

ENDOMETRIAL PATHOLOGY REPORTING: WHAT REALLY MATTERS- WHEN AND WHY

W Glenn McCluggage

Belfast

United Kingdom

OUTLINE OF TALK

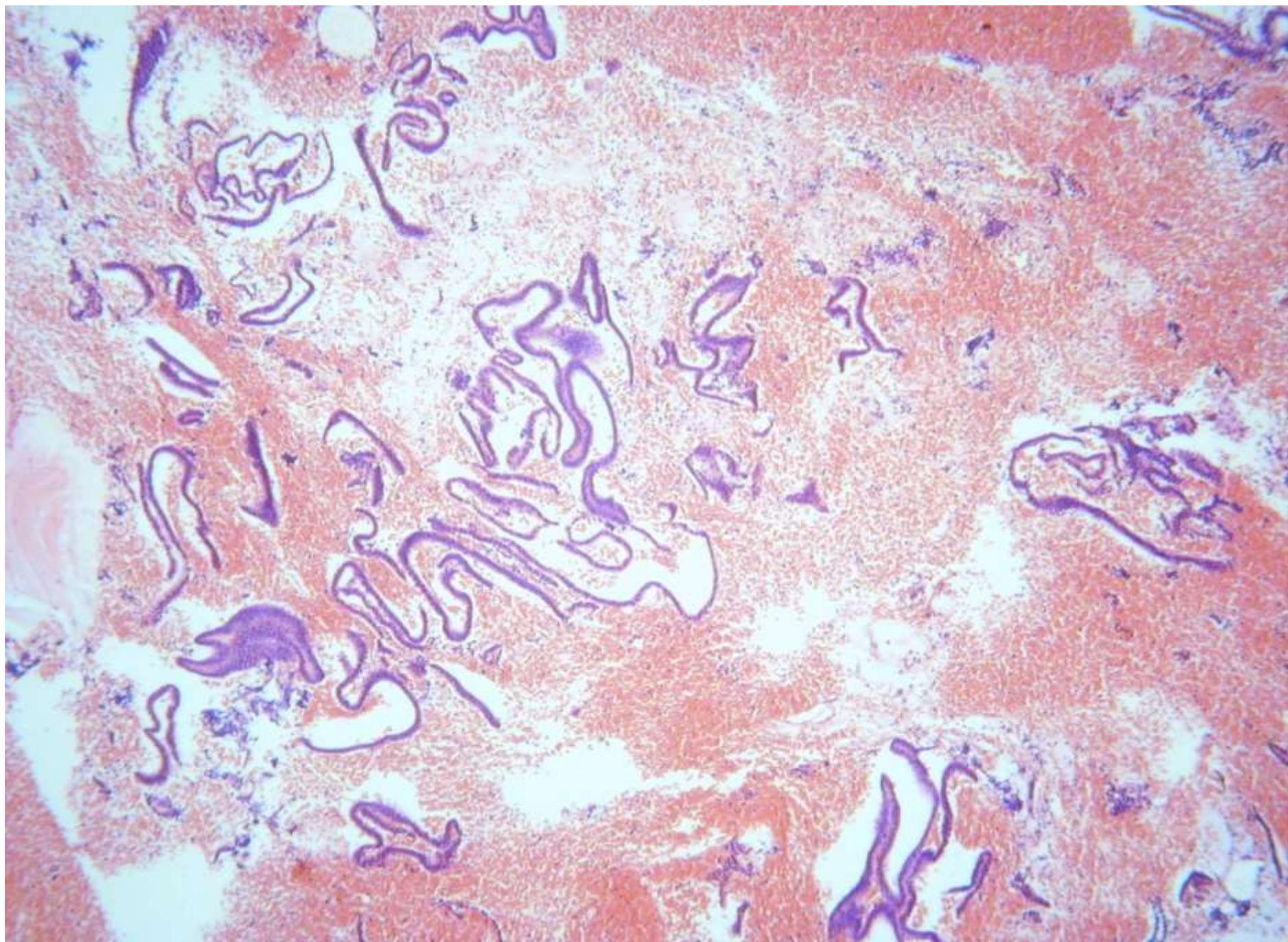
- General points (Murali Varma covered)
- Benign endometrial pathology
- Premalignant and malignant endometrial pathology (biopsies and resections)
- **MANY OF TIPS ARE PERSONAL AND EVERYONE MAY NOT AGREE**

BENIGN ENDOMETRIAL BIOPSIES

- In general- don't need to perform levels
- Try to explain every individual piece of tissue (lower uterine segment; myometrium; cervix etc)
- Criteria for adequacy
- Be aware of and don't stress about artefacts
- Be aware of features of breakdown
- Don't need to look for plasma cells in every endometrial biopsy (unless some clue that there may be an endometritis)
- Don't need to date endometria (proliferative, secretory etc is enough)
- Endometrial polyps- things not to worry about

CRITERIA FOR ADEQUACY OF ENDOMETRIAL BIOPSY

- most biopsies are outpatient pipelles (often contain scant tissue)
- considerable disagreement amongst pathologists as to criteria for adequate/inadequate
- classification as inadequate/ insufficient may have clinical implications
- in postmenopausal woman with atrophic endometrium, scant tissue is the norm- usually superficial strips of endometrial glands
- examine under high power to look for mitotic activity (abnormal in postmenopausal) and atypia
- often take longer to assess than intact biopsies



(PIPELLE OR CURETTAGE) (J Clin Pathol 2005;58;417-419)

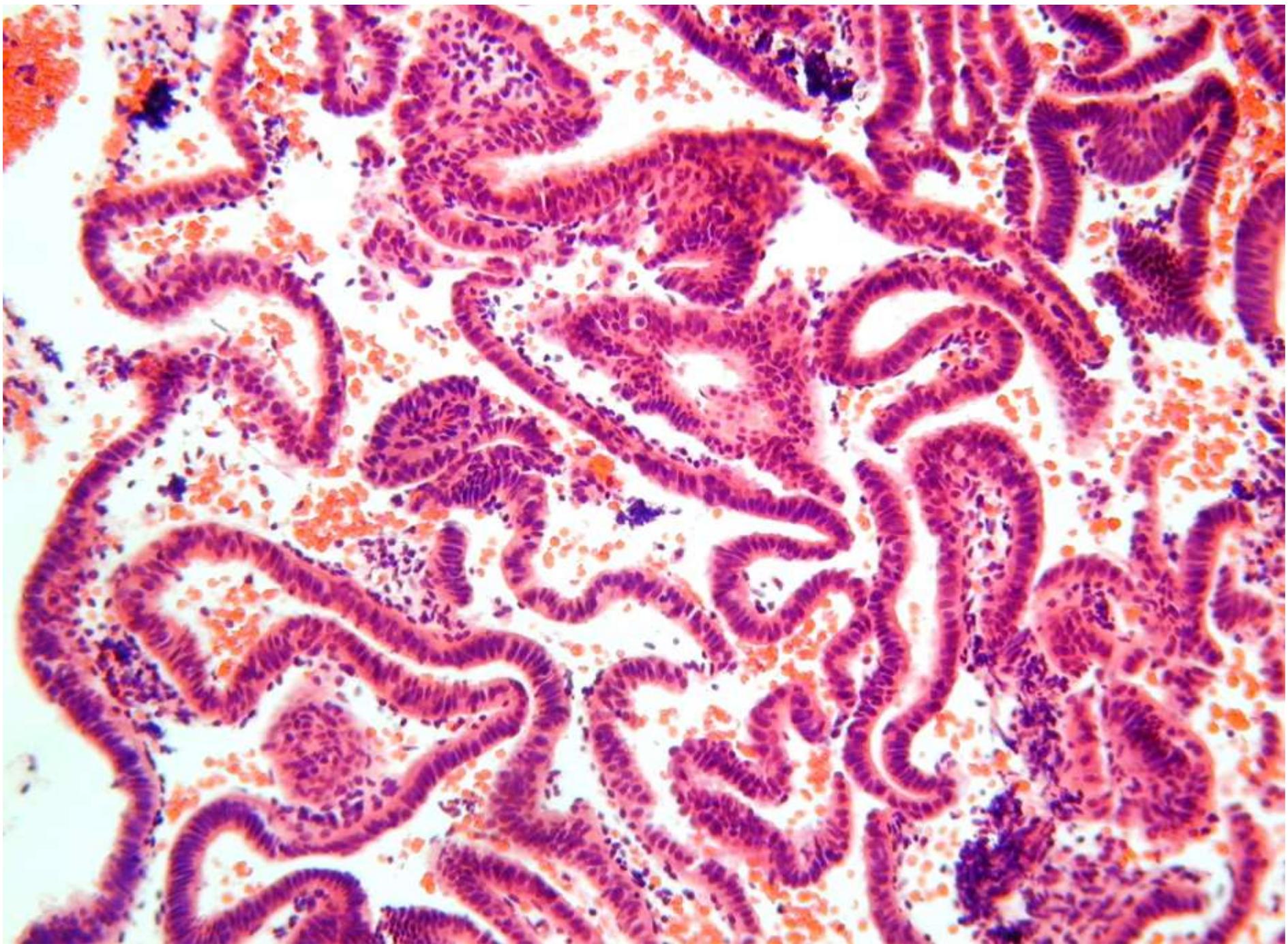
- INADEQUATE (no endometrial tissue)
- UNASSESSABLE (minimal endometrial tissue – provides evidence that endometrial cavity has been entered)
- TYPE (if significant amount of tissue)

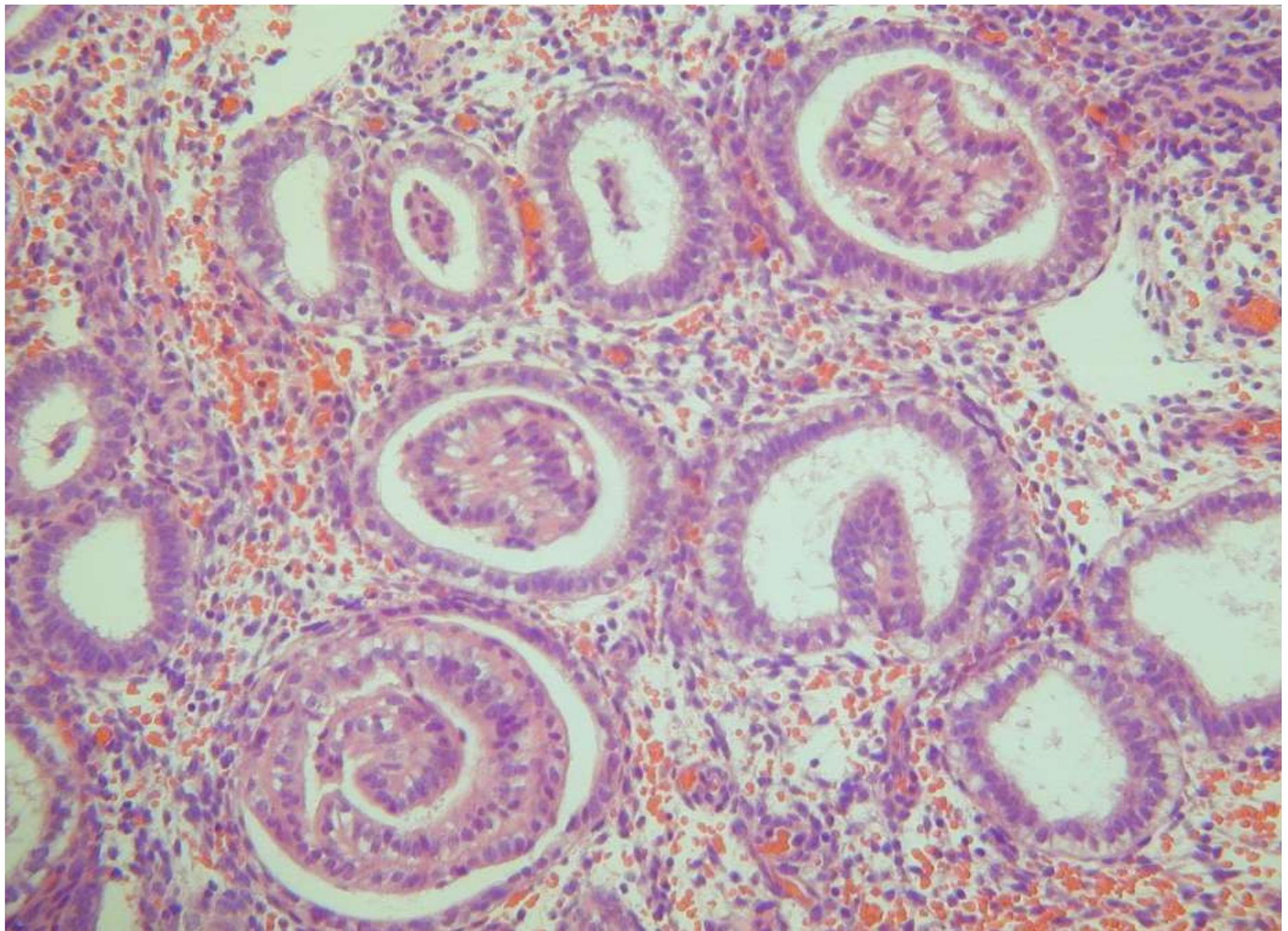
RECENT PROPOSAL

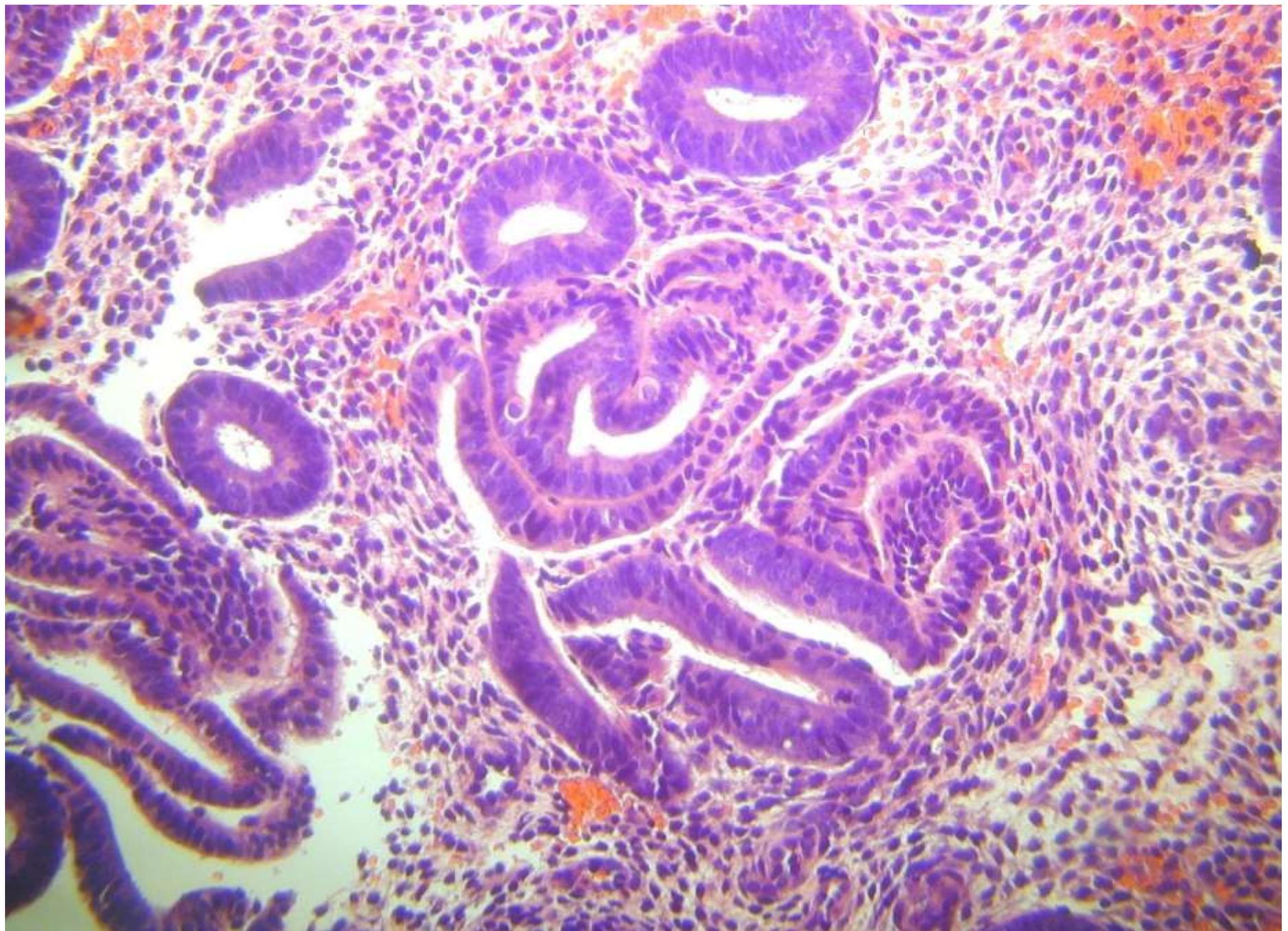
- IJGP- PMID 26990506
- No well defined criteria for adequacy
- 1768 endometrial samples (used repeat procedure outcomes as reference)
- At least 10 endometrial strips- negative predictive value of close to 100%
- Proposed 10 endometrial strips as minimum criteria for adequacy in postmenopausal women
- DON'T ASK FOR OR EVEN SUGGEST TO DO A REPEAT BIOPSY WITH SCANTY SPECIMENS

ARTEFACTS

- Pseudopapillary architecture (especially in postmenopausal atrophic endometrium)
- Telescoping (glands within glands)
- Glandular moulding



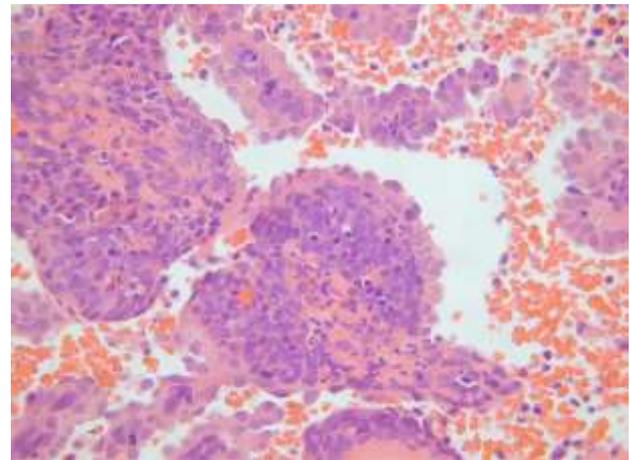
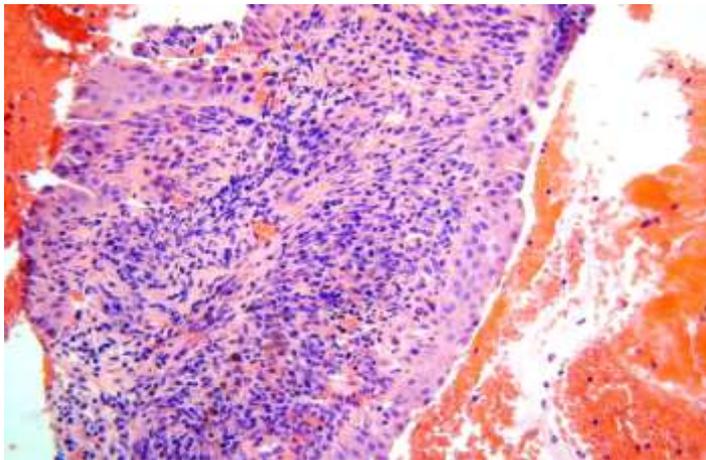
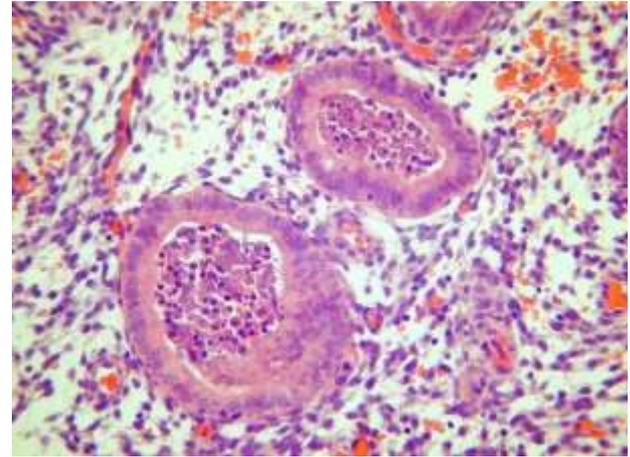
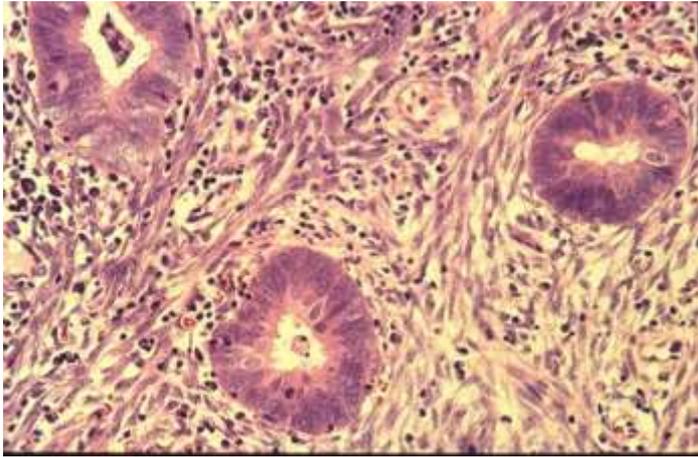




