

Endometrial carcinoma: histological typing

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Prevalence of endometrial Ca

- Flanders 1997-1999: 670 new cases/year
- 5,3 % of all malignancies in women
- third after breast (34%) and colorectum (13%)
- Increase !!
- 2000-2001: 761 new cases/year

WHO-classification of EM-Ca

Endometrioid adenoCa

Special types:

Villoglandular
Secretory

Ciliated cell

With squamous differentiation

Mucinous Ca

Serous Ca

Clear cell Ca

Mixed cell adenoCa

Squamous cell Ca

Transitional cell Ca

Small cell Ca

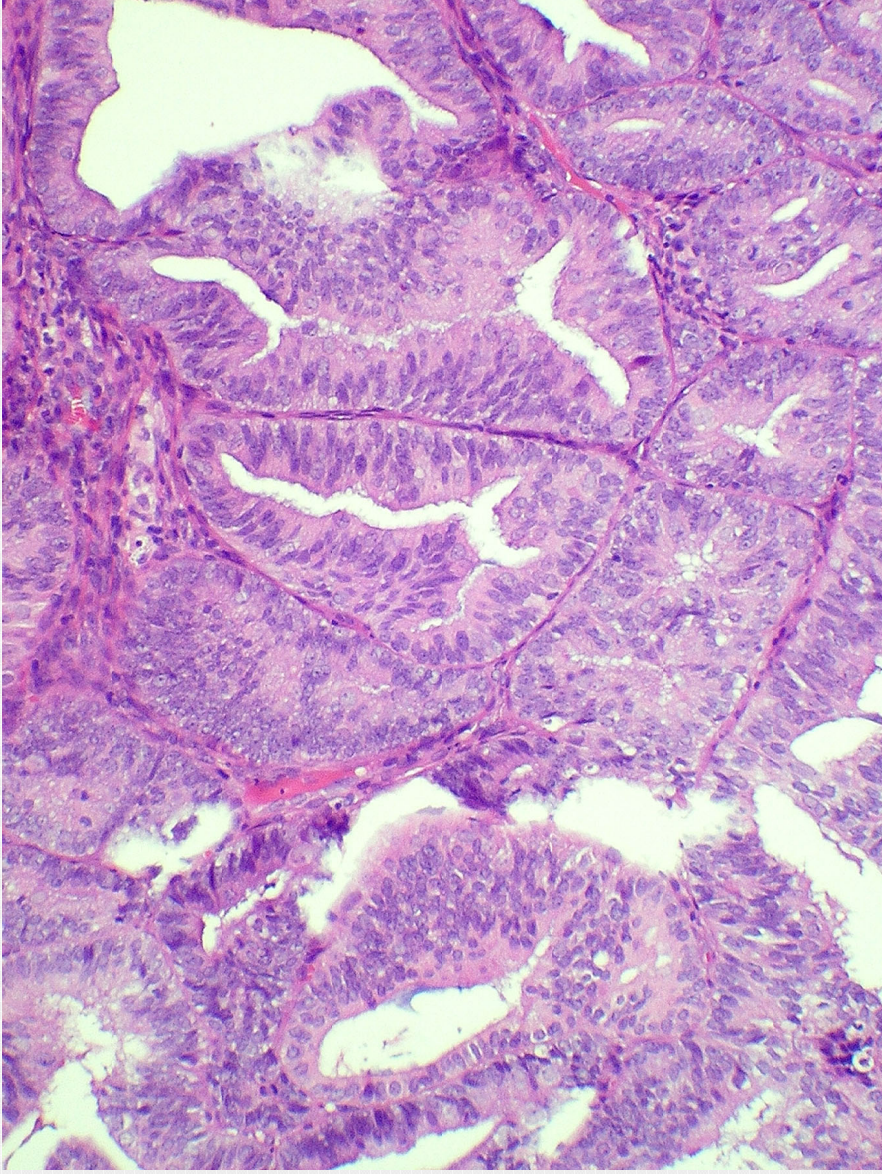
Undifferentiated Ca

Others

Endometrioid Carcinoma NOS

- Glands resembling those of normal endometrium in proliferative phase
- Max 10% zones with squamous, serous, clear cell, mucinous differentiation
- If >10% : mixed type

Endometrioid Ca, NOS



Endometrioid Ca: grading

- Mostly based on architectural grade
- Nuclei only important if grade 3

Architectural grade

- Depends on the extent of solid zones in comparison to the glands
- Do not consider squamous zones !!

Architectural grade

- Grade 1: Max 5 % solid
- Grade 2: 6-50 % solid
- Grade 3: > 50 % solid

Cytological grade

- Nuclei grade 1:
 - oval
 - slightly enlarged
 - fine dispersed chromatin
- Nuclei grade 3:
 - strongly pleomorphic
 - strongly enlarged
 - unregular coarse chromatin
 - prominent eosinophilic nucleoli

Cytological grade

- Nuclei grade 2: between 1 and 3
- Number of mitosis not important

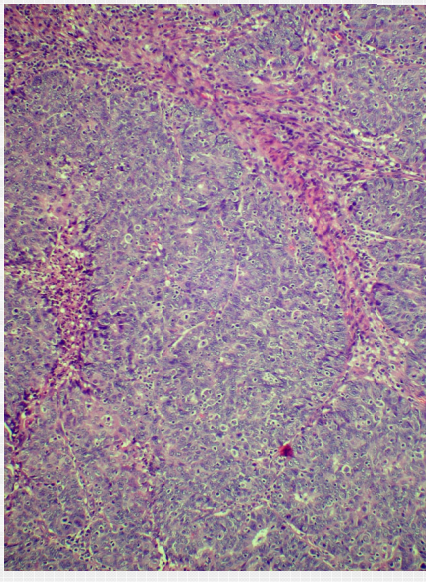
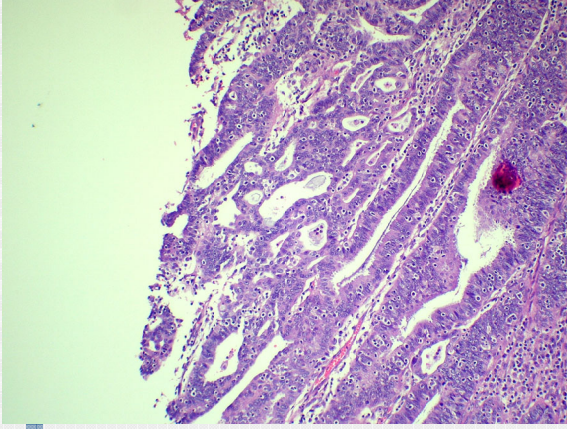
Determination of grade

- Architectural grade primordial
- Cytologic grade 3 augments
architecturale grade 1 or 2 by 1
- If really discordant: think of
 - Serous Ca
 - Clear cell Ca

Examples

- Arch 1 + Cyt 1 or 2
 - → **Grade 1**
- Arch 2 + Cyt 1 or 2
 - → **Grade 2**
- Arch 1 + Cyto 3
 - → **Grade 2**
- Arch 2 + Cyt 3
 - → **Grade 3**

Grade can be very heterogenic



- 1 tumour with zones grade 1 and zones grade 3

Grading

- Heterogeneity in grade very often
- Reason for discordance between curettage and hysterectomy
- Grade 1 remains grade 1 in 45%

Grade 1 + undifferentiated Ca

- Silva: Association of low-grade endometrioid Ca of the uterus and ovary with undifferentiated Ca: a new type of dedifferentiated Ca?
I J Gynecol Pathol (2006) 25: 52-58
- Indicates aggressive behavior
- In asynchronous cases: can explain absence of second primary

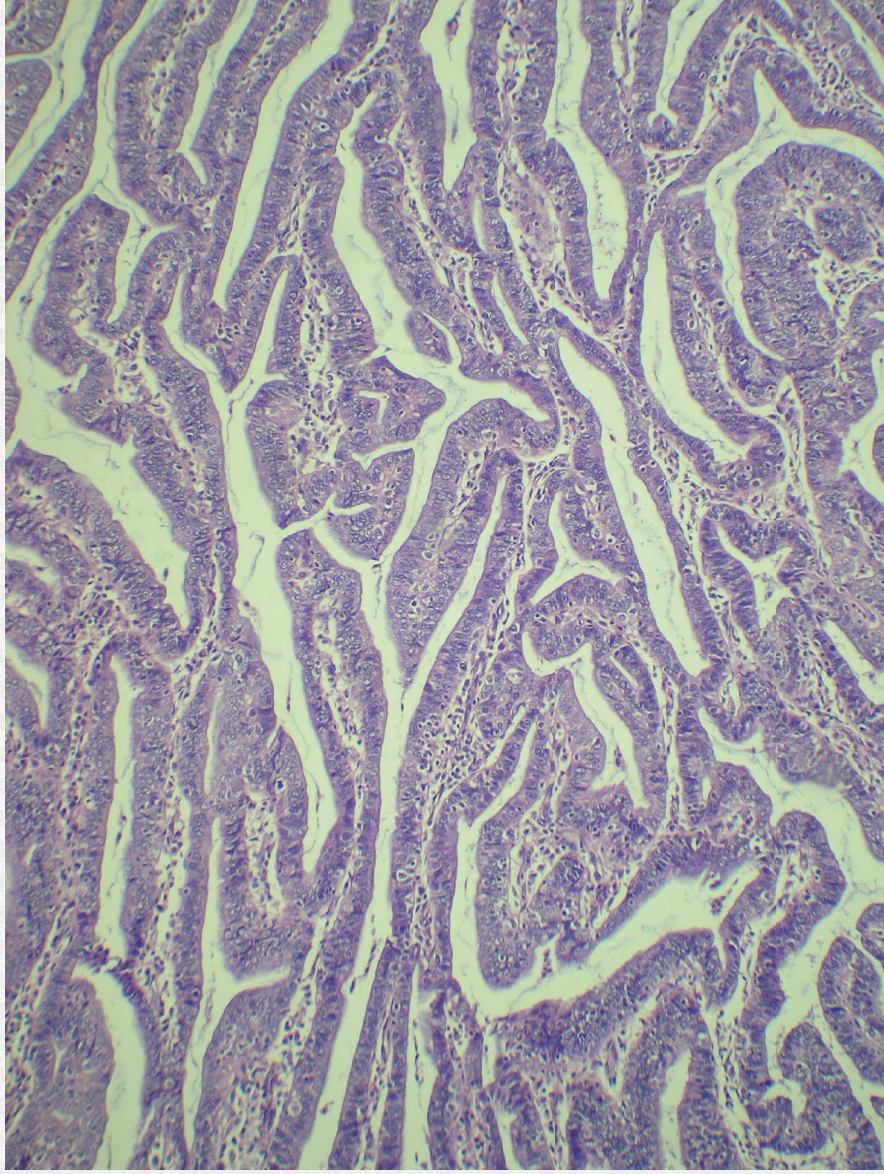
Endometrioid Ca: variants

- Villoglandular Ca
- Secretory Ca
- Ciliated cell Ca
- Endometrioid Ca with squamous differentiation

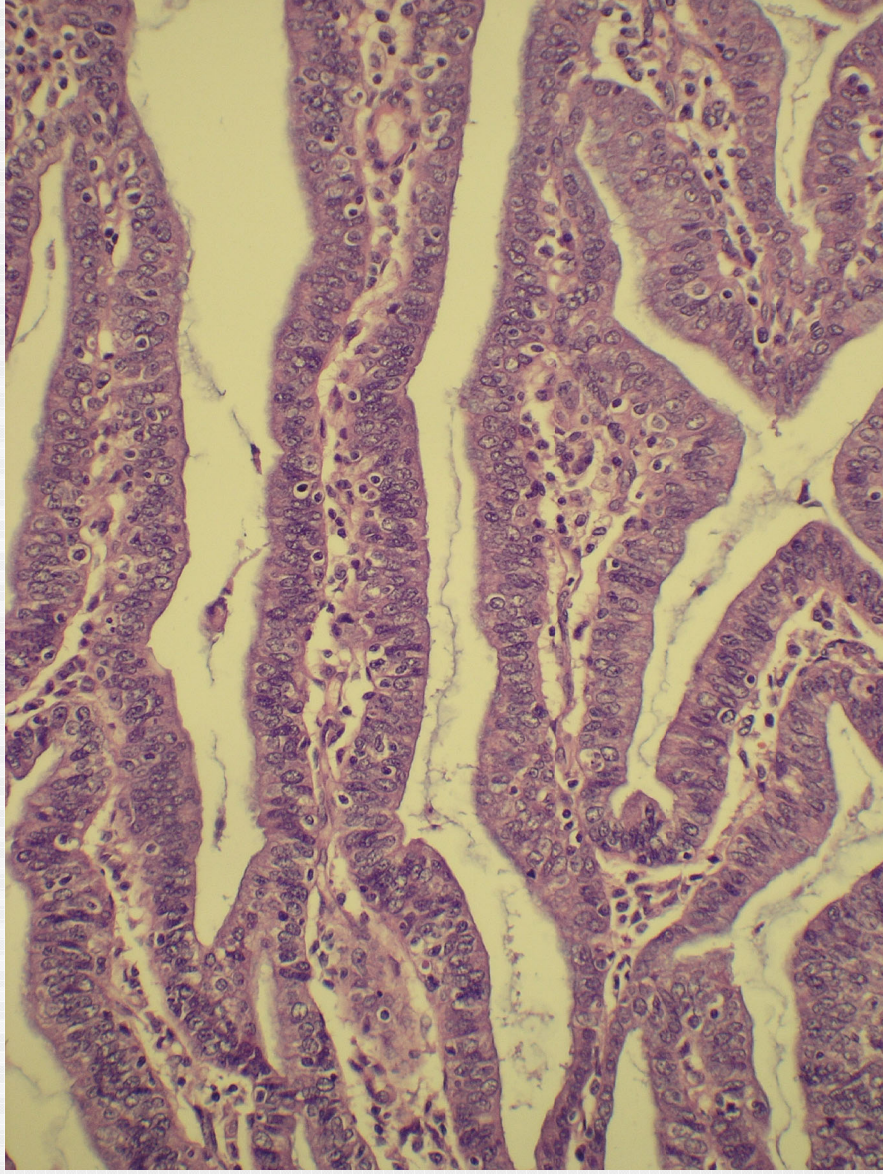
Villoglandular Ca

- Numerous villous fronds, long and slender
- Delicate fibrovascular core
- Columnar cells , polarity maintained
- Nuclei: usual grade 1 or 2

