ENDOMETRIAL CANCER

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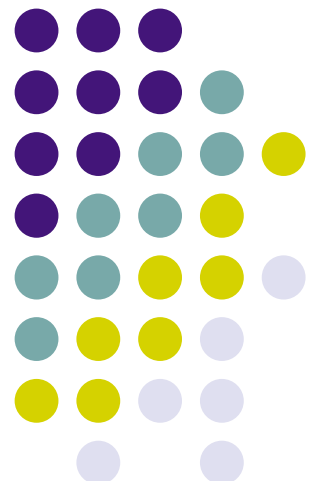


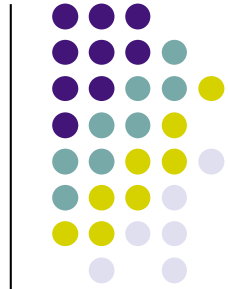
Endometrial tumours

- Epithelial
- Mesenchymal
- Mixed epithelial and mesenchymal
- Trophoblastic
- Lymphoid
- Miscellaneous tumours e.g. sex cord like tumours
- Secondary tumours

Endometrial Carcinoma

- Endometrial carcinoma (EC) is the 4th most common cancer in European and North American women
- 80-85% endometrioid type
- Aetiology – hormones, obesity, diabetes, nulliparity, diet and molecular genetics

Endometrial carcinoma

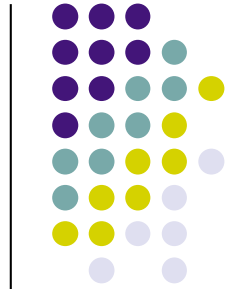


- Type 1 - oestrogen related carcinomas – young female, perimenopausal, background hyperplasia, favourable prognosis.
- Type II - non oestrogen related – elderly, atrophic endometrium, higher grade, poor prognosis.
- Mixed carcinomas
- Hybrid tumours
- HNPCC – lower uterine segment

Tamoxifen

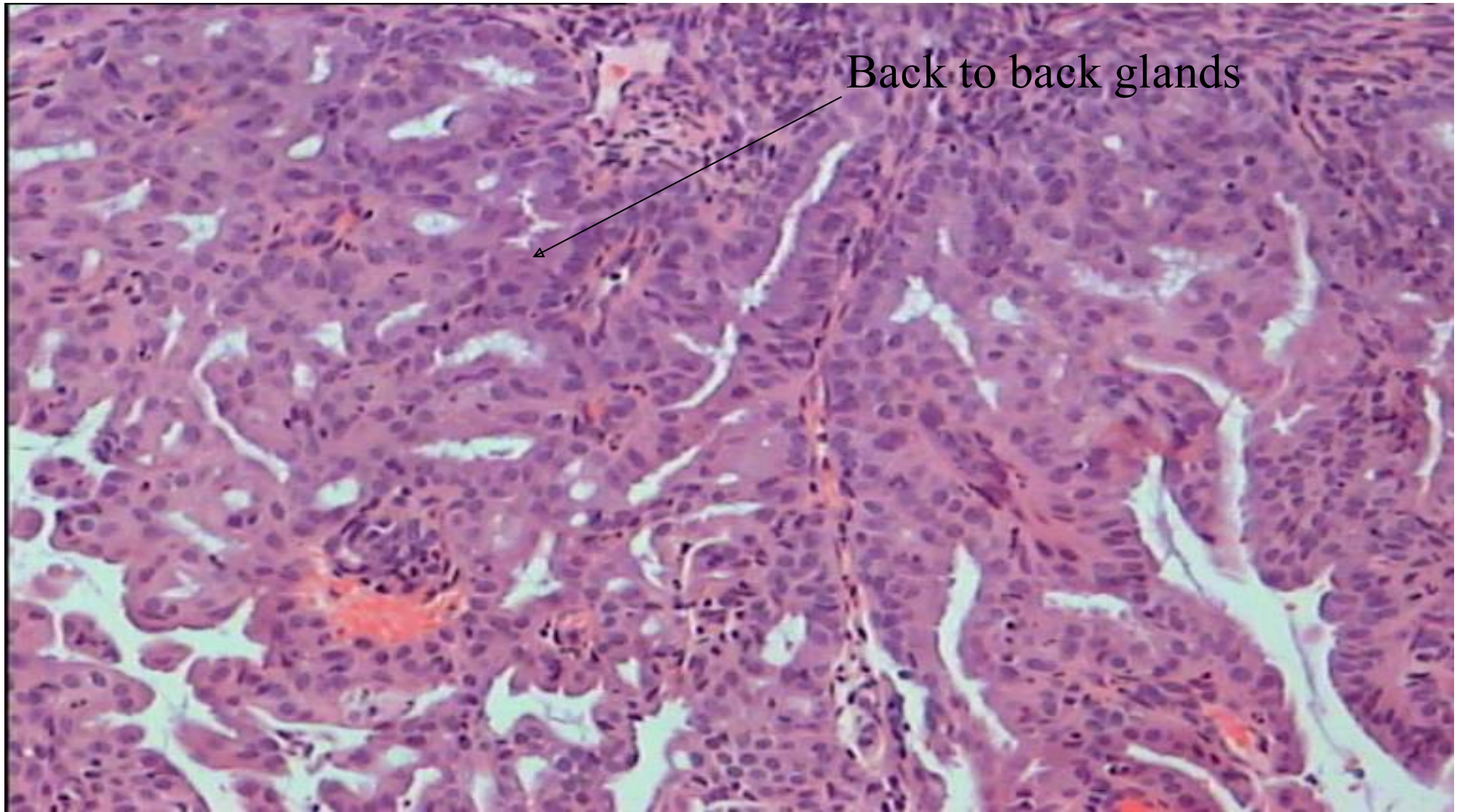
- Weak oestrogen agonist.
- In young female- blocks effect of oestrogen.
- In elderly female – stimulates proliferation of endometrium.
- Histology – Hyperplasia, large polyps with cystic glands, carcinoma (high grade), carcinosarcoma, metaplasias

Endometrial Hyperplasia

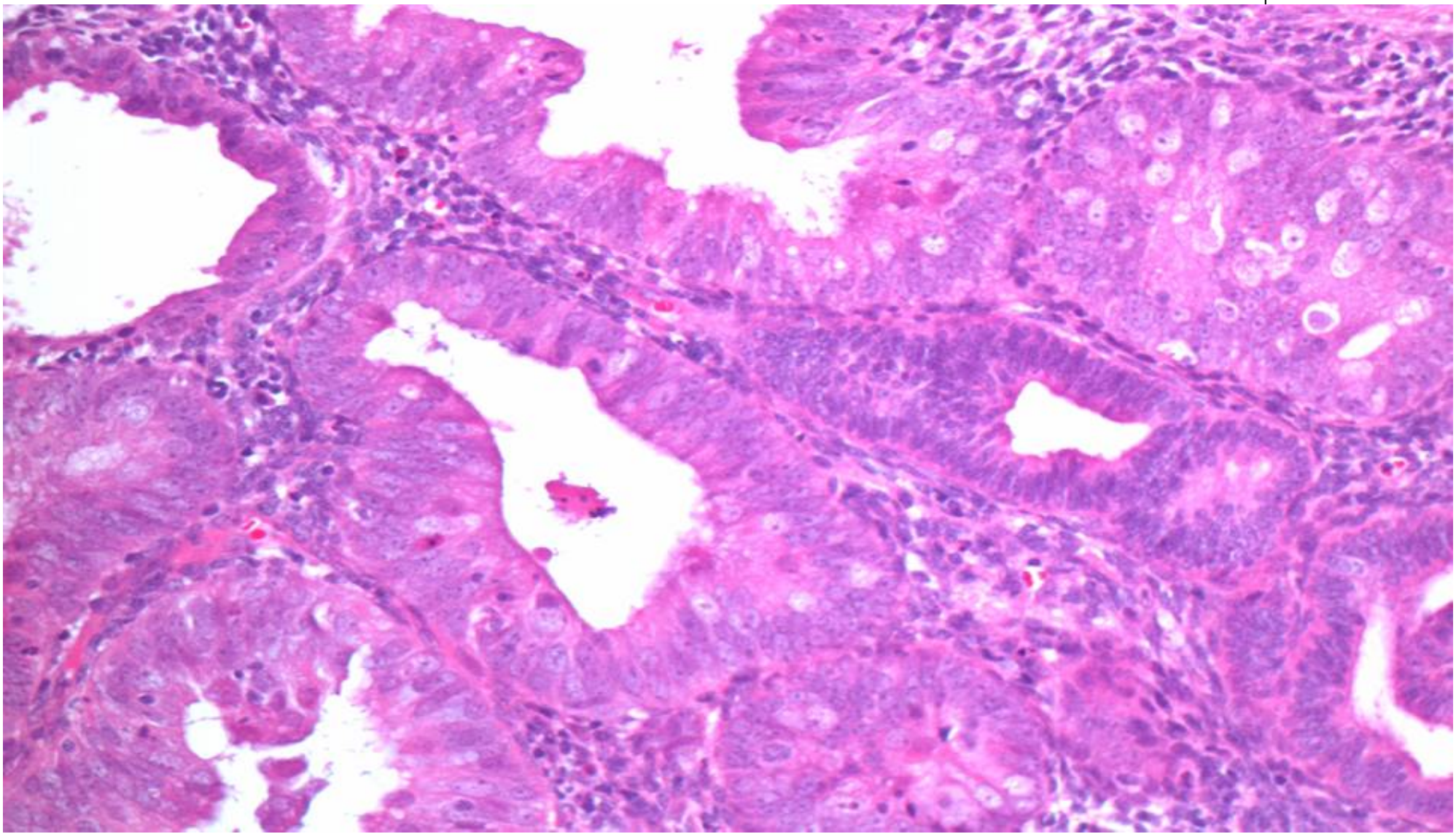


- Hallmark – increased glandular tissue relative to stroma.
- Simple hyperplasia with or without atypia
- Complex hyperplasia with or without atypia.
- Associations – polycystic ovaries, sex cord stromal tumours etc i.e. excess oestrogen

