some, but by no means all, of these lesions are associated with AIS, HSIL, or invasive adenocarcinoma
- These lesions appear to occur at a younger age and may harbor high-risk HPV, suggesting they may be precursor lesions of AIS
- However, significant interobserver disagreement about diagnosis of "dysplasia"

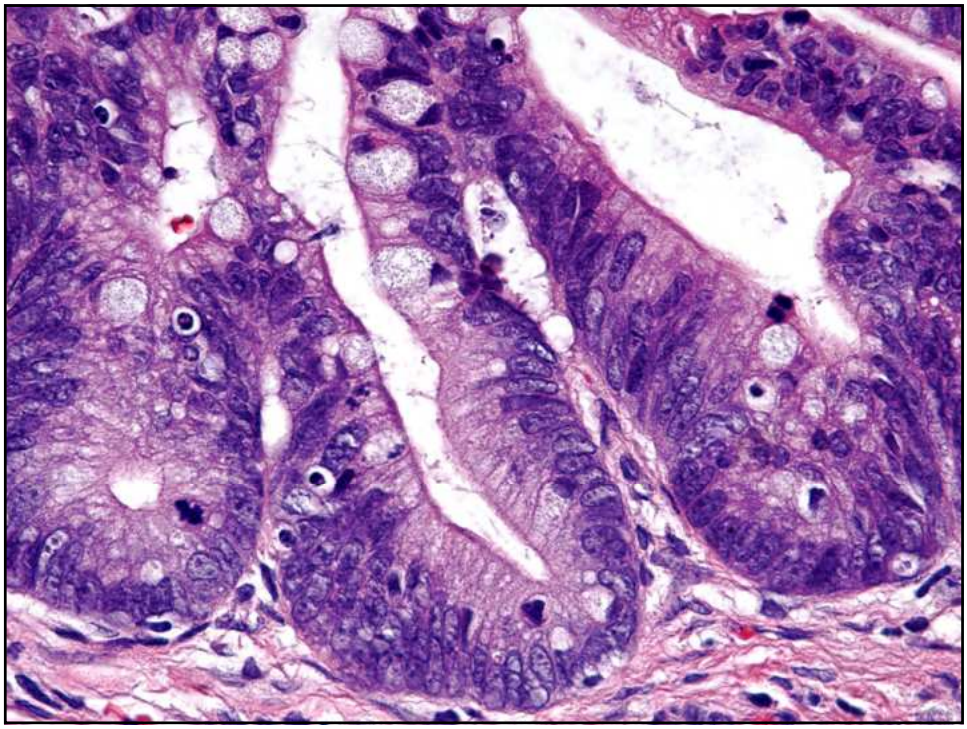
So, What To Do?

Am J Surg Pathol 2003;27:452-460

	0	1	2	3
Stratification	None	Mild	Moderate	Severe
Nuclear atypia	None	Mild	Moderate	Severe
Mitosis + Apoptosis	None	<0.5	0.6-3.0	>3.0

Nuclear enlargement, anisocytosis, hyperchromasia, dyspolarity, nucleoli (at least 2)

Average number per gland in 2 most active glands



Endocervical Glandular Score

Am J Surg Pathol 2003;27:452-460

- Total score 0-3 = benign (kappa=0.6)
- Total score 4-5 = endocervical glandular dysplasia (EGD) (kappa=0.6)
- Total score 6-9 = adenocarcinoma in situ (AIS) (kappa=0.8)

The Downside of Dysplasia

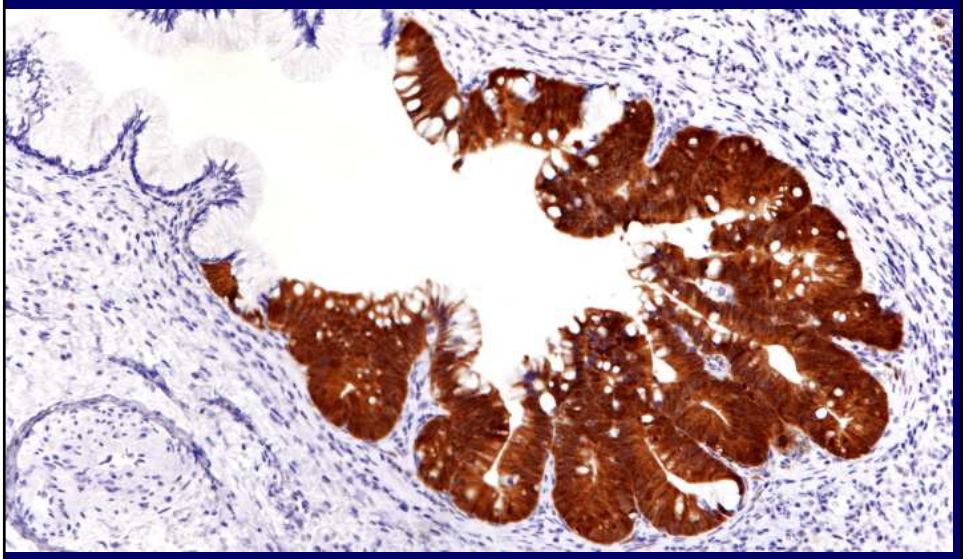
Am J Surg Pathol 2003;27:452-460

- Reproducibility of diagnosis of dysplasia, even with scoring method is at best "good"
- Collapsing benign & dysplasia into one category (benign) gives high concordance (94%)
- Clinical implications, prevalence, progression rate to AIS, & diagnostic criteria not uniformly agreed upon
- Enter "borderline" or "glandular atypia, cannot exclude" diagnosis → ***p16***

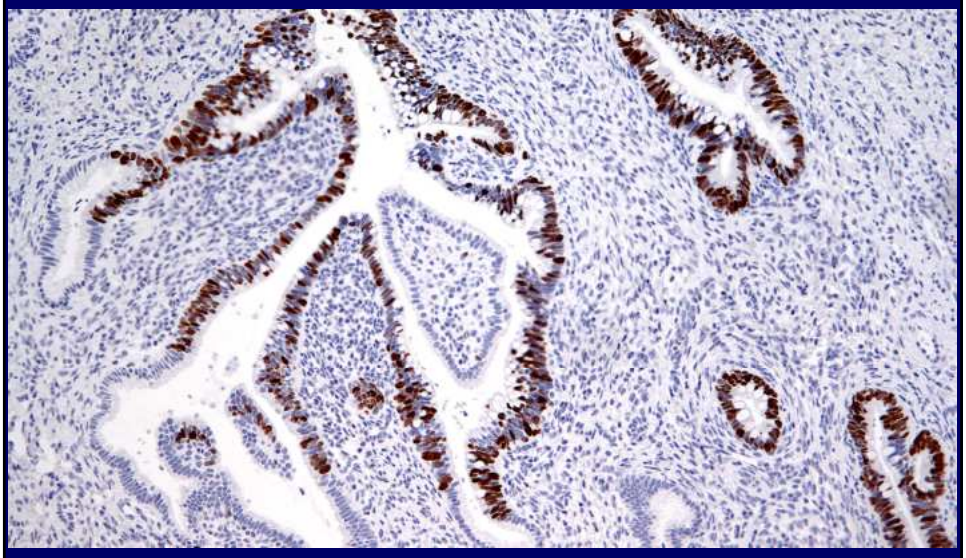
Use of p16 in AIS

- Since AIS is assoc w/ high-risk HPV, AIS demonstrates diffuse, strong expression of p16
- Ki-67 is also elevated & can be used as complimentary marker
- This can be used in confirming diagnosis of AIS in biopsy or curettage samples, but requires experience

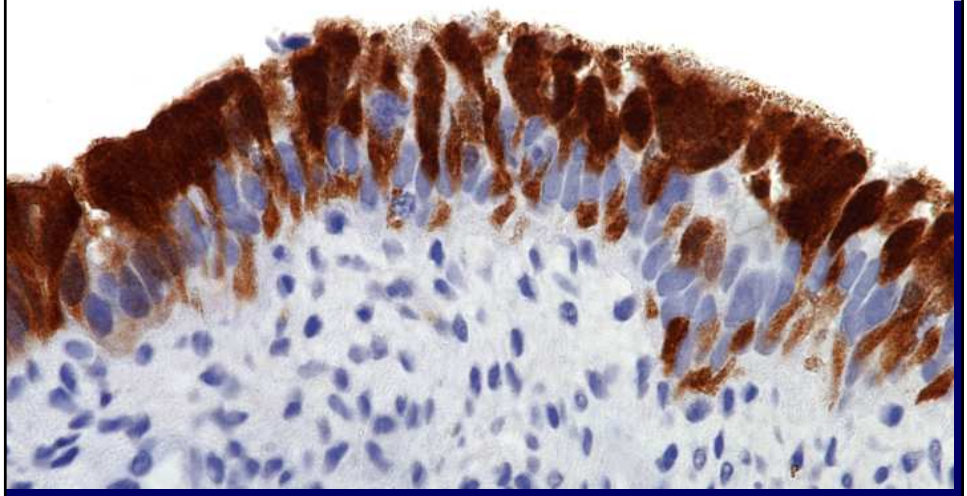
Endocervical Adenocarcinoma in Situ: Positive p16



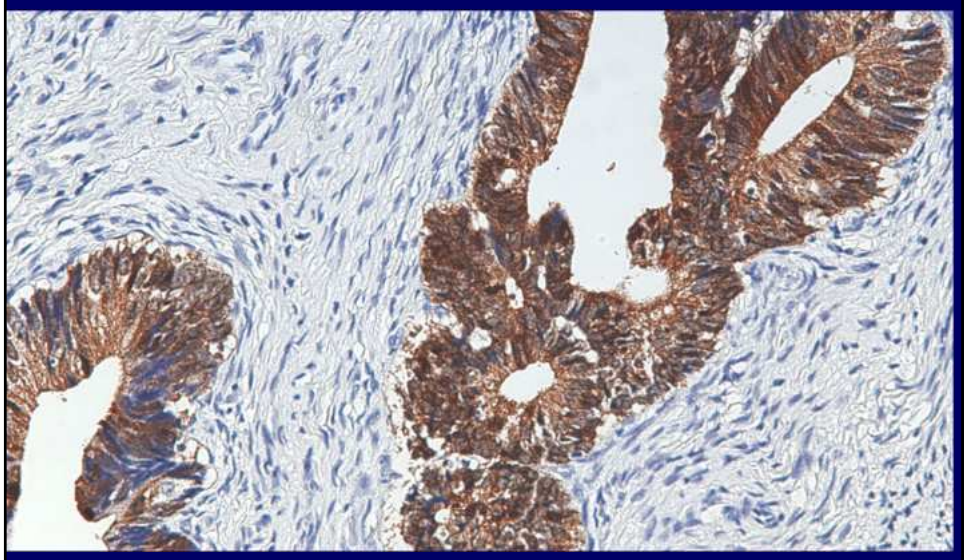
Endocervical Adenocarcinoma in Situ: Ki-67

