Challenge Cases #1

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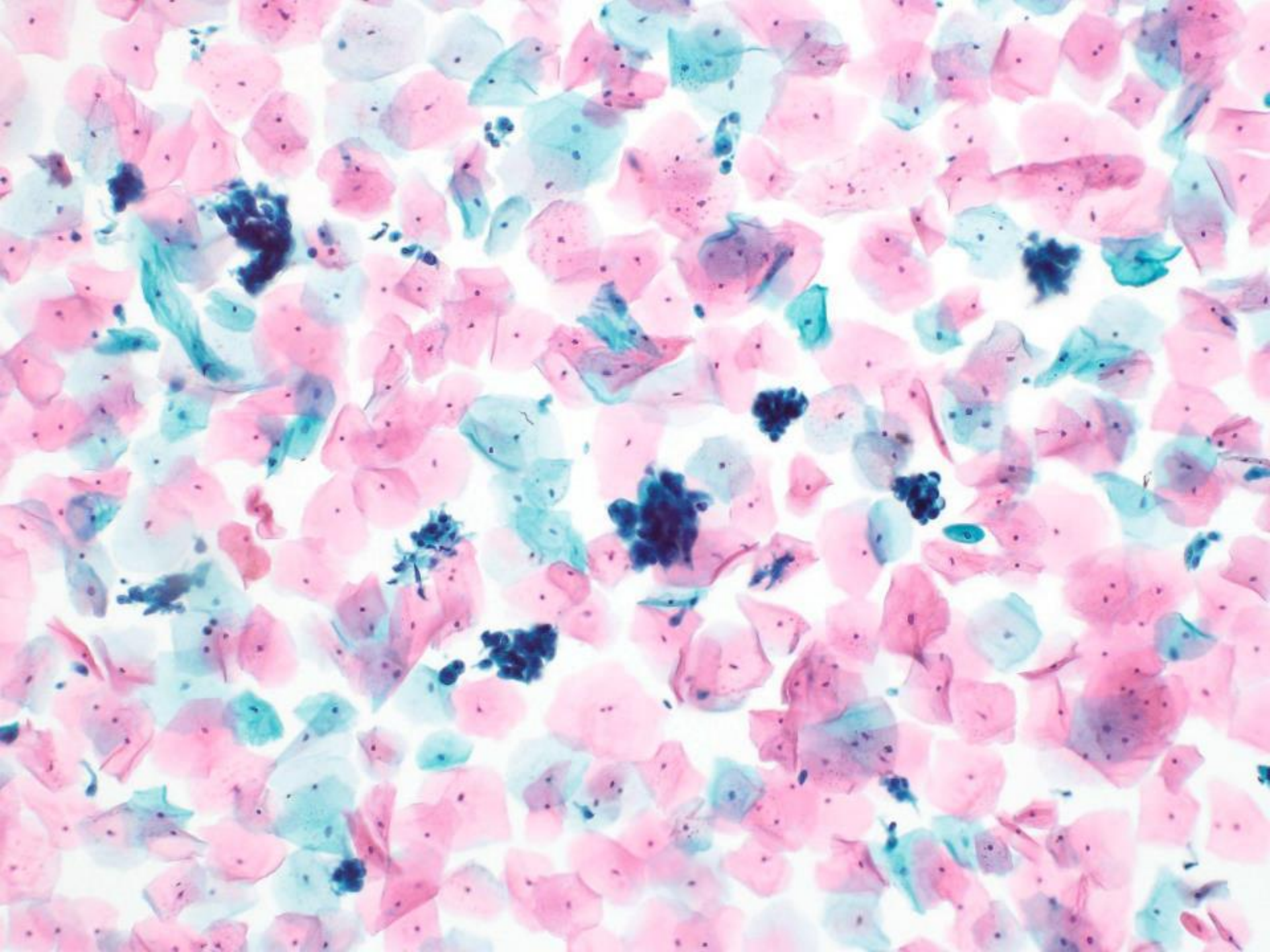
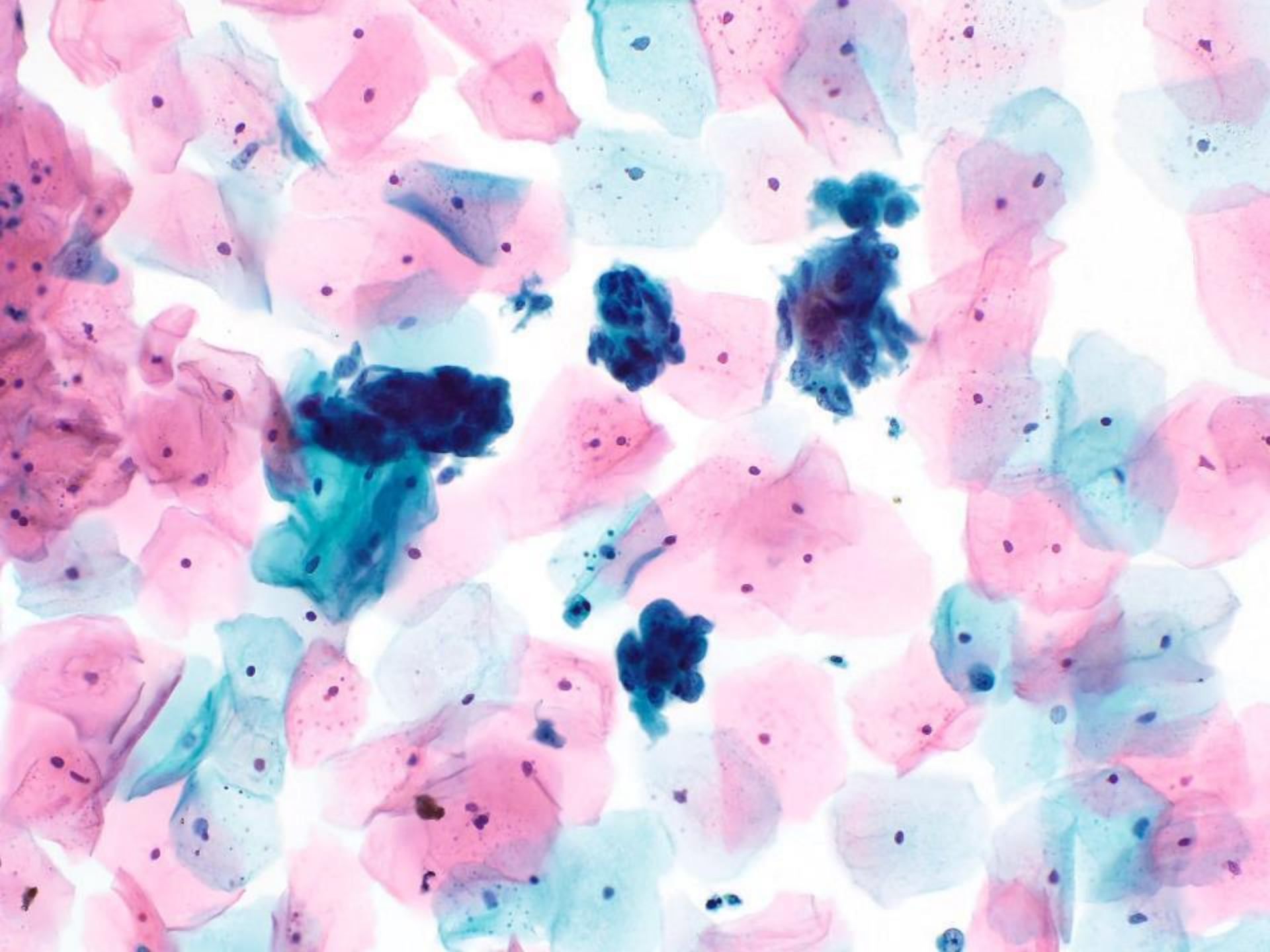