ENDOMETRITIS

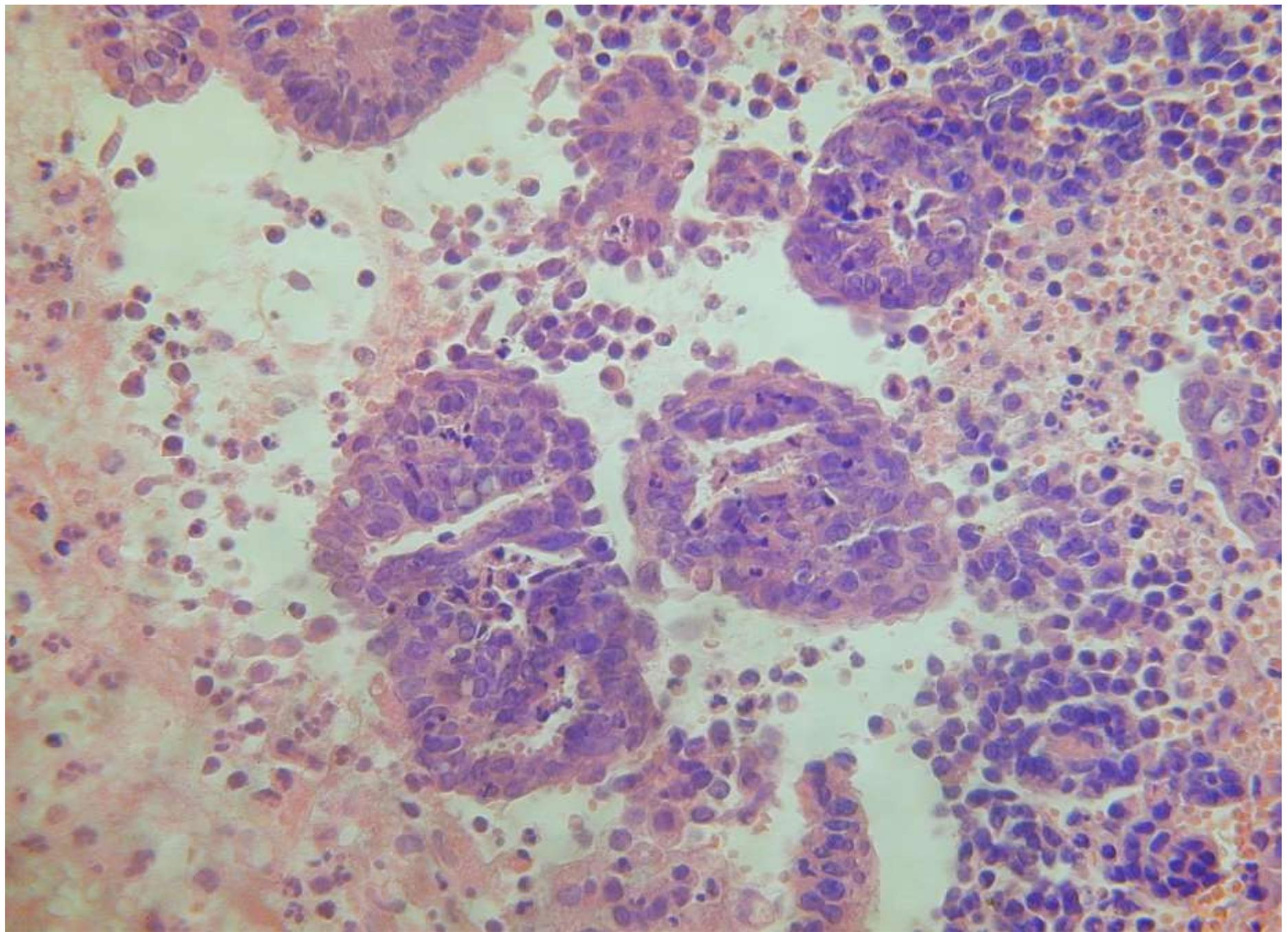
- Don't look for plasma cells in every endometrial biopsy
- Plasma cells best seen at intermediate power
- Only look if clues that an endometritis may be present (almost never with secretory features)
- Lymphoid cells are present in many endometrial biopsies (NK cells in secretory and progesterone effect endometrium; lymphoid aggregates especially in postmenopausal; polymorphs with breakdown)
- Don't do plasma cell markers (don't need and very non-specific; glands often stain)
- Plasma cells normal in cervix; abnormal in endometrium- can be helpful

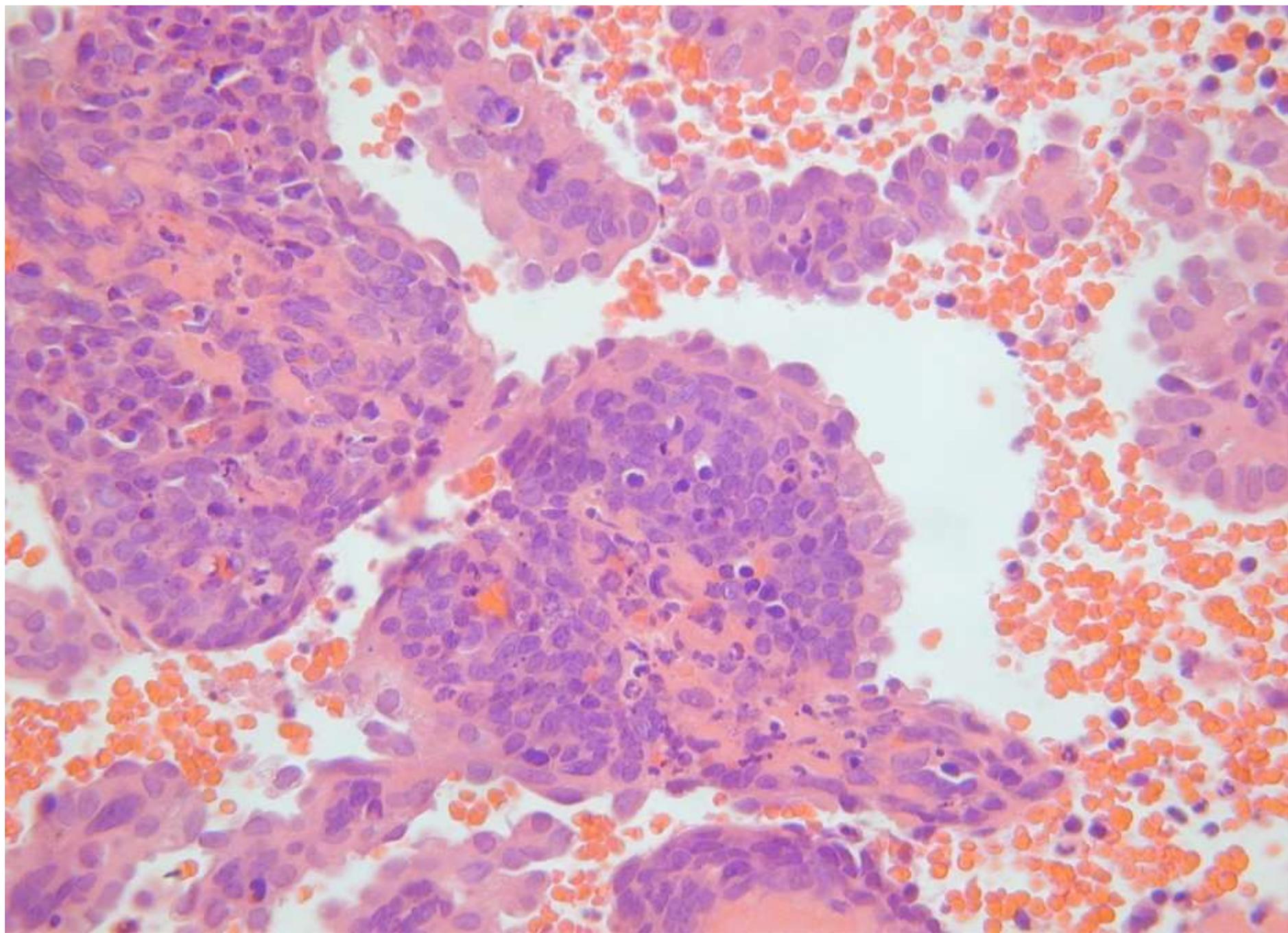
LOW POWER CLUES TO ENDOMETRITIS

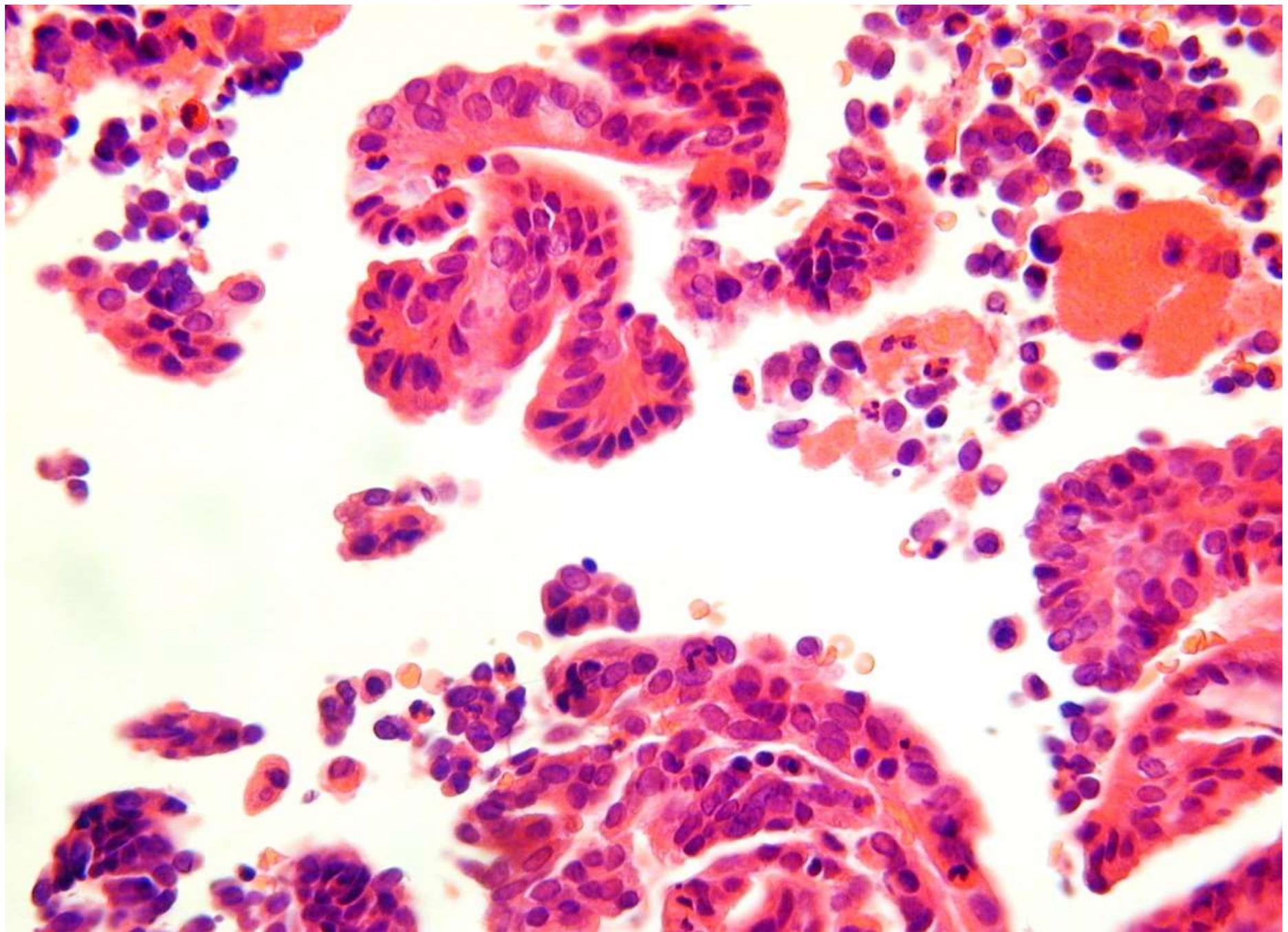


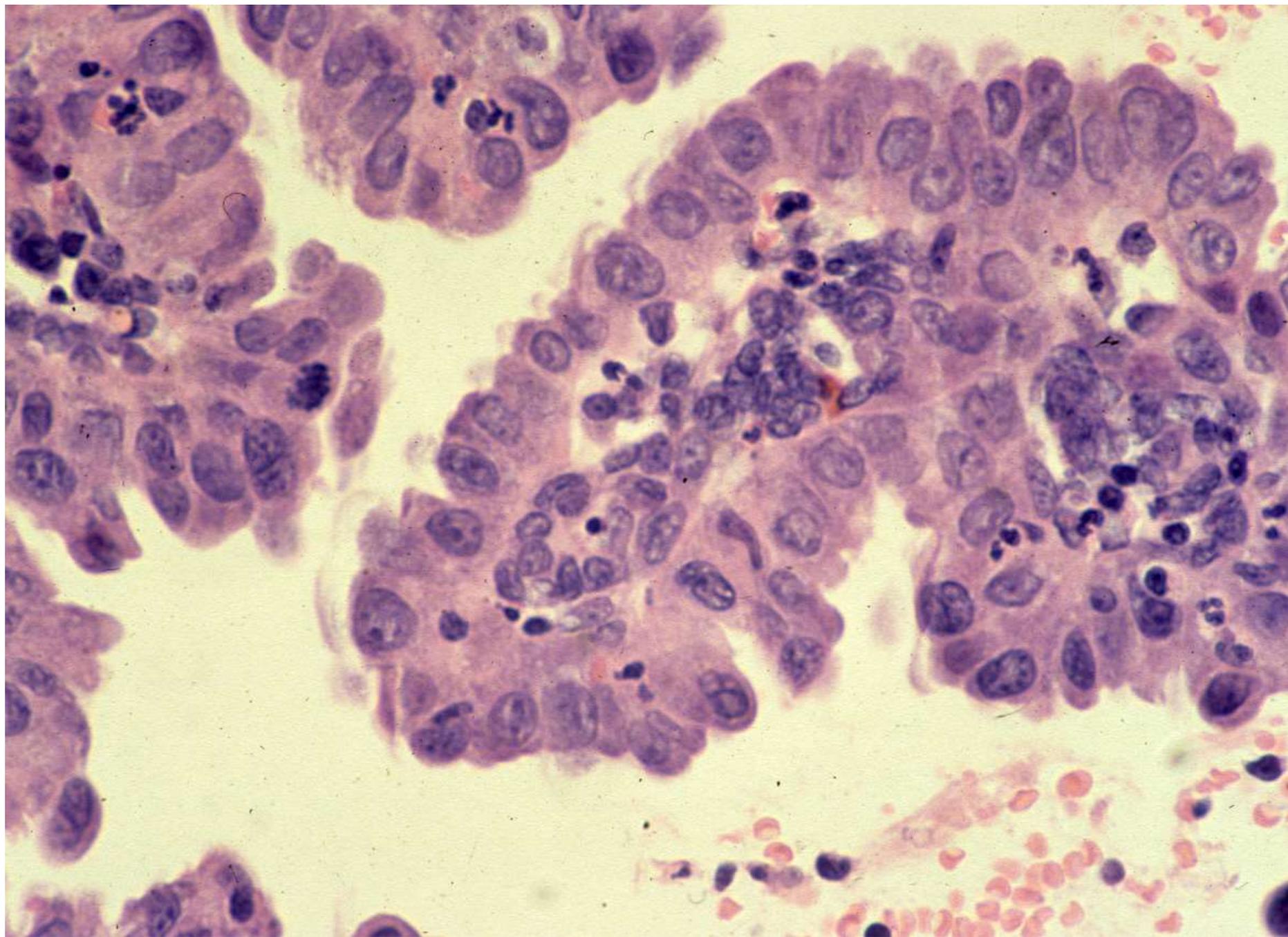
ENDOMETRIAL BREAKDOWN

- menstrual or non-menstrual
- in non-menstrual endometrium may be sign of hormone imbalance and cause of abnormal bleeding
- very florid breakdown with papillary syncytial metaplasia (PSM) may mimic serous proliferation; look for other signs of breakdown; can be very worrying at high power





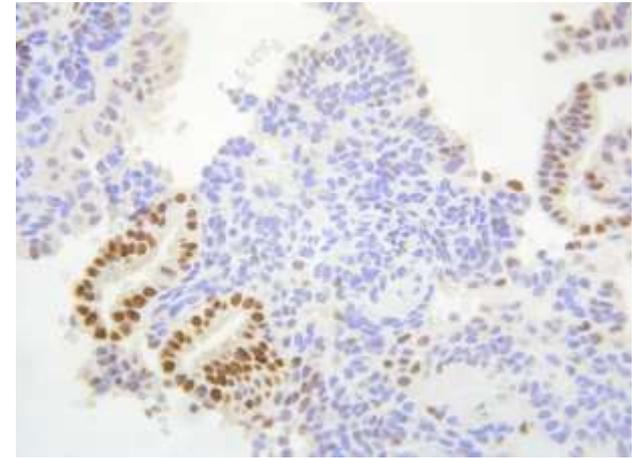
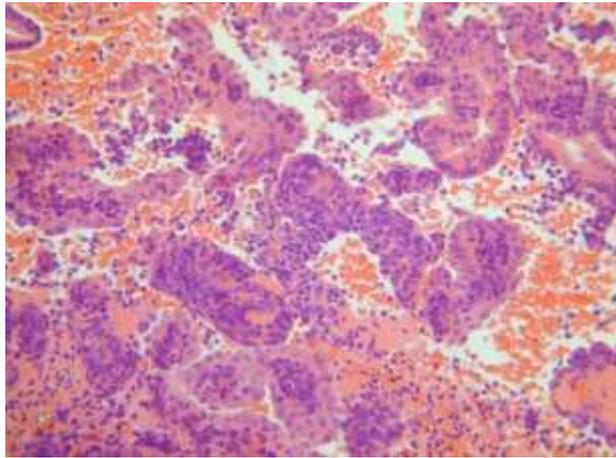




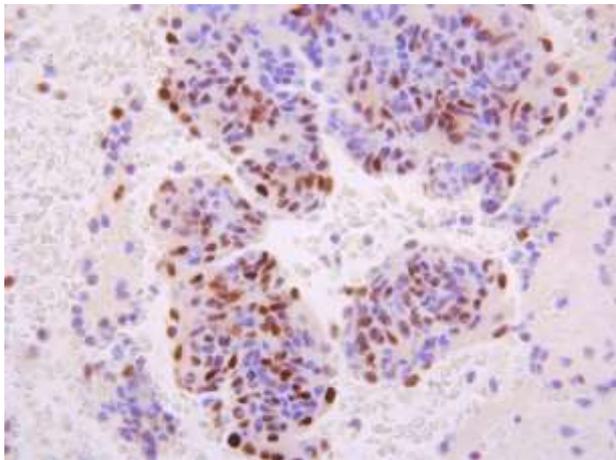
DIFFERENTIAL FROM SEROUS PROLIFERATION

- look for other signs of breakdown
- immunohistochemistry- p53, ER, p16 (BUT BEWARE)
- Immunohistochemistry of PSM (and other “metaplastic” lesions): ER often decreased; p53 often increased but “wild-type”; p16 often strongly expressed

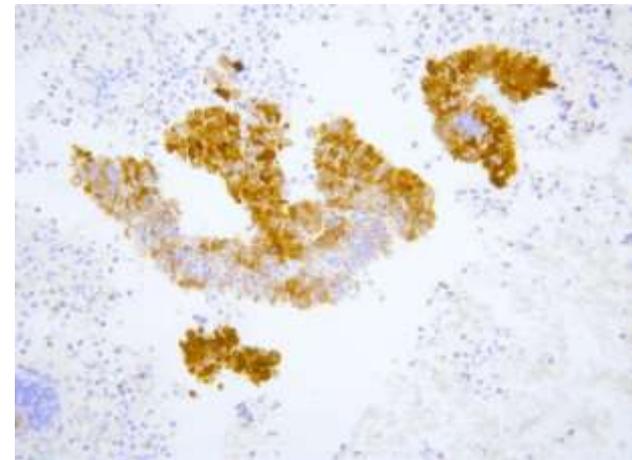
IMMUNOHISTOCHEMISTRY- SURFACE METAPLASTIC CHANGES/ PSM/ IUD EFFECT



ER



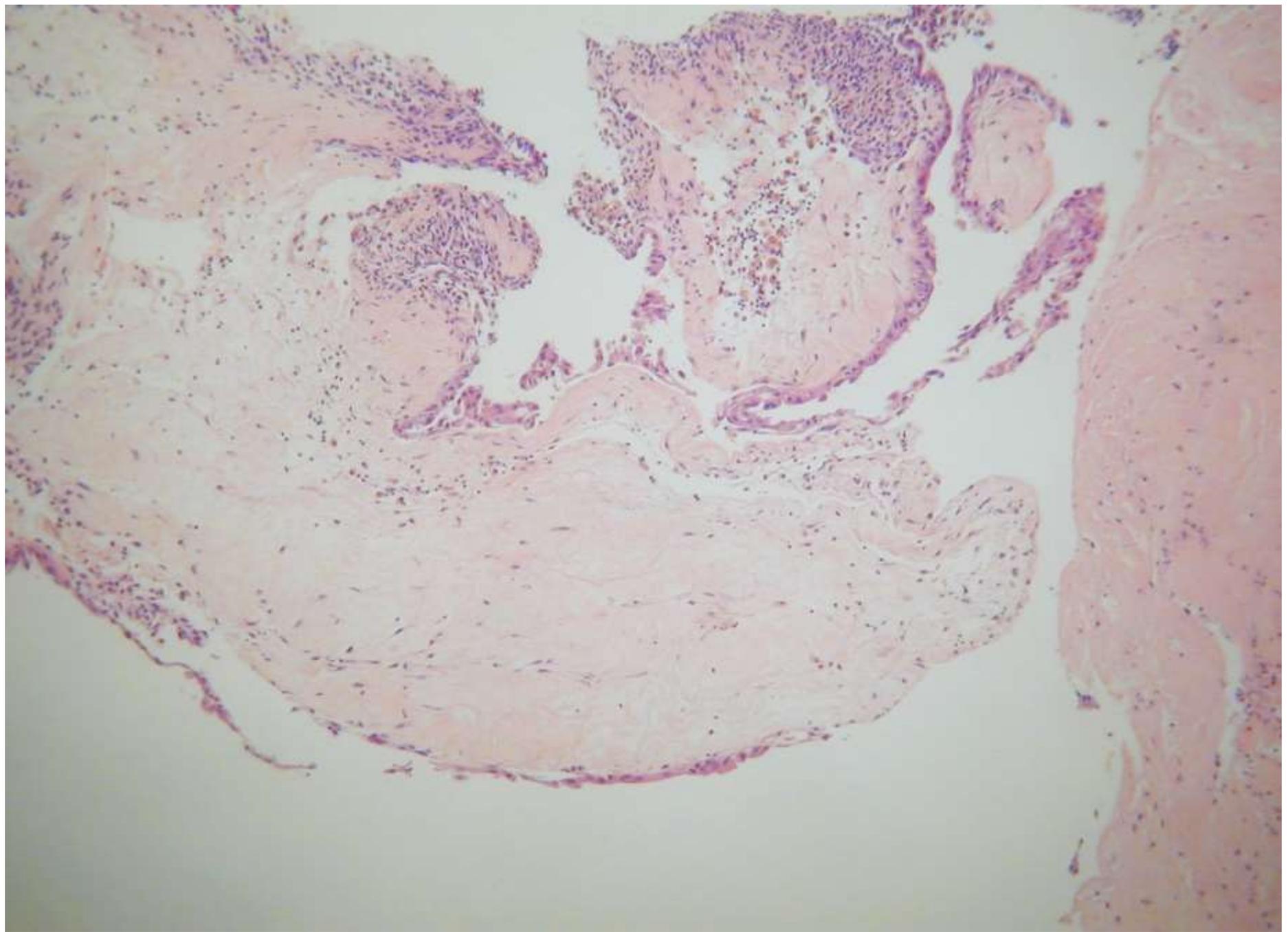
p53



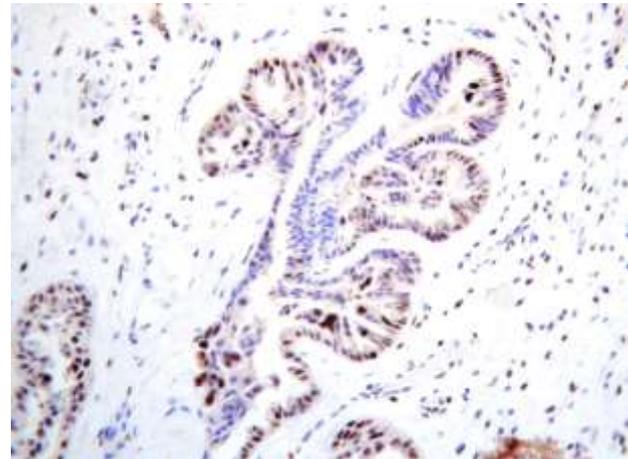
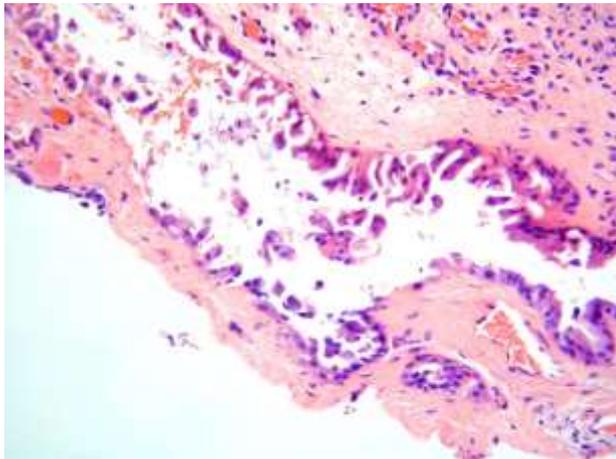
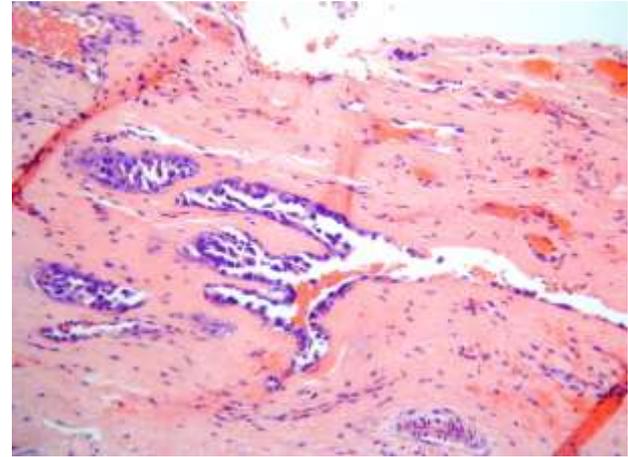
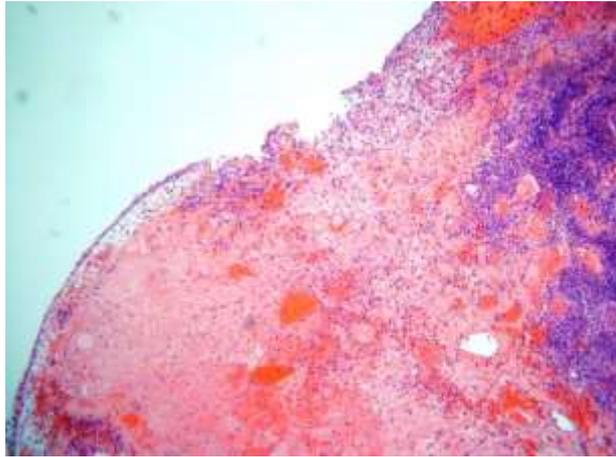
p16