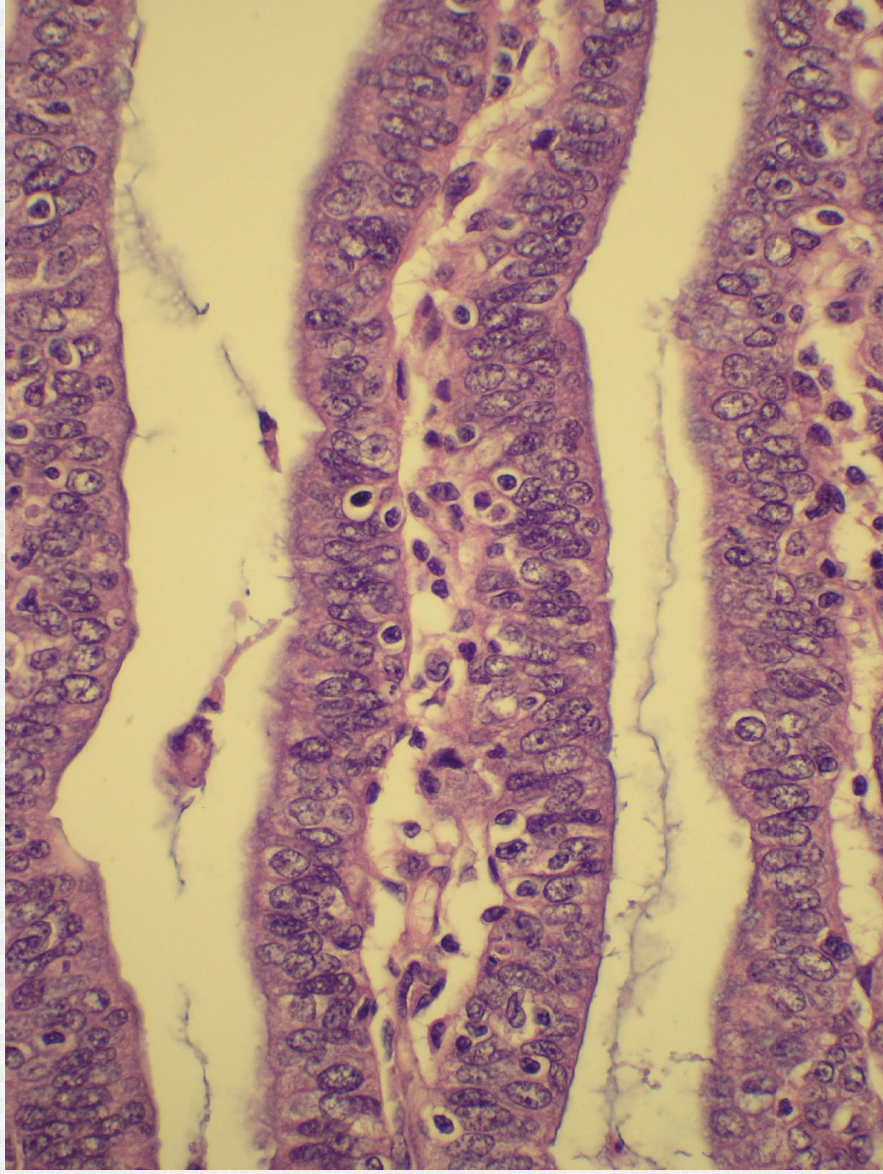
Villoglandular Ca



Villoglandular Ca



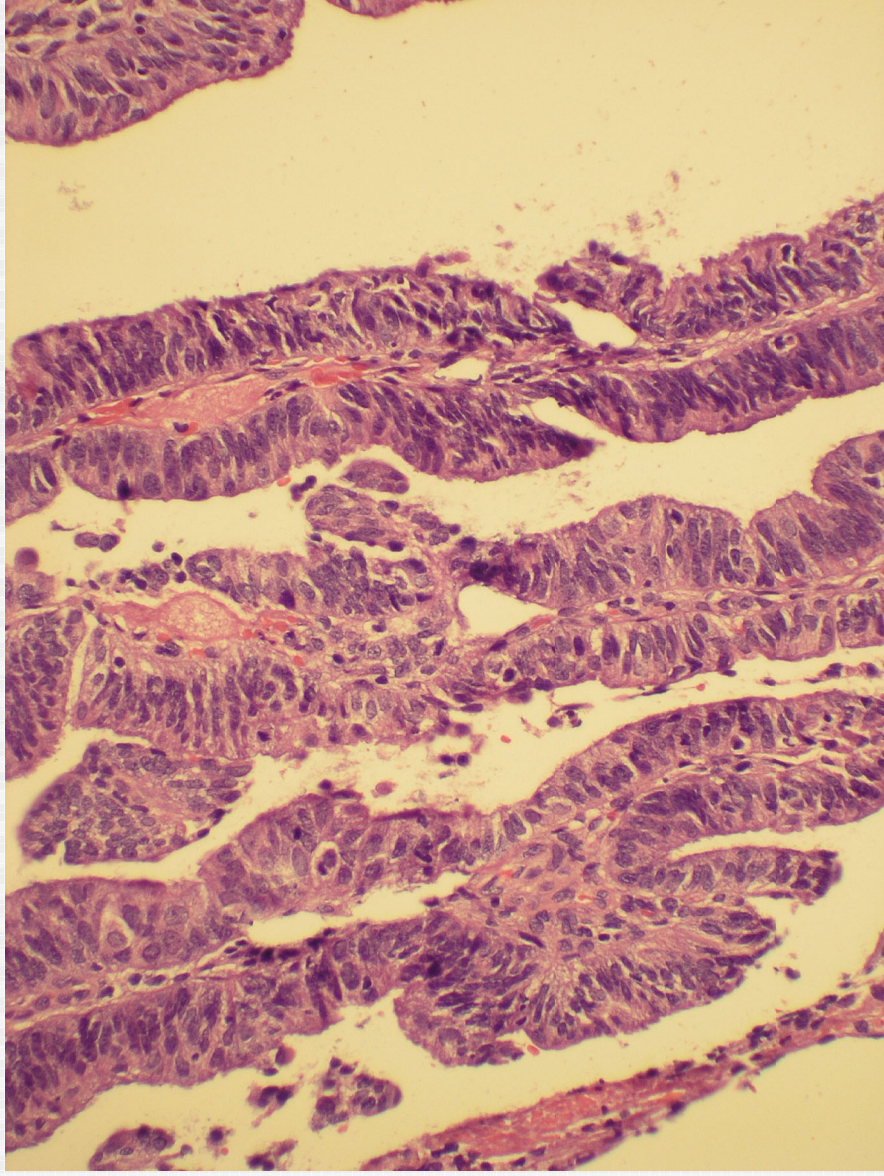
Villoglandular Ca



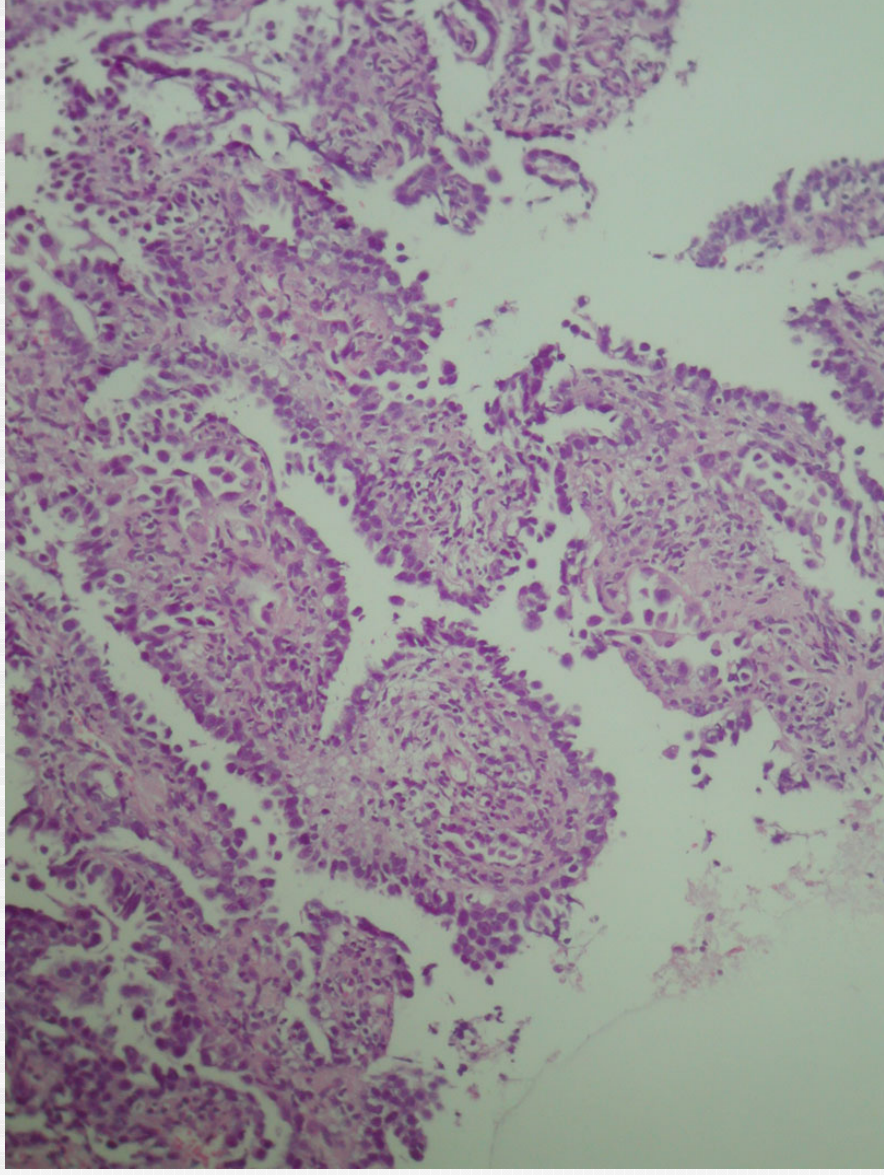
Villoglandular Ca: DD

- | | |
|-----------------------------------|--|
| ■ Villoglandular Ca: | ■ Serous Ca: |
| ■ long papillae | ■ short papillae |
| ■ slender papillae | ■ broad papillae |
| ■ fibrovascular connective tissue | ■ fibrous connective tissue |
| ■ little atypia | ■ severe atypia |
| ■ regular luminal border | ■ irregular luminal border:
micropapillae |
| ■ cohesive cells | ■ dyscohesive cells |

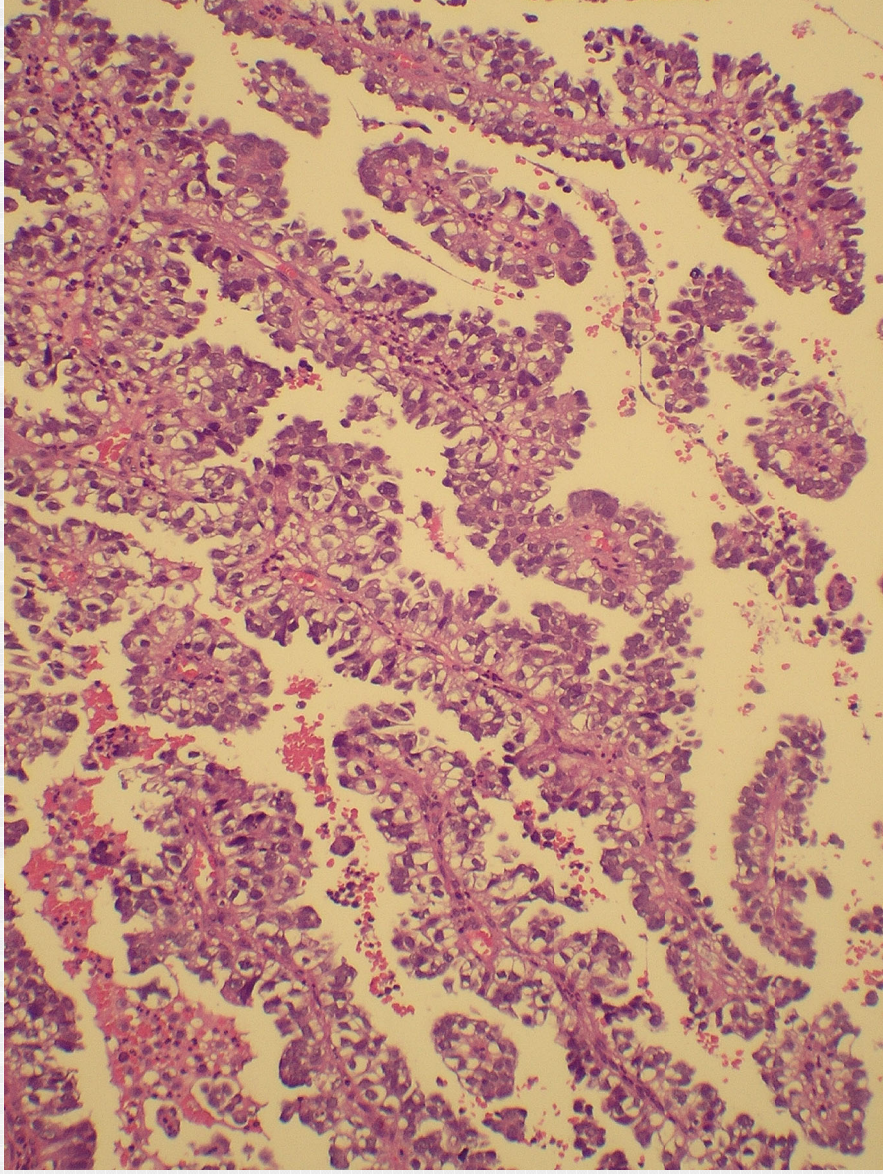
Villoglandular Ca



Serous Ca: typical presentation

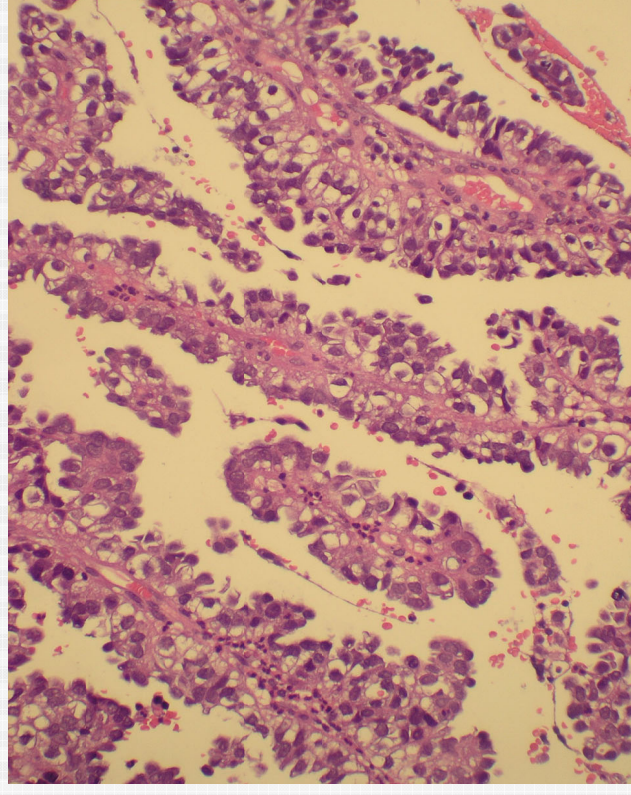
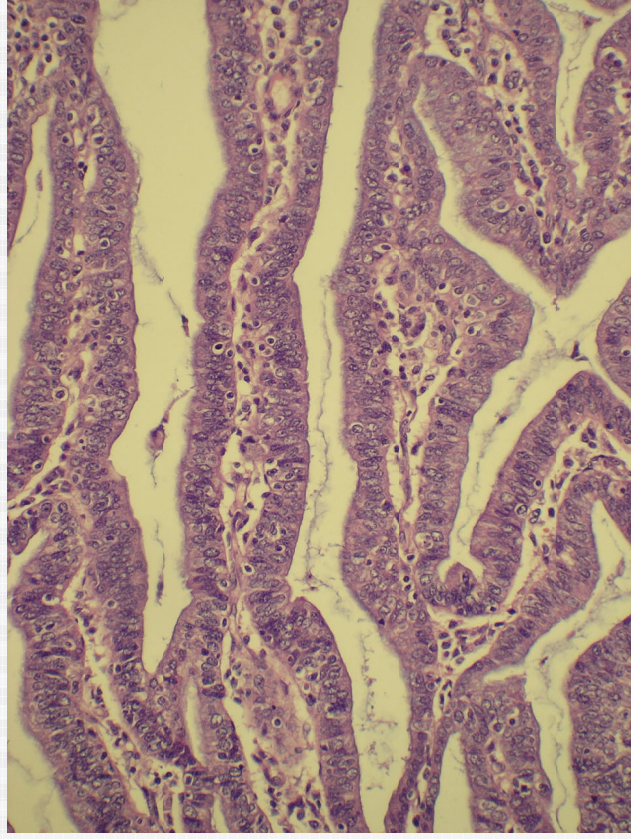