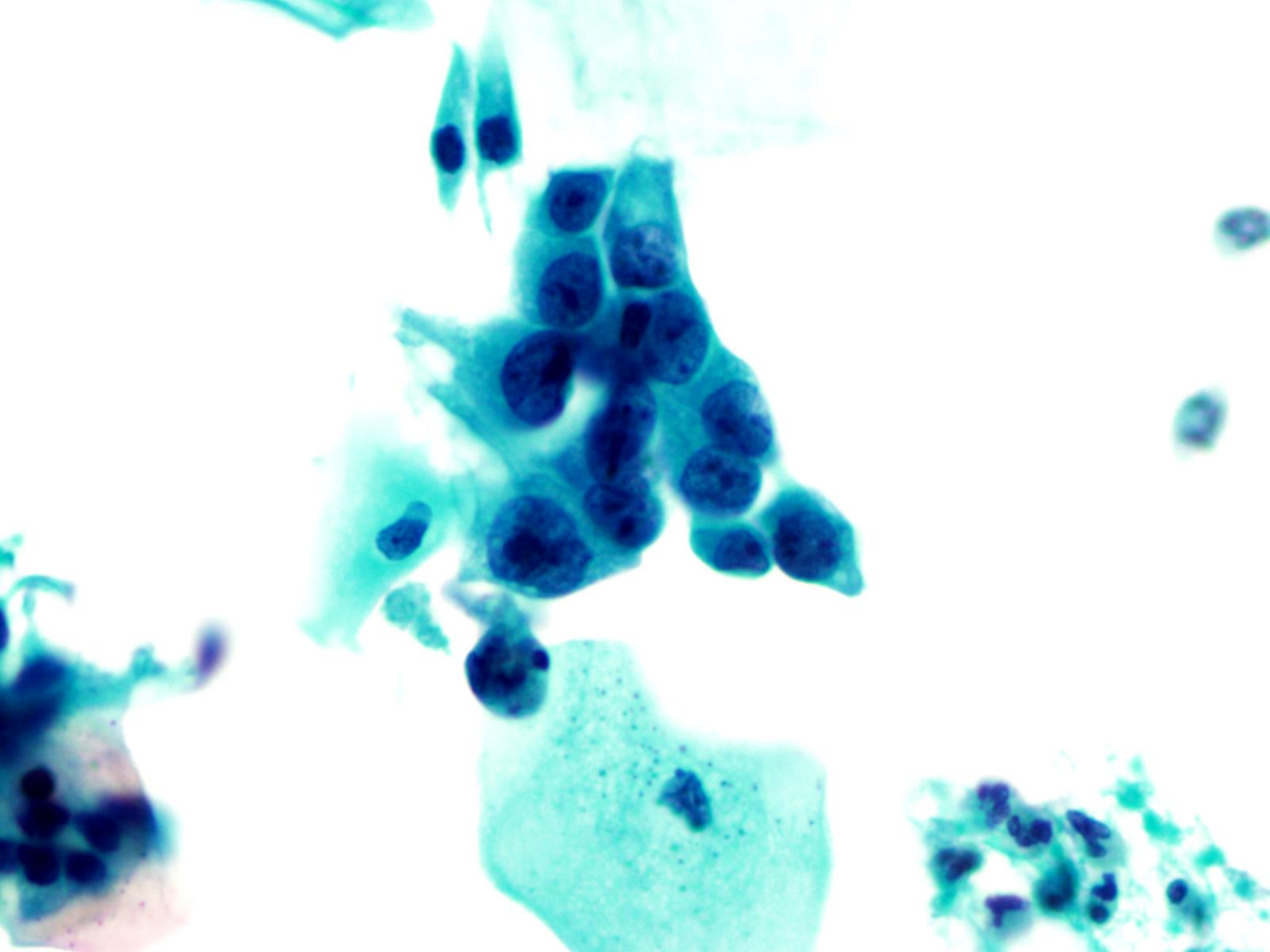
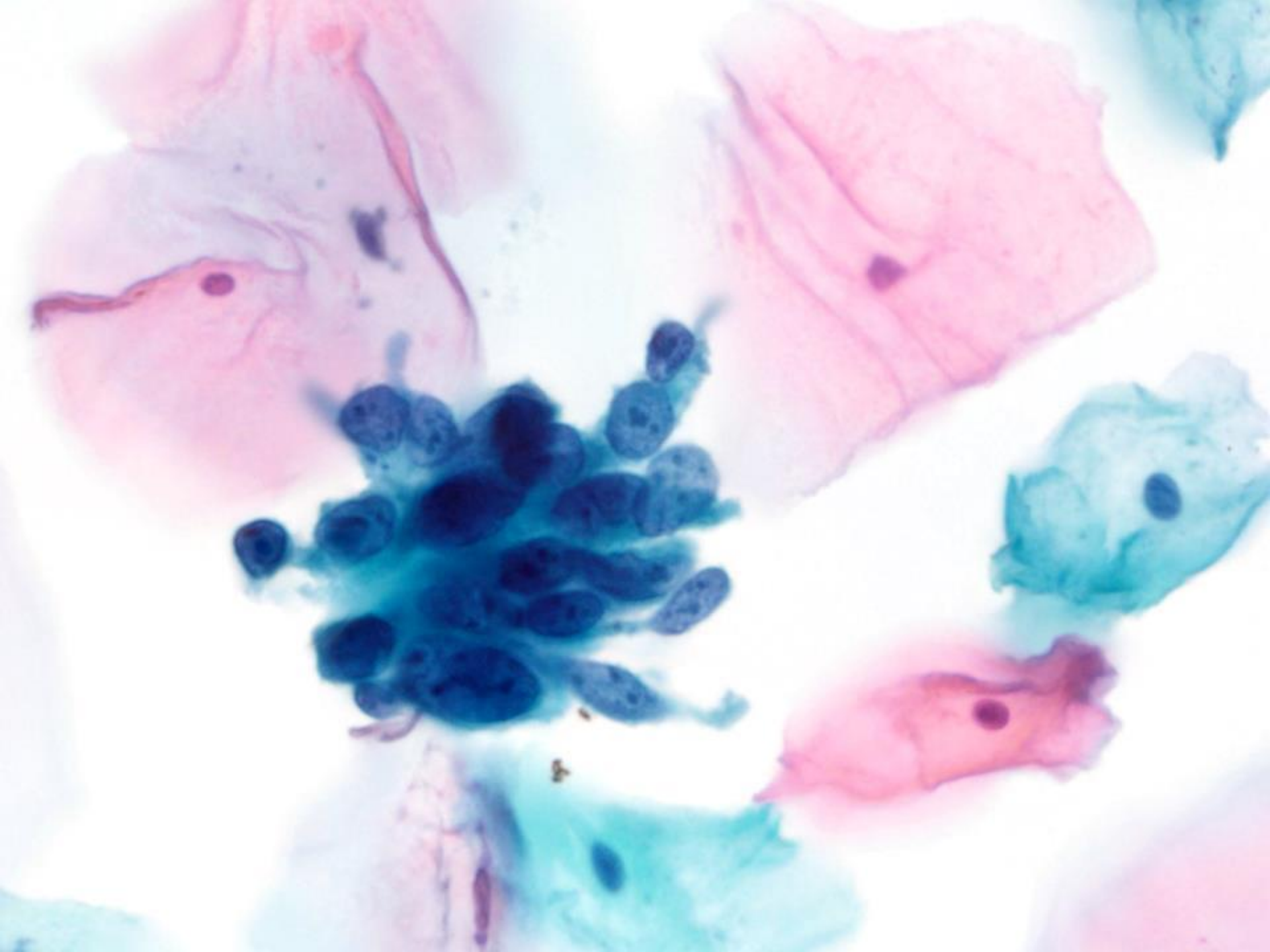
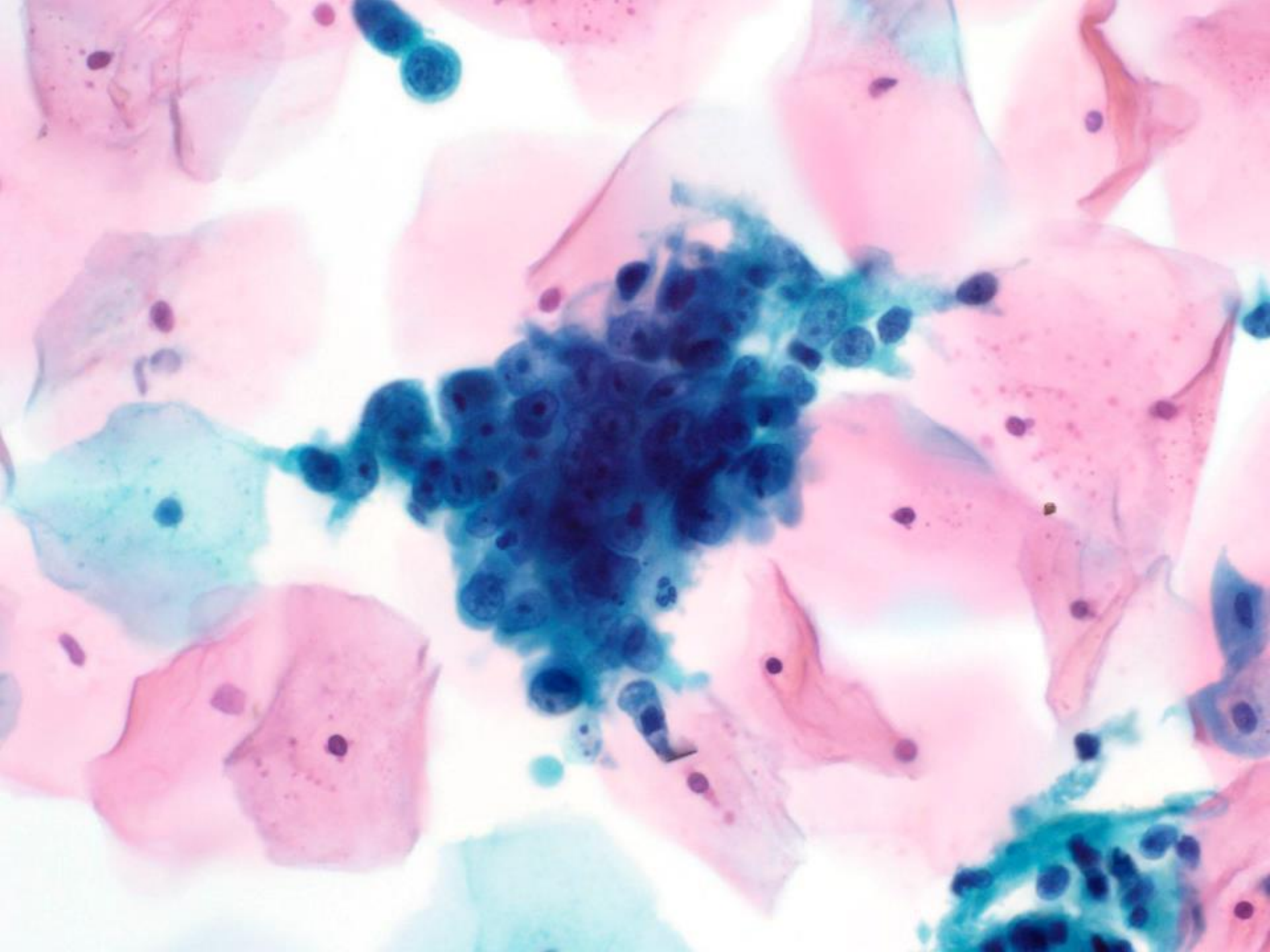
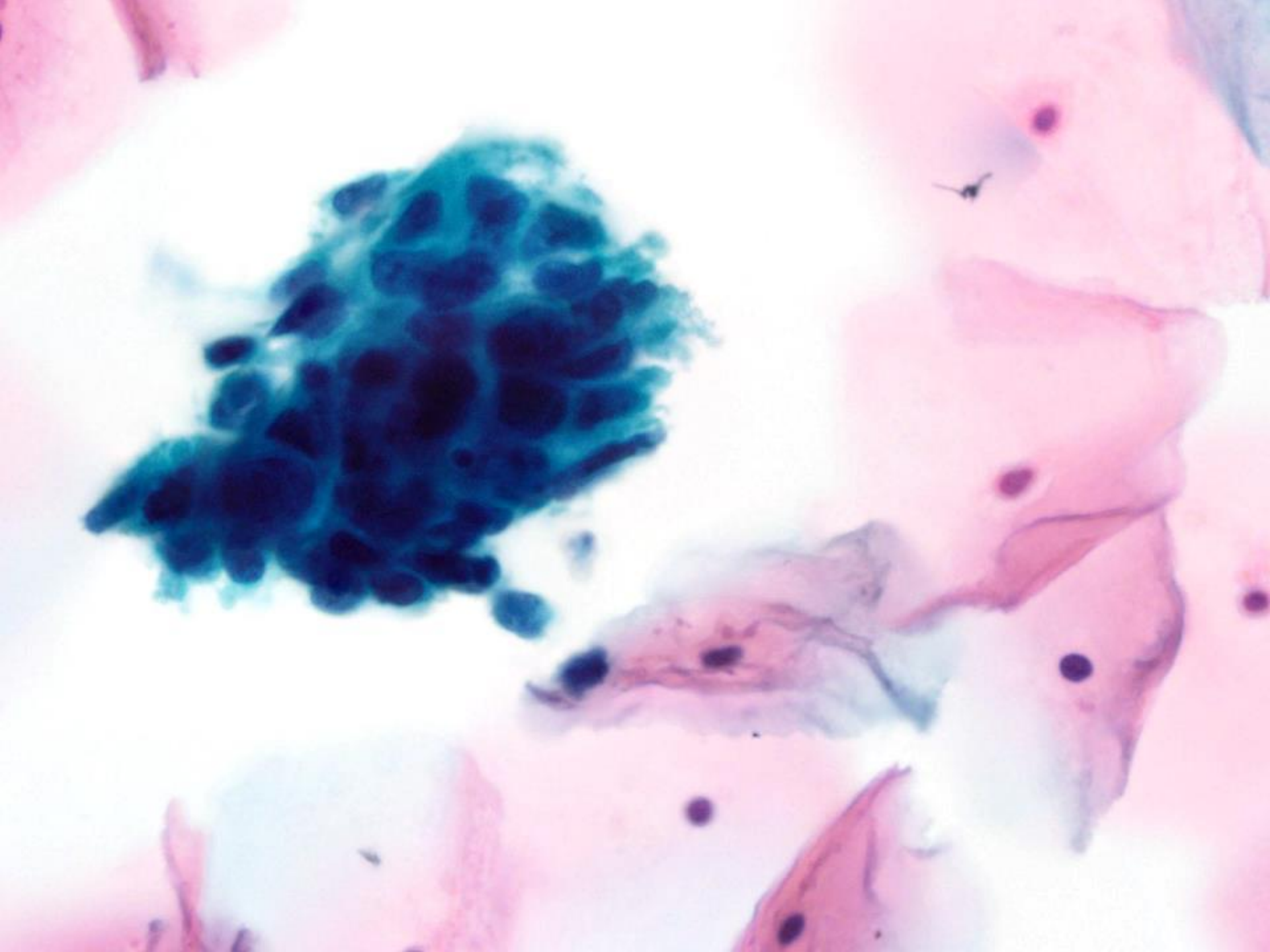