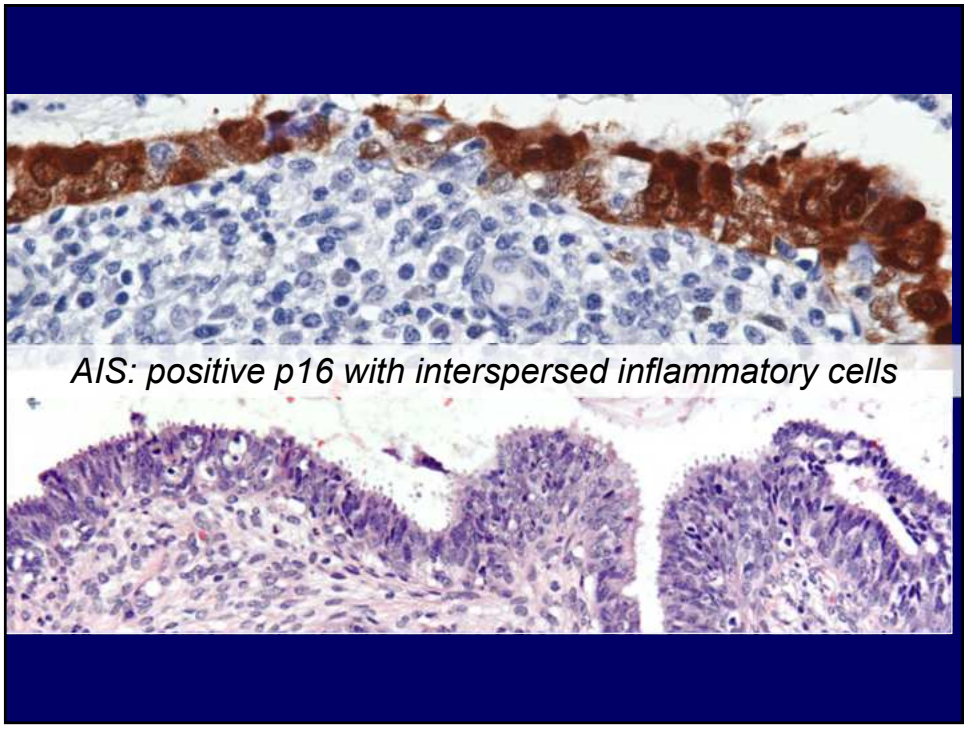


Negative p16

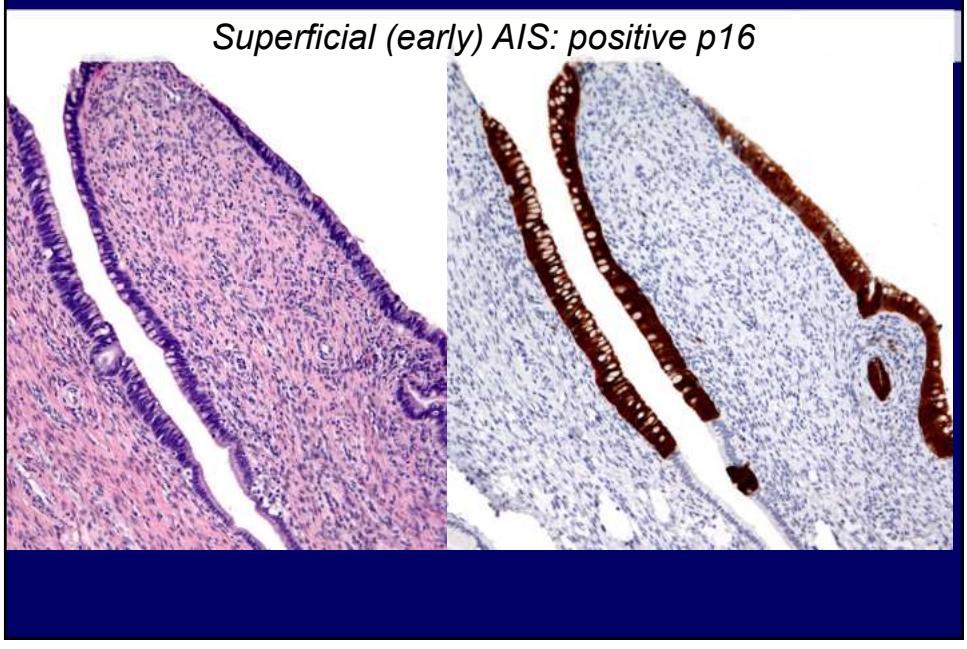


Equivocal p16



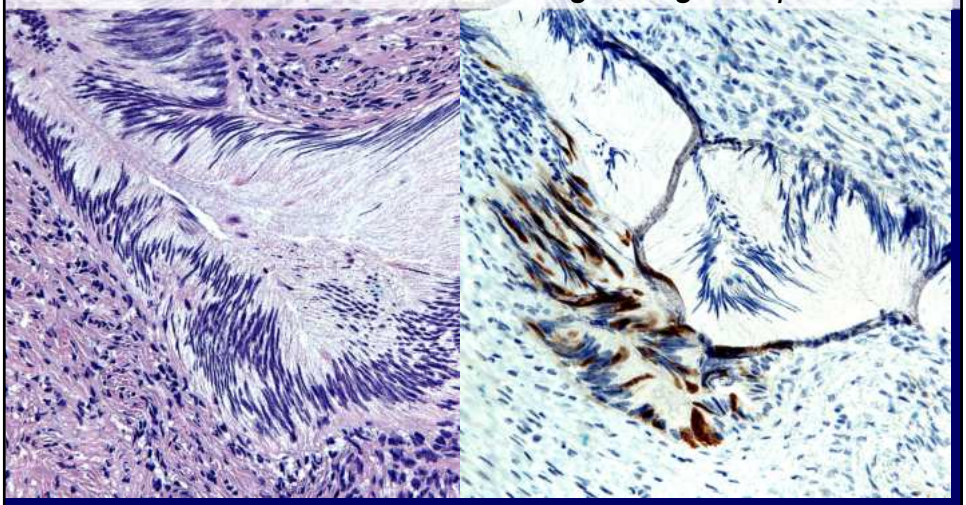


AIS: positive p16 with interspersed inflammatory cells

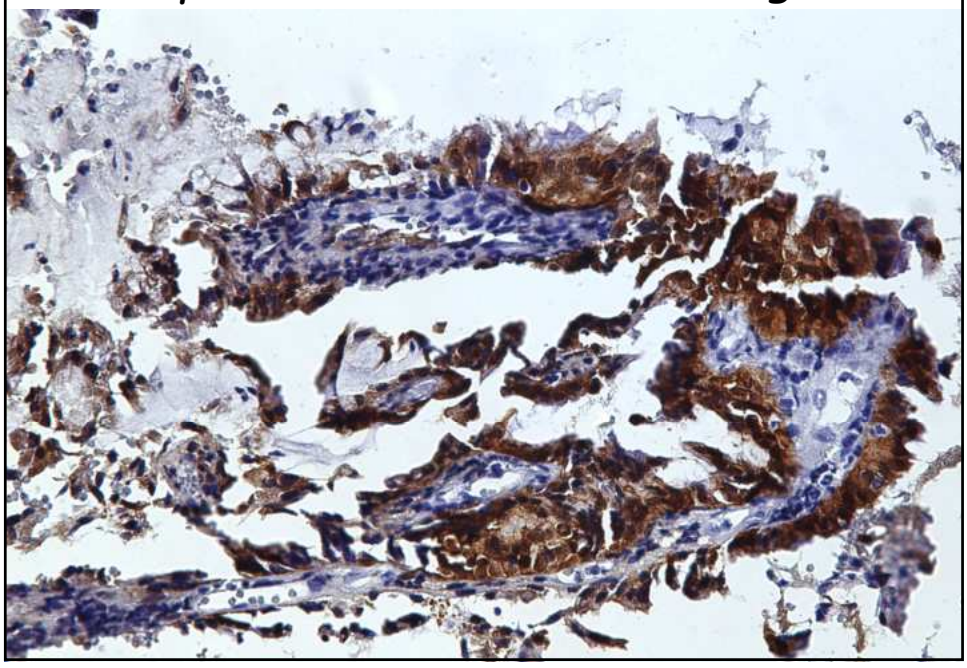


Superficial (early) AIS: positive p16

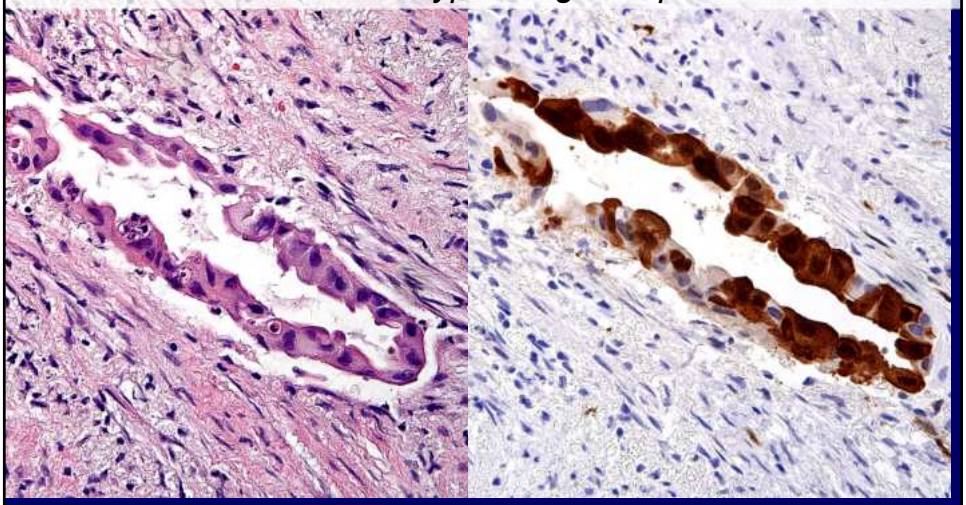
Evaluation of cauterized margin: negative p16



p16 – Endocervical curettage



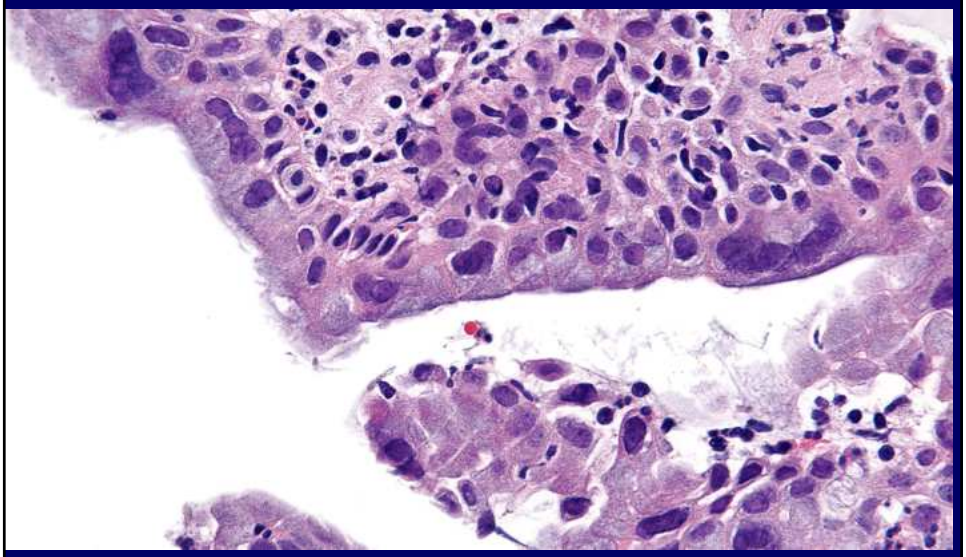
Radiation atypia: negative p16



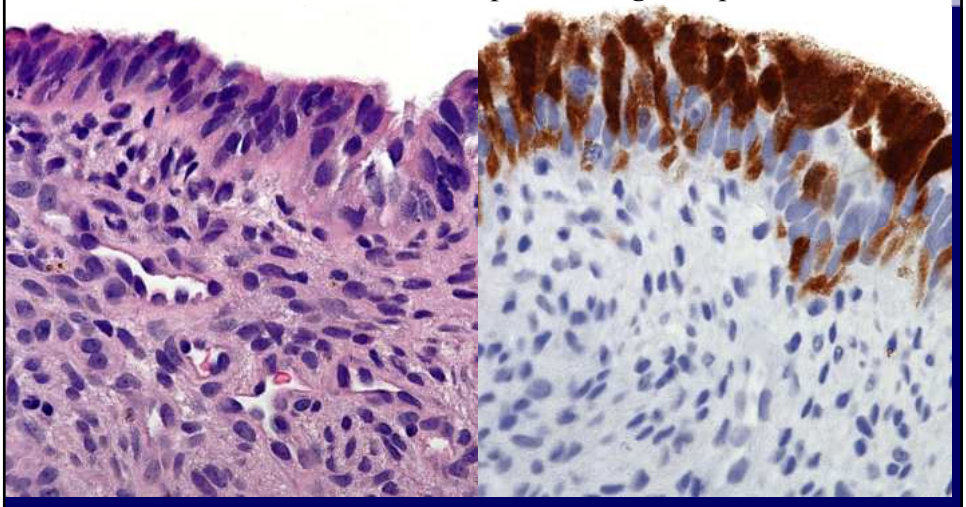
AIS: Differential Diagnosis

- Tuboendometrioid metaplasia
- Cervical endometriosis
- Reactive endocervical atypia
- Endocervical glandular hyperplasia
- Mitotically active endocervical mucosa
- Stratified endocervical mucosa
- Other: radiation, viropathic effect, some hormones

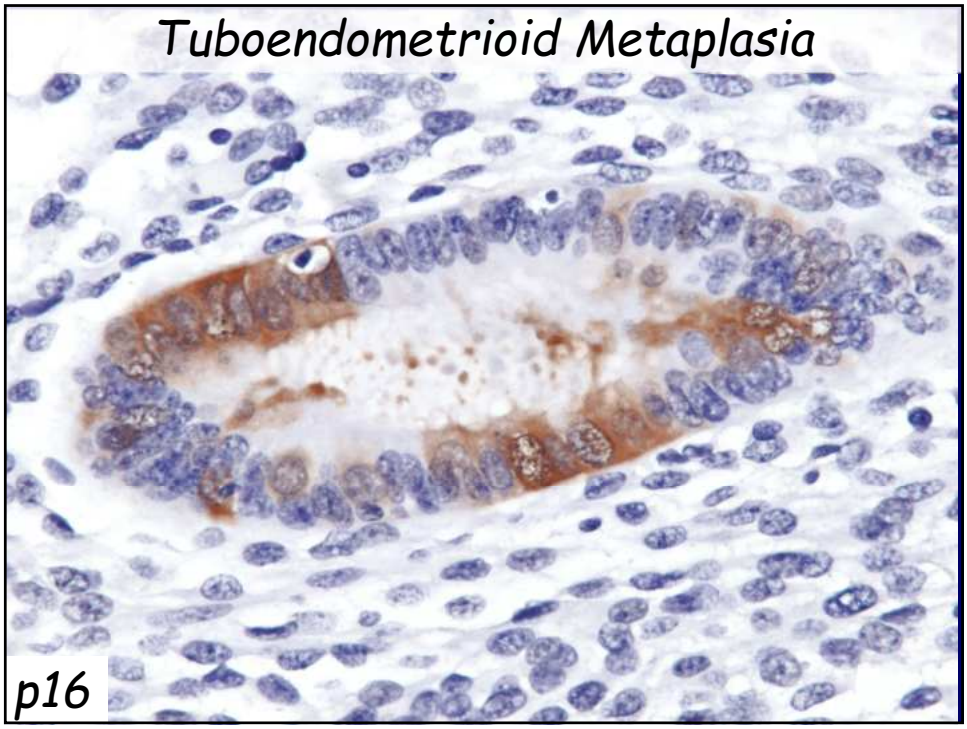
Reactive Endocervical Cells



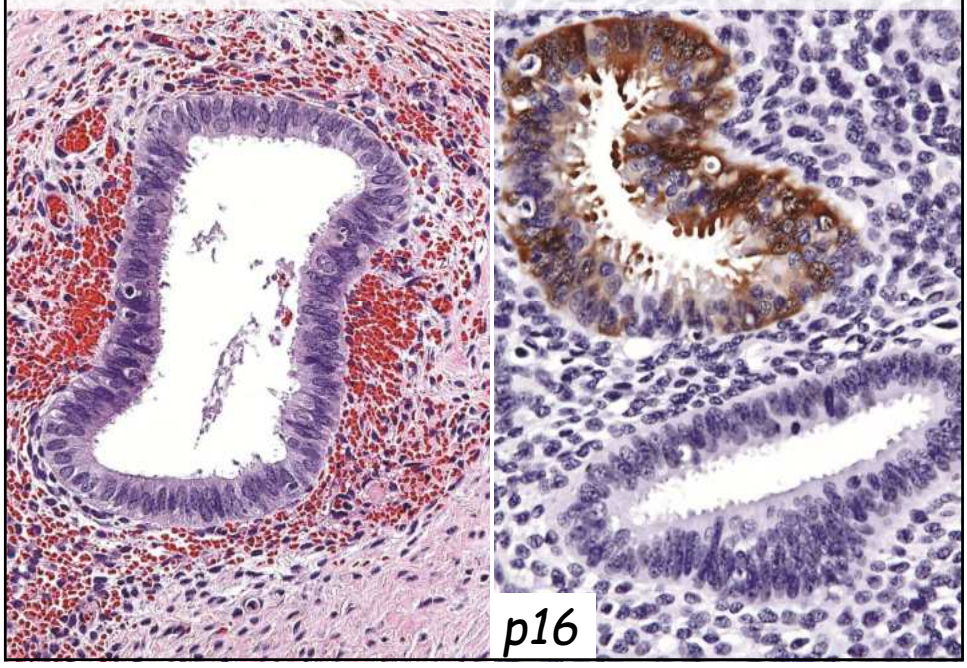
Tuboendmetrioid metaplasia: Negative p16



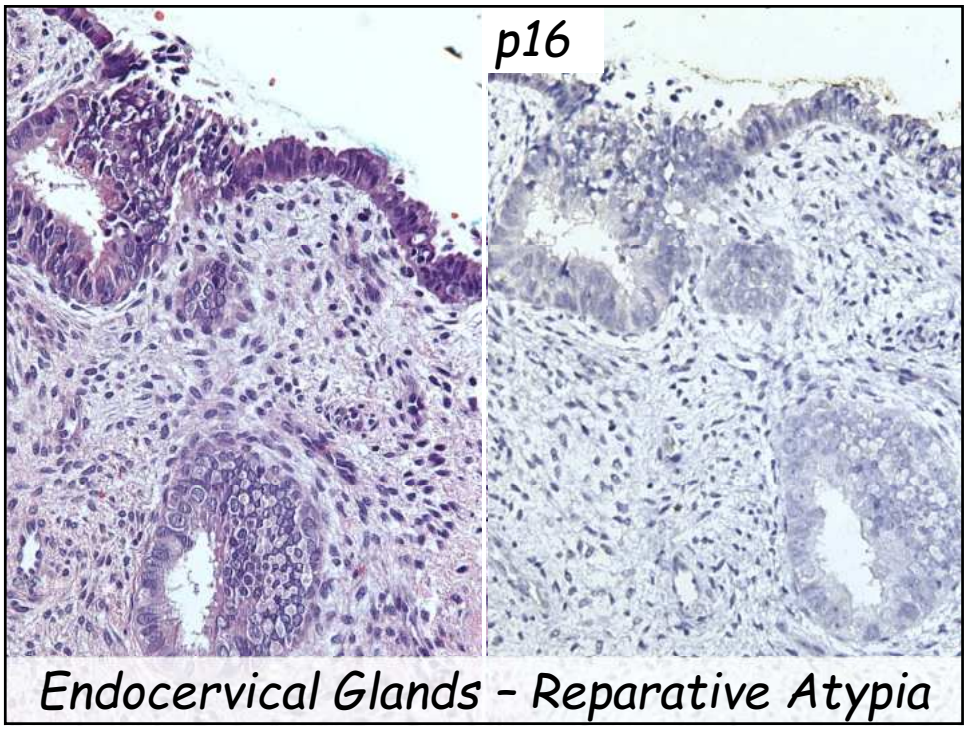
Tuboendometrioid Metaplasia



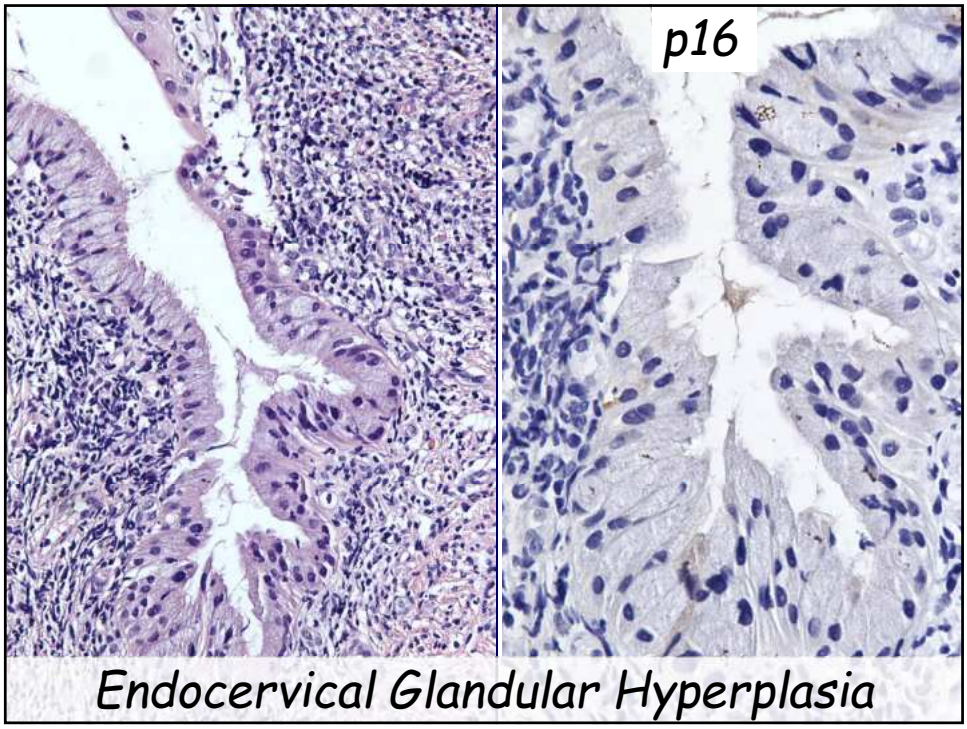
Cervical Endometriosis



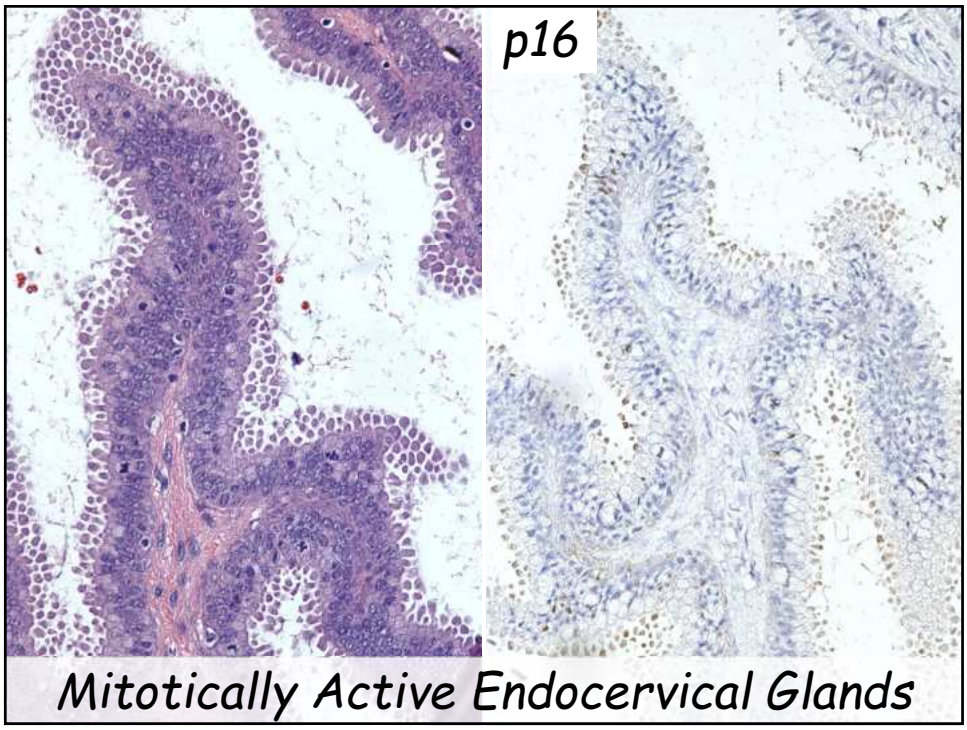
IHC	Endometriosis	AIS
p16	Patchy	Diffuse, continuous
Ki-67	Variable	High
PAX2	Positive	Negative (mostly)