PROBLEMS IN ENDOMETRIAL POLYPS (NO NEED TO SCRUTINISE ALL POLYPS UNDER HIGH POWER)

- **proliferative activity may occur in glands in postmenopausal women (don't talk about atrophic, hyperplastic, proliferative polyps)**
- **inflammatory cells, including plasma cells, may occur- not endometritis**
- **epithelial metaplasias common**
- rarely stromal metaplasias
- **necrosis secondary to torsion; surface atypia and hobnail change secondary to torsion**
- symplastic stromal cells
- sex cord-like elements in stroma
- papillary proliferation of endometrium
- **adenofibroma/ adenosarcoma-like areas**
- cellular stroma mimicking endometrial stromal neoplasm
- **hyperplasia in polyp (DON'T CONSIDER UNLESS SIGNIFICANT GLANDULAR CROWDING)**
- carcinoma in polyp (any morphological type)



HOBNAIL "METAPLASIA" IN NECROTIC POLYP



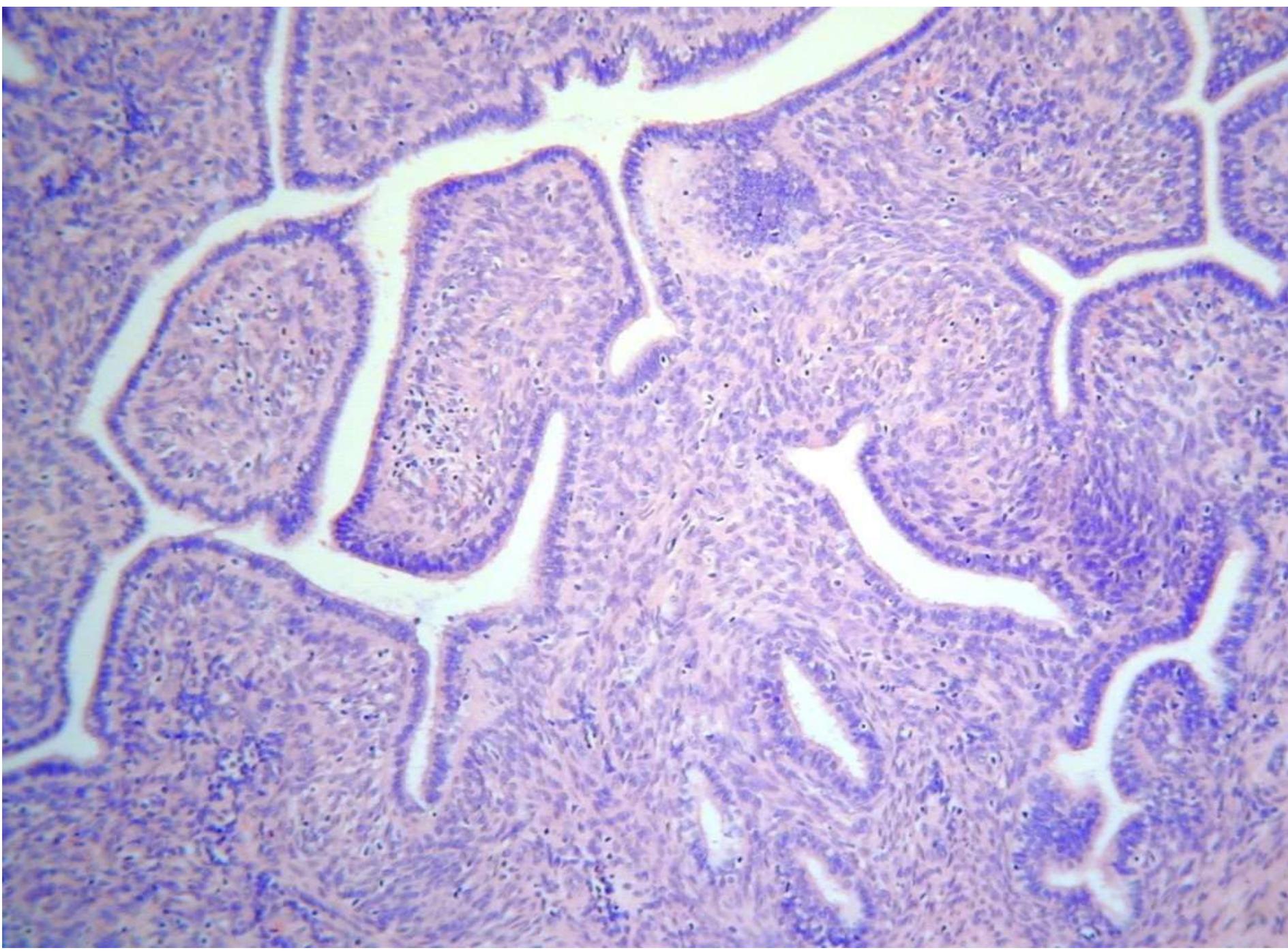
p53

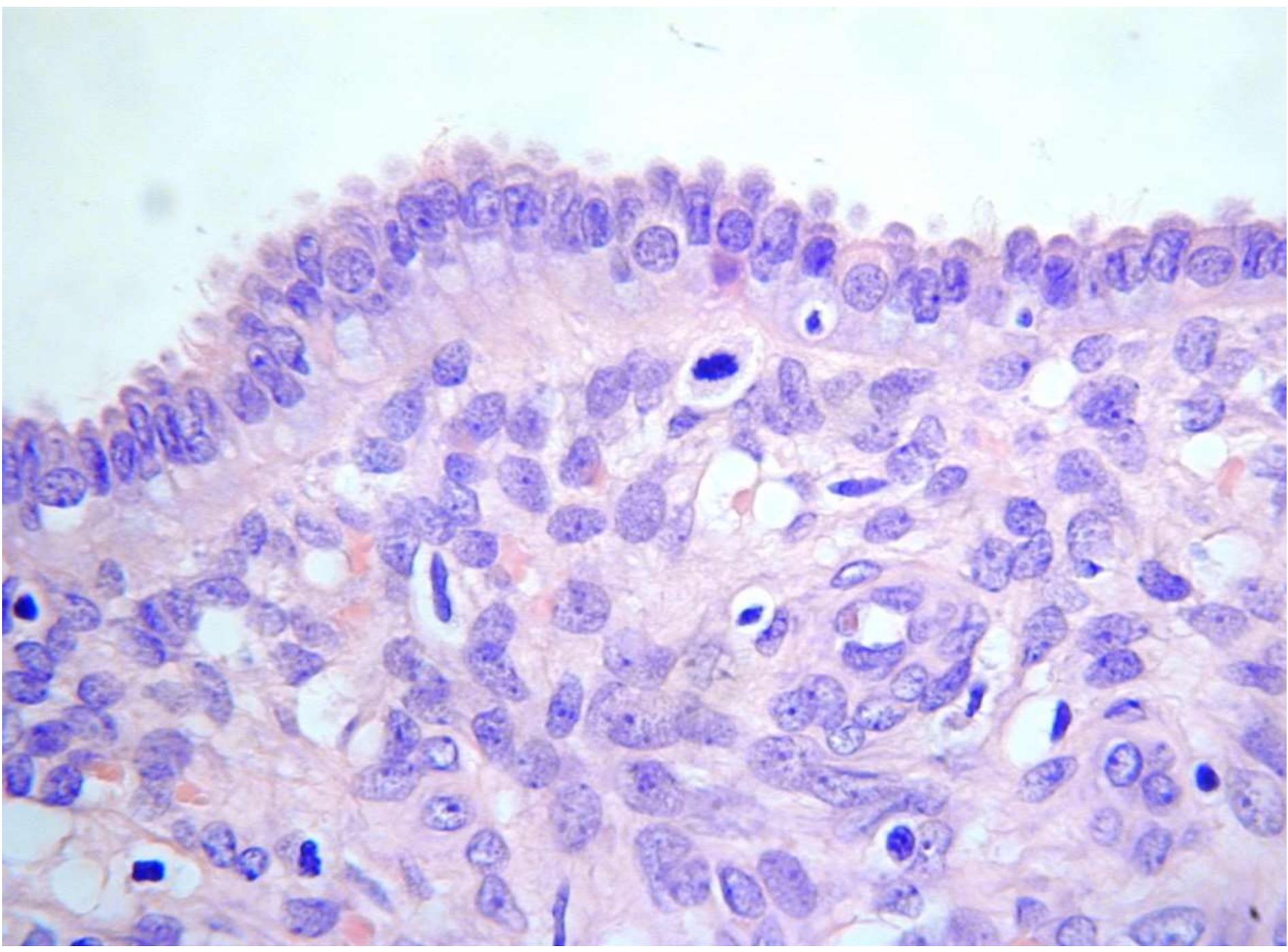
ENDOMETRIAL OR CERVICAL POLYP

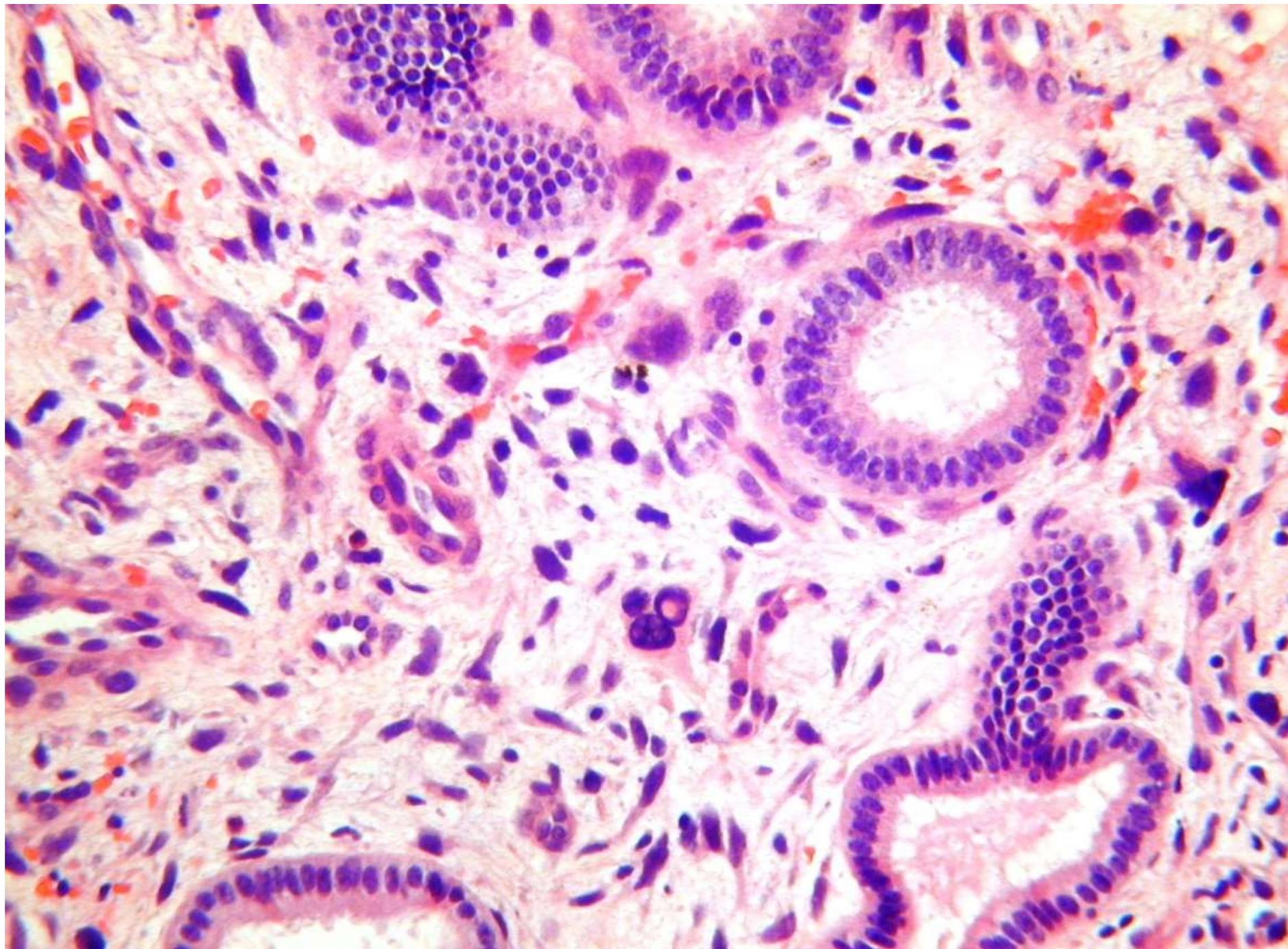
- some endometrial or cervical polyps have some features of adenofibroma/adenosarcoma but not all (polyps with features overlapping with or subdiagnostic of adenosarcoma)
- examples include phyllodes-like architecture, intraglandular projections, periglandular increased cellularity, stromal atypia or mitoses
- recent study- follow up in such cases uneventful (AJSP 2015; 39;116-126)

ENDOMETRIAL POLYP- ADENOSARCOMA LIKE



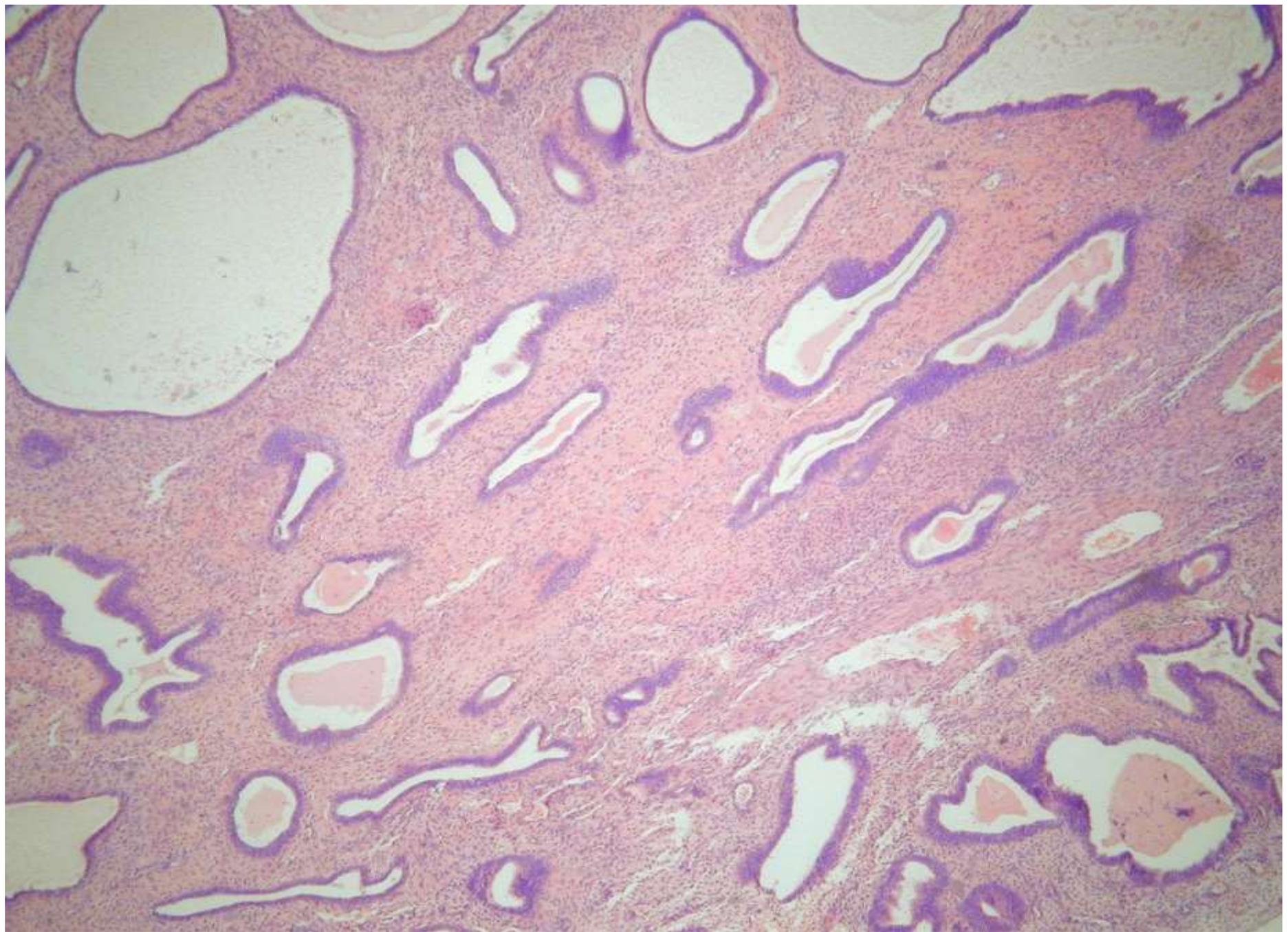


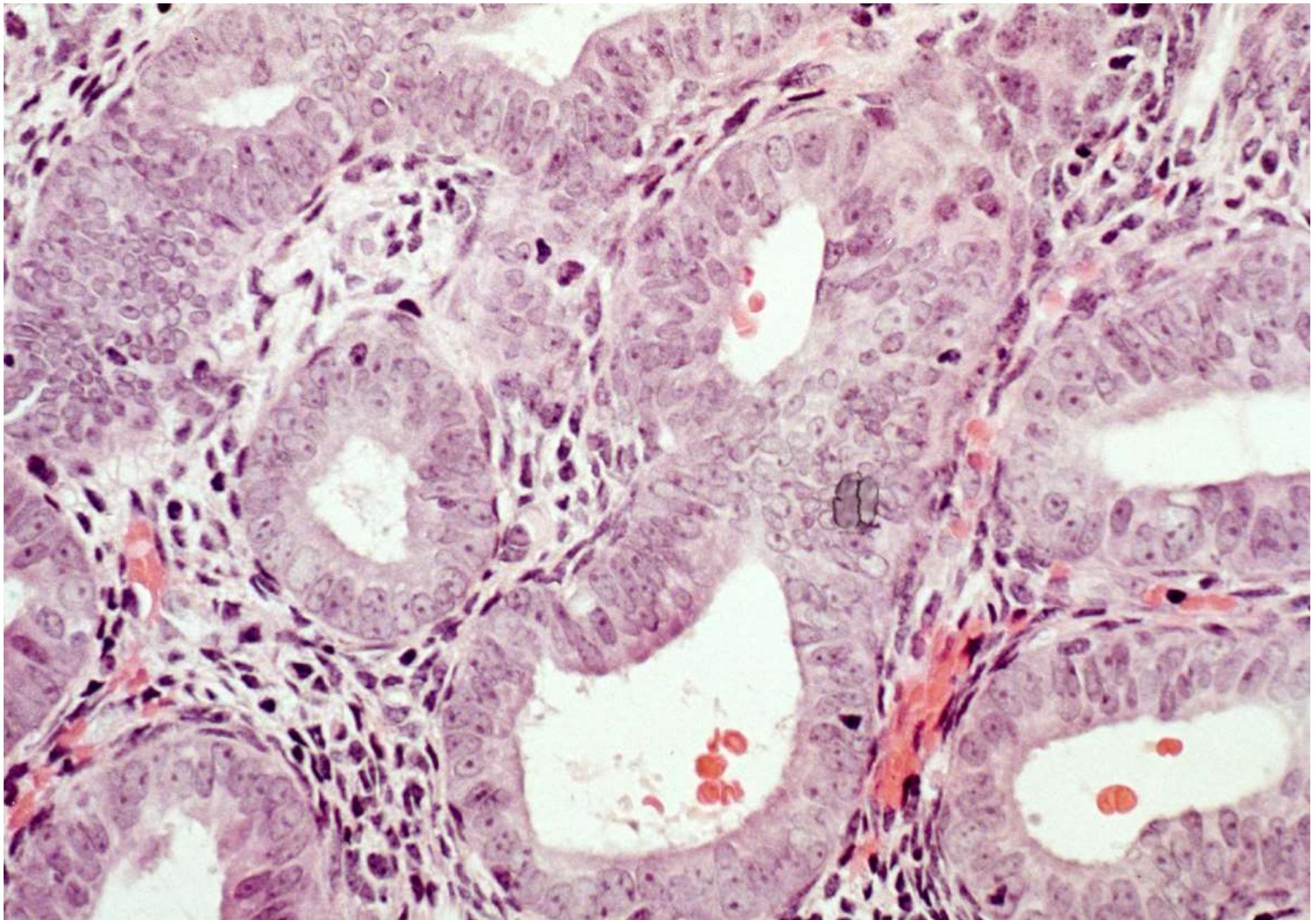




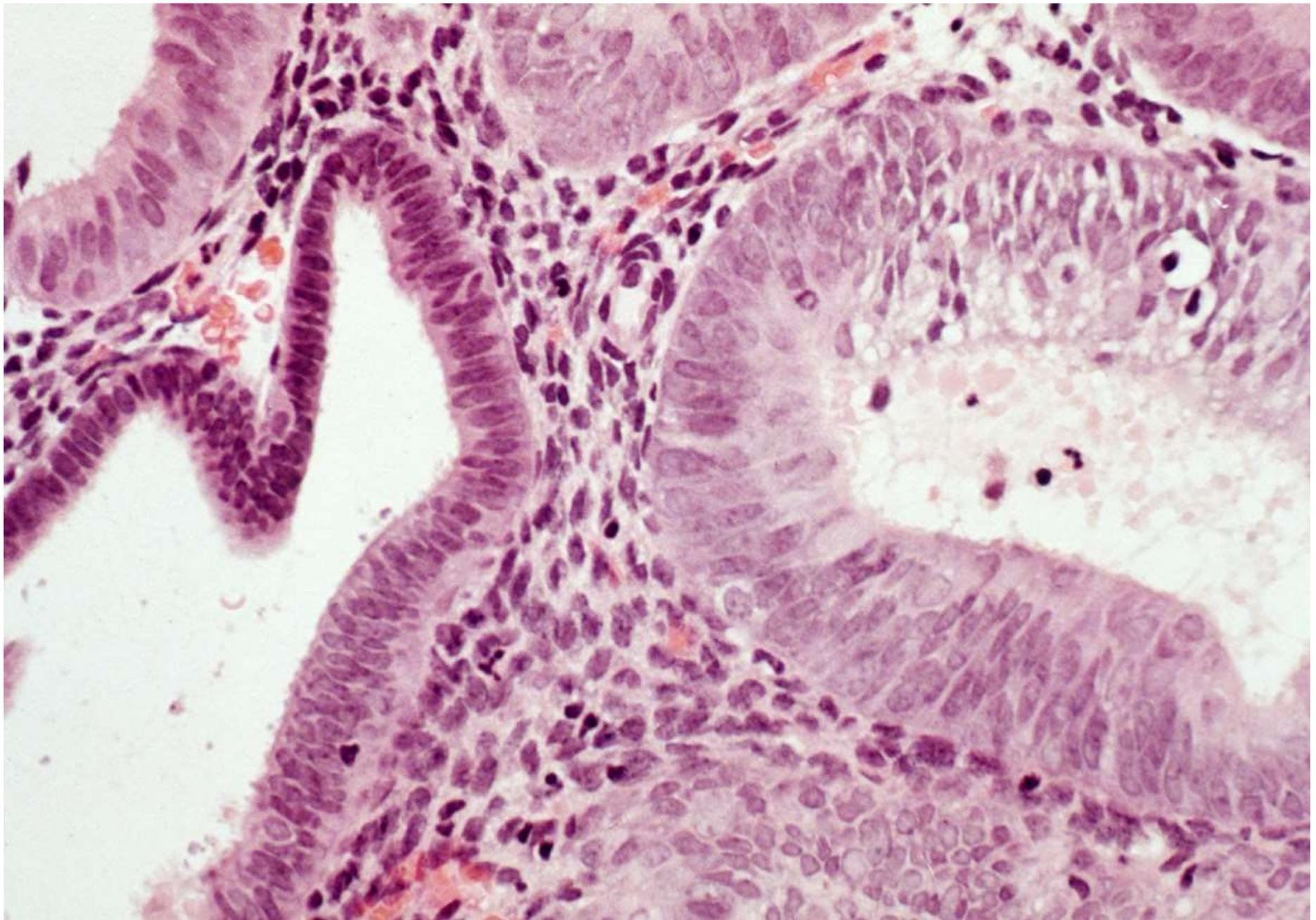
ENDOMETRIAL HYPERPLASIA IN POLYP

- not uncommon for hyperplasia to be identified in endometrial polyp
- don't diagnose simple hyperplasia in polyp
- diagnose complex hyperplasia (hyperplasia without atypia) or atypical hyperplasia using same criteria as in non-polypoid endometrium
- ? significance of hyperplasia in polyp





