

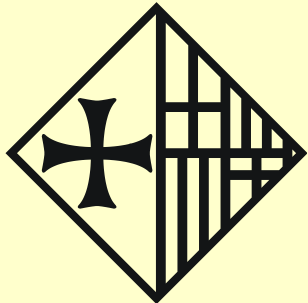
XX Congreso Chileno de Anatomia Patologica

SCHAP, Santiago de Chile
Jueves, 10 de noviembre, 2016

Adenocarcinoma de Cérvix

Dr. Jaime Prat

Hospital de la Santa Creu i Sant Pau
Universitat Autònoma de Barcelona, España



Cervical Cancer

WHO-2003

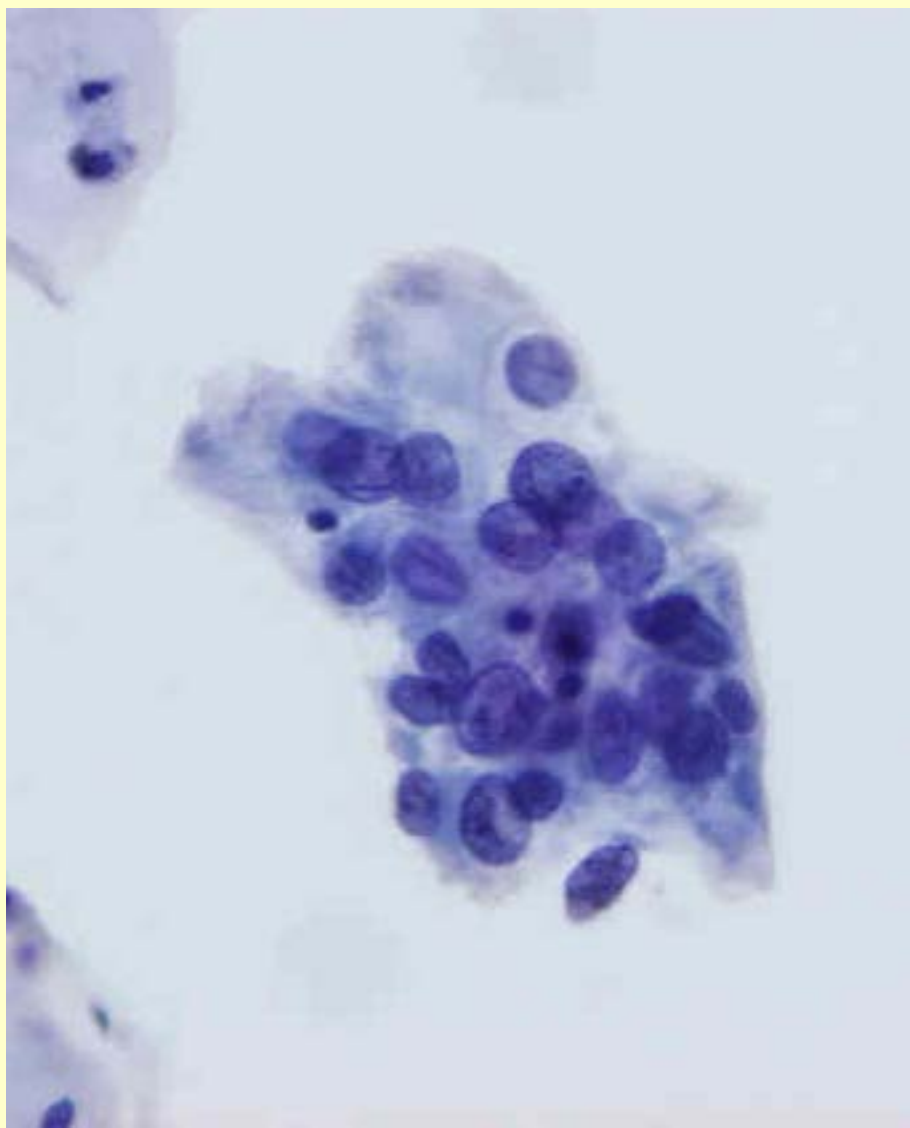
- Squamous cell carcinoma (60-80%)
- Adenocarcinoma (15-20%)
- Other epithelial tumors

Preinvasive Glandular Lesions (Cervix - WHO-2003)

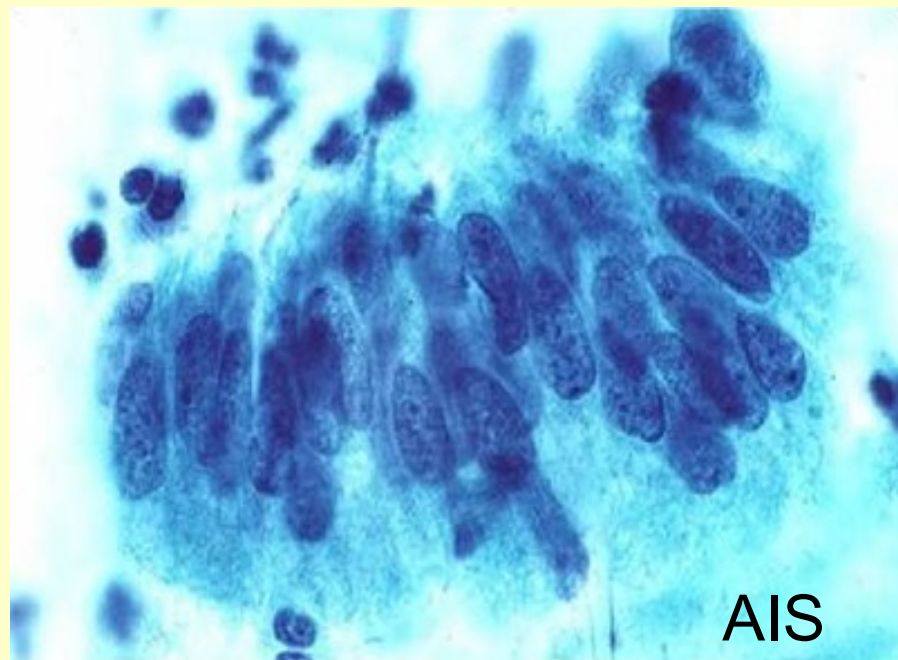
- Glandular Atypia
- Glandular Dysplasia
- Adenocarcinoma in Situ (AIS)

Adenocarcinoma In Situ (AIS)

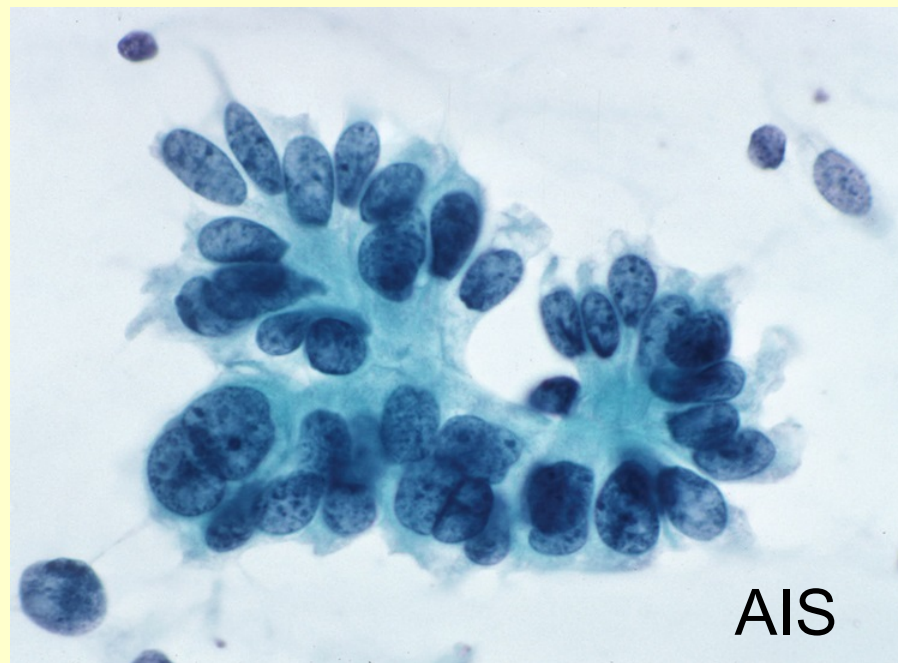
- Age 39-46 yrs (10 yr < Inv Adca)
- Assoc with Inv Adca
- AIS → Inv Adca (rare)
- hPV 16, 18, 31
- 10-20% of Adca of Cx
- Most asymptomatic (Pap smears)



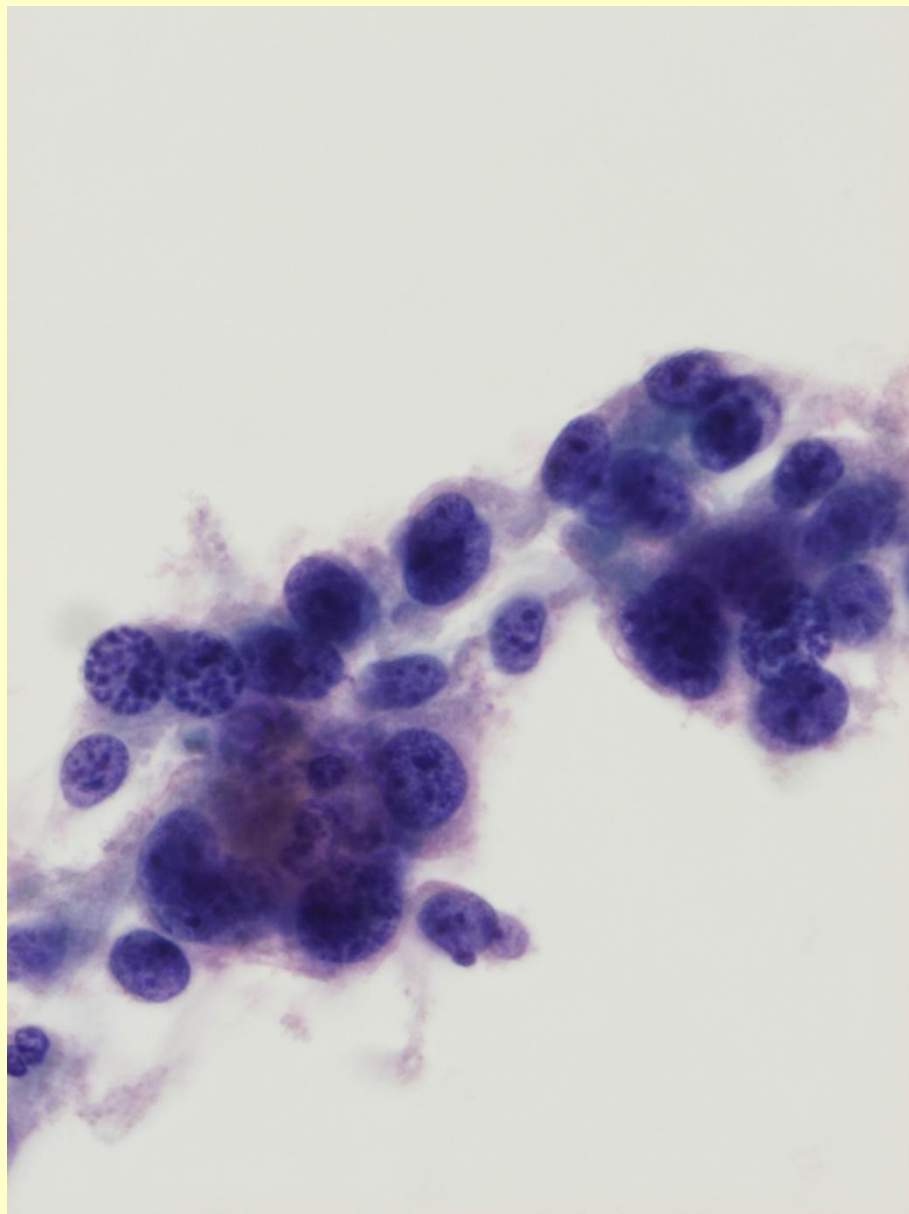
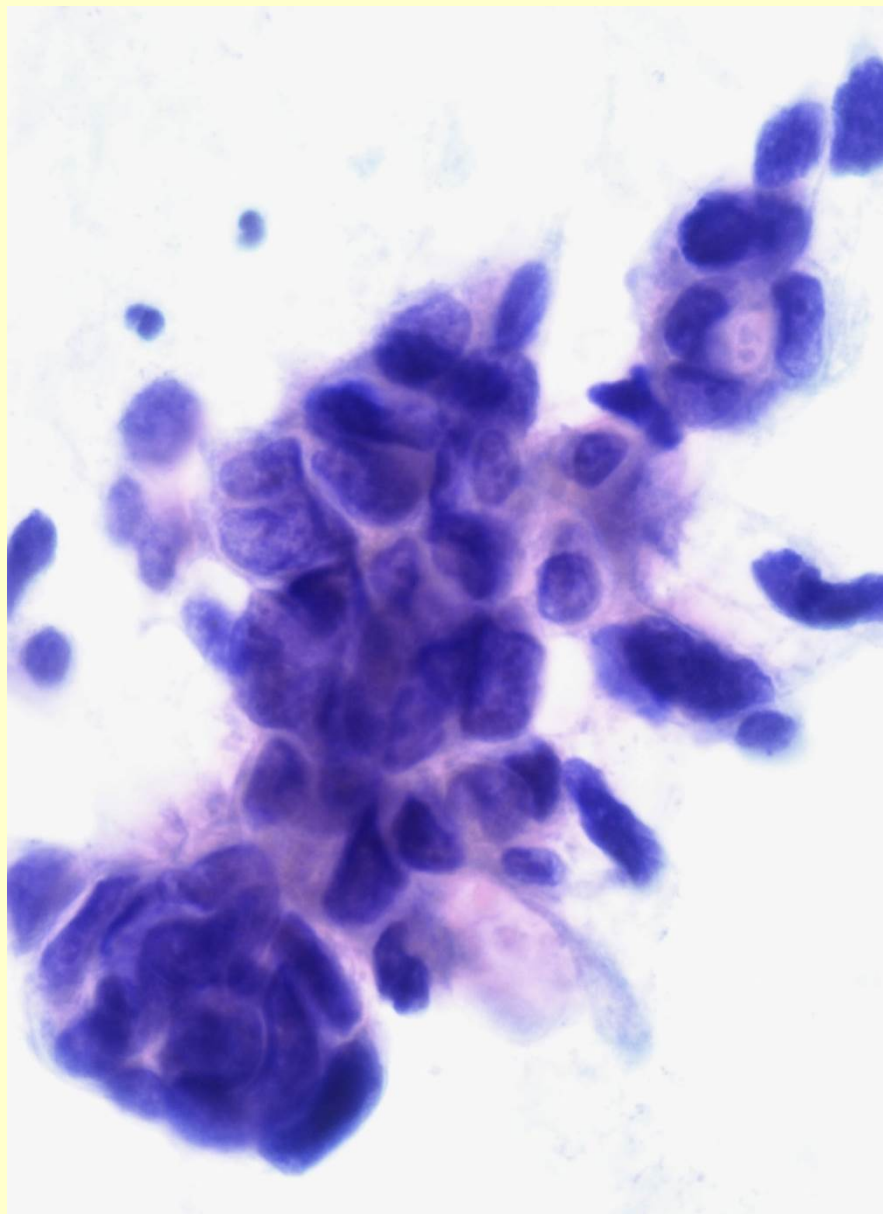
AGUS



AIS



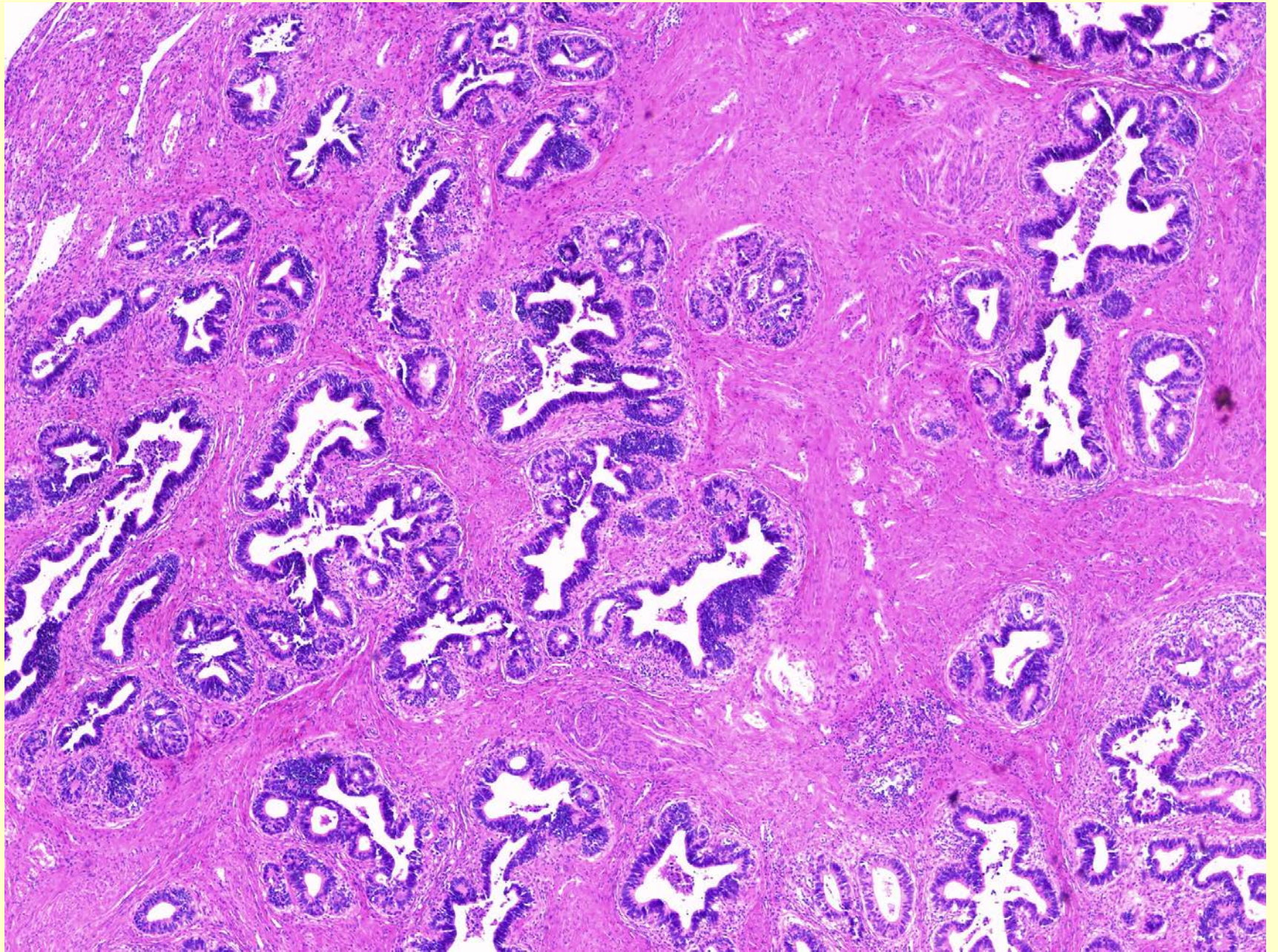
AIS

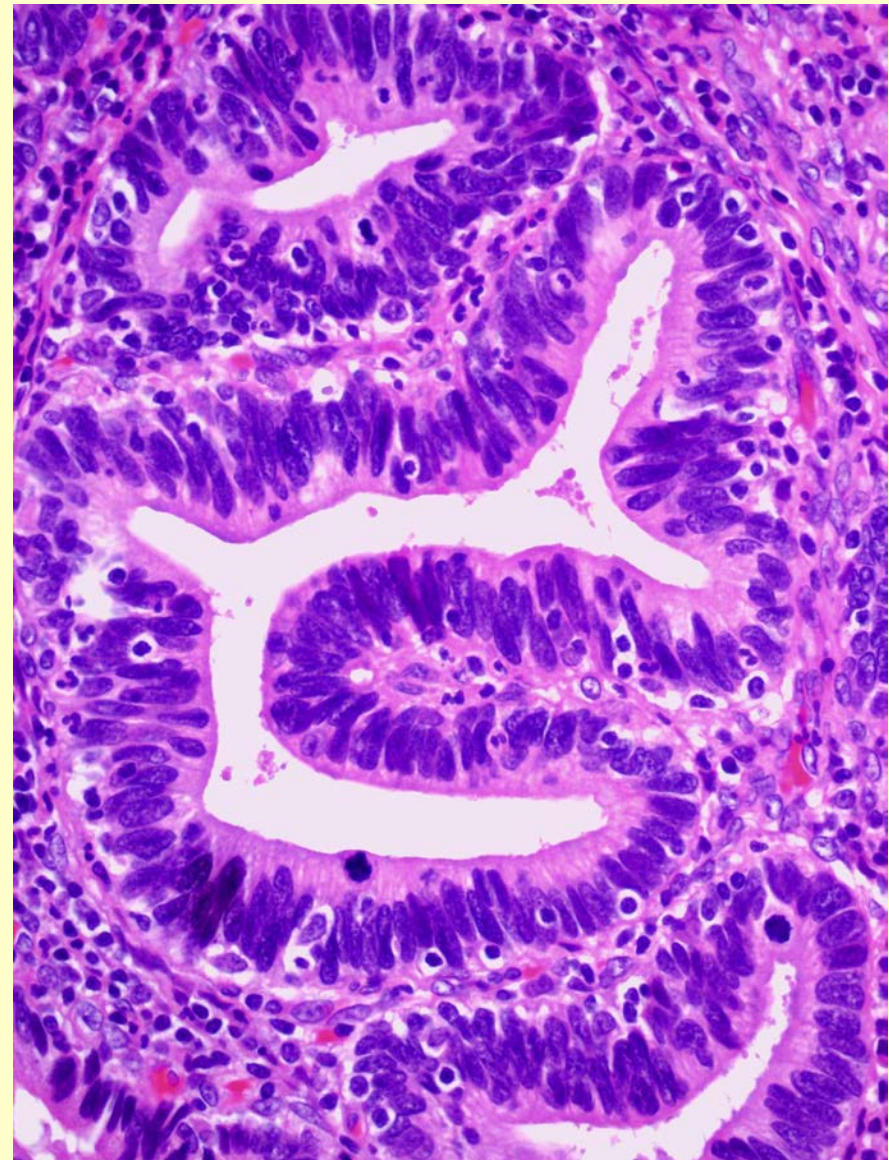
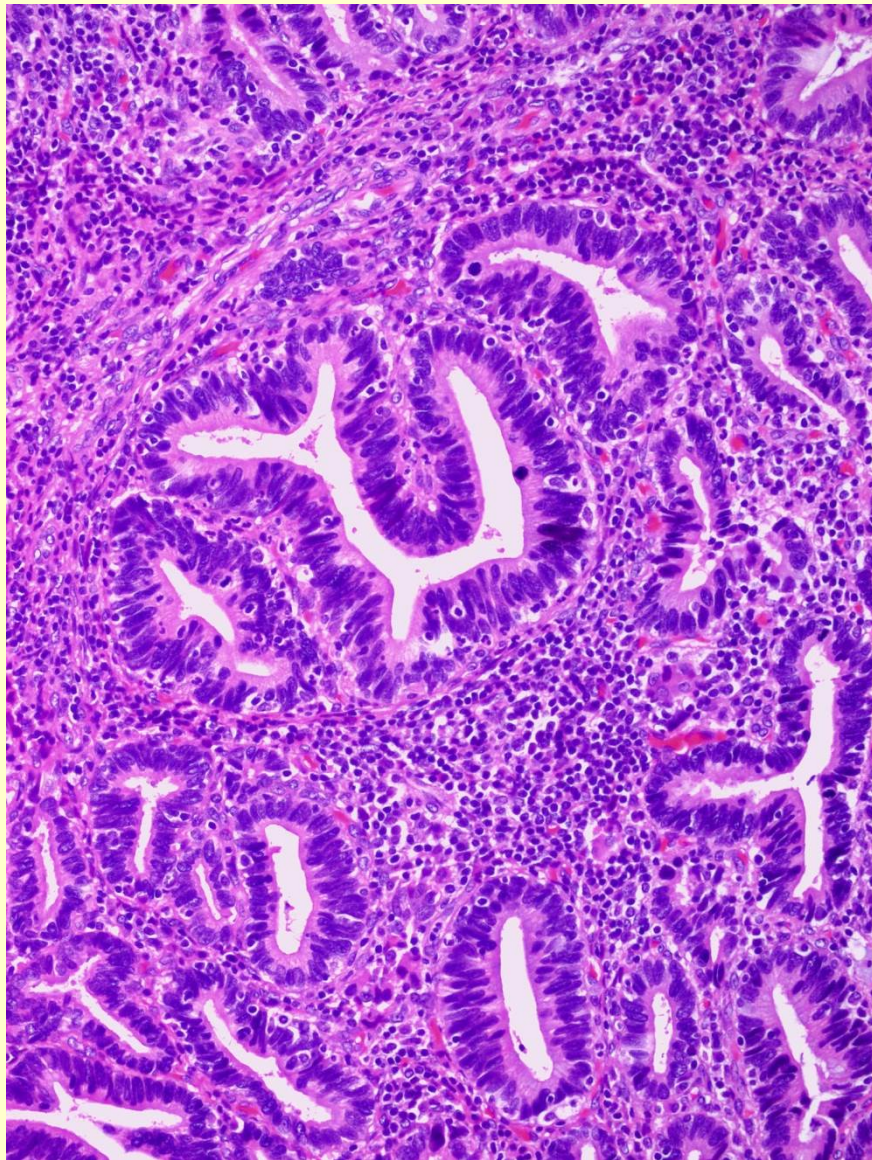


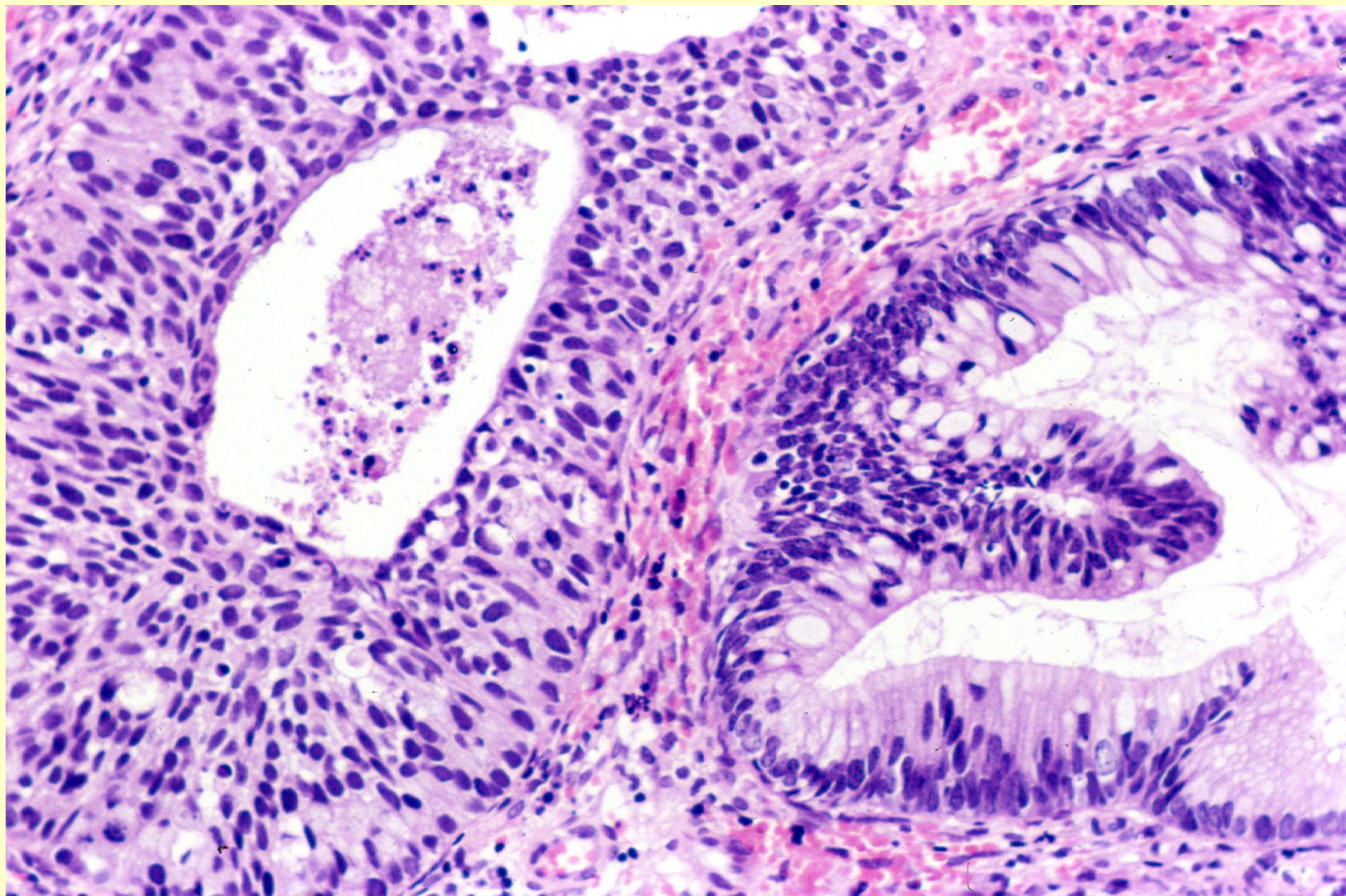
Adenocarcinoma

Adenocarcinoma In Situ (AIS) (10-20% of Adca Cx)

- T Zone involvement
- Multifocal (15%)
- Av Size 12 mm
- Assoc with CIN/Sq Cell Ca (60%)

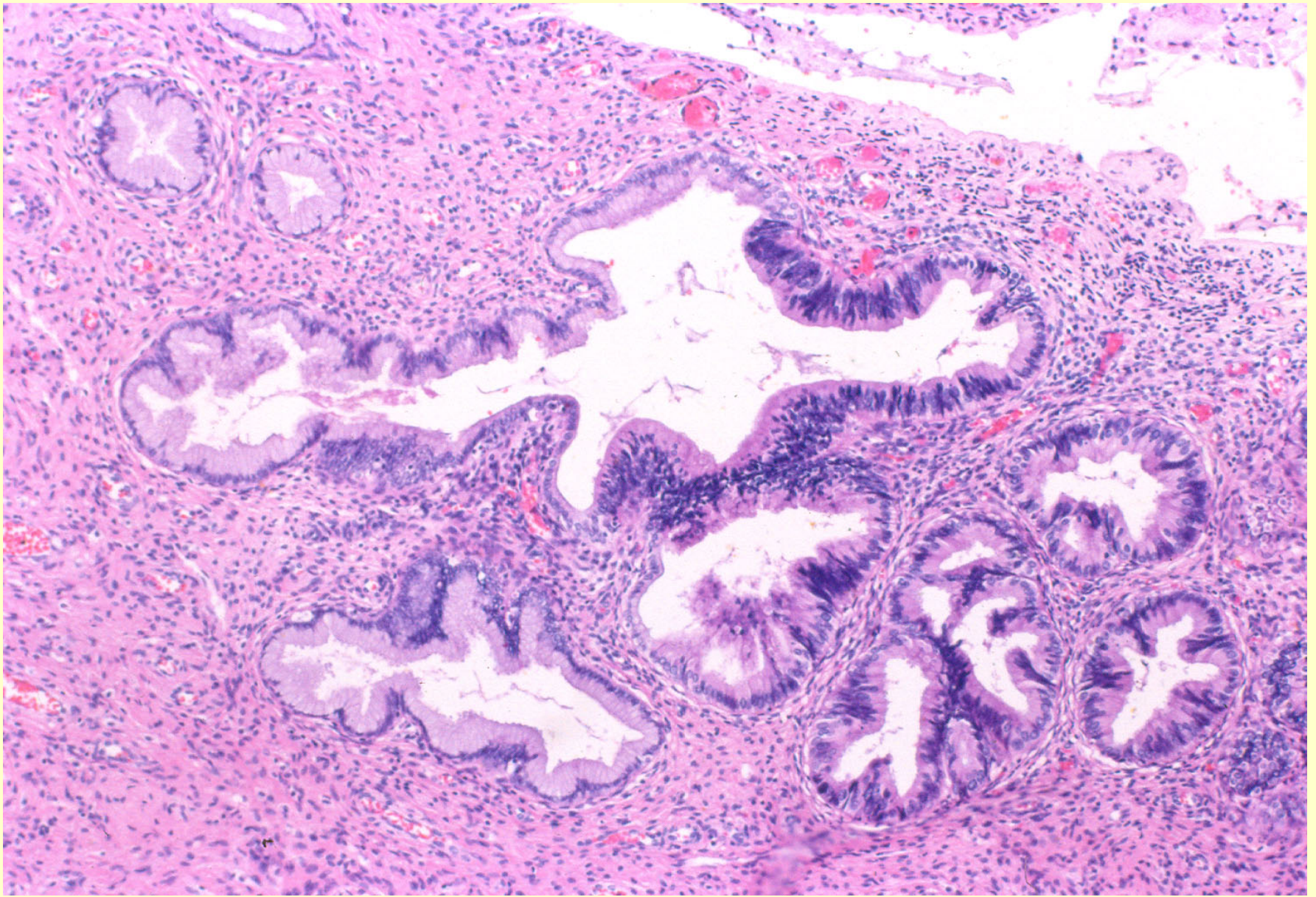






CIN

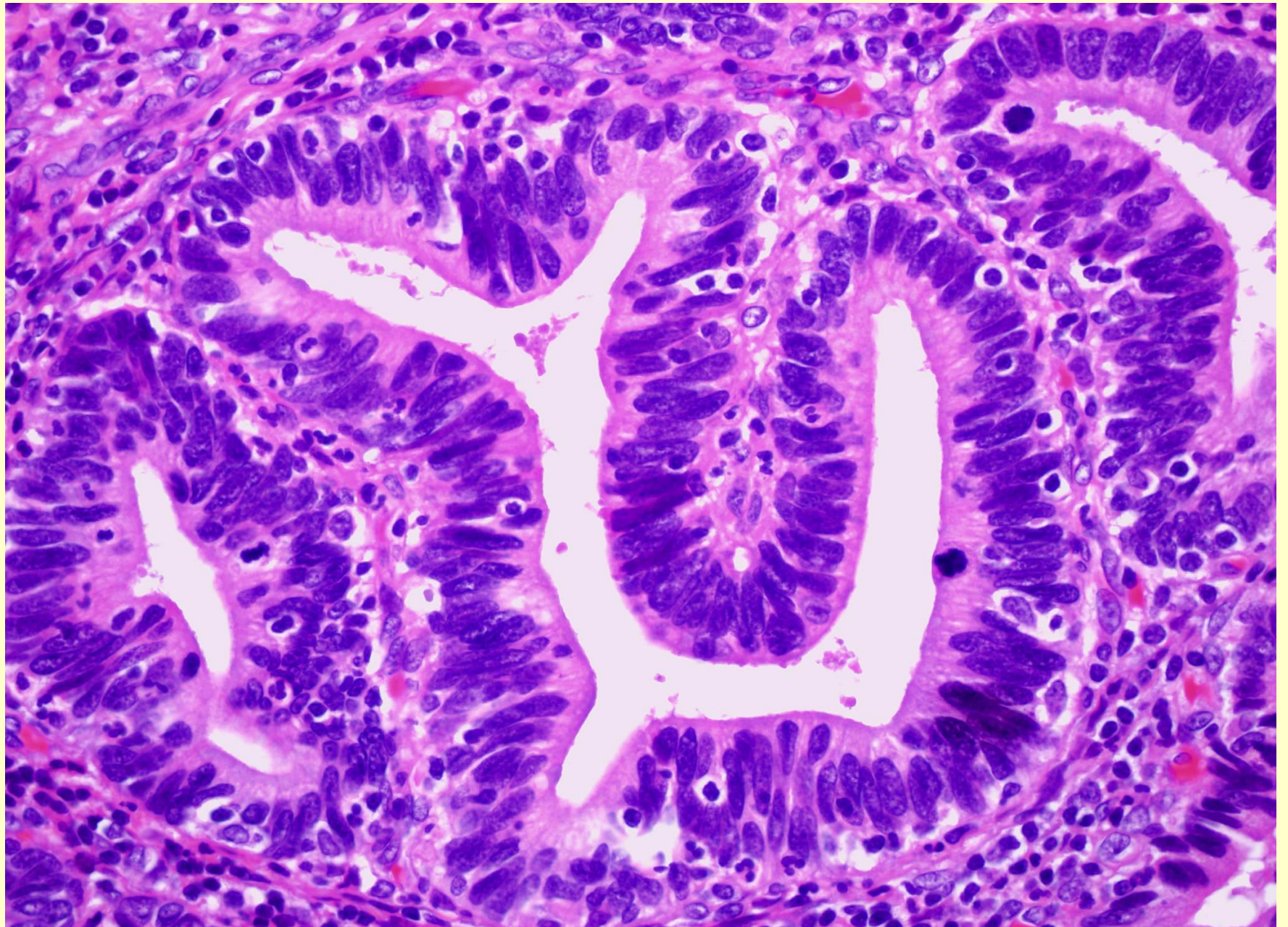
AIS

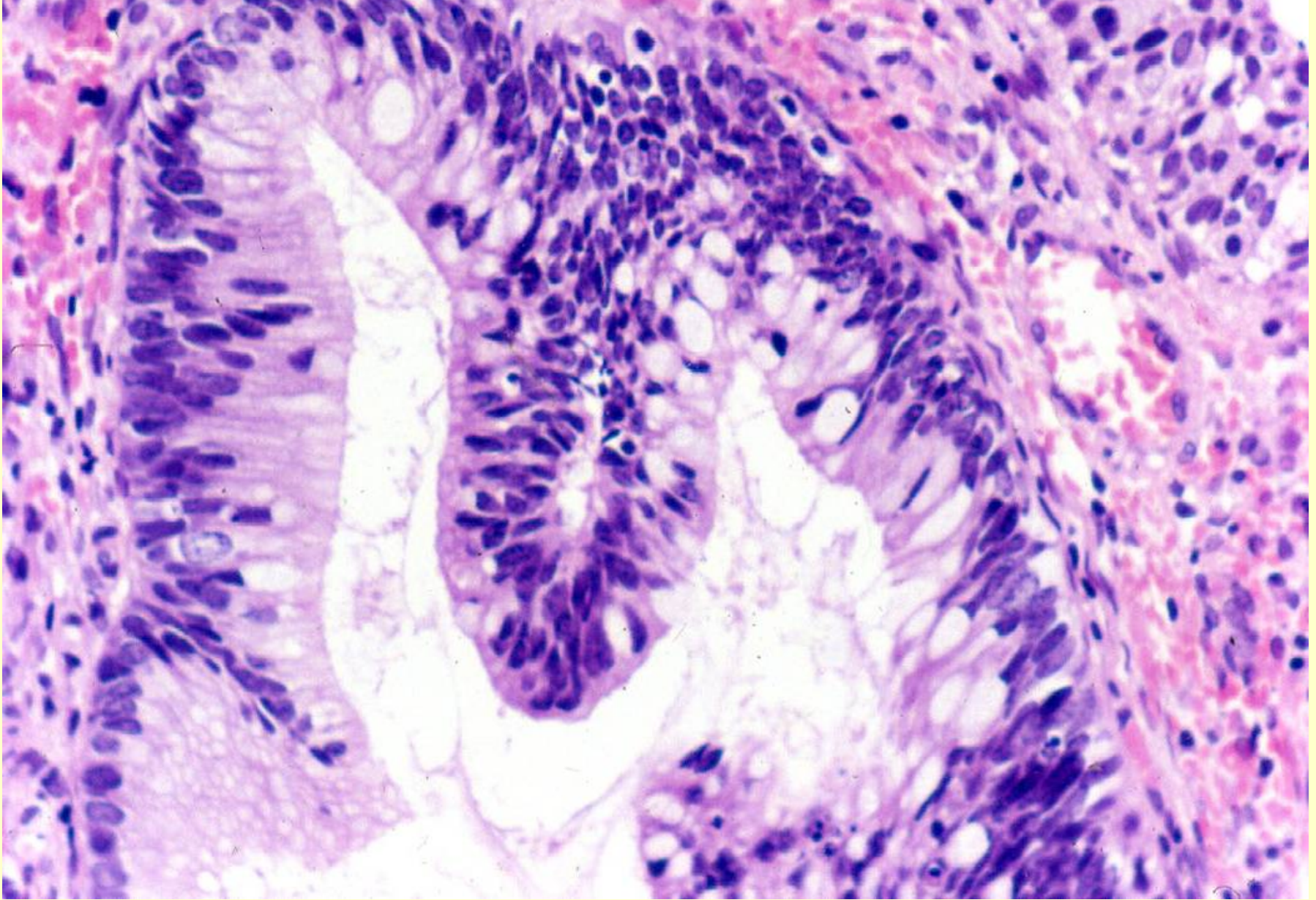


AIS – Focal glandular involvement

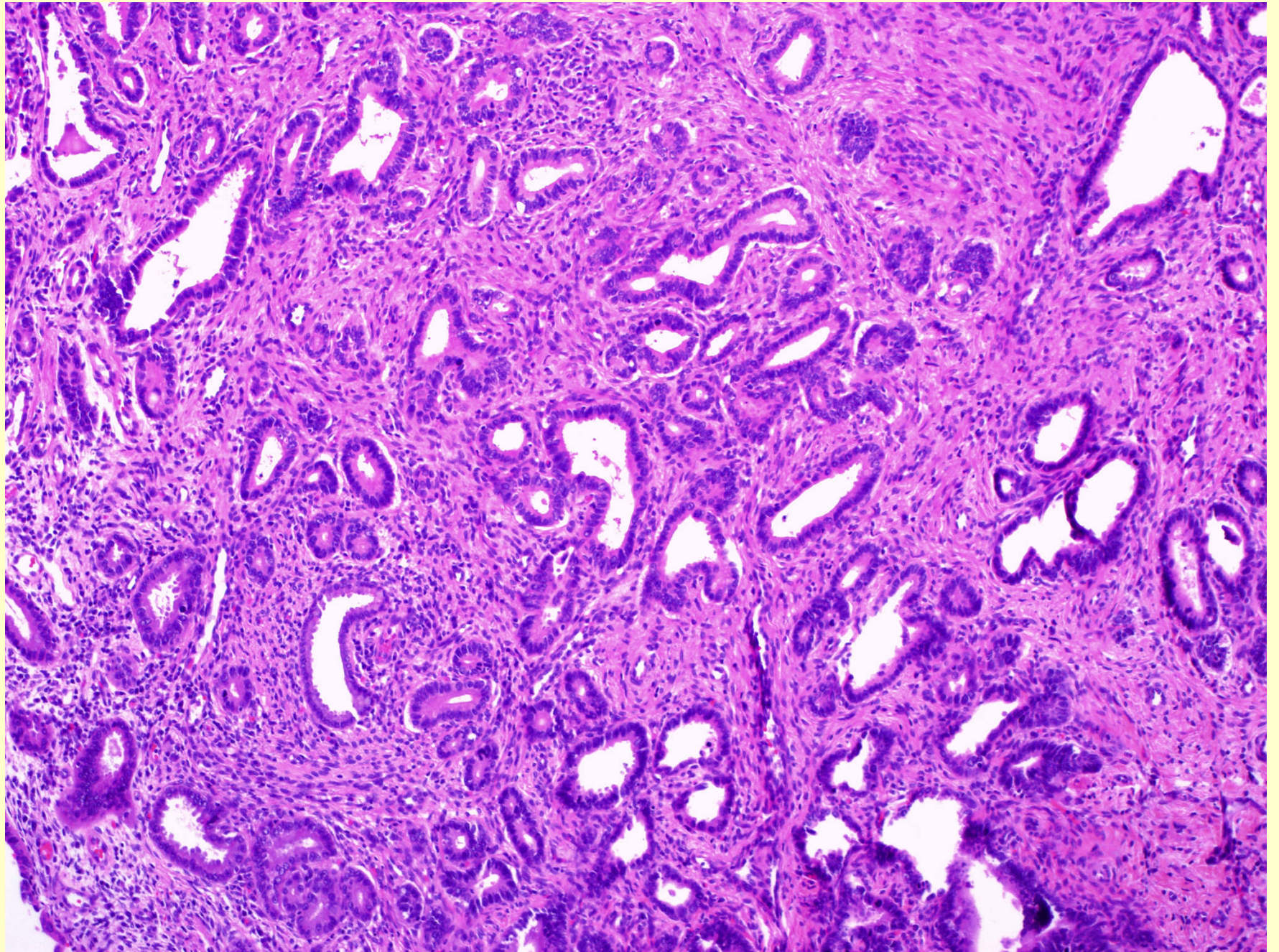
Adenocarcinoma In Situ (AIS) (Pathology)

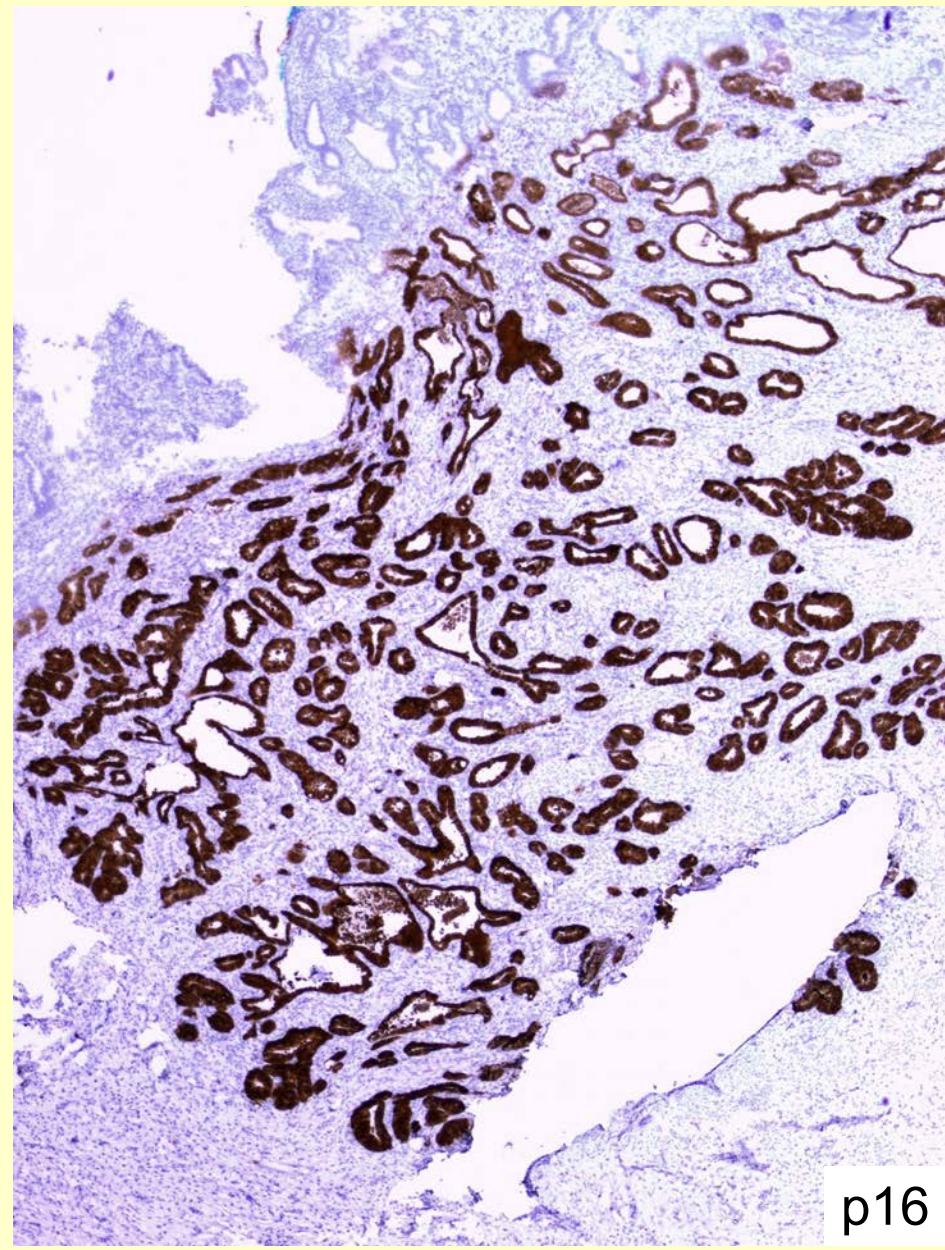
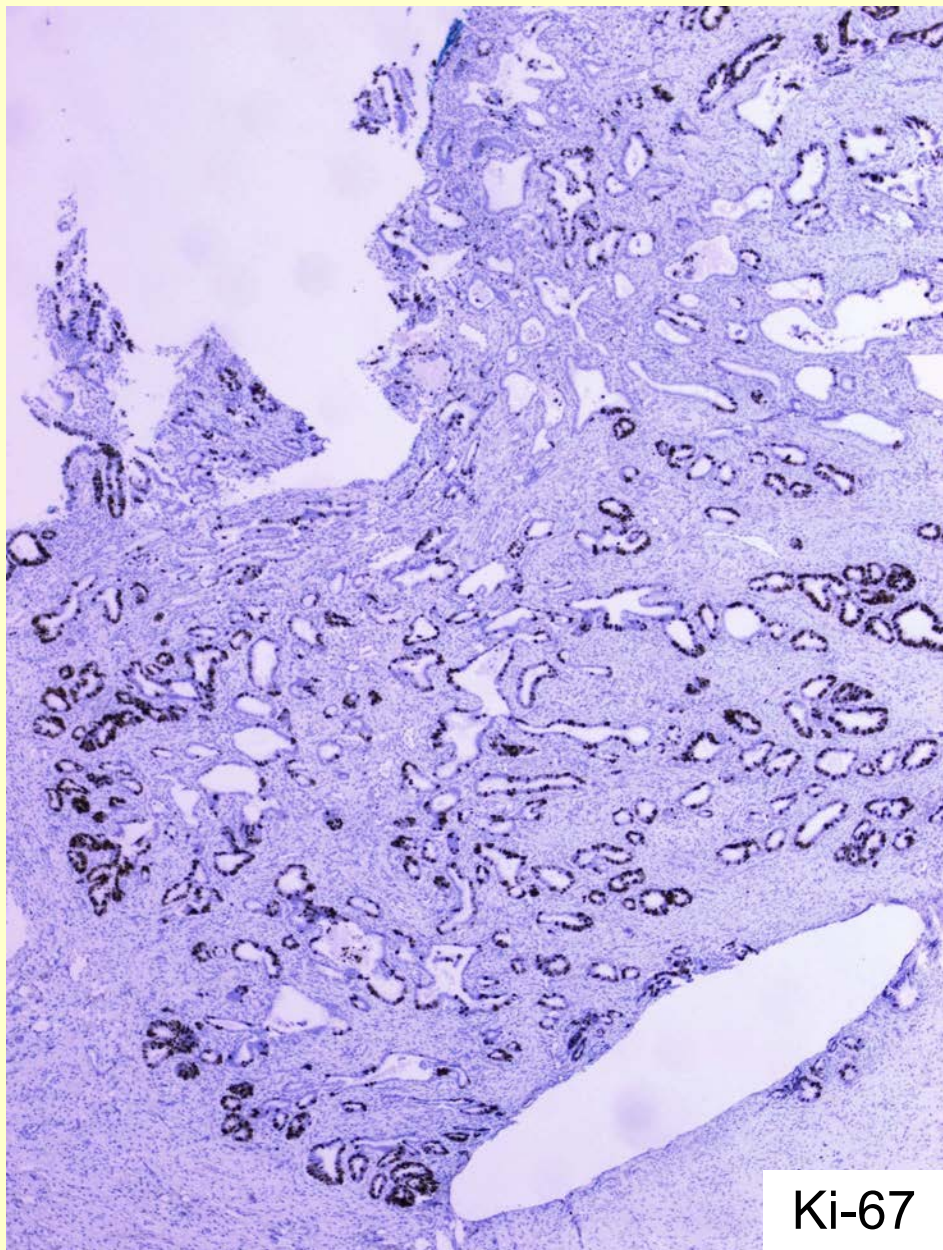
- Endocervical (Mucinous)
- Intestinal (goblet cells)
- Endometrioid
- Adenosquamous





AIS – intestinal type

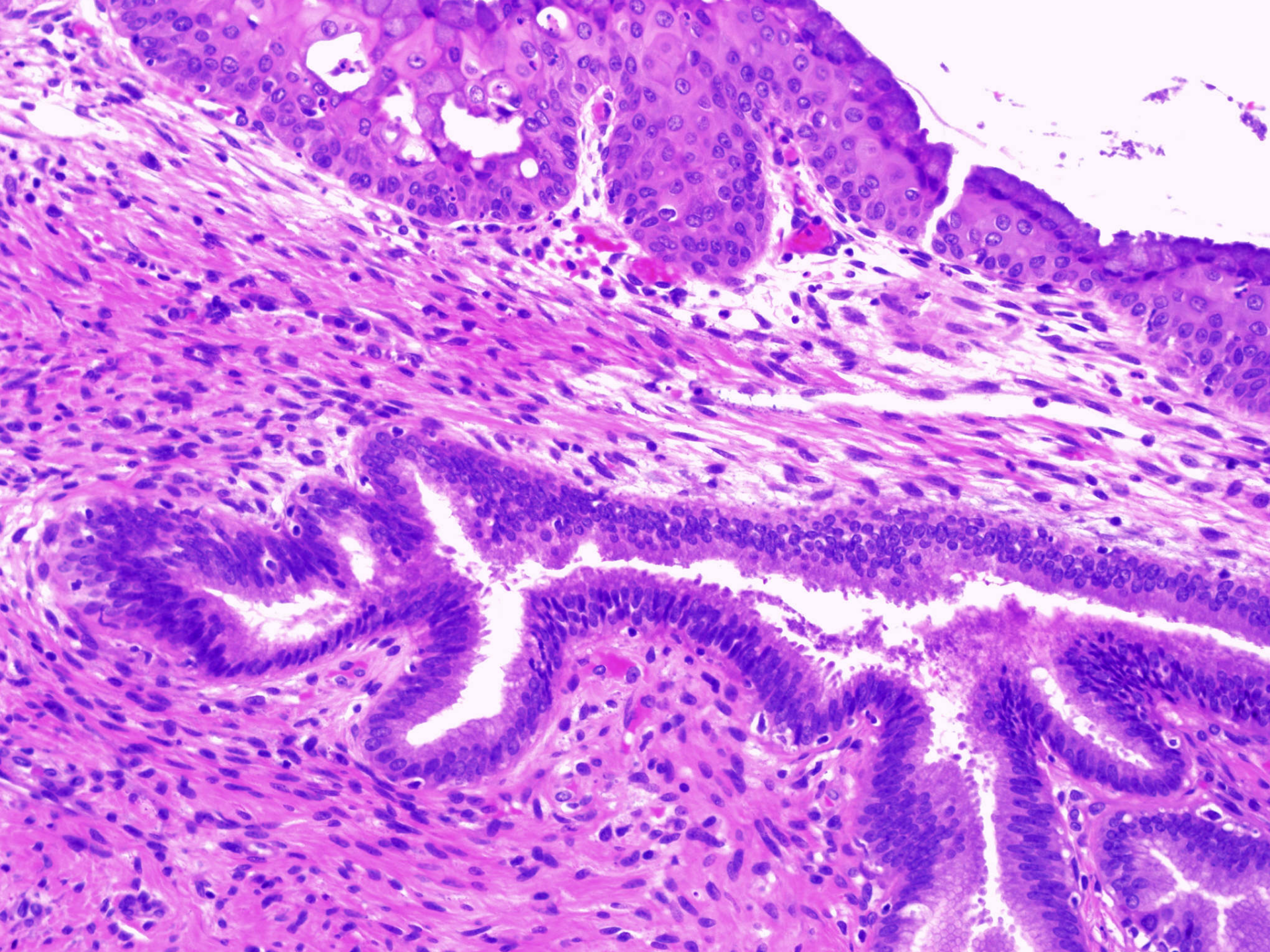


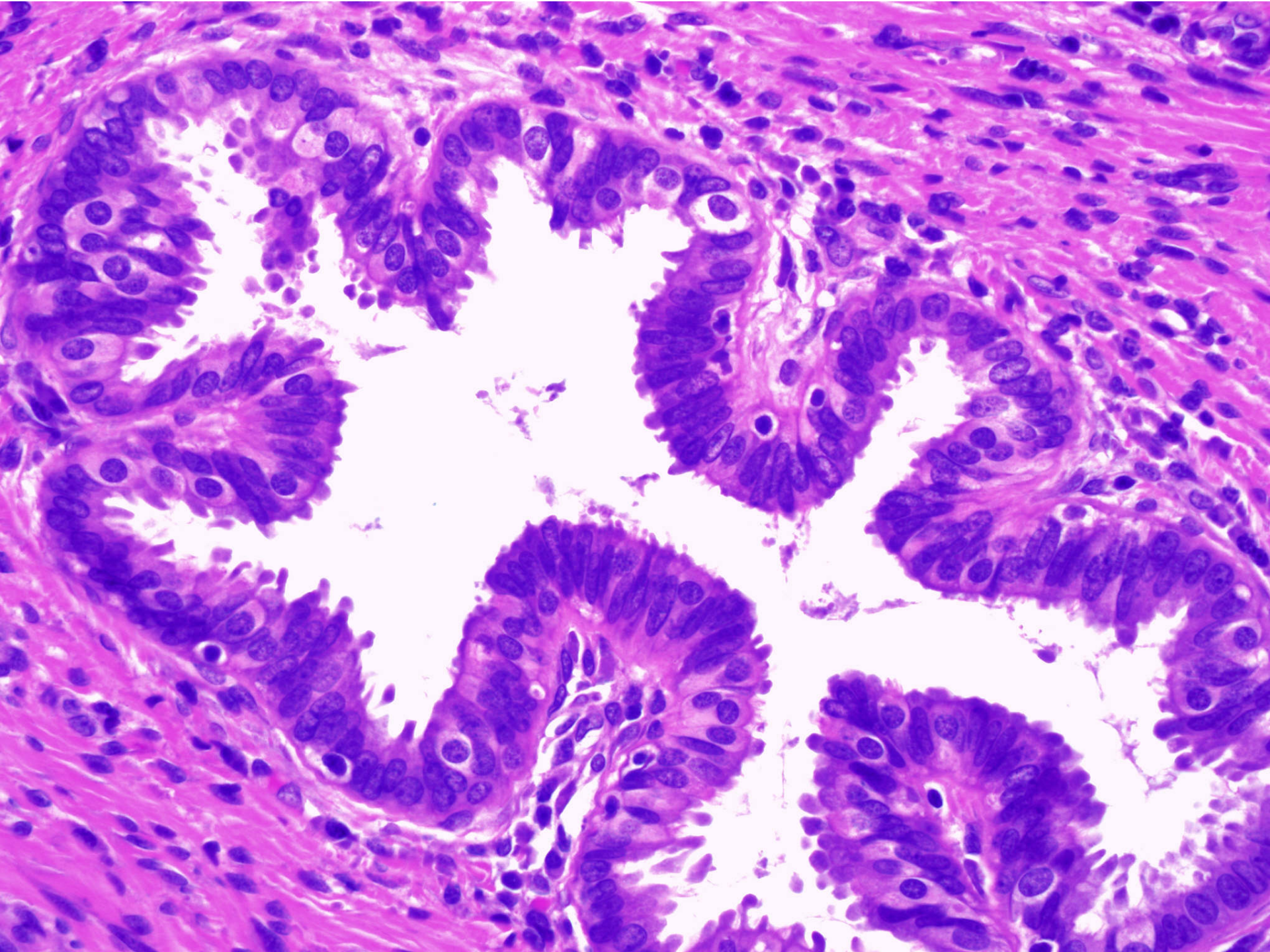


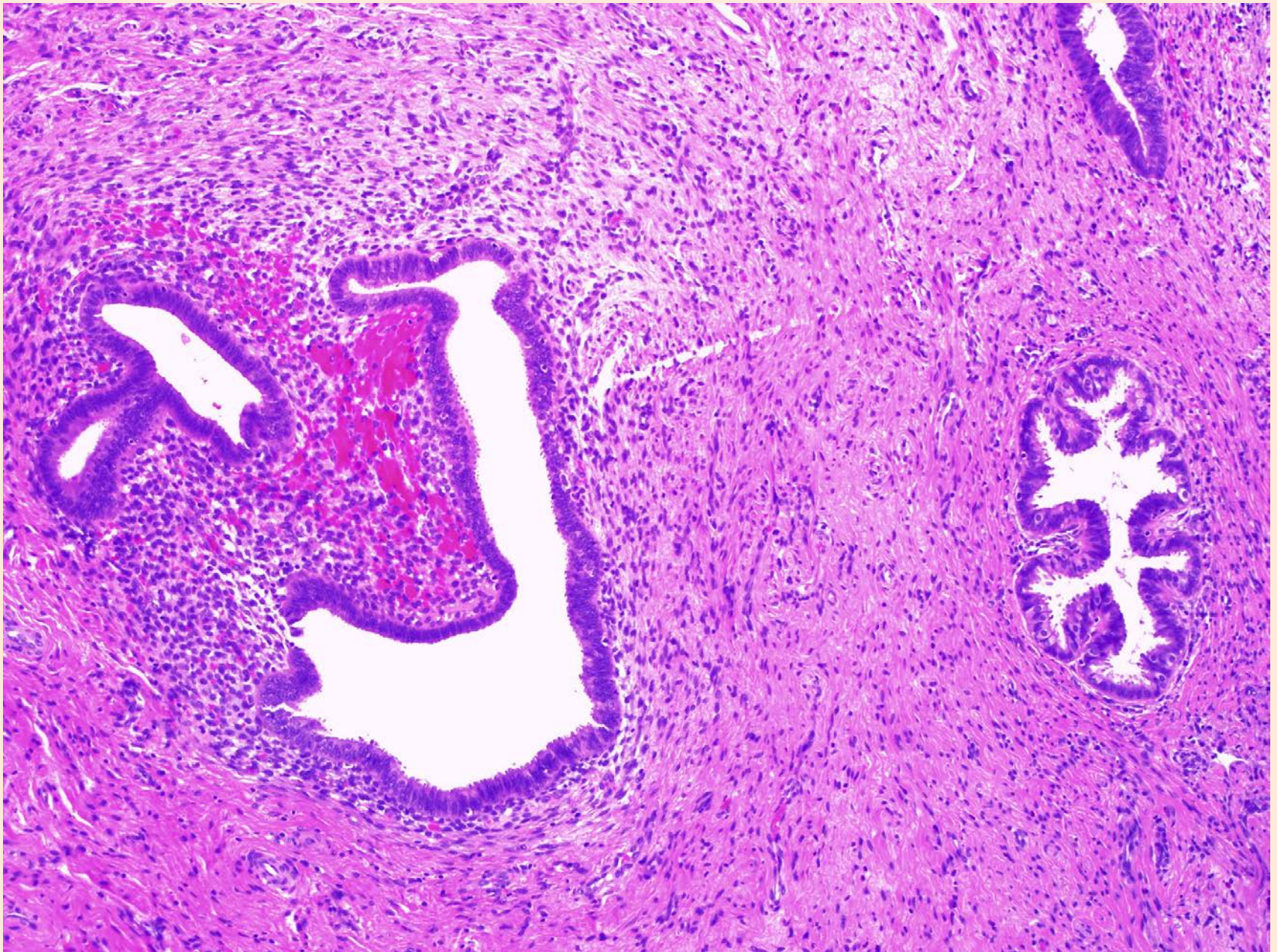
Clinical History

(15B-3370)

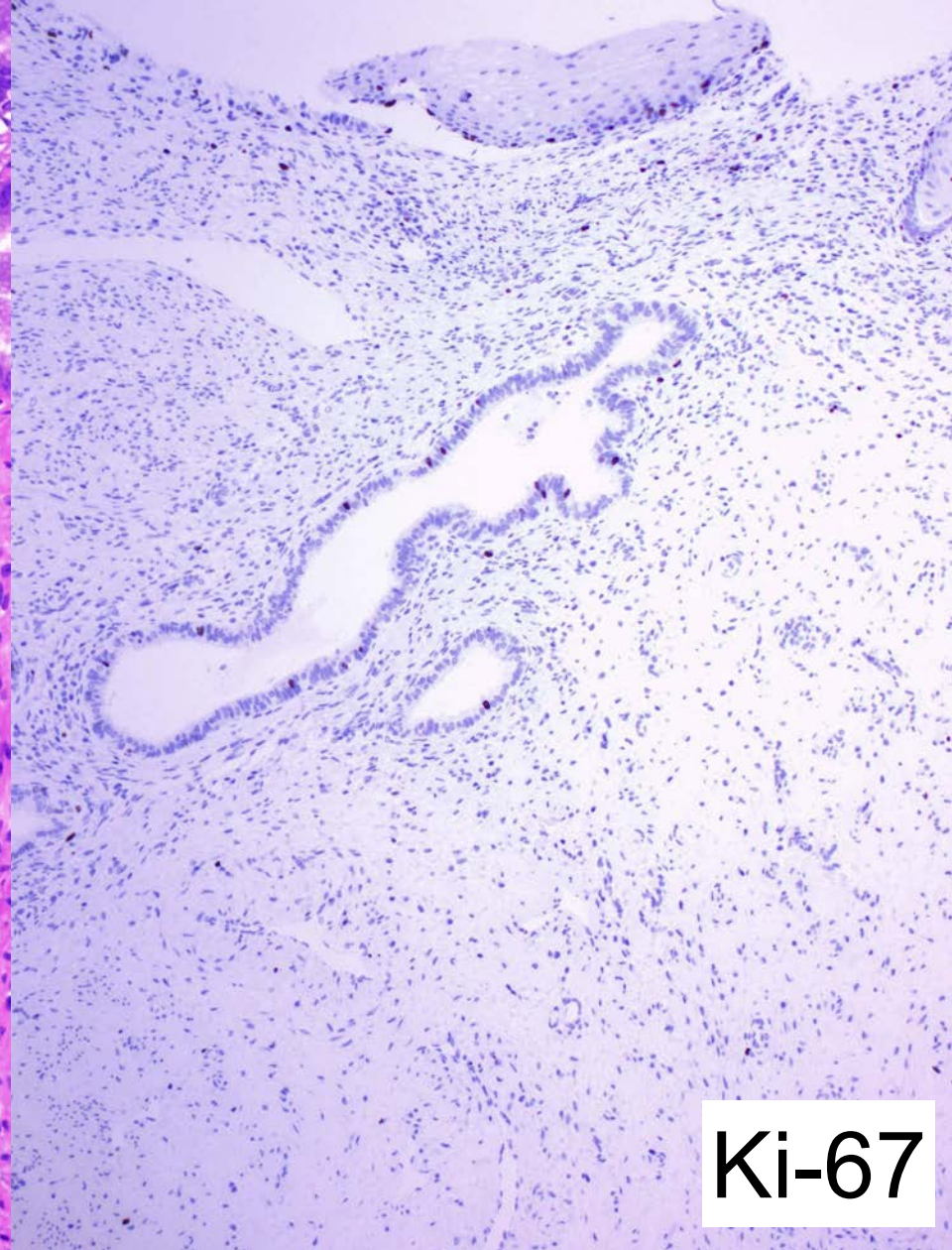
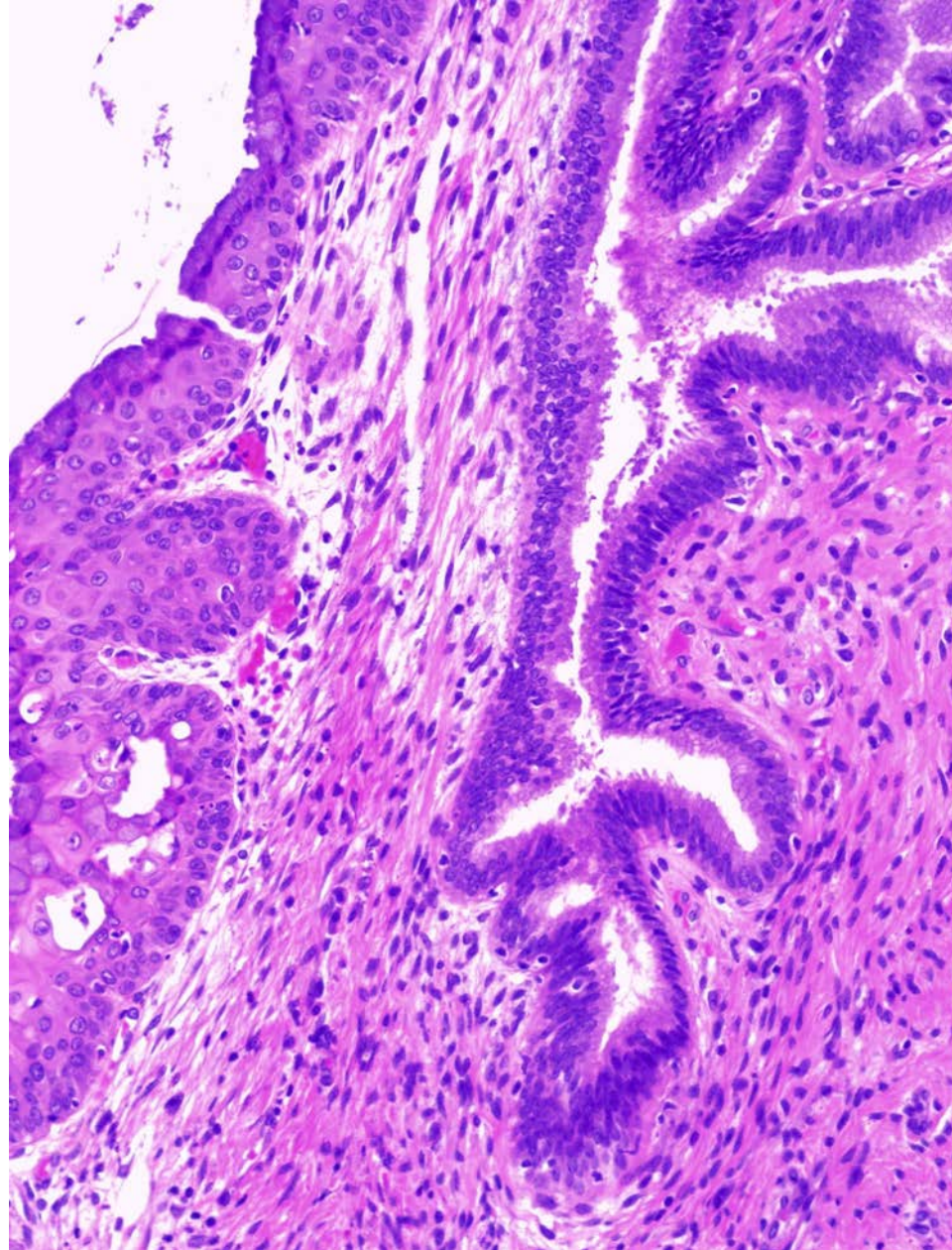
- 53 y.o. woman
- Cervical cone for CIN3-with negative margins
- Pap test: adenocarcinoma in situ (AIS)?
- Colpo & Pap test: negative
- 2nd conization





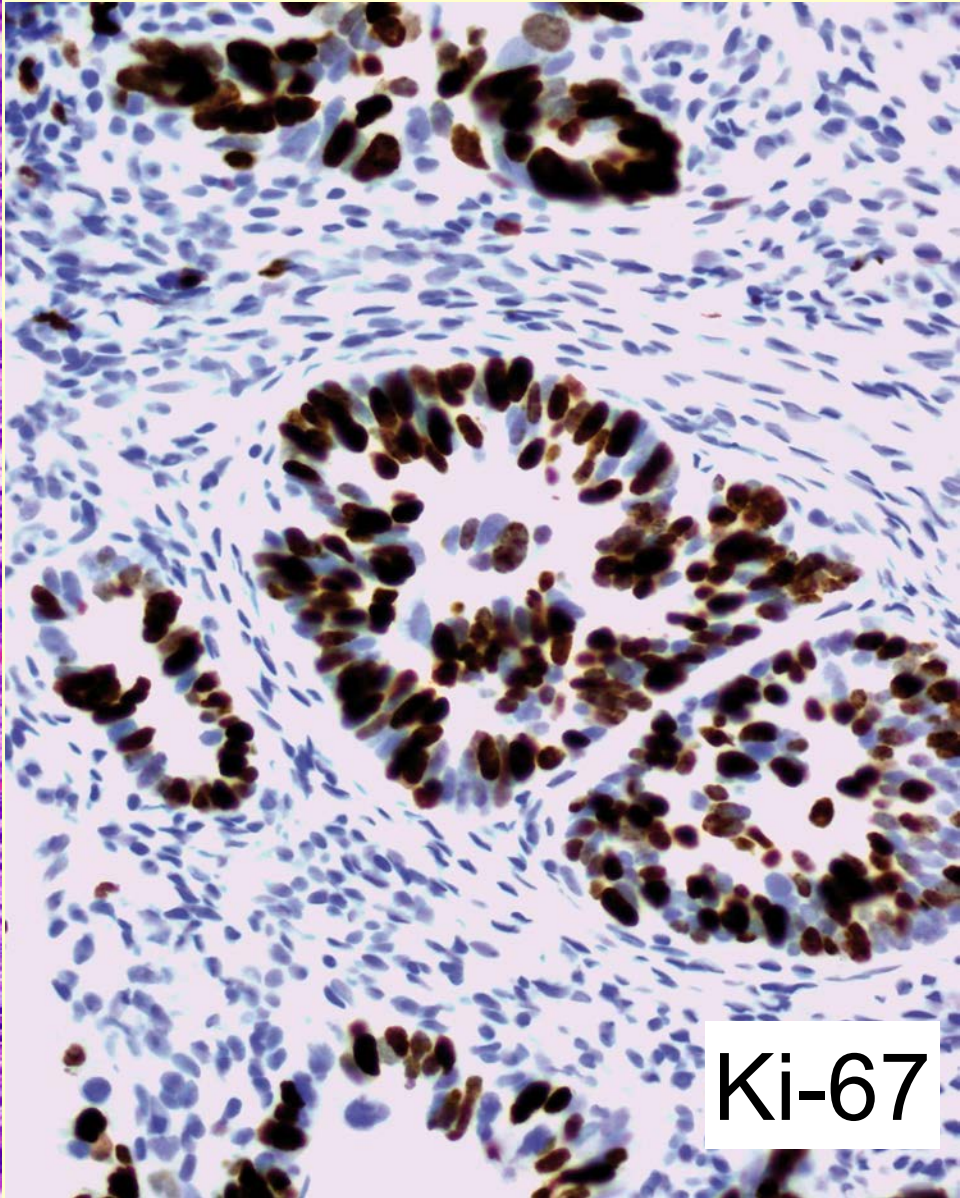
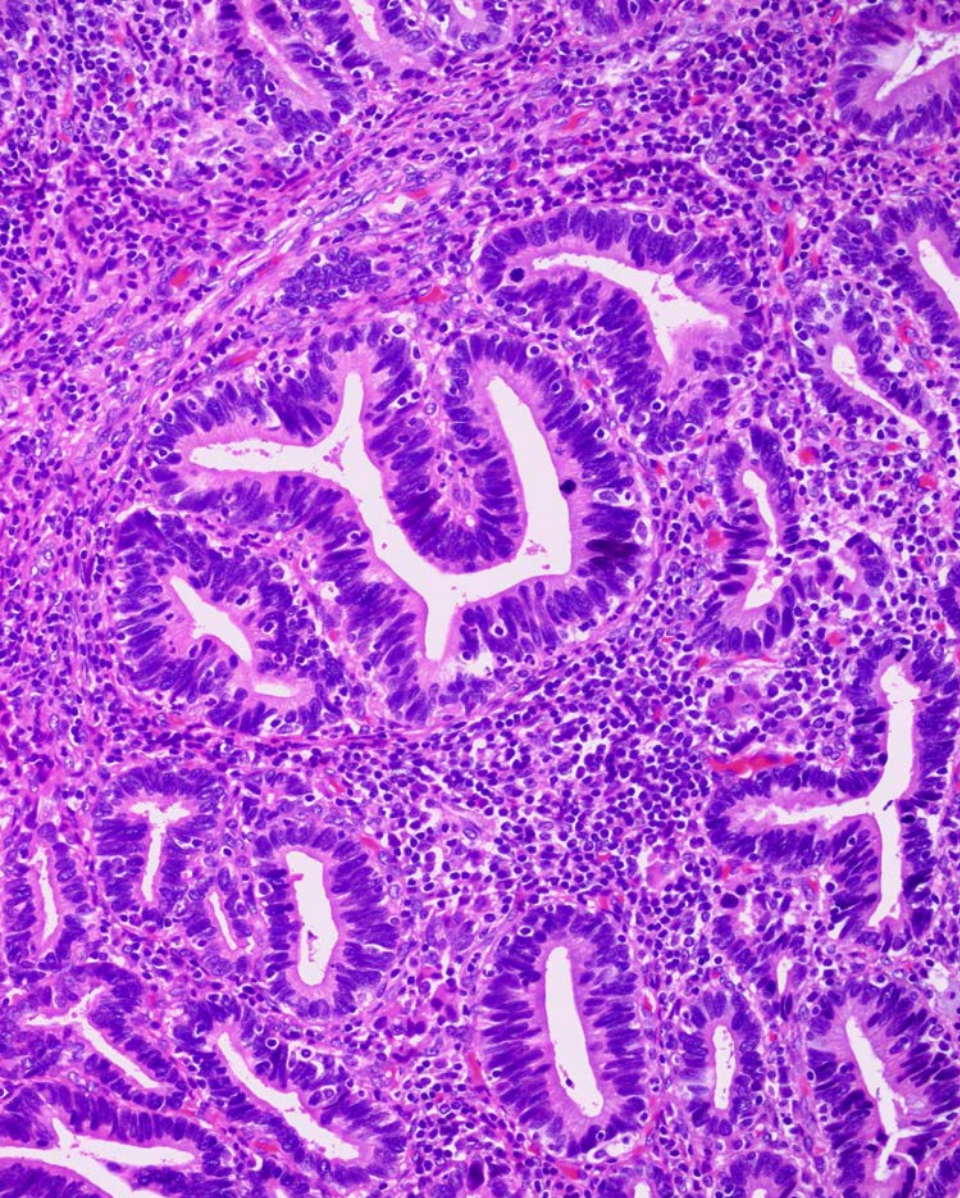


Endometriosis

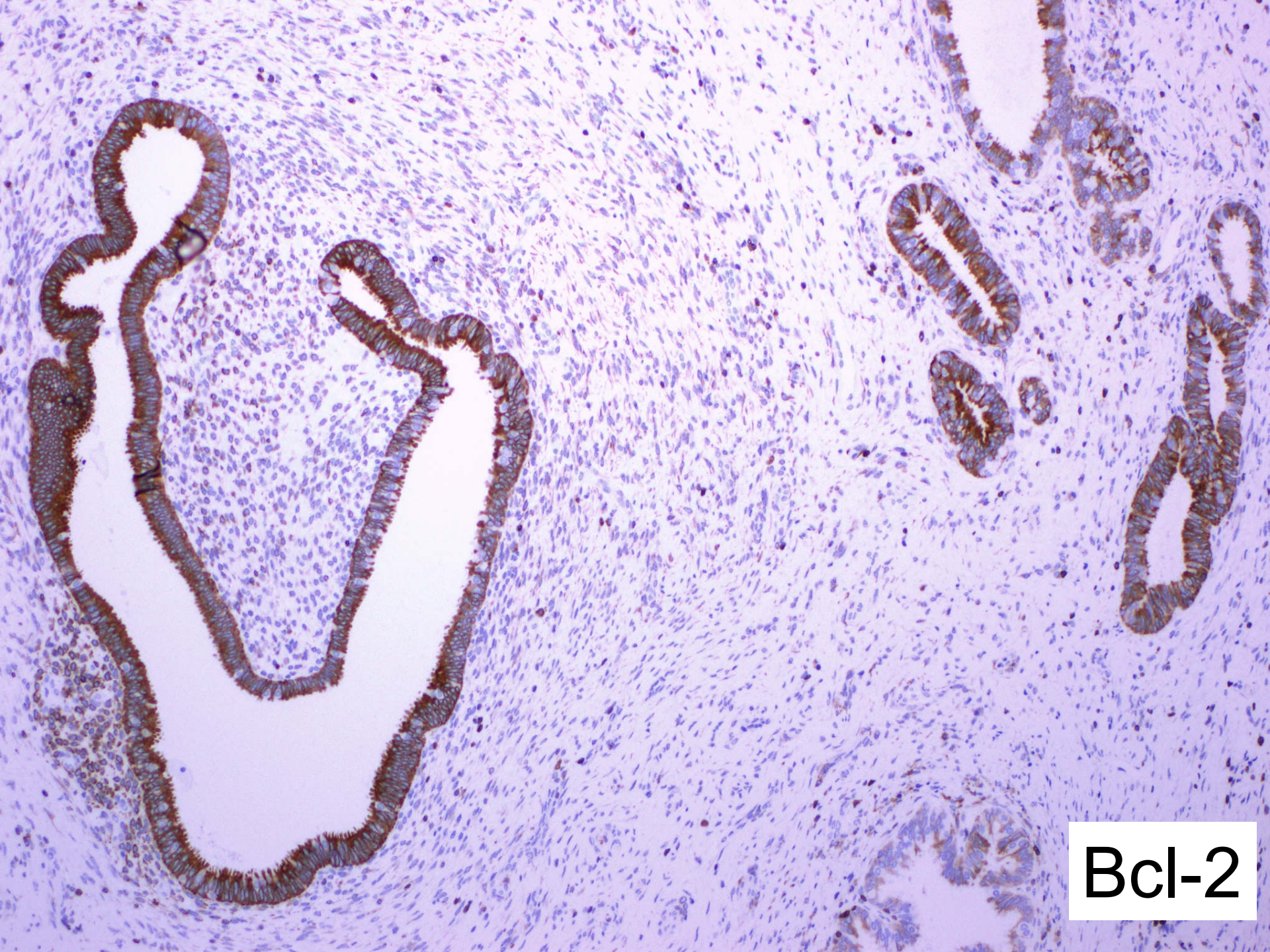


Ki-67

Tuboendometrioid metaplasia



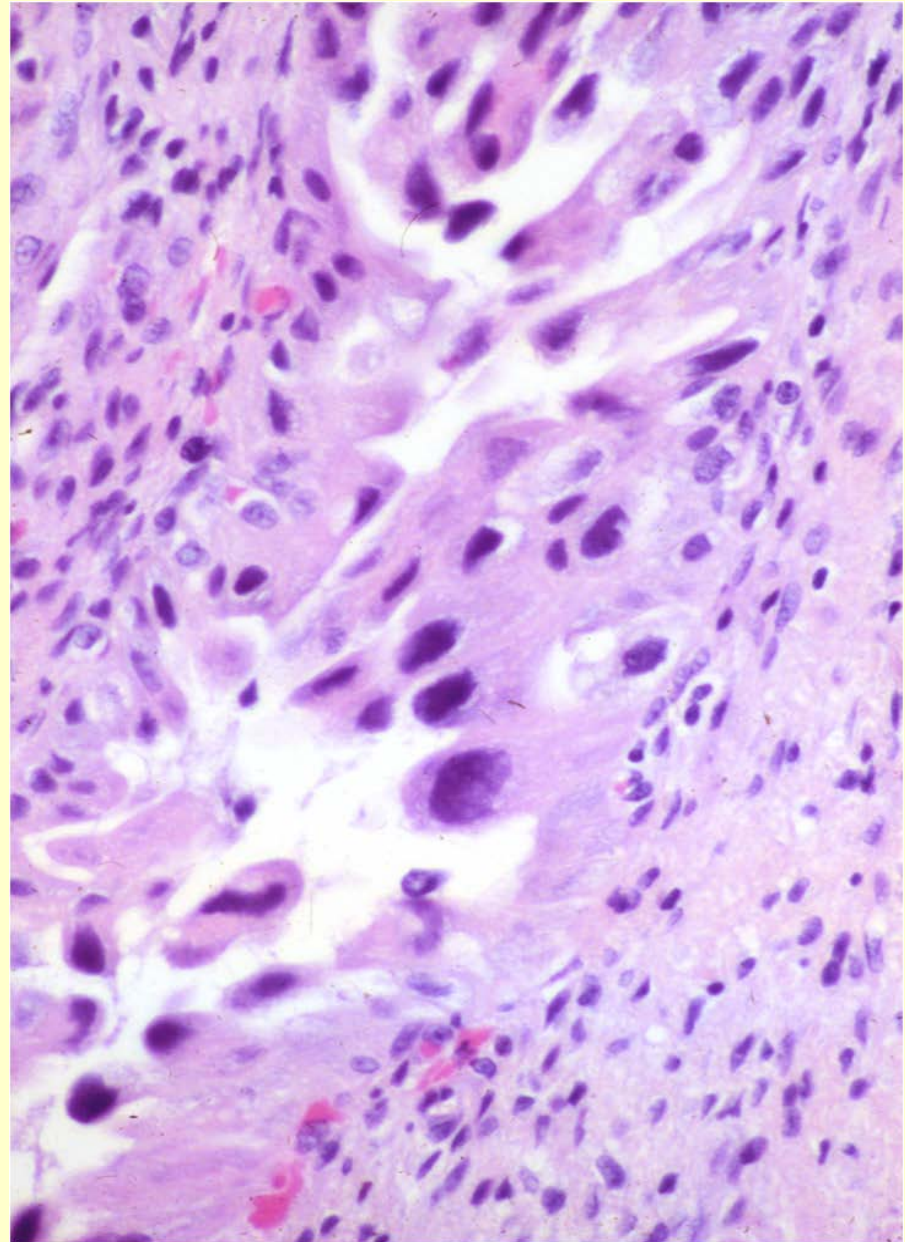
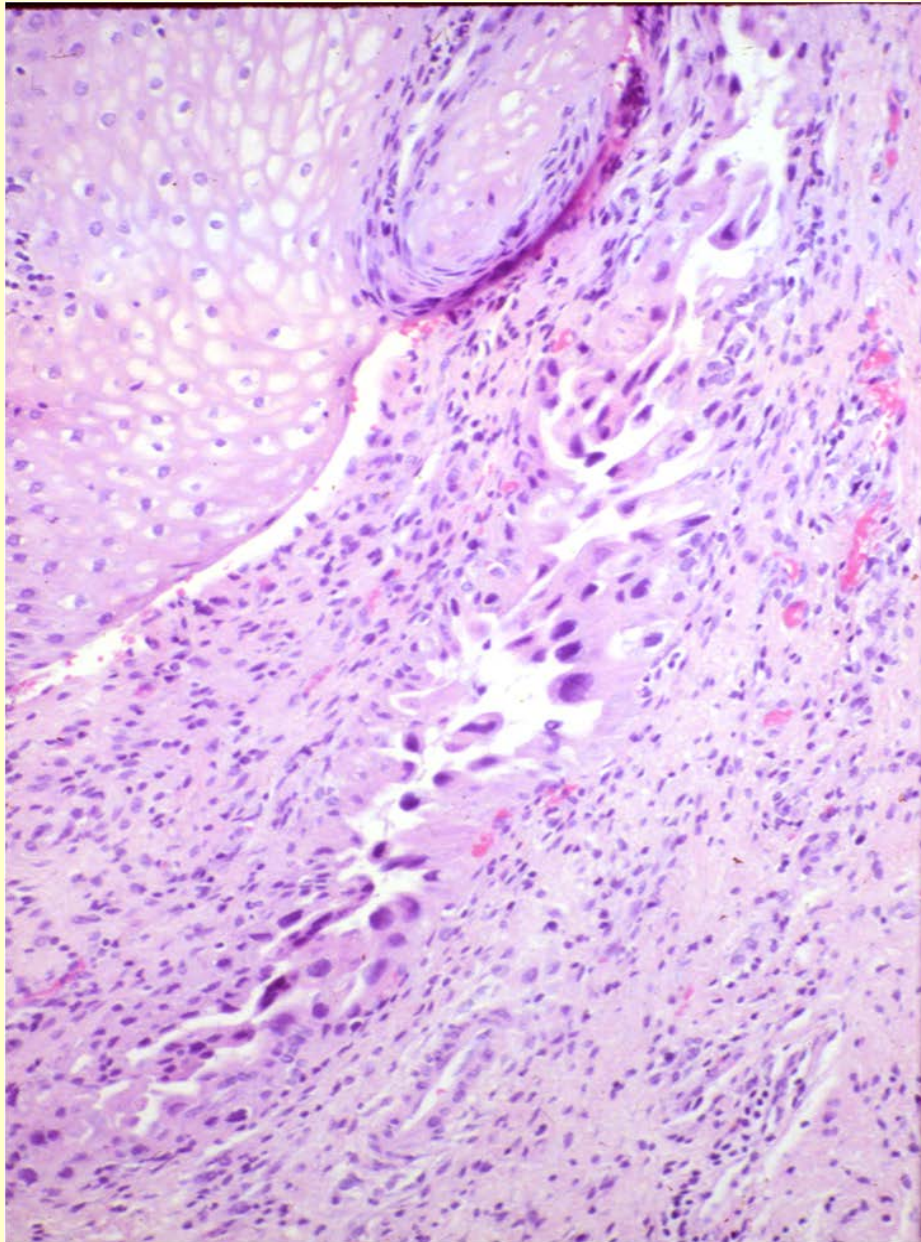
Adenocarcinoma in situ



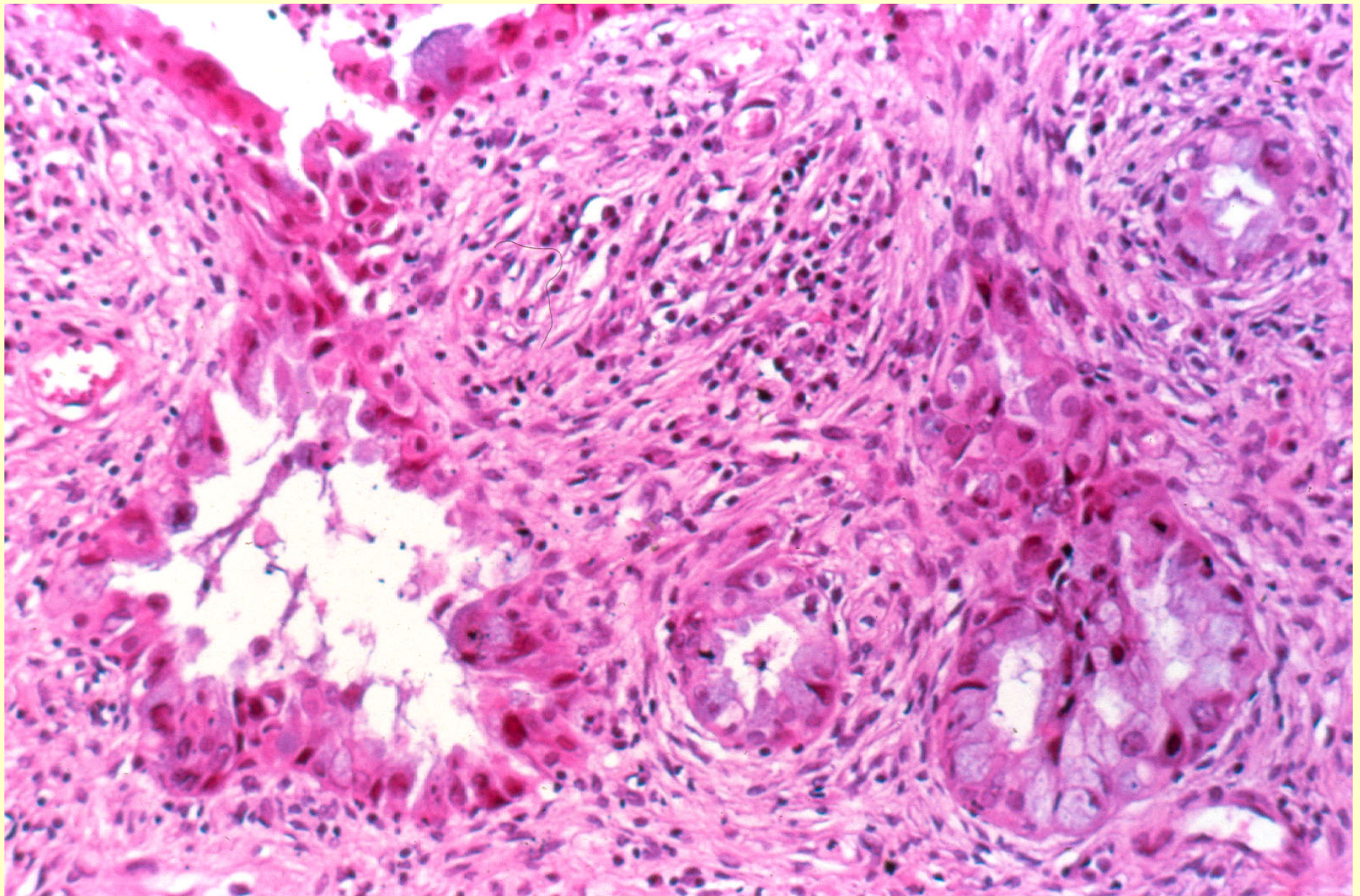
Bcl-2

Adenocarcinoma In Situ (AIS) (Differential Diagnosis)

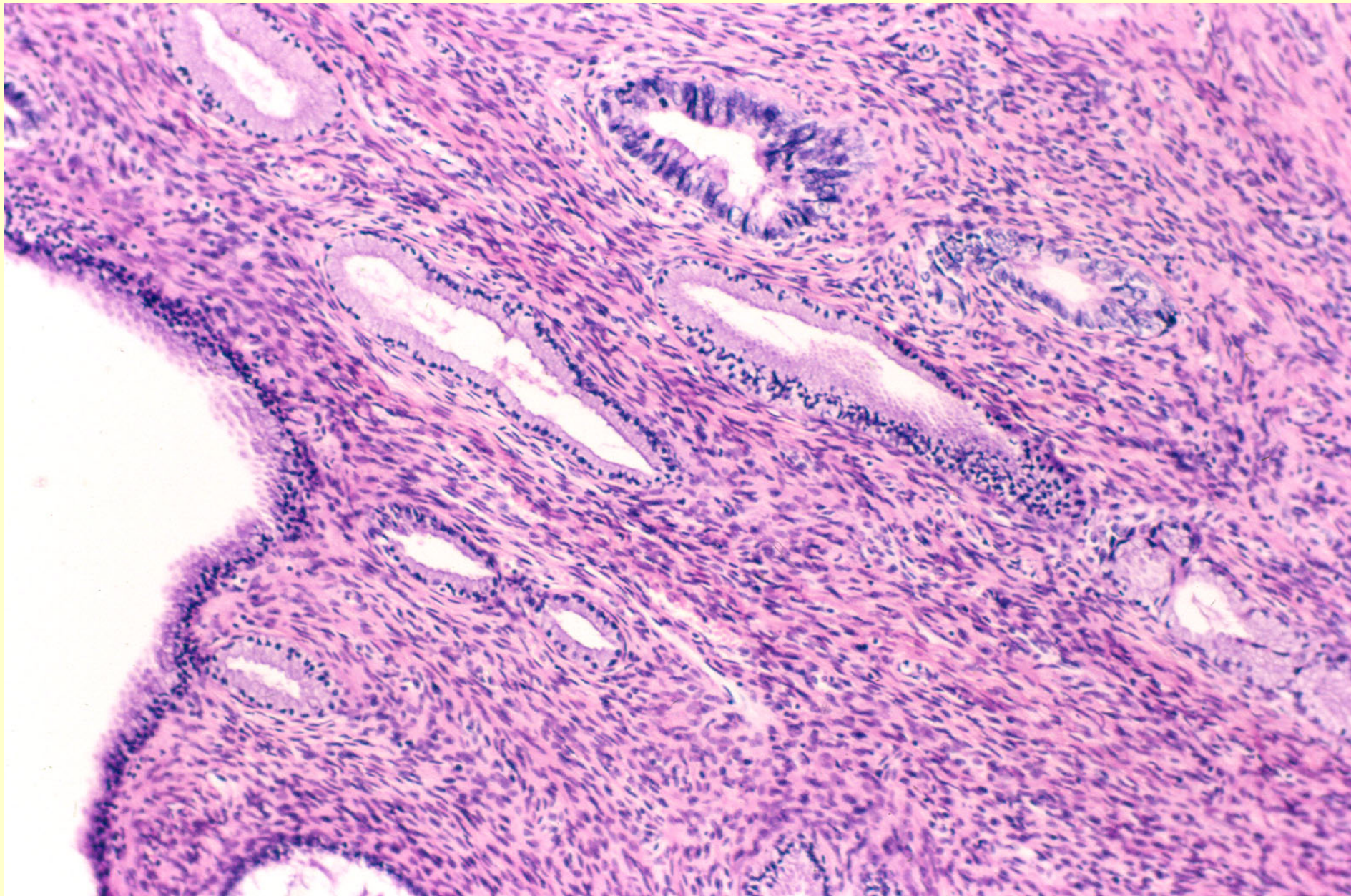
- Inflammation/repair
- Tubal metaplasia
- Endometriosis
- Arias-Stella
- Radiation effect
- Viral infections (CMV)



Arias-Stella Reaction



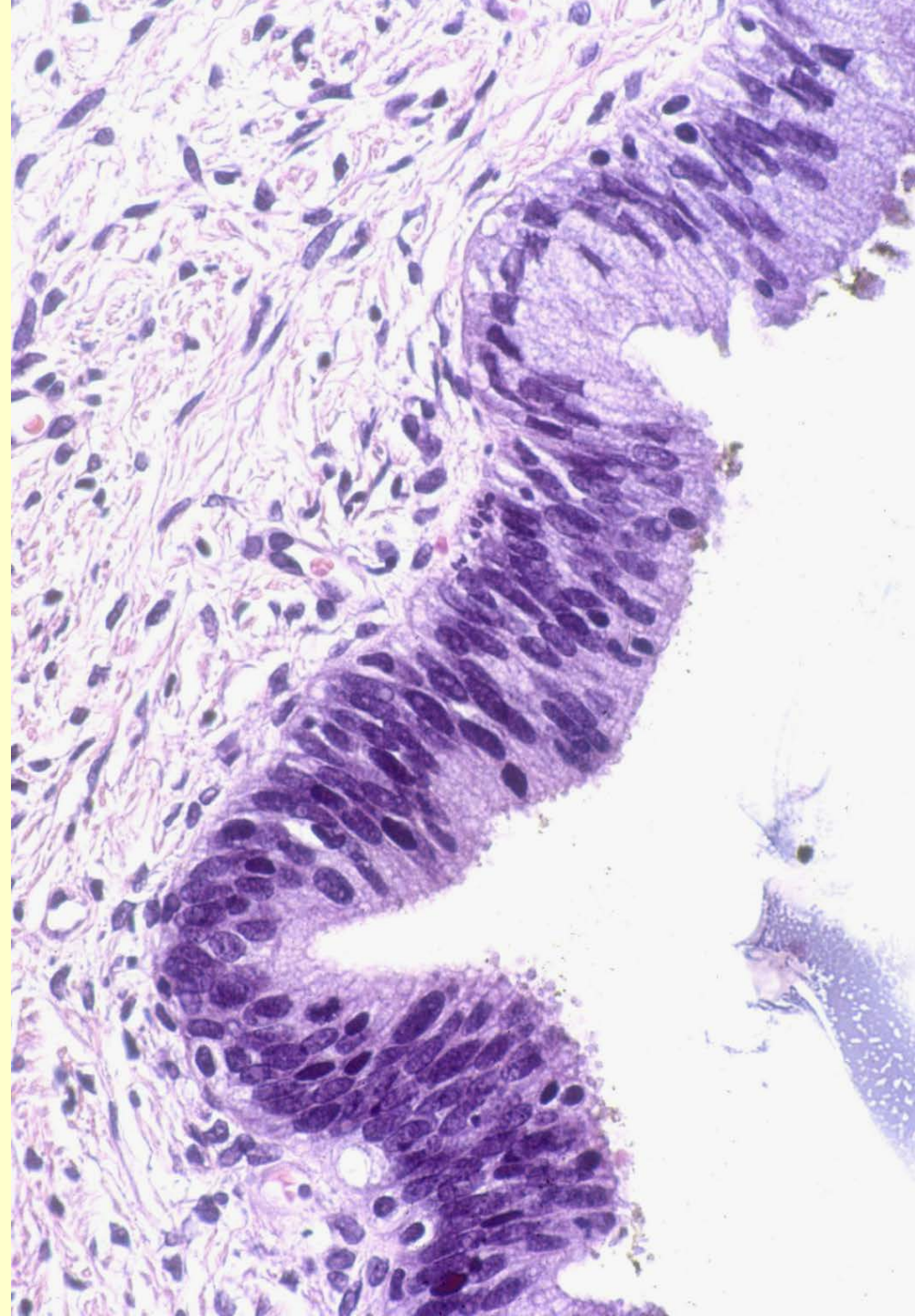
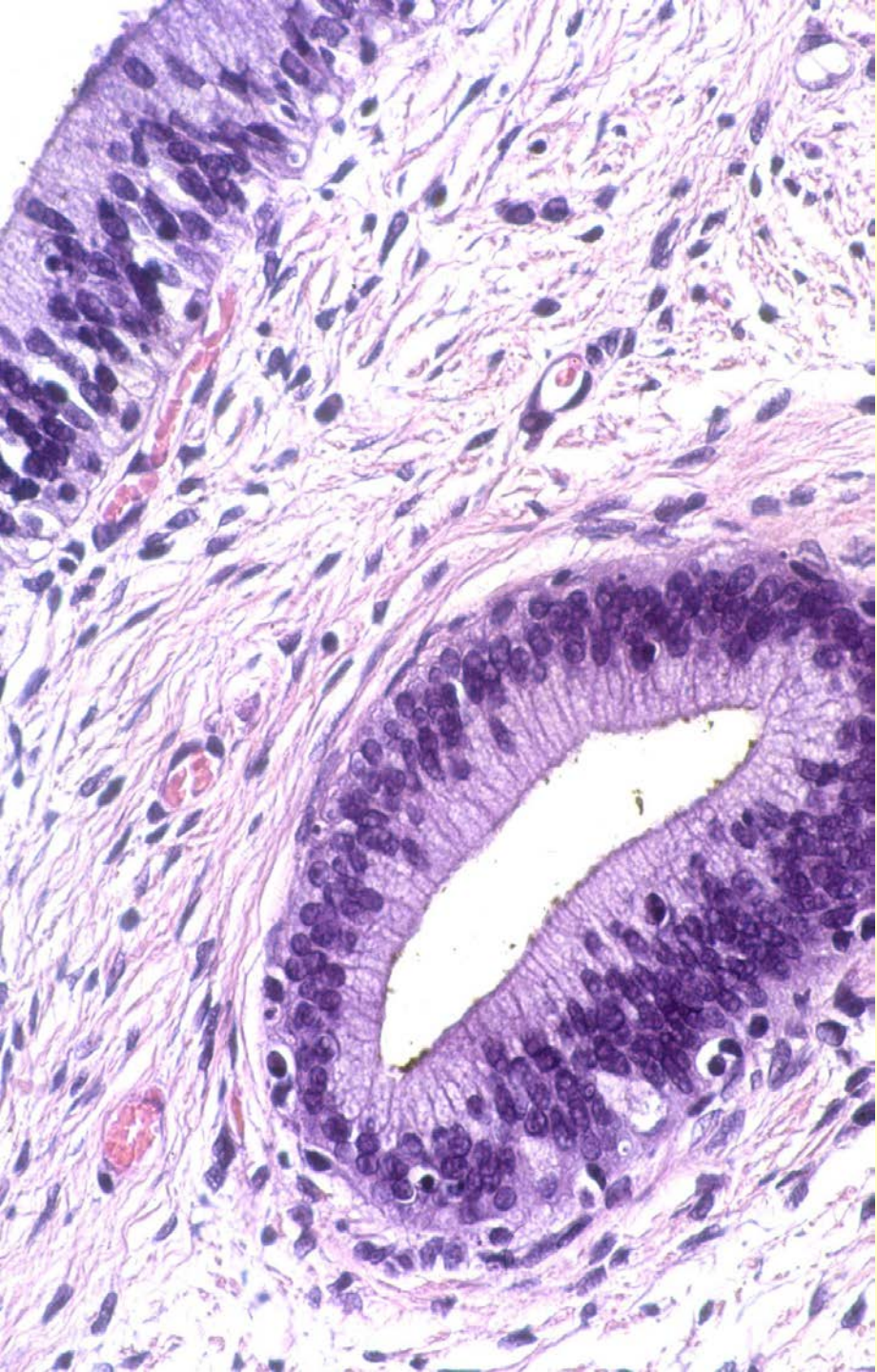
Radiation effect



Hysterectomy: residual AIS

Endocervical Gland Dysplasia

- Nebulous entity not universally accepted
- High variability on diagnostic criteria with no consistent reproducibility
- Clinical significance not established yet
- HPV-glandular precursors differs from HPV-squamous precursors
- There is no glandular LSIL-equivalent lesion



Cervical Adenocarcinoma

(Frequency)

1970	5%	of Ca Cx
2000	15-20%	of Ca Cx

Cervical Adenocarcinoma

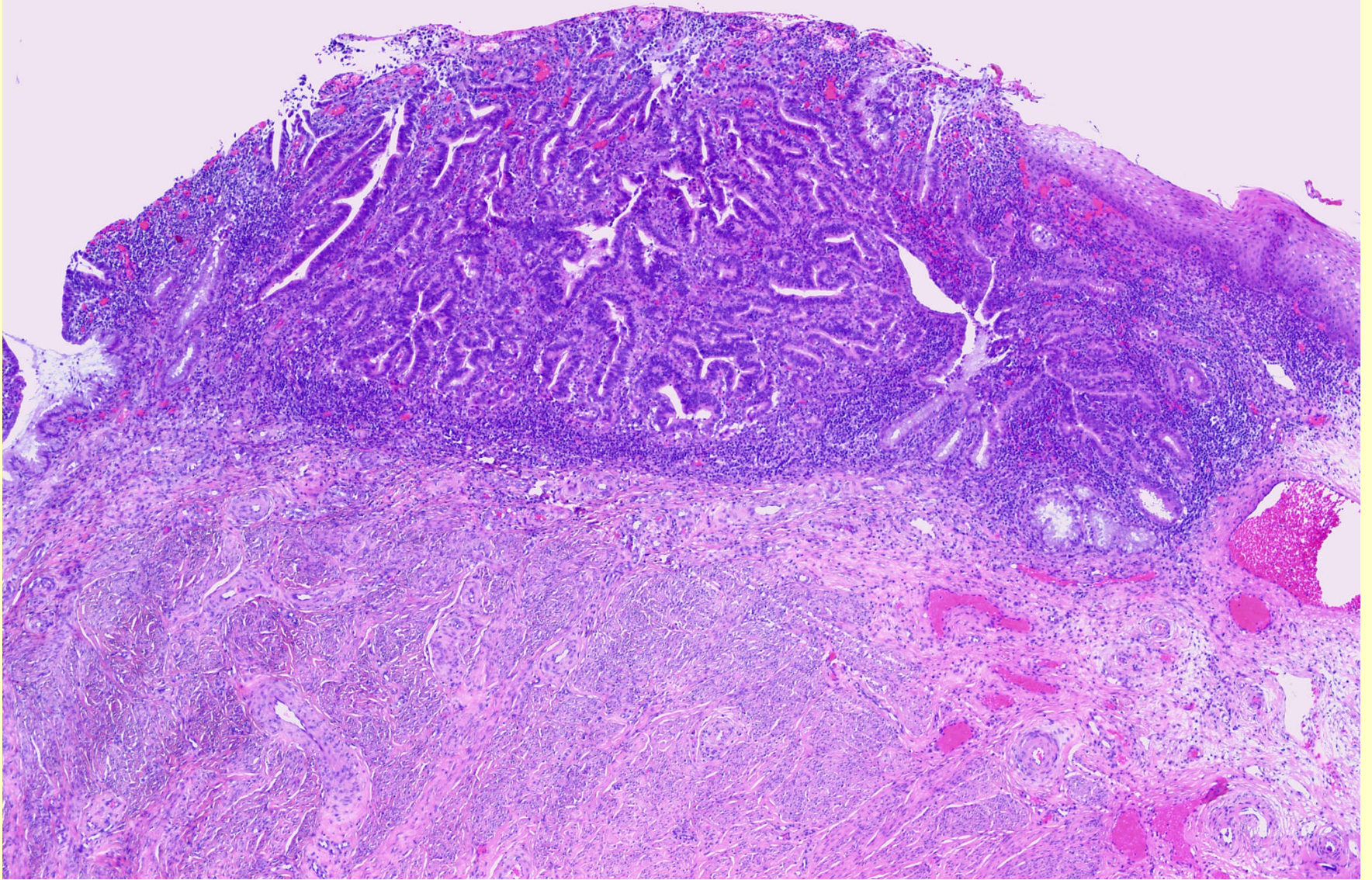
(Epidemiol & Pathogenesis)

- CIN (SIL): 60%
- hPV 16, 18, 31 (Adsq Ca: 80%)
- Oral Contraceptives (?)
- DES (Clear Cell Ca, 50s-60s)
- Peutz-Jeghers (Min Dev Adca)

Cervical Adenocarcinoma

(Clinical Features)

- Av Age 47-53 yrs
- Vaginal Bleed (80-90%)
- Asymptomatic (20%)
- Pap smears (49%)



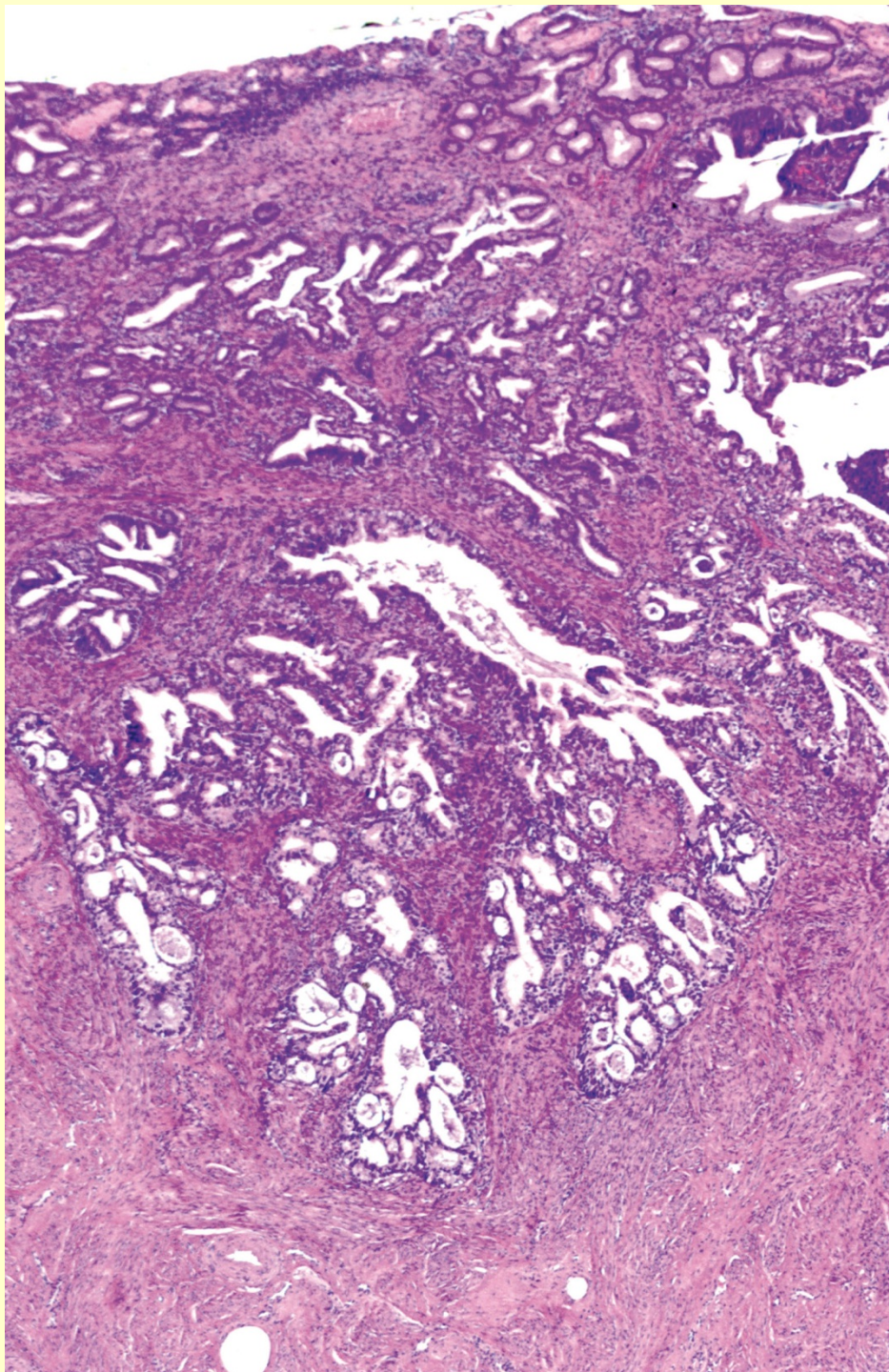
Superficially Invasive Adenocarcinoma

Microinvasive Adenoca (MIA)

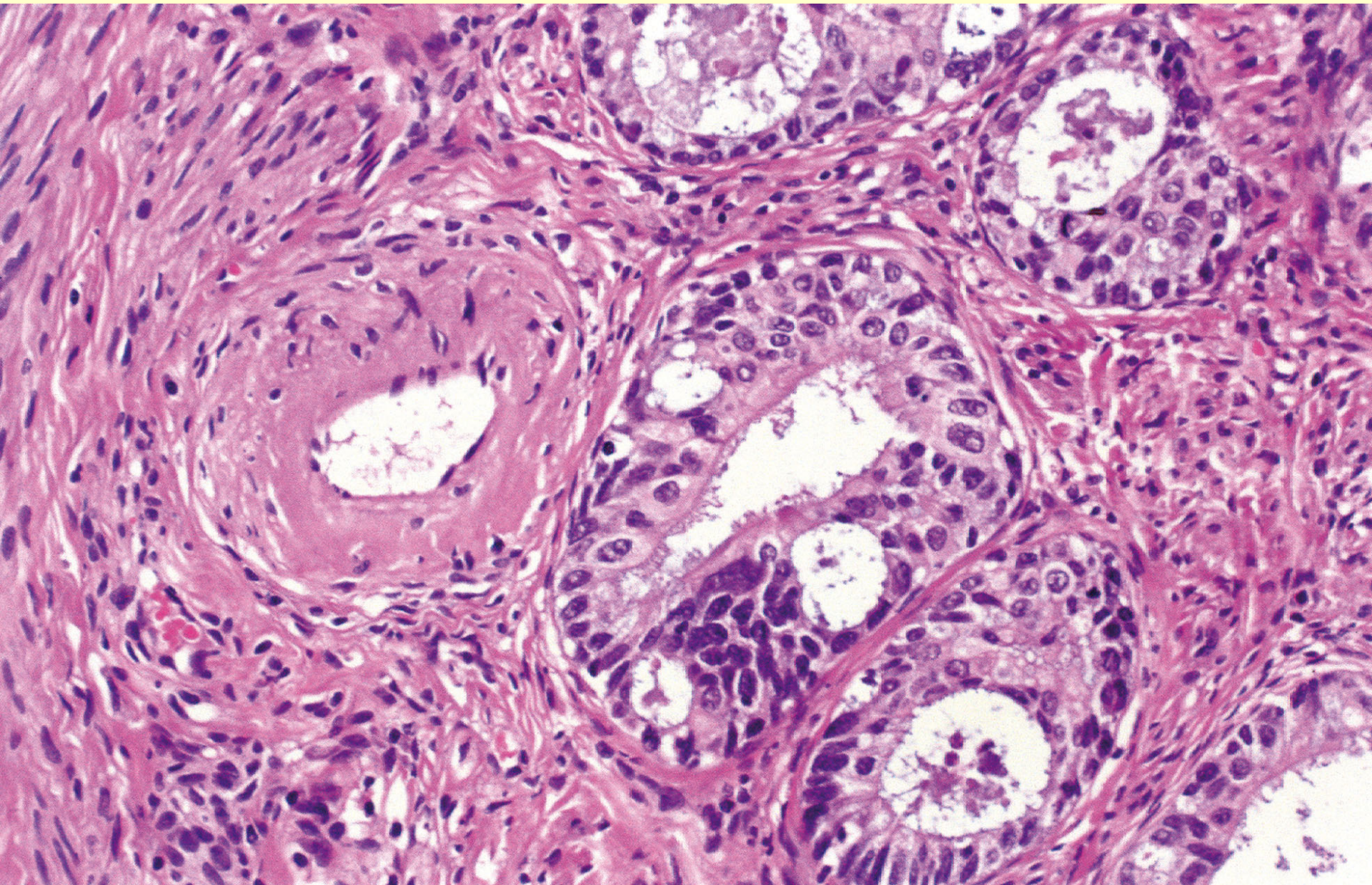
- Invasive adenocarcinoma small enough not to be associated with metastasis
- Conservative therapy is safe

Microinvasive Adenoca (MIA)

- MIA vs AIS
- Depth of invasion ≤ 5 mm
- Ext below nl endocx glands
- Stromal desmoplasia
- Dx: Cone/Hysterectomy
- 5/219 (2%) + Pelvic LN



Superficially
Invasive
(Microinvasive)
Adenocarcinoma



Superficially Invasive (Microinvasive) adenocarcinoma

Cervical Adenocarcinoma – WHO 2014

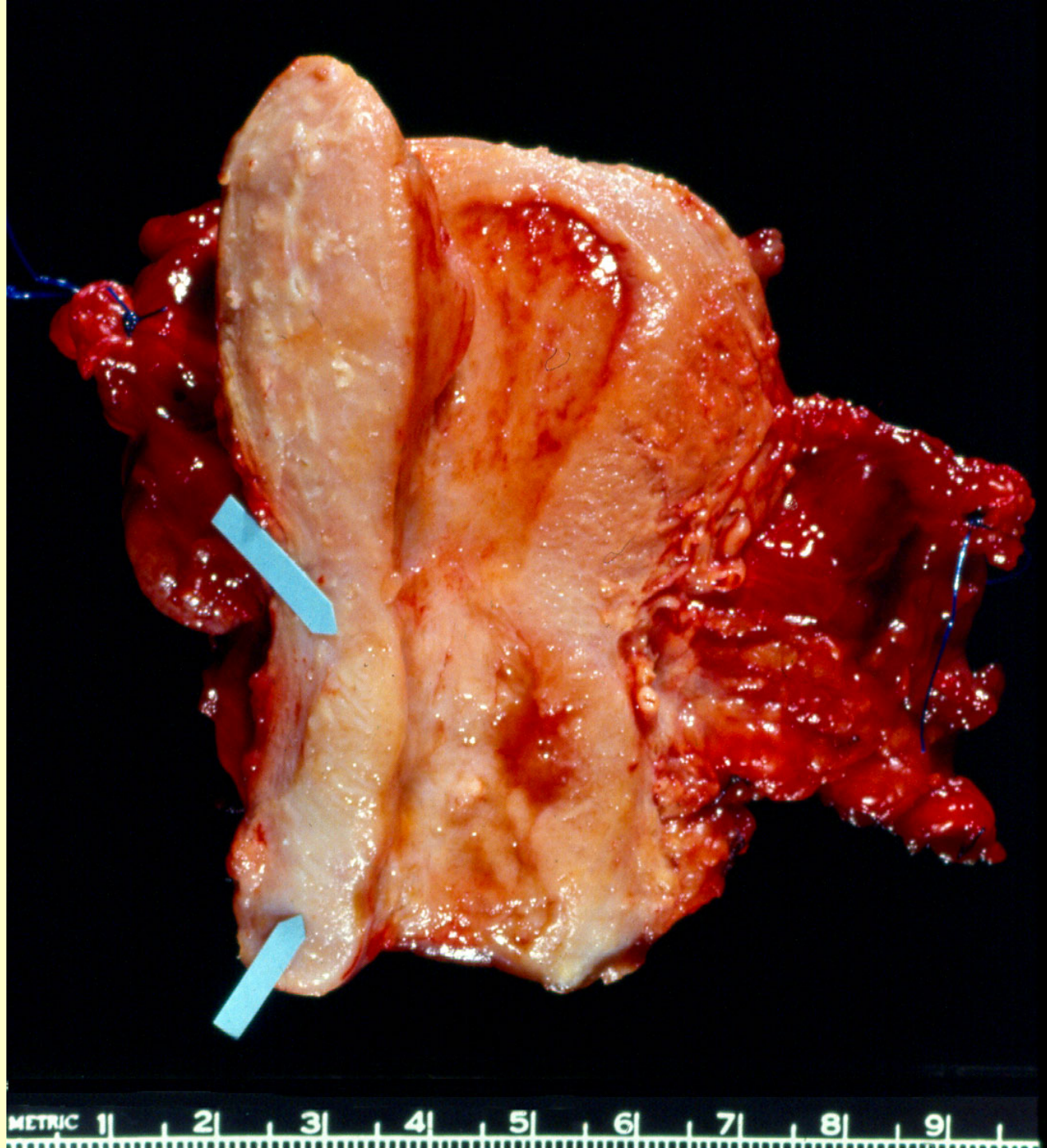
Adenocarcinoma

1. Endocervical adenocarcinoma (usual type)
2. Mucinous carcinoma NOS
 - Gastric type (minimal deviation adenocarcinoma, "adenoma" malignum)
 - Intestinal type
 - Signet-ring cell type
 - 3. Villoglandular carcinoma
4. Endometrioid carcinoma
5. Clear cell carcinoma
6. Serous carcinoma
7. Mesonephric carcinoma

Cervical Adenocarcinoma – WHO 2014

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Endocervical Adenocarcinoma (Usual type)

- Most common type (70%)
- Mod differentiated adenocarcinoma
- Papillae rarely conspicuous
- Prominent fibrous stroma

Original Article

**Invasive Endocervical Adenocarcinoma: Proposal for a
New Pattern-based Classification System With Significant
Clinical Implications: A Multi-institutional Study**

Andrea Diaz De Vivar, M.D., Andres A. Roma, M.D., Kay J. Park, M.D.,
Isabel Alvarado-Cabrero, M.D., Golnar Rasty, M.D., Jose G. Chanona-Vilchis, M.D.,
Yoshiki Mikami, M.D., Sung R. Hong, M.D., Brent Arville, D.O., Norihiro Teramoto, M.D.,
Rouba Ali-Fehmi, M.D., Joanne K.L. Rutgers, M.D., Farah Tabassum, M.D.,
Denise Barbuto, M.D., Irene Aguilera-Barrantes, M.D., Alexandra Shaye-Brown, M.D.,
Dean Daya, M.D., and Elvio G. Silva, M.D.

TABLE 1. *Proposed new classification system for invasive endocervical adenocarcinomas based on pattern of invasion (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 lymph-vascular invasion
- Well or moderate differentiation

Pattern B

- Early destructive stromal invasion arising from well-demarcated glands (Pattern A-like glands)
- ± Lymph-vascular invasion

Pattern C

- Diffuse destructive invasion
-

Invasive Endocervical Adenocarcinoma

(Classification based on pattern of invasion)

Pattern A

Well demarcated glands, rounded contours, groups

No desmoplastic reaction, no single cells

Complex glands, cribriform, papillae

No LVSI

Well-moderate diff

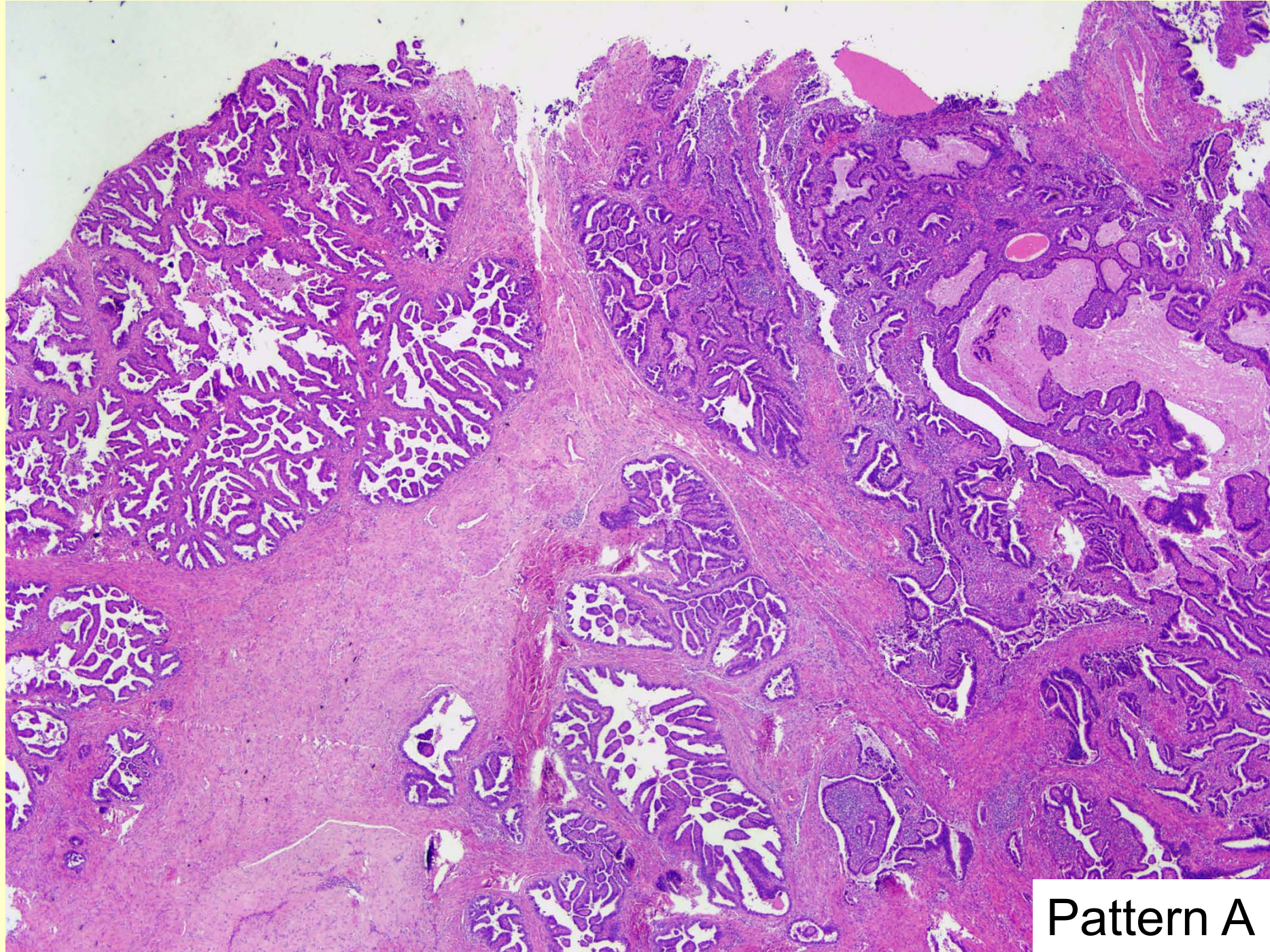
Pattern B

Early destructive invasion arising from well
demarcated glands (Pattern A)

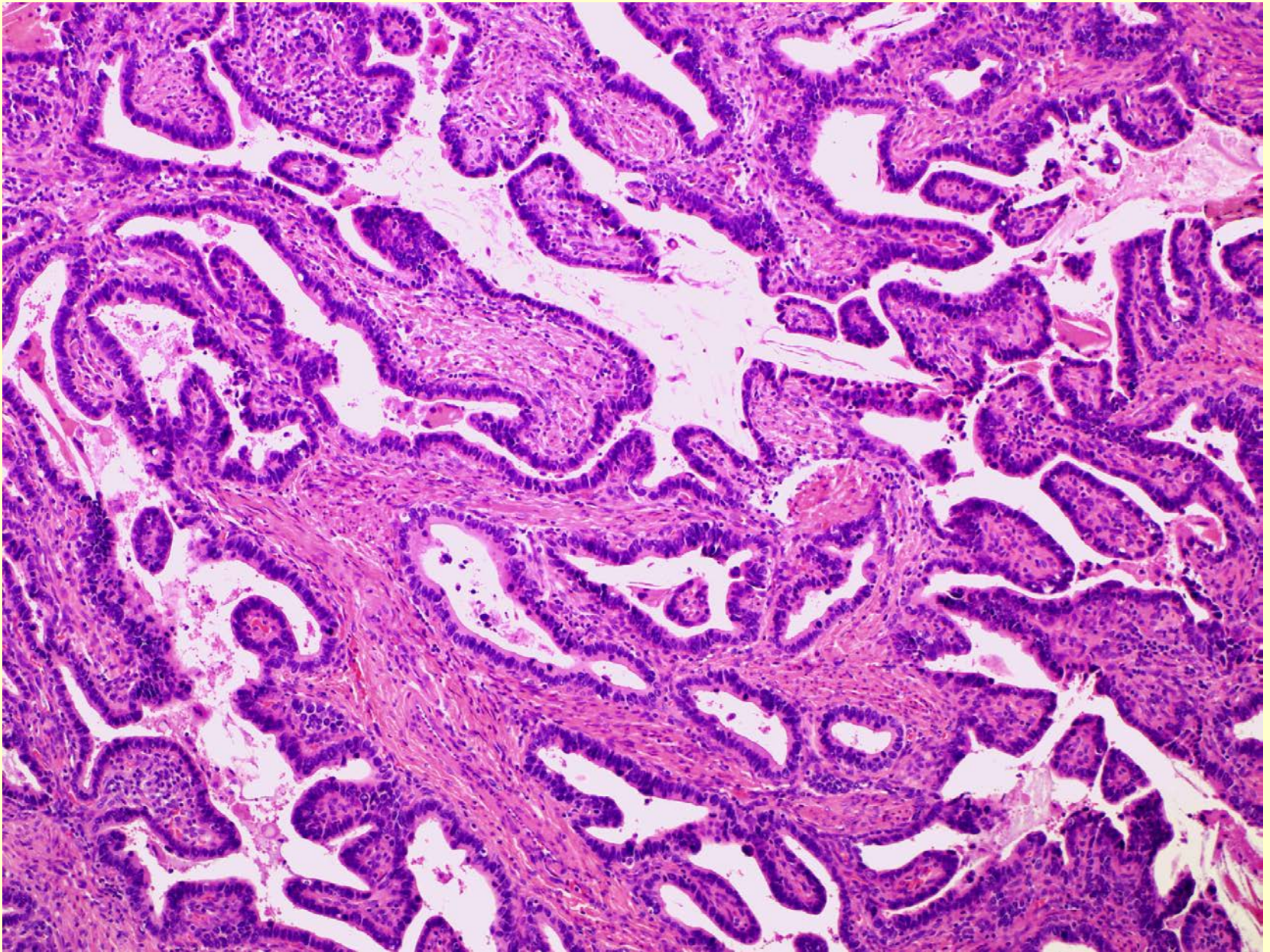
Pattern C

Diffuse destructive invasion

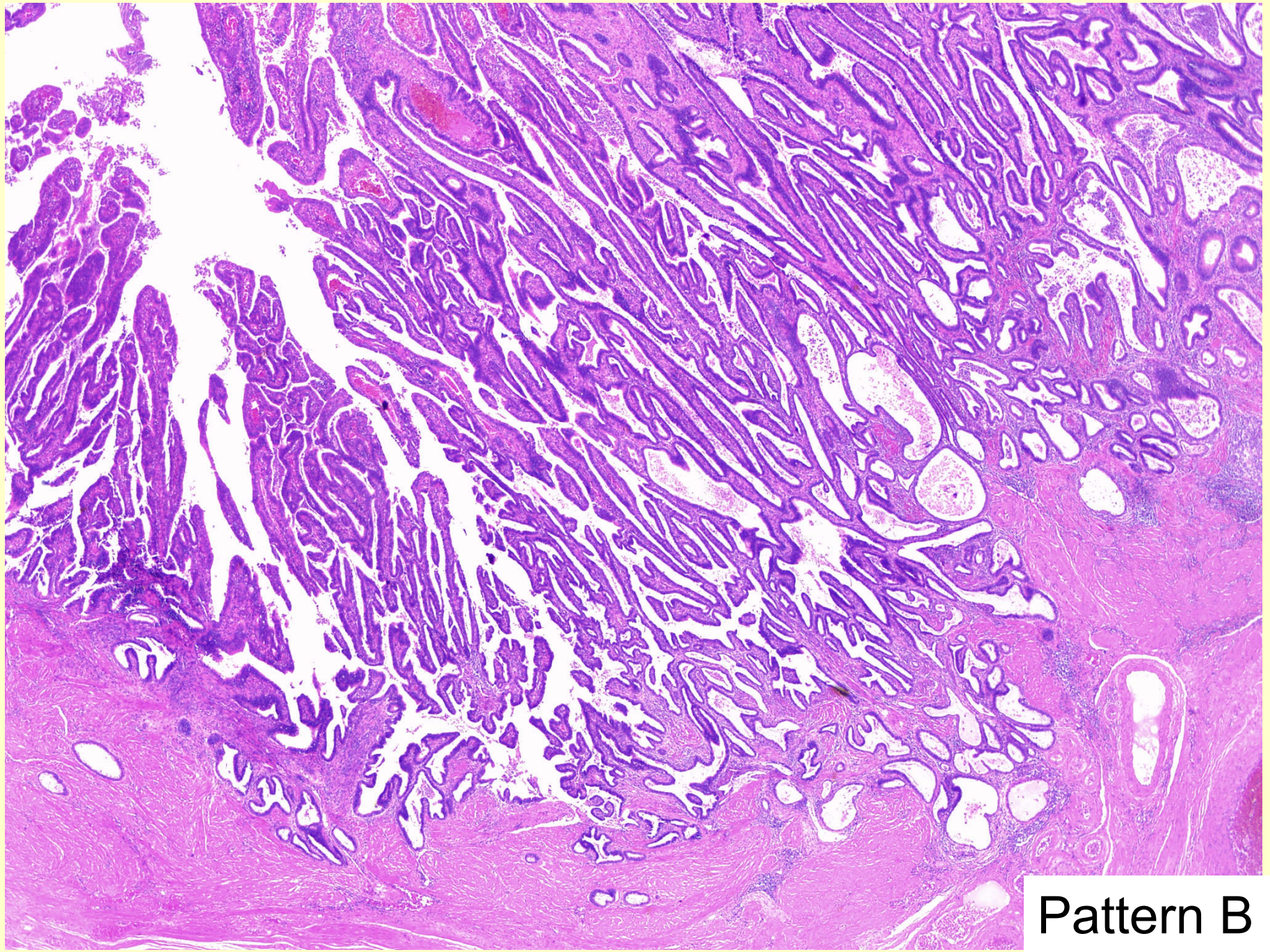
Diaz de Vivar A, et al.
IJGP 2013;32:592



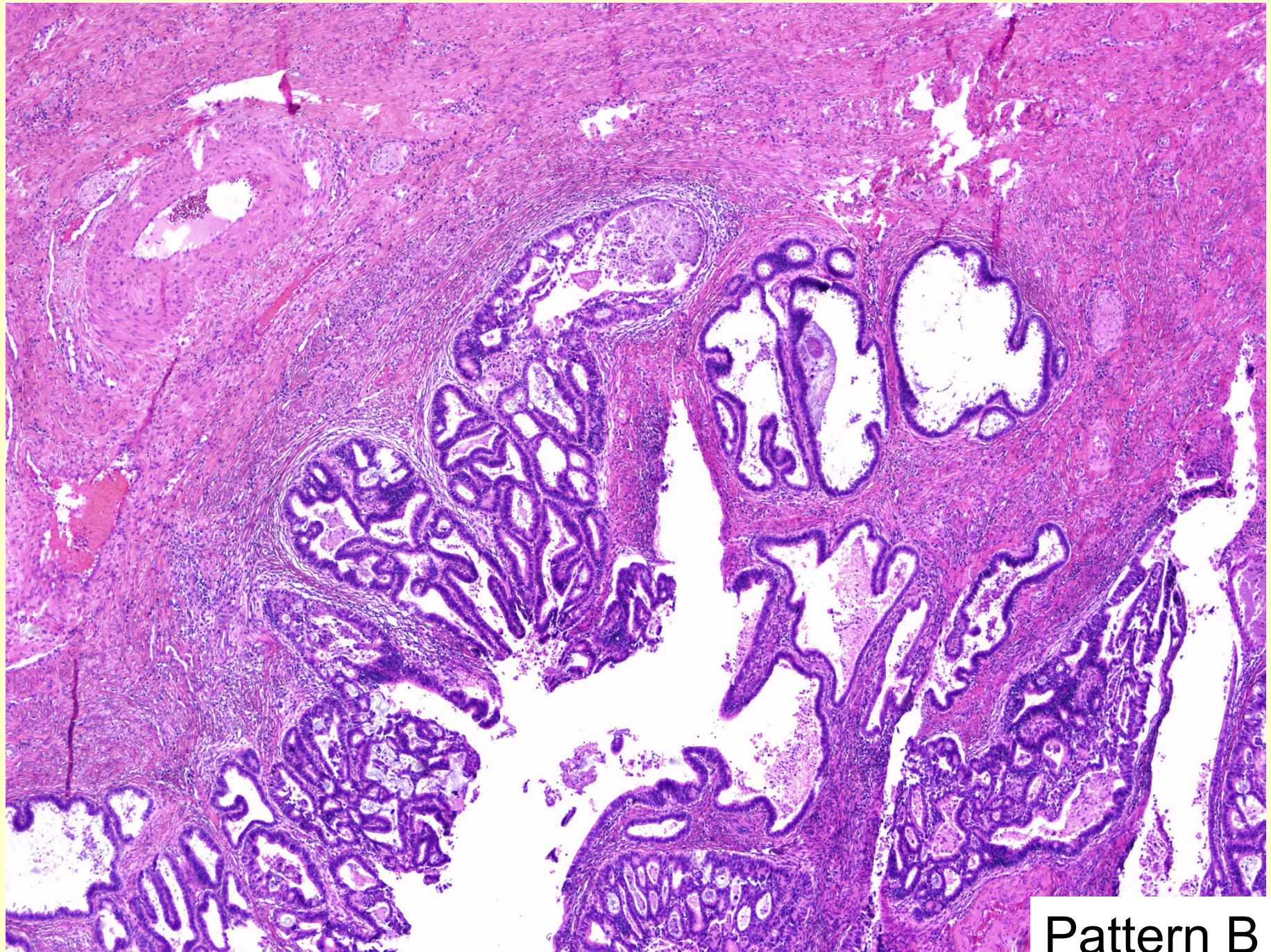
Pattern A



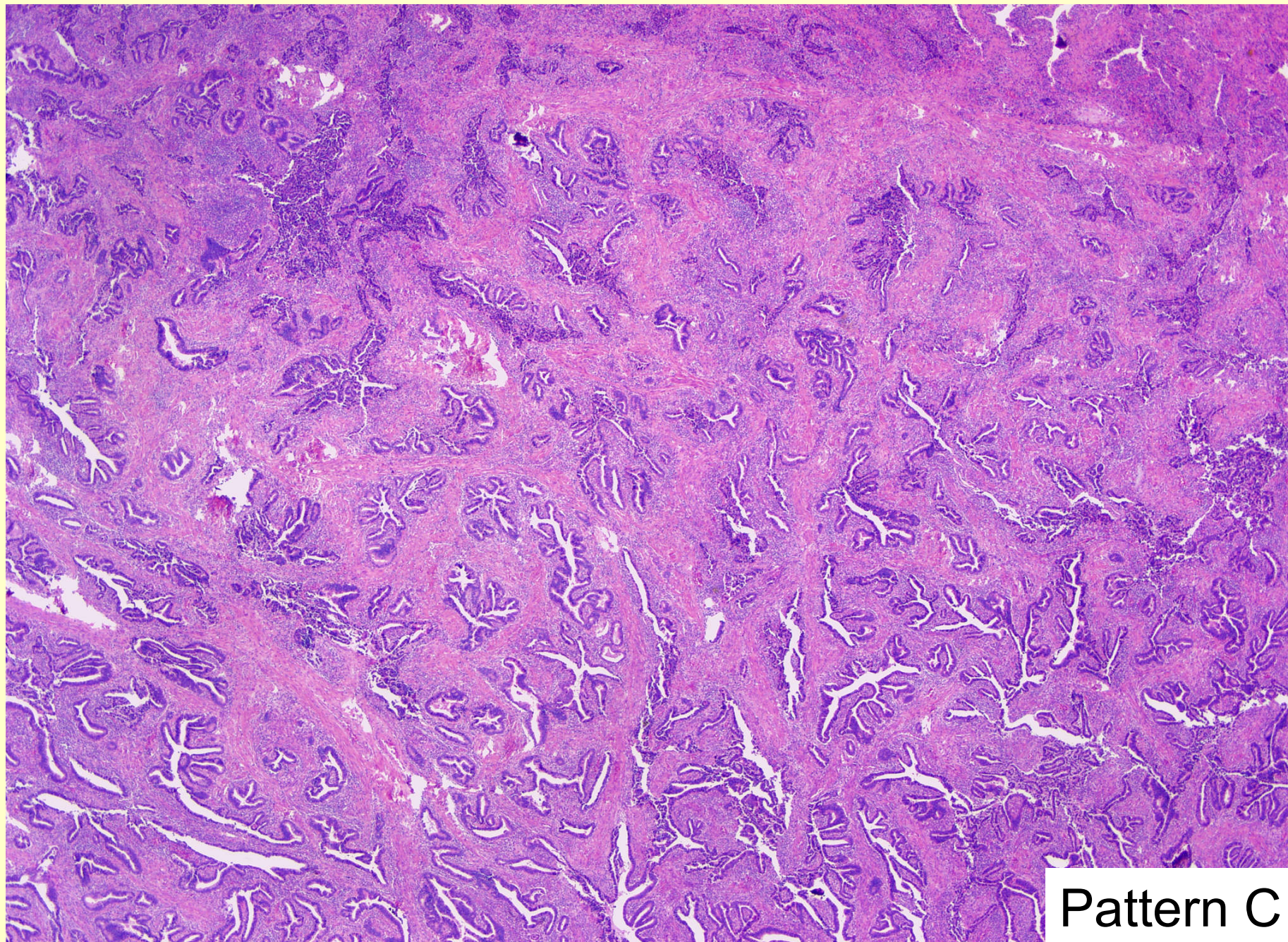
Endocervical adenocarcinoma – Usual type – Pattern A



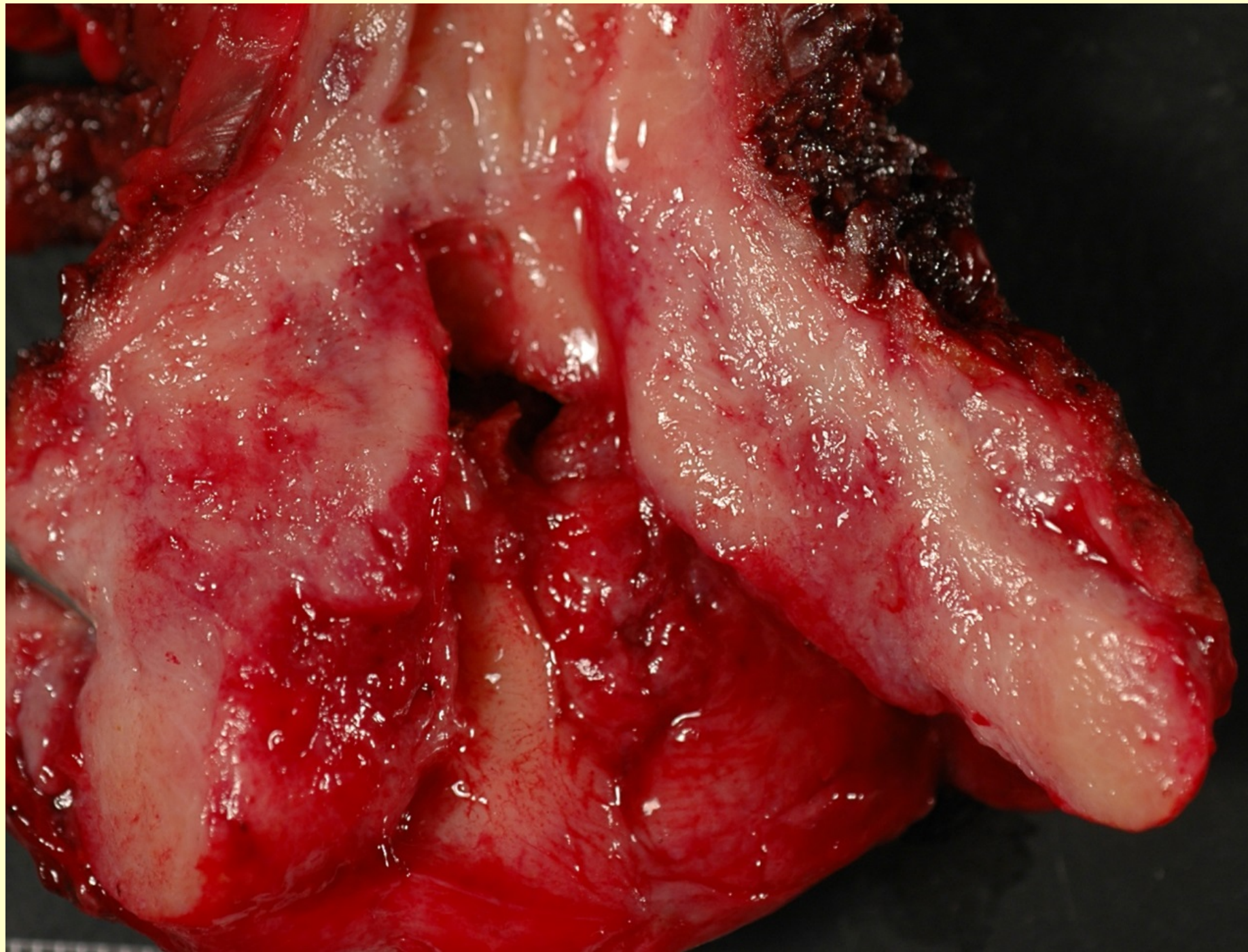
Pattern B

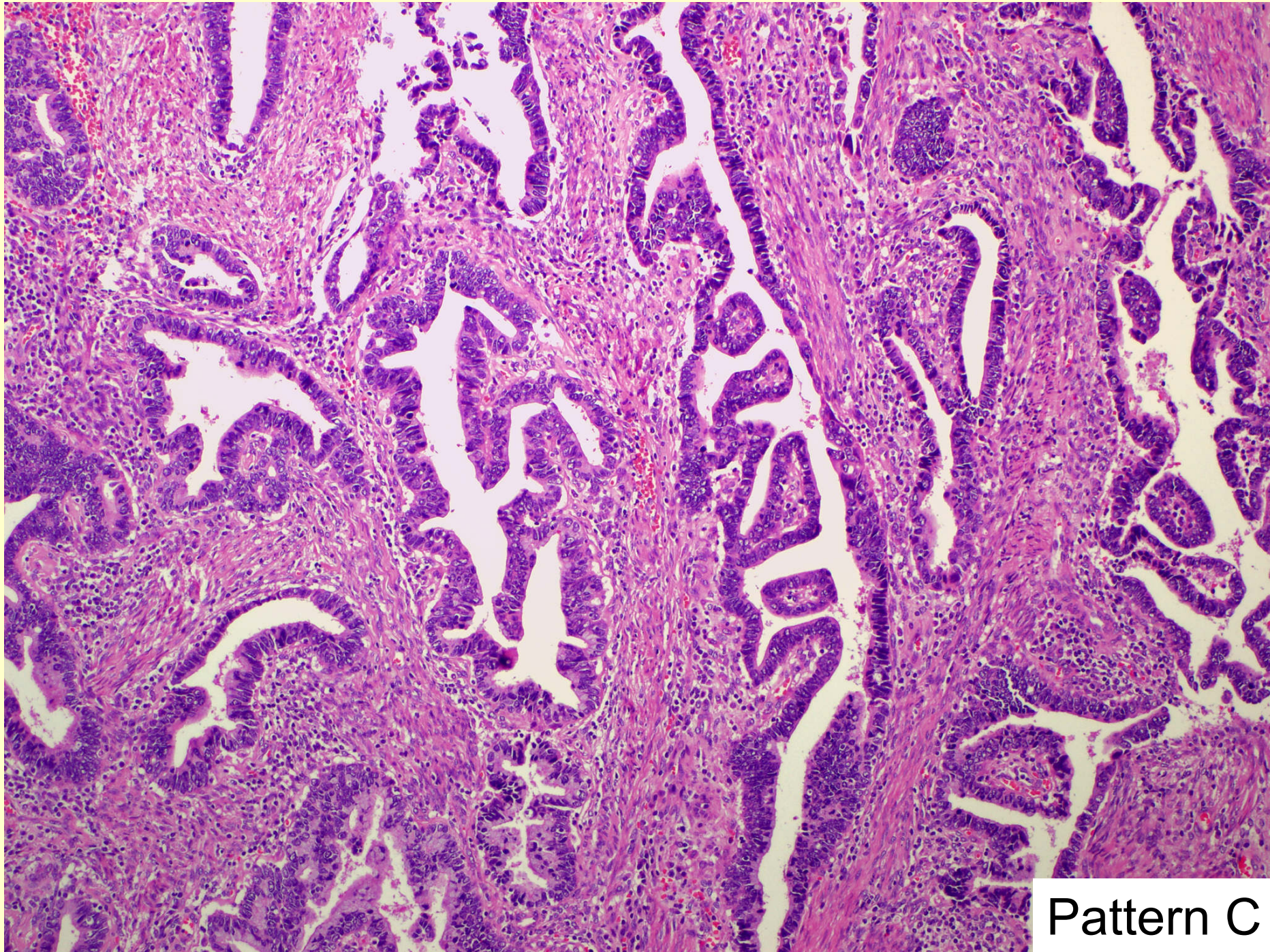


Pattern B



Pattern C





Pattern C

TABLE 2. Outcome data comparing the standard method of tumor evaluation (depth of invasion) versus the newly proposed pattern-based method

Method	N	DOI (mean in mm)	Patients with (+) LN	Total (+) LN/total resected LN	Recurrences	DOD	Stage I	Stages II–IV
Standard	352 (100%)	6.7	49 (13.9%)	78/6506	39 (11.4%)*	16 (4.6%)*	311 (88.3%)	41 (11.7%)
Pattern A	73 (20.7%)	3.8	0 (0%)	0/1333	0 (0%)	0 (0%)	73 (100%)	0 (0%)
Pattern B	90 (25.6%)	4.0	4 (4.4%)	5/1750	1 (1.2%)*	0 (0%)	86 (95.6%)	4 (4.4%)
Pattern C	189 (53.7%)	9.2	45 (23.8%)	73/3423	38 (22.1%)*	16 (8.8%)*	152 (80.4%)	37 (19.6%)

*Percentages from available outcomes.

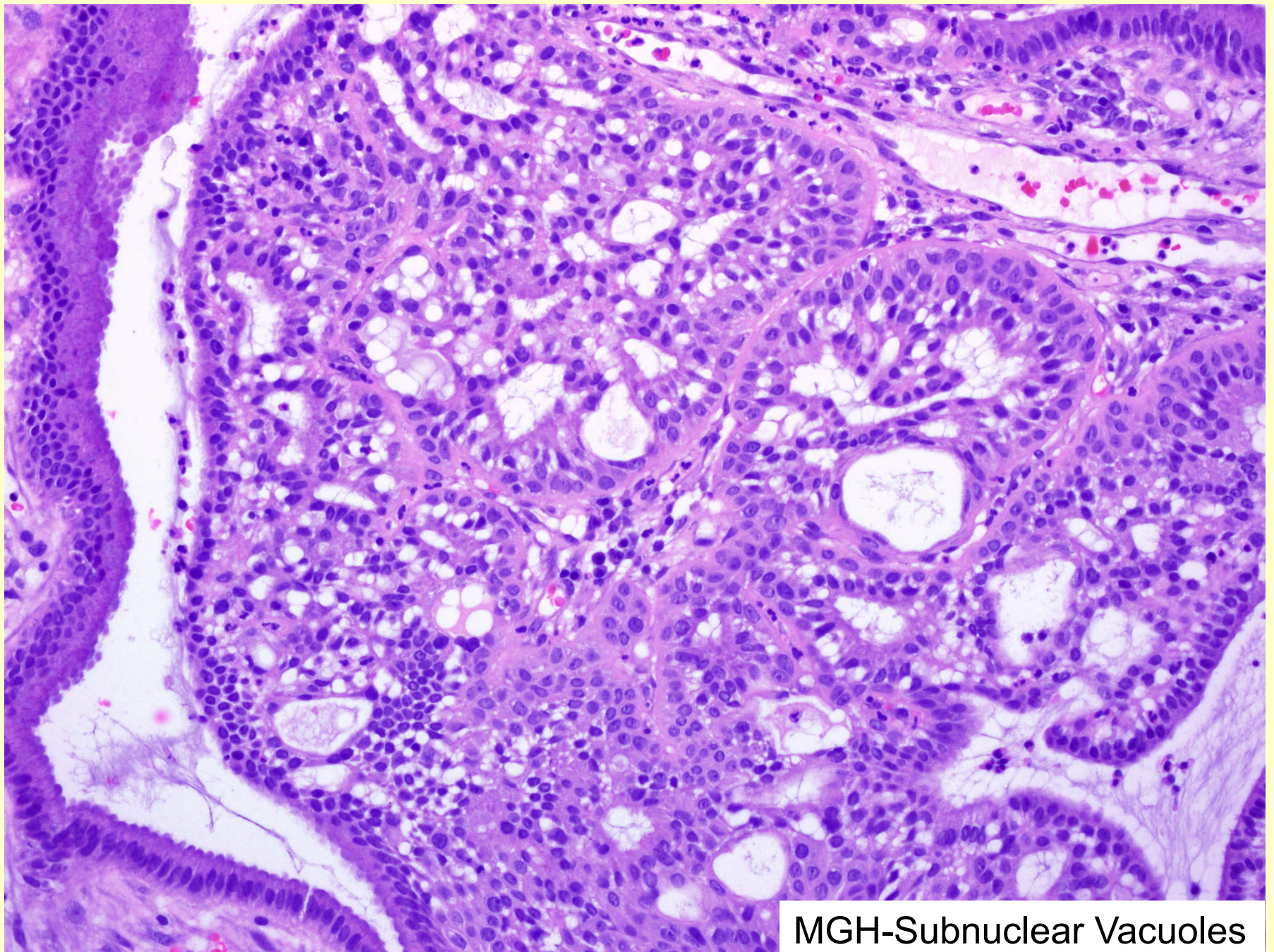
LN metastases: $P < 0.001$ comparing Pattern A with B/C; $P < 0.05$ comparing Pattern A with B; $P < 0.0001$ comparing Pattern A with C.

Stage I versus II or higher: $P < 0.005$ comparing Pattern A with B/C; $P = 0.147$ comparing Pattern A with B; $P < 0.0001$ comparing Pattern A with C.

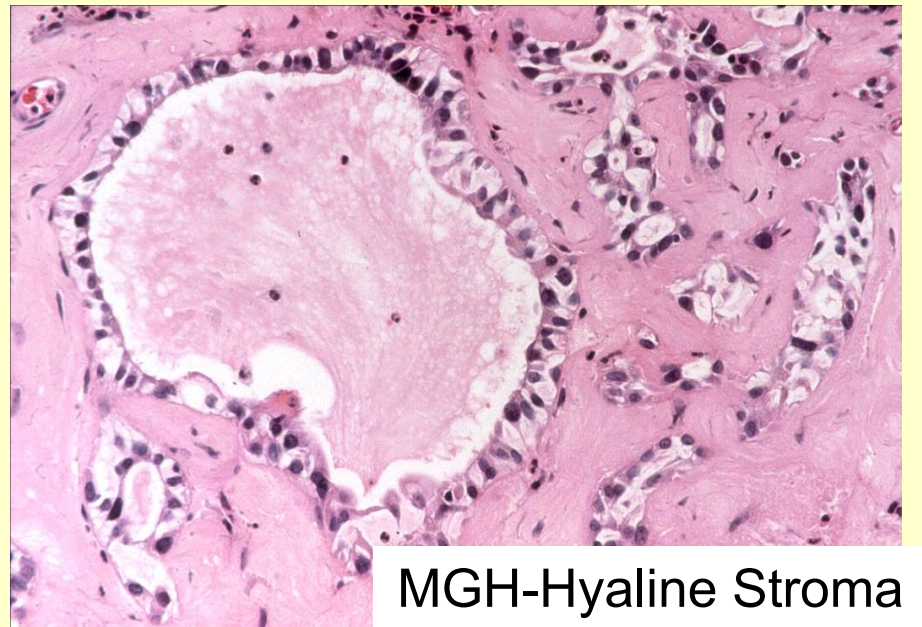
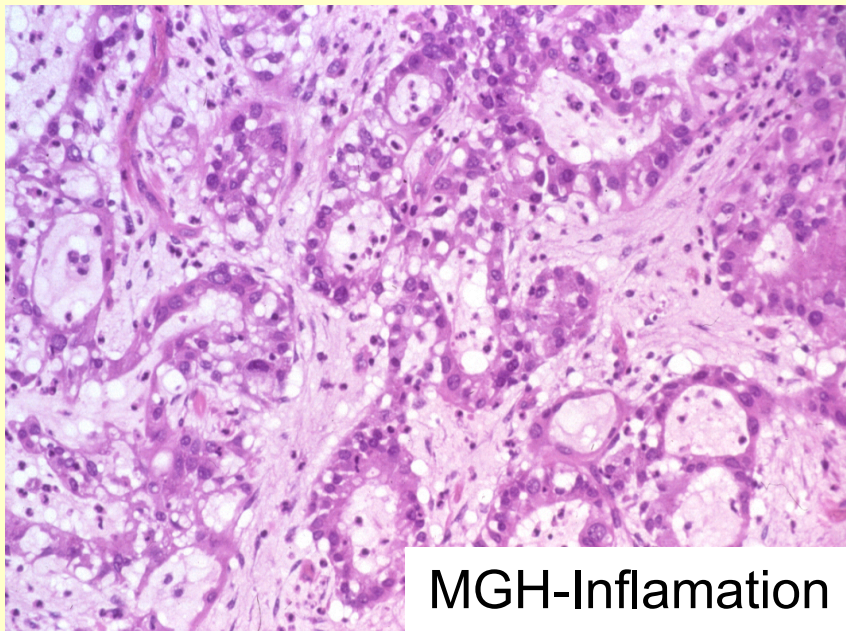
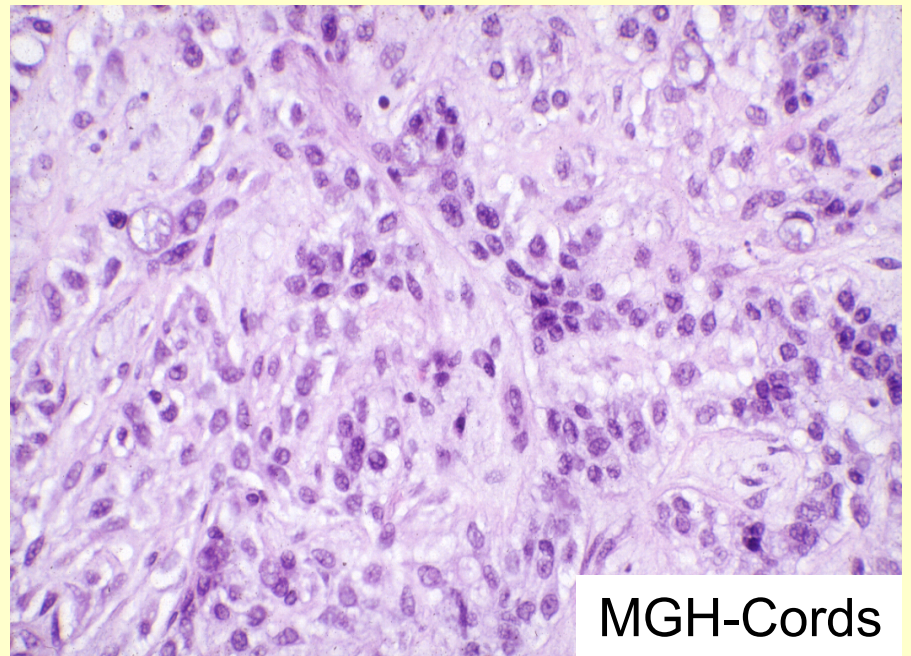
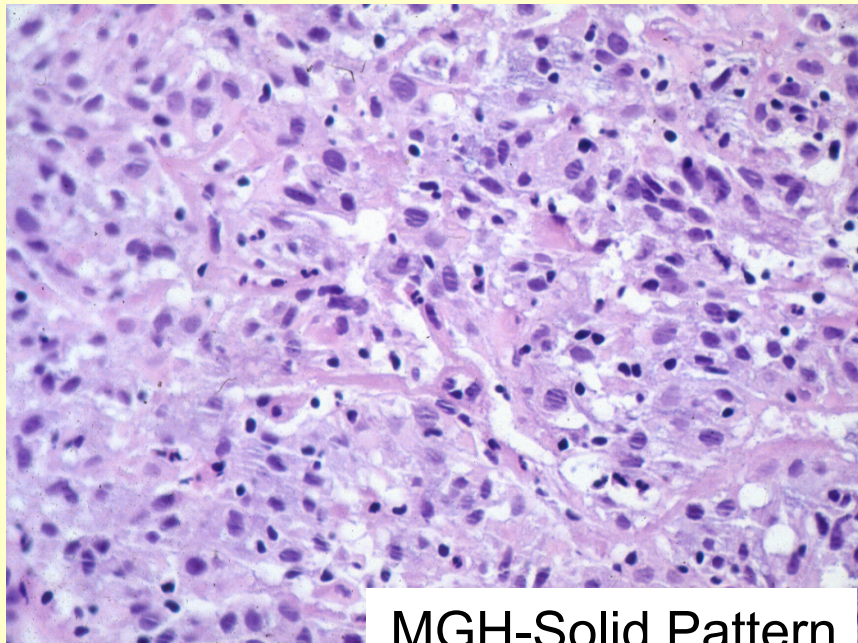
DOD indicates died of disease; DOI, depth of invasion; LN, lymph node/s.

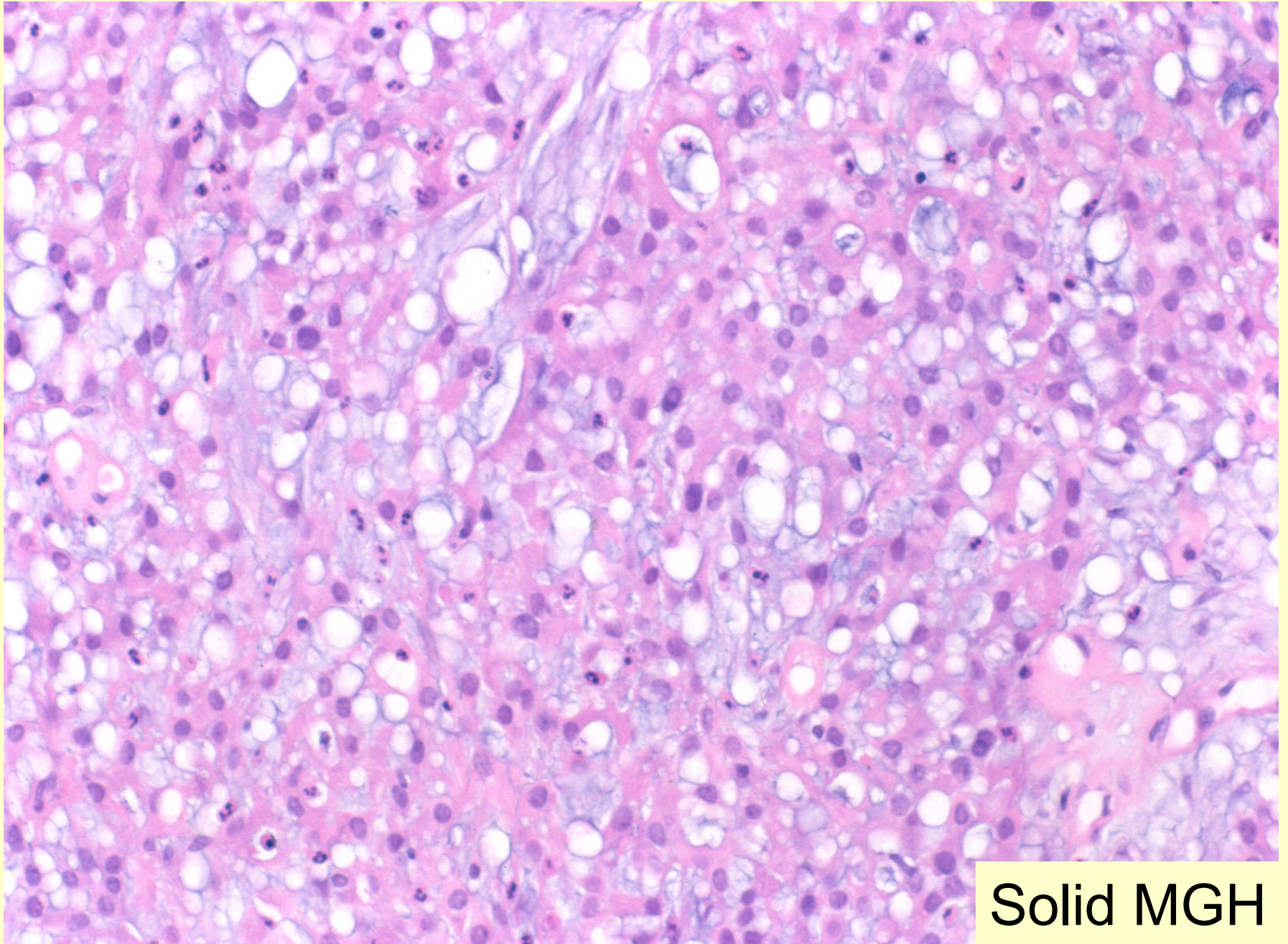
Cervical Adenocarcinoma (Differential Diagnosis)

- Microglandular hyperplasia
- Lobular endocervical glandular hyperplasia (LEGH)
- Mesonephric remnants
- Cervical extension of endometrial carcinoma

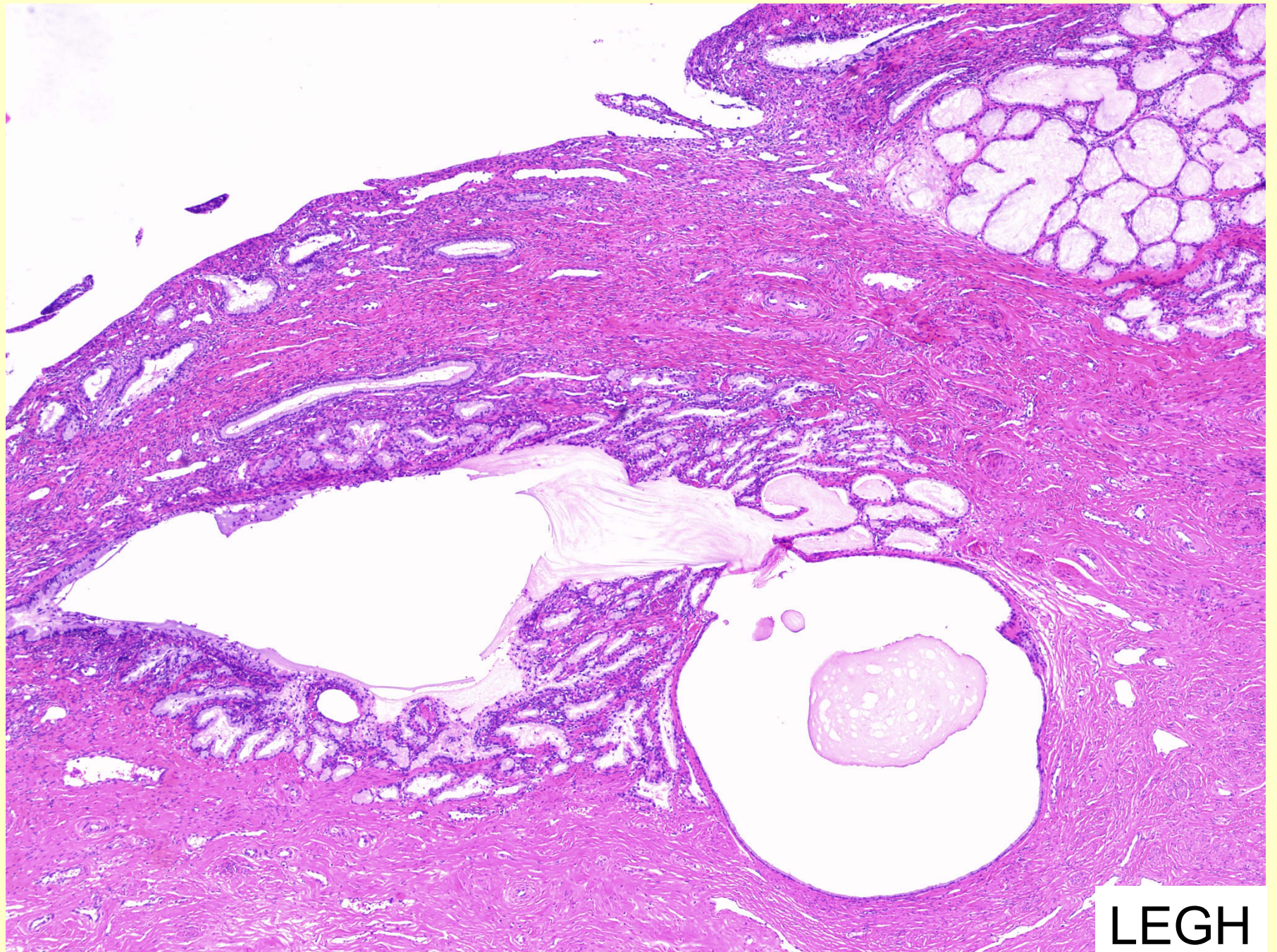


MGH-Subnuclear Vacuoles

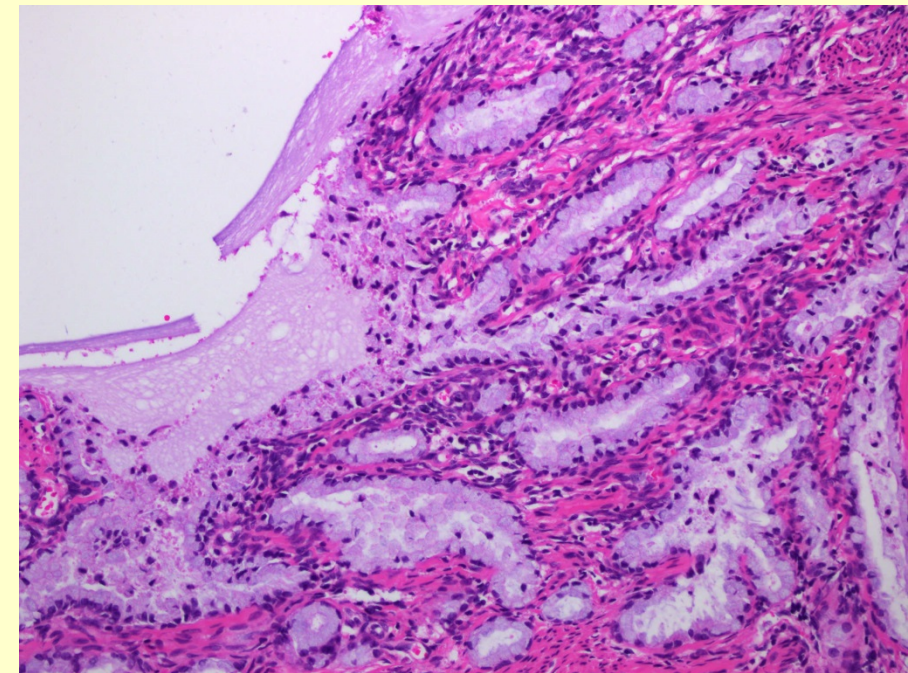
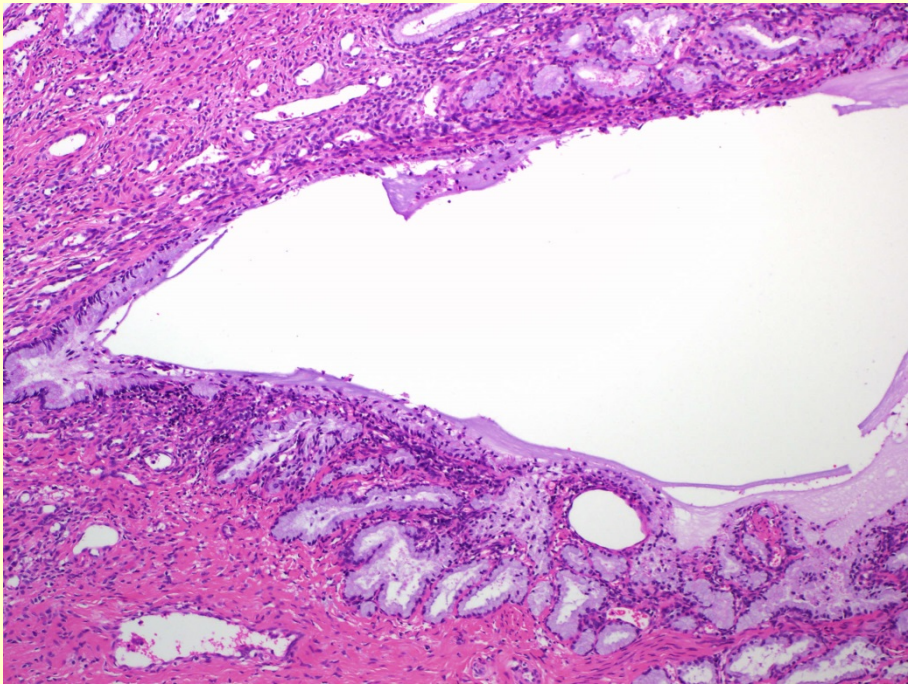




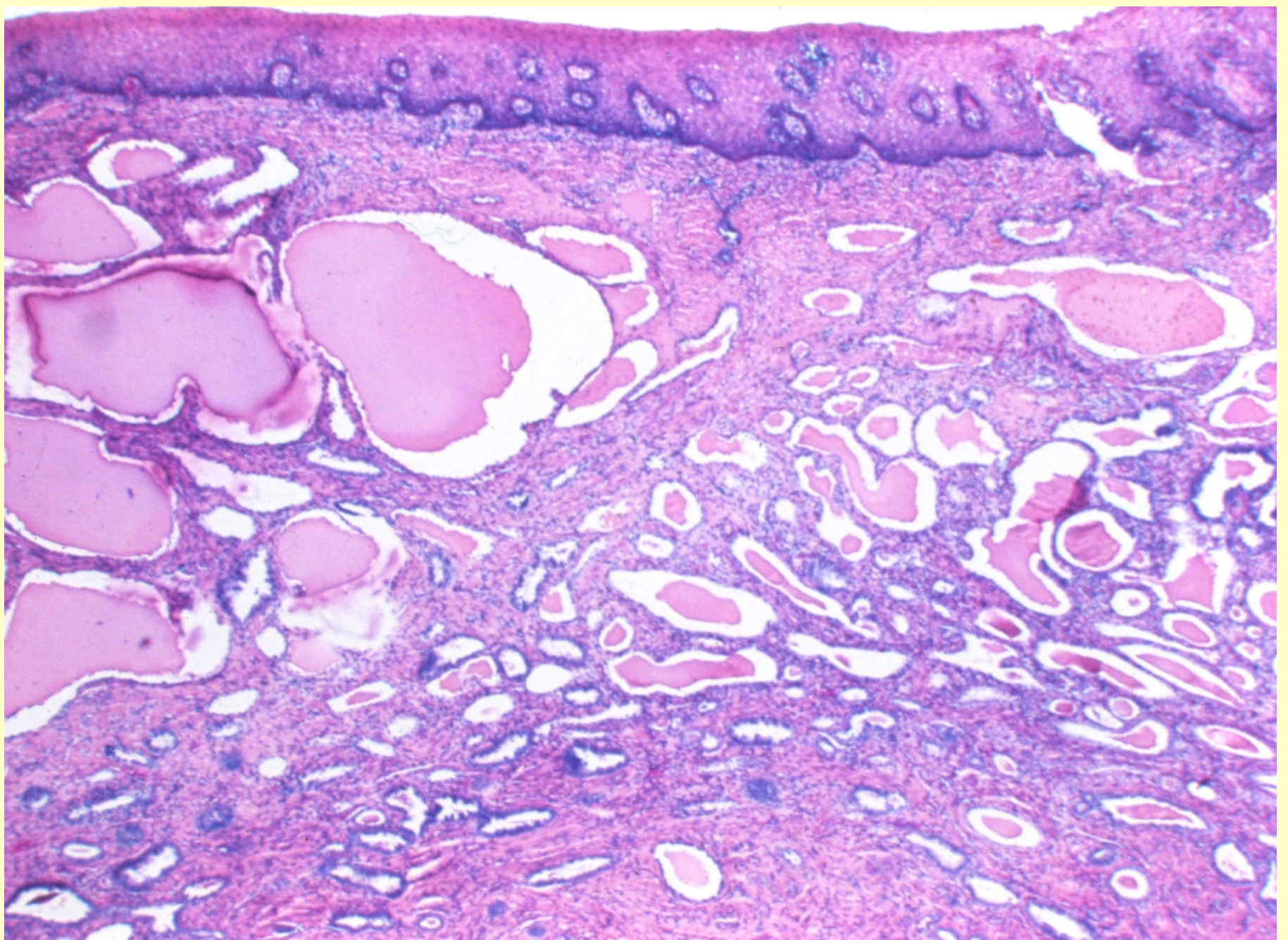
Solid MGH



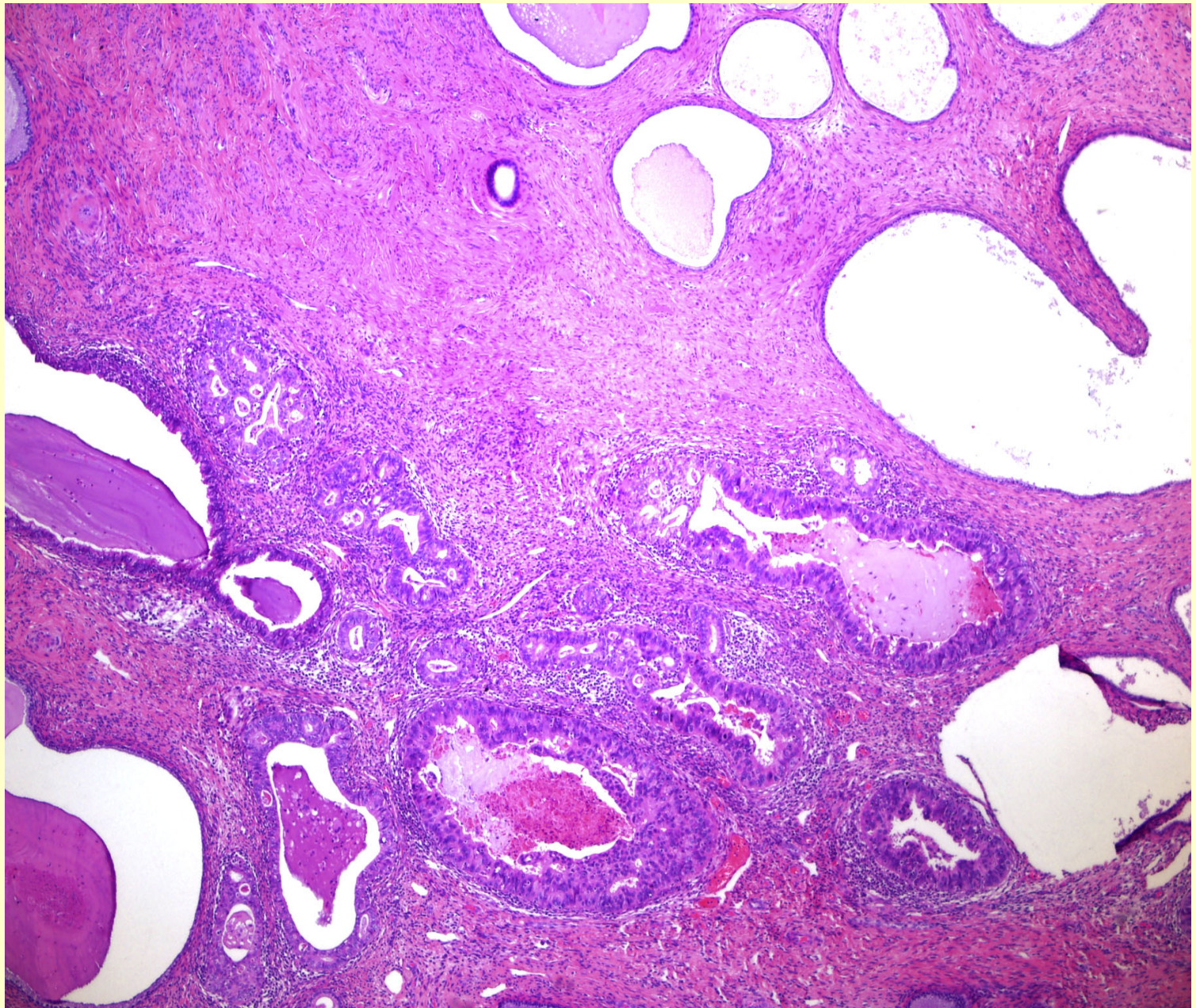
LEGH



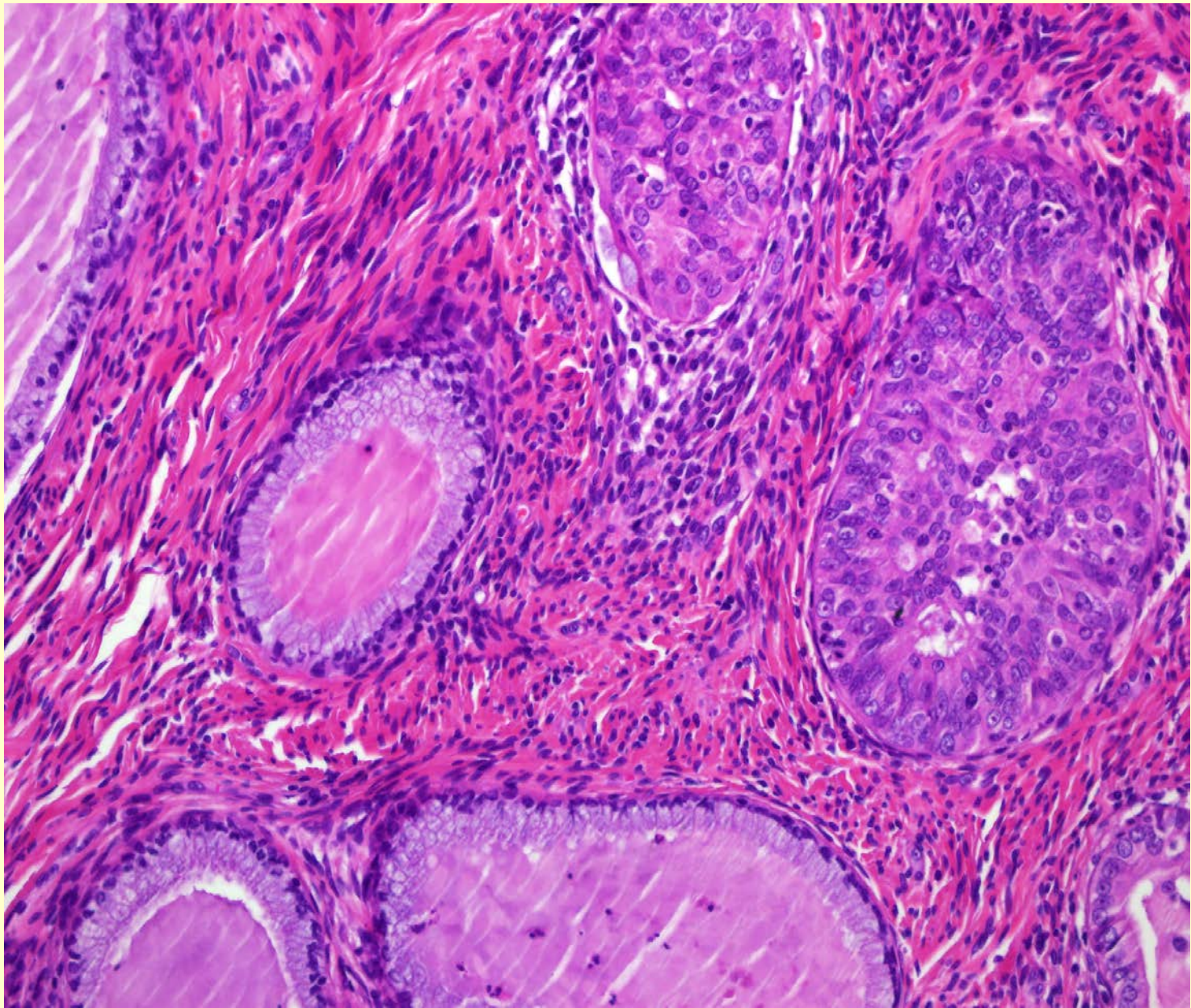
LEGH



Mesonephric hyperplasia



Endocervical or endometrial adenocarcinoma?

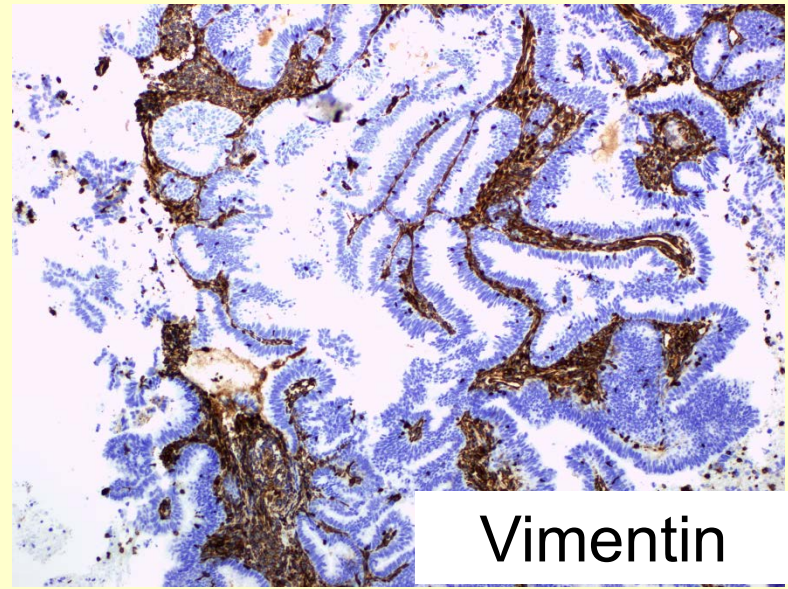
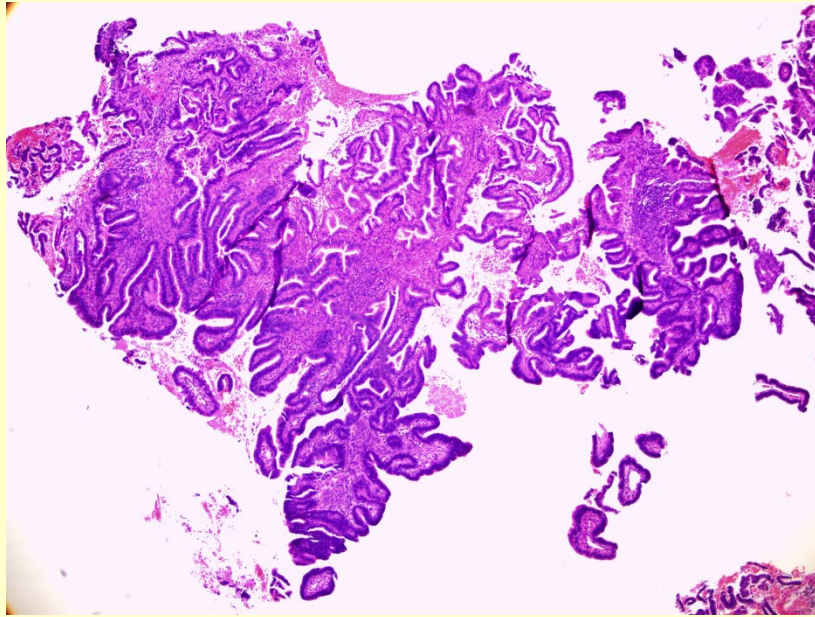


Cervical extension of endometrial adenocarcinoma

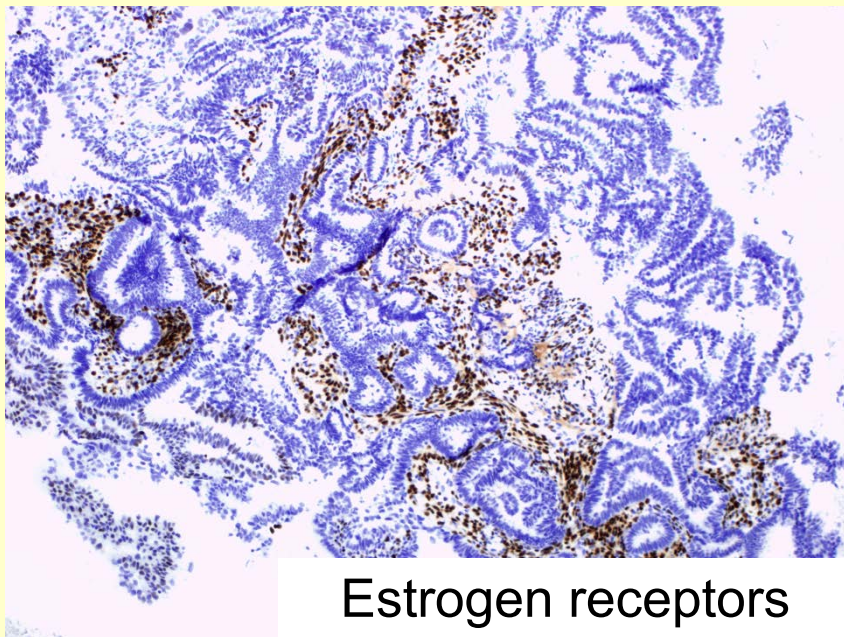
Adenocarcinoma

Cervical Endometrial

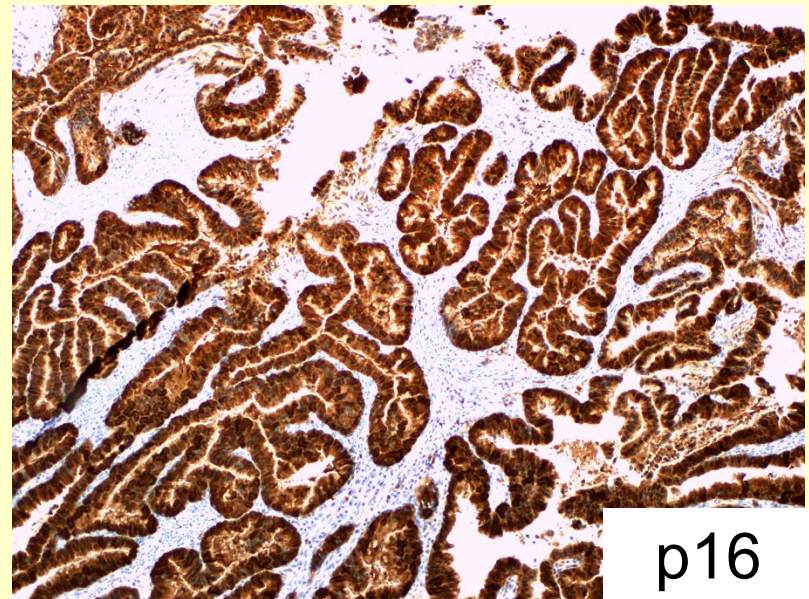
Vimentin	-/+	+++
ER/PR	-	++
hPV	+	-



Vimentin



Estrogen receptors



p16

Cervical Adenocarcinoma – WHO 2014

Adenocarcinoma

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