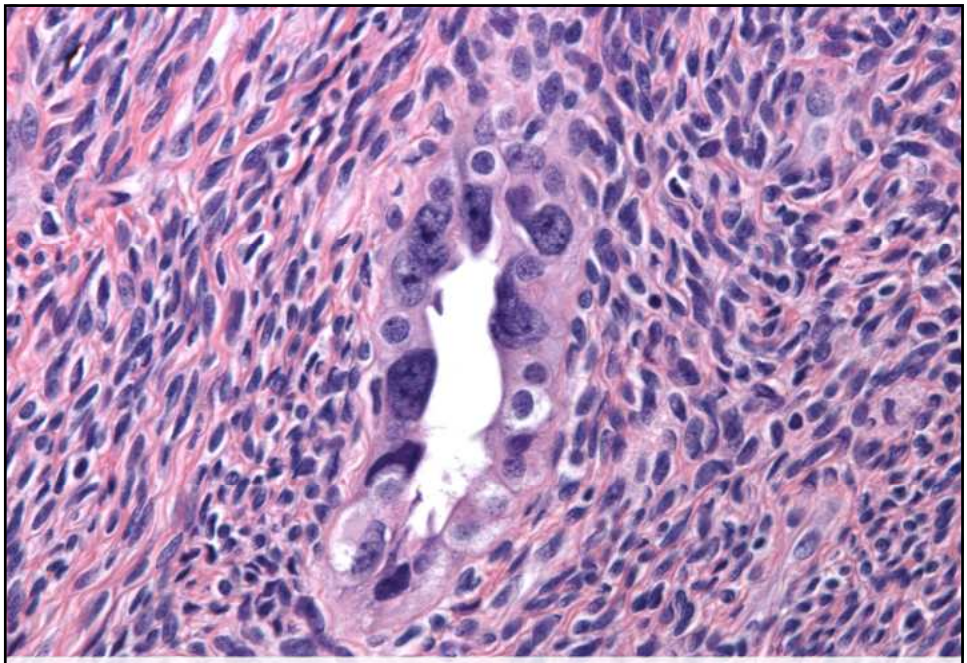
Endocervical Glands – Reparative Atypia



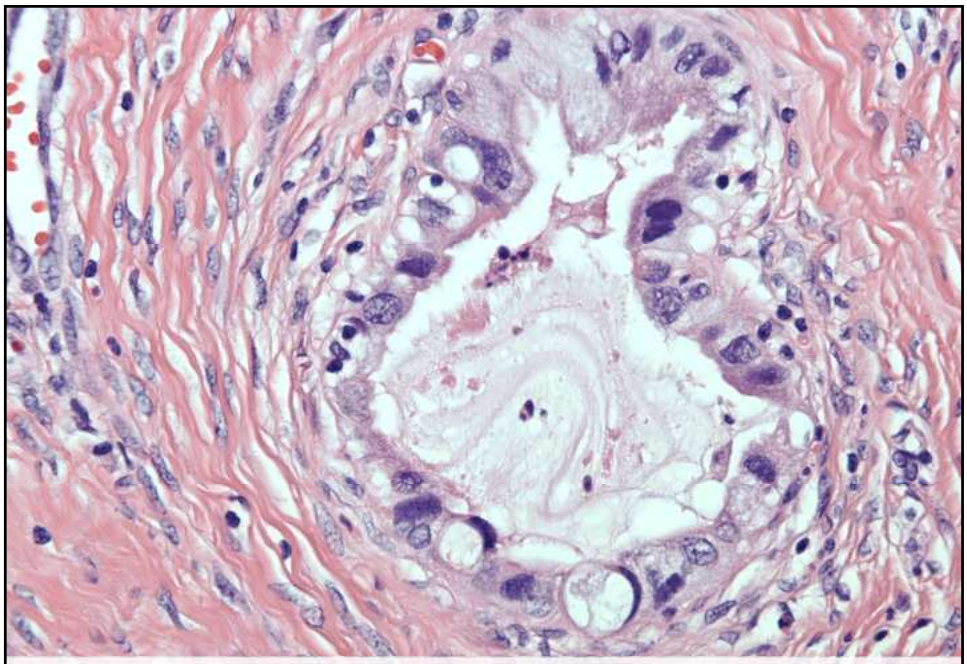
Endocervical Glandular Hyperplasia



Mitotically Active Endocervical Glands



Radiation Atypia



Hormone Effect

AIS: Screening Errors

- Miss on colposcopy
- Miss on ECC and/or biopsy for SIL
- Miss on polypectomy

AIS: Extrauterine Spread

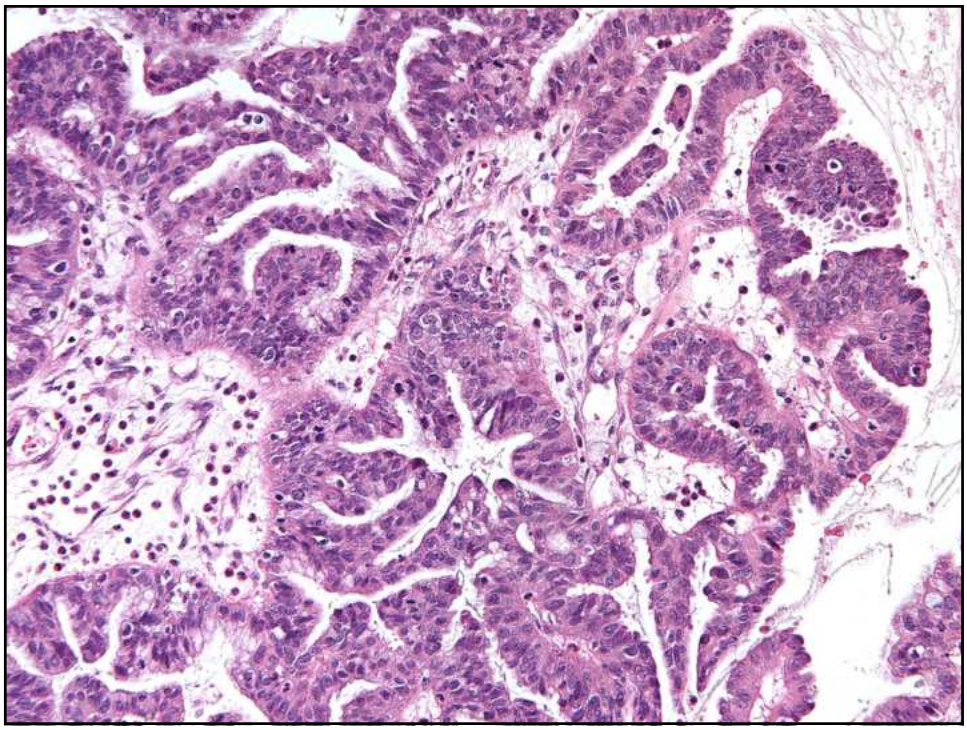
- Recent literature has described apparent spread of AIS to the ovary
- Involved ovary may be small or large, but masquerades as primary ovarian tumor
- Diagnostic clues: hybrid tumor, tumor difficult to classify or otherwise "odd"
- Colonization of endometrium also seen

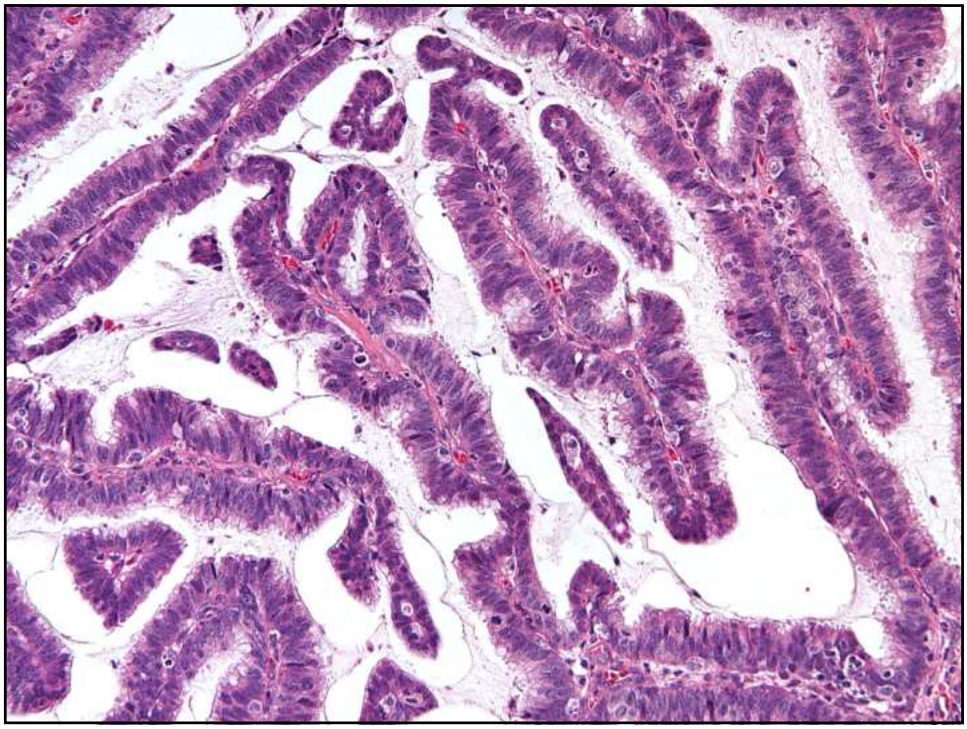
Am J Surg Pathol. 2008;32:1835-53

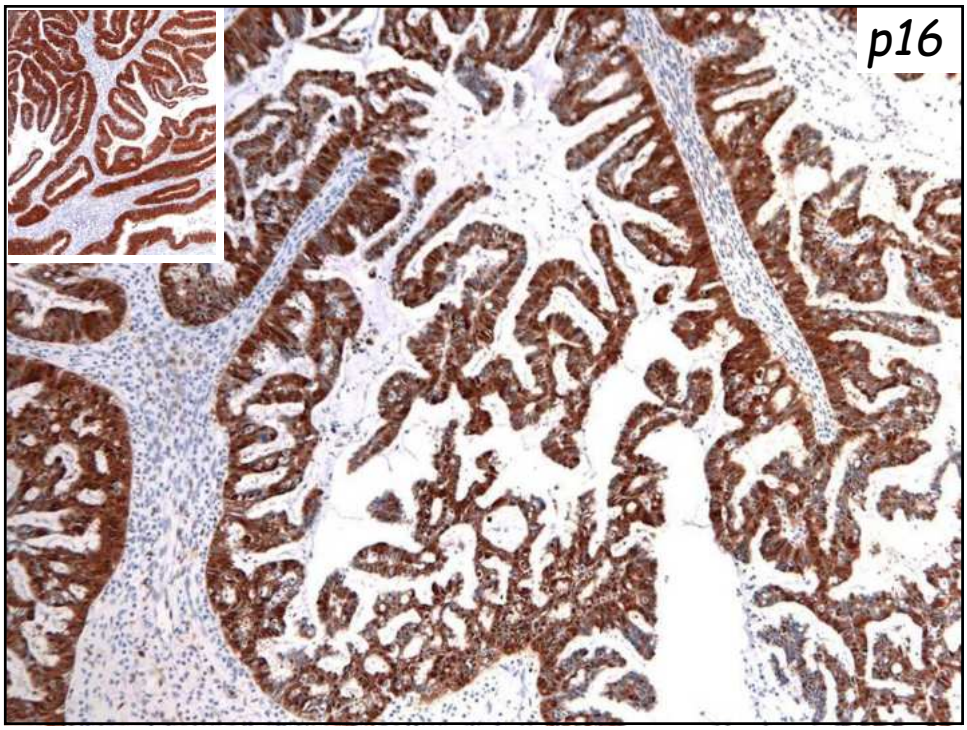
AIS: Extrauterine Spread

- High-risk HPV present, p16 strong & diffuse
- How does it get there? undiagnosed, superficially invasive adenocarcinoma or transtubal spread to the ovary with encystation (subject to debate)
- Prognosis is more favorable than usual stage IV

Am J Surg Pathol. 2008;32:1835-53






p16

The AIS Work Up

- Can be focal & superficial – requiring level sectioning to identify
- Can be extensive and diffuse – requiring level sectioning to exclude invasion
- Perform IHC only if indicated (p16)
- Evaluate for squamous intraepithelial lesion

The AIS Report

- Extent of AIS
- Early invasion
- LVSI
- SIL component
- Margins (if cone)

AIS: Clinical Management

- Hysterectomy for women who have completed their family or are of post child-bearing age.
- Cone followed by long-term surveillance for reproductive age women
- Positive margins in a cone biopsy is managed by re-excision or follow-up colposcopy, cervical cytology and HPV testing at 6 months.

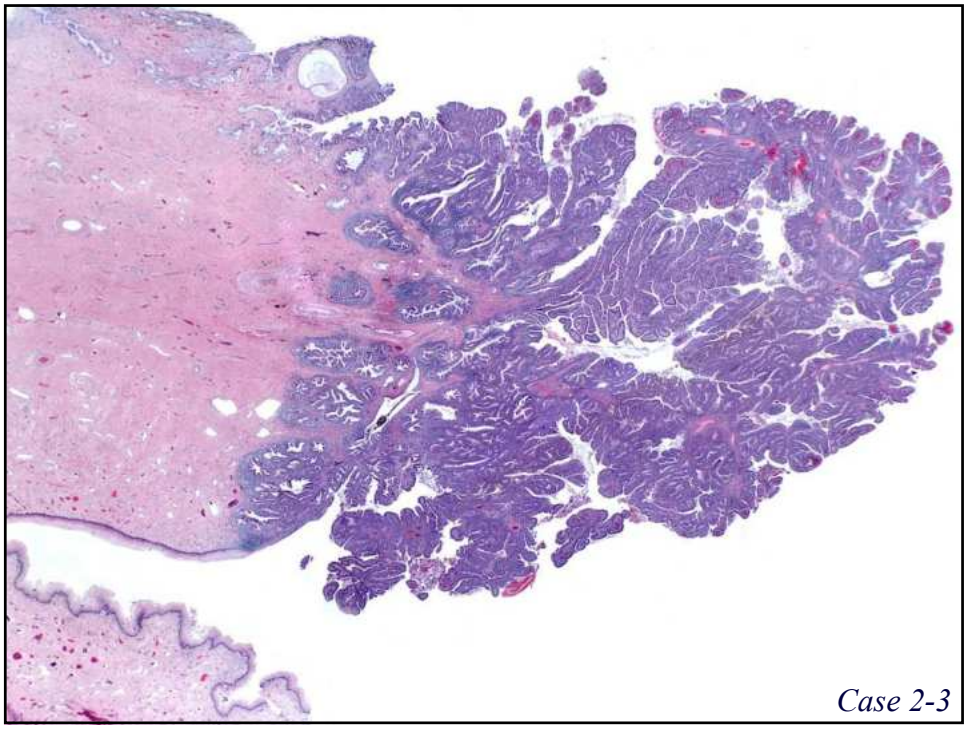
Summary

- Co-existing SIL in ~50% AIS
- Scan on low power for hyperchromatic glands with abrupt transition from normal mucinous epithelium
- Look on high power for floating (apical) mitoses and apoptotic bodies (often on-luminal)