AH



AH

ENDOMETRIAL HYPERPLASIA IN POLYP

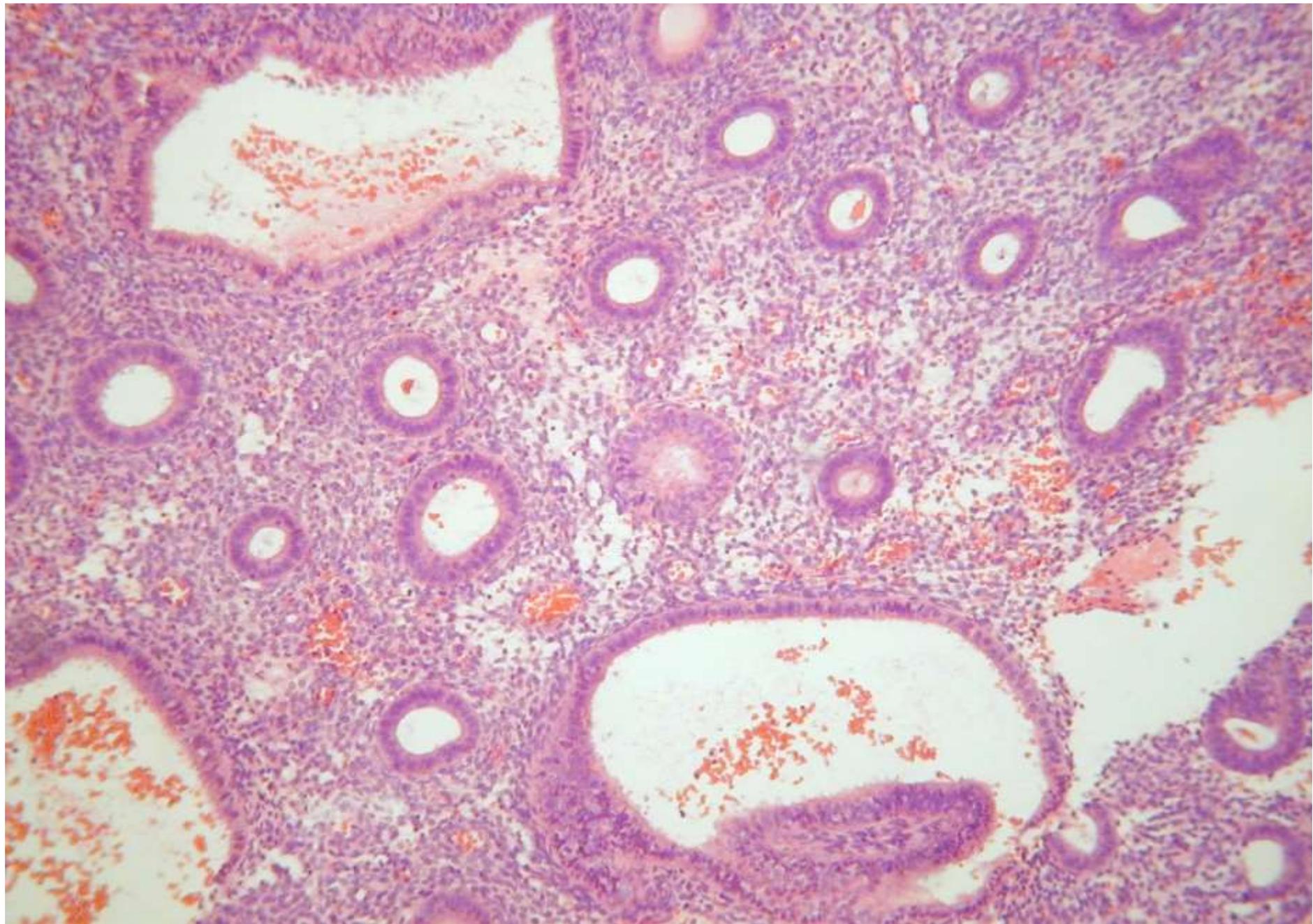
- little information in literature
- BJOG 2007;114;944-950
- in about 50% of cases, hyperplasia will involve non-polypoid endometrium
- not much difference whether complex or atypical hyperplasia

HYPERPLASIA WITHOUT ATYPIA (SIMPLE HYPERPLASIA) VERSUS DISORDERED PROLIFERATIVE ENDOMETRIUM

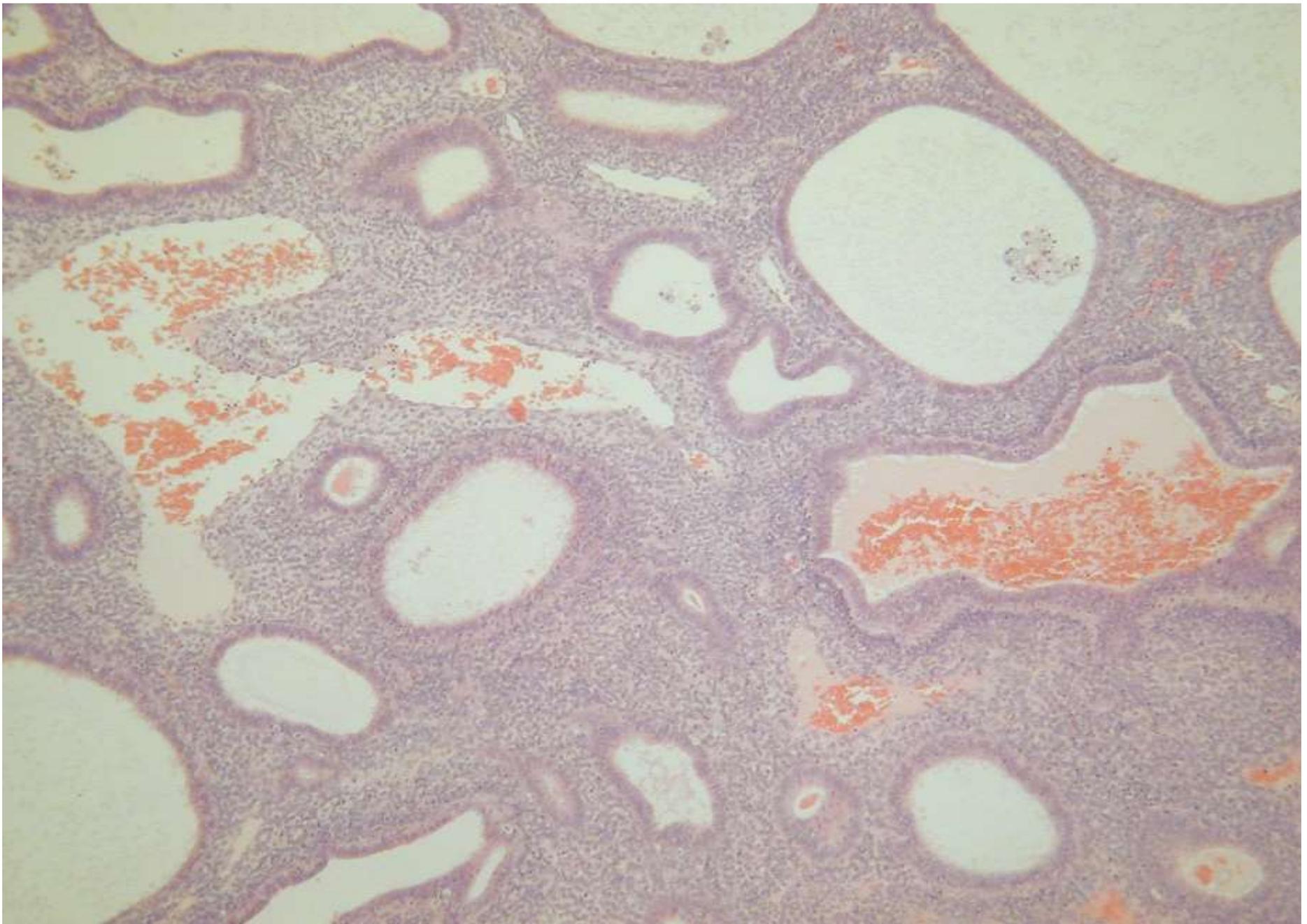
- All part of a spectrum
- Probably no (at most minimal) risk of progression
- Don't worry too much about distinction- not clinically important (don't let clinicians tell you it is)
- Tend to call disordered proliferative in perimenopausal years; tend to call hyperplasia without atypia in younger or older

DISORDERED PROLIFERATIVE ENDOMETRIUM (anovulatory)

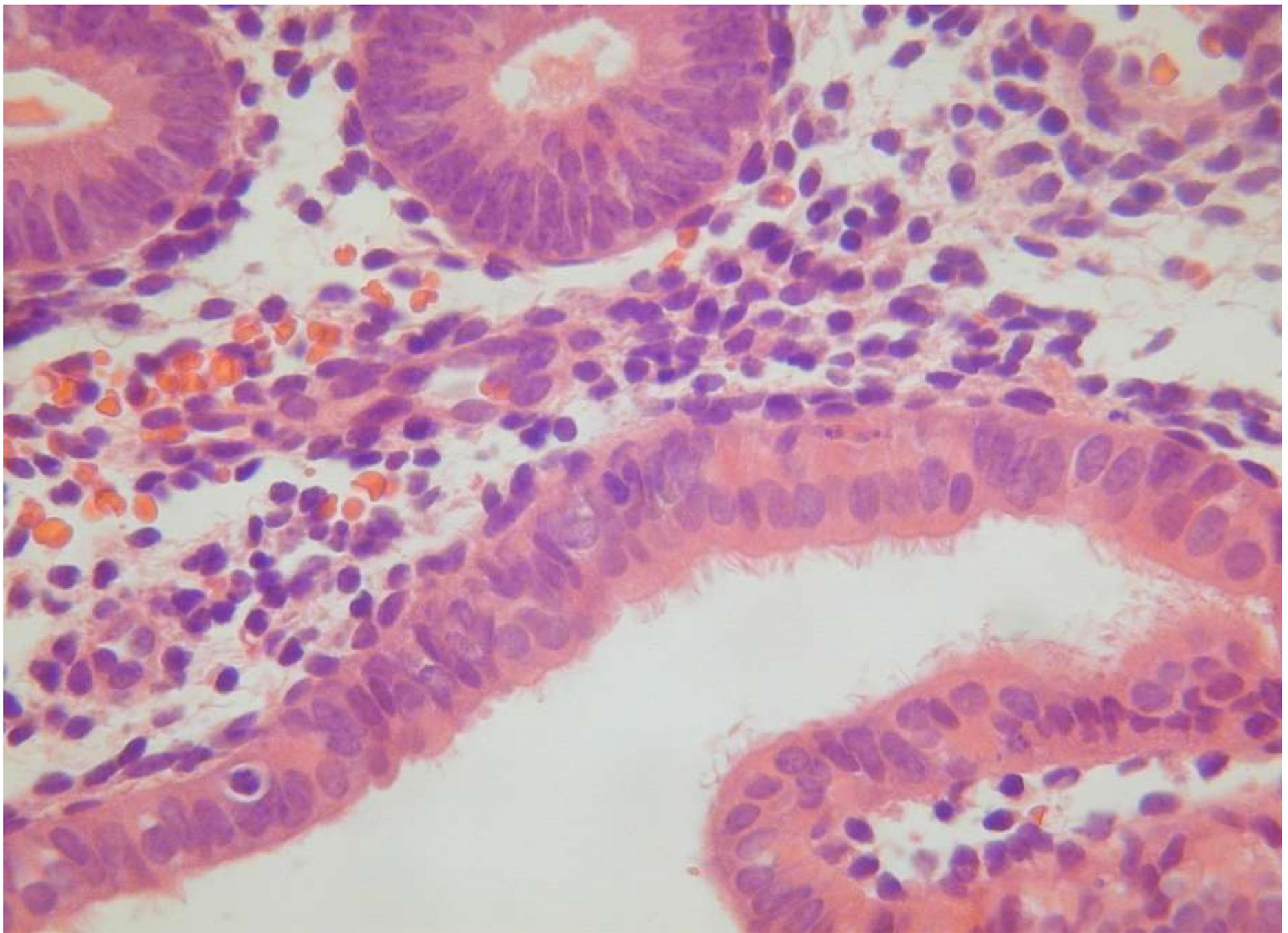
- common, especially in perimenopausal years
- response to increased oestrogenic drive without opposition of progestogen, usually secondary to anovulatory cycles
- merges with simple hyperplasia (part of same spectrum) (tend to diagnose disordered proliferative endometrium in perimenopausal years)
- occasional dilated glands with proliferative activity, stromal breakdown, metaplasias (especially ciliated)



Disordered proliferative endometrium



HYPERPLASIA WITHOUT ATYPIA- SH



PROGESTIN TREATMENT OF ATYPICAL HYPERPLASIA OR ENDOMETRIOID CARCINOMA

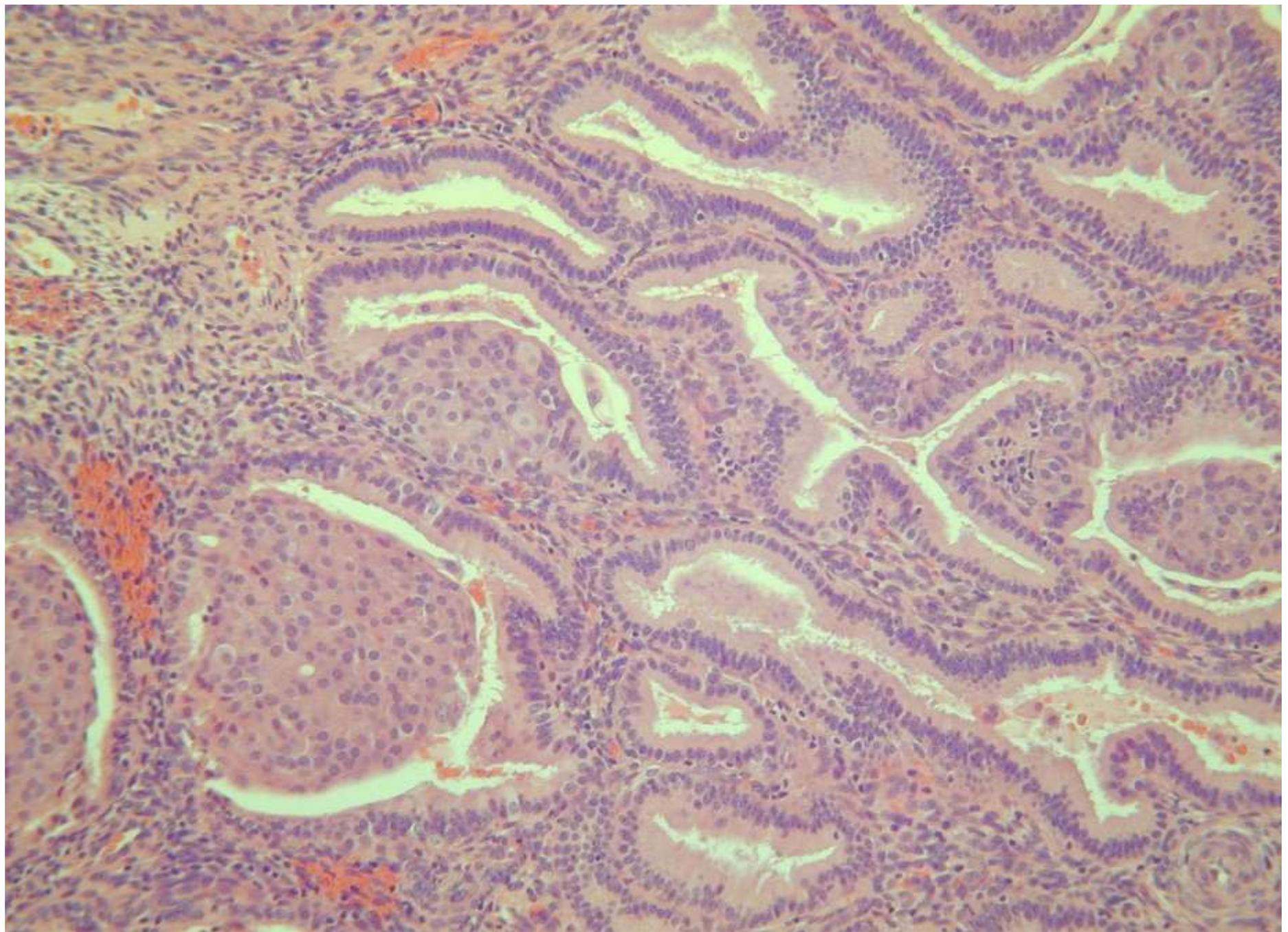
- occasionally used in management of low grade endometrioid adenocarcinoma or atypical hyperplasia
- IN GENERAL, DISTINCTION BETWEEN ATYPICAL HYPERPLASIA AND GRADE 2 ENDOMETRIOID CA NOT THAT IMPORTANT
- usually when fertility preservation is an issue or poor operative risk
- oral progestogens or Mirena IUD or both
- perform MRI to try to exclude myoinvasive disease
- reasonable response rate but risk of recurrence
- need regular endometrial biopsies
- may need to stay on progestogens for some time before reverting to normal

ALTERATIONS INDUCED BY PROGESTOGENS

- decreased gland to stroma ratio
- decreased cytologic atypia
- decreased mitotic activity
- epithelial metaplasias/ cytoplasmic changes
- stromal decidualisation/pseudo-decidualisation
- ? increased papillary and cribriform architecture

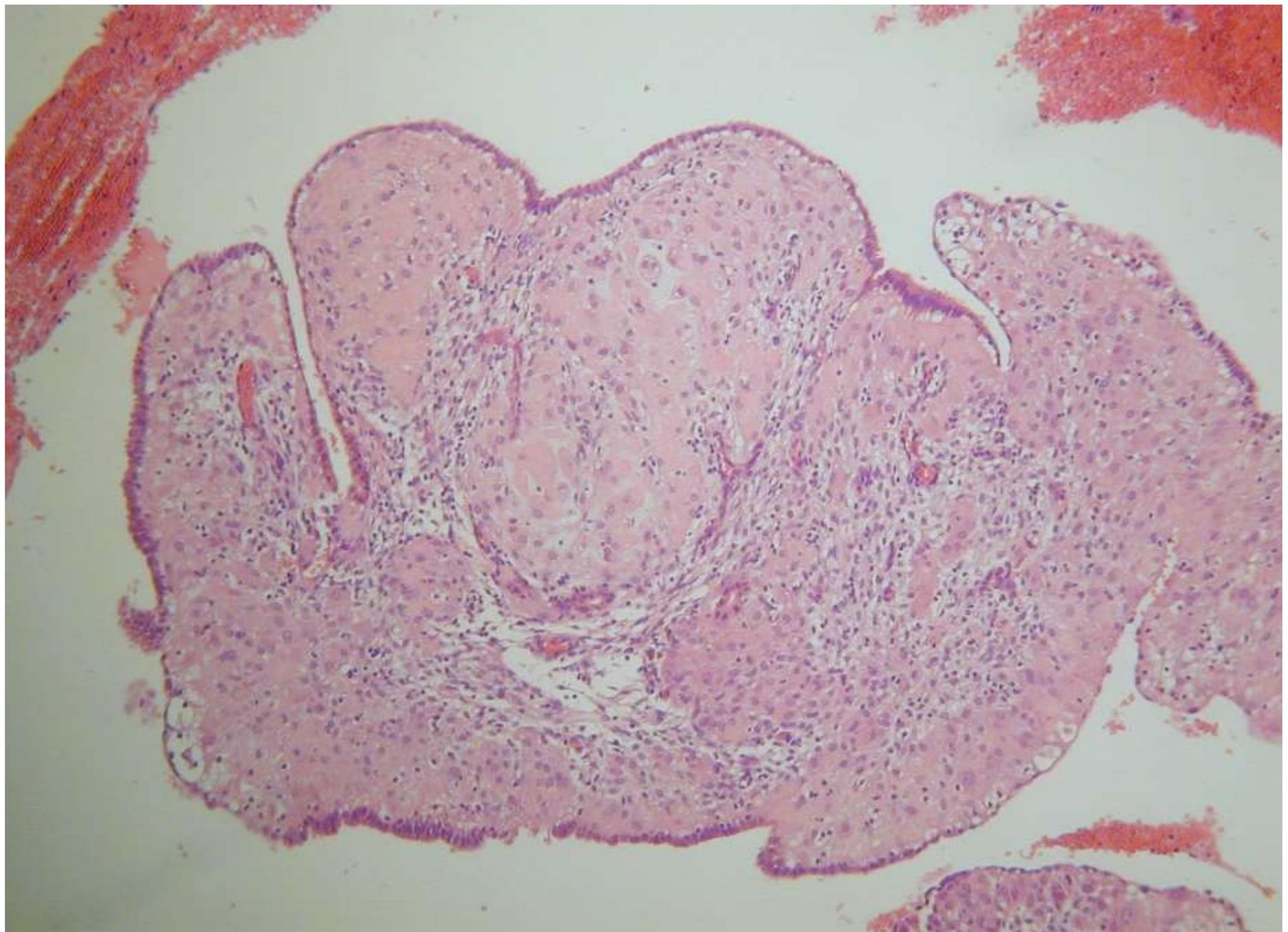
CASE

- mixture of atypical hyperplasia and grade 1 endometrioid adenocarcinoma
- treated with progestogens for 3 months
- further biopsy