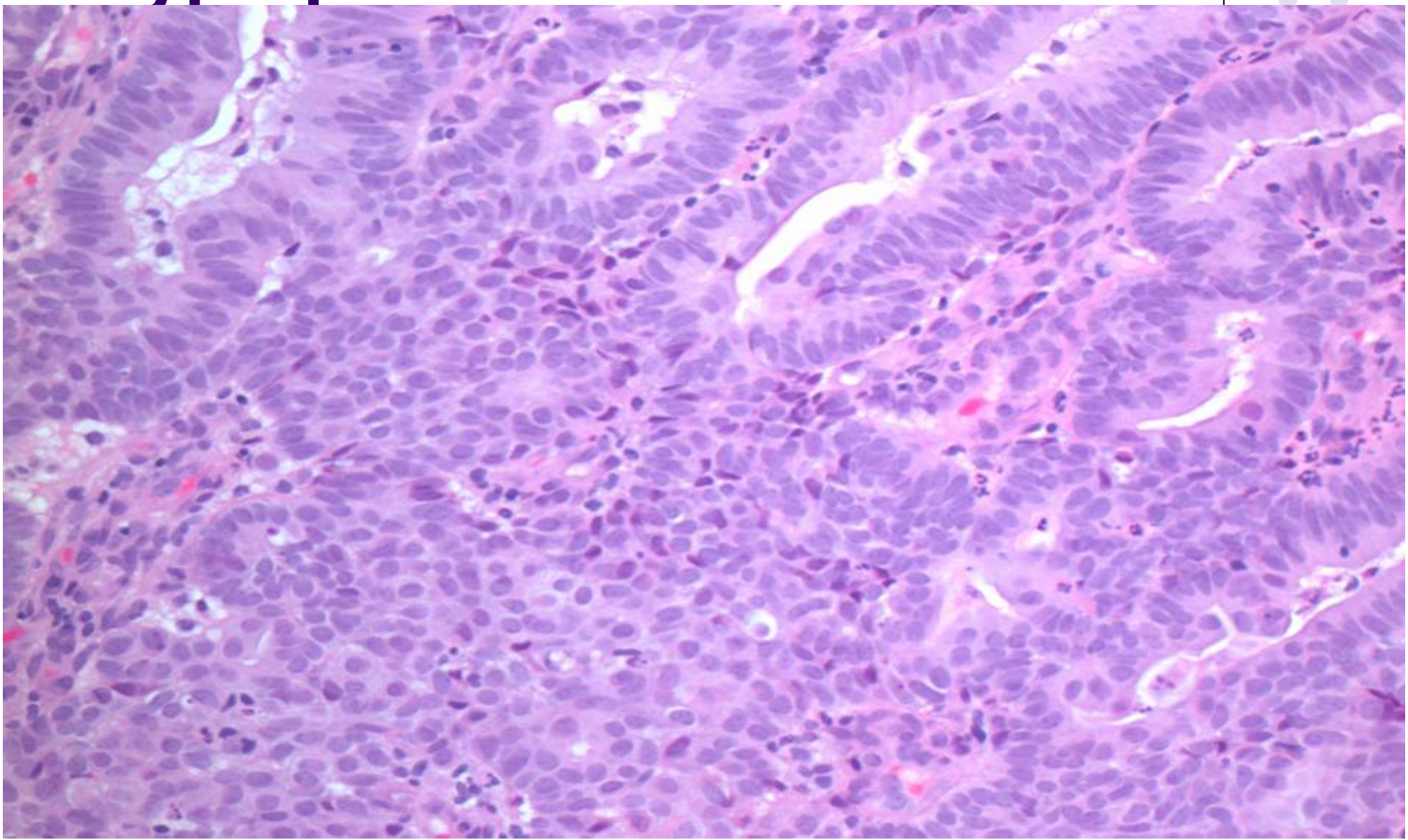
Atypical hyperplasia



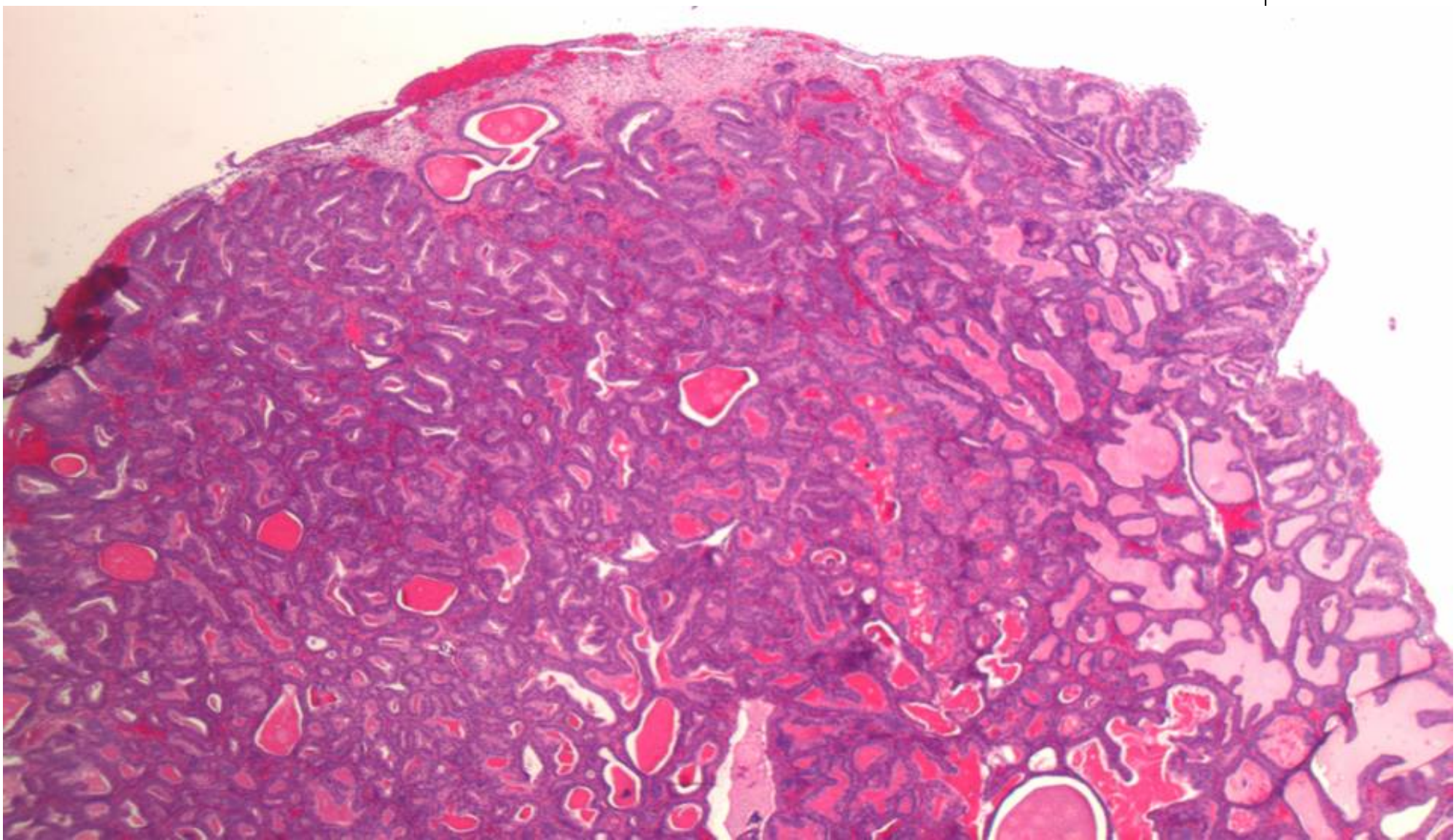
Hyperplasia



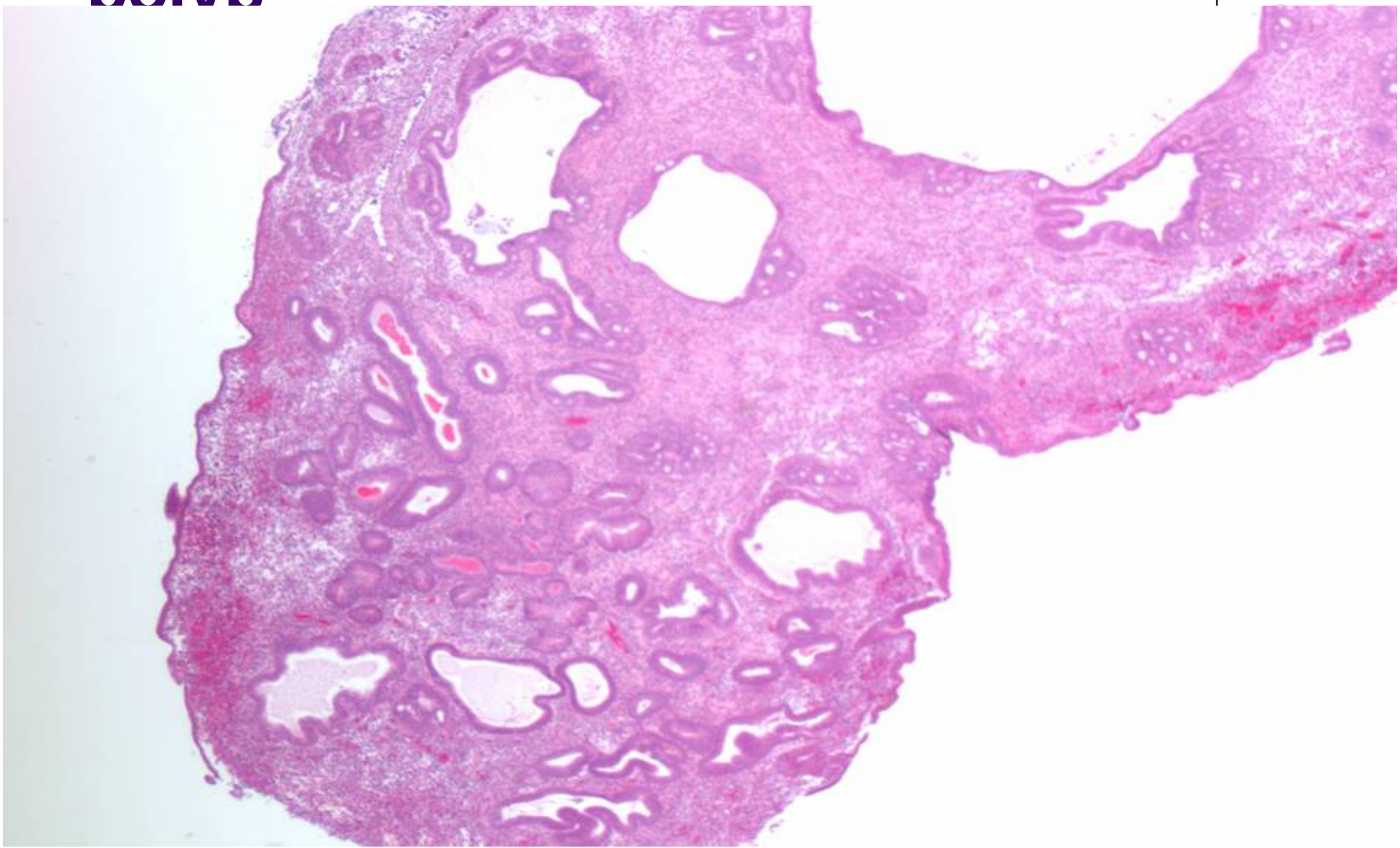
Hyperplasia



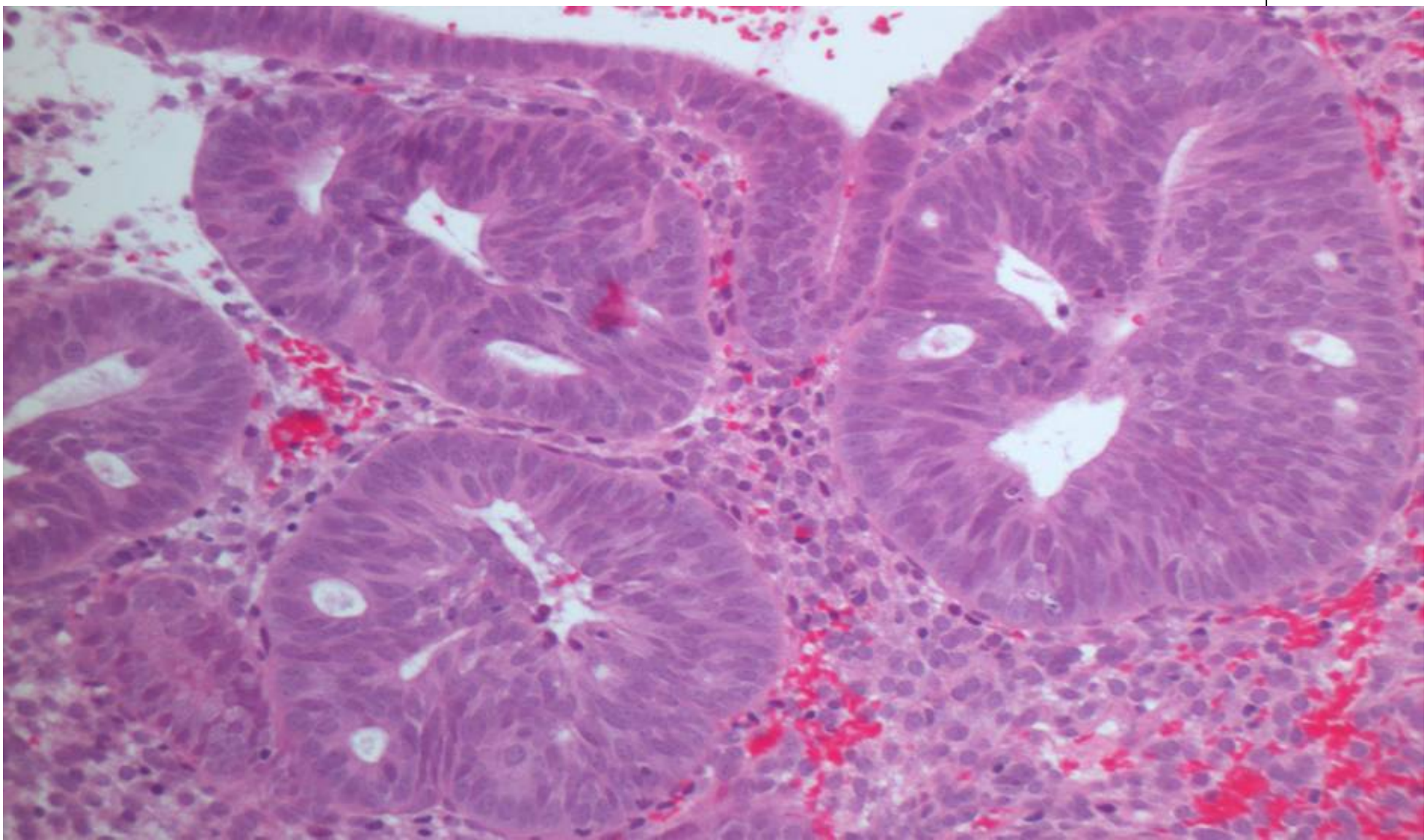
Atypical hyperplasia in polyp



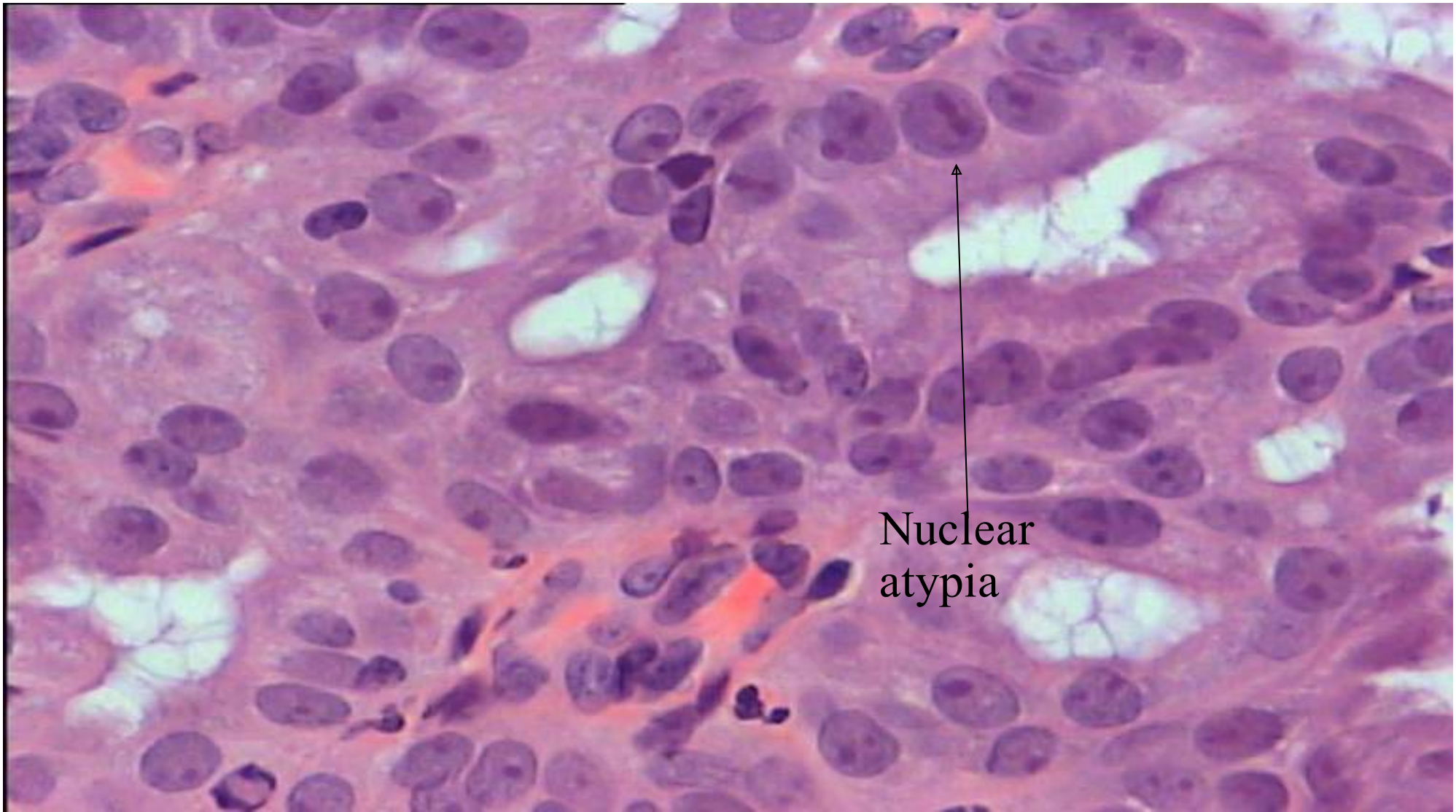
Complex atypical hyperplasia in polyp



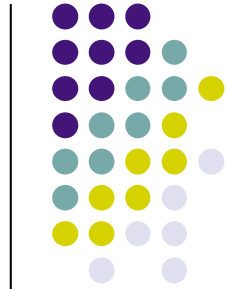
Polyp with CAH



Atypical hyperplasia

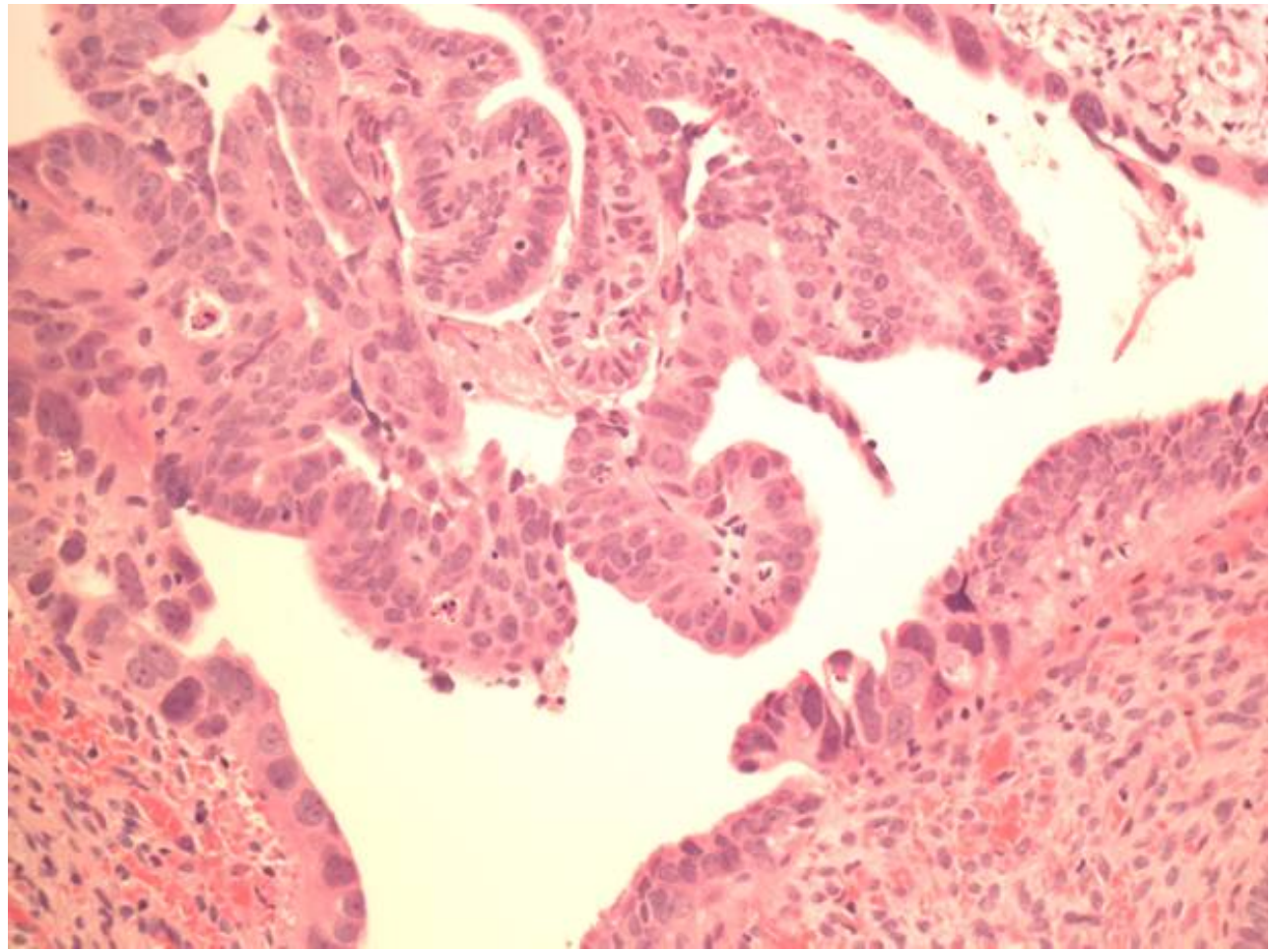


Endometrial intraepithelial carcinoma (EIC)

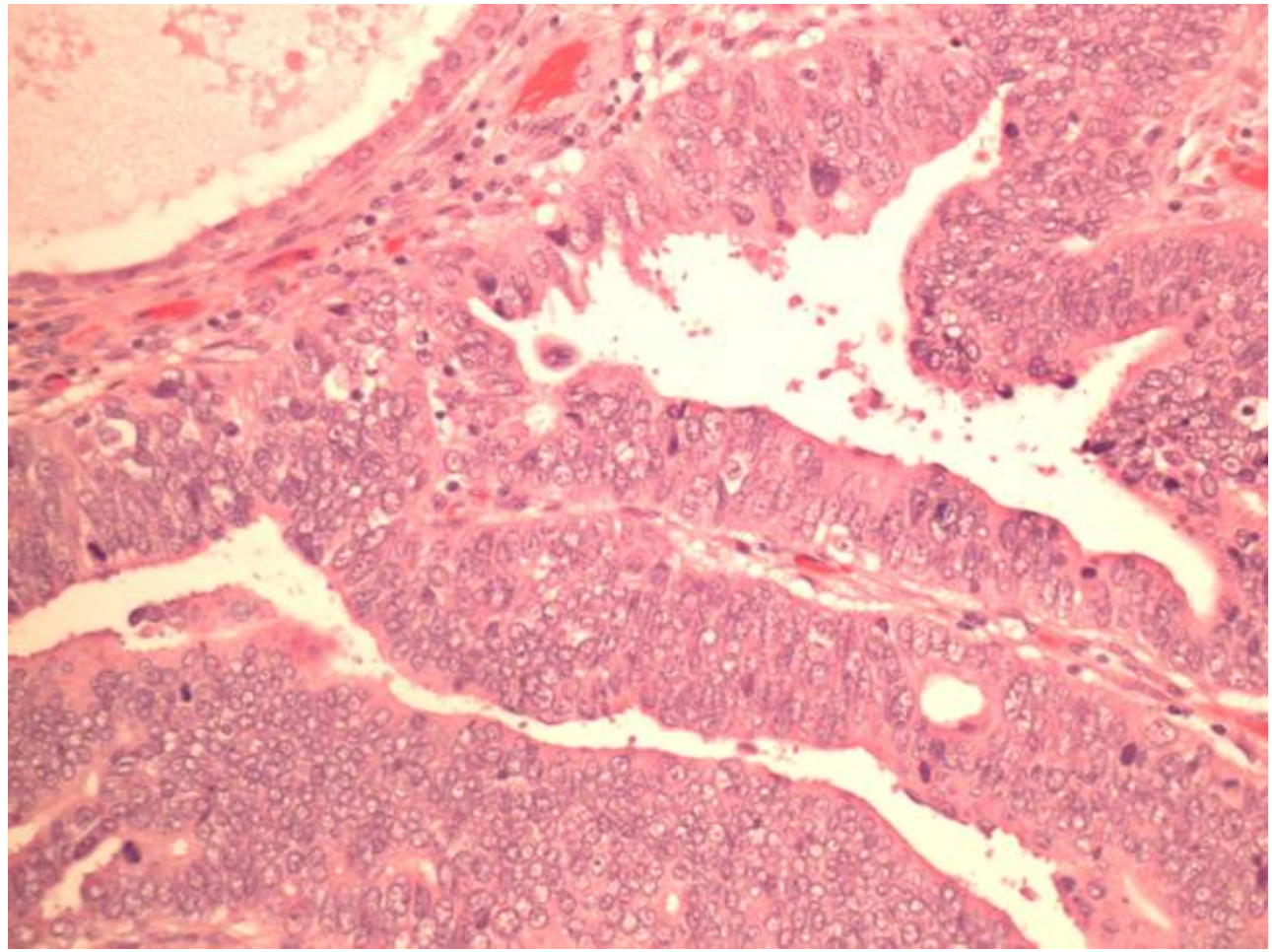


- Markedly atypical cells identical to invasive serous carcinoma lining the surface of glands of polyps or atrophic endometrium
- P53 expression
- Minority p53 negative – truncated or unstable protein
- Distinguish from early serous carcinoma/metaplasia
- Can disseminate

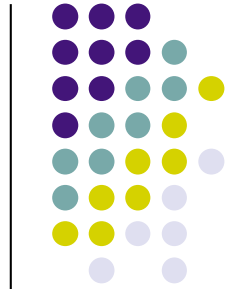
EIC



Polyp with EIC/Invasive serous carcinoma

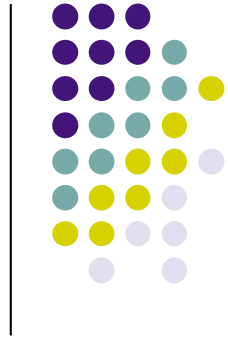


Endometrial carcinoma



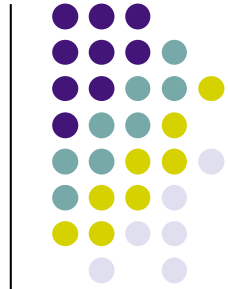
- Type I – endometrioid adenocarcinoma and variants, mucinous adenocarcinoma (80-90%)
- Type II – serous adenoca and clear cell ca.
- Mixed carcinomas
- Mixed epithelial and mesenchymal tumours
- Other – squamous cell ca, small cell etc

WHO classification of endometrial Ca



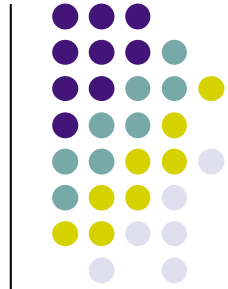
- Endometrioid adenoca – villoglandular variant, secretory variant, ciliated cell, variant with squamous differentiation.
- Mucinous adenoca
- Serous adenoca (not papillary)
- Clear cell adenoca
- Mixed cell adenoca
- Small cell carcinoma
- Undifferentiated carcinoma/de-defferentiated ca
- others

Molecular pathology