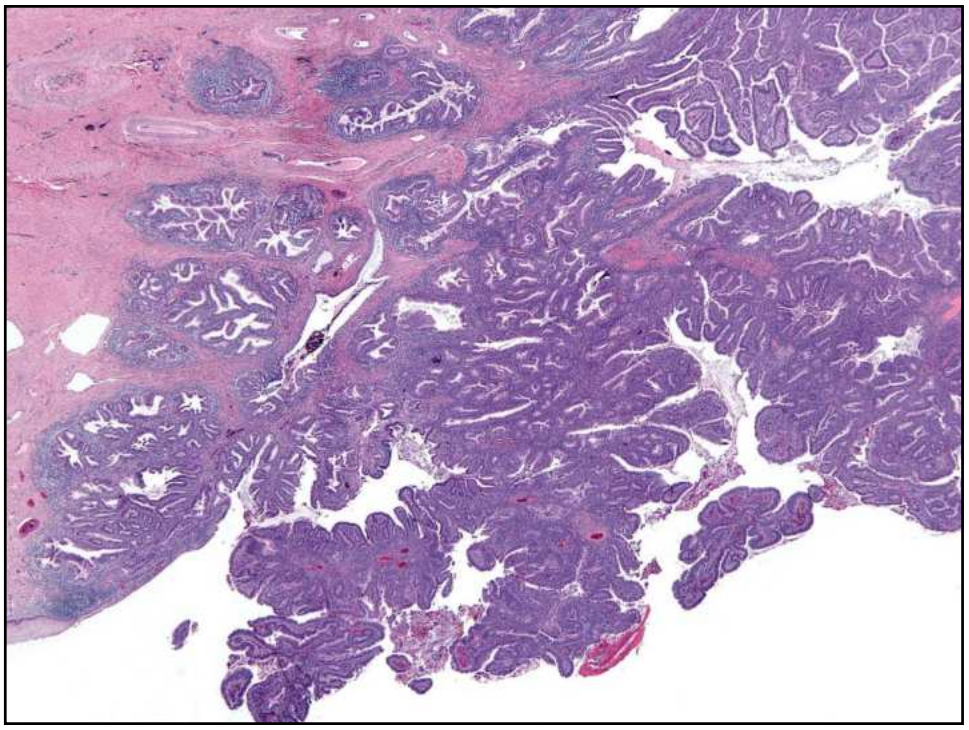
Summary

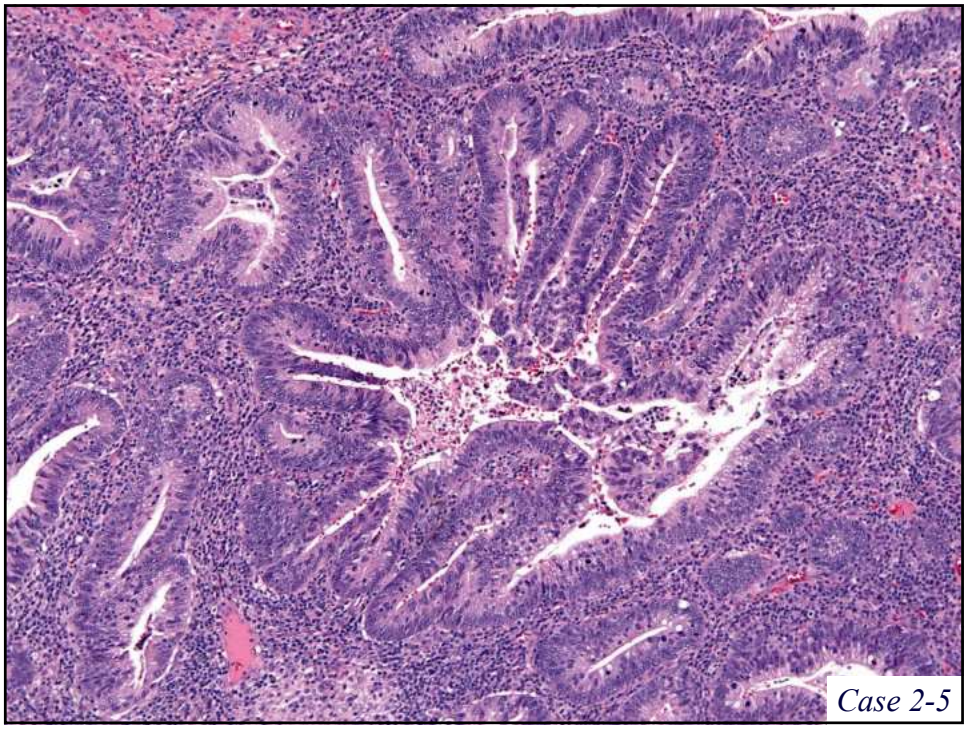
- Differential diagnosis includes tuboendometrioid metaplasia, endometriosis and reactive/reparative changes
- Continuous strong p16 supports AIS

31- year- old female with abnormal Pap test and biopsy, undergoes cervical LEEP (photomicrographs of LEEP)

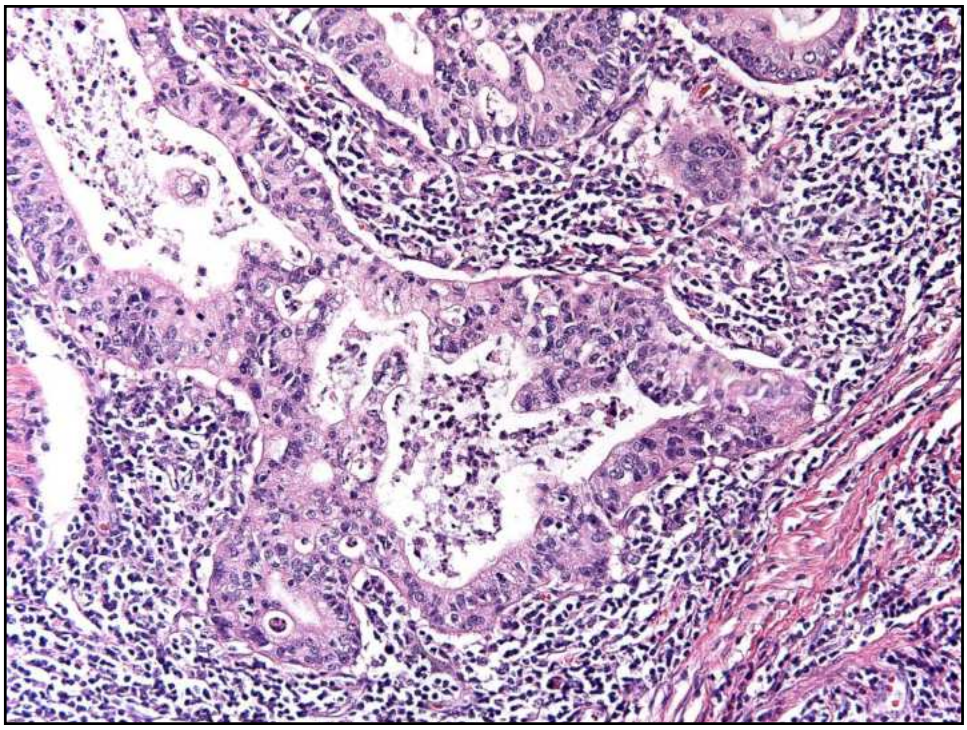


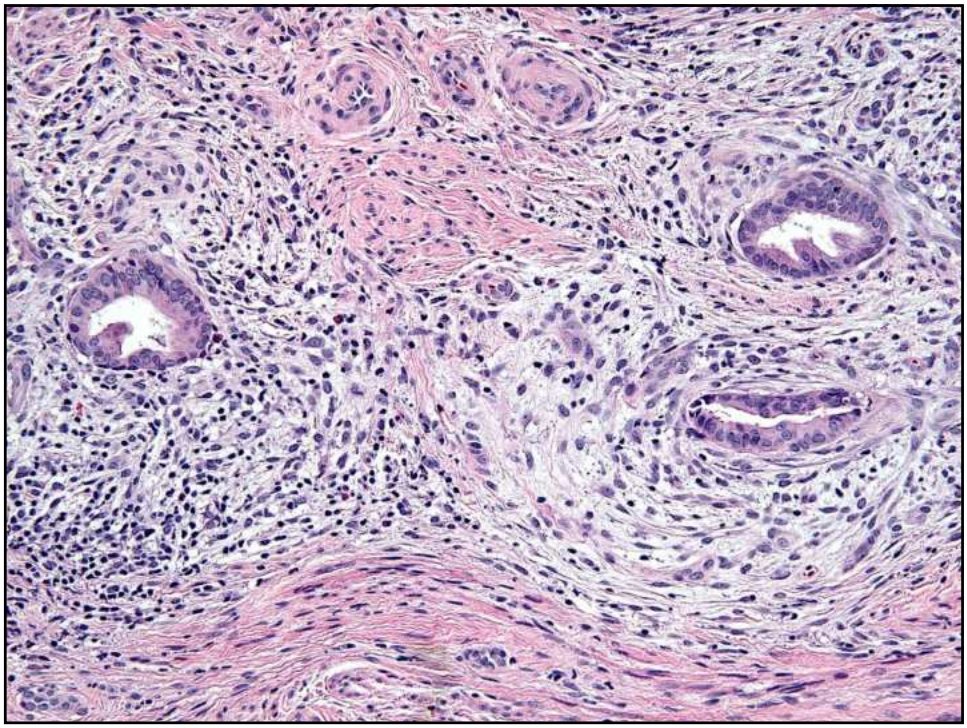
Case 2-3





Case 2-5





INVASIVE ADENOCARCINOMA

Adenocarcinoma

- Cytologic criteria
- Terminology and definition
- Histologic criteria
- Measuring and reporting
- Prognosis and treatment

Terminology

- “Microinvasive carcinoma” not used for glandular lesions
  - Not advised for squamous
- Adenocarcinomas with minimal invasion are referred to as “early” invasive adenocarcinoma
  - Associated with low rate of LN metastases

Definition

FIGO Stage IA1:

≤3mm depth, ≤7mm linear extent

FIGO Stage IA2:

3-5 mm depth, ≤7mm linear extent

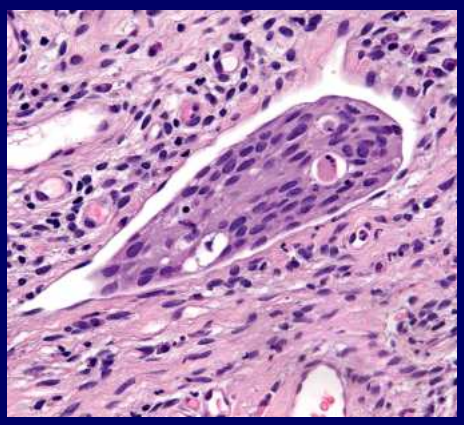
Vascular invasion does not alter stage

Entire lesion must be evaluable (negative margins)

Lymphatic-Vascular Invasion: *Challenges*

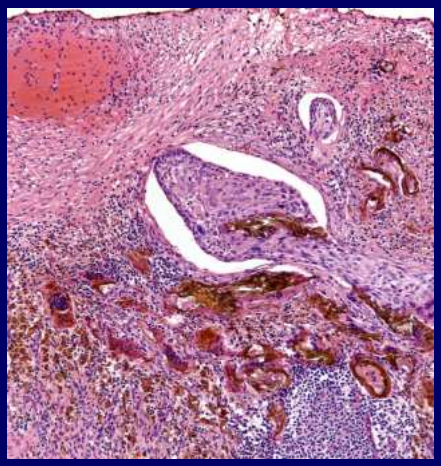
Variability in criteria

- Tumor in endothelial-lined spaces and/or spaces with rbcs
- Tumor partially or completed surrounded by endothelial cells in vascular channels
- Tumor attached to vascular wall with adherent thrombus



Lymphatic-Vascular Invasion: *Challenges*

- Extensive retraction around tumor cells
- Micropapillary architecture
- Prior biopsy site
- Limited LVI



Identifying Early Invasion

- Overall pattern:
  - Infiltrative, superficial, or expansile
- Abnormal architecture:
  - Extension beyond depth of normal endocervix
  - Haphazard arrangement of glands
  - Irregular glands
  - Cribriform, papillary or solid nests
  - Partial Glands

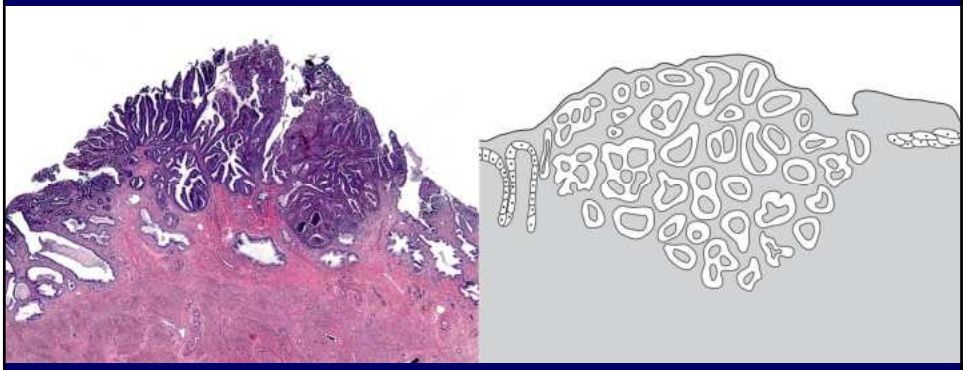
New Classification Scheme for Invasive Adenocarcinoma *Silva Method*

- Proposed 3 patterns based on well-demarcated glands vs destructive invasion

Int J Gynecol Pathol 2013;32:592-601

	Silva system
Pattern A	- Well-demarcated glands with rounded contours, frequently forming groups - No single cells or desmoplastic stromal reaction - Irrelevant relationship to large cervical vessels or depth of the tumor - Complex intraglandular growth allowed (i.e. cribriform, papillae) - No lymphovascular invasion - Well or moderate differentiation
Pattern B	- Early destructive stromal invasion arising from well-demarcated glands (pattern A-like glands) - +/- Lymphovascular invasion
Pattern C	- Diffuse destructive invasion

Silva System: Pattern A



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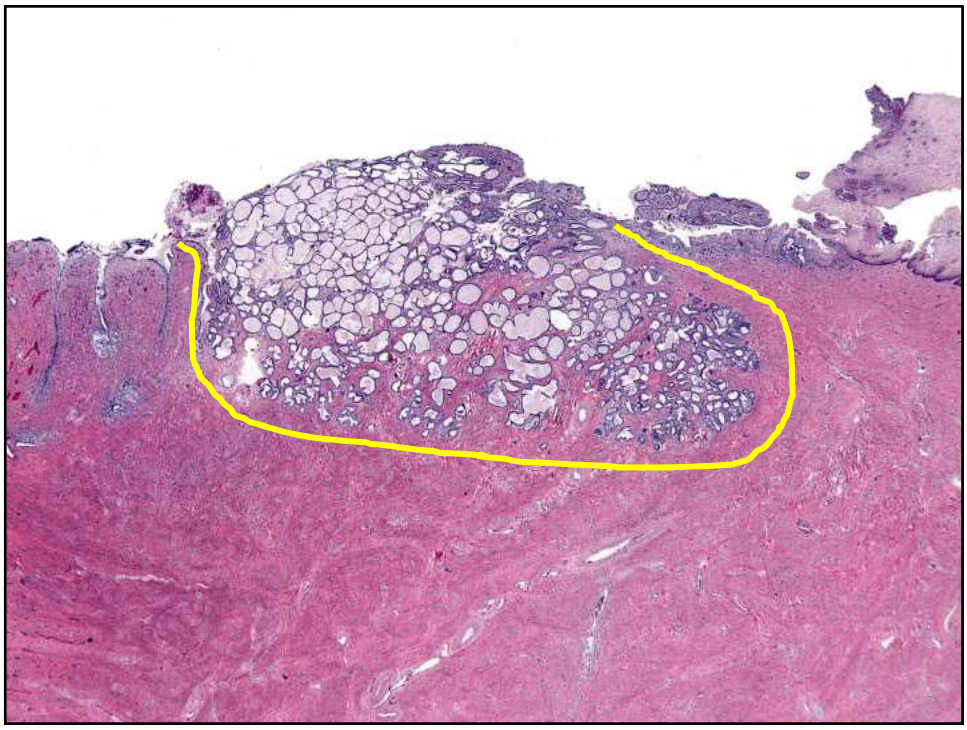
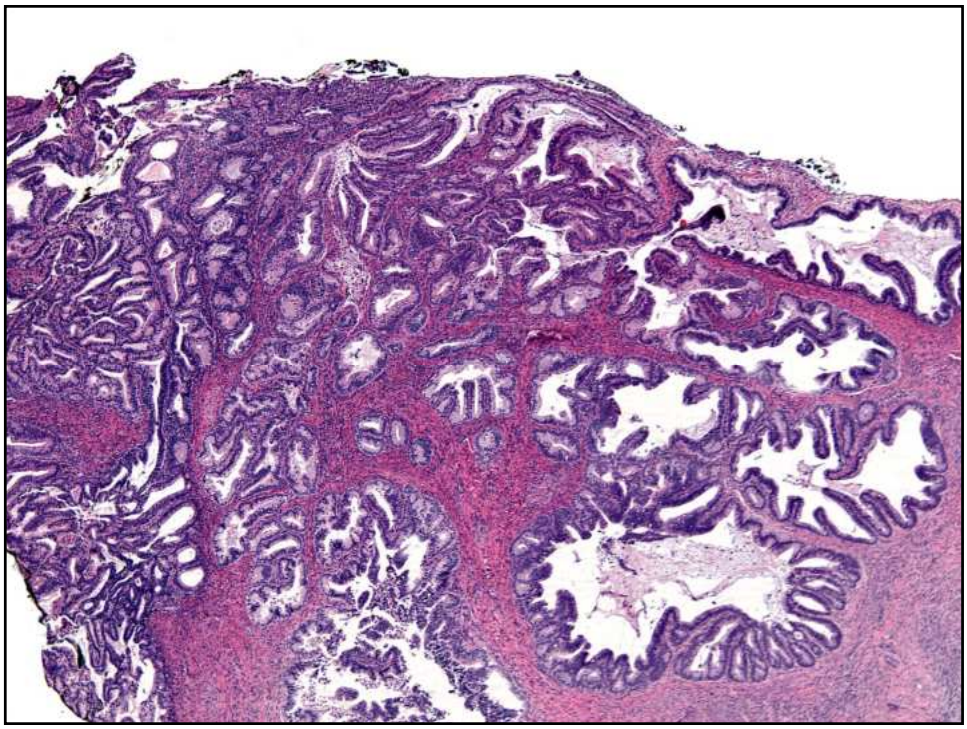
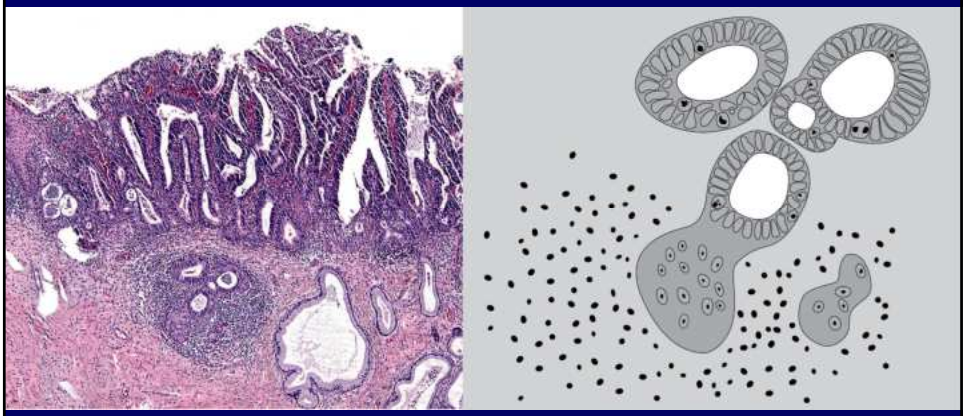