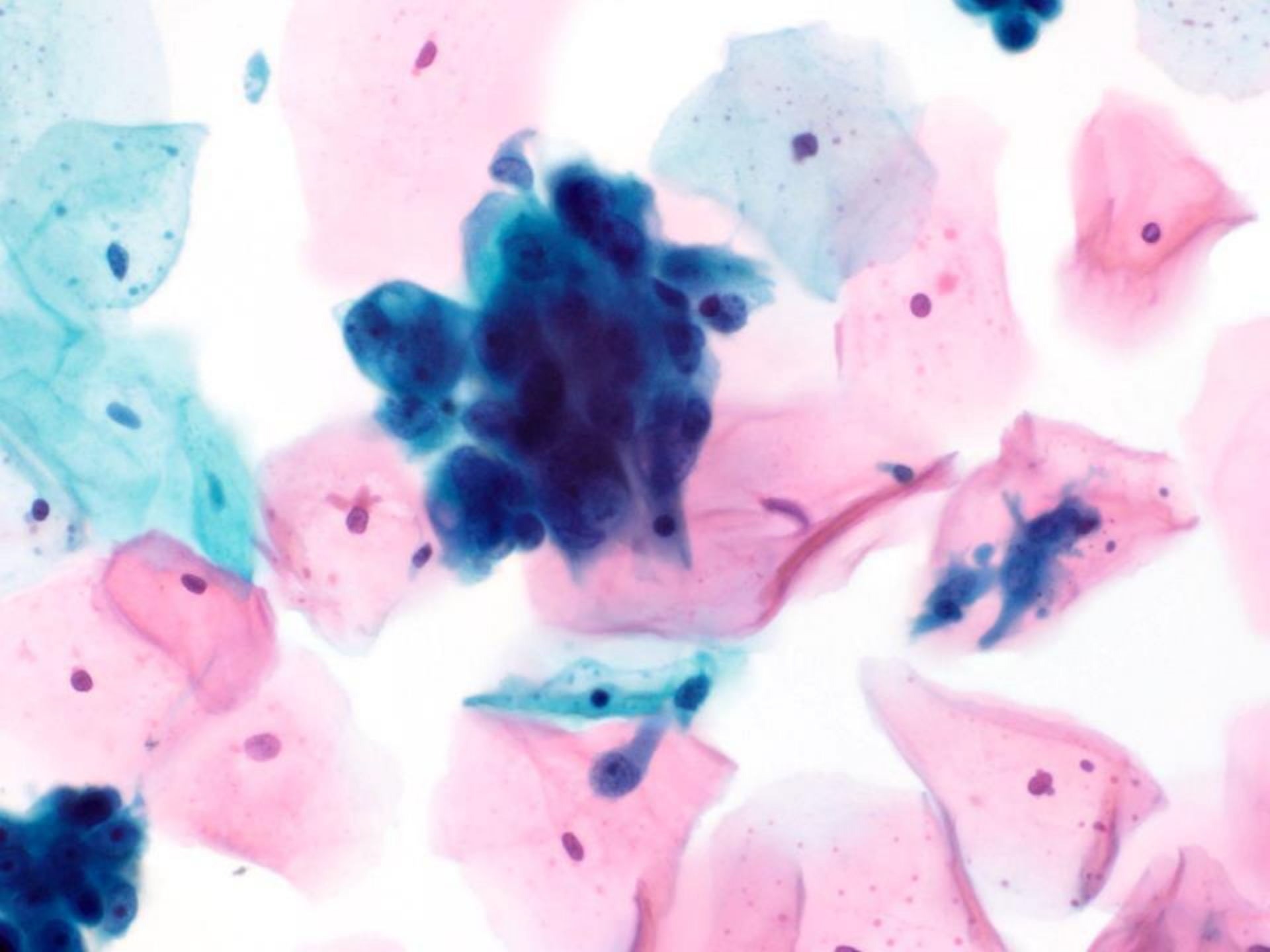












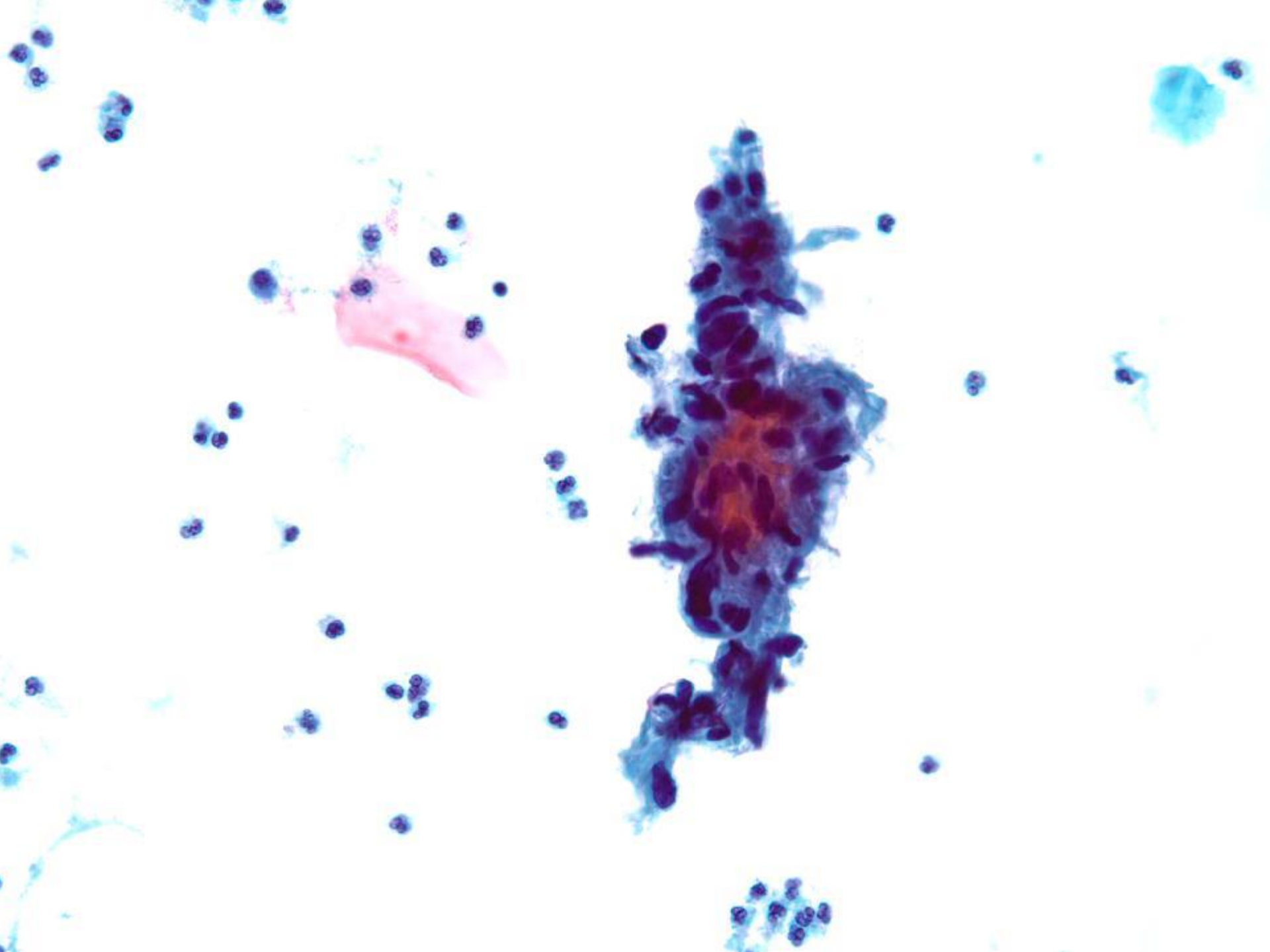
Assessment?

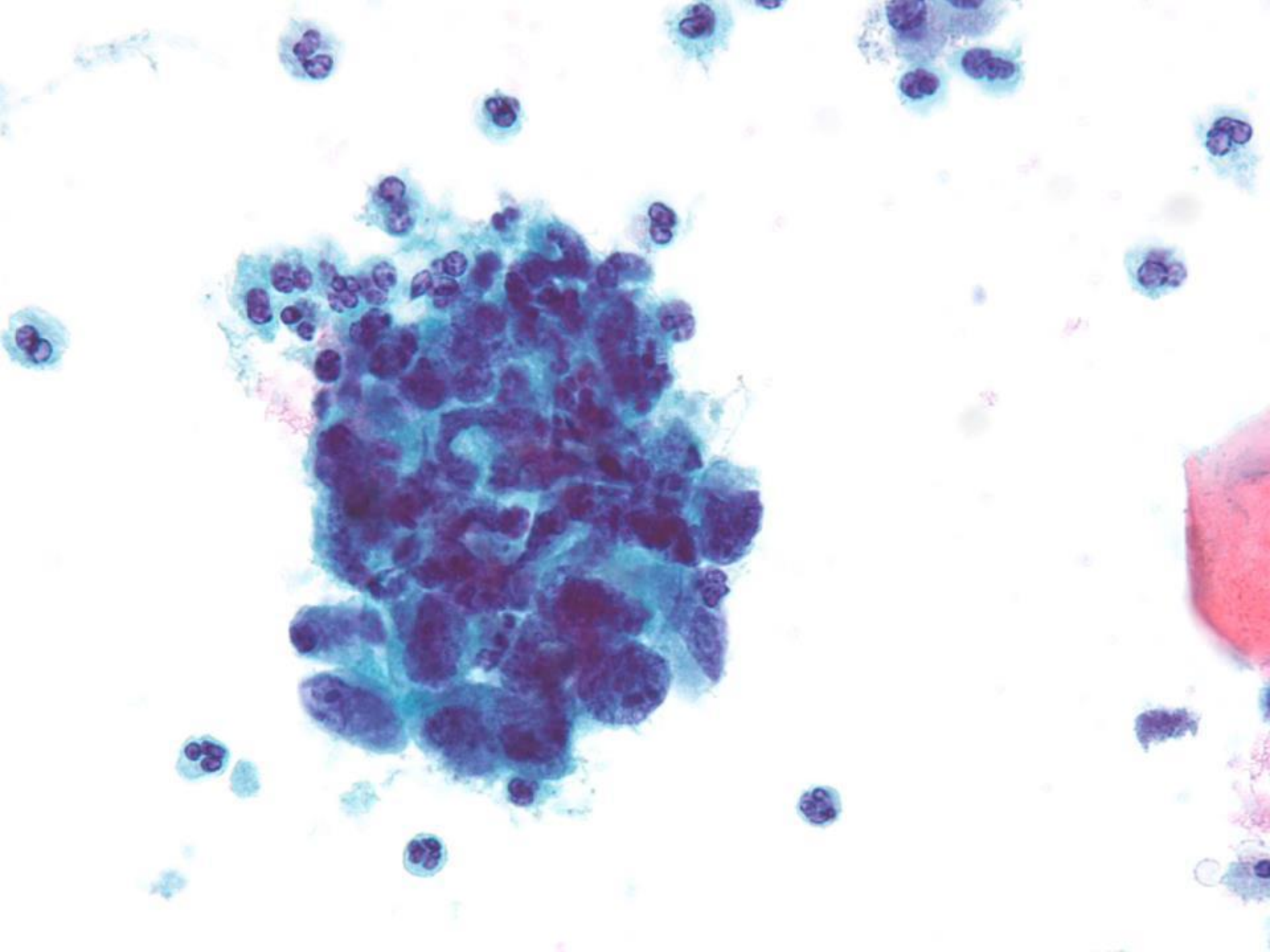
Assessment?