CASE

- treated with progestogens for further 6 months
- further biopsy



INTERPRETATION DIFFICULT

- ? persistent hyperplasia, ? responding hyperplasia
- must report in knowledge of prior biopsy
- useful to look at prior biopsy when reporting
- difficulties if no prior biopsy or not available
- ? should take off progestogens before biopsy (in practice doesn't happen)
- **SOME GUIDELINES- 2 NEGATIVE BIOPSIES BEFORE TAKING OFF PROGESTOGENS**

USEFUL WAY TO THINK ABOUT

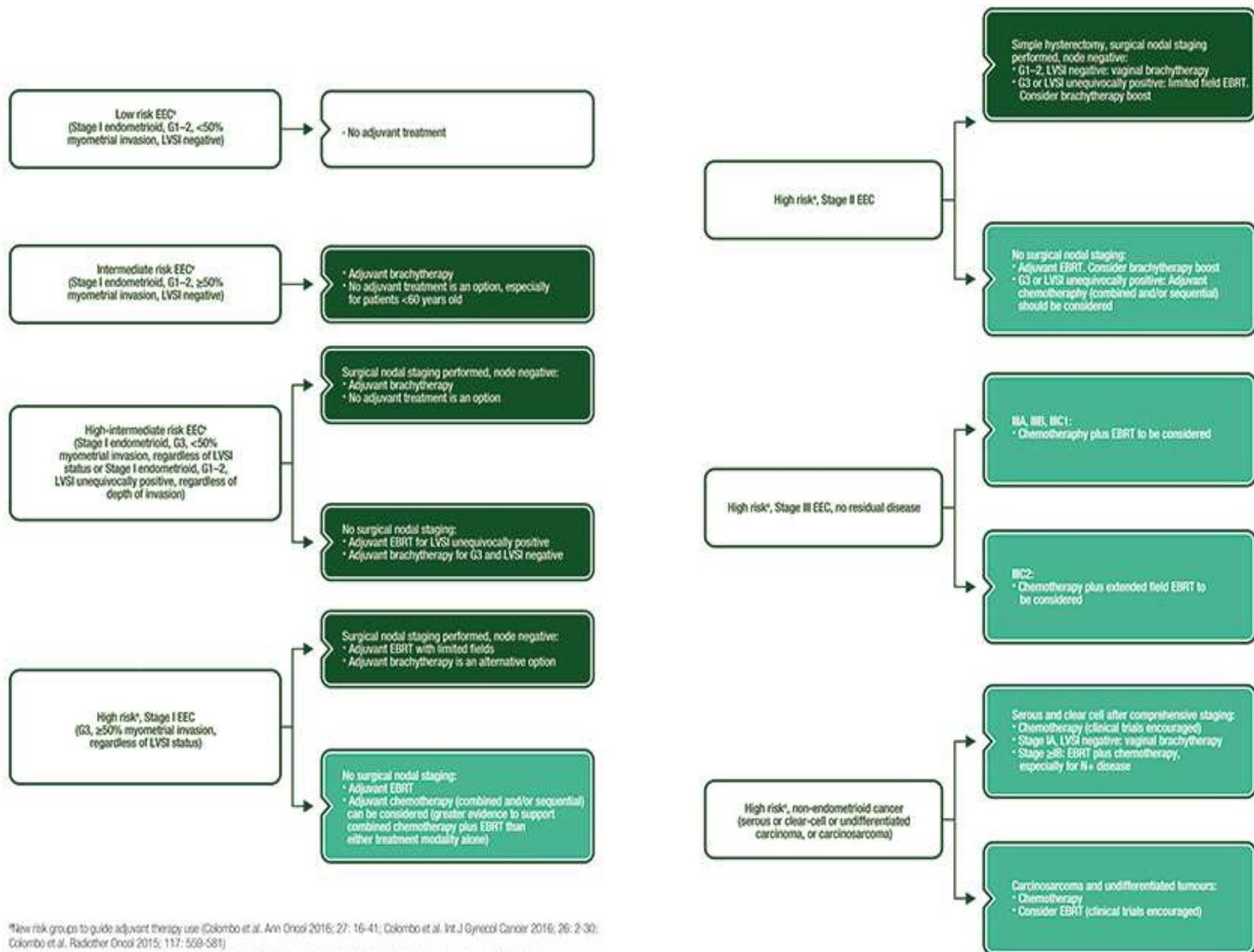
- PROGRESSION
- PERSISTENCE
- PARTIAL RESPONSE
- TOTAL RESPONSE

ENDOMETRIAL CARCINOMAS

- What is important is what is needed for STAGING, PROGNOSIS, PATIENT MANAGEMENT
- ICCR definition:-

REQUIRED ELEMENTS- those which are unanimously agreed by the panel to be essential for the histological diagnosis, clinical management, staging or prognosis

RECOMMENDED ELEMENTS- non-mandatory, which are clinically important, recommended as good practice and should ideally be included in the dataset but which are not yet validated or regularly used in patient management



*New risk groups to guide adjuvant therapy use (Colombo et al. Ann Oncol 2016; 27: 16-41; Colombo et al. Int J Gynecol Cancer 2016; 26: 2-30; Colombo et al. Radiother Oncol 2015; 117: 559-581)

EBRT, external beam radiotherapy; EEC, endometrioid endometrial cancer; G, grade; LVSI, lymphovascular space invasion; N, node

CRITICAL REGARDING REPORTING OF ENDOMETRIAL CARCINOMA IN HYSTERECTOMY SPECIMEN- ESMO GUIDELINES

- FIGO Grade (1 or 2 versus 3)
- Myometrial invasion (<50%; ≥50%)
- Lymphovascular space invasion (LVSI)
- Tumour stage

GENERAL POINTS

- Uterine weight irrelevant (weights of organs in general)
- Measuring organs in 3 dimensions irrelevant
- No point in looking hard for LVSI if distant metastasis present

Hysterectomy for Endometrial Carcinoma, Gross Examination



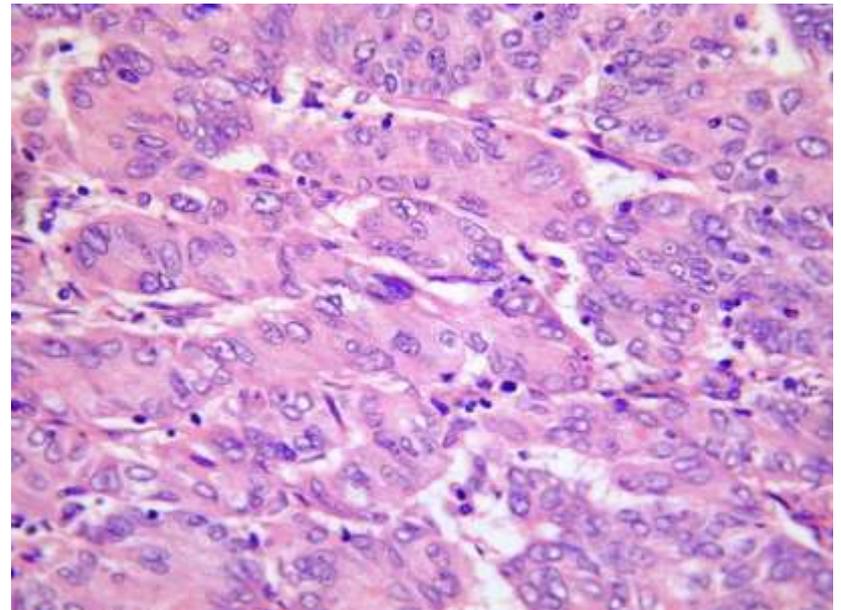
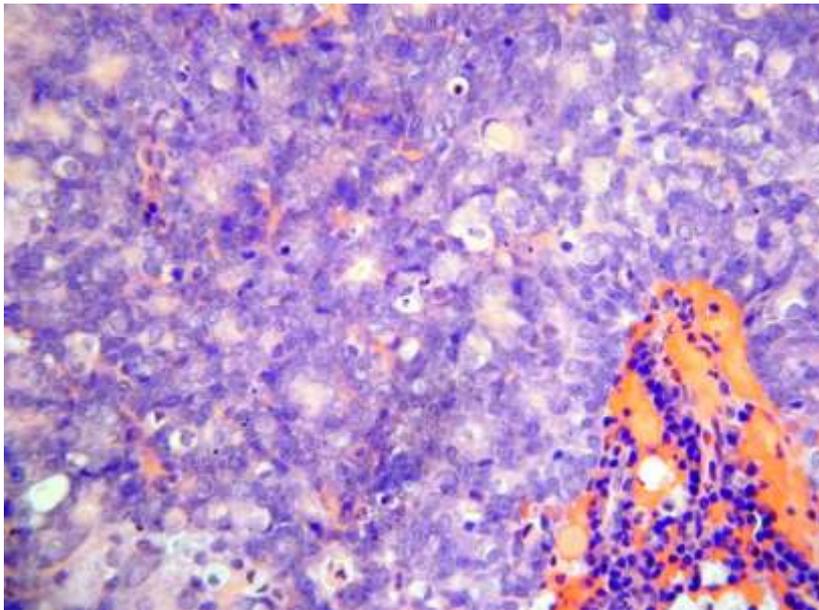
- Uterine weight will determine the CPT code to be used

CPT code	Surgery	Medicare Physician Fee Schedule, Houston, TX region
58570	Tlh uterus 250 g or less	\$804.61
58571	Tlh w/t/o 250 g or less	\$928.62
58572	Tlh uterus over 250 g	\$1,054.19
58573	Tlh w/t/o uterus over 250 g	\$1,259.08

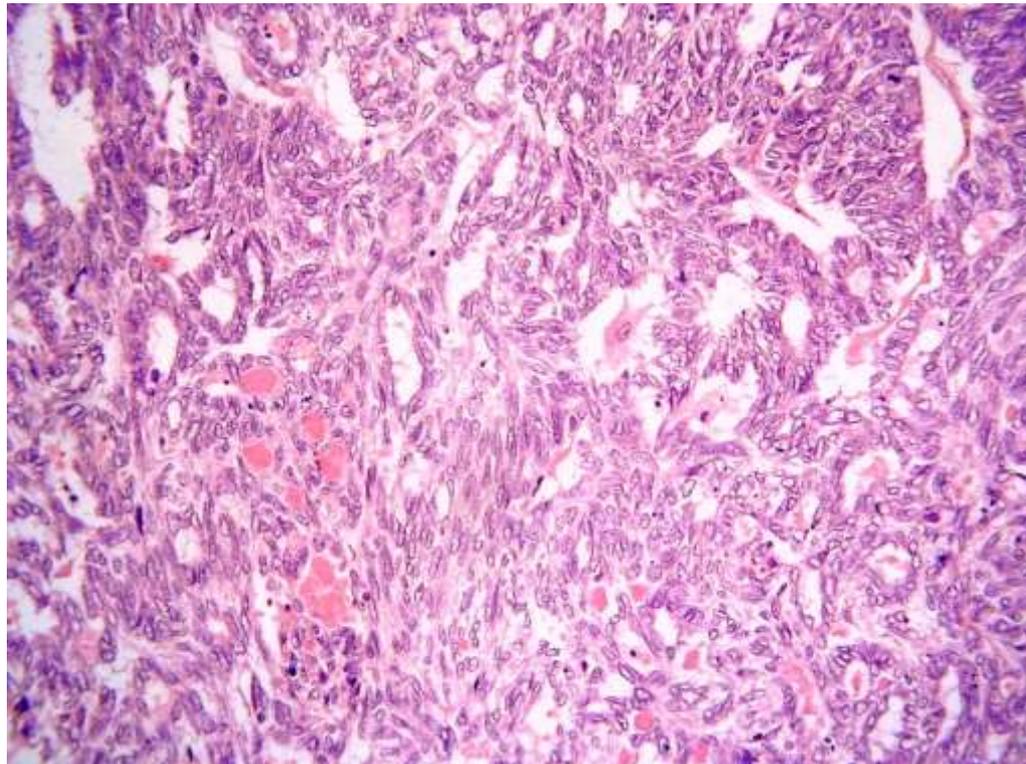
FIGO GRADING OF ENDOMETRIAL CARCINOMAS

- Basically “made-up” with little evidence
- Only for endometrioid (and mucinous) carcinomas
- Distinction between grade 1 and 2- clinically unimportant SO DON'T STRESS (ISGyP 2018 consensus recommendations- low grade versus high grade; BINARY FIGO) (grade 1 versus 2- some studies small but significant differences in outcome but dependent on other factors)
- Don't stress percentage solid versus glandular; don't go onto high power and evaluate every endometrioid adenocarcinoma for marked nuclear atypia

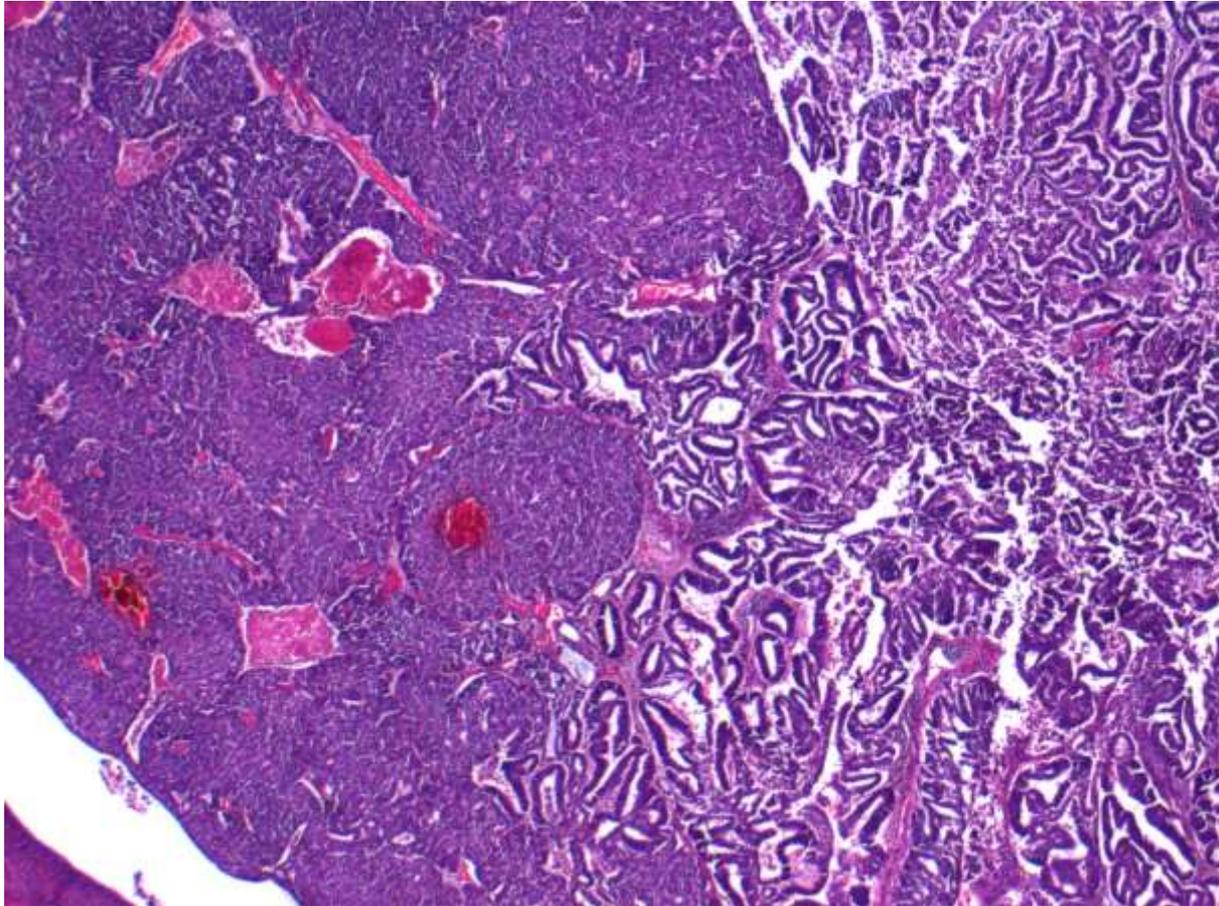
PROBLEM- WHAT IS SOLID? WHAT IS CLOSELY PACKED MICROGLANDULAR?



PROBLEM- WHAT IS SOLID
GLANDULAR? WHAT IS SQUAMOUS?



INTRATUMORAL HETEROGENEITY- ?
Give different grades; probably not at present
present



GRADING OF ENDOMETRIOID CARCINOMAS

- Don't give a default grade of grade 2
- Most endometrioid adenocarcinomas are grade 1
- Rarely upgrade an endometrioid adenocarcinoma on basis of nuclear atypia (no need to scrutinise every cell on high power) (NEED SEVERE NUCLEAR ATYPIA AT LOW POWER IN AT LEAST 50% OF CELLS; THIS IS RARE AND MOST WILL BE GLANDULAR VARIANTS OF SEROUS)

TYPING OF HIGH GRADE ENDOMETRIAL CARCINOMAS

- Marked interobserver variability in distinguishing between different types of high-grade endometrial carcinoma (grade 3 endometrioid, serous, clear cell, carcinosarcoma, undifferentiated)
- At present, management is similar, although MAY CHANGE IN FUTURE
- Surgical treatment more dependent on tumour grade than type (some differences between grade 3 endometrioid and others but not consistent)
- Adjuvant treatment more dependent on tumour grade than type (some differences between various high grade carcinomas but not consistent)

INTEROBSERVER VARIABILITY IN HIGH GRADE ENDOMETRIAL CARCINOMAS

- grade 3 endometrioid, serous, clear cell, carcinosarcoma, undifferentiated/ dedifferentiated, mixed
- AJSP 2013;37;874-881- Gilks, Oliva, Soslow
- 56 cases diagnosed as “high grade” endometrial carcinoma
- 62% - agreement between all 3
- 36% - major disagreement (subtype or even whether high grade carcinoma was present)
- no consistent pattern between observers
- major problems- serous v clear cell; serous v grade 3 endometrioid; serous versus undifferentiated
- need for molecular tools and development of biomarkers
- MUCH MORE PROBLEMATIC THAN TYPING OF OVARIAN CARCINOMAS

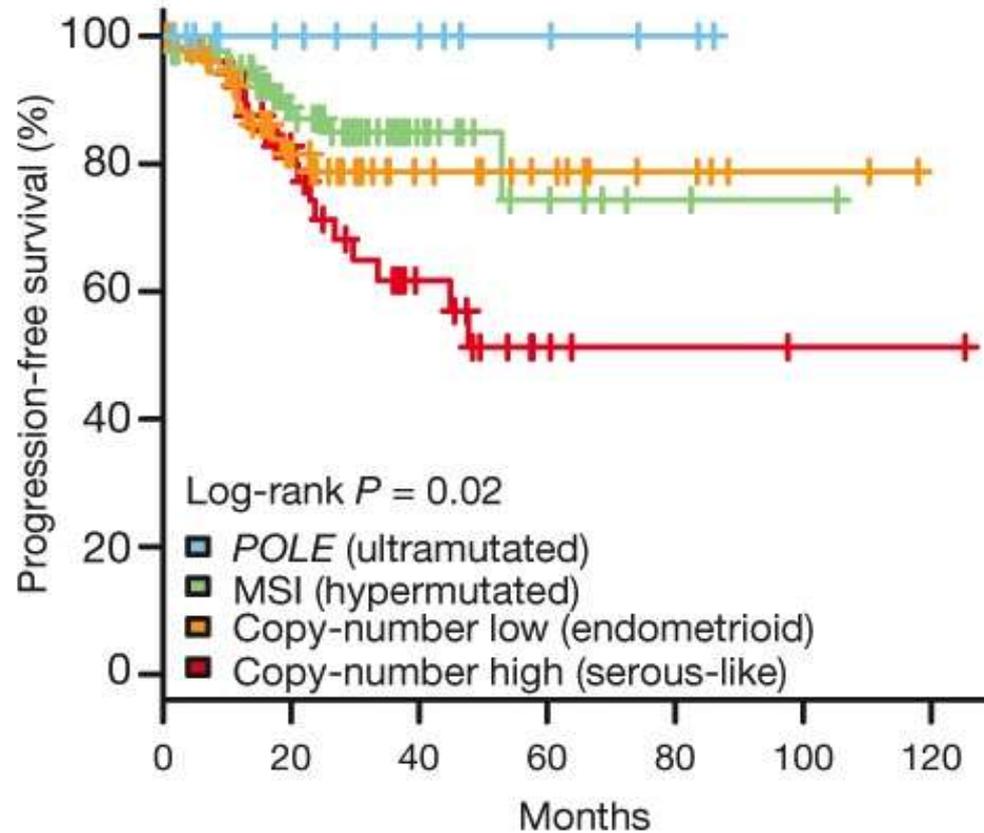
WHY IS IT SO DIFFICULT TO TYPE ENDOMETRIAL CARCINOMAS?