Pattern A: Expansile Invasion

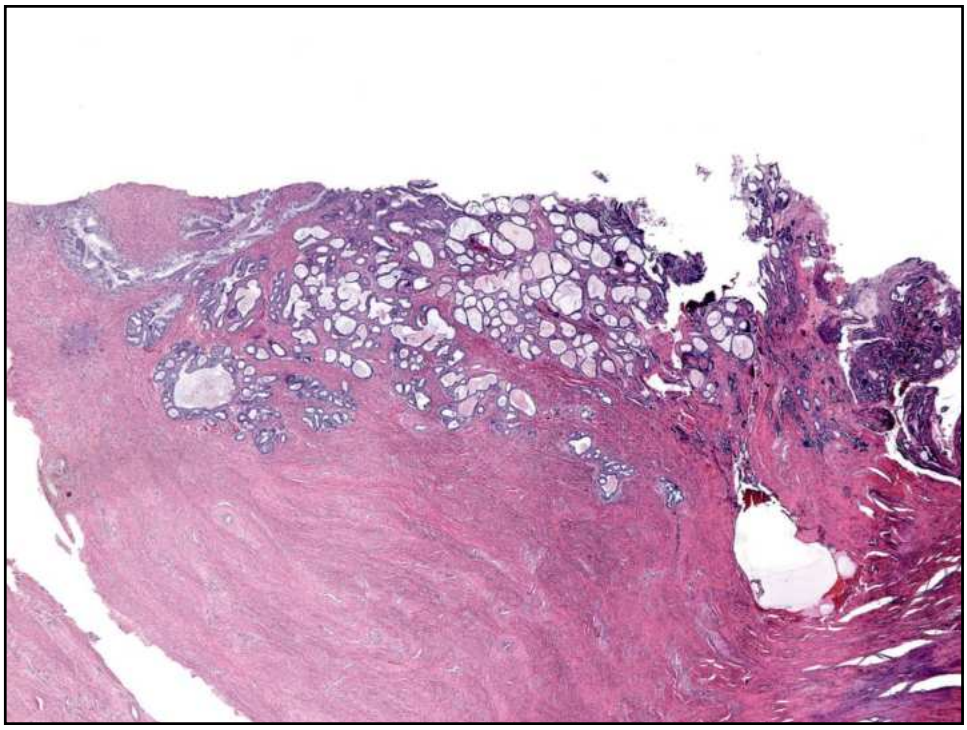
- Bulky expansion into stroma with sharply circumscribed border
- Often lacks stromal reaction
- AIS-like glands, may appear as cribriform, papillary or solid nests
- Distinction from AIS tough

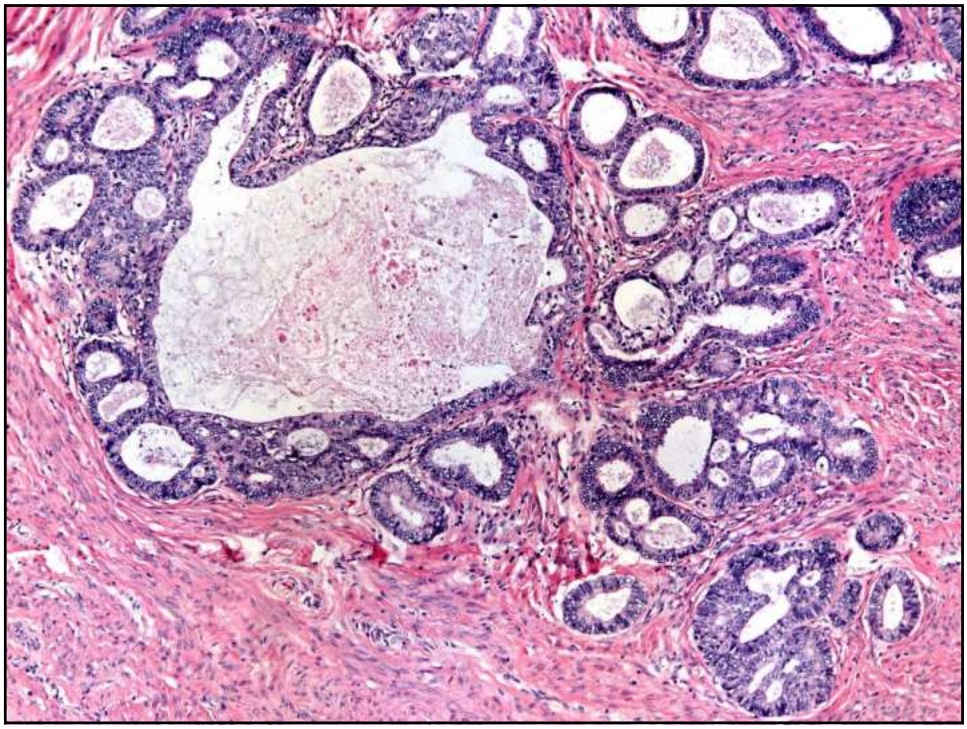


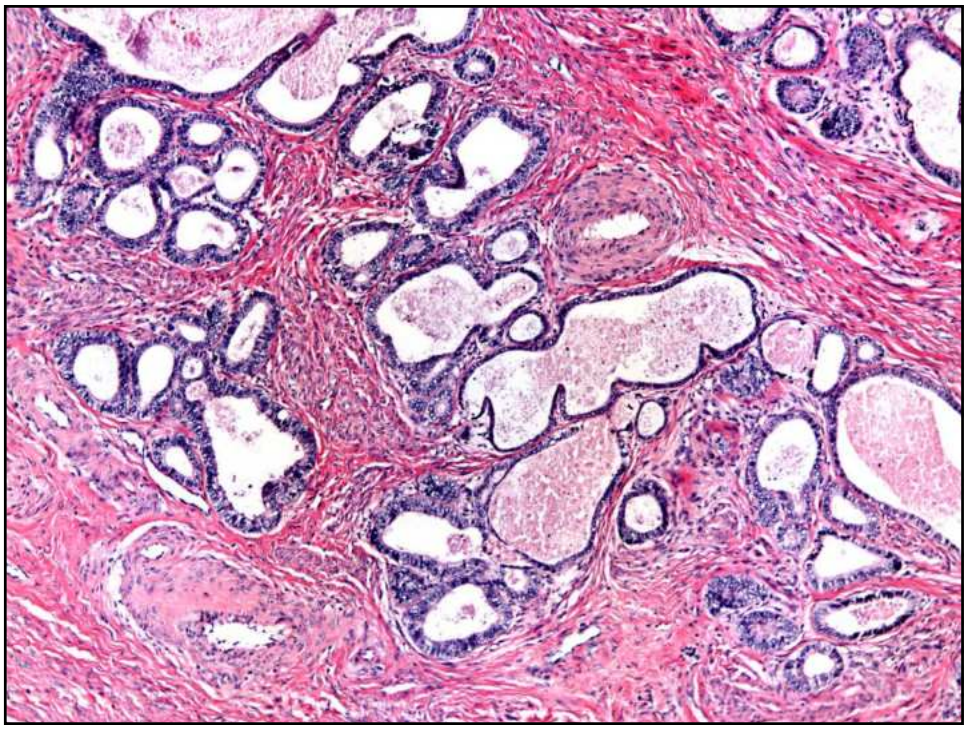
Silva System: Pattern B

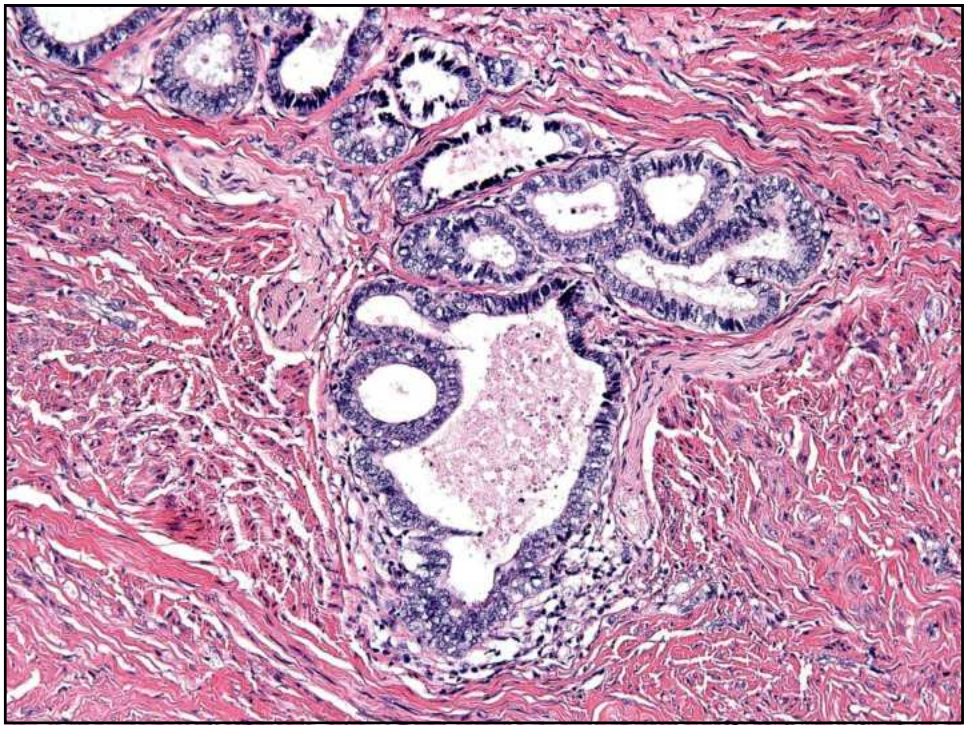


Int J Gynecol Pathol 2013;32:592-601

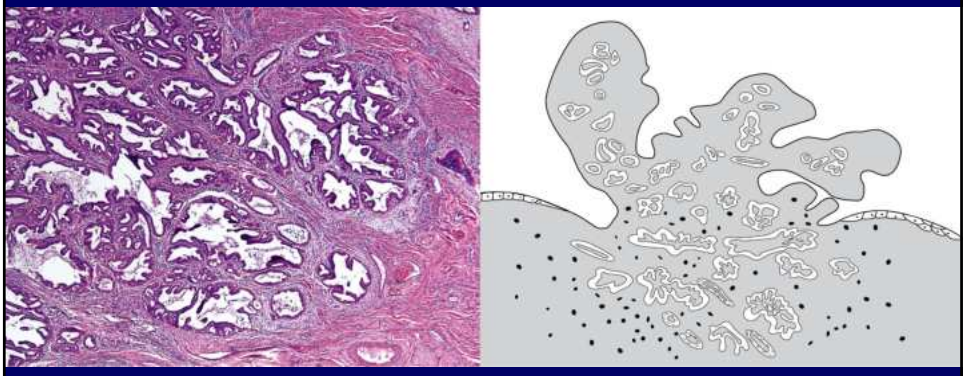








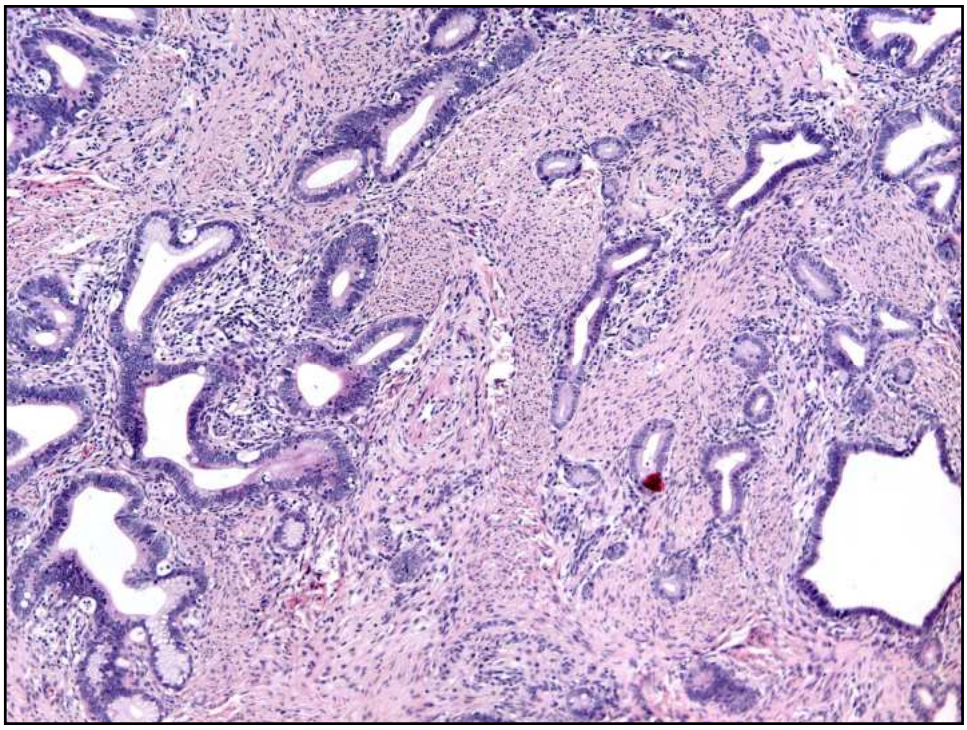
Silva System: Pattern C

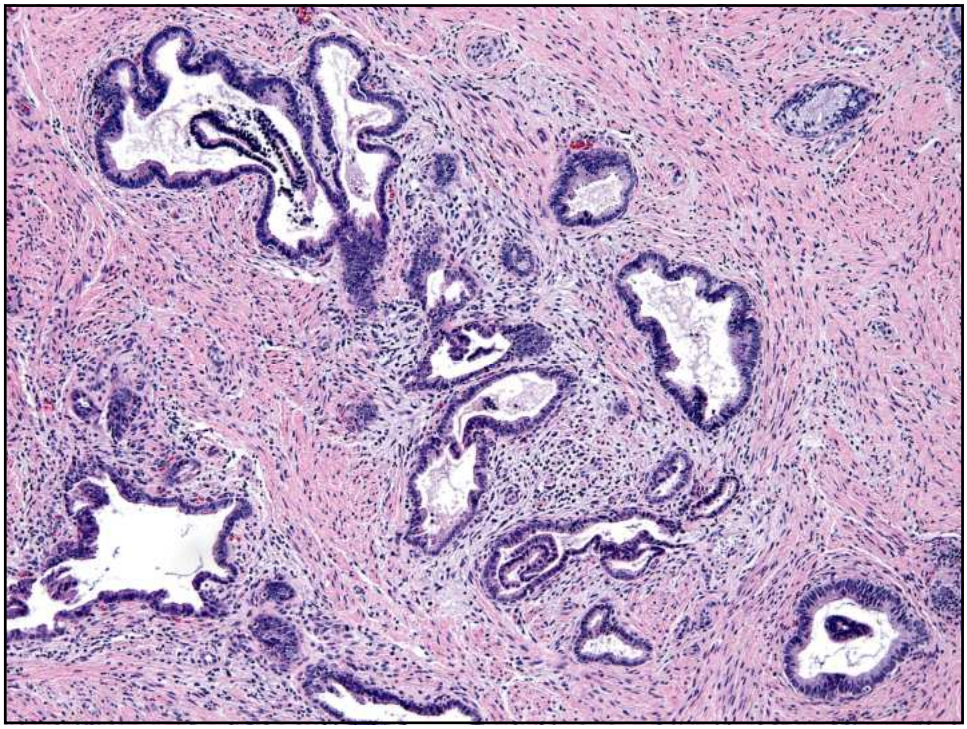


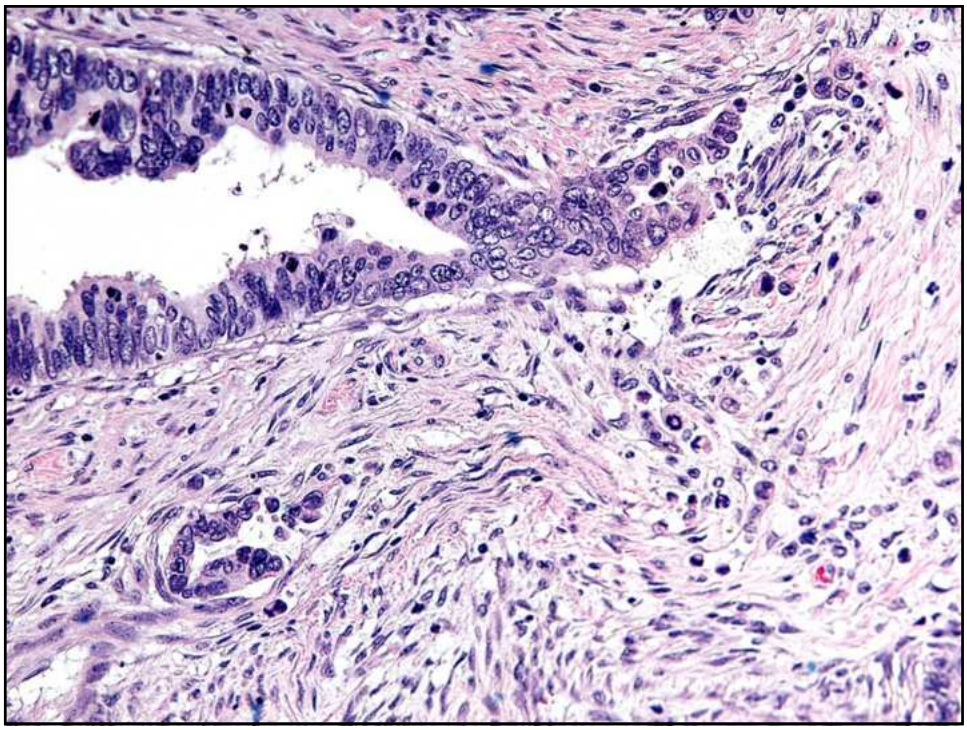
Int J Gynecol Pathol 2013;32:592-601

Pattern C: Infiltrative Pattern

- Glands permeate stroma with abnormal architectural pattern
  - Marked gland irregularity
  - Haphazard arrangement of glands
  - Glands adjacent to large vessels: not reliable
- +/- Altered, edematous stroma and inflammation