USC: cove slender papillae



Villoglandular

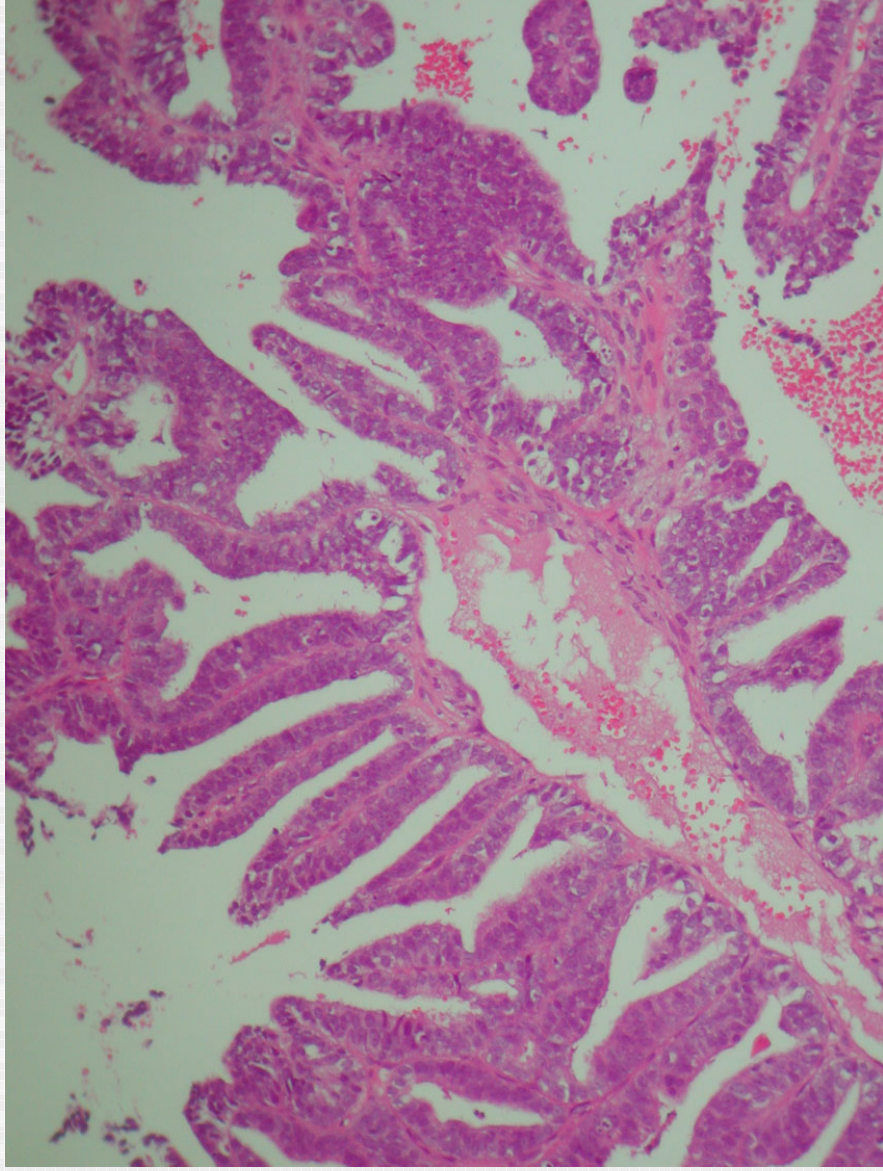
USC



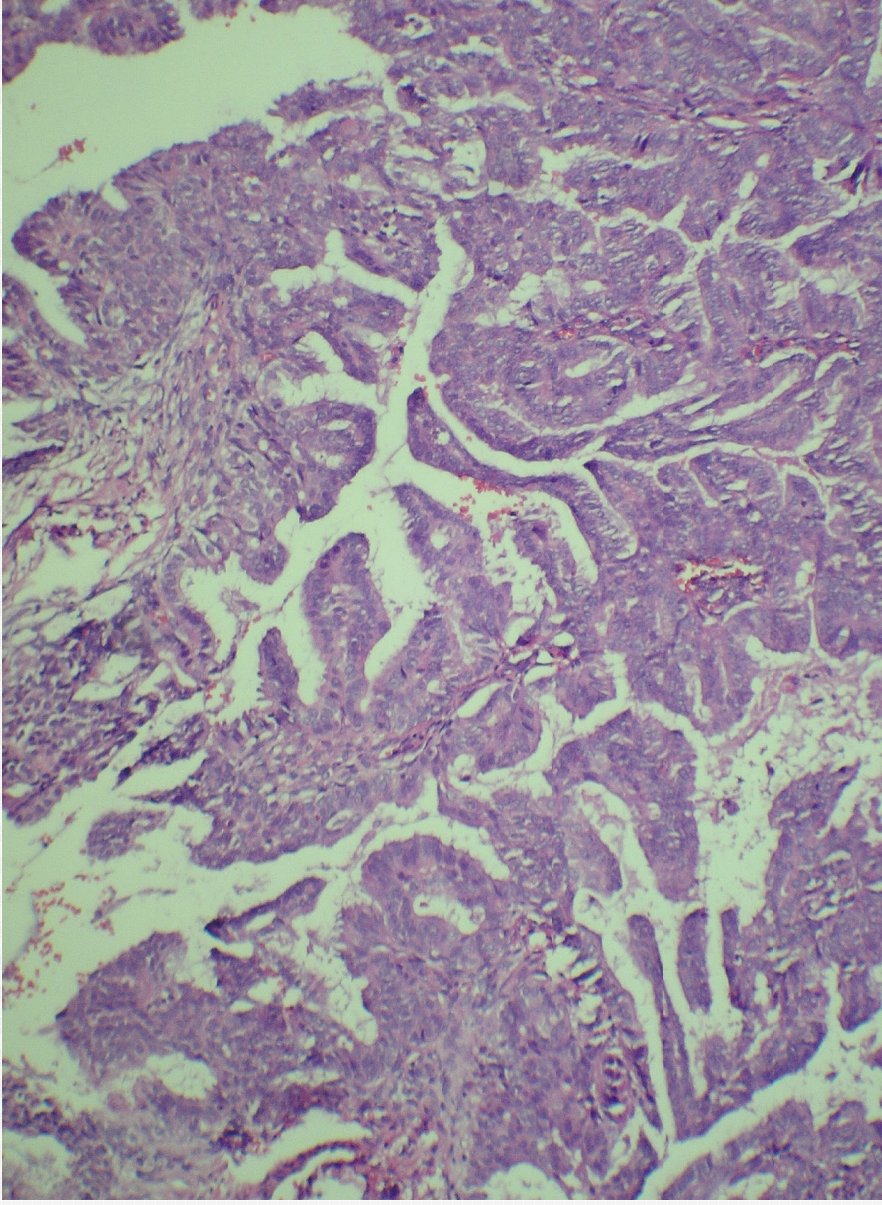
CAVE !!!!!

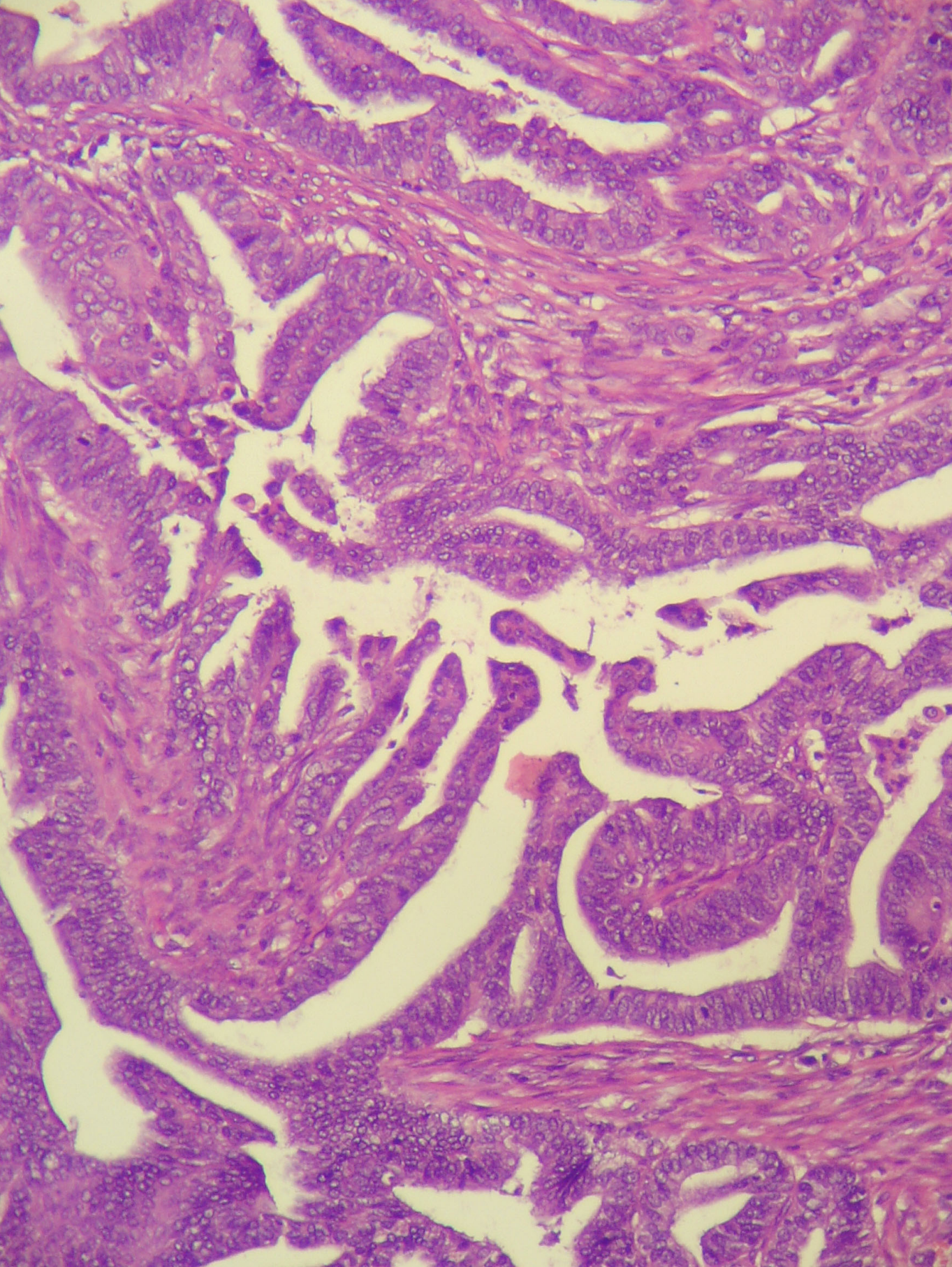
- Micropapillary variant of endometrioid Ca
 - Short papillae, not complex
 - Bland cytology
 - Cells not discohesive
- Not an official WHO-variant
- Prognosis worse than endometrioid NOS