- Endometrioid adenoca - microsatellite instability, PTEN, KRAS, PIK3CA, CTNNB1 (beta-catenin).
- Familial – HNPCC, MLH1+ MSH2 mutations.
- Serous carcinoma – P53, HER/NEU amplification and others.
- Targeted therapies

LYNCH SYNDROME (HNPCC)



- Autosomal dominant, increases risk for multiple cancers, usually patients >50yrs.
- Germline mutations in DNA mismatch repair genes – MLH1, MSH2, MSH6, and rarely PMS2
- Endometrial cancer – sentinel cancer
- Predilection for lower uterine segment
- Immunohistochemistry to screen patients followed by mutational analysis
- Consent issues.

EIC VS EIN

- EIC – serous intraepithelial carcinoma.
- EIN – Clonal proliferation of architecturally and cytologically altered premalignant endometrial glands – Type 1 (endometrioid) adenoca.

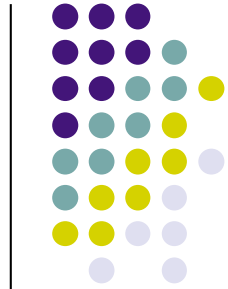
Features of endometrial cancer

- Uterus – small, normal or enlarged in size
- On sectioning – single lesion, multiple lesions or diffuse.
- Polypoid
- Commoner on posterior wall
- Histological types – Endometrioid,serous,clear cell, squamous cell, mixed types, undifferentiated..
- Metastatic tumours.

Prognostic factors.

- Histological type
- Grade
- Depth of invasion
- Vascular invasion
- Stage
- Age at diagnosis.

Grading (endometrioid/mucinous adenoca) – FIGO.



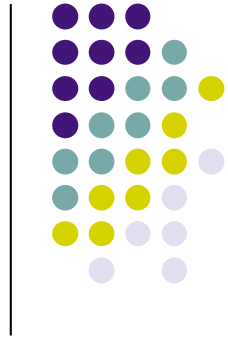
- G1 – 5% or less solid pattern.
- G2 – 6-50%
- G3 - >50%
- Cytology – raise by one grade

Binary grading

- Two part grading system better
- Binarised FIGO (G1/2 – low grade; G3 – high grade)
- Binary Gilks' grading system – can be used with any cancer. Based on:

2 out of 3 features considered "high grade" – papillary or solid architecture; high nuclear grade; >6 mitotic figures/10 high power field