Comparison of histologic features encountered in patterns A, B & C

Pattern	No. Of Patientts	DOI mm	Patients with LN +	Tumor size mm (mean)	Recurrences	DOD
A	73 (20.7%)	3.8	0(0%)	2.5-42 (13.5)	0 (0%)	0 (0%)
B	90 (25.6%)	4.0	4 (4.4%)	0.7-65 (15.9)	1 (1.2%)	0 (0%)
C	189 (53.7%)	9.2	45 (23.8%)	1.2-87 (23.7)	38 (22.1%)	16 (8.8%)

Int J Gynecol Pathol 2013;32:592-601

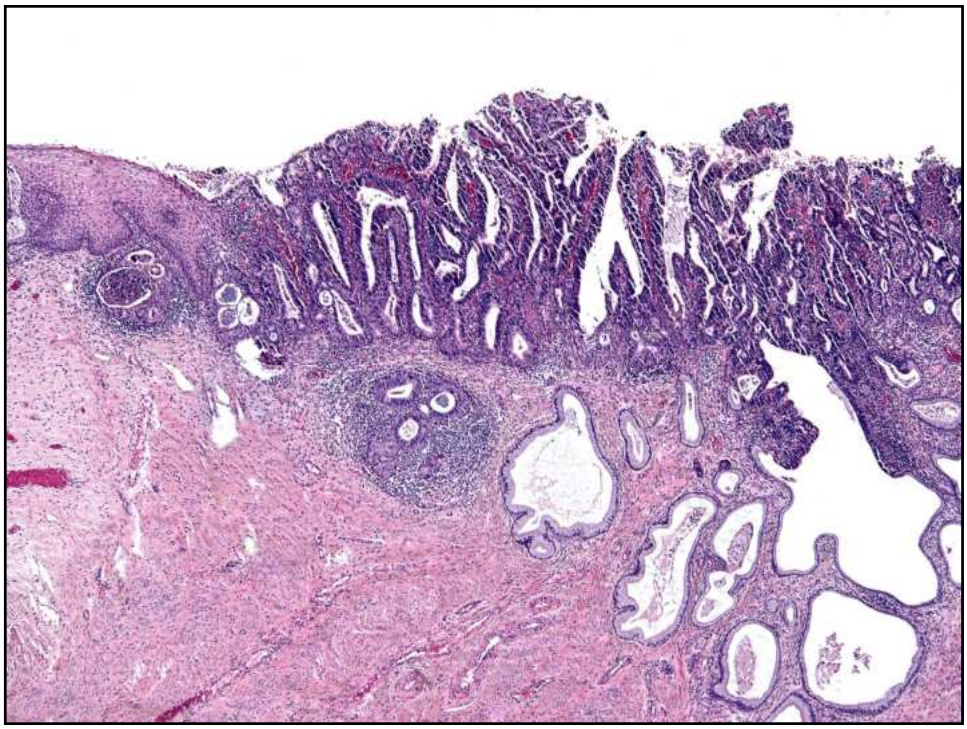
Reproducibility of Pattern Diagnoses

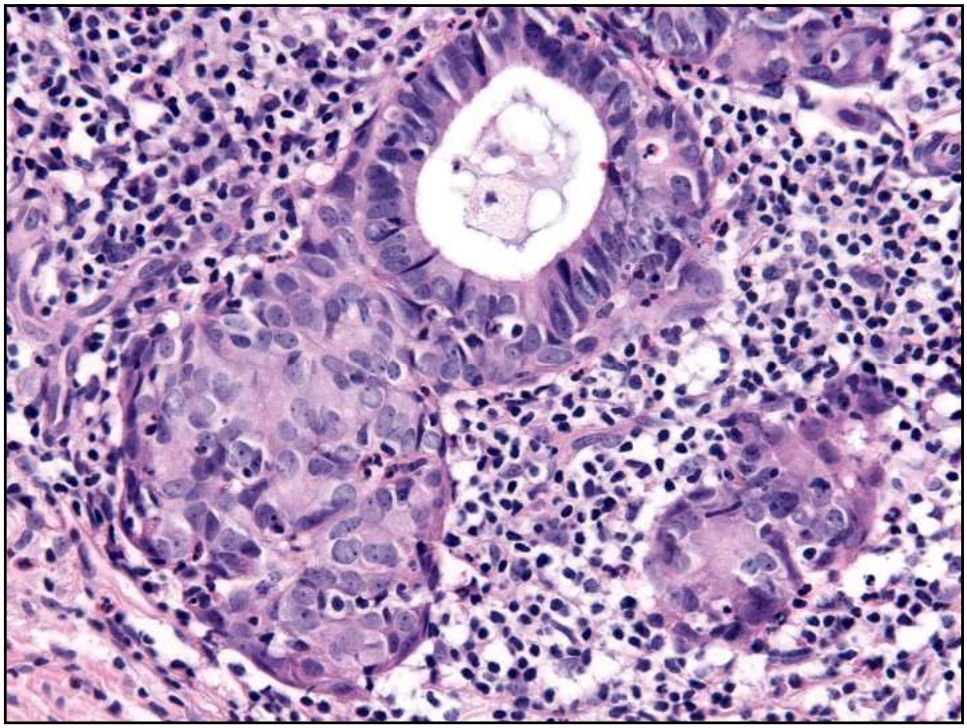
- Overall concordance 74%
- Missing a few individually infiltrative cells is the most common cause of undercalling pattern B
- Small foci of inflamed, loose or desmoplastic stroma lacking infiltrative tumor cells in pattern A appeared to account for those cases up-graded to pattern B

Mod Pathol 2016;29:1083-94

Superficial Invasion Pattern

- Malignant glands budding off of AIS
- Aberrant maturation: invasive glands have more abundant eosinophilic cytoplasm and larger nuclei than AIS
- Invasive partial glands and single cells
- Associated with desmoplastic response





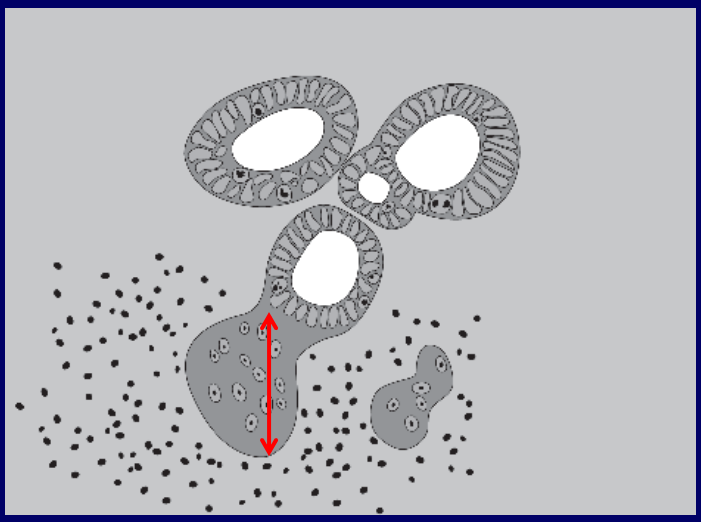
Reporting

- Measurement (use calibrated optics):
  - Depth of invasion
  - Tumor thickness
  - Linear (horizontal) extent of invasion
- Grade?
- Lymphatic-vascular invasion

Measurement: *depth*

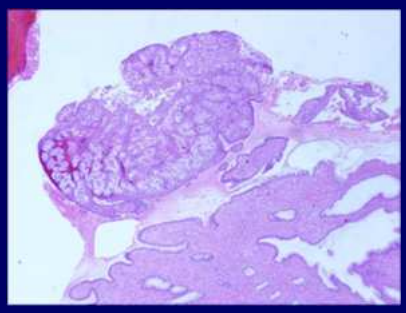
- Measure from basement membrane of surface mucosa to deepest point of invasion
- If point of origin can be identified, measure from gland of origin to deepest point of invasion

Depth from Gland of Origin



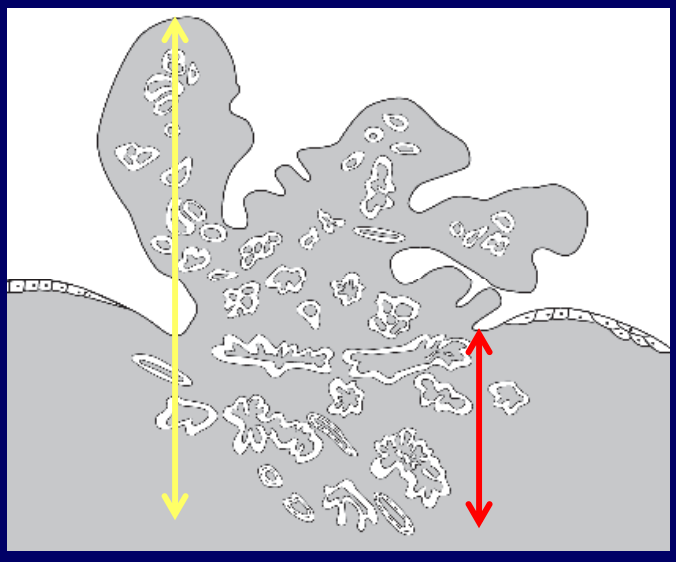
Measurement: *tumor thickness*

Tumor thickness is often the same as depth of invasion, except if exophytic.

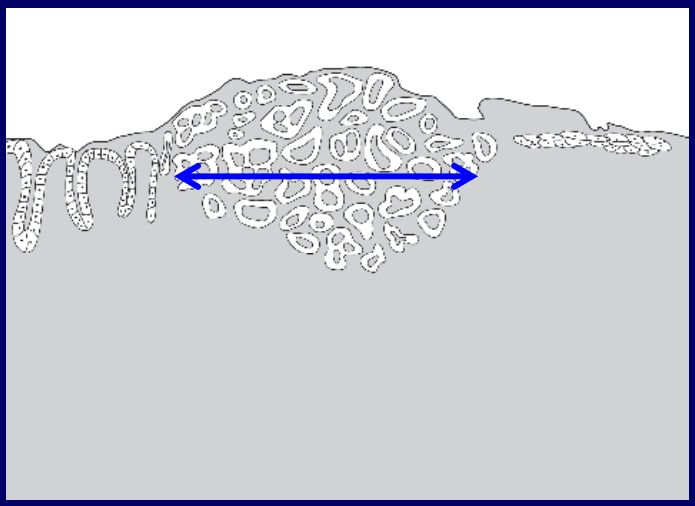


Measure from basement membrane of surface mucosa to deepest point of invasion.

Tumor Thickness & Depth



Horizontal Extent (diameter)



Do not include AIS in measurement

Measurement: *horizontal extent (diameter)*

- Discontinuous foci of invasion:
  - Report largest focus and overall area involved
- Multiple sections/blocks involved:
  - Estimate extent: # consecutive sections involved multiplied by section thickness (e.g. 3mm)

Cone Biopsy

EXTENT	MARGIN	MANAGEMENT
≤3 depth *and* ≤7 horizontal extent	Negative	**AIS or early invasive:** Clinical follow-up
Unknown	Positive	**AIS or early invasive:** Repeat cone
		Invasive: Radical hysterectomy or trachelectomy

Cone Biopsy

Focus suspicious for invasion:

- Levels of problematic area
- Embed all tissue
- If still unclear, indicate uncertainty in report; include depth, thickness & horizontal extent
- Repeat cone and/or imaging studies may be helpful

Management

Stage 1A1 (≤3mm depth; ≤7 mm diameter):

Conservative treatment with cone biopsy or with simple hysterectomy

Lymphatic or parametrial involvement not identified in patients treated with radical hysterectomy and pelvic lymphadenectomy

McHale, 2001

Management

- Stage 1A2-1B1:
  - Variable
  - Radical hysterectomy or radical trachelectomy

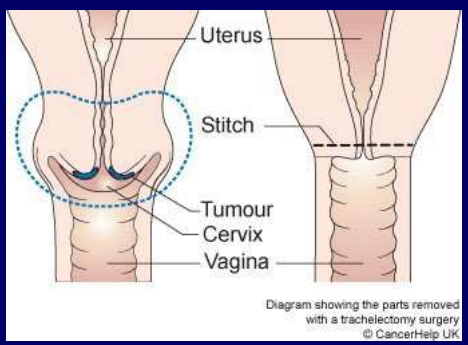


Diagram showing the parts removed with a trachelectomy surgery

Radical Trachelectomy: *indications*

- Fertility preservation desired
- No clinical evidence of impaired fertility
- Tumor < 2.0 cm size (FIGO stage 1A-1B1)
- Upper endocervical canal not involved
- No pelvic lymph node metastasis
- No lymphatic-vascular invasion

Koliopoulos 2004

Radical Trachelectomy *frozen section*

- Pelvic lymph node FS
- FS evaluation of margin not standardized:
  - Perform on all cases vs. visible lesions only
  - Complete en face (transverse) margin *vs.* representative or complete longitudinal (perpendicular) sections

Chenevert 2009; Park, 2008

Radical Trachelectomy
frozen section

- Require >5 mm margin
- If <5mm margin:
  - Additional tissue excised, or
  - Completion hysterectomy

Trachelectomy Outcome

- Recurrence rate 0-8%
- Miscarriage rate:
  - 1st trimester: 16-20%
  - 2nd trimester: 8.6% (vs. 4% general population)
- Preterm delivery
  - <32 weeks: 0-29%
  - 33-36.6 weeks: 0-43%

Plante 2008

Endocervical Adenocarcinoma: WHO Classification

- Endocervical, usual
  - 70-80% cervical adenocarcinomas
- Endometrioid
- Mucinous NOS
  - Gastric
  - Intestinal
  - Signet ring cell
- Villoglandular
- Clear cell
- Serous
- Mesonephric
- Adenocarcinoma with admixed neuroendocrine carcinoma

Endocervical Adenocarcinoma: HPV Classification

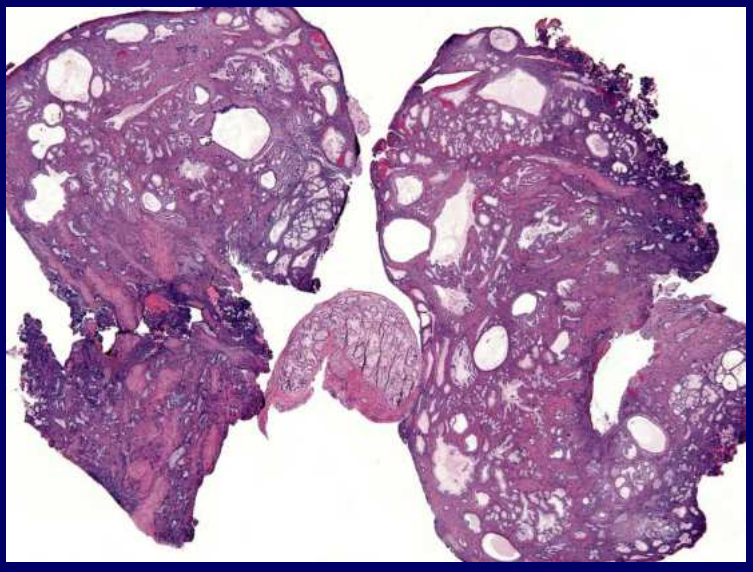
HPV positive

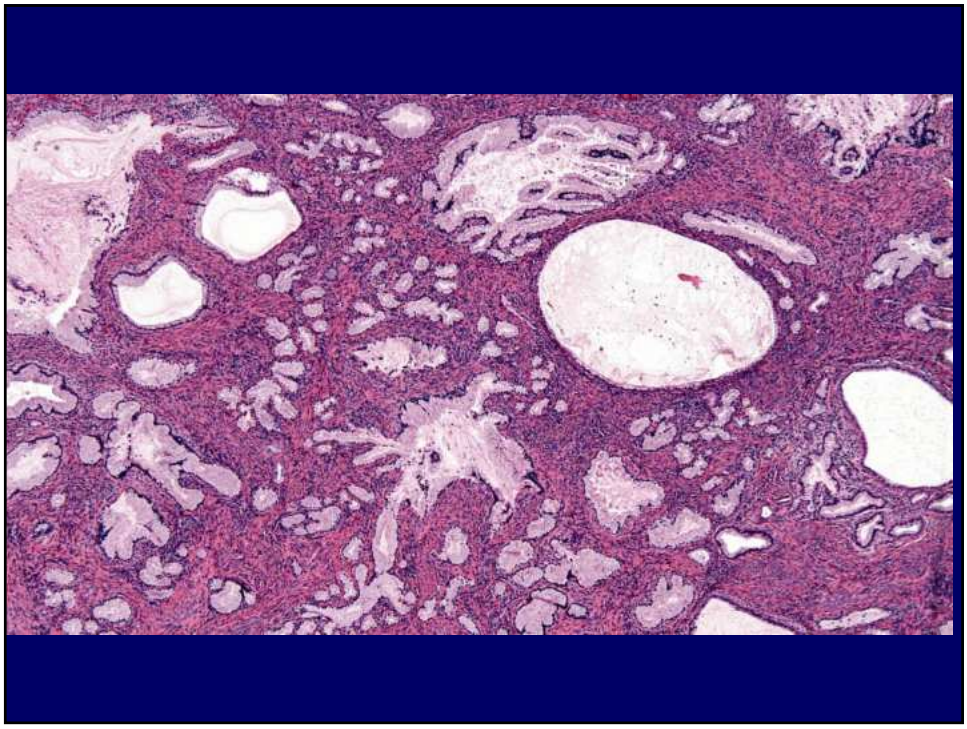
- Usual
- Villoglandular
- Endometrioid
- Adenoid basal cell
- Neuroendocrine