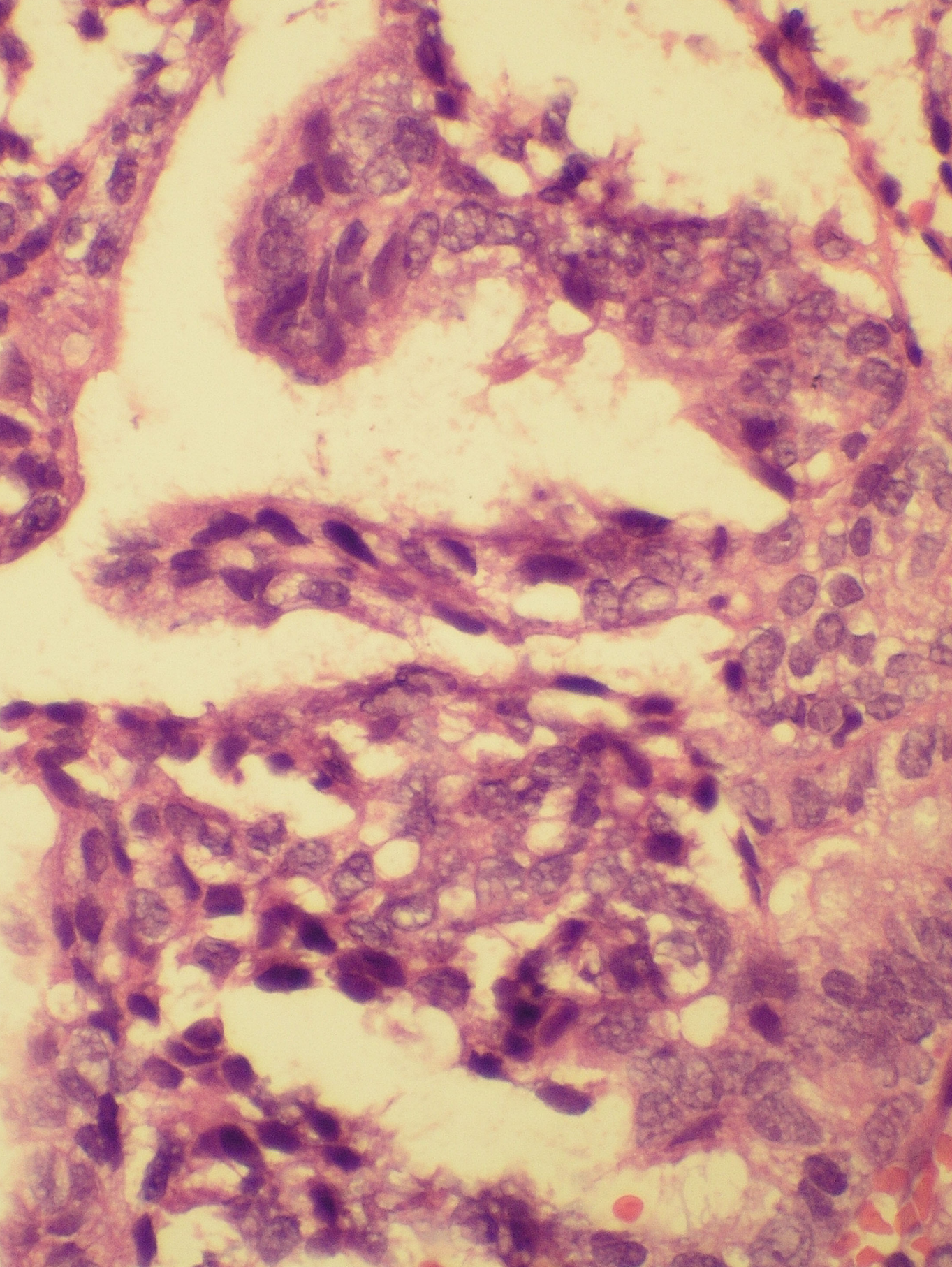
Micropapillary endometrioid Ca



Endometrioid Ca: micropapillary



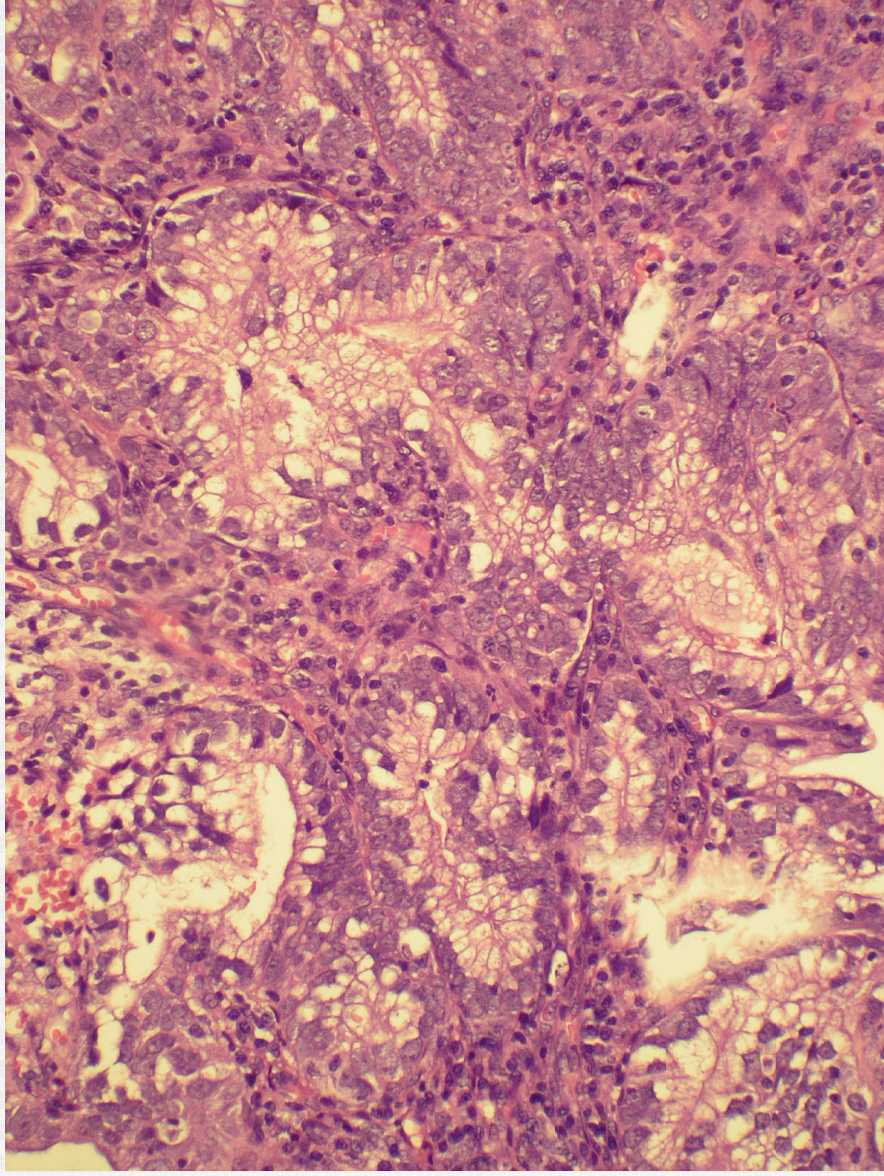




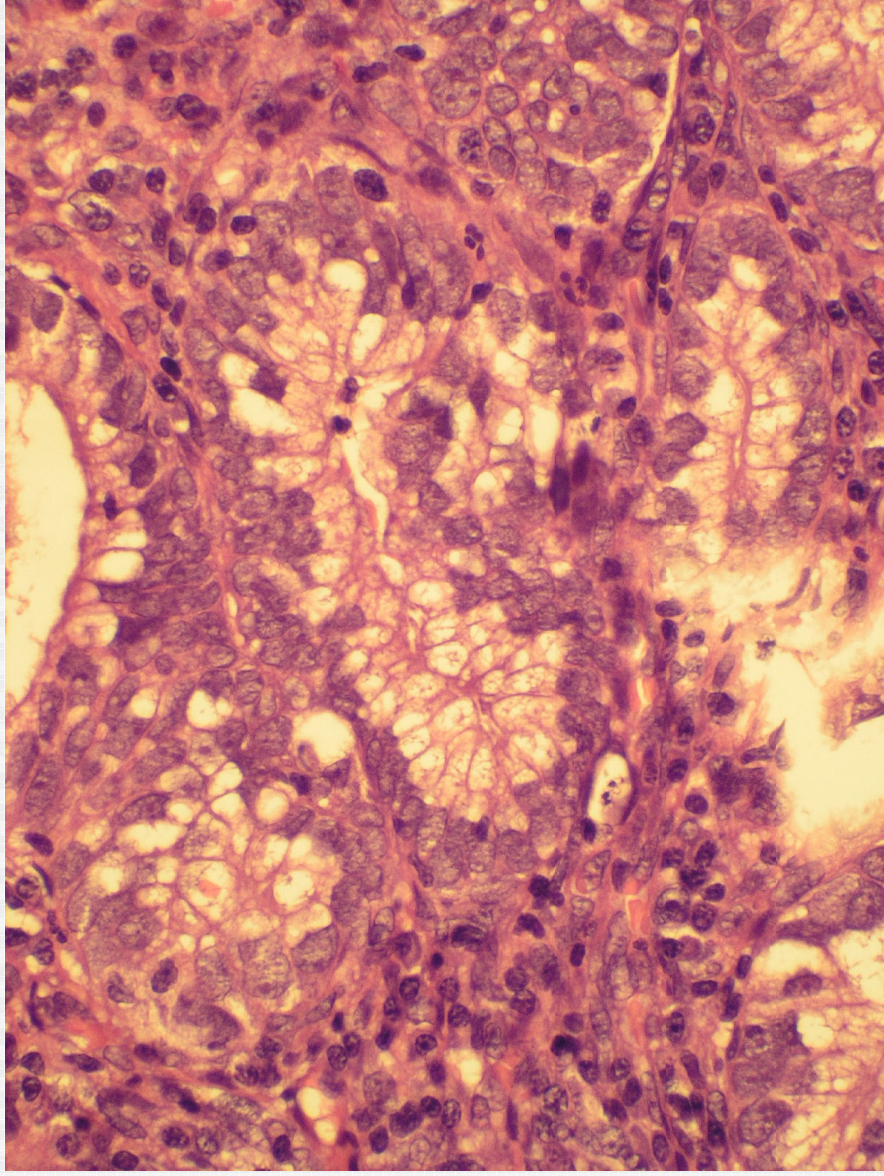
Secretory Ca

- resembling early secretory endometrium
- vacuoles in cytoplasm of most cells
sub- or supranuclear
- nuclei usual grade 1 without stratification

Secretory Ca



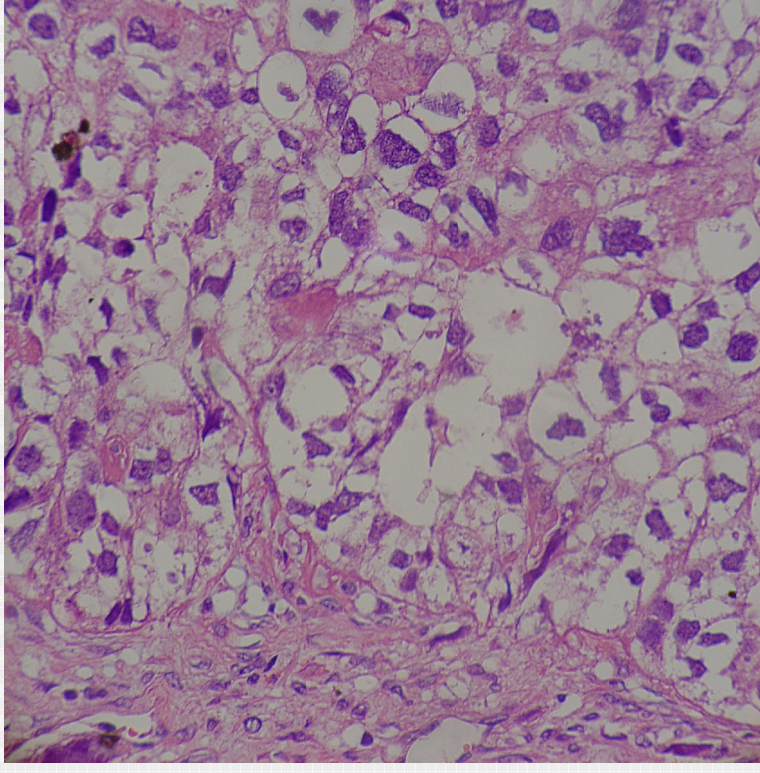
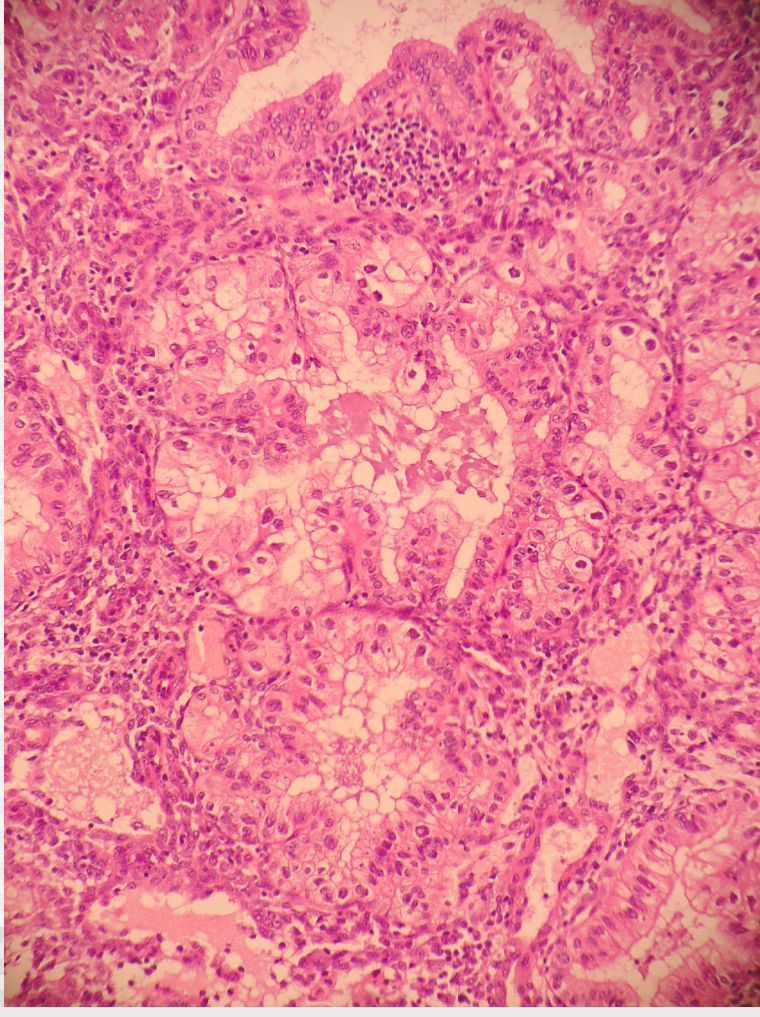
Secretory Ca



Secretory Ca: DD

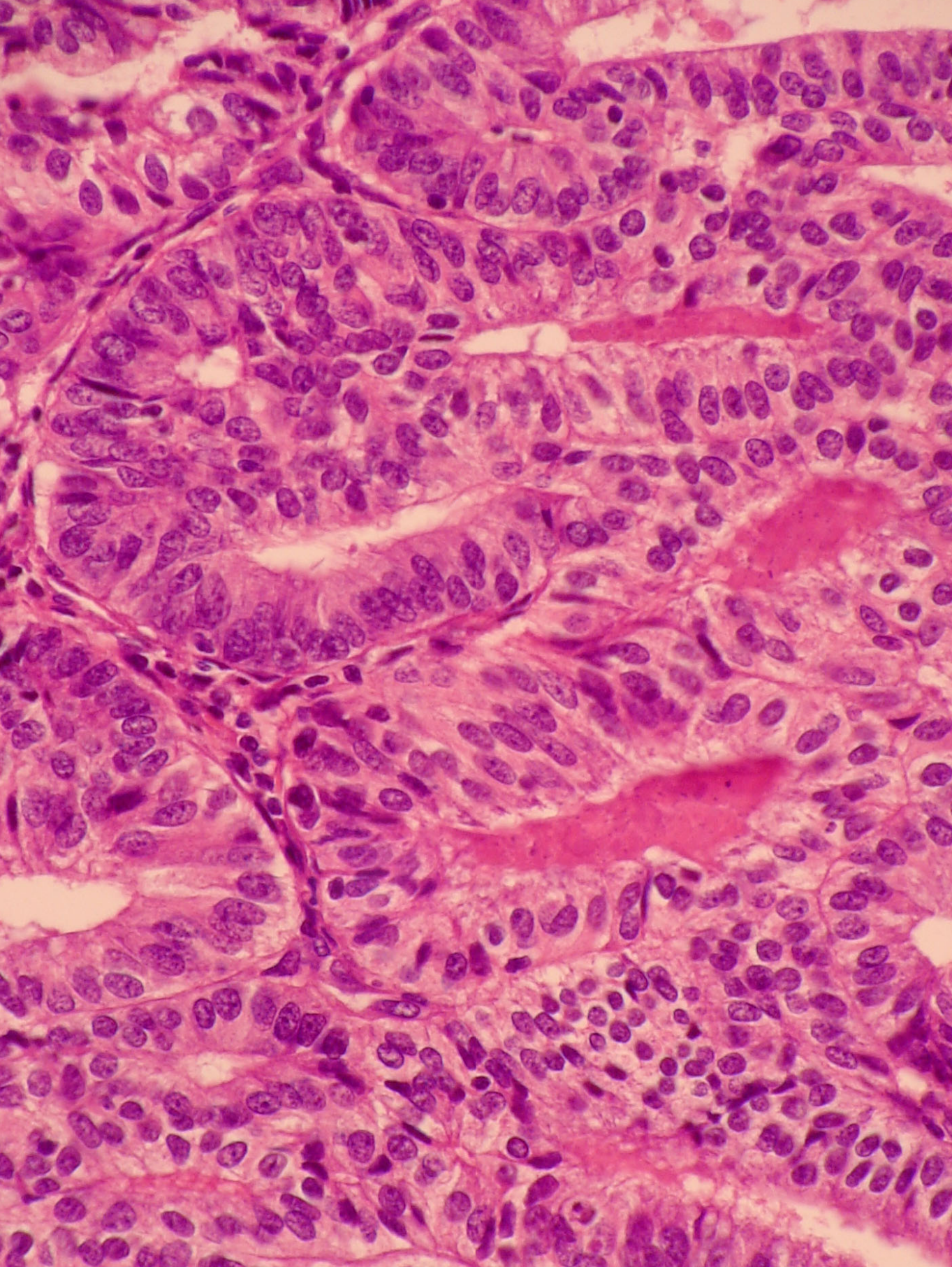
- Secretory Ca
 - glandular
 - endometrioid NOS
 - cells columnar
 - nuclei eccentric
 - grade 1
- Clear Cell Ca
 - often solid
 - serous Ca
 - cells round, polygonal
 - nuclei central
 - severe atypia
 - frequent hobnail