Immunohistochemistry

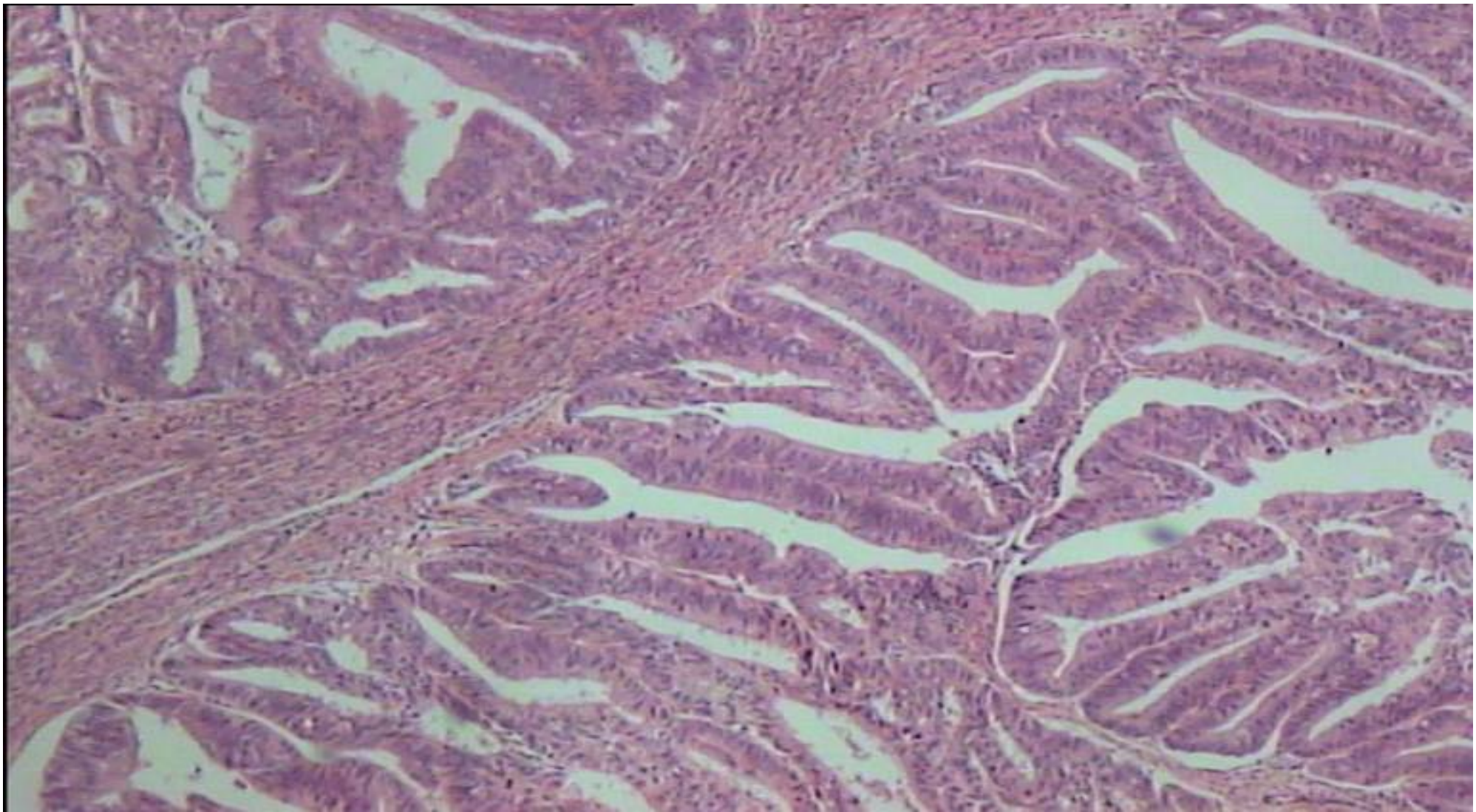


- Vimentin
- Cytokeratins
- ER, PR
- CEA
- P16, P53, MIB-1
- Immuno available for MSI - DNA mismatch repair proteins: MLH1, MSH2, MSH6, PMS2 (consent issues and counseling)

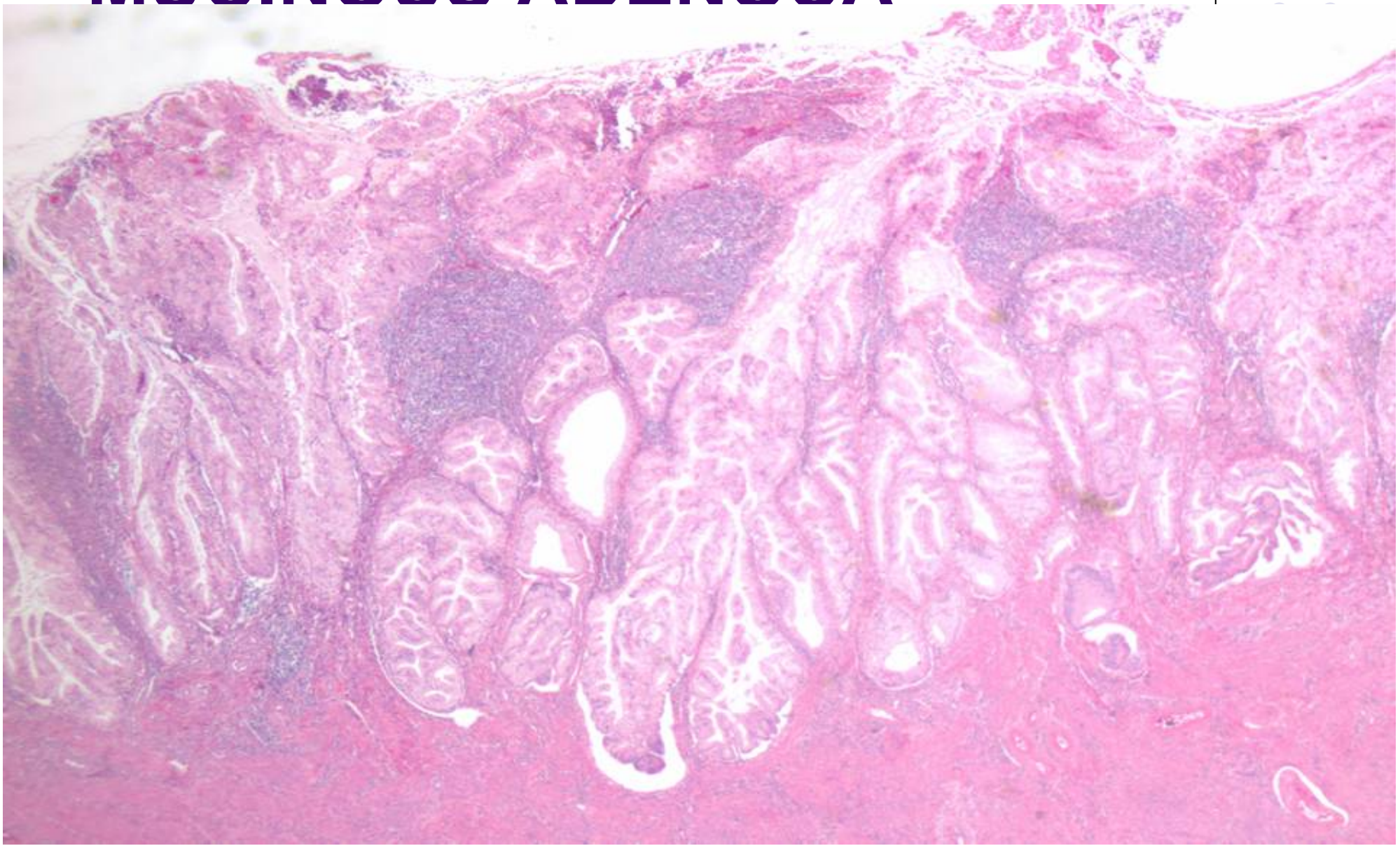
Reporting of endometrial Ca

- MDS – tumour type,location, size, depth of invasion, distance from serosal surface, involvement of cervix, parametria, ovaries, fallopian tubes, background hyperplasia etc.
- Biopsies – tumour type, grade, background endometrium.
- FIGO 2009