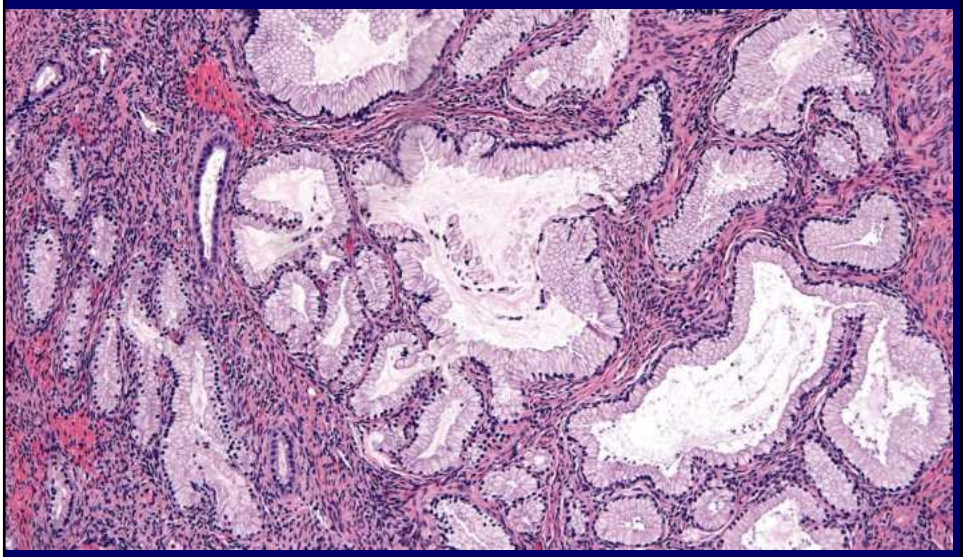
HPV negative

- Gastric/Minimal deviation
- Clear cell
- Mesonephric

49 year old has cervical polyp







MINIMAL DEVIATION ADENOCARCINOMA

Gastric-type Adenocarcinoma (GAS)

- Non-HPV related variant of mucinous adenocarcinoma
- Encompasses minimal deviation adenocarcinoma (adenoma malignum) at the very well-differentiated end of spectrum
- Worse prognosis than usual type endocervical adenocarcinoma
- Putative precursor lesion: lobular endocervical glandular hyperplasia

Karamurzin 2015

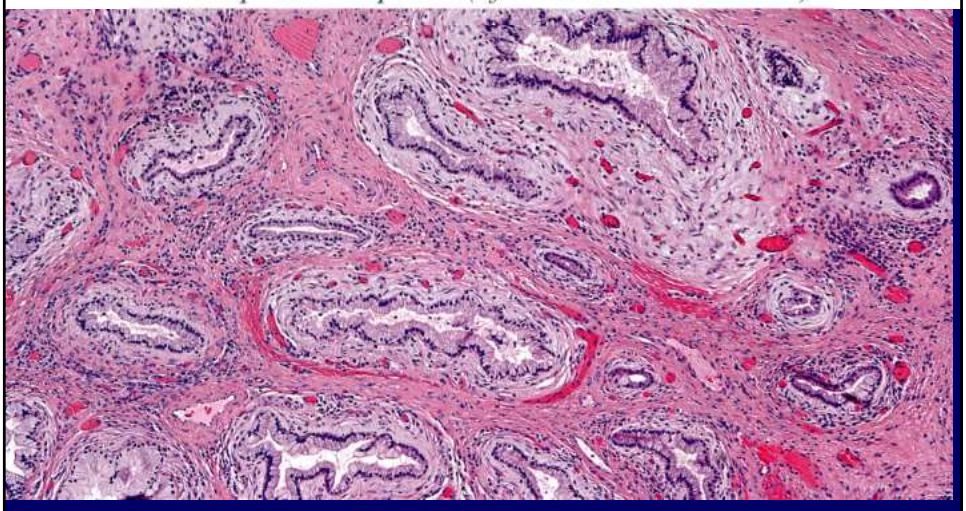
Minimal Deviation Adenocarcinoma

- Presentation
  - Asymptomatic, watery discharge, bleeding
- Physical exam
  - Normal, thickened cervix; barrel solid cervix, polyp
- Predisposition
  - 1% of all cervical adenocarcinomas
  - ~10% linked to Peutz-Jeghers Syndrome

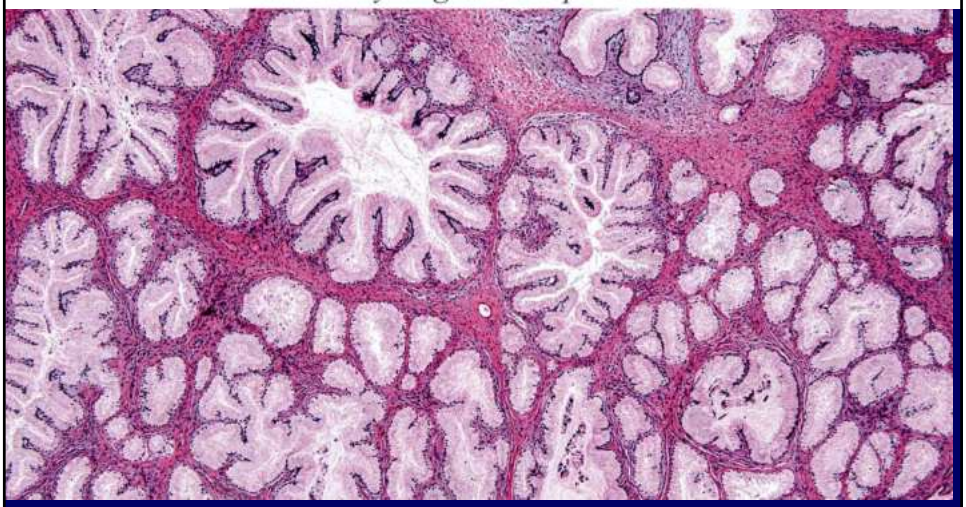
Minimal Deviation Adenocarcinoma: Helpful Features

- Desmoplastic response
- Variability in gland shape and size; irregular gland contours
- Focal cytologic atypia
- Loss of polarity and nuclei that look like usual AIS
- Mitoses
- Glands deep in cervical stroma

Desmoplastic response (often absent on small bx)



Variability in gland shape and size



Deep Glands

Minimal Deviation

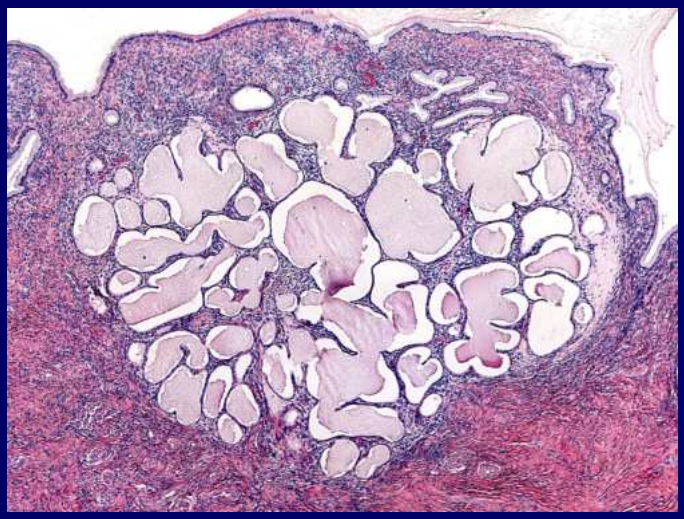
- Estimated by glands beyond the majority of the baseline endocervical glands
- Where is the baseline?

Benign Lesions in Deep Stroma

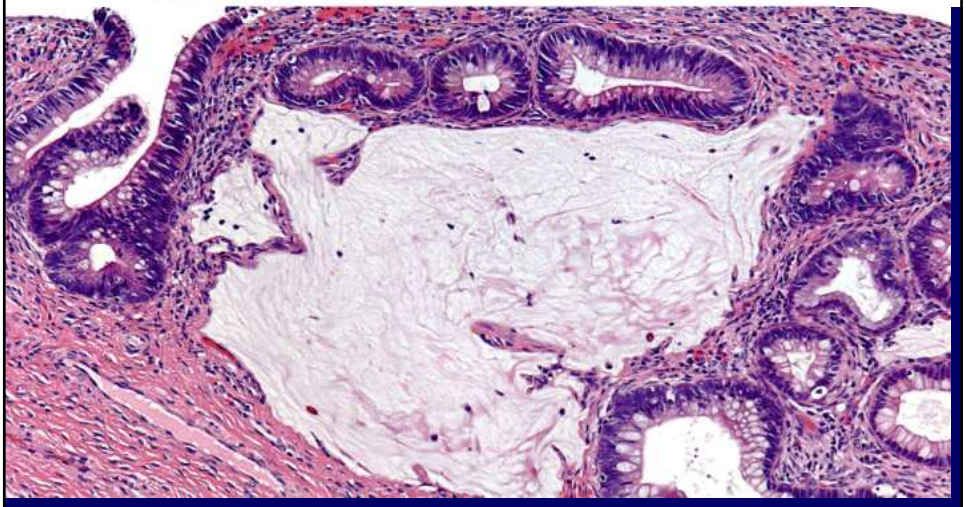
- Mesonephric hyperplasia
- Nabothian cysts
- Endocervical adenomyoma
- Endocervicosis
- Endometriosis/ adenomyosis

- Normal endocervical glands

Tunnel Clusters: can be deceiving on small biopsies



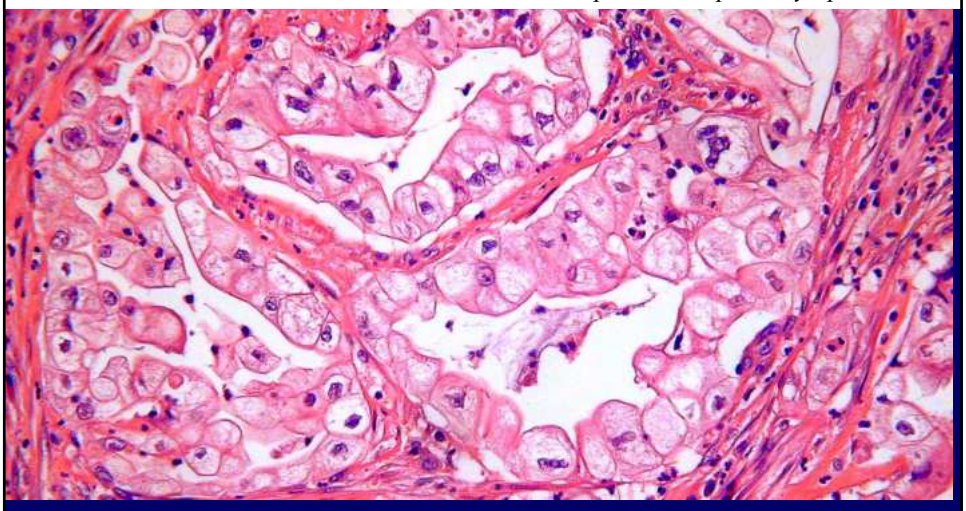
Adenocarcinoma in situ with mucin extravasation



Gastric-type Adenocarcinoma (GAS)

- Distinct cell borders, voluminous clear, eosinophilic or foamy cytoplasm
- Goblet cells
- Glands with elongated, stratified nuclei
- Glands with small cuboidal cells
- Glands with flattened cells or papillary growth
- Single cell infiltration and infiltration with microcystic elongated and fragmented pattern

GAS: distinct cell borders, voluminous clear to pale eosinophilic cytoplasm



Special Variants:

GOOD PROGNOSIS

- Villoglandular – strictly defined
- Adenoid basal carcinoma – strictly defined

POOR PROGNOSIS

- Gastric (or enteric)
- Neuroendocrine
- Clear cell (?)

Neuroendocrine Tumors: WHO Classification

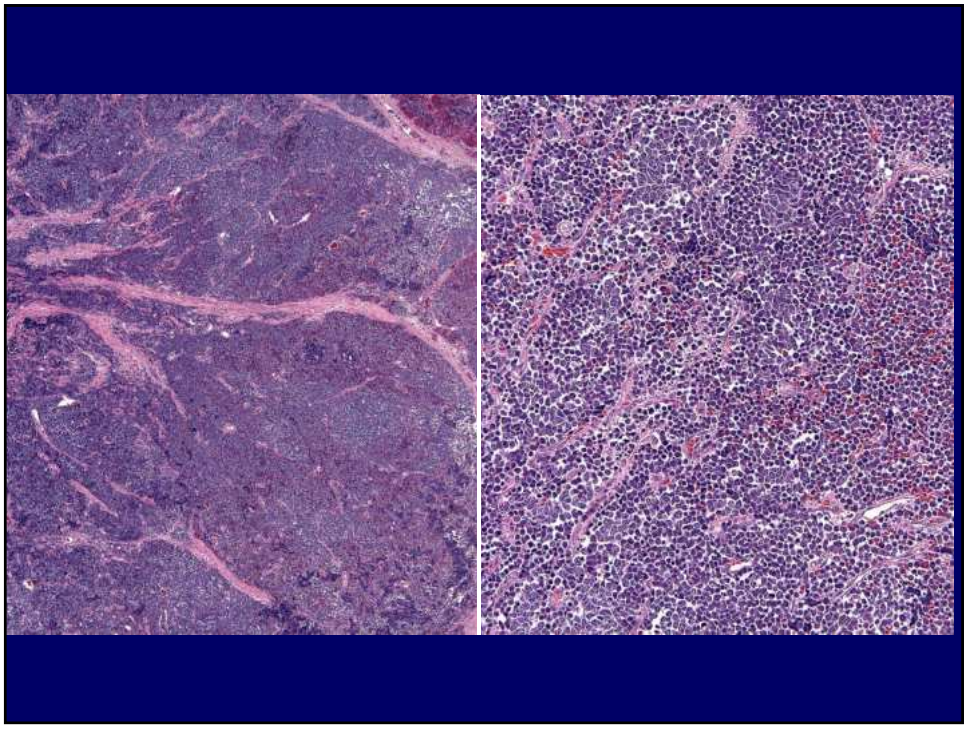
- Low-grade neuroendocrine tumor
  - Carcinoid tumor
  - Atypical carcinoid tumor
- High-grade neuroendocrine tumor
  - Small cell neuroendocrine tumor
  - Large cell neuroendocrine tumor

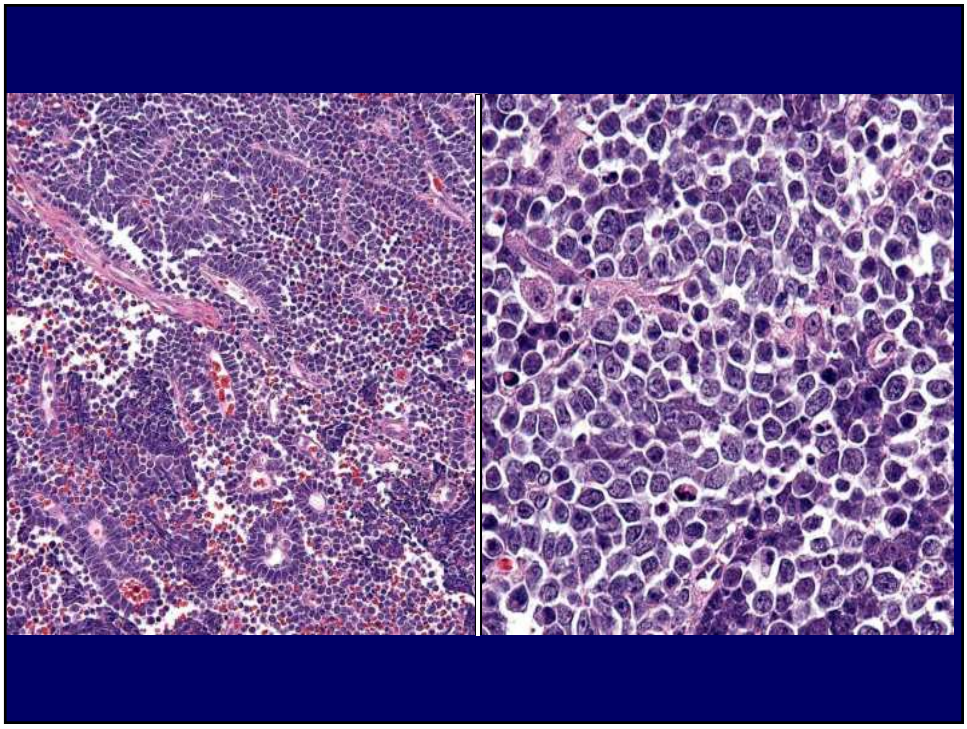
Cervical Neuroendocrine Carcinoma

- <5% of all cervical cancer
- Most present in mid 50's
- Bulky & deeply invasive, necrotic tumors
- Most express one or more neuroendocrine markers
- Often associated with AIS, HSIL, and conventional invasive cervical adenocarcinoma
- Both small and large cell types are p16-positive and harbor high-risk HPV (esp HPV 18) – so not typical neuroendocrine carcinoma

Neuroendocrine Carcinoma, Small Cell Type

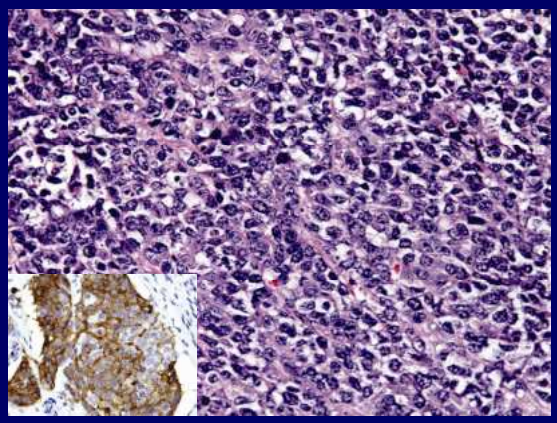
- Usual features of small cell neuroendocrine carcinoma
- Nuclear hyperchromasia, nuclear molding, dispersed chromatin, inconspicuous nucleoli
- High mitotic index, apoptosis
- Necrosis





Neuroendocrine Carcinoma, Large Cell Type

- Medium to large cells
- Moderate to abundant cytoplasm; may contain eosinophilic granules
- Nucleoli may be present but are not required



Cervical Neuroendocrine Carcinoma

- Chromogranin
- Synaptophysin
- Cytokeratin & EMA
- Ki-67 >20%
- All other NE markers – not specific
  - NSE, CD56, S100, etc
- Approximately 40% express TTF1
- P16 positive

Neuroendocrine Tumor Grading

NE Grade	Mitotic Index (MF/10HPF)	Ki-67 (%)
Grade 1	< 2	≤2%
Grade 2	≥ 2	>2%
Grade 3	>20	>20%

Cervical Neuroendocrine Carcinoma

- Clinically aggressive
- 50% present at high stage (FIGO III/IV)
- Common sites of metastases include bone, brain, liver, and bone marrow
- High incidence of regional lymph node metastases
- Systemic chemotherapy with cisplatin or carboplatin and etoposide
- Response durations are often short

Special Variants:

GOOD PROGNOSIS

- Villoglandular – strictly defined
- Adenoid basal carcinoma – strictly defined

POOR PROGNOSIS

- Gastric (or enteric)
- Neuroendocrine
- Clear cell (?)