Secretory Ca vs Clear cell Ca

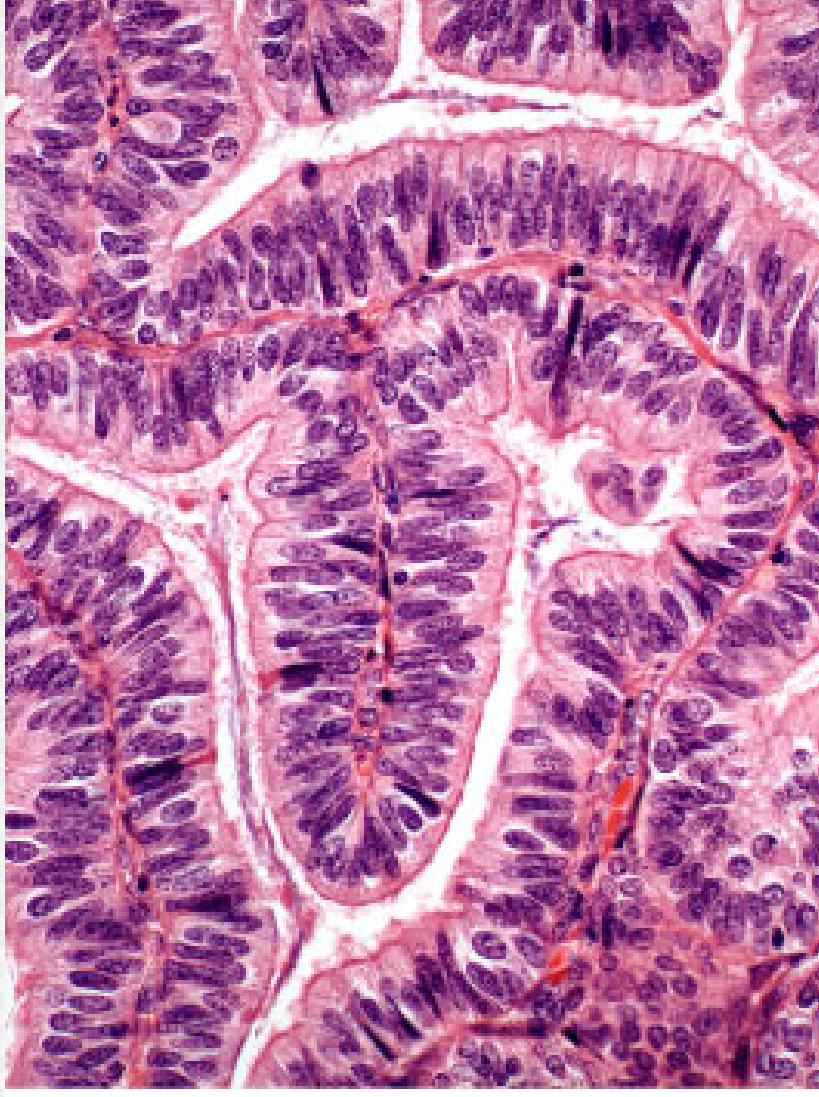


Ciliated cell Ca

- Almost always grade 1
- often cribriform pattern
- prominent eosinophil cytoplasm
- Cilia (not always) - cuticula
- Nuclear membrane irregular
- Coarse chromatin
- Prominent nucleoli



Ciliated cell carcinoma



Ciliated cell Ca

- Associated with endometrioid Ca NOS, or mucinous Ca
- Ciliated cells must predominate

Endometrioid Ca with squamous differentiation

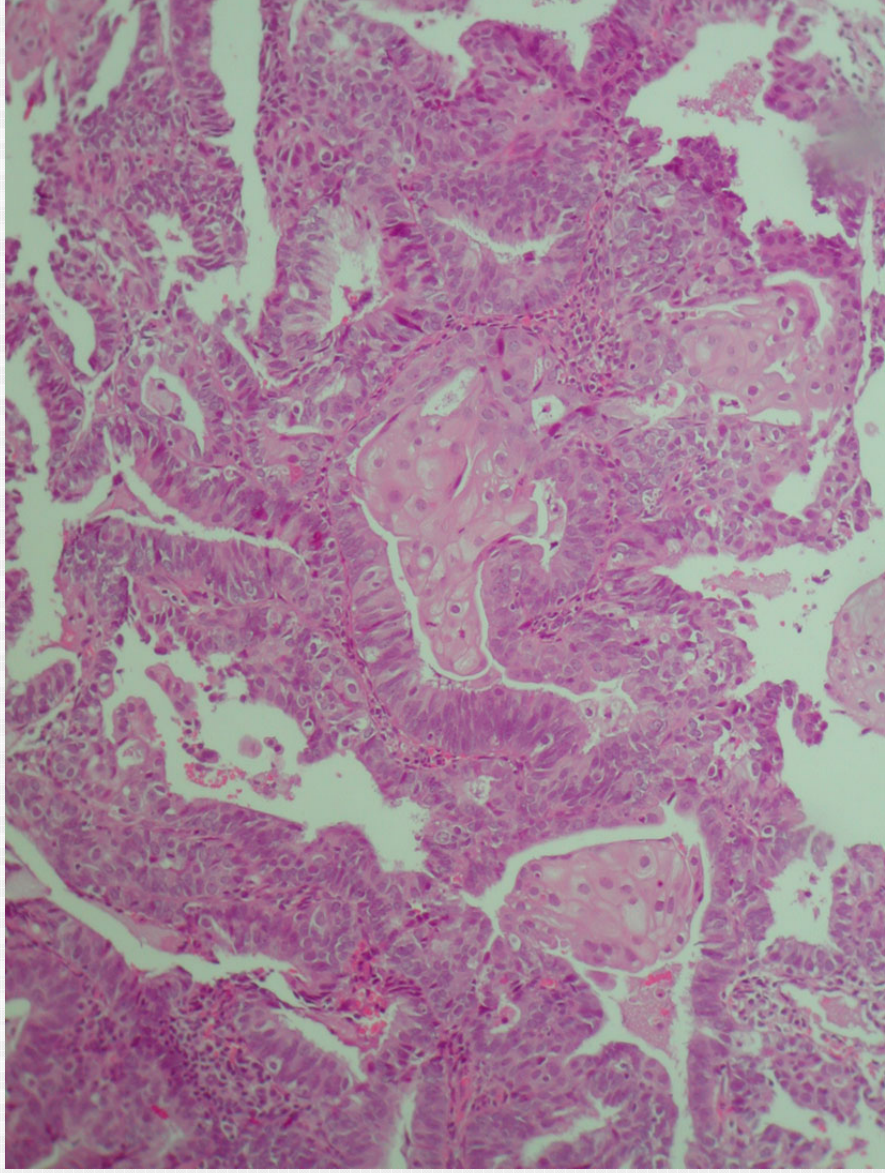
= adenosquamous Ca + adenoacanthoma

- is squamous component malignant ?
 - difficult to assess
 - no clinical significance

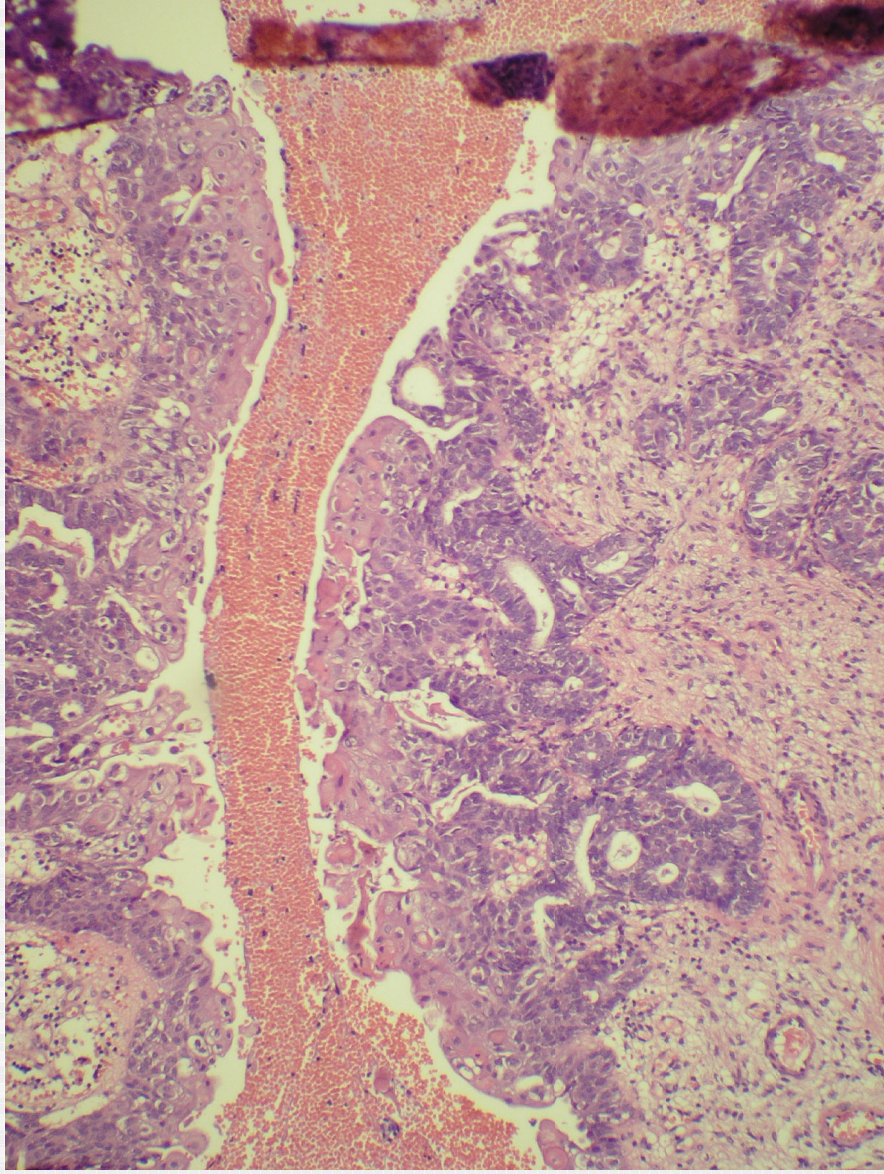
Endometrioid Ca with squamous differentiation

- 10% of the tumour has to be squamous
- Sometimes only intraluminal
- Glandular component predominates