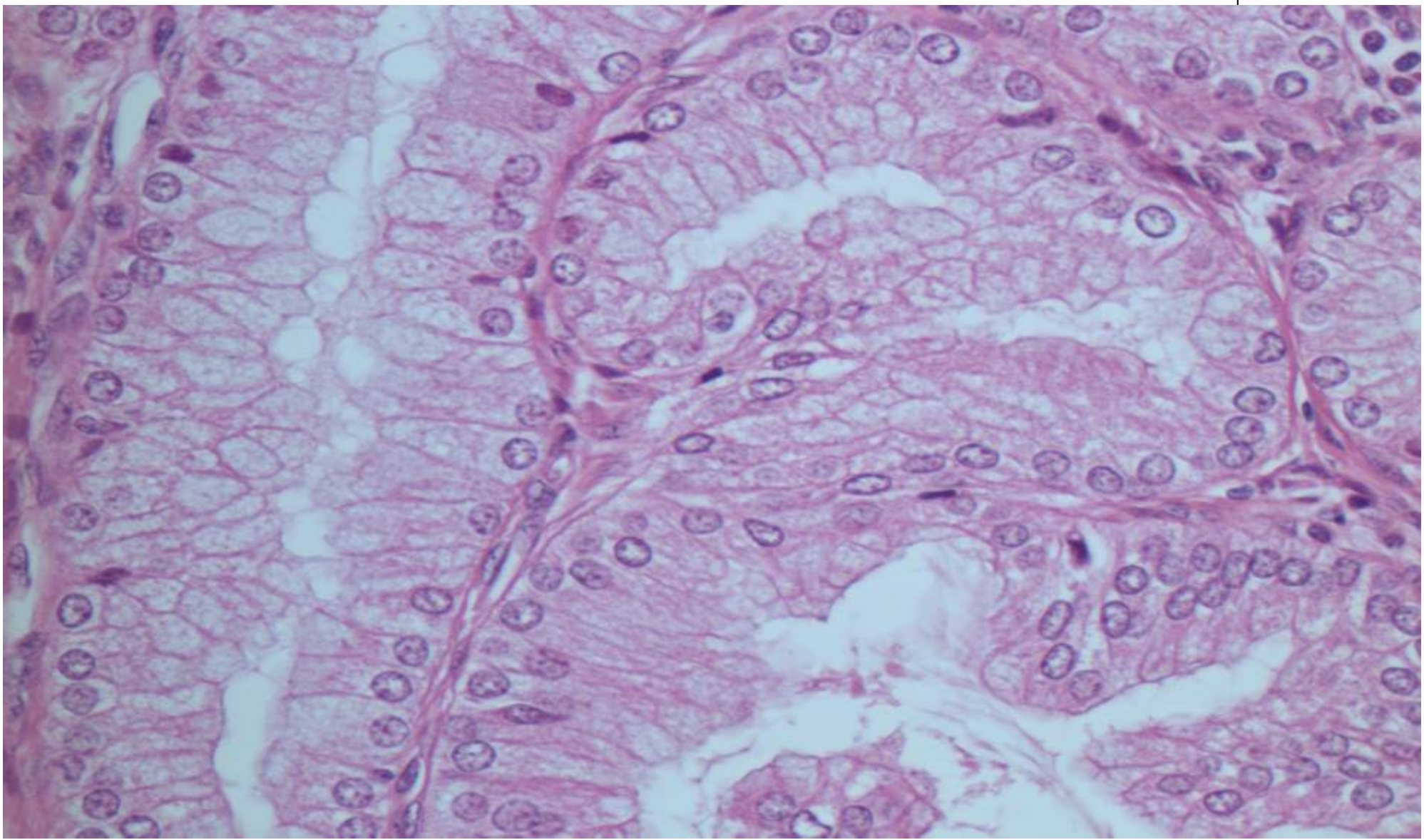
Endometrioid adenocarcinoma grade 1



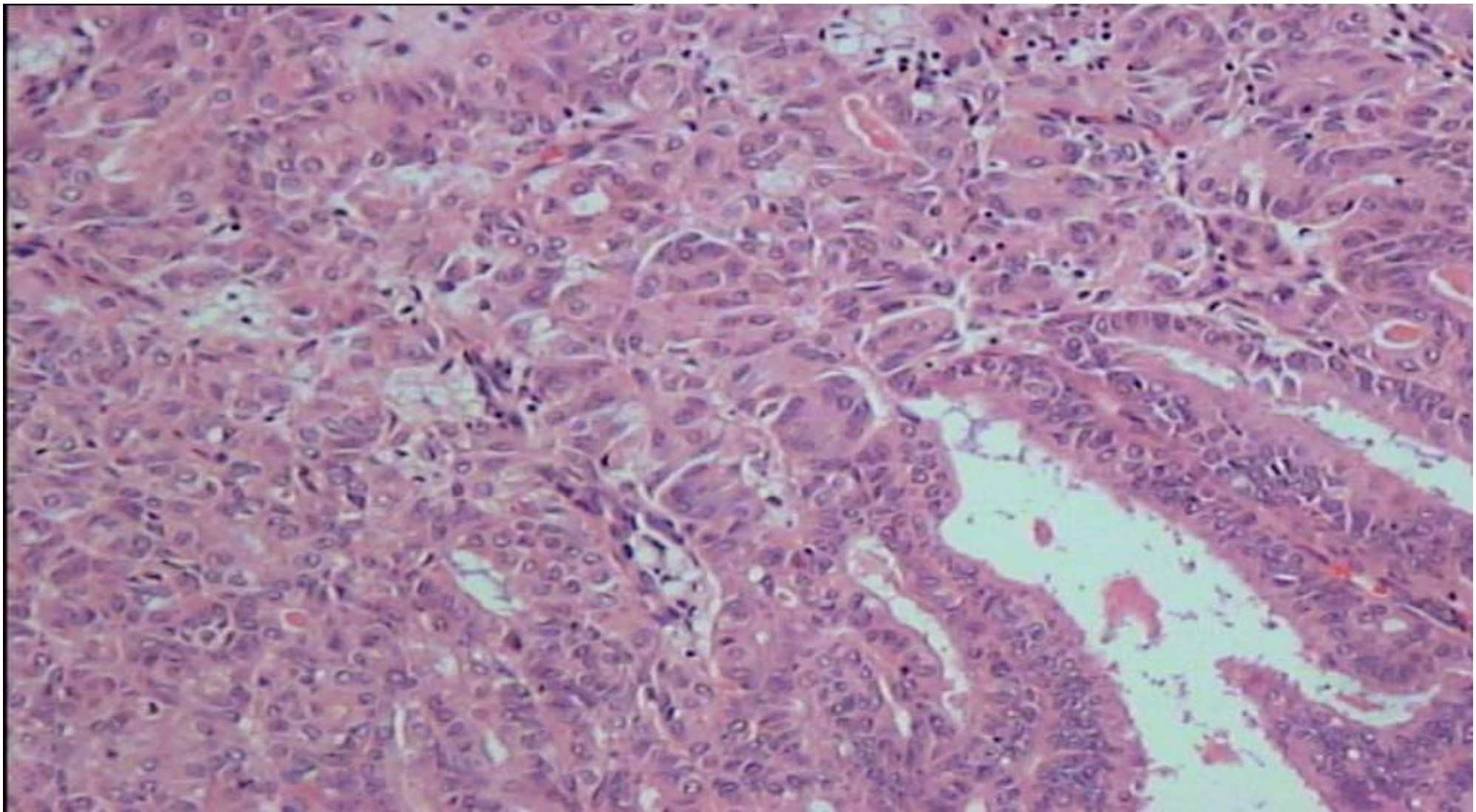
MUCINOUS ADENOCA



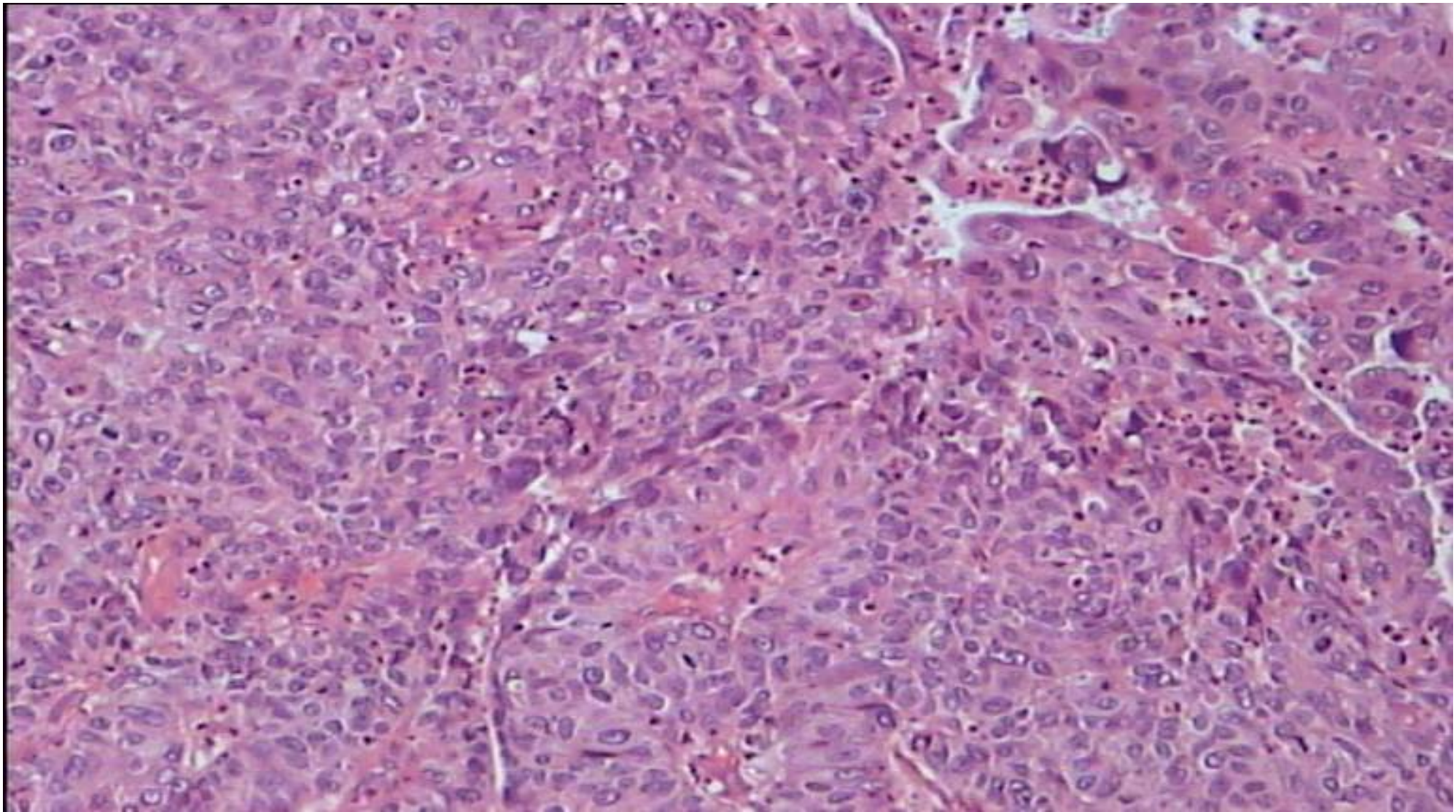
MUCINOUS ADENOCA



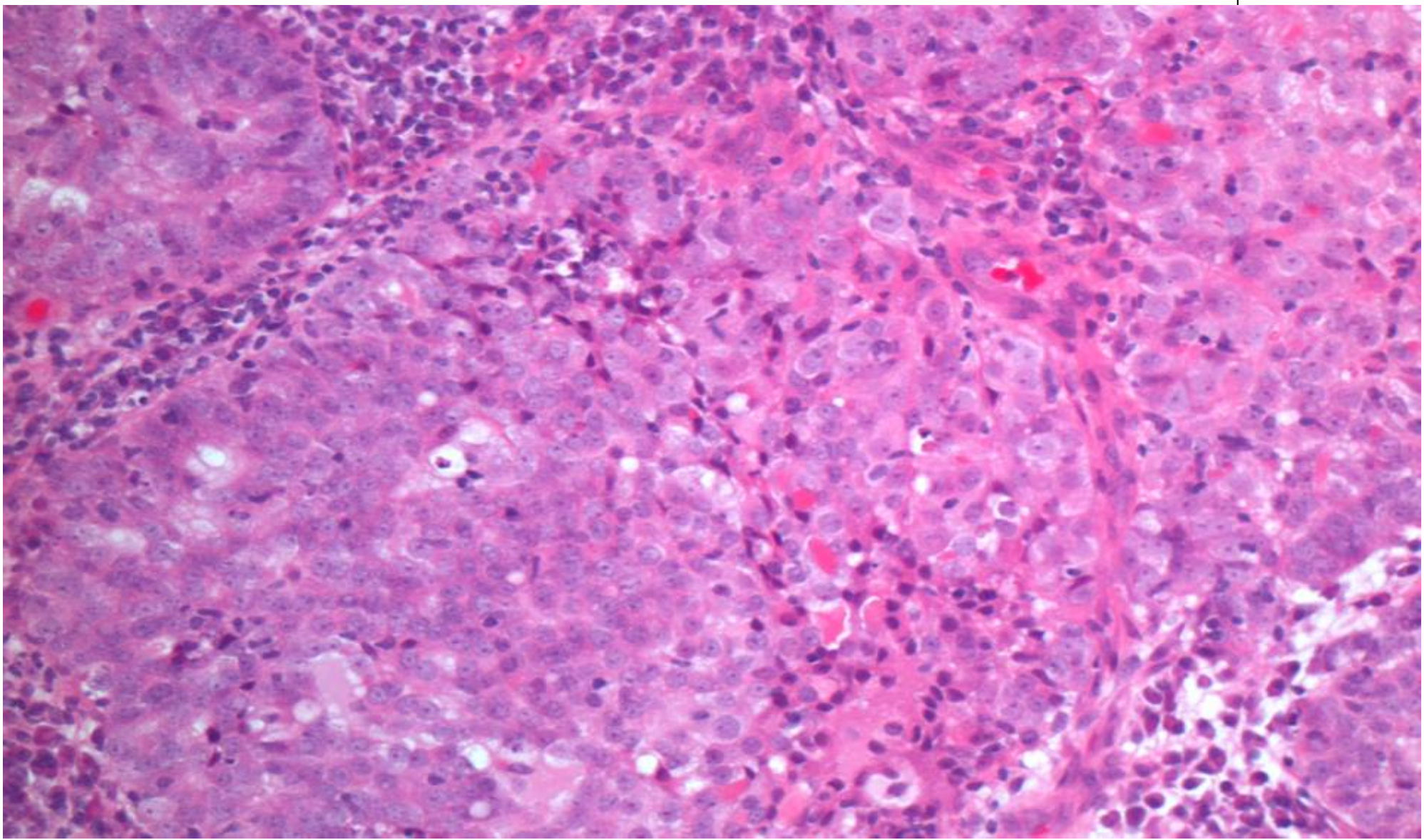
Endometrial adenocarcinoma grade 2



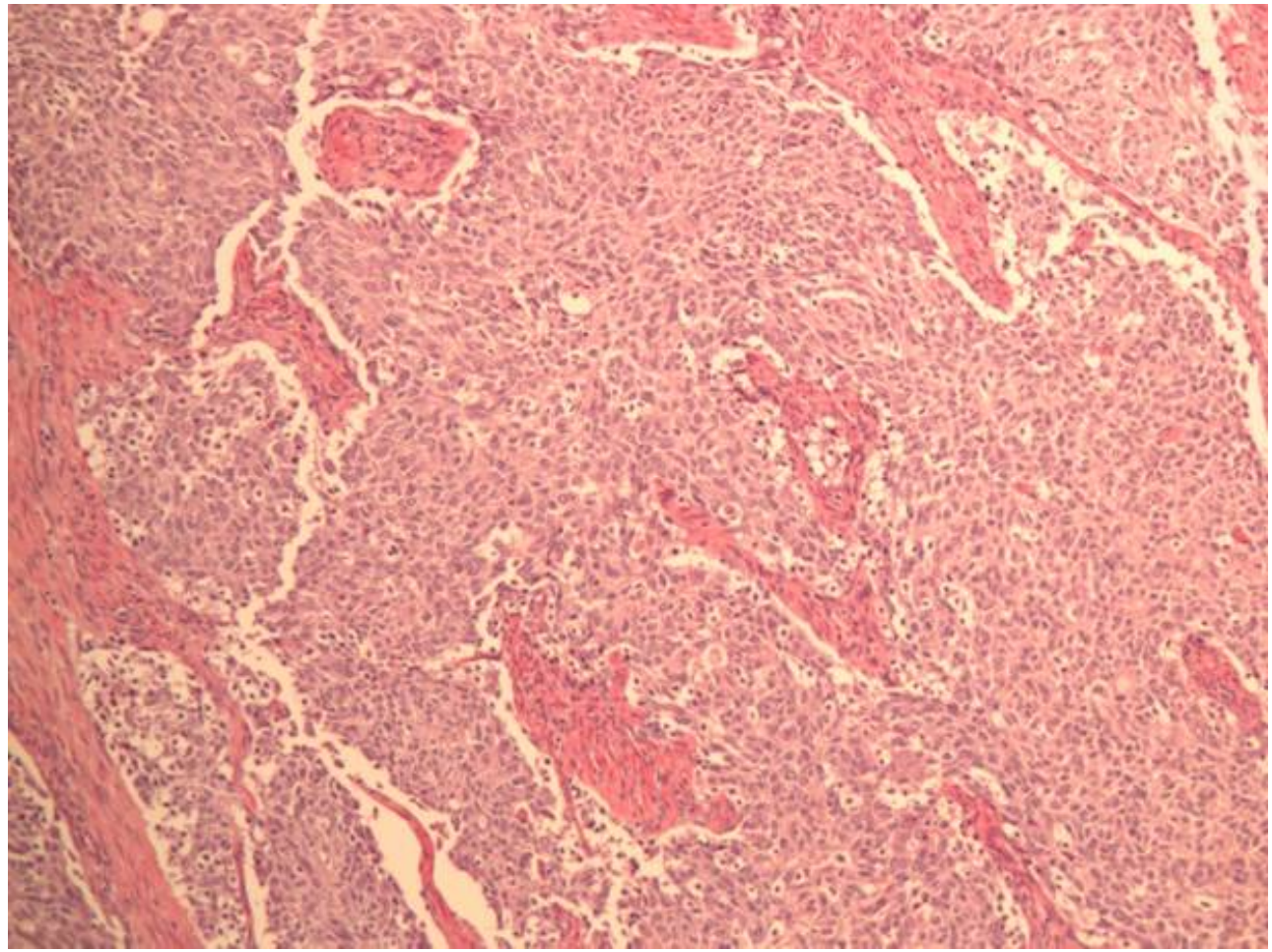
Endometrial Adenocarcinoma grade 3



G3 ENDOMETRIOID ADENOCA



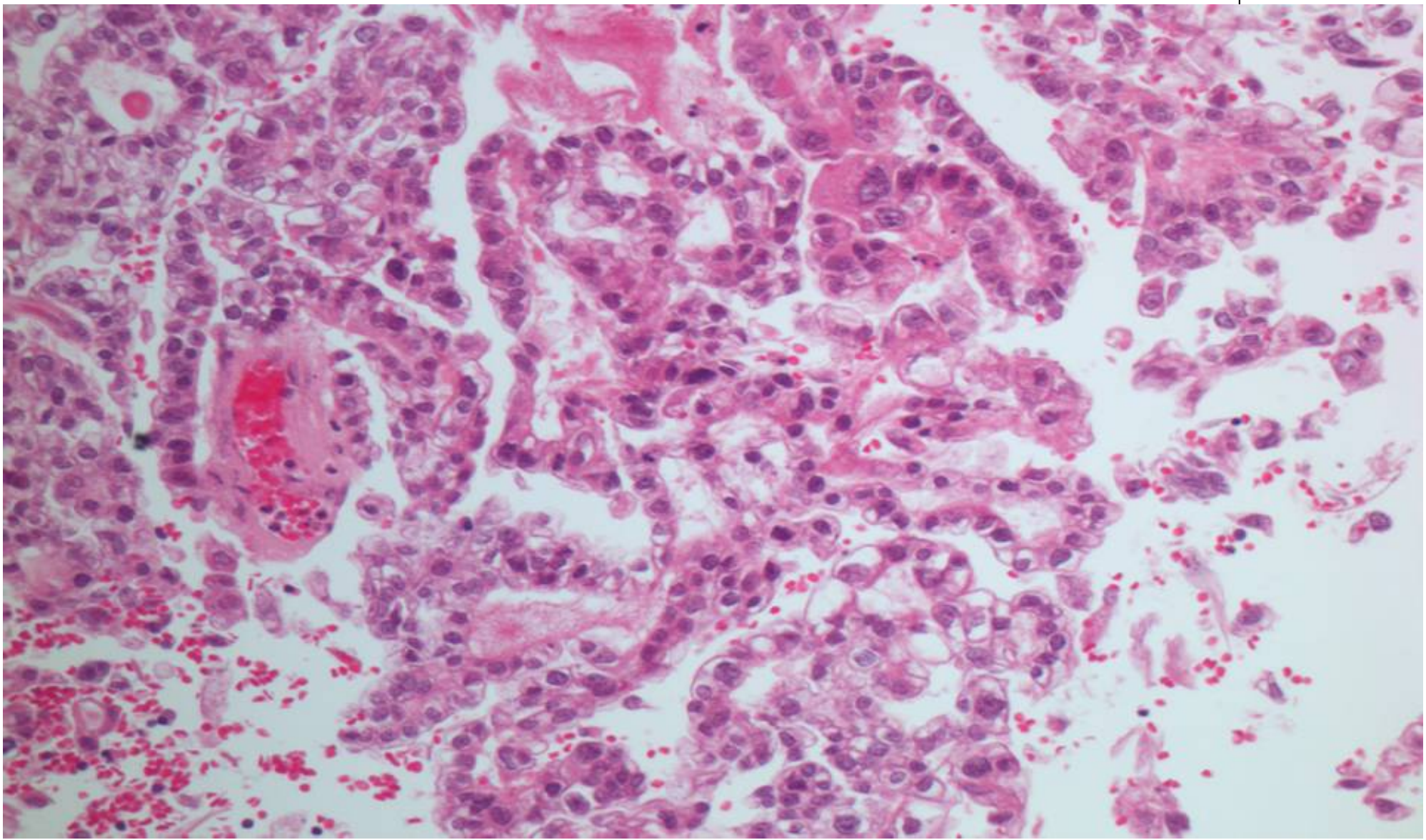
Grade 3 endometrioid adenoca



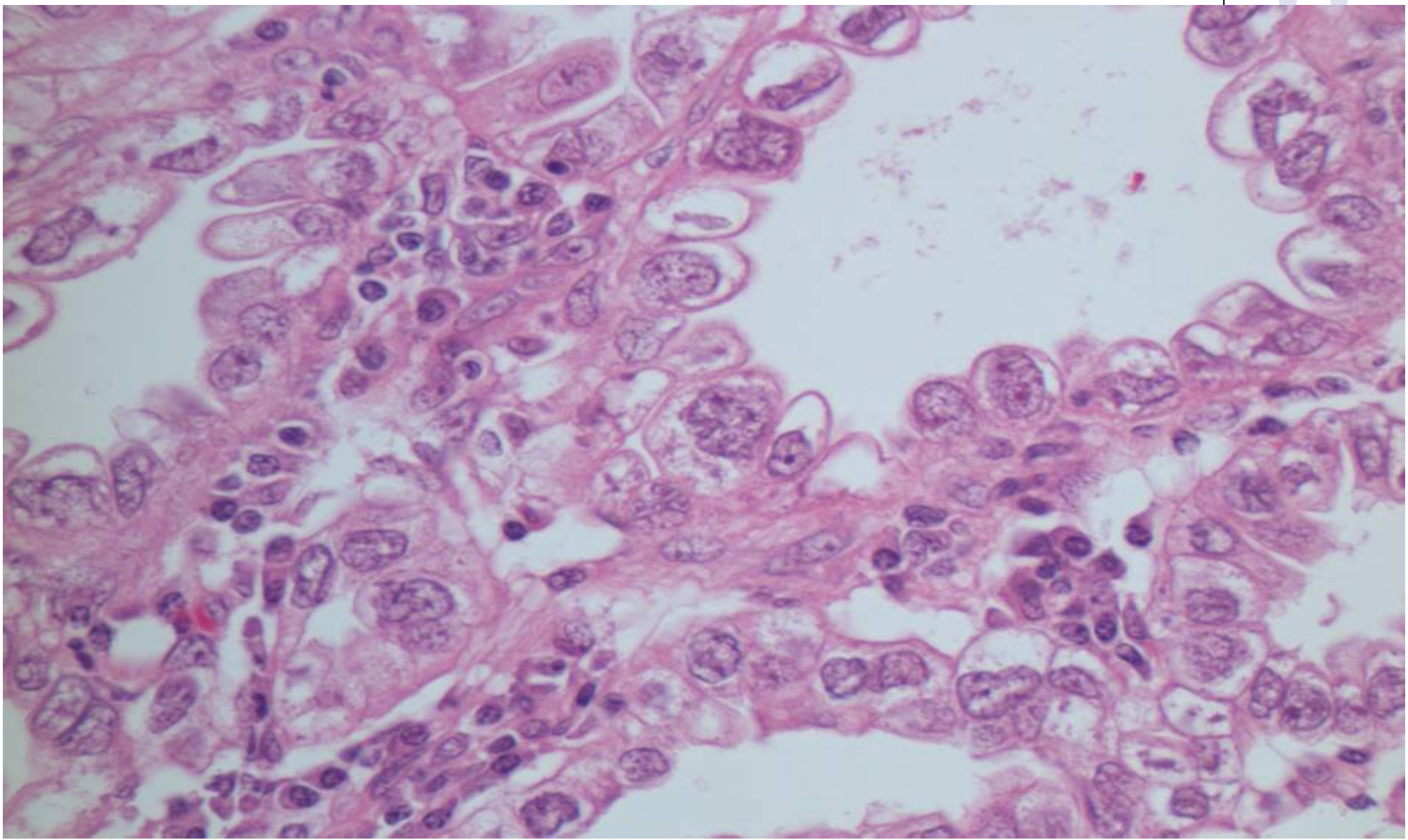
Clear cell carcinoma

- Type II carcinoma
- 1-5% of endometrial carcinomas