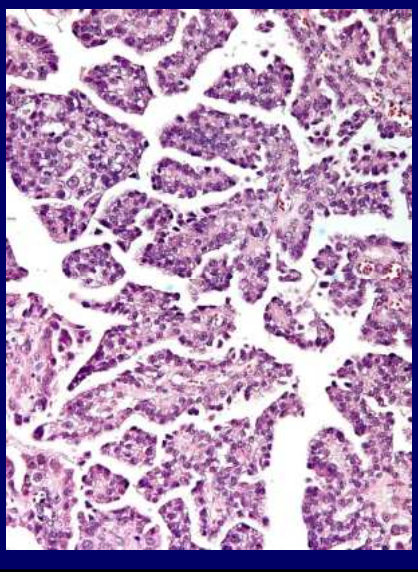
Clear Cell Carcinoma

Non-DES related:

- Wide age range (mean 53 yrs)

DES related:

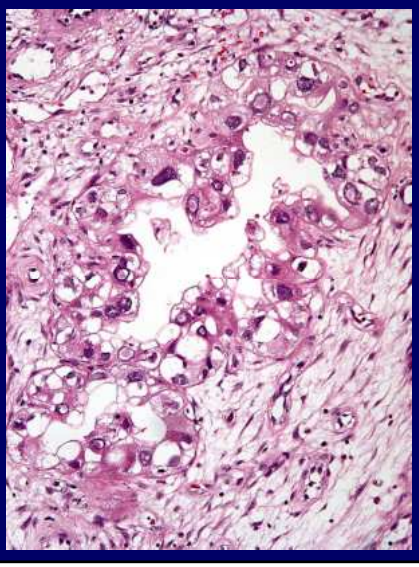
- Arise in adenosis in upper 1/3 vagina or cervix
- Incidence 1/1000
- Peak age 19 years



Clear Cell Carcinoma

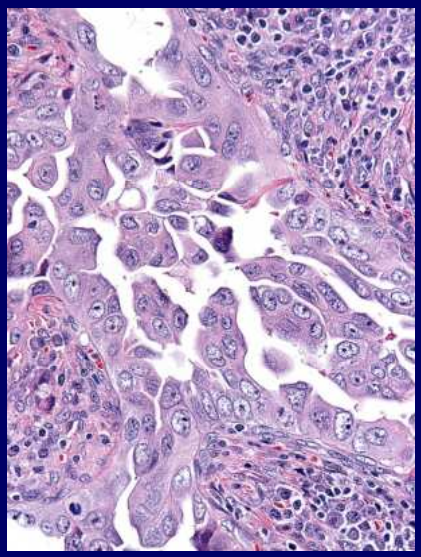
Arias-Stella reaction:

- Dense smudged nuclear chromatin
- Paucity of MF & apoptotic bodies
- No invasion, no mass lesion
- Lacks various patterns of clear cell



Serous Carcinoma

- Cervical primary extraordinarily rare to nonexistent
- Differential diagnosis:
  - Clear cell carcinoma
  - Papillary architecture in usual endocervical CA
  - Extension from endometrium



Special Variants:

PROGNOSIS UNCERTAIN

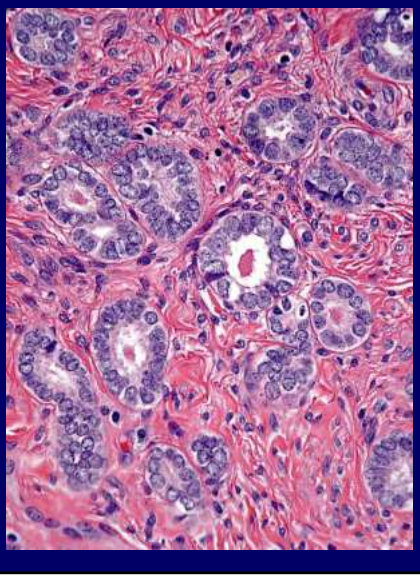
- Mesonephric – early reports suggest good prognosis, but recent data (limited) indicate potential for more aggressive clinical course

Mesonephric Carcinoma

- Patients range in age from 24 years to greater than 60 years.
- Does not arise in transformation zone
  - Arises in lateral, deep cervix, but may be superficial
- Not associated with high-risk HPV
- Often asymptomatic, incidental finding during work-up for other reason
- Most are undetected in cervical cytology

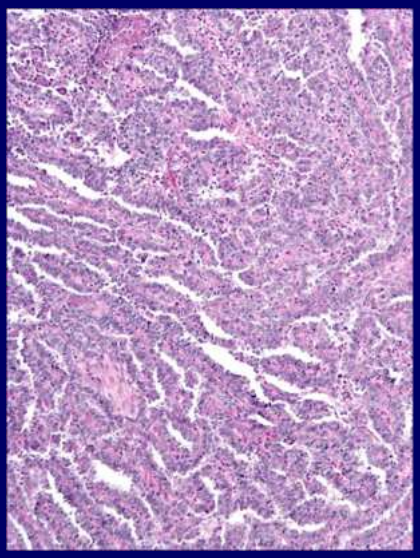
Mesonephric Carcinoma

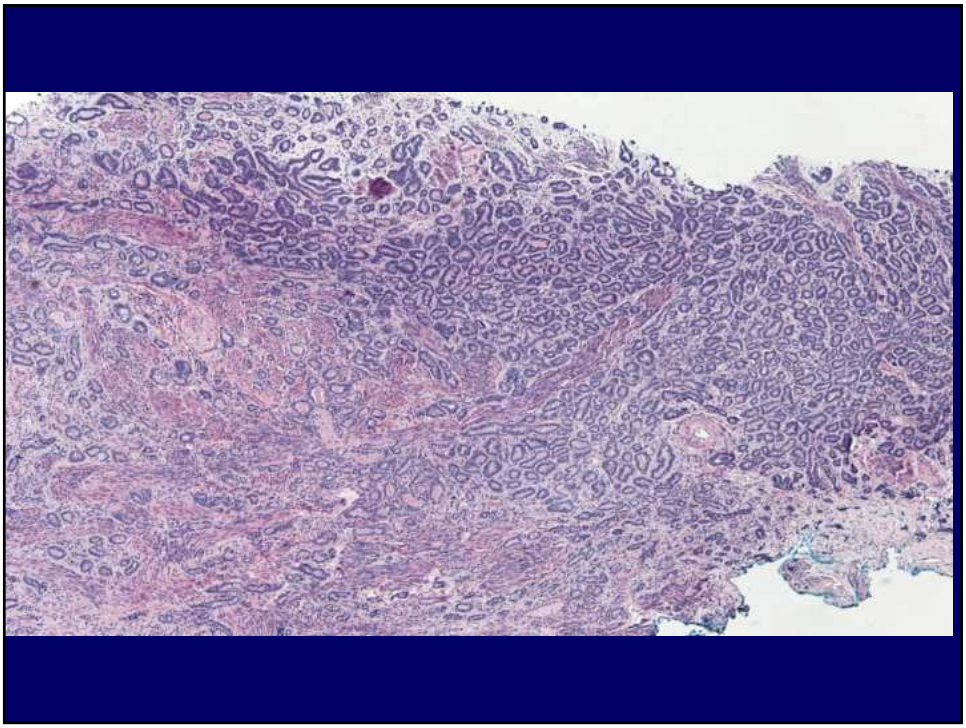
- Small, uniform glands with intraluminal eosinophilic secretions, resembling the adenoid areas of adenoid basal carcinoma, but squamoid areas are absent



Mesonephric Carcinoma

- Ductal, retiform, tubular, solid, & spindle patterns
- Most are low to moderate nuclear grade
- Often merge with florid mesonephric hyperplasia.
- HSIL may be present, but usually appears disparate.





Mesonephric Carcinoma

- Positive for calretinin, inhibin, GATA-3 and CD10 (luminal aspect)
- Generally negative for CEA, ER, and PR
- But, most cases best diagnosed on morphology
- Not known to be associated with HPV; p16 negative

Howitt 2015

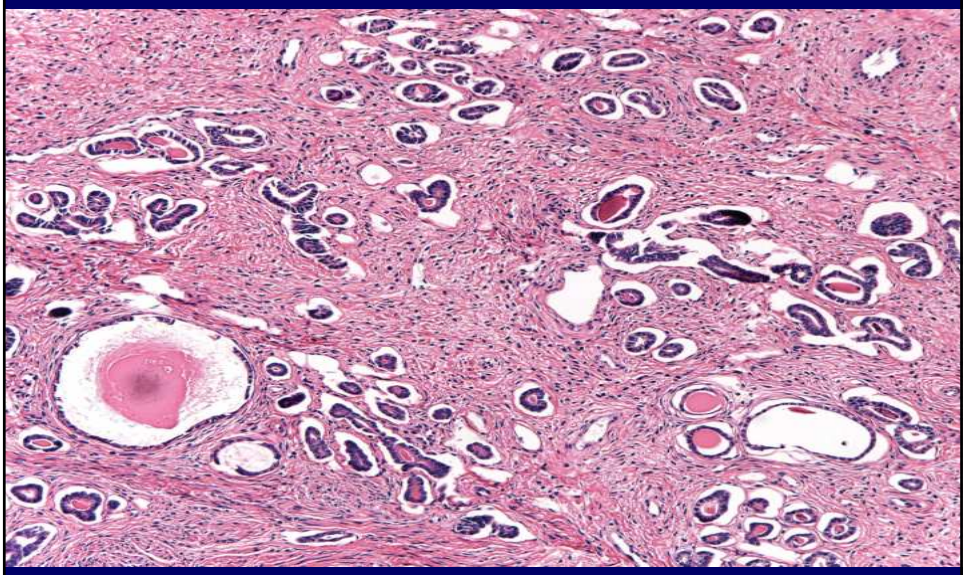
Mesonephric Hyperplasia

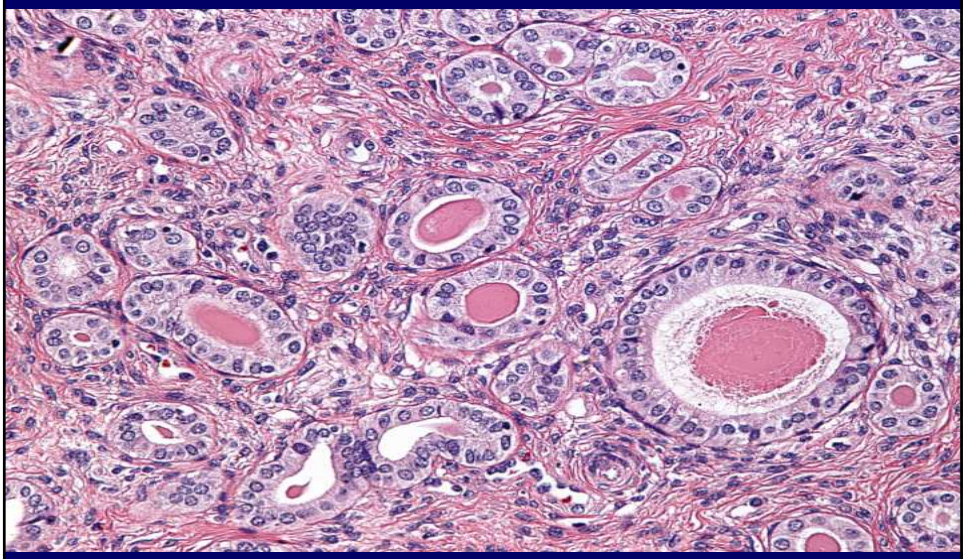
HYPERPLASIA

- Lobular pattern
- Mild cytologic atypia
- Mitotic figures often absent, but may be present

CARCINOMA

- Infiltrative pattern
- Cytologic atypia
- Mitotic figures may be present, often increased





Special Variants:

GOOD PROGNOSIS

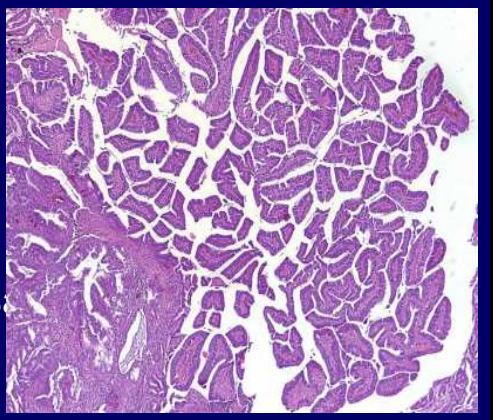
- Villoglandular Adenocarcinoma
- Adenoid Basal Carcinoma

POOR PROGNOSIS

- Gastric type
- Neuroendocrine CA

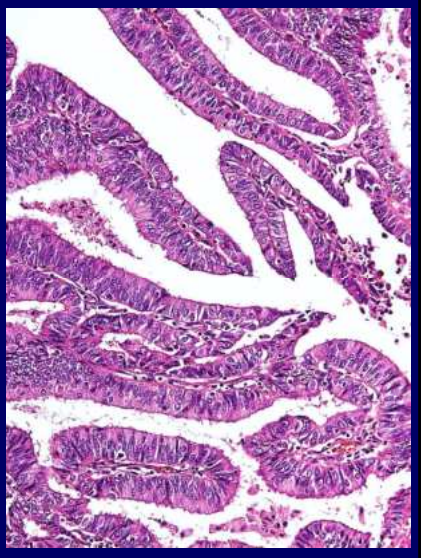
Villoglandular Adenocarcinoma

- Young women
- Good prognosis
- Exophytic tumor
- Minimal invasion
- Caution, if limited s



Villoglandular Adenocarcinoma

- Frond-like growth pattern
- Low nuclear grade
- Cell types: endometrioid, mucinous, or eosinophilic
- Commonly associated with HSIL or AIS
- HPV18 more frequent than HPV16

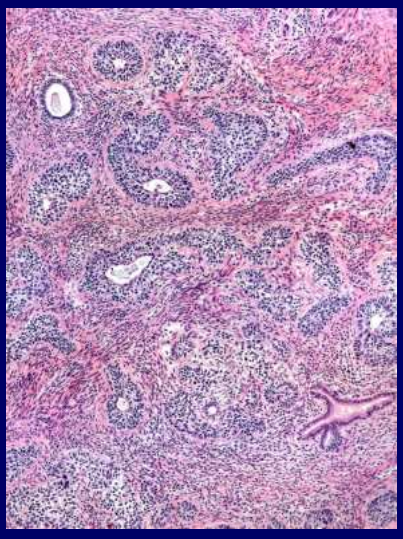


Adenoid Basal Carcinoma

- Other diagnostic term: *Adenoid basal cell epithelioma*
- Elderly, postmenopausal (mean age, 65 years)
- Often asymptomatic – discovered during Pap smear (associated with HSIL)
- Cervix is often normal on colposcopic and physical exam
- Favorable prognosis, as classically defined
- Tumors with deep cervical stromal invasion, foci of higher grade tumor, or lymphovascular involvement may be higher risk

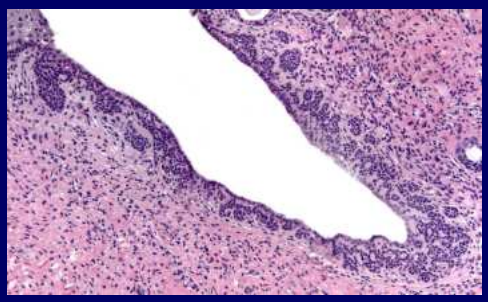
Adenoid Basal Carcinoma

- Features squamoid, basaloid, & adenoid differentiation
- Widely separated clusters of small glands with basaloid, adenoid, & squamoid differentiation
- Typically no stromal response
- Often superficial, but may rarely invade deeply
- CD117 negative



Adenoid Basal Hyperplasia

- Uncommon, incidental finding
- May be associated with adenoid basal cell CA
- If biopsy, need to exclude adenoid basal carcinoma
- If hysterectomy, thorough sectioning to exclude a more severe lesion



Summary

- Pattern-based Classification System: correlates with prognosis
  - Pattern A: pushing border, no LVI
  - Pattern B: limited invasion
  - Pattern C: diffuse, destructive invasion; confluent growth or solid foci

Summary

- Gastric type carcinoma
  - HPV-negative
  - Encompasses minimal deviation adenocarcinoma
- Neuroendocrine carcinoma
  - HPV-positive
  - Almost all high-grade
- Mesonephric carcinoma
  - HPV-negative
  - Infiltrative vs. lobular architecture for mesonephric hyperplasia

Summary: Subtyping *Does* Matter

- Neuroendocrine carcinoma
- Adenoid basal carcinoma
- Gastric-type adenocarcinoma/Adenoma malignum (minimal deviation)
- Villoglandular
- Clear cell
- Mesonephric carcinoma


Thank you
Stanford University