Squamous differentiation: intraluminal



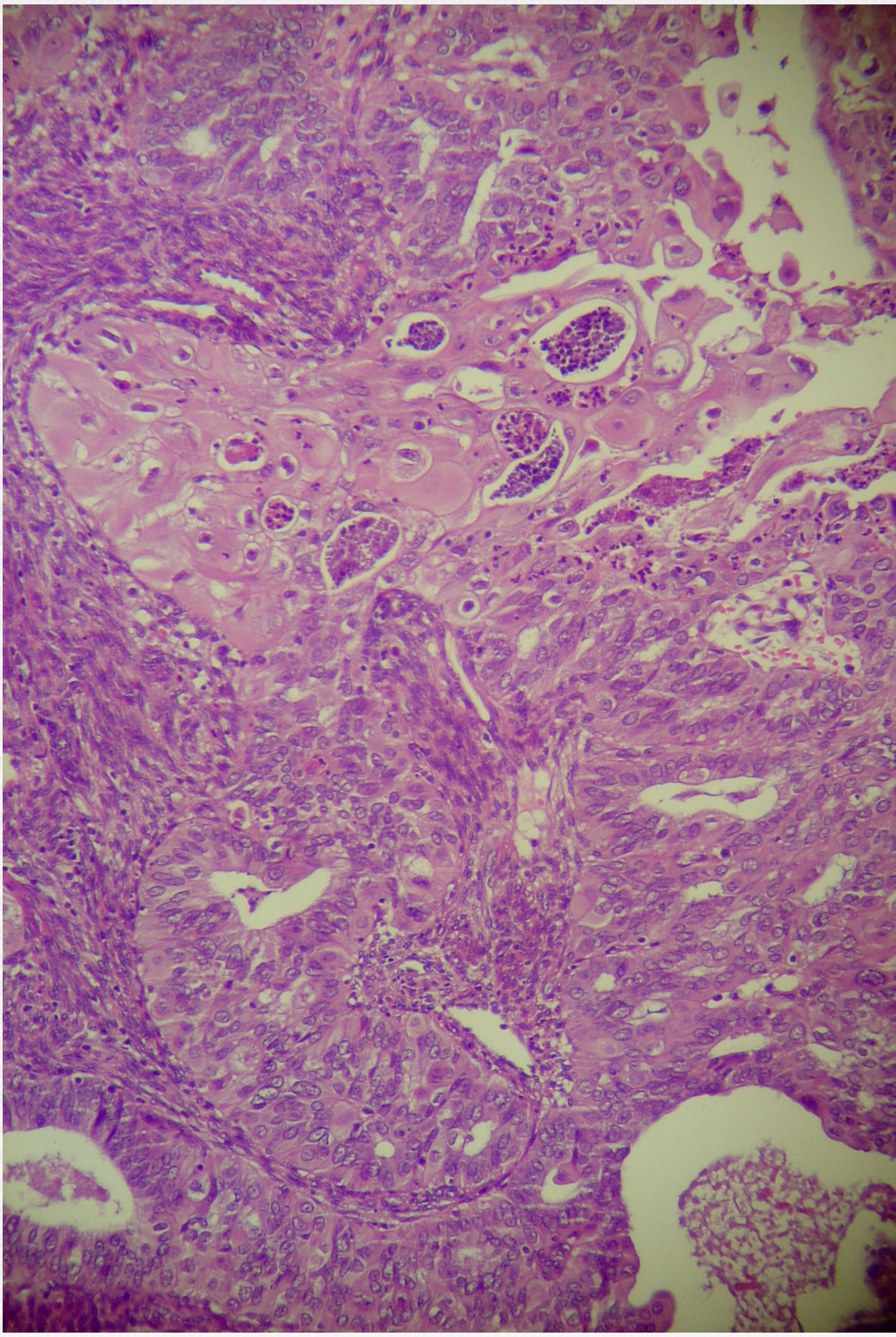
Squamous differentiation: surface



Endometrioid Ca with squamous differentiation: grading

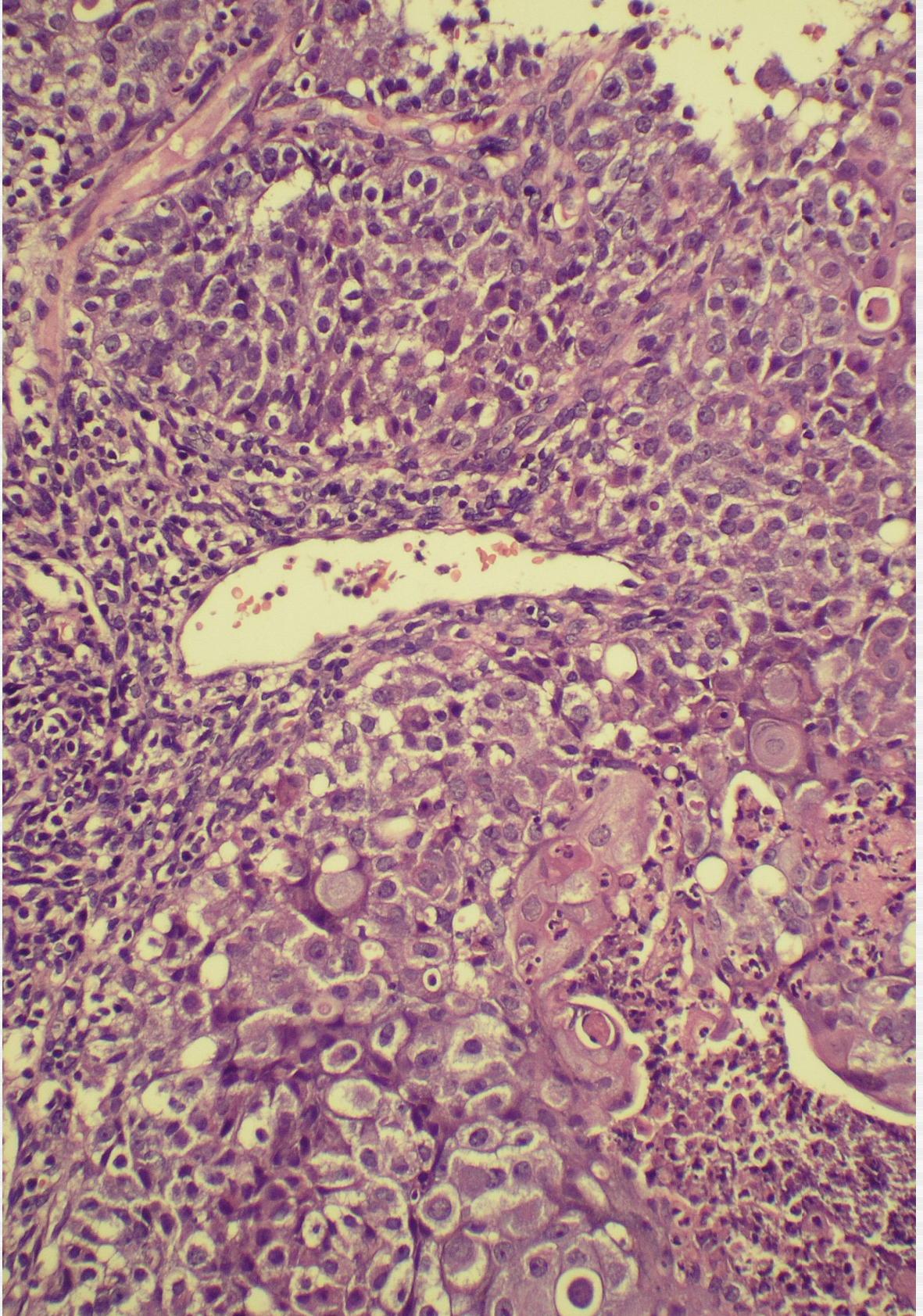
- Prognosis does not depend on assessment of malignancy of squamous zones
Architectural grade of glandular component
- **Identify** squamous zones and **IGNORE** them while grading

Endometrioid Ca with squamous differentiation: grading



Endometrioid Ca with squamous differentiation

- Solid zones of undifferentiated cells: regard as glandular unless:
 - Intercellular bridges
 - Large cells with eosinophilic cytoplasm and clear cellboundaries



Endometrioid Ca with squamous differentiation: DD

- Atypical hyperplasia with metaplasia/EIN
- Granuloma
- High-grade non-squamous component !!!
- Primary Cx:
 - Signet cells: rather in Cx

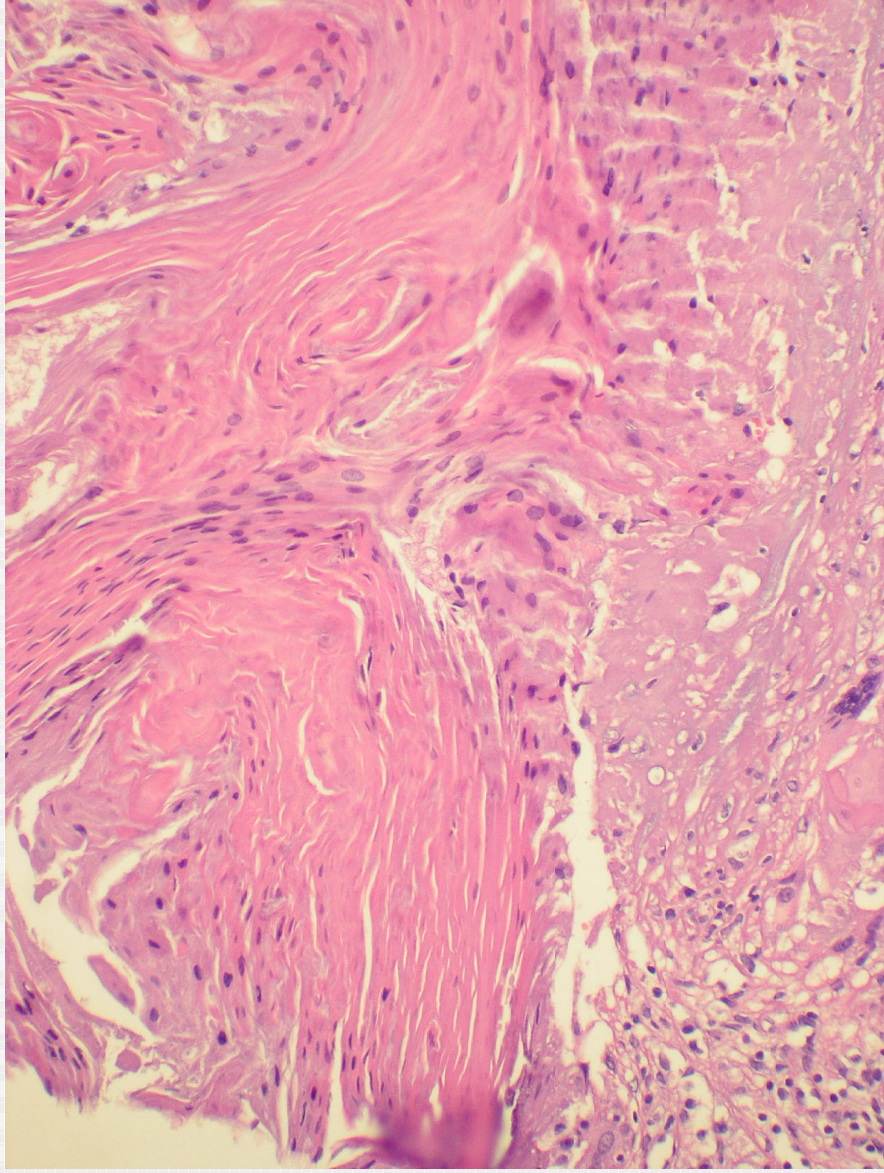
Endometrioid Ca with squamous diff: metastasis

- Remains glandular and squamous
- 20% only glandular component
- 8% only squamous component

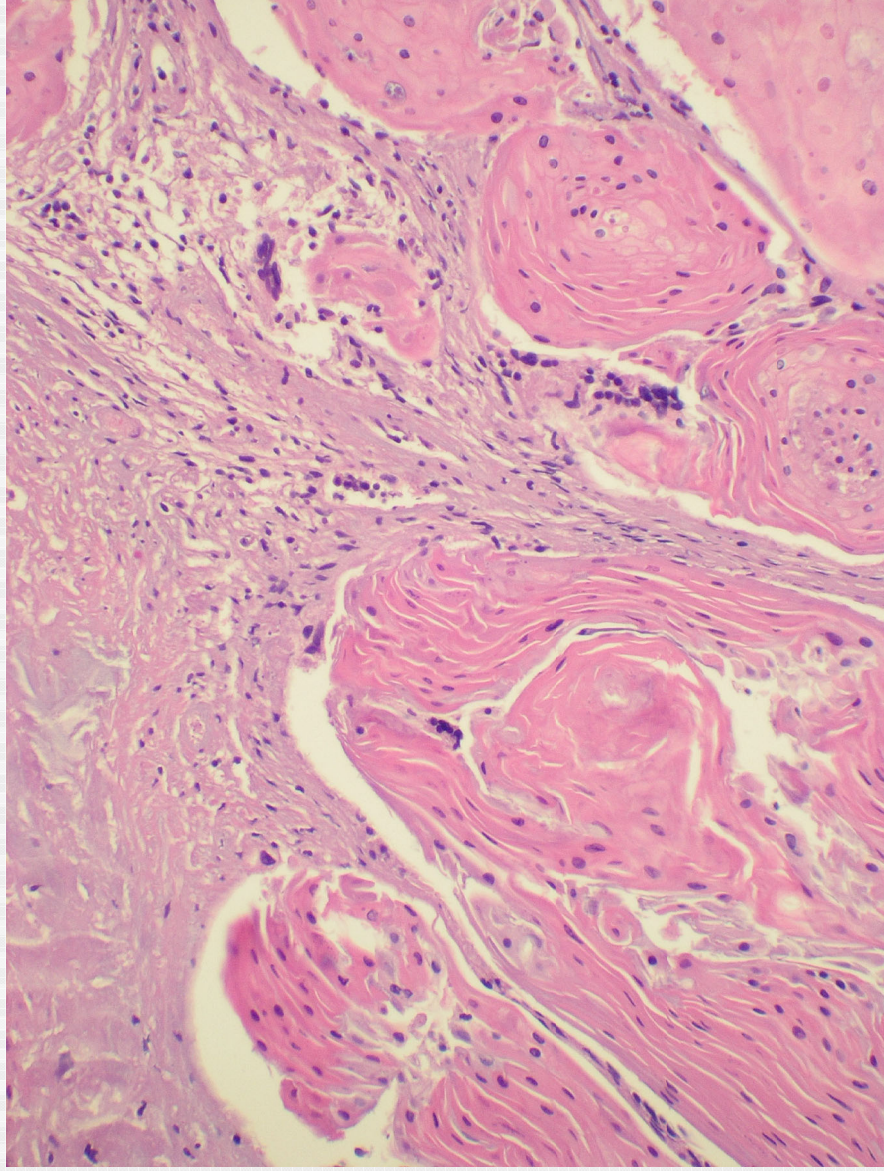
Endometrioid Ca with squamous differentiation and keratingranulomas

- If keratin without viable tumourcells:
ignore while staging
- Consider only as tumour if also viable
tumourcells are present !!

Keratingranuloma



Keratingranuloma



Glassy cell carcinoma

- Very rare in Em: no official variant
- More frequent in cervix
- Considered to be an undifferentiated adenosquamous Ca
- Very aggressive

Glassy cell Carcinoma

- Polygonal cells in solid sheets
- “glassy” cytoplasm
- Fibrous stroma
- Abundant inflammatory cells
- In Cx: eosinophils !!

WHO-classification of EM-Ca

Endometrioid adenoCa

Mucinous Ca

Serous Ca

Clear cell Ca

Undifferentiated Ca

Mixed cell adenoCa

Squamous cell Ca

Transitional cell Ca

Small cell Ca

Others

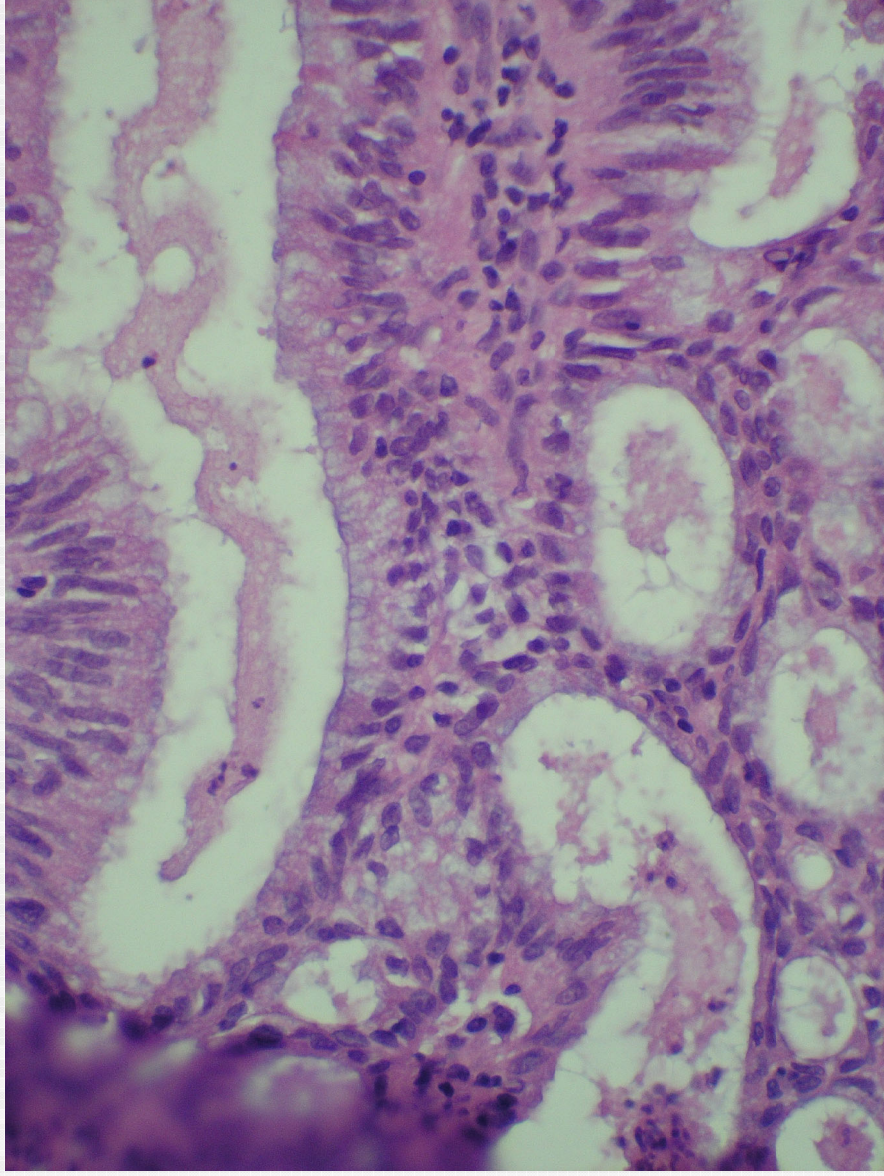
Mucinous carcinoma

- Rare in pure form
- Looks like mucinous Ca of endocx
- 50 % of cells : PAS+ mucin in cytoplasm
- diastasis resistant