- Predominantly older patient
- Frequently diagnosed in advanced clinical stage
- Strong expression of p53 associated with aggressive behaviour

CLEAR CELL CARCINOMA



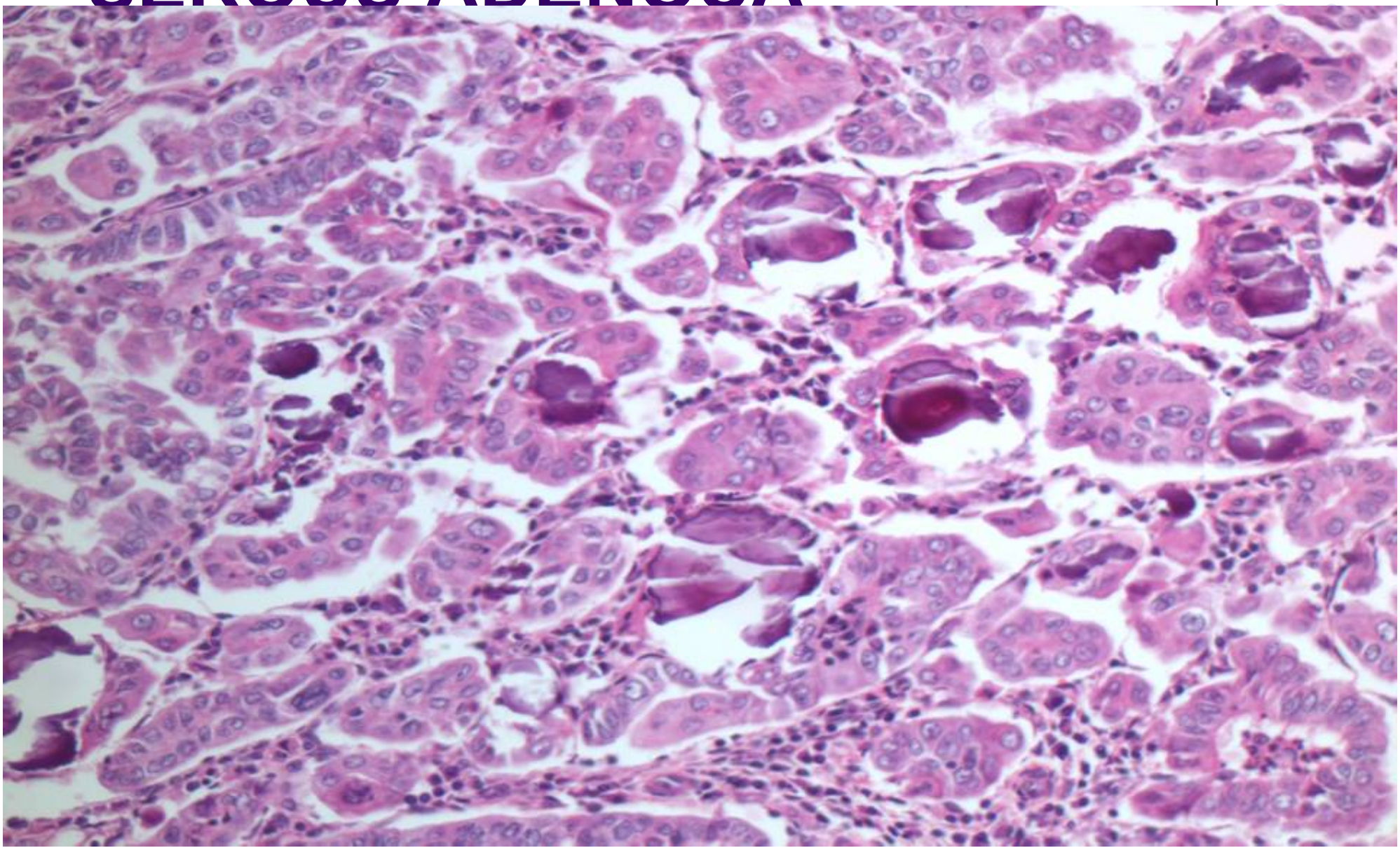
CLEAR CELL CARCINOMA



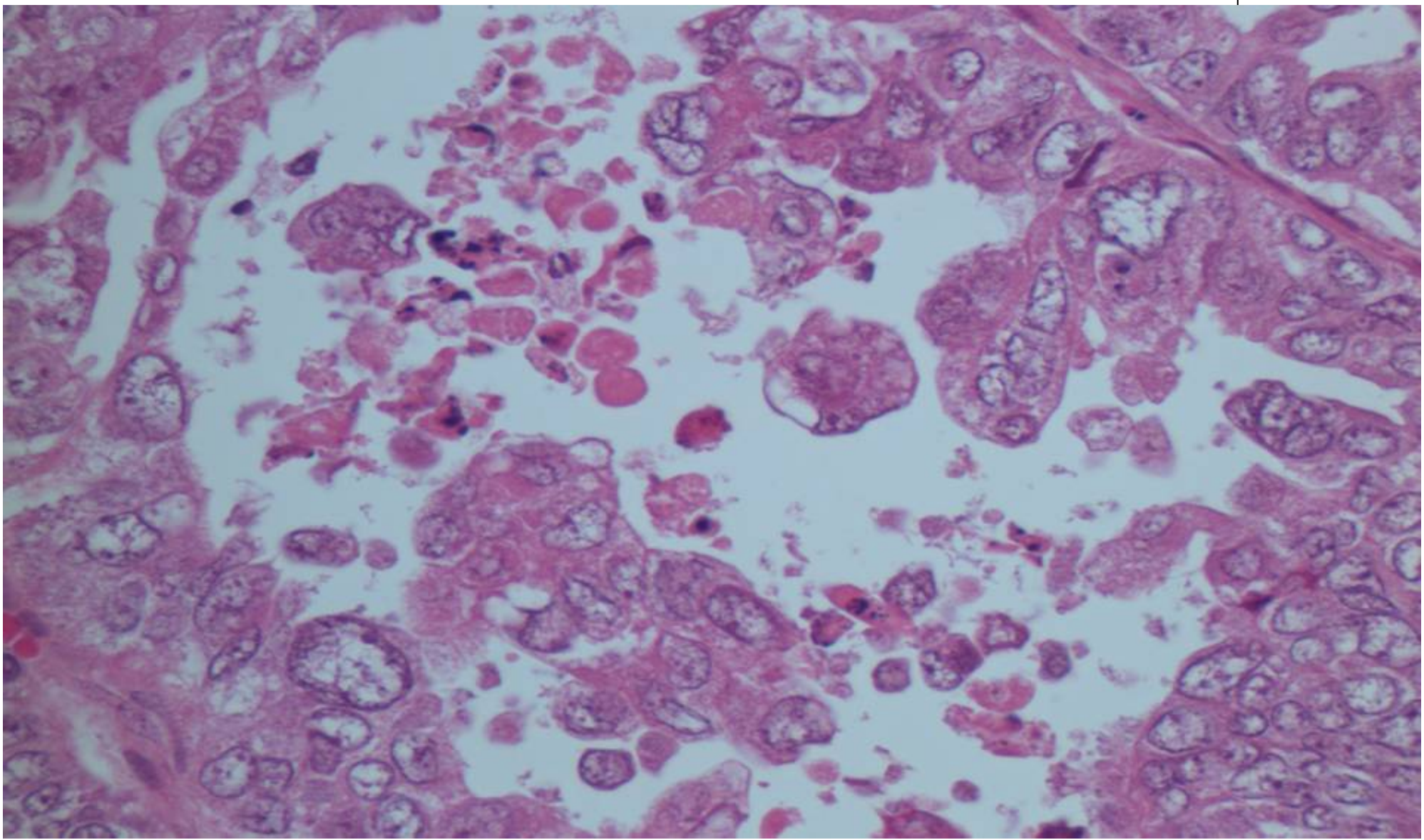
Serous adenoca

- 5-10% of endometrial carcinomas
- Type II carcinoma
- Aggressive tumour
- May show LVSI and peritoneal deposits with minimal myometrial invasion
- Staging recommended in patients with pre-operative diagnosis of SC
- Non-invasive precursor lesion - EIC/intraepithelial serous carcinoma.