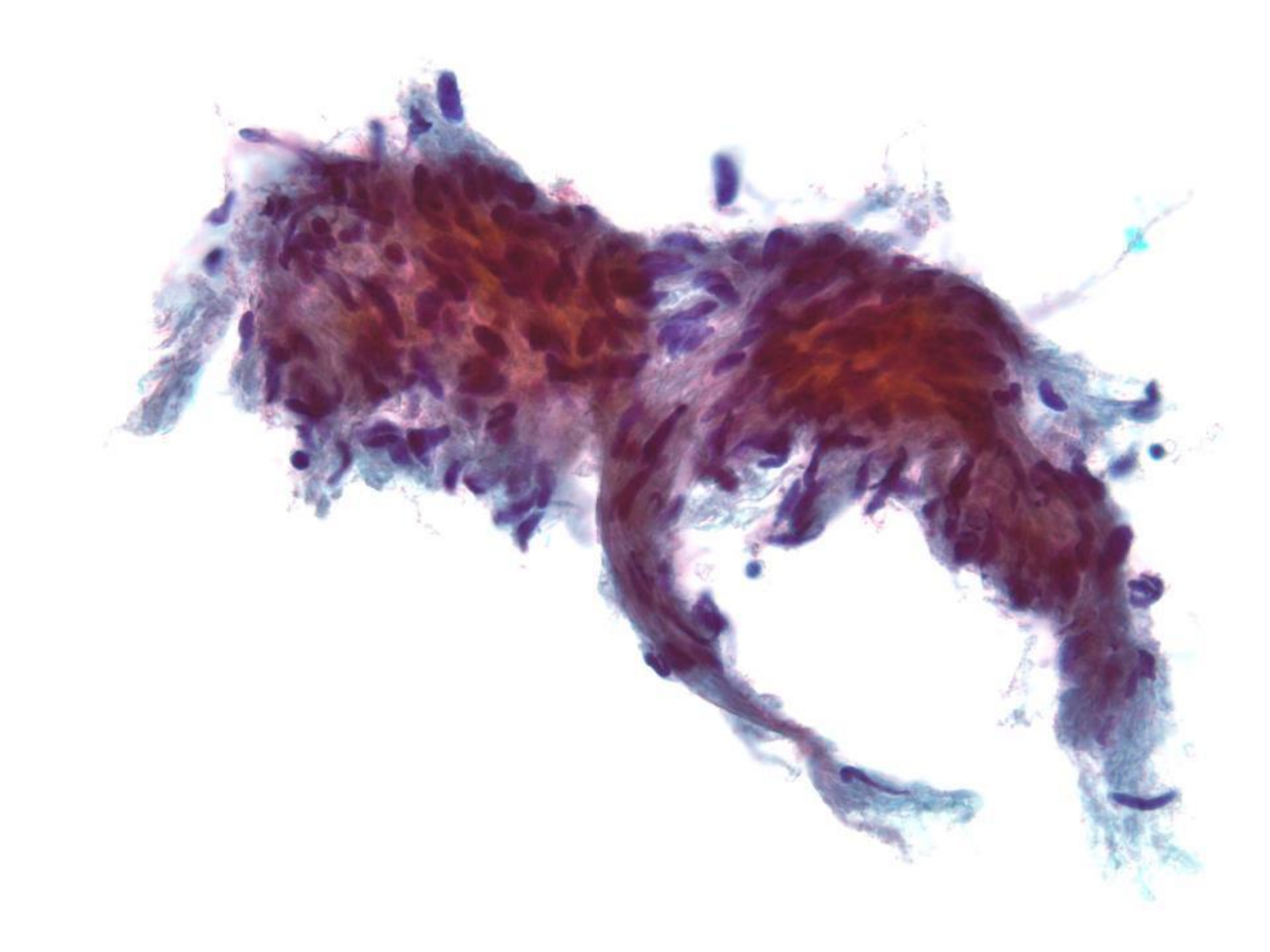
Malignant epithelial cells
Glandular features
Prominent nucleoli seen
Clean background

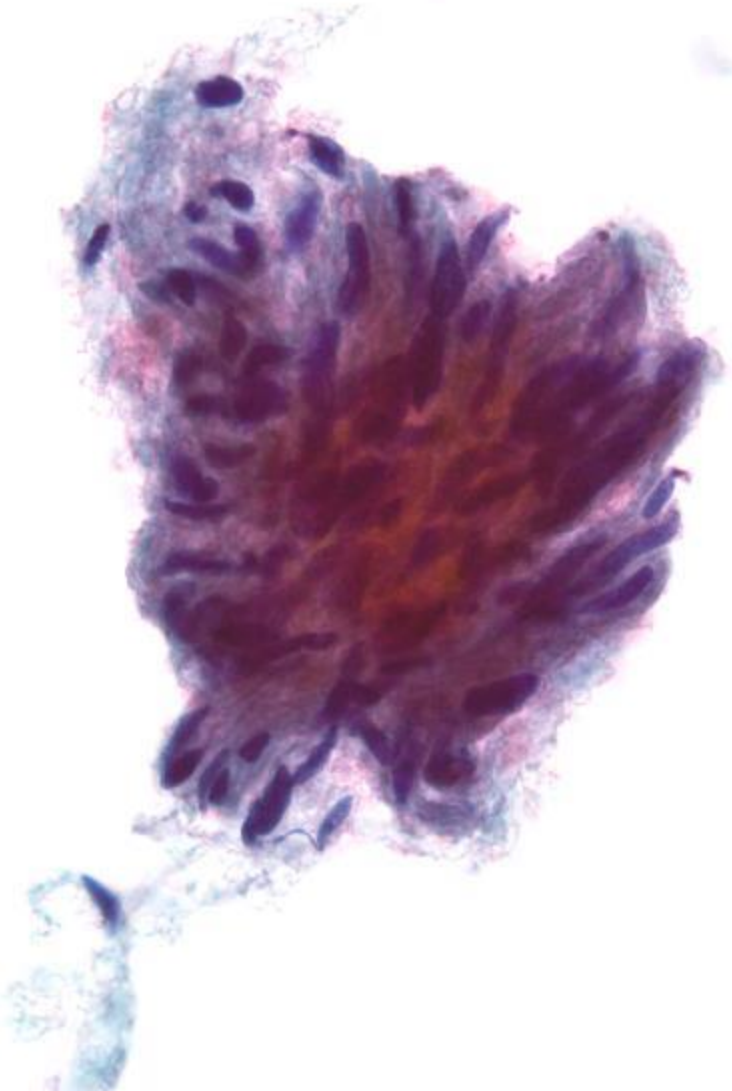
Diagnosis: Carcinoma with glandular features. See note.
Note: An extrauterine primary site cannot be excluded.

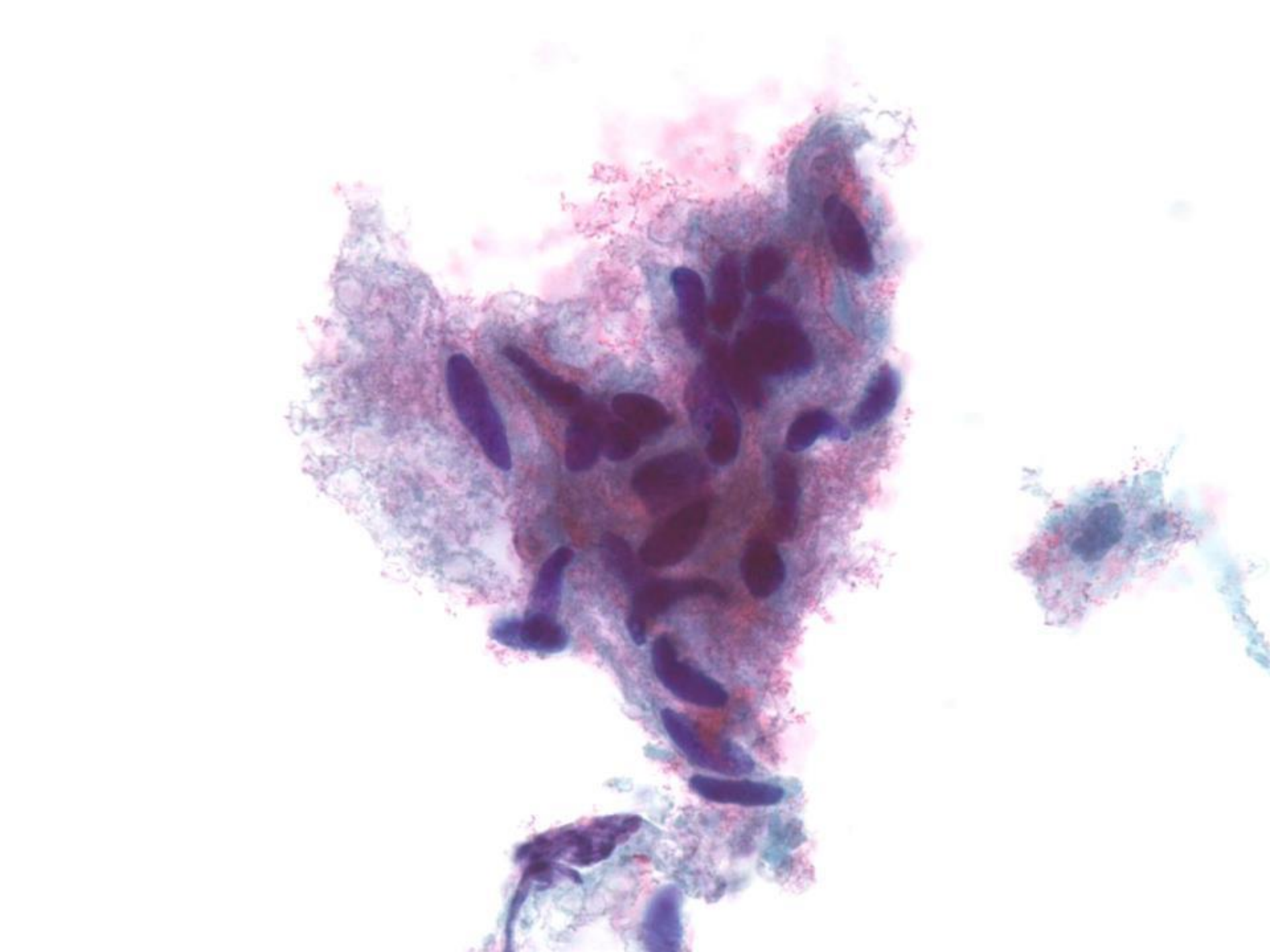
Follow up diagnosis:
Endometrioid ovarian carcinoma