- mixed tumours (possibly slightly more common than in ovary but probably being over-diagnosed)
- morphologically ambiguous tumours
- intratumoral heterogeneity
- **no good marker (WT1 in ovary)**

TCGA Molecular Classification of Endometrial Cancers

- **COPY NUMBER LOW/ NO SPECIFIC MOLECULAR TYPE** (INTERMEDIATE PROGNOSIS) (39%)
- **MICROSATELLITE INSTABILITY HYPERMUTATED** (INTERMEDIATE PROGNOSIS) (28%) (OFTEN LOOK HIGH GRADE/ AMBIGUOUS/ INTRATUMORAL HETEROGENEITY)
- **COPY NUMBER HIGH (*TP53* mutations)** (mostly, but not all, serous) (WORST PROGNOSIS) (26%)
- **POLE ULTRAMUTATED** (BEST PROGNOSIS) (7%) (OFTEN LOOK HIGH GRADE/ AMBIGUOUS/ INTRATUMORAL HETEROGENEITY)

Mutation Spectra Across Endometrial Carcinomas



TYPING OF ENDOMETRIAL CANCERS

- **TCGA classification of endometrial cancers is of prognostic significance**
- Tumour histotyping is not (because of poor interobserver reproducibility)
- Morphology is not reliable in separating into TCGA categories

STRATEGIES FOR TYPING (TCGA)

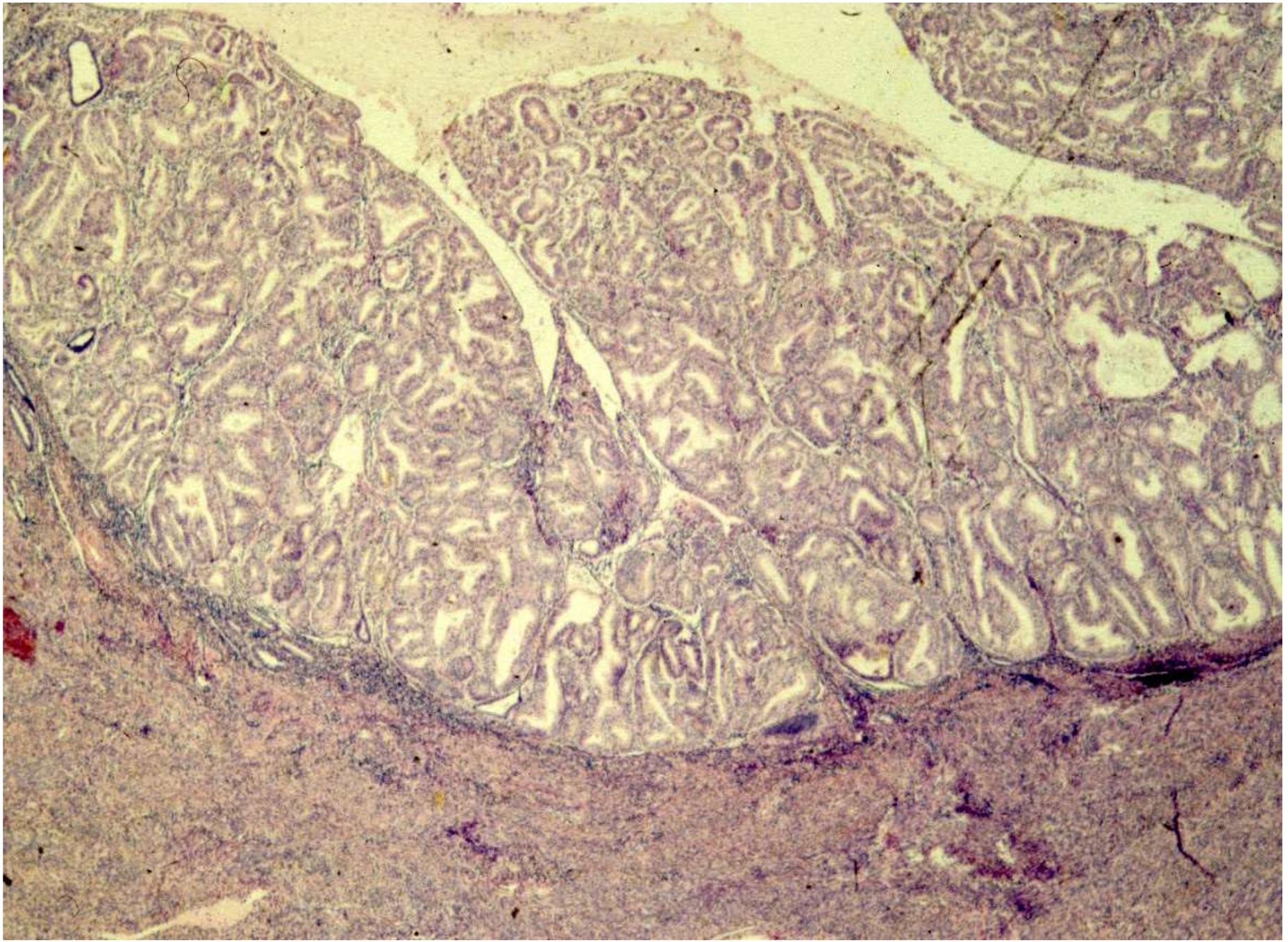
- POLE mutation analysis- identifies POLE ULTRAMUTATED (NEED TO DO FIRST)
- MMR staining (PMS2 and MSH6)- identifies MICROSATELLITE INSTABILITY HYPERMUTATED
- p53 staining- mutation-type staining identifies COPY NUMBER HIGH
- Left with COPY NUMBER LOW
- Important for prognosis, management/ targeted therapies
- ProMisE (Proactive Molecular Risk Classifier for Endometrial Cancer) classifier

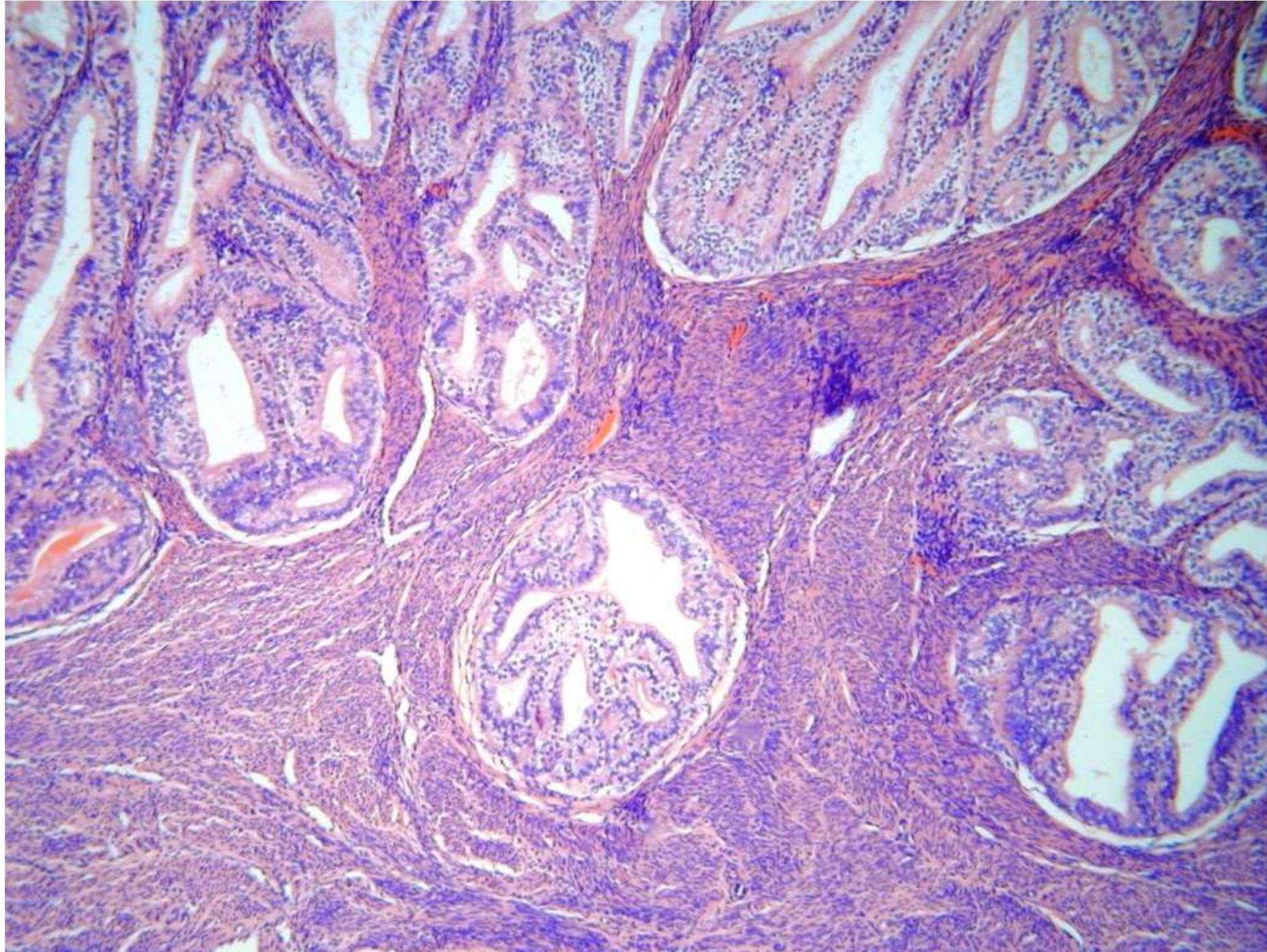
IMMUNOHISTOCHEMISTRY

- Don't need in every endometrial carcinoma
- p16- probably only diffuse block-type in two-thirds of serous carcinomas; most serous carcinomas are ER positive; p53 can be mutation-type in all high-grade (and even some grade 1-2)
- Don't need to perform ER histoscore (hormone receptors sometimes needed in recurrent tumours)
- ANYTHING CAN HAPPEN WITH ANY MARKER

MYOMETRIAL INVASION

- ONLY IMPORTANT FACTOR IS INNER/ OUTER HALF (exactly 50% is IB)
- Absolute depth of myometrial invasion, percentage of myometrial invasion, distance to serosa not important in management
- DON'T WORRY ABOUT DISTINCTION BETWEEN NO MYOMETRIAL INVASION AND EARLY SUPERFICIAL MYOMETRIAL INVASION (both FIGO IA; significant interobserver variability; more likely to overdiagnose early invasion; no difference in management or outcome)



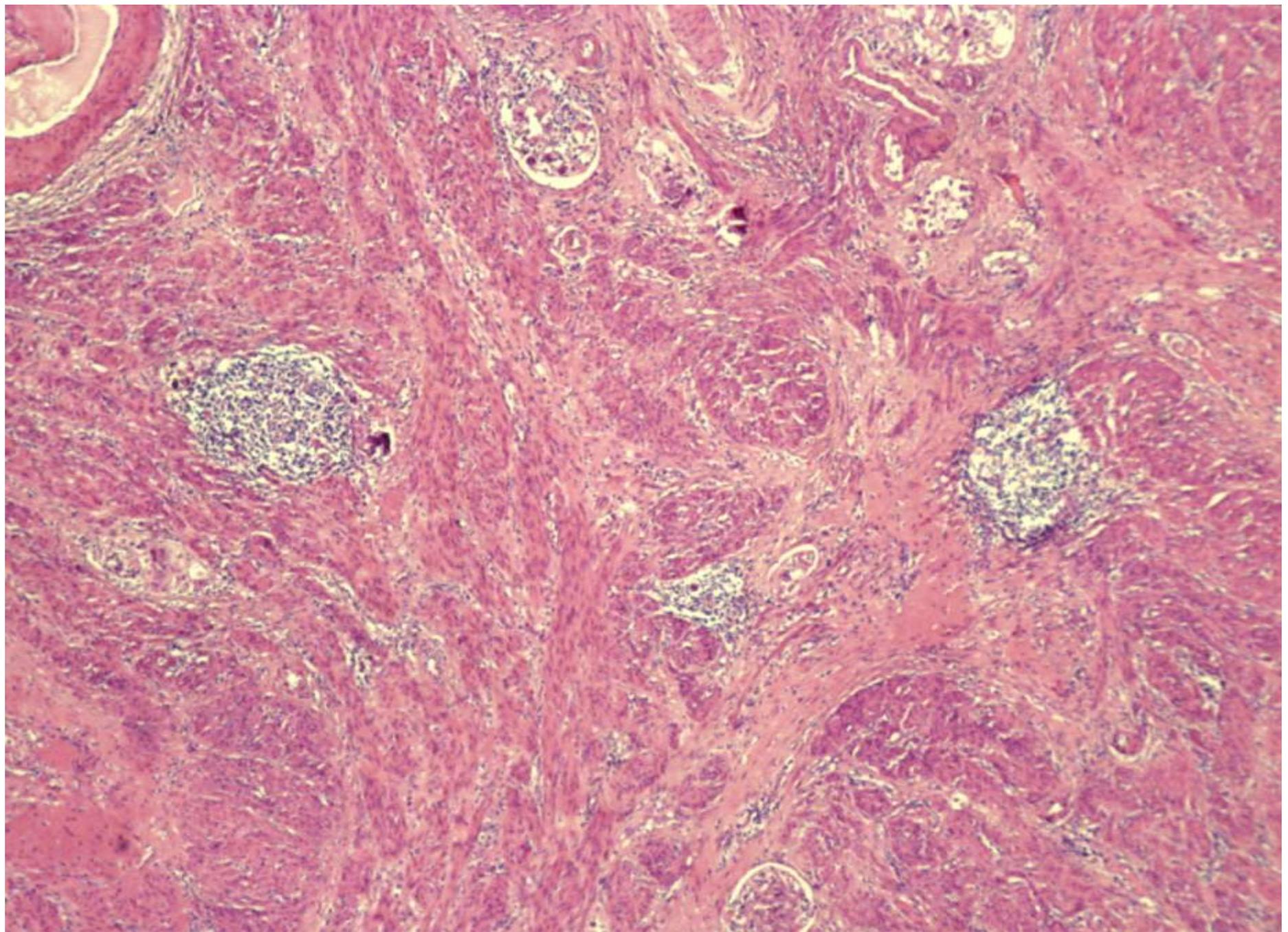


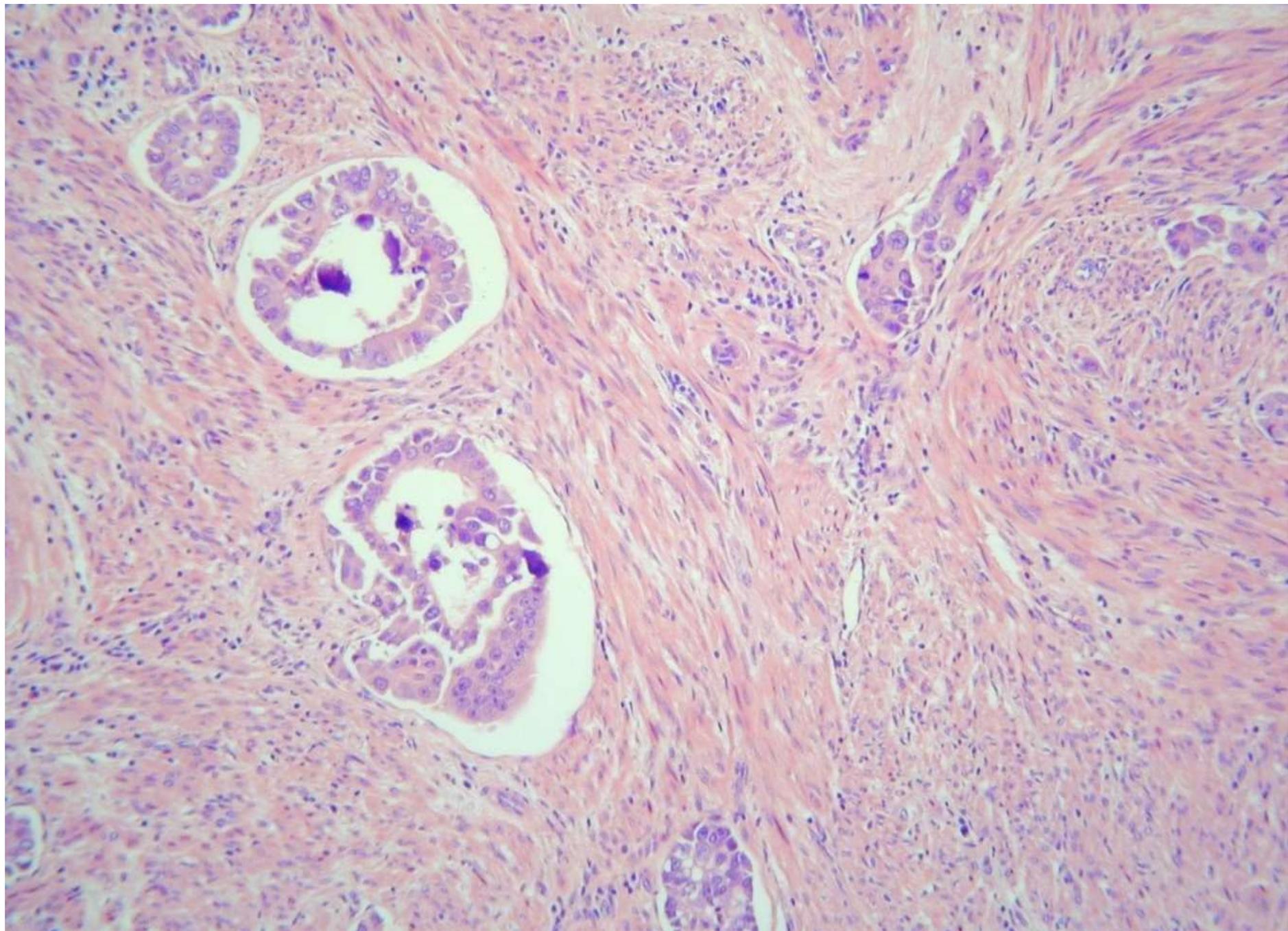
LYMPHOVASCULAR INVASION IN ENDOMETRIAL ADENOCARCINOMAS

- independent prognostic factor in stage I endometrioid adenocarcinomas (nodal metastasis and disease recurrence)
- more likely with deep myometrial invasion
- **NOW decisions regarding management taken on presence or absence (IMPORTANT TO DIAGNOSE ACCURATELY) BUT ONLY IN CERTAIN CIRCUMSTANCES**
- often see at advancing edge of tumour
- lymphoid aggregates may be a clue
- DO NOT UPSTAGE IN ABSENCE OF TUMOUR OUTSIDE VESSELS- BUT MENTION IN REPORT
- MELF may simulate vascular invasion (may also be associated)
- RECENT EVIDENCE THAT AMOUNT OF LVSI MAY BE PROGNOSTICALLY IMPORTANT (FOCAL VERSUS SUBSTANTIAL)

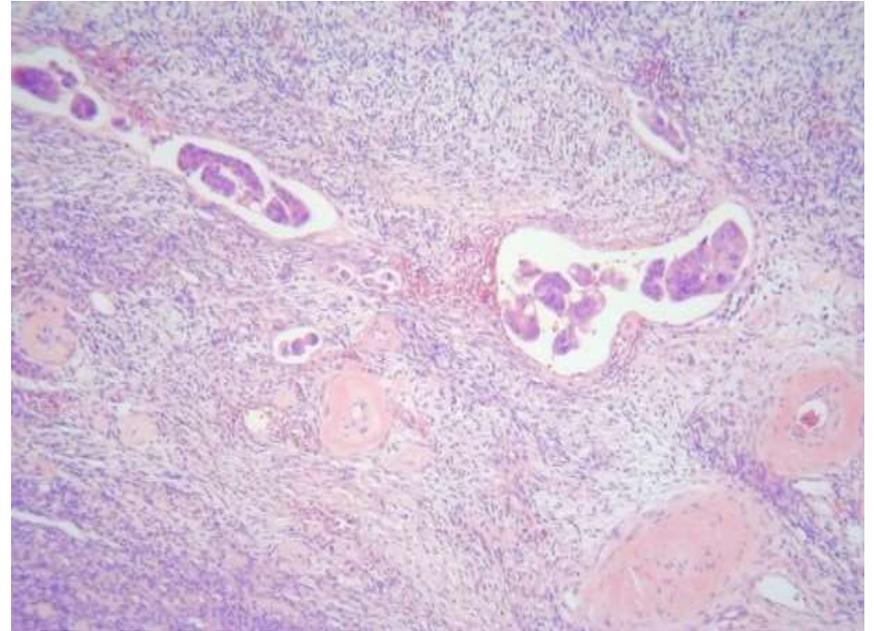
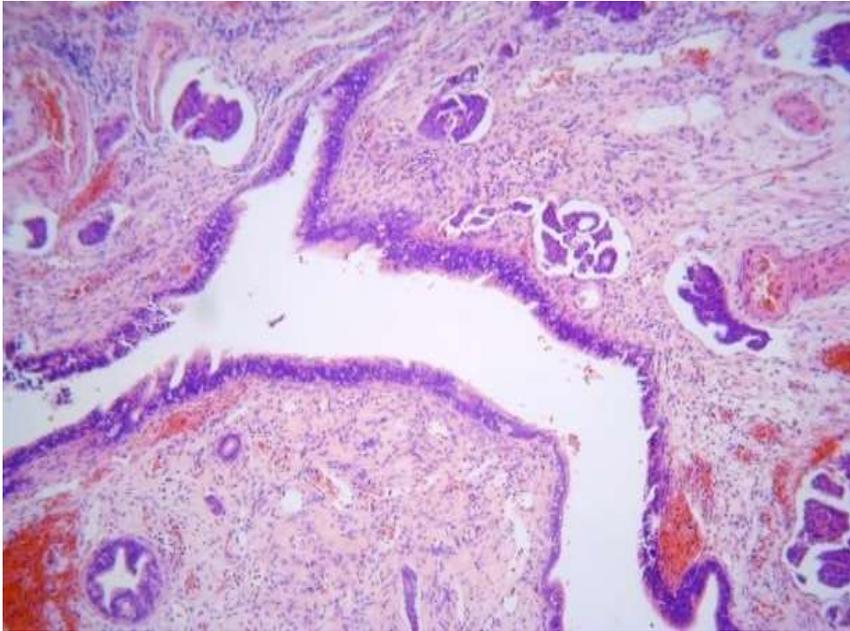
LYMPHOVASCULAR SPACE INVASION- MANAGEMENT

- Not important in grade 1 or 2, stage IA
- Not important in advanced stage
- Generally not important in grade 3
- IMPORTANT IN GRADE 1 or 2, stage IB
- **Clinicians think it is straightforward and reproducible**
- **Pathologists know it is difficult and poorly reproducible**





LVSI OUTSIDE ORGAN OF ORIGIN- DOESN'T UPSTAGE IN ABSENCE OF TISSUE INVOLVEMENT



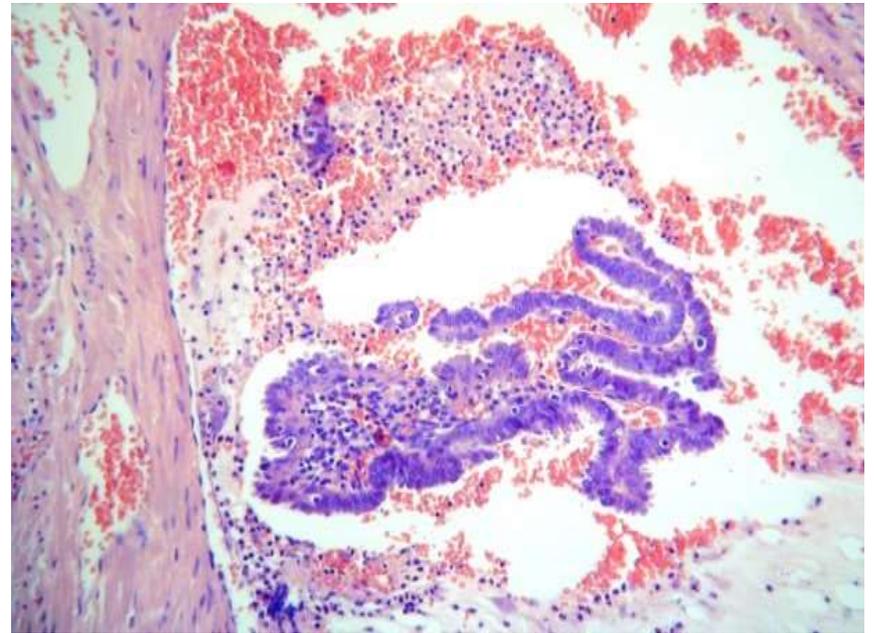
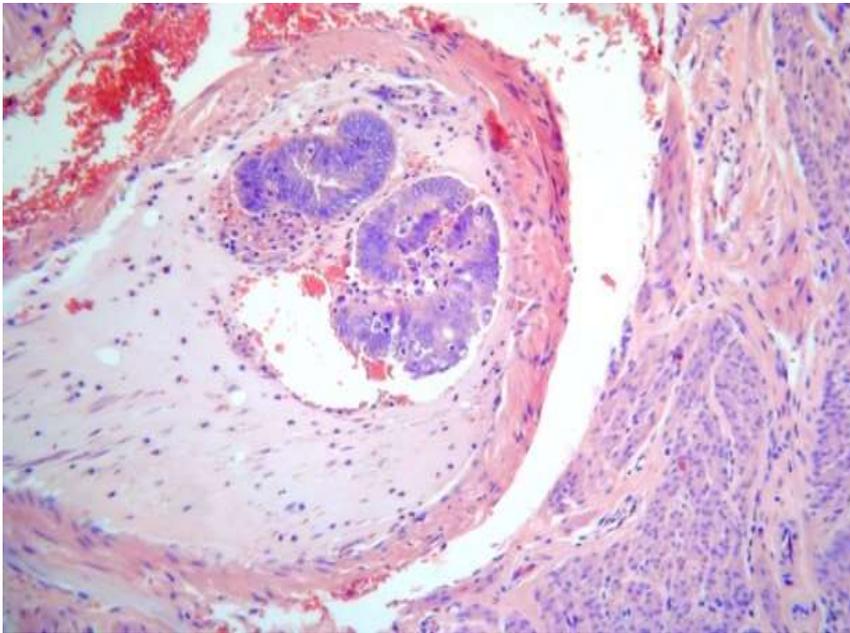
REASONS FOR POOR REPRODUCIBILITY IN ASSESSING LVSI

- Focal LVSI
- “Solid” extensive tumours
- Retraction artefact
- Smearing artefact (poor fixation/ autolysis)
- Surgical manipulation (vascular pseudoinvasion)
- Patterns of invasion mimicking LVSI (MELF)

VASCULAR PSEUDOINVASION

- common with laparoscopic hysterectomies and intrauterine balloon manipulators
- more common with polypoid tumours
- benign or malignant tissue displaced into vessels
- predominantly thick-walled vessels in outer half of myometrium
- often clue is that degree of vascular invasion inconsistent with low tumour grade and stage
- often crush artefact
- associated stroma with glands
- inflammatory debris in vessels
- PROBABLY NO PROGNOSTIC SIGNIFICANCE (BUT UNKNOWN)
- **MENTION ON REPORT BUT STATE THAT NOT TRUE LVSI**

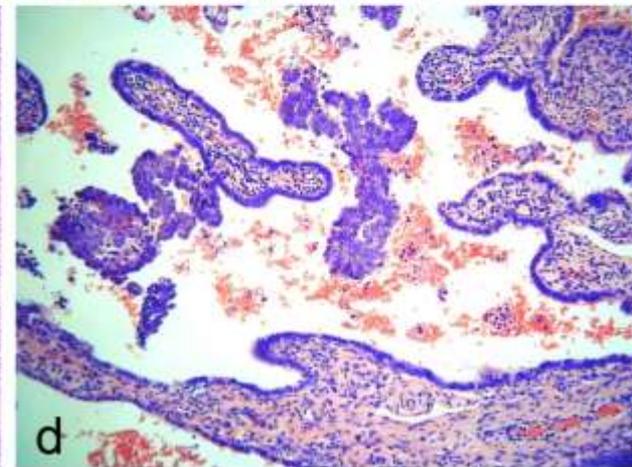
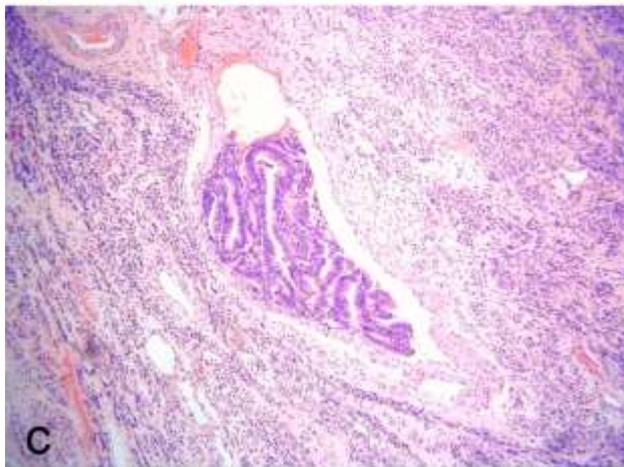
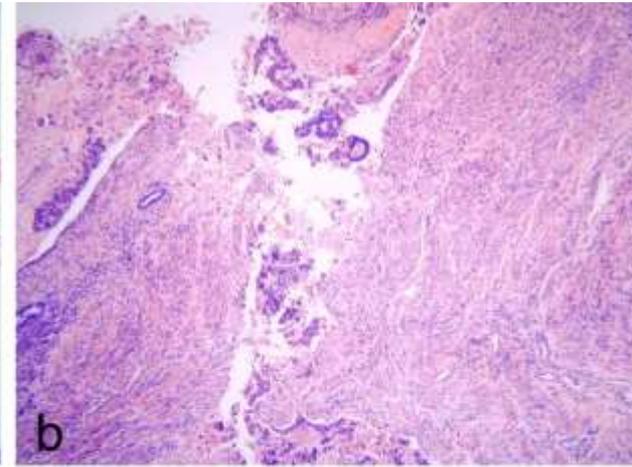
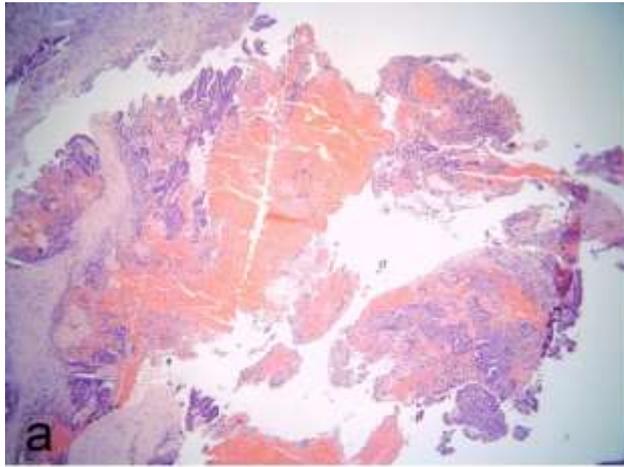
VASCULAR PSEUDOINVASION



OTHER FEATURES

- disruption of endometrial lining
- myometrial clefts
- floaters in tubal lumina and cervix
- serosal carry-over
- increased incidence of positive peritoneal washings (can be prevented by ligating tubes)

INTRAUTERINE BALLOON MANIPULATORS



EUROPEAN JOURNAL OF CANCER

2015; 51; 1742-1750

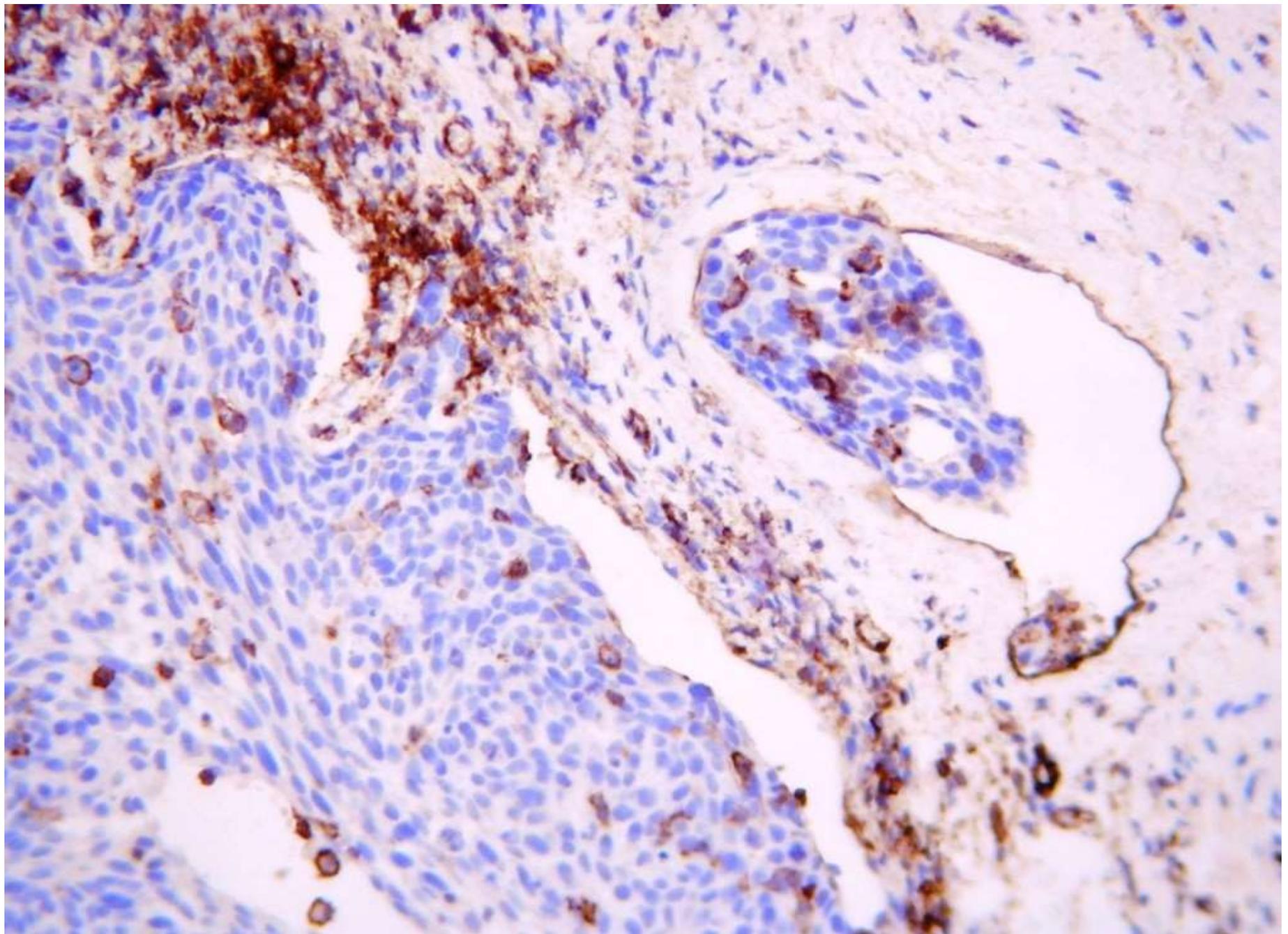
- Cases from PORTEC trials (pooled data from PORTEC 1 and 2)
- Large number (926) of stage I endometrial cancers
- **Multivariate analysis (age, depth of invasion, grade, treatment)-substantial LVSI was strongest independent prognostic factor for local pelvic recurrence, distant metastasis and overall survival**
- LVSI was not predictive of vaginal recurrence
- Conclusions- therapeutic decisions should be based on substantial LVSI (**3 OR MORE**) (as opposed to no or focal) (LVSI defined as presence of tumour cells in a vascular space **OUTSIDE** the immediate invasive tumour border)
- AGREEMENT BETWEEN ORIGINAL REPORTS AND CASE REVIEW WAS LOW (6.9% versus 13.9% for any LVSI)
- 4.8% SUBSTANTIAL LVSI

? USE OF VASCULAR MARKERS

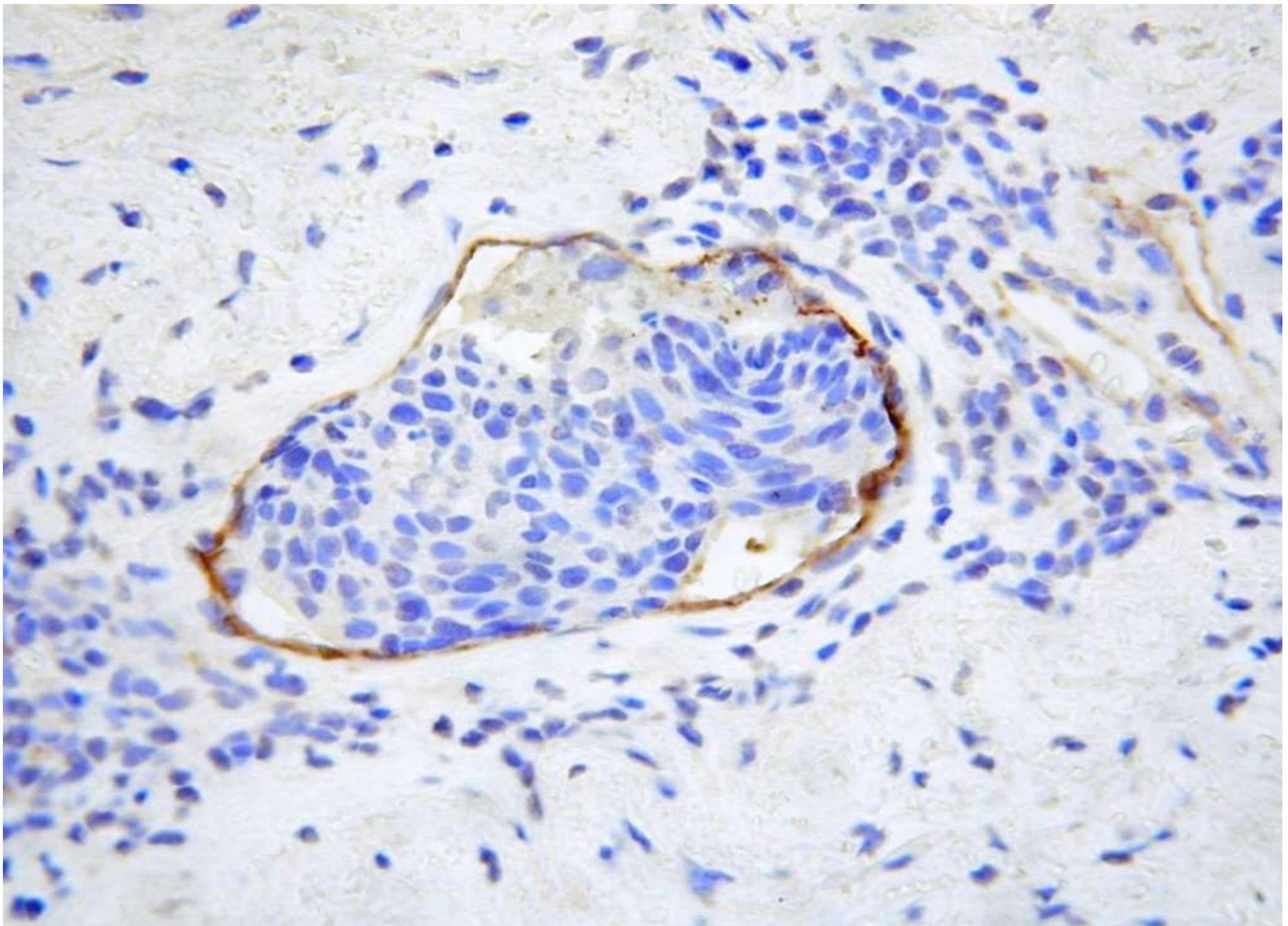
- Not routinely
- May be of use in equivocal cases
- CD34, CD31, D2-40, ERG

IS IT WORTH DISTINGUISHING BETWEEN LYMPHATIC AND BLOOD VESSEL INVASION?

- D2-40 (lymphatic vessels); CD31 and CD34 (all vessels)
- In endometrial cancer- blood vessel involvement shown to have worse prognosis than lymphatic involvement (more likely distant spread than nodal involvement) (Histopathology 2009;54;174-183)
BUT NOT IMPORTANT FOR TREATMENT SO DON'T NEED TO DO



CD34



D2-40

PARAMETERS FOR STAGING

- Cervical stromal involvement
- Serosal and extrauterine disease
- We don't do peritoneal washings any more

CERVICAL INVOLVEMENT IN ENDOMETRIAL ADENOCARCINOMA

- FIGO 2009- only one category of stage II disease defined by stromal involvement (still mention glandular involvement in report)
- multiple problems in assessment
- significant interobserver variability (AJSP 2011;35;289-294)
- important for adjuvant therapy (glandular- sometimes; **stromal-usually**)
- few guidelines regarding how to assess

PROBLEMS

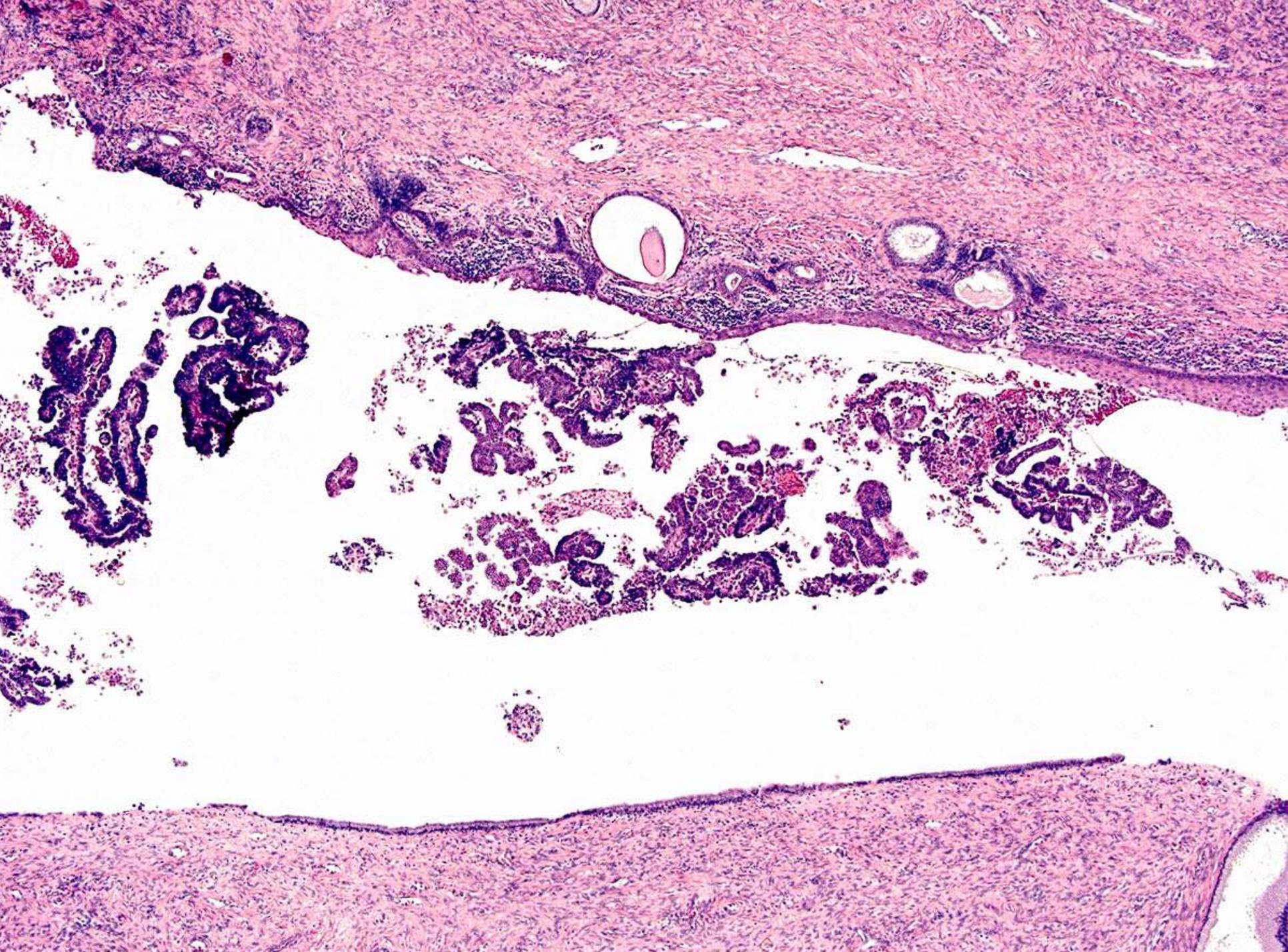
- where does endocervix start and isthmus/ LUS end (no anatomical landmarks)
- floaters versus true glandular involvement
- tumour superficially implanted in granulation tissue related to prior biopsy
- glandular versus stromal involvement
- subtle patterns of stromal involvement without a stromal response
- florid reactive changes in endocervix (TEM, reaction to recent curette)
- sampling issues (how many blocks of cervix)

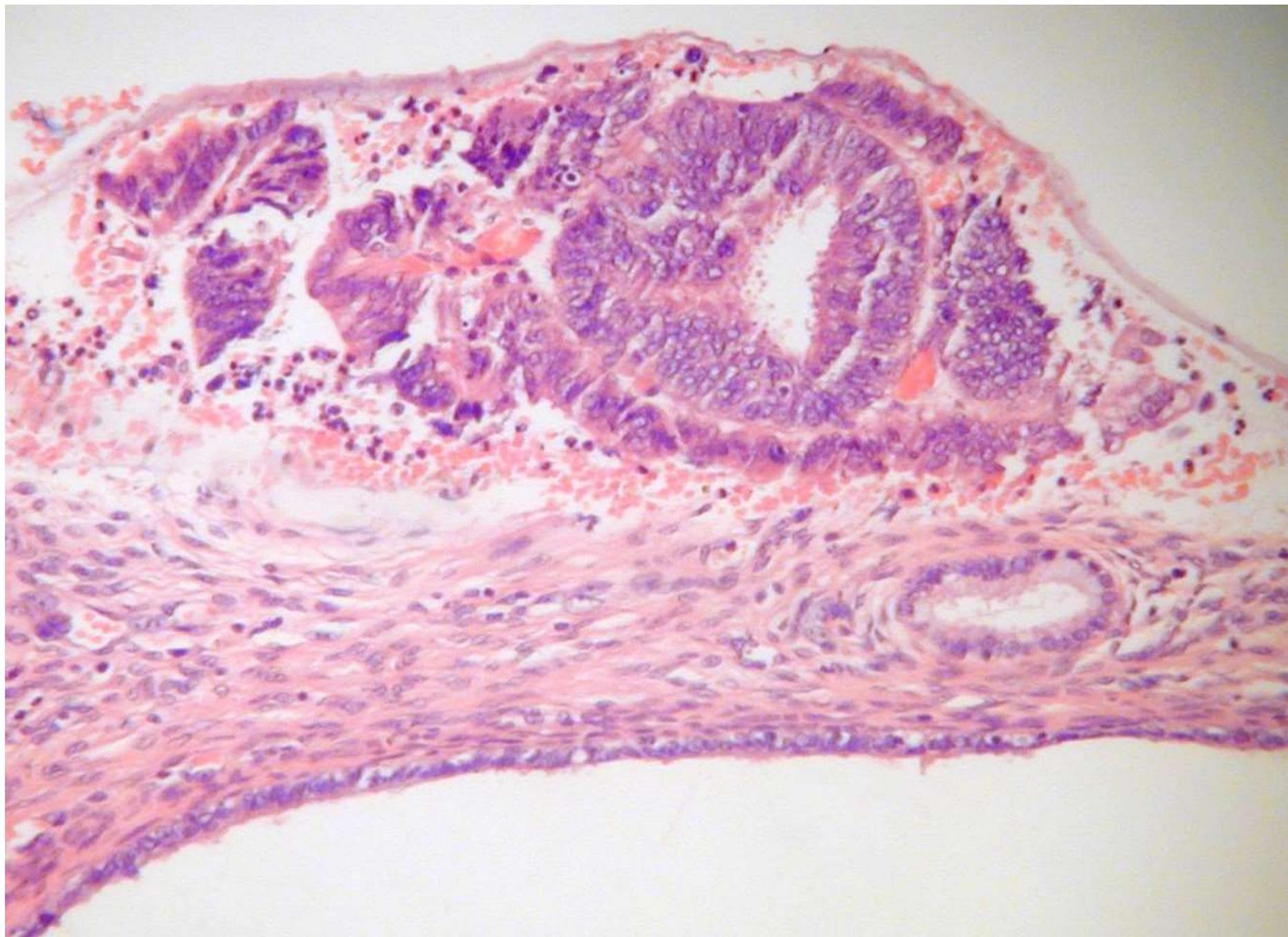
HOW MANY BLOCKS OF CERVIX NEEDED?

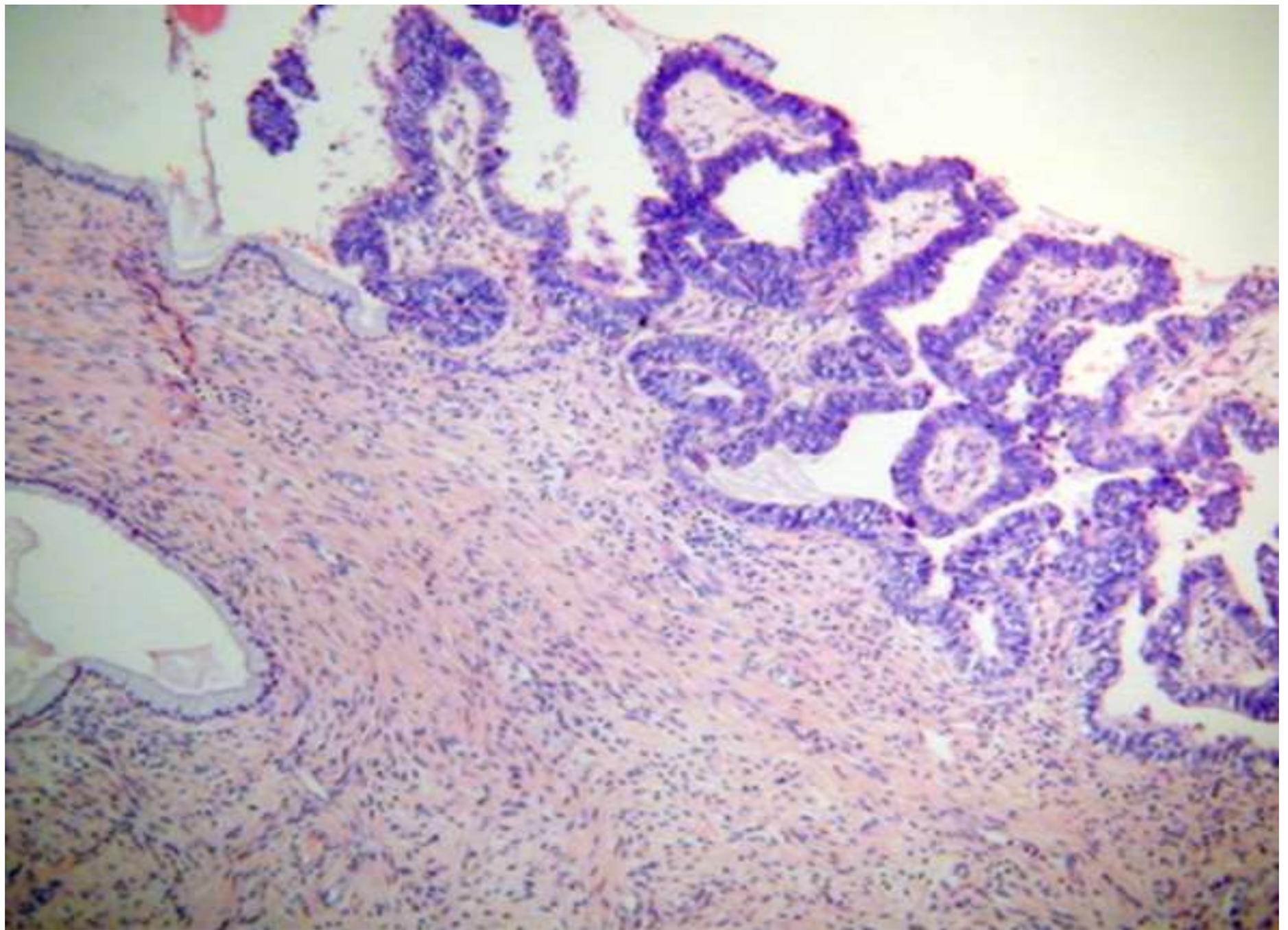
- I only take 2
- J Clin Pathol 2008;61:621-2:PMID 18006669.
Conclusion- **sampling of two blocks from the cervix appears sufficient for histological staging of endometrial cancer in hysterectomy specimens.**

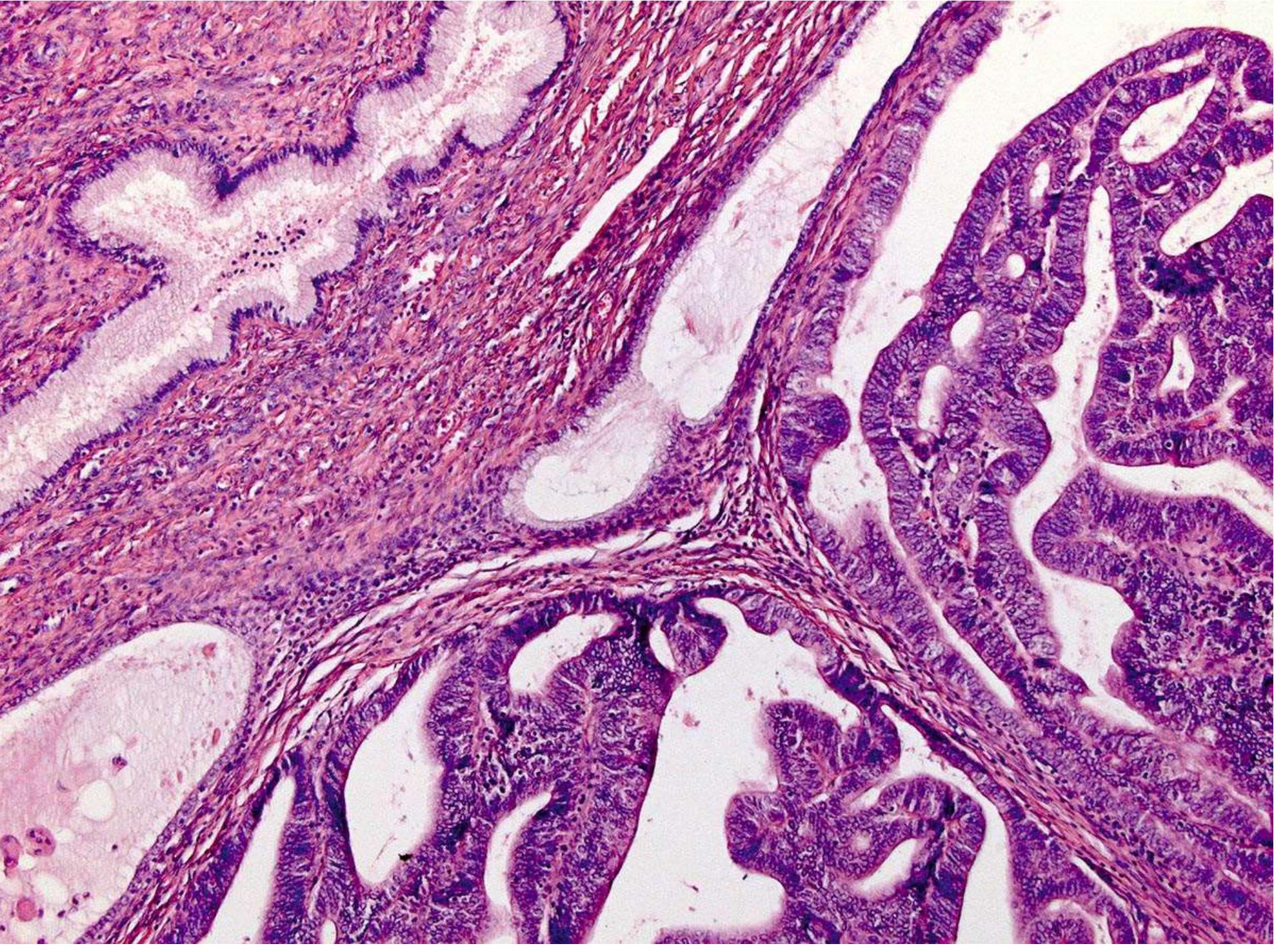
RECOMMENDATIONS

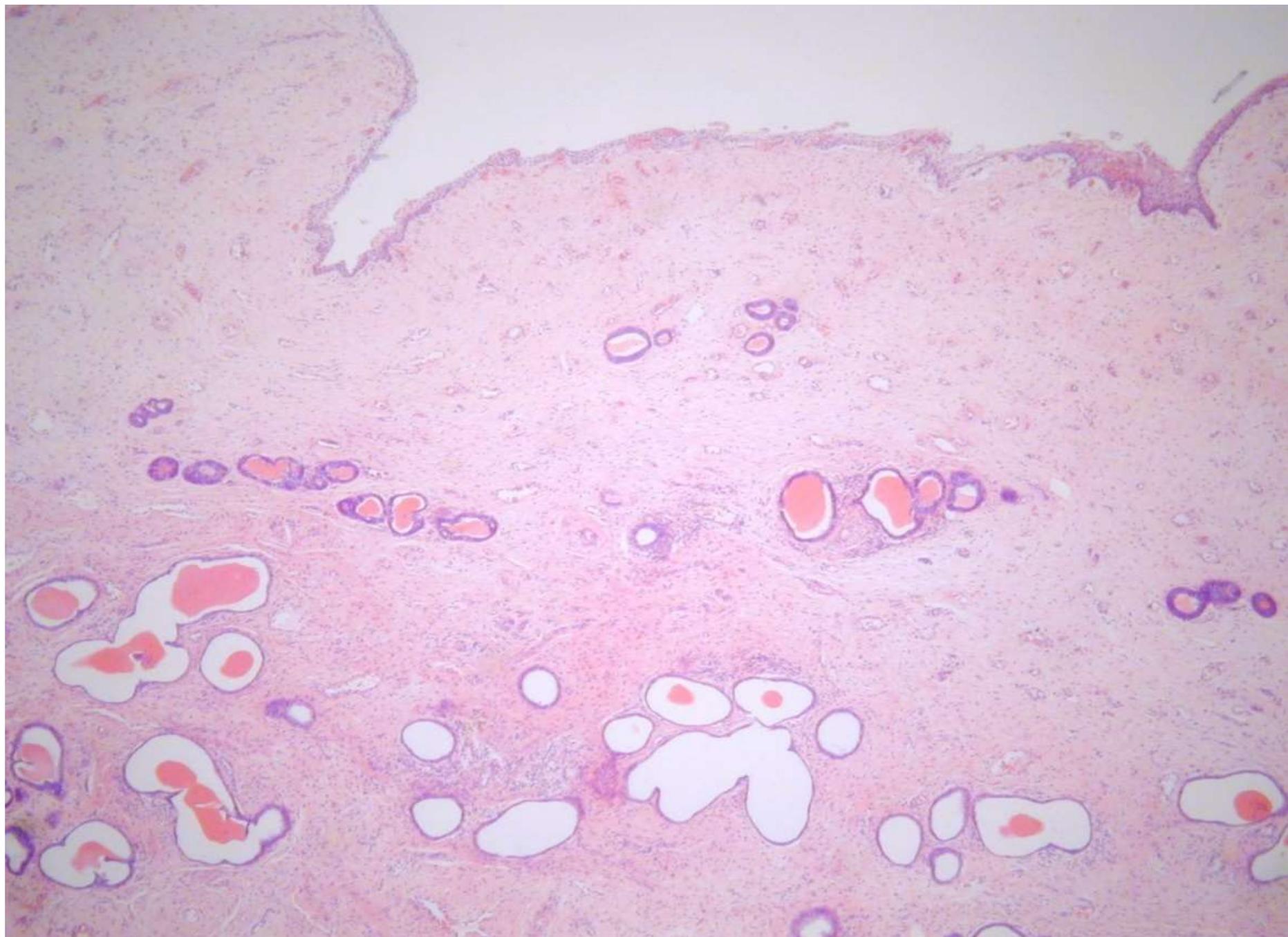
- Mention cervical surface/gland involvement in pathology report but not part of staging
- Disregard free-lying tumour in canal or tumour in granulation tissue
- Use uppermost mucinous gland as boundary with isthmus/ lower uterine segment
- Tumour must surround mucinous glands

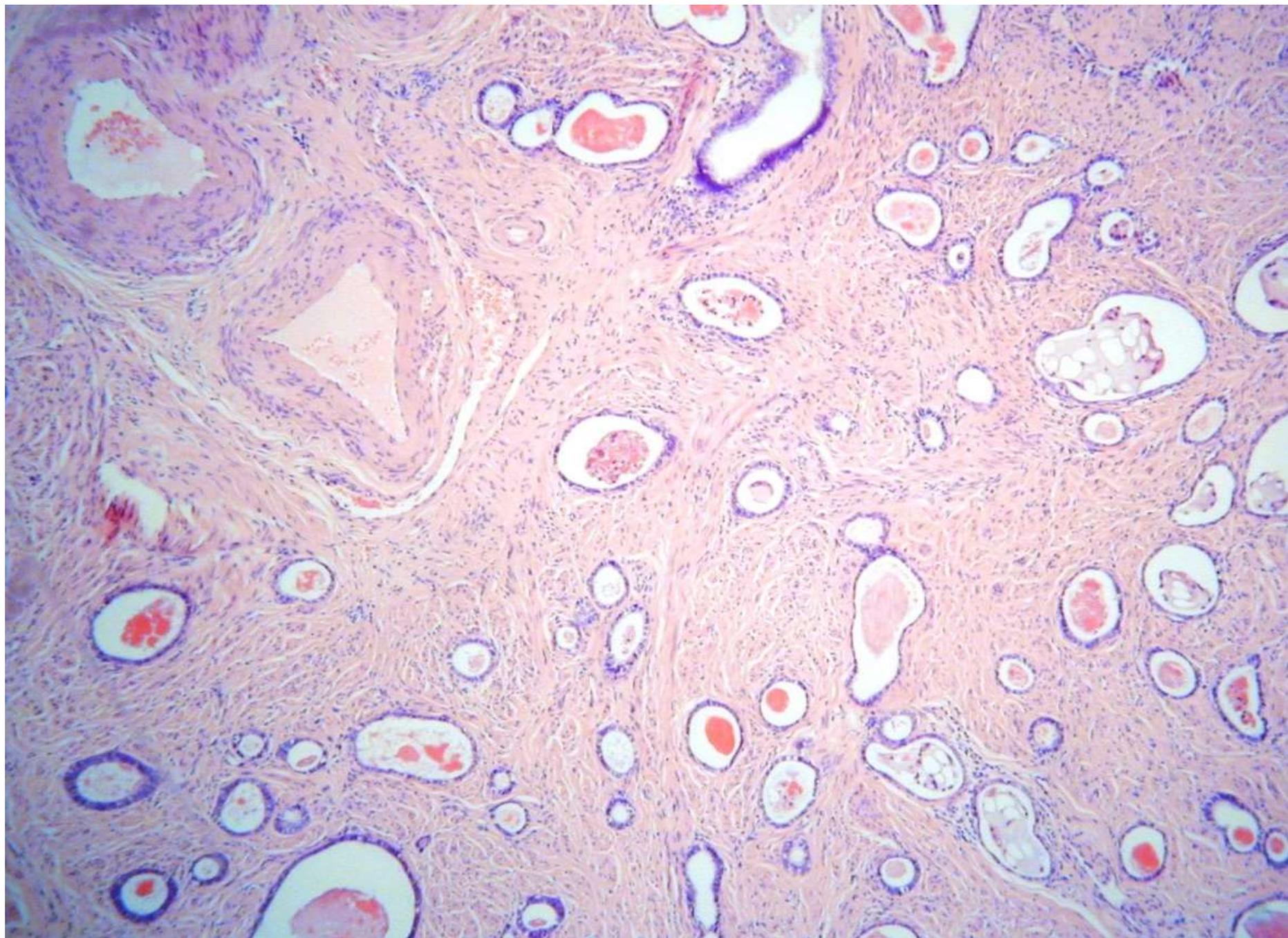












HOW MANY BLOCKS OF GROSSLY NORMAL ADNEXA

- 1 of each ovary
- 1 of each tube (include whole of fimbria)
(argument for more sampling in serous carcinoma-
PMID 27776011)

HOW MANY BLOCKS OF OMENTUM IN ENDOMETRIAL CARCINOMA

- If grossly involved- 1
- If grossly uninvolved- RCPATH suggests 4- argument that 1 is enough
- Some suggest depends on morphological subtype
- IJGP- PMID 25760907 (ovarian and endometrial carcinomas)- suggest 10 blocks but not convincing paper

PRIOR DIAGNOSIS OF ATYPICAL HYPERPLASIA OR ENDOMETRIAL ADENOCARCINOMA

- Not rare for endometrial cancers to be totally removed by biopsy/polypectomy
- Do we need to block the entire endometrium if nothing grossly and nothing on initial sections
- CONTROVERSIAL AREA
- TAKE CORNUAL BLOCKS
- Easy to block all if small uterus; not so easy if large
- If AH or low-grade endometrioid carcinoma, probably little risk of missing anything significant

PARAMETRIAL INVOLVEMENT IN SIMPLE HYSTERECTOMY FOR ENDOMETRIAL CARCINOMA

- Some confusion regarding whether to sample/
include on report since this does not constitute a
formal parametrectomy
- I tend to shave off or include with LUS blocks
- I mention on report

RCPATH FEBRUARY 2014

ENDOMETRIAL CARCINOMA DATASET

- Parametrial tissue should be sampled completely. Generally one block on each side will suffice to completely sample the parametrium. However, in those cases where radical hysterectomy has been performed (usually when cervical involvement is suspected preoperatively), more than one block from each side may be needed

RCPATH 2014- CORE ELEMENTS

- **PATHOLOGICAL CORE DATA: MACROSCOPIC:**
- - specimen type
- - attached anatomical structures
- - accompanying specimens
- - maximum dimension of tumour **(DO WE REALLY NEED) -WORTH RECORDING AND SOME SYSTEMS (MAYO CLINIC) FACTOR IT IN BUT USUALLY NOT USED IN MANAGEMENT**
- **❓ PATHOLOGICAL CORE DATA: MICROSCOPIC:**
- - tumour type
- - tumour grade
- - myometrial invasion
- - **tumour free distance to serosa (do we really need?)**
- - lymphovascular invasion
- - cervical stromal invasion
- - vaginal involvement
- - uterine serosal involvement
- - parametrial involvement

RCPATH 2014- NON-CORE ELEMENTS

- **PATHOLOGICAL DATA: MACROSCOPIC**
- - specimen weight and measurements.
- **☒ PATHOLOGICAL DATA: MICROSCOPIC**
- - percentages of different components of mixed carcinomas
- - morphological components of carcinosarcomas
- - cervical surface and gland (crypt) involvement
- - distance of tumour from cervical (or vaginal) margin
- - percentage of myometrium involved by tumour
- - background endometrium
- - peritoneal involvement
- - peritoneal cytology
- - distant metastases
- - extracapsular spread of lymph node metastases
- - ancillary investigations
- - block key
- - provisional TNM stage.

BLOCK-KEY

- Non-core item
- BUT very important should need for internal or external review arise (sometimes impossible without)
- ALSO USEFUL TO PUT MOST REPRESENTATIVE TUMOUR BLOCK IN PATHOLOGY REPORT (FURTHER STUDIES) (SAVES TIME IN FUTURE)

QUESTIONS

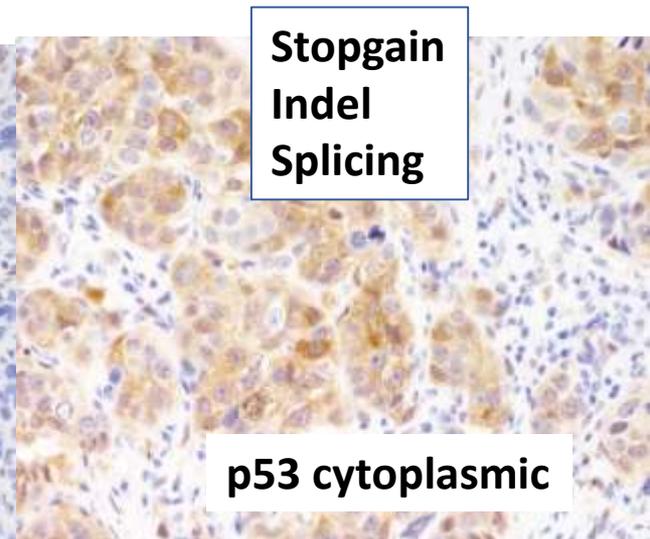
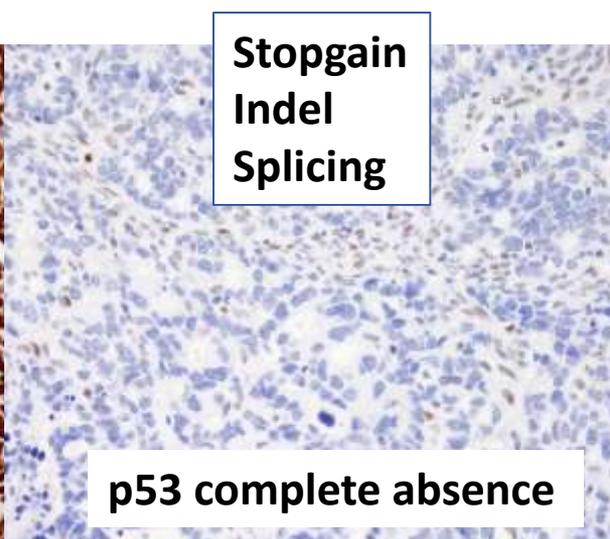
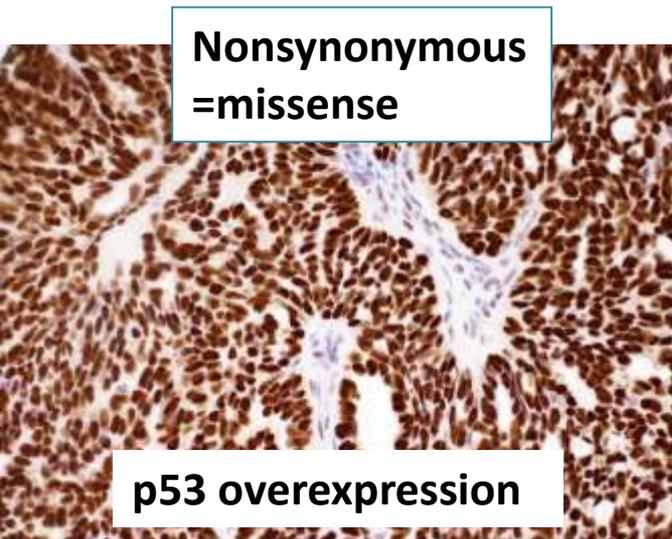
p53

- p53 immunohistochemistry- lot of confusion
- only consider positive/significant if diffuse strong nuclear immunoreactivity (75-80% cells suggested- associated with missense mutation)
- p53 null consistent with serous carcinoma (different type of mutation (nonsense) or deletion resulting in truncated protein which is not detected by immunohistochemistry)
- third pattern of mutation-type staining- cytoplasmic (rare pattern)
- most normal tissues and tumours exhibit focal, weak, heterogenous staining (“wild-type” staining) (usually <50%) (**about 5% of HGSCs with *Tp53* mutation exhibit wild-type staining**)
- DON'T REPORT AS POSITIVE OR NEGATIVE- REPORT AS “WILD-TYPE” or “MUTATION-TYPE”
- OCCASIONALLY DIFFICULT TO INTERPRET (“wild-type” at upper end; negative “mutation-type” versus “wild-type”)

Interpretation of p53 immunohistochemistry



Normal



abnormal; mutation-type

p53 immunohistochemistry pattern and interpretation

Pattern	p53 IHC Interpretation	TP53 mutation type	% in HGSC
TP53 MUTATION ABSENT			
Wild type	Normal	No mutation	0
TP53 MUTATION PRESENT			
Overexpression	Abnormal	Non-synonymous (missense); also in-frame deletion, splicing	66%
Complete absence/ null	Abnormal	Indels, stopgains, splicing mutations	25%
Cytoplasmic	Abnormal	Indels and stopgains with disruption of the nuclear localization domain	4%
Wild type	Normal*	Truncating mutation	5%

HGSC- high-grade serous carcinoma