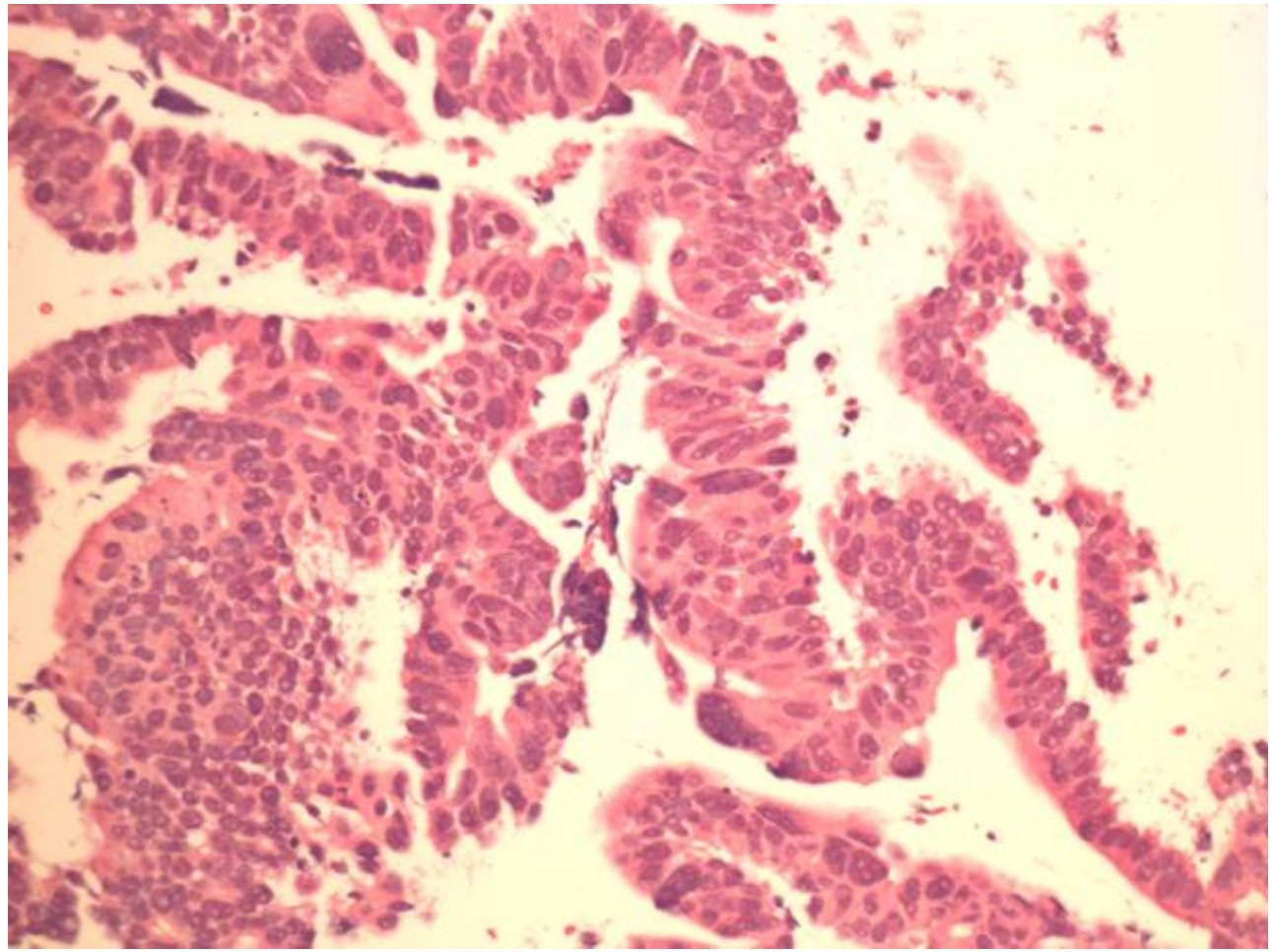
SEROUS ADENOCA



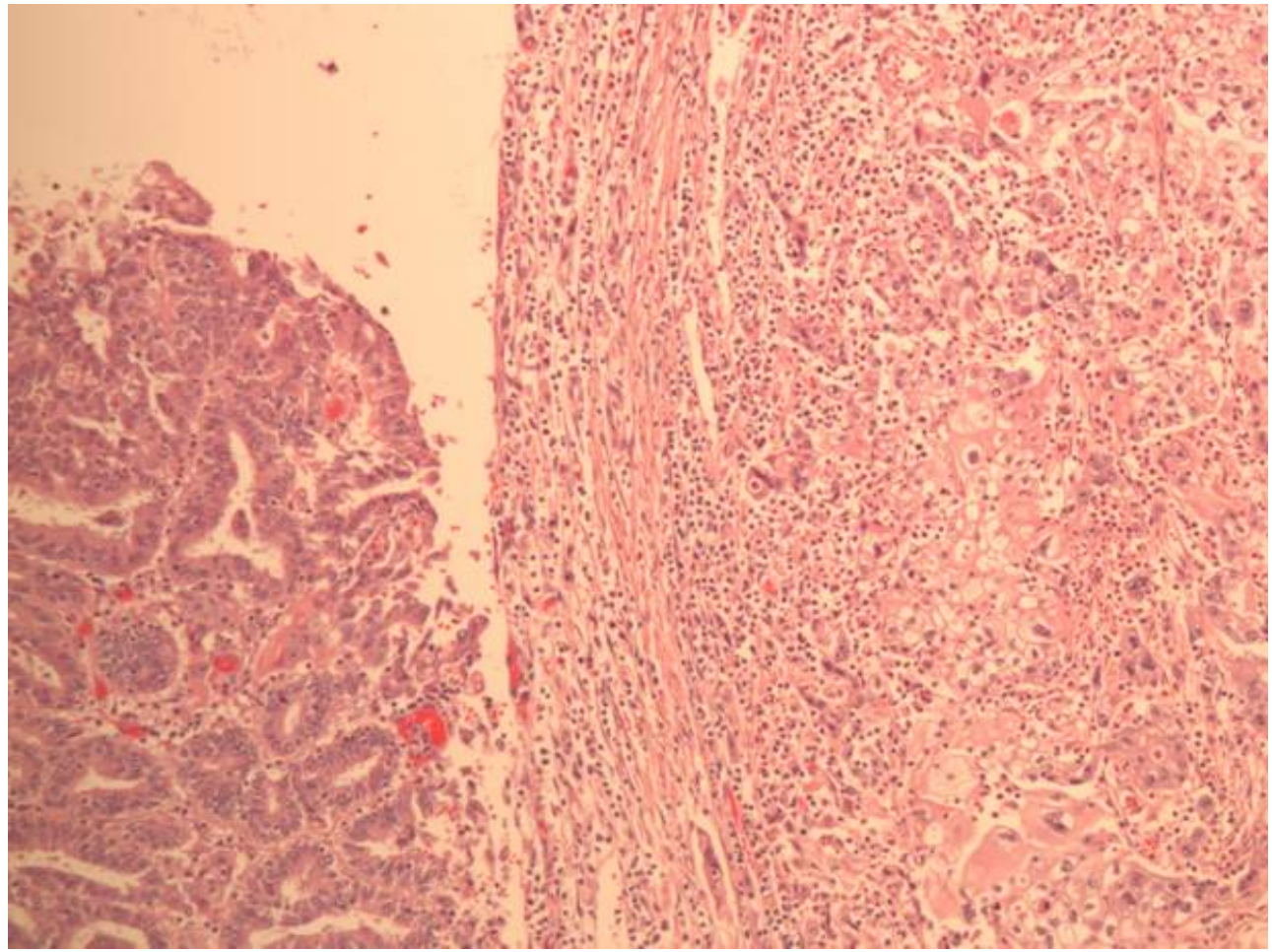
SEROUS ADENOCA



Serous carcinoma



Mixed adenoca/De-differentiated adenoca?



Hybrid tumours

- Some tumours may be difficult to assign a histologic subtype:

  gland forming or papillary tumour exhibits nuclear pleomorphism and a high mitotic rate but lacks confirmatory endometrioid or serous features

- FIGO grading inappropriate - useful to use Gilk's grading system
- P53 can be useful in such cases

Endometrial tumours with a stromal component

Divided into 2 groups

1) Pure stromal tumours

2) Tumours with an epithelial component

Other subtypes

- De-differentiated endometrial adenocarcinoma
- Undifferentiated adenocarcinoma
- Endometrioid adenocarcinoma with spindle cell elements – spindle cell elements never histologically high grade

Carcinosarcoma

- Definition – mixed tumour of malignant glands and mesenchyme

Histology

- Admixed malignant epithelial and mesenchymal elements
- Epithelial- endometrioid,squamous,mucinous,serous,clear cell.
- Mesenchymal- striated muscle,chondroid,osteoid etc

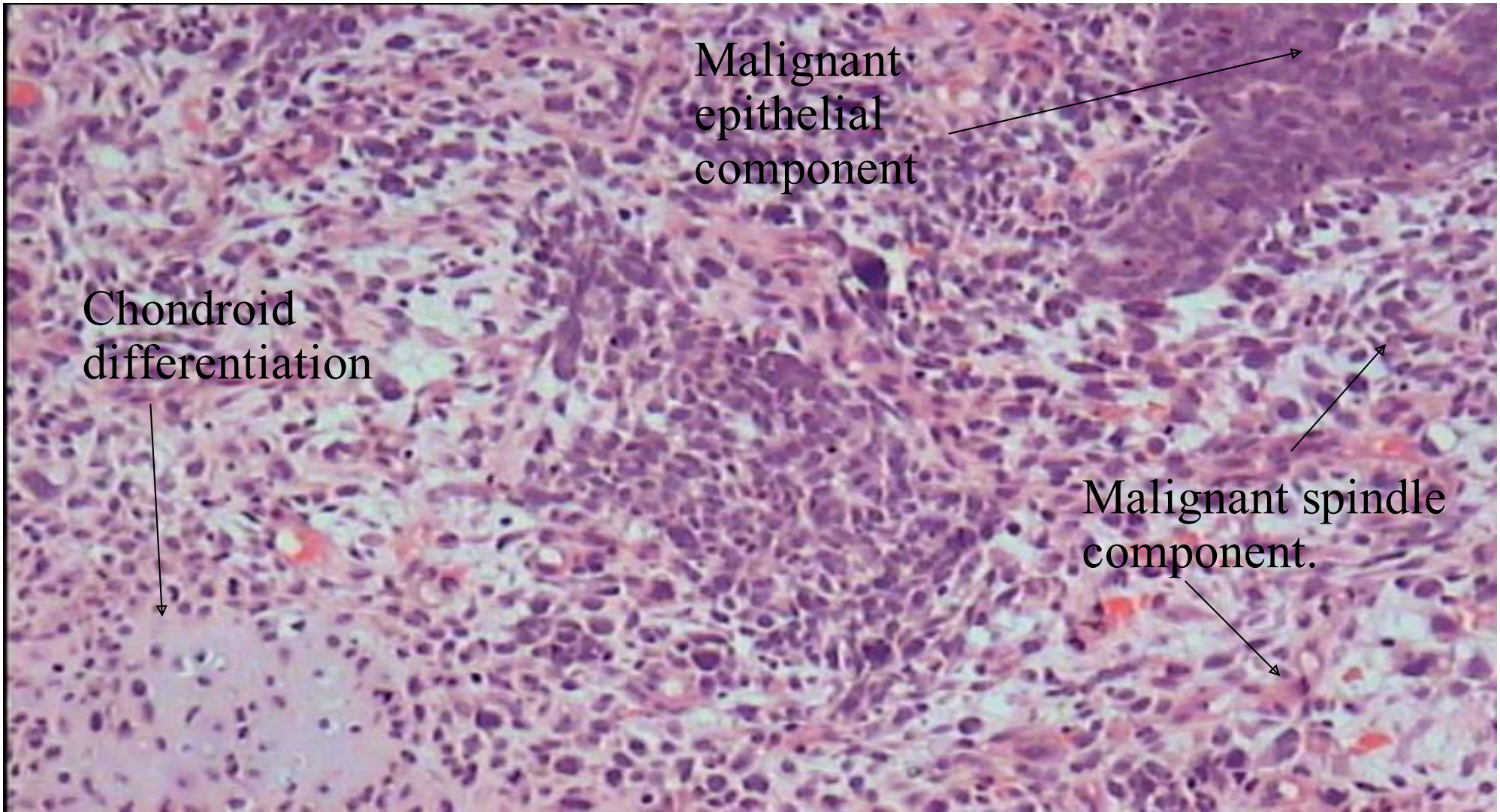
Carcinosarcoma/MMMT

- <5% of malignant uterine tumours
- Carcinomas with sarcomatoid differentiation i.e. biphasic
- Gynaecologists/oncologists persist in classifying as sarcomas
- Mean age - 7th decade, age range 4th to 9th decades
- Polypoid tumours
- Heterologous and homologous elements.

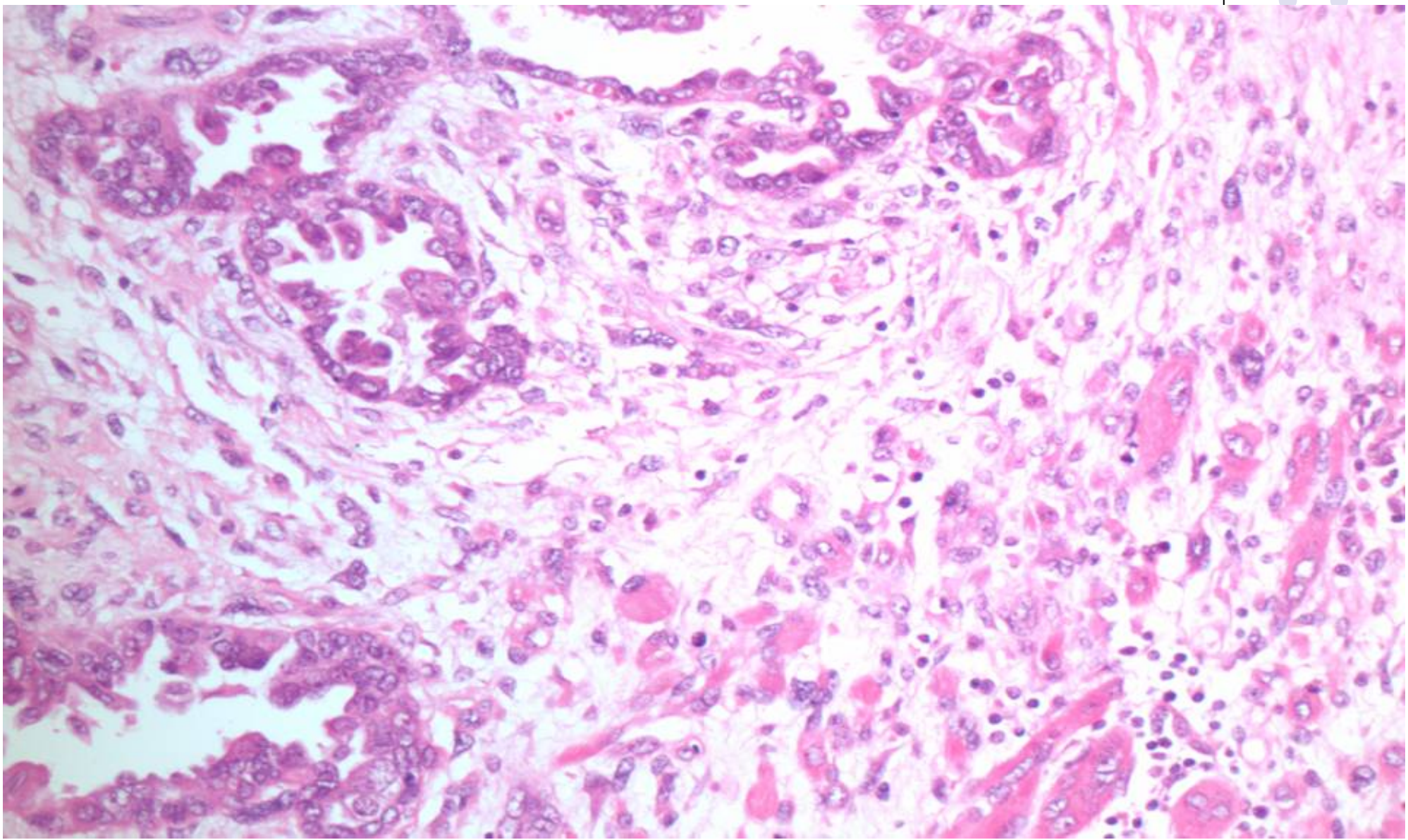
Continuation

- Histogenesis – Single progenitor cell?
- Metastases usually epithelial
- Prognosis dependant on epithelial component