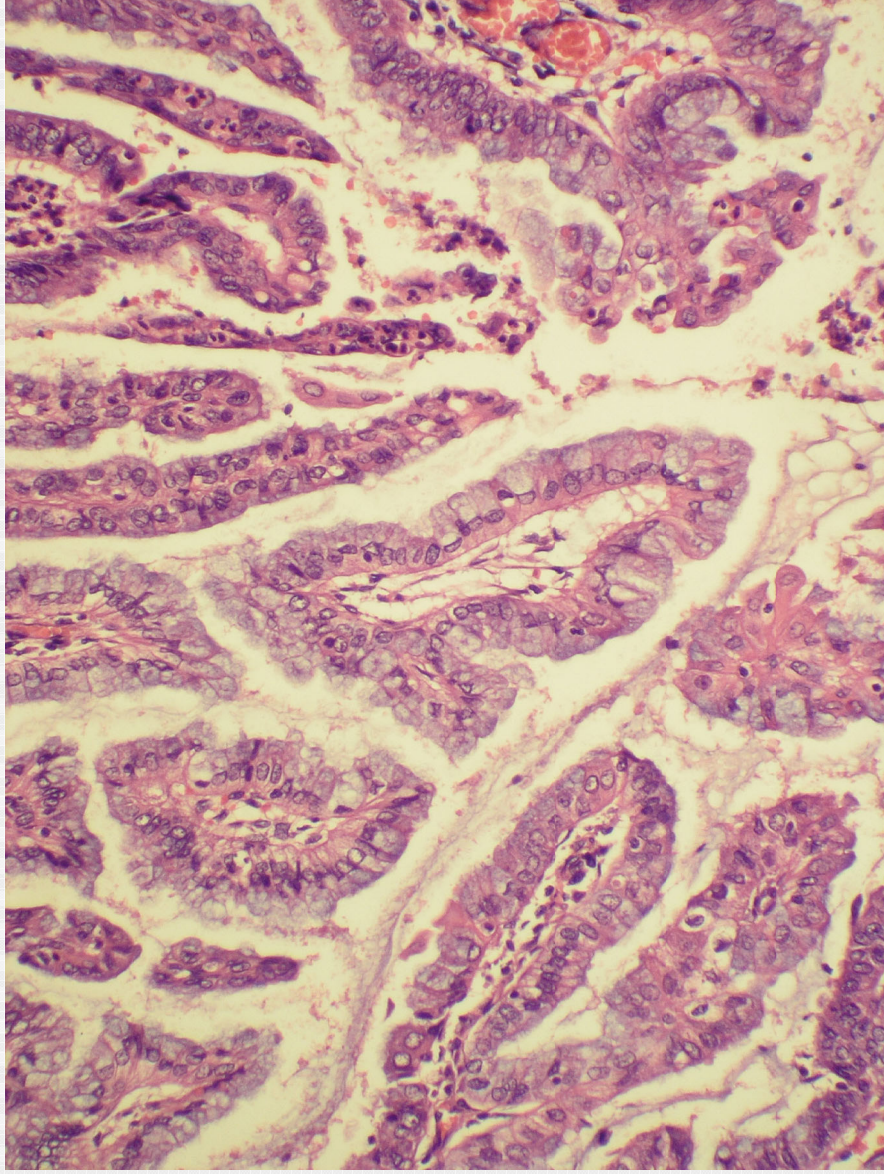
Mucinous carcinoma

- (villo)glandular pattern
- uniform columnar cells
- HE: granular, not clear !
- dilated glands with mucin and leukocytes

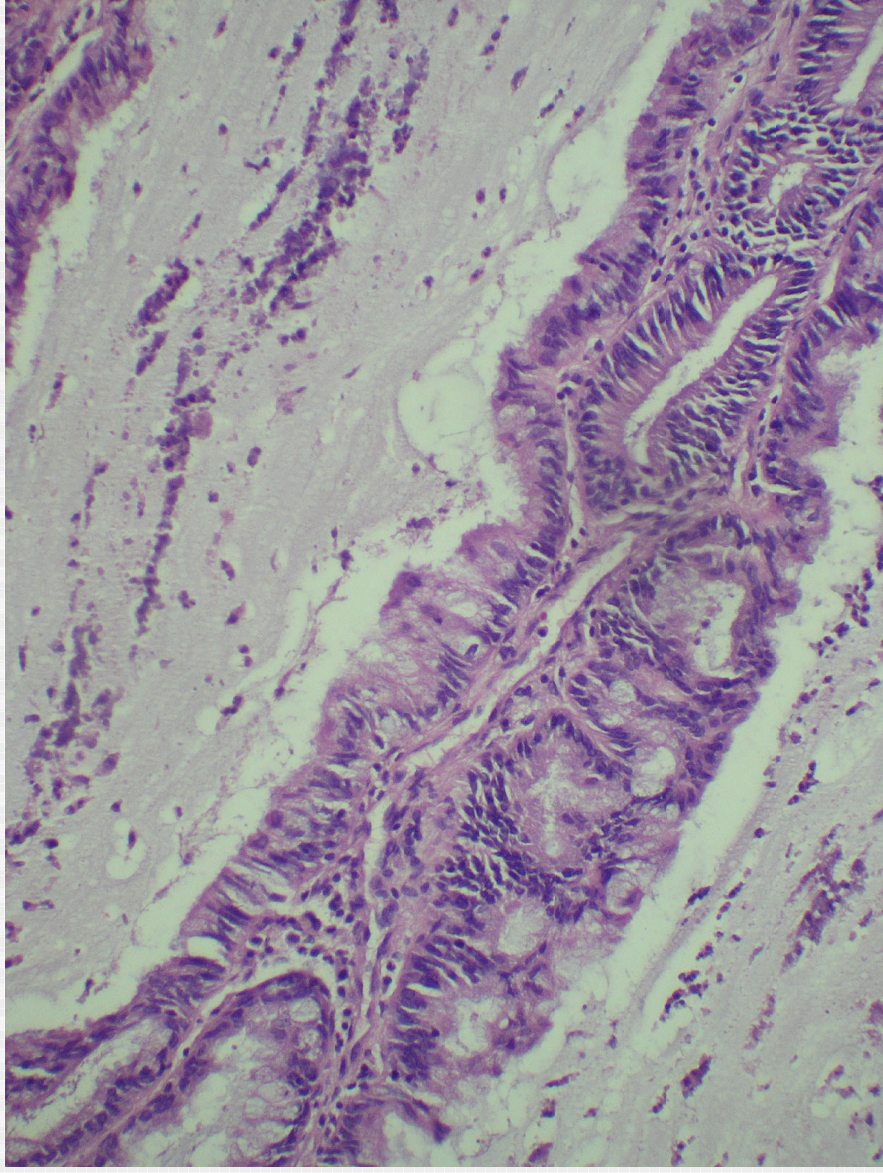
Mucinous Ca



Mucinous Ca

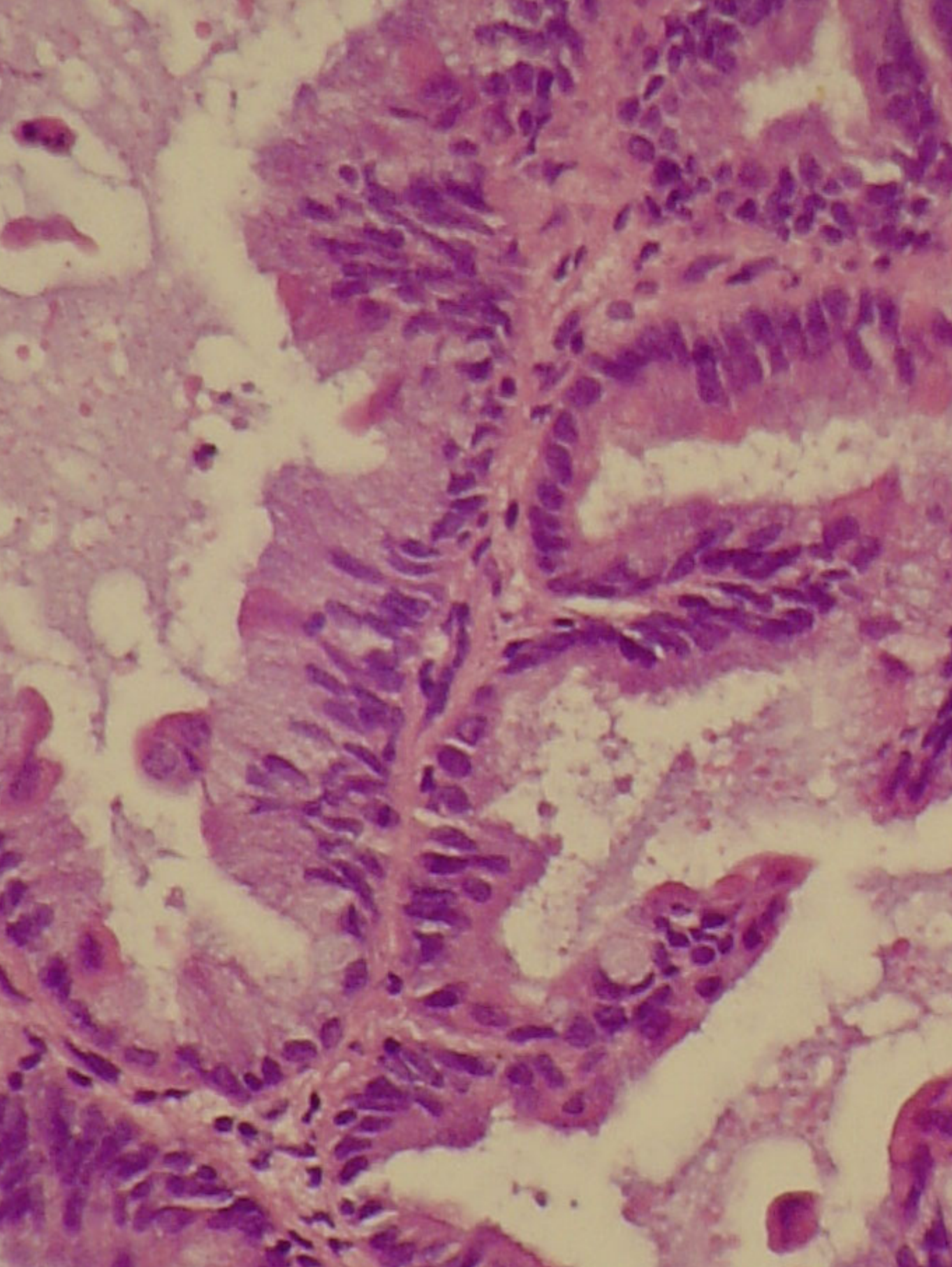


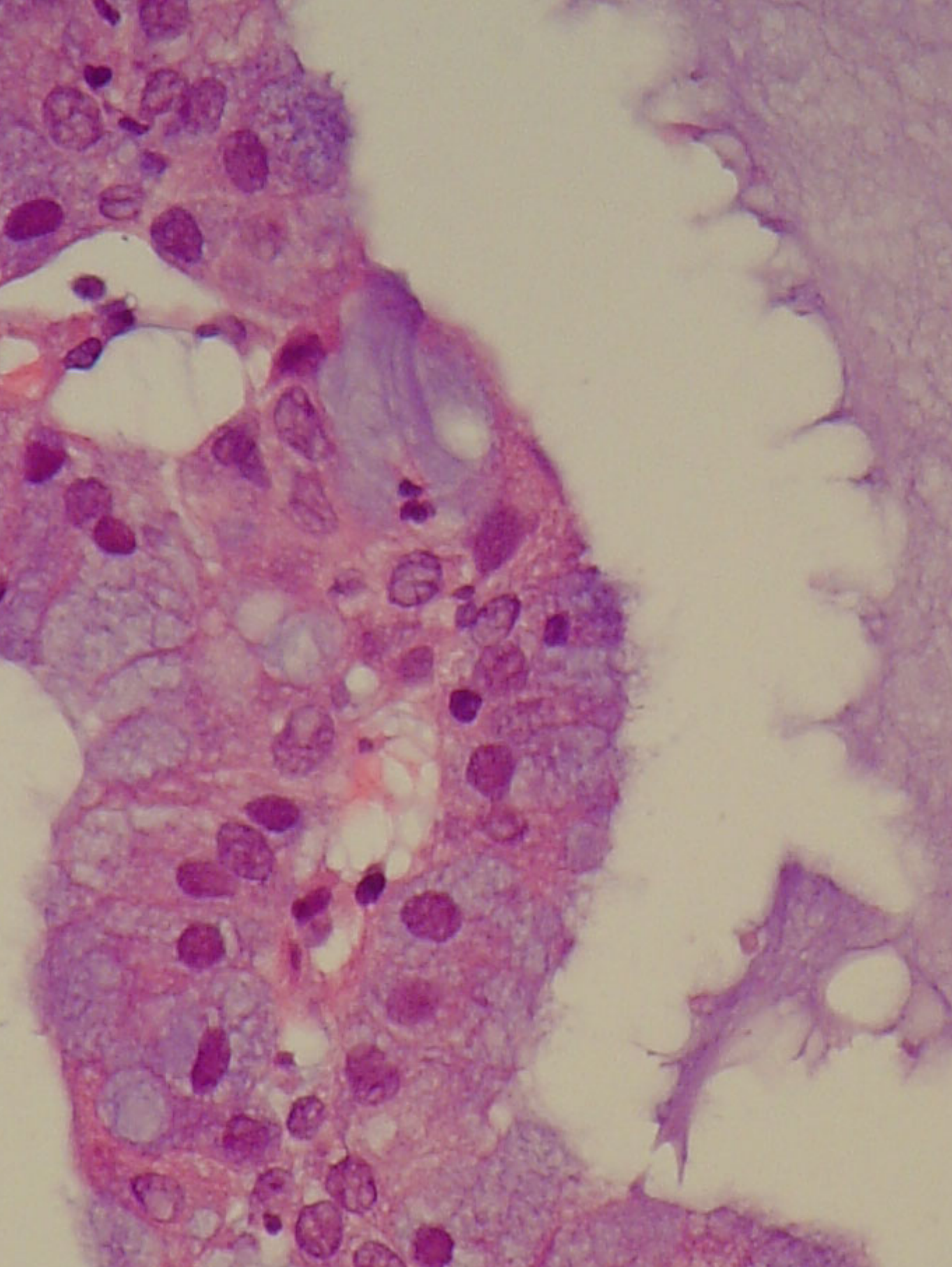
Mucinous Ca



Mucinous carcinoma: nuclei

- Few mitoses
- mild to moderate atypia
- minimal stratification





Grading mucinous carcinoma

- No rules !!!
- By convention : rules of endometrioid
- Most are grade 1

Mucinous Ca: DD

- Other types Em Ca
- MGH Cx
- Mucinous Ca Cx

Mucinous Ca:

DD with other types of Em-Ca

serous Ca, clear cell Ca:

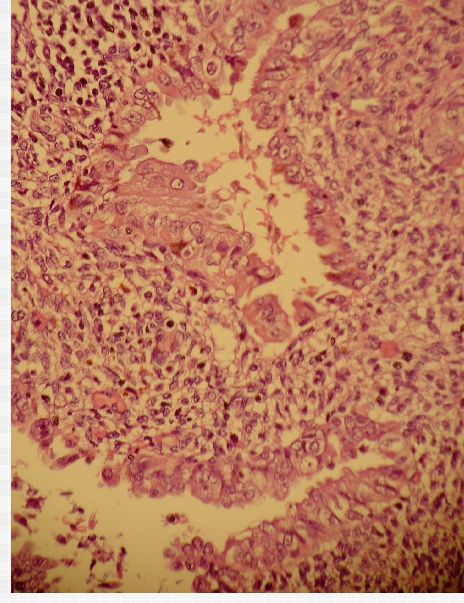
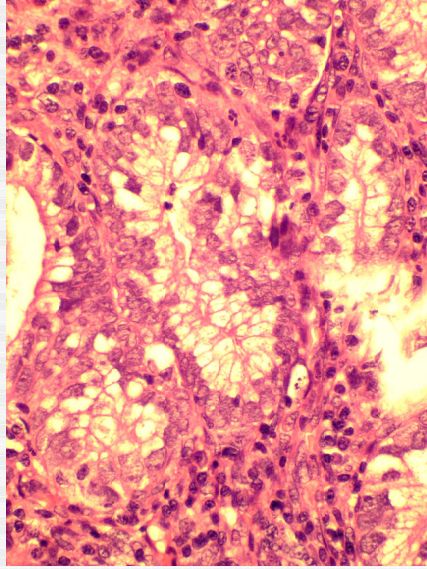
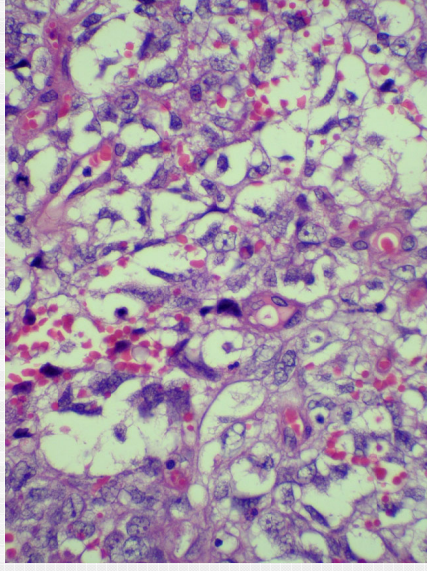
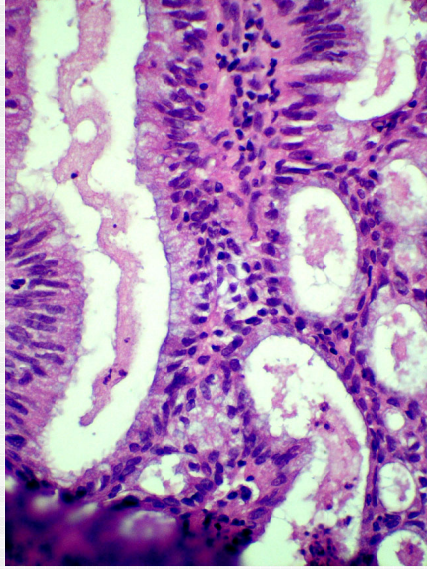
PAS: not diastasis resistant

morphology: clear or eosinophil, not granular
cells more polygonal, hobnail
atypia

secretory Ca

clear cytoplasm

Mucinous Ca: DD



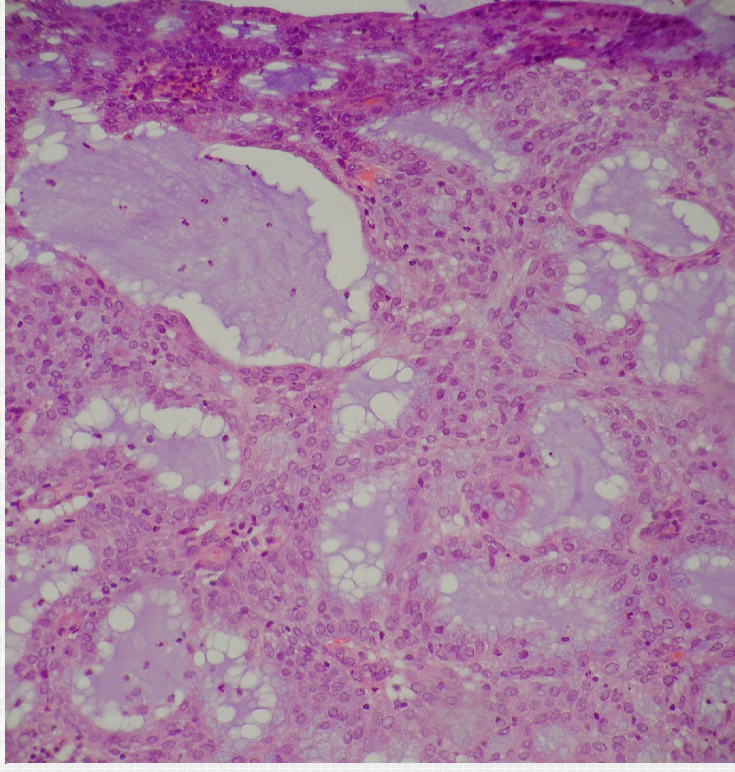
Mucinous Ca: DD with benign MGH

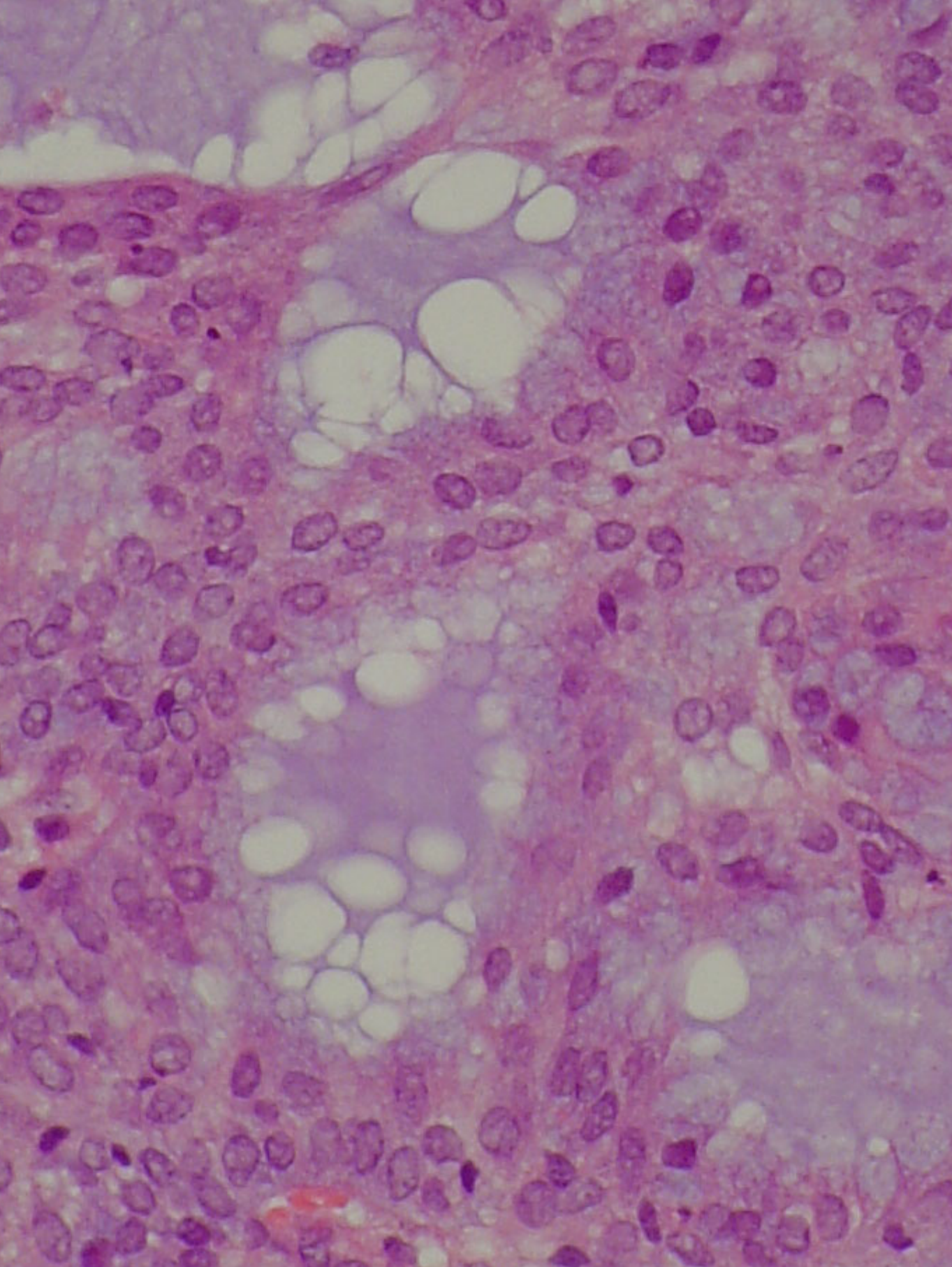
microglandular hyperplasia cx:

- age
- less atypia, less complex
- mitoses: up to 3/10 HPF in MGH
- subnuclear vacuoles only in MGH
- subcolumnar squamous metaplasia: MGH
- Vim - in MGH, + in 90% of MGC

Microglandular Ca

- Variant of mucinous Ca





DD Em - endocervical ?

- Site
- Age
- HE
- IHC

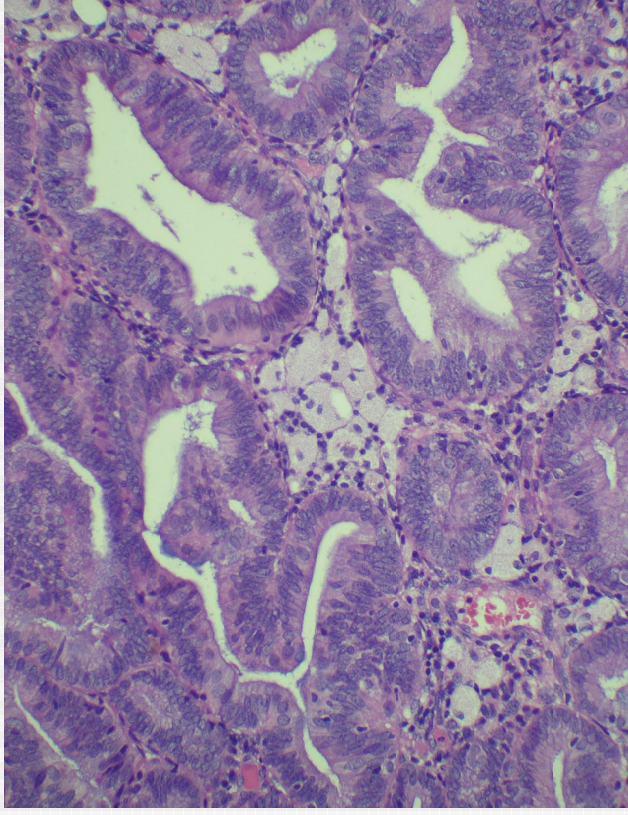
HE in DD Em-Endocx

- Foam cells
- Squamous component
- Mucinous component
- Endometrioid

Foam cells

Not only in carcinoma

If in carcinoma:
rather Em than Ecx



Squamous component

- Benign squamous component: EM
- Extensive squamous component: EM
- Luminal squamous component: EM

Mucinous component

- Endocx: more atypia
 - hyperchromatic nuclei
 - more mitoses and apoptosis
 - coarse chromatine

Look for associated CIN or EGD

Endometrioid features

- Endometrioid Ca of endocx is **NOT recognised** by most authors
- Considered to be “Mucinous Ca with little or no mucin”
- Endometrioid features do **NOT** help

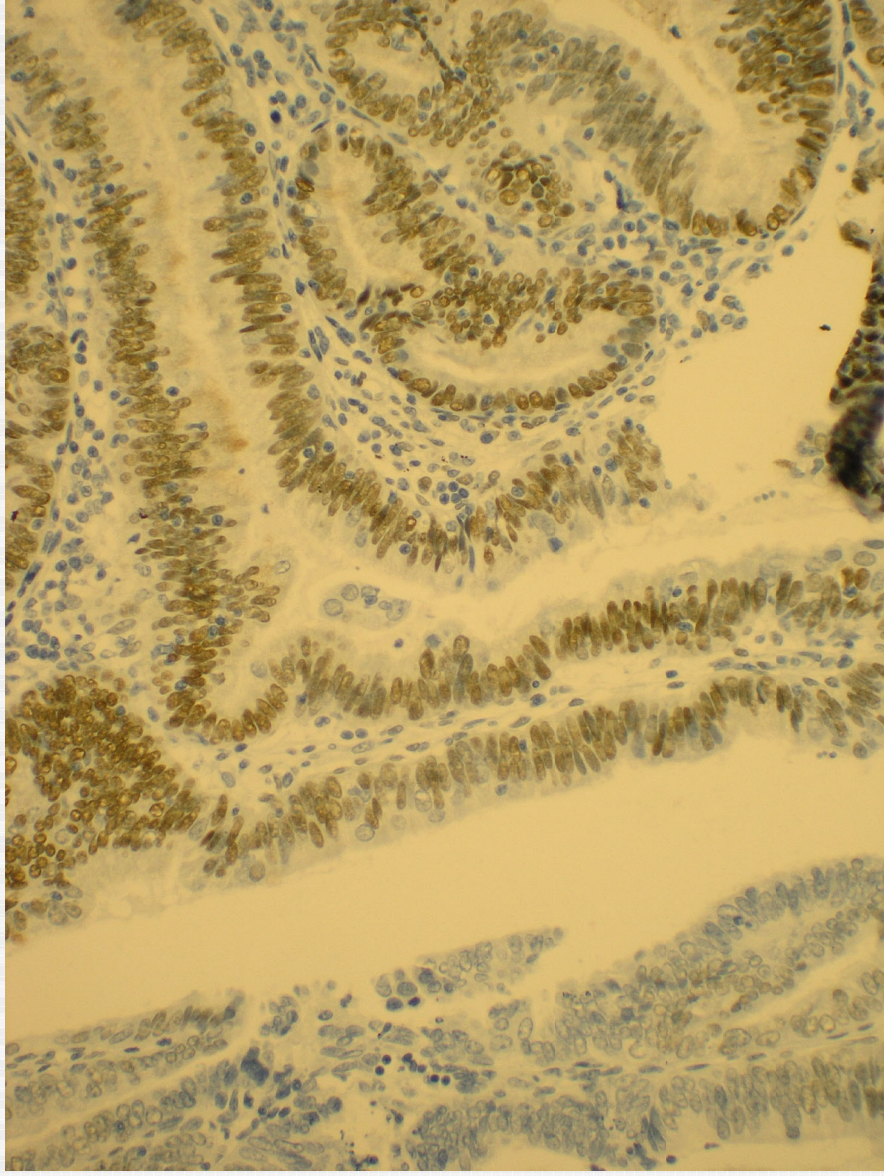
Em Ca vs Ecx Ca: IHC

- McCluggage: A panel of immunohistochemical stains, including CEA, Vim and ER, aids in the distinction between primary endometrial and endocervical adenoCa
Int J Gynecol Pathol 2002; 21: 11-15
- Kamoi: Immunohistochemical staining in the distinction between primary endometrial and endocervical adenoCa: another viewpoint
Int J Gynecol Pathol 2002; 21: 217-223

DD Em/Cx: IHC

- Primary Em
- ER +
- Vim +
- CEA -
- P16 -
- Primary endocx
- ER -
- Vim -
- CEA +
- P16 +

Endometrial Ca: Receptor +



Vimentin

- Dabbs: Intermediate filaments in endometrial and endocervical carcinomas. The diagnostic utility of vimentin patterns.

Am J Surg Path 1986; 10: 568-576

- Endometrial Ca +, Ecx -
- Not completely specific

CEA

- Cohen: Endocervical and endometrial adenocarcinoma: an immunoperoxidase and histochemical study.

Am J Surg Pathol 1982; 6:151-157

- Often present in Ecx Ca, not in Em Ca
- Not completely specific

DD Em - Ecx: p16

- Mc Cluggage: p16 may assist in distinction between endometrial and endocx adenoca

I J Gynecol Pathol 2003, 22: 231-235

- Ecx: 22/23 diffusely +
- Em: most are + but focal (sometimes 100 % +)

Type I endometrial Ca

- Endometrioid Ca
 - Villoglandular
 - Secretory
 - Ciliated cell
 - With squamous differentiation
- Mucinous Ca