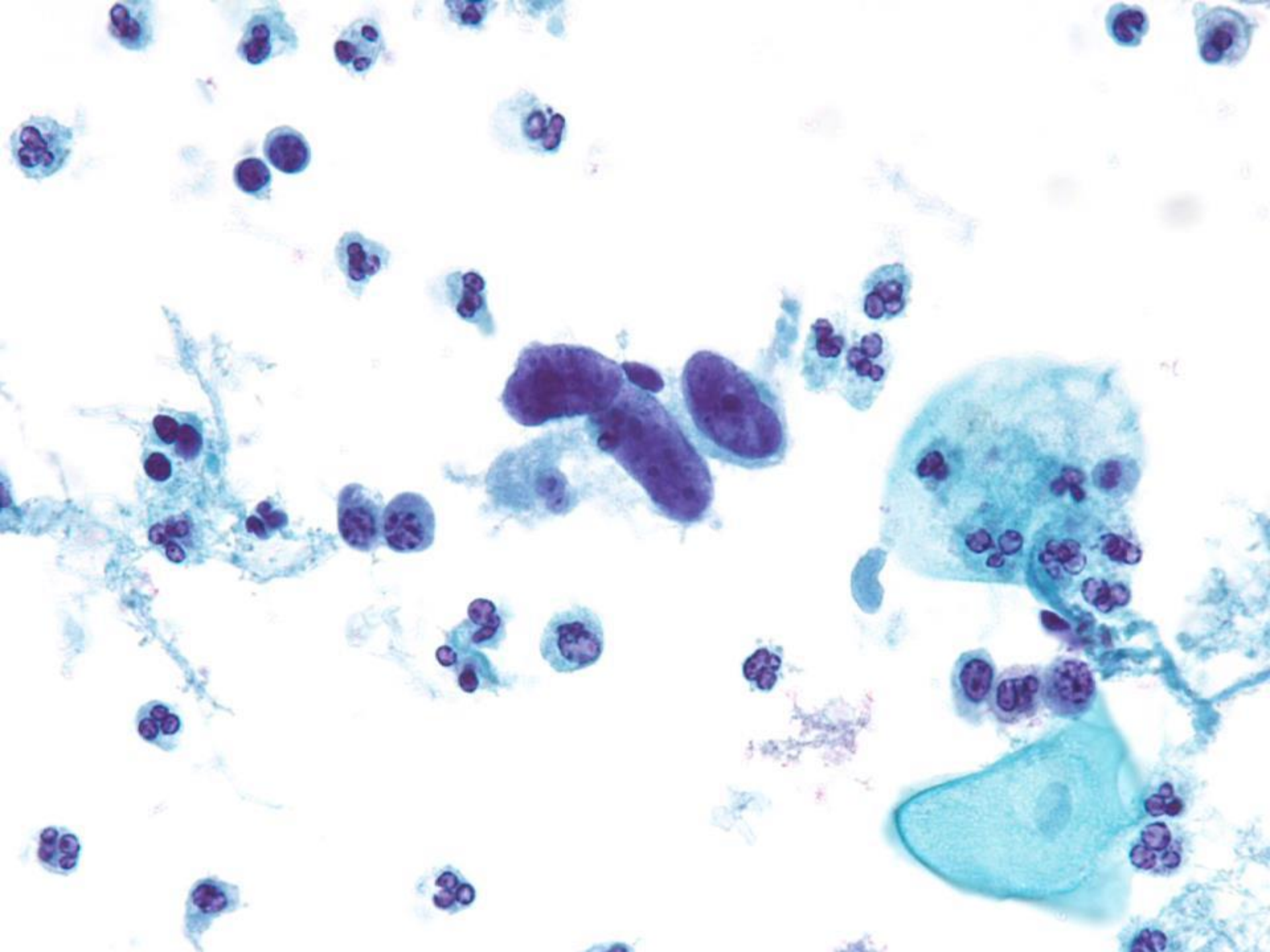












Assessment?

Assessment?

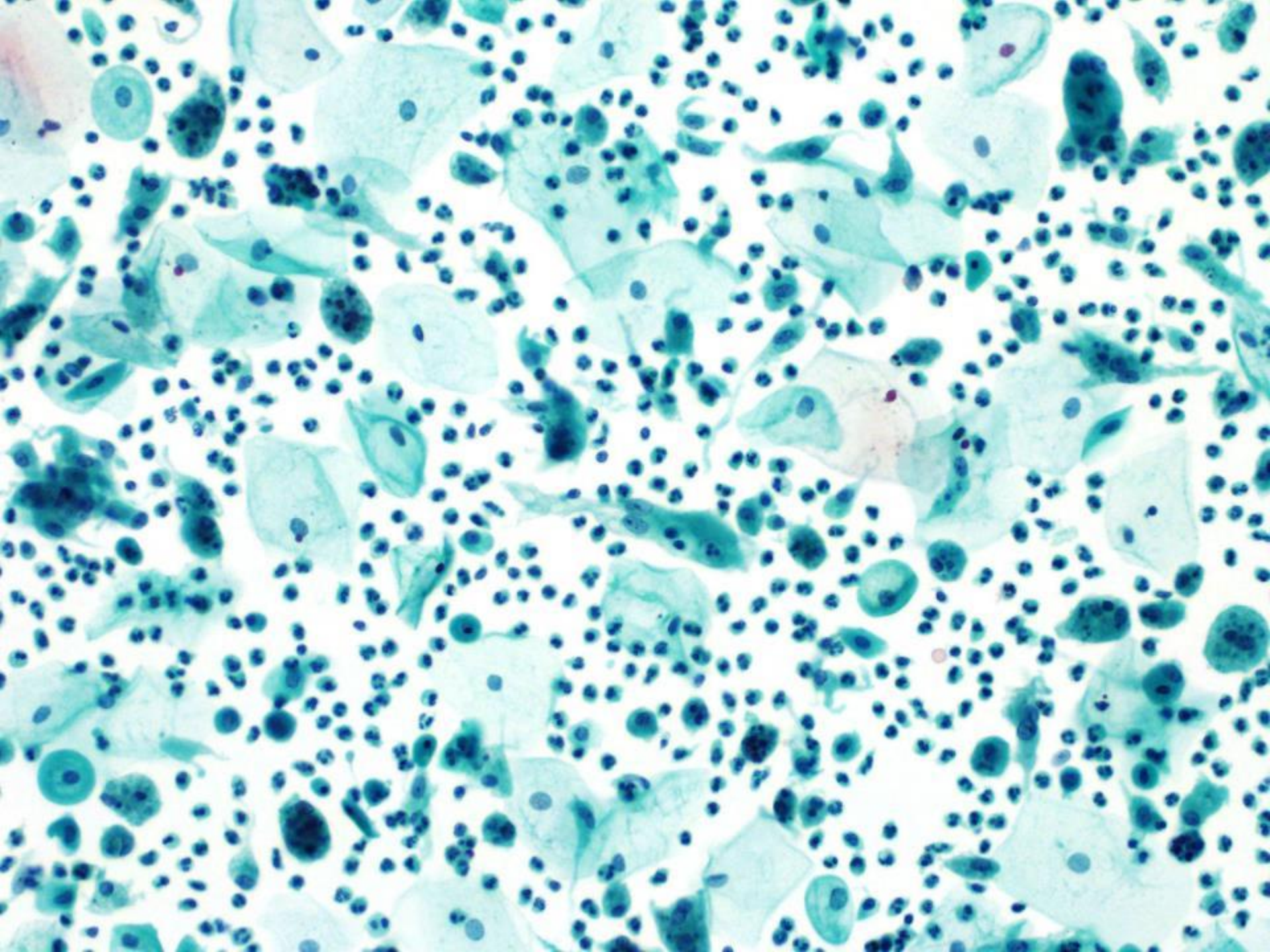
Malignant spindle cells

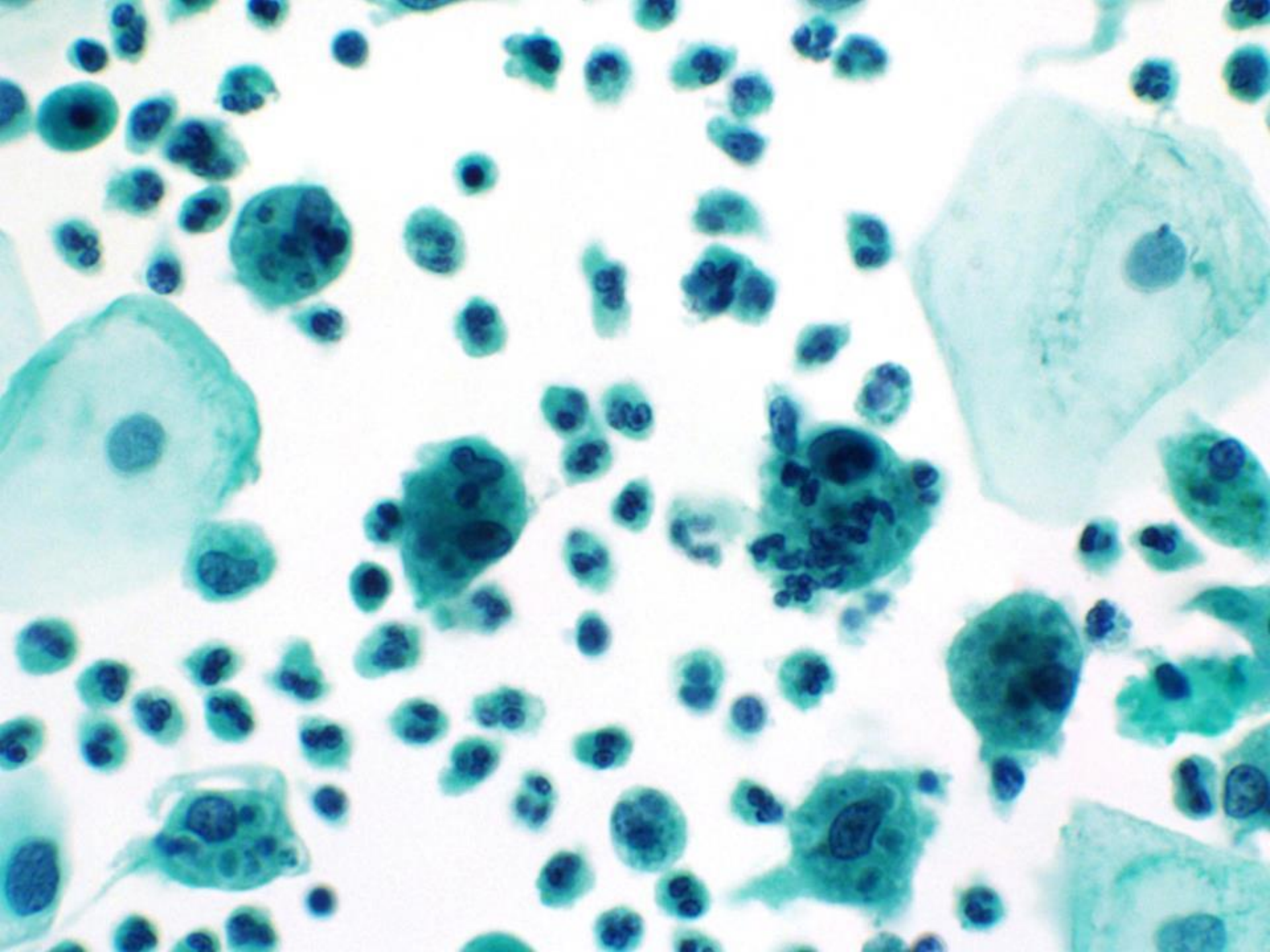
- Leiomyosarcoma
- Endometrial Stromal Sarcoma
- Sarcomatoid SqCCa
- Spindle Cell Melanoma
- MMMT

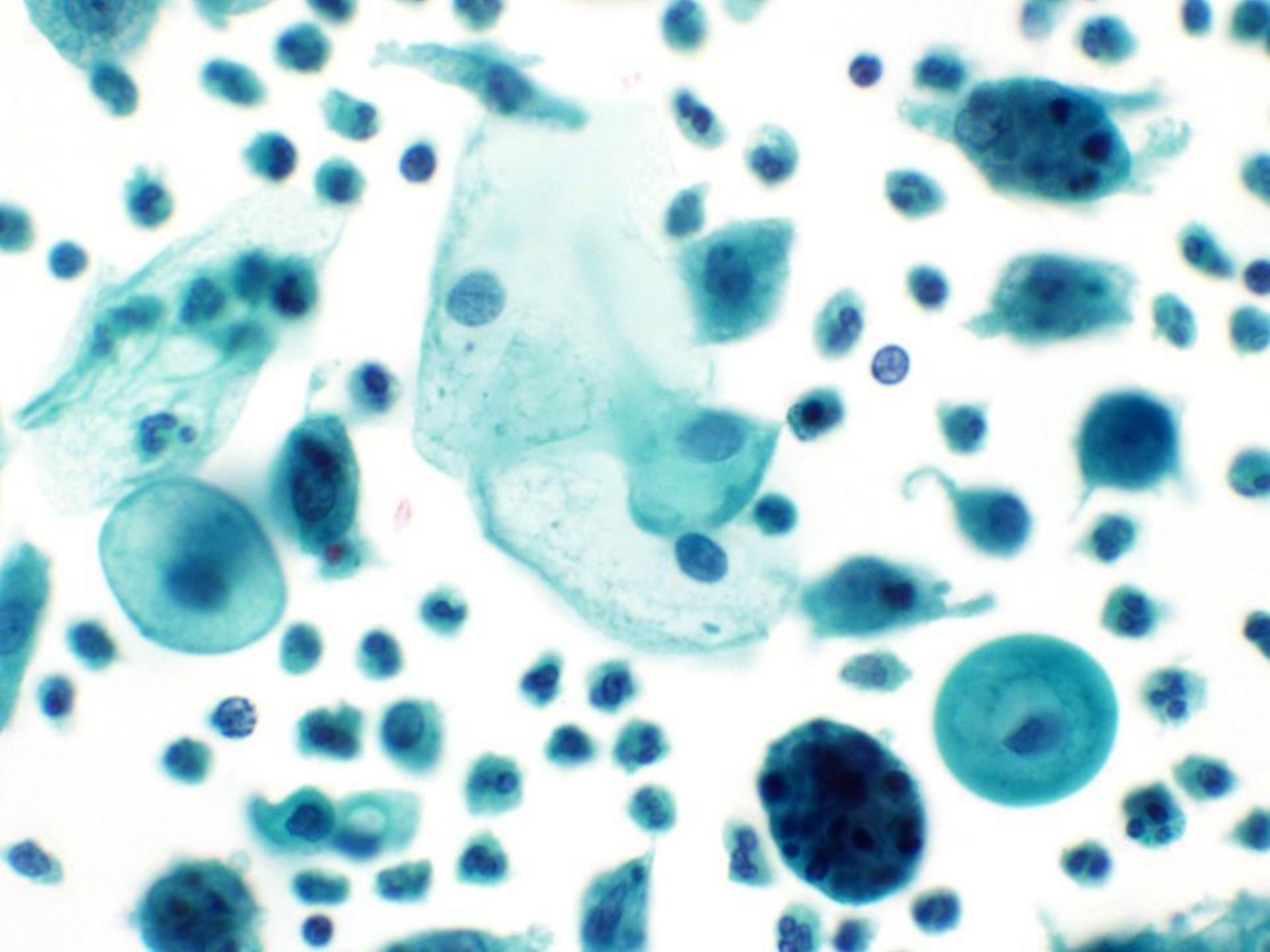
Clinging diathesis

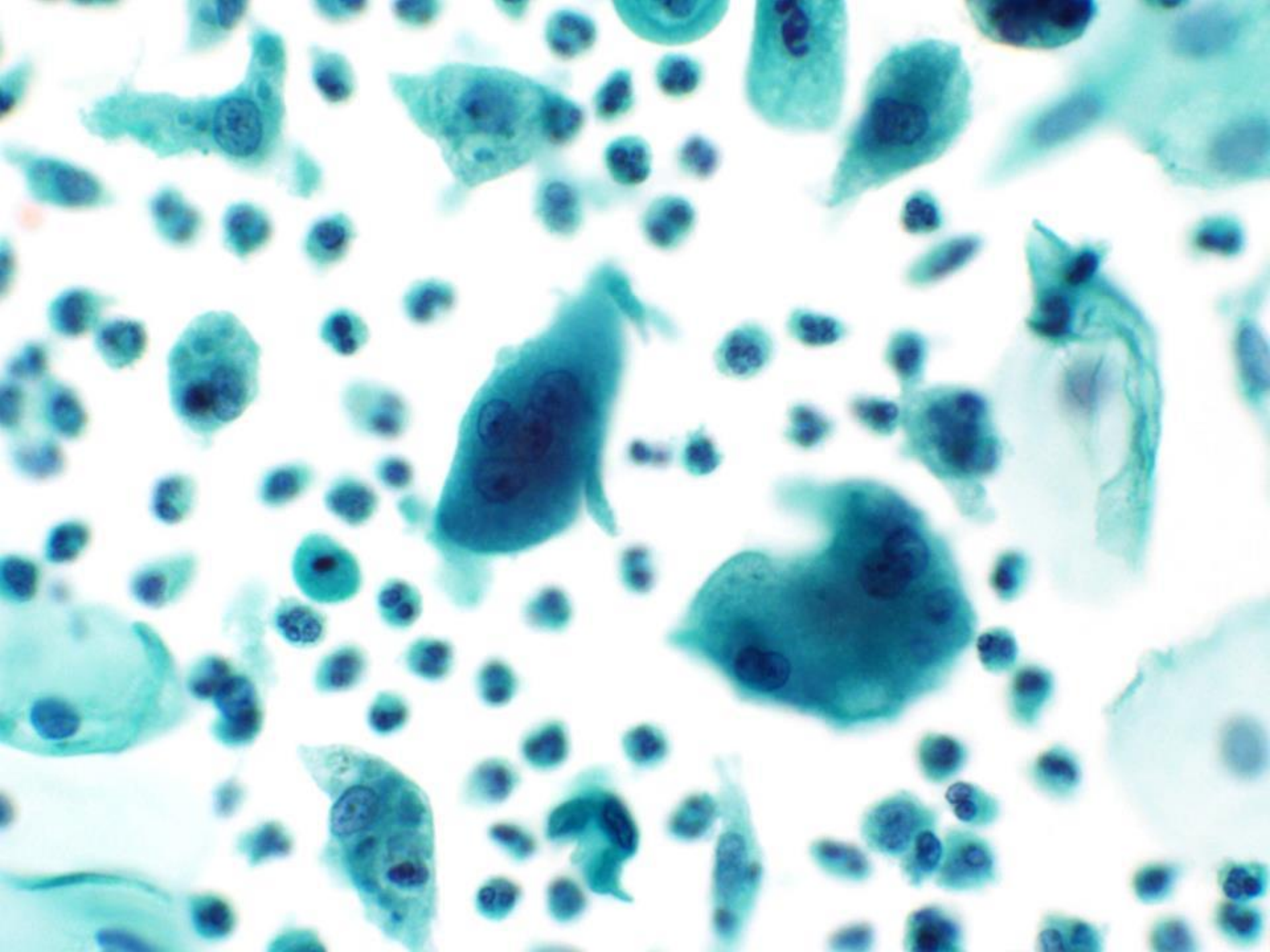
Diagnosis: Malignant spindle cell neoplasm

Follow up diagnosis: Leiomyosarcoma









Histiocytes in Pap Test

Table I. Characteristics of Cases of Endometrial Pathology (i.e., Carcinomas and Hyperplasias) and Their Controls

Variable	*Categories*	*Cases*		*Controls*
		Carcinomas	*Hyperplasias*	
Age (yr)	40–55	12 (27.9%)	30 (50.8%)	47 (46.5%)
	56–69	20 (46.5%)	20 (33.9%)	48 (47.5%)
	>69	11 (25.6%)	9 (15.3%)	6 (5.9%)
Mean age		62.9	57.3	56.5
Free histiocytes	Present	12 (27.9%)	8 (13.6%)	12 (11.9%)
Histiocytes with PIC	Present	19 (44.2%)	5 (8.5%)	17 (16.8%)
	Absent	12 (27.9%)	46 (77.9%)	72 (71.3%)
Normal	Present	4 (9.3%)	8 (13.6%)	5 (5.0%)
Endometrial cells	Absent	39 (90.7%)	51 (86.4%)	96 (95.0%)

Nguyen et al. Diag Cytopathol 1998 19(2):89-93

Histiocytes in Pap Smear

Table II. Logistic Regression Analysis of Cytopathological Attributes and Risk of Endometrial Carcinoma and Endometrial Hyperplasia

	Odds ratio[a] and 95% confidence interval		
Variable	*Crude*	*Age-adjusted*	*Multivariate[b]*
Endometrial pathology			
Free histiocytes	1.81 (0.83–3.93)	1.58 (0.71–3.50)	1.23 (0.50–3.00)
Histiocytes with PIC	1.52 (0.76–3.04)	1.33 (0.65–2.71)	1.10 (0.50–2.48)
Normal endometrial cells	2.56 (0.87–7.56)	3.11 (1.03–9.40)	2.84 (0.90–8.72)
Endometrial carcinoma			
Free histiocytes	2.87 (1.17–7.05)	2.03 (0.77–5.38)	1.02 (0.32–3.22)
Histiocytes with PIC	3.91 (1.76–8.67)	3.19 (1.37–7.43)	3.00 (1.16–7.70)
Normal endometrial cells	1.97 (0.50–7.72)	2.80 (0.64–12.21)	2.19 (0.43–11.08)
Endometrial hyperplasia			
Free histiocytes	1.16 (0.45–3.03)	1.11 (0.42–2.95)	1.10 (0.37–3.30)
Histiocytes with PIC	0.46 (0.16–1.31)	0.44 (0.15–1.27)	0.33 (0.10–1.06)
Normal endometrial cells	3.01 (0.94–9.68)	3.23 (0.99–10.53)	4.09 (1.14–14.67)

Nguyen et al. Diag Cytopathol 1998 19(2):89-93

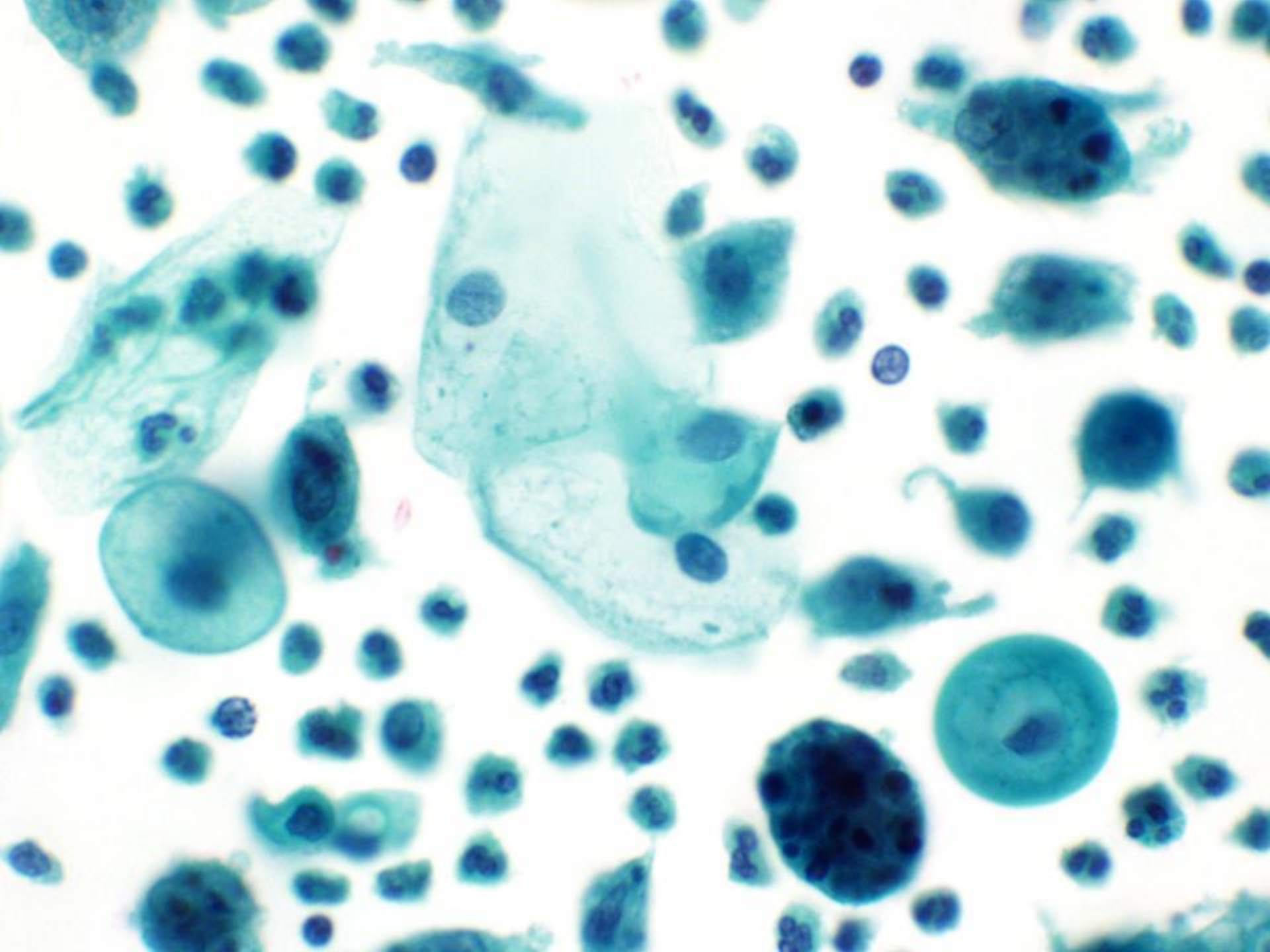
Histiocytes in Pap Smear

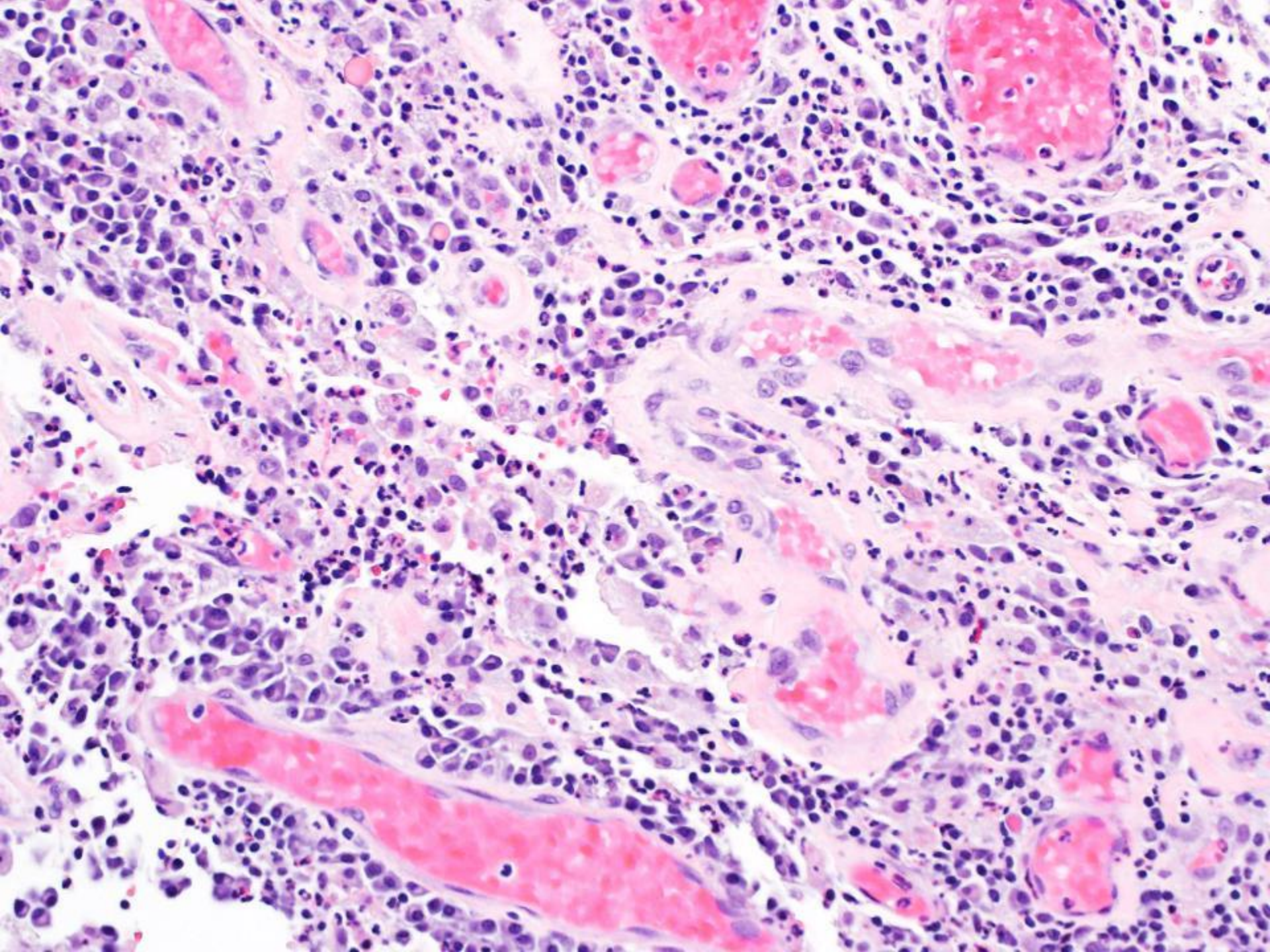
Table II *PPV for Women with Histiocytes Only and with Additional Clinical and/or Pap Smear Findings*

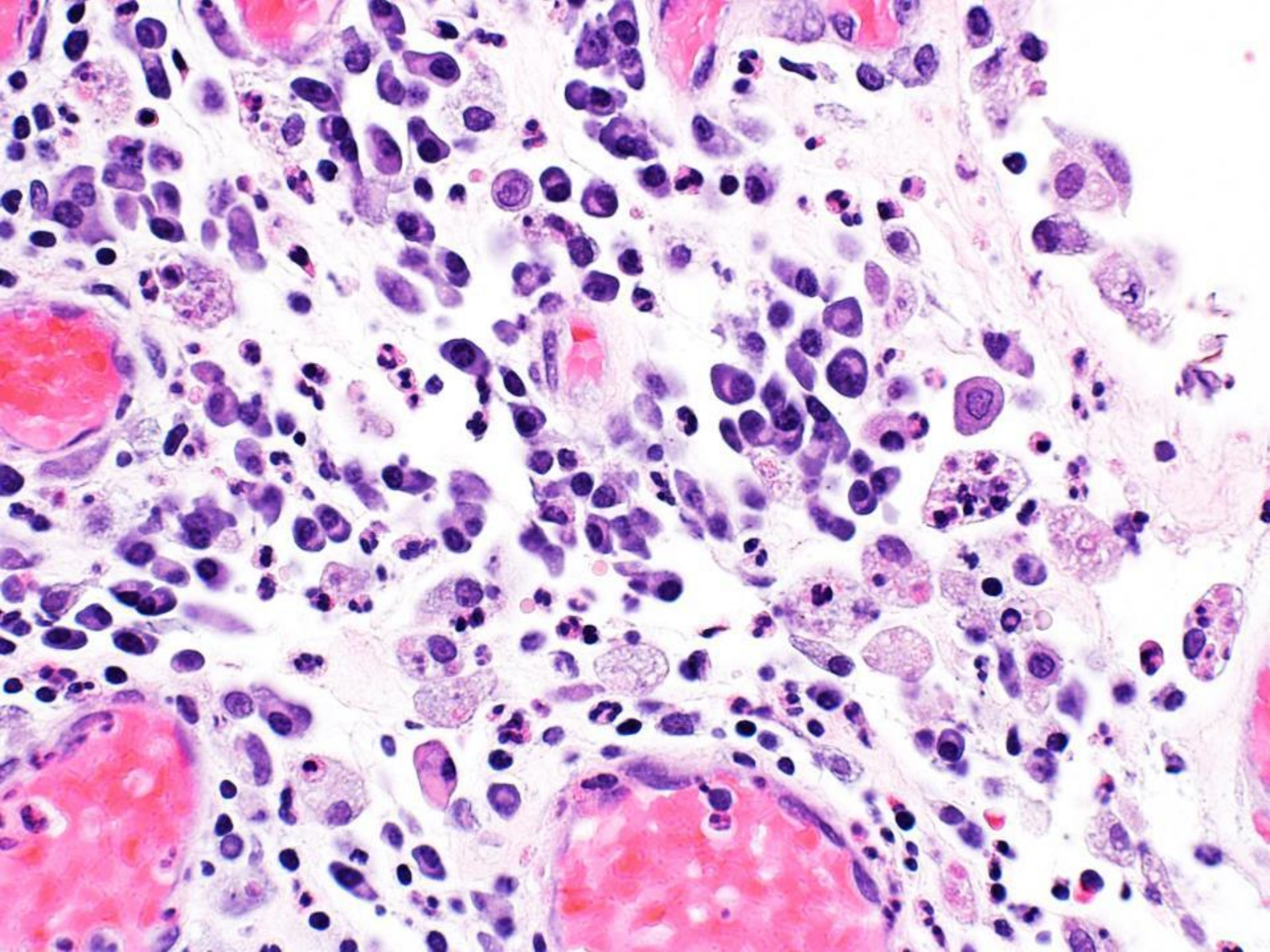
Patients with:	Uterine pathology (%)	Endometrial pathology (%)	Endometrial malignancy (%)
Additional clinical and/or Pap smear findings	60	36.7	20
Histiocytes only	5.5	2.9	1.3

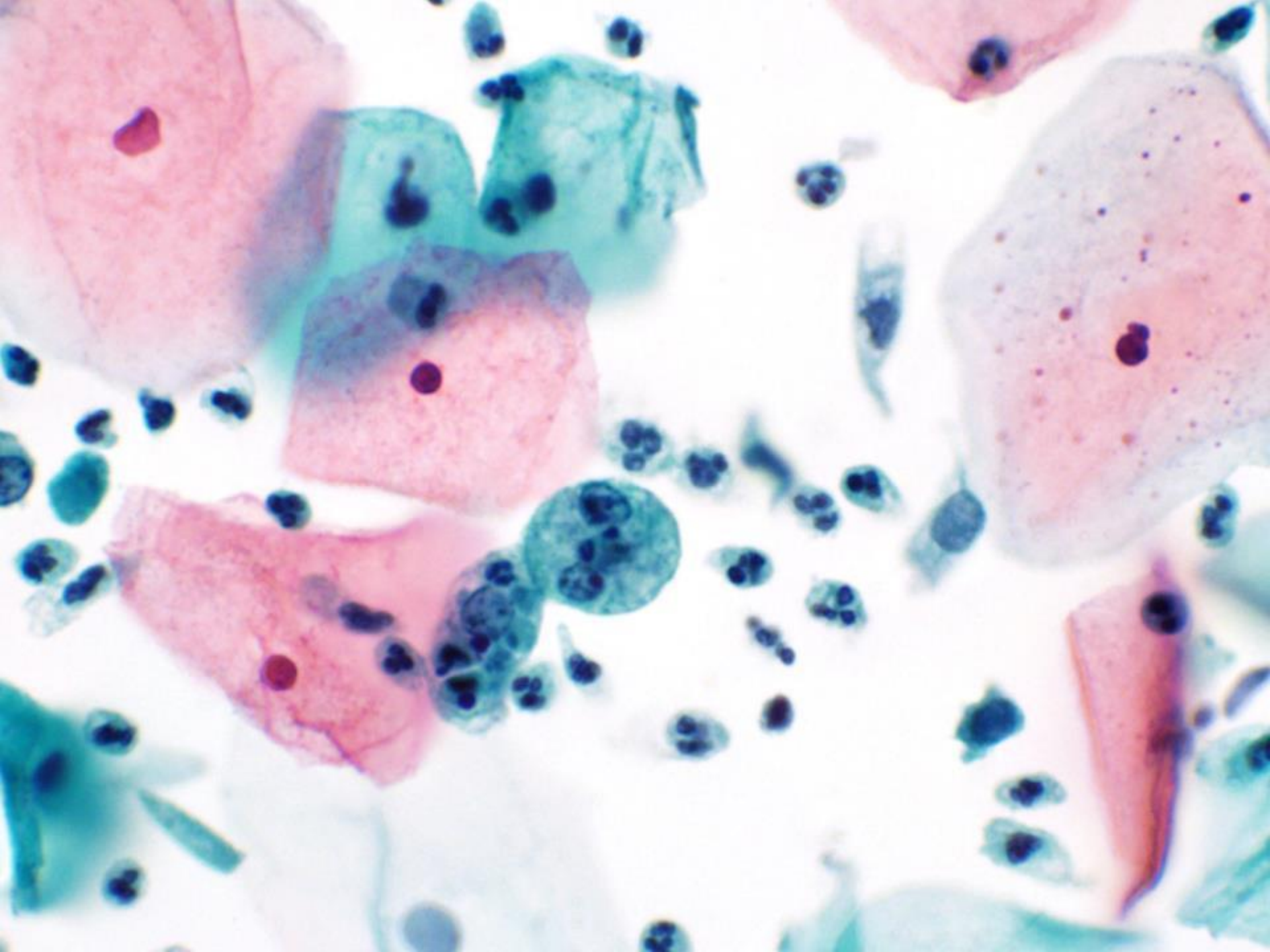
Uterine pathology = all primary and metastatic uterine malignancies, endometrial hyperplasias, endometrial and endocervical polyps, submucosal leiomyomata and tamoxifen-related endocervical glandular atypia; endometrial pathology = all endometrial primary malignancies, endometrial hyperplasias and endometrial polyps; endometrial malignancy = all primary endometrial carcinomas and malignant mixed müllerian tumors.

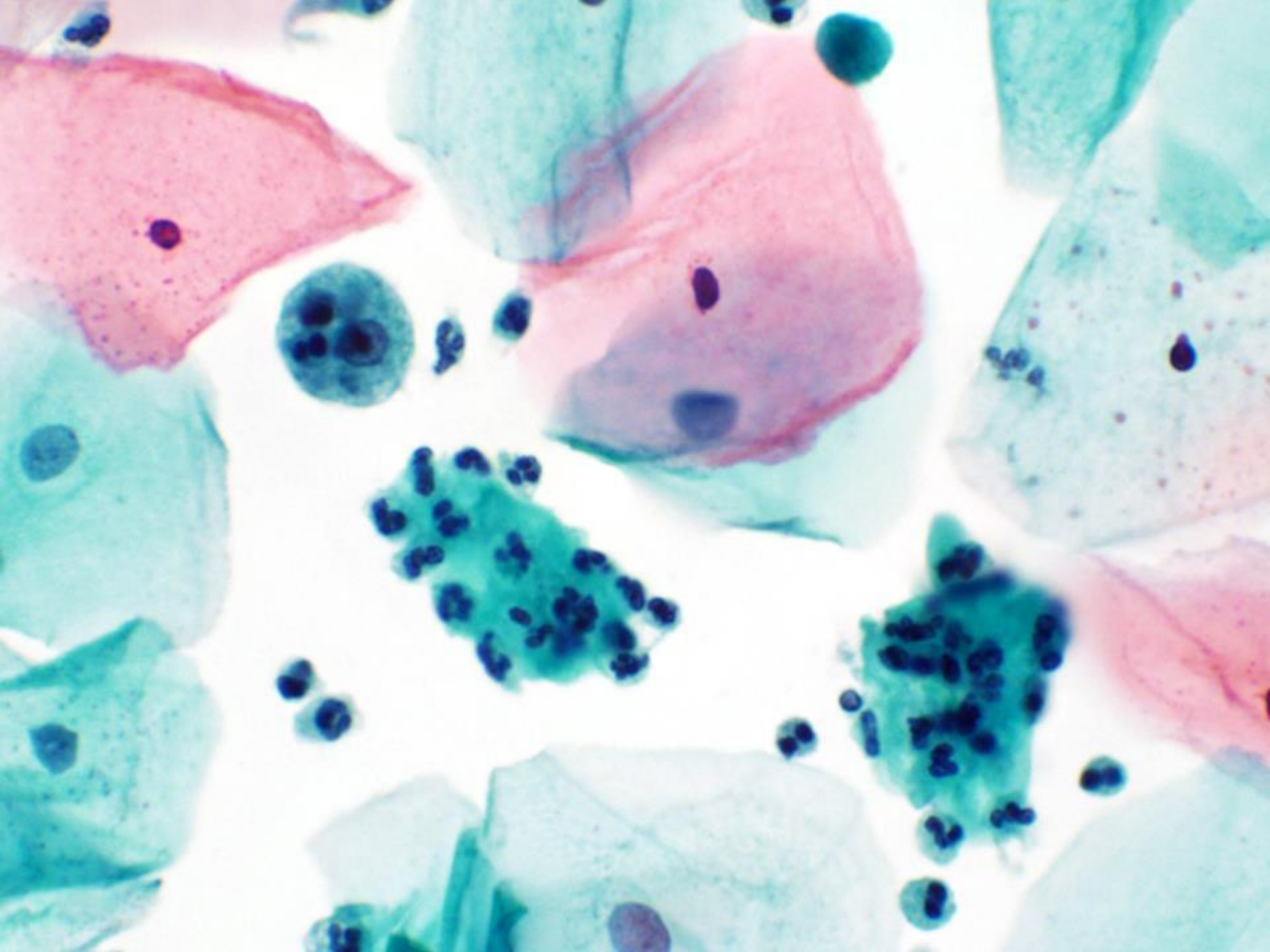
Nassar A et al. Acta Cytologica 2003 47(5):762-7

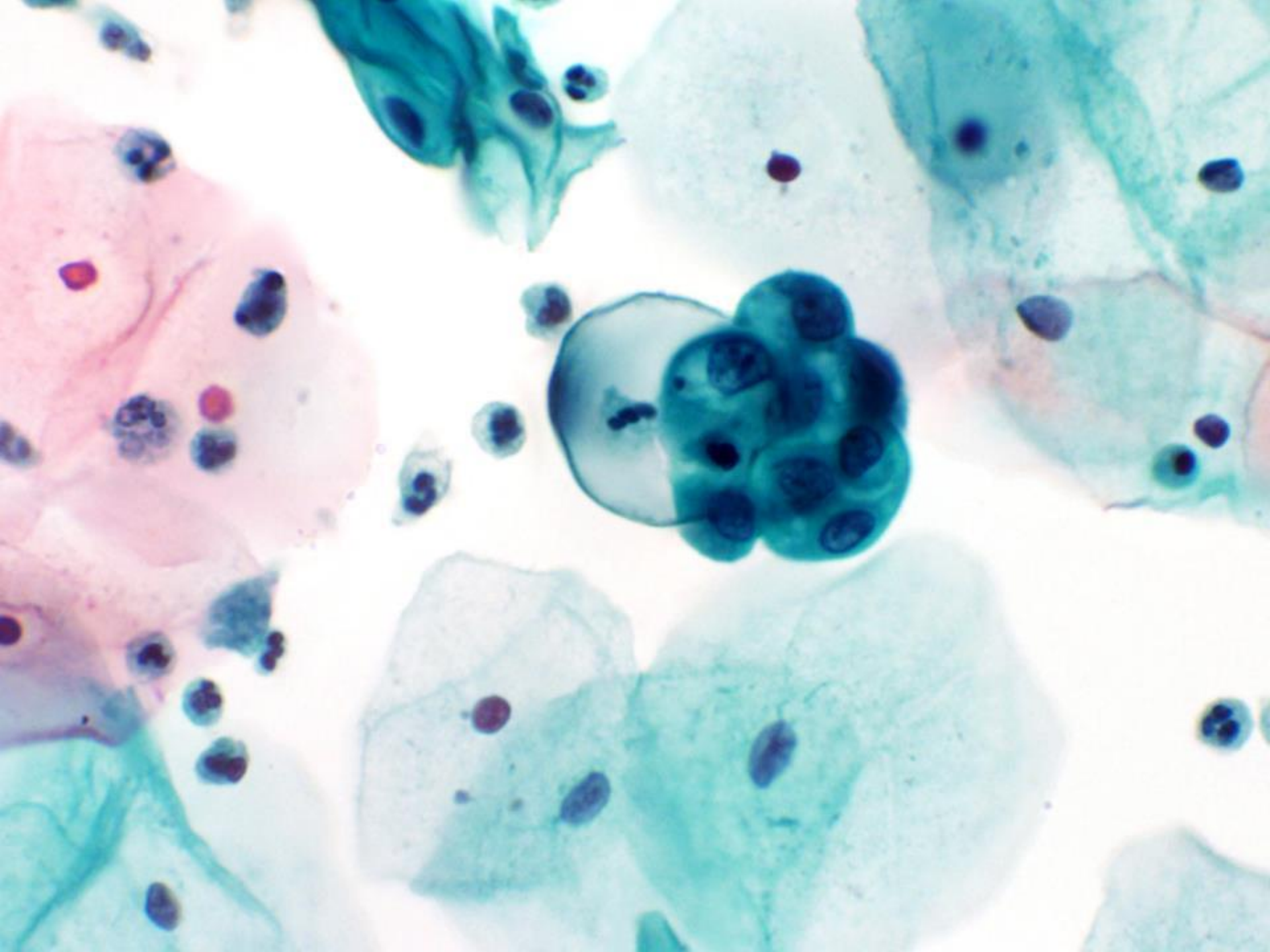