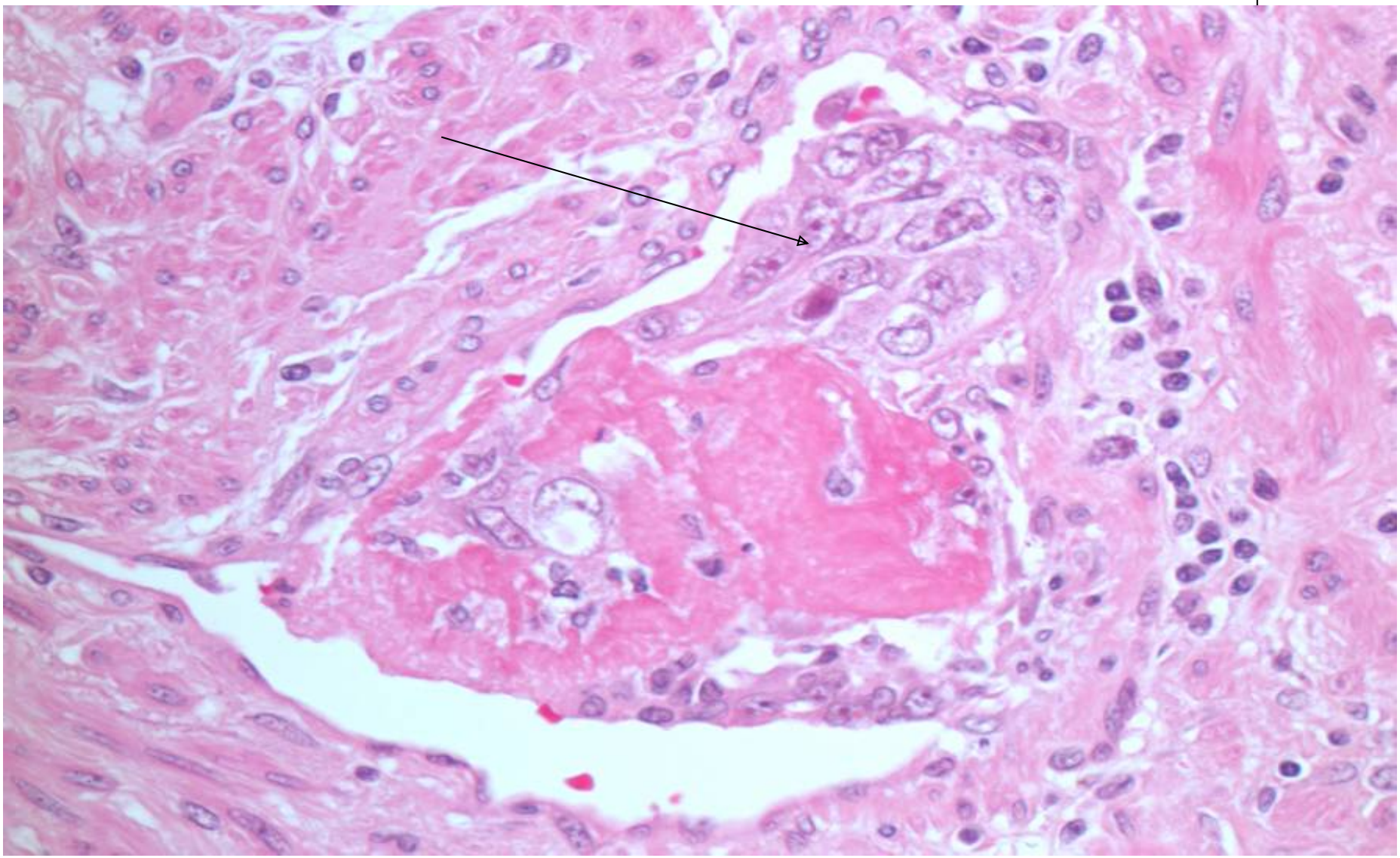
Malignant Mixed Mullerian Tumour



MMMT



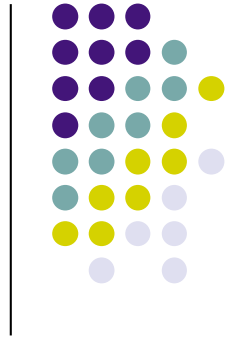
LVSI



Pure stromal tumours

- Endometrial stromal nodule
- Endometrial stromal sarcoma
- Undifferentiated uterine sarcoma

Tumours with an epithelial component

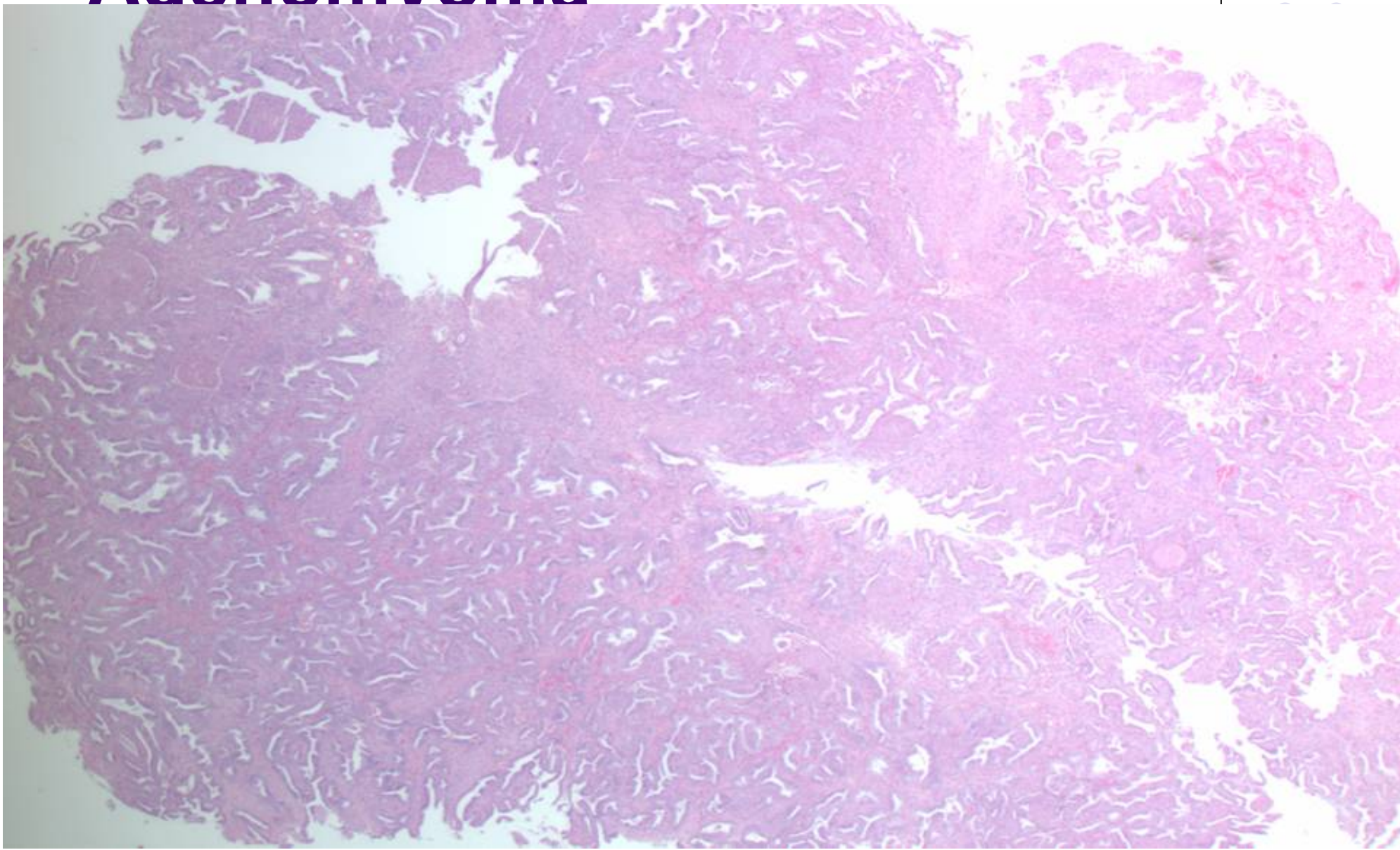


- Adenofibroma
- Adenomyoma
- Atypical polypoid adenomyoma

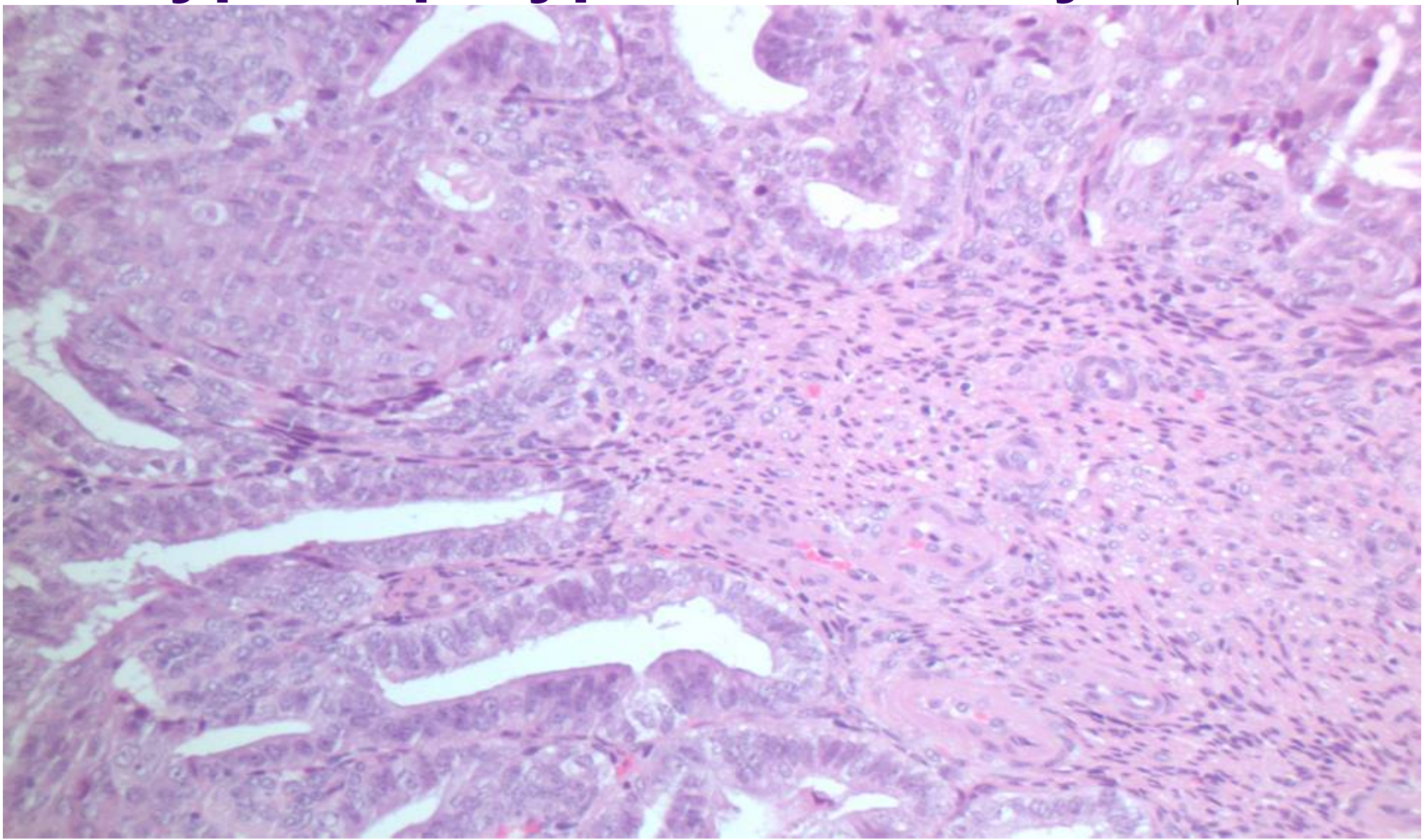
- Adenosarcoma

- Carcinosarcoma- with homologous or heterologous elements

Atypical Polypoid Adenomyoma



Atypical polypoid adenomyoma



Endometrial stromal nodule

- Well circumscribed
- Fleshy and focally yellow in appearance

Histology

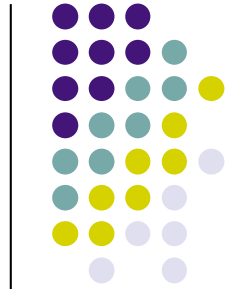
- Densely cellular
- Maybe hypocellular,fibrous,hyalinized,myxoid/oedematous
- Arterioles (spiral arteriole calibre)

PATHOLOGY REPORT

- Histological type of tumour
- High grade/ low grade
- LVSI
- Stage – FIGO
- Margins – if any

- Biopsy specimen – type of tumour and grade.

Is immunohistochemistry of value?



- Tumours don’t read books!
- Serous ca – p53, p16, ER, PR, MIB-1, WT-1
- EIC – p53 useful
- Low grade endometrioid – p53, vimentin, ER, PR, PTEN
- Grade 3 endometrioid – limited value
- Clear cell – ER and PR negative. P53,p16and Ki-67 intermediate between serous and endometrioid ca

Thank you

Questions?

Quiz

Highly recommend: Histopathology Volume 62 Number 1 January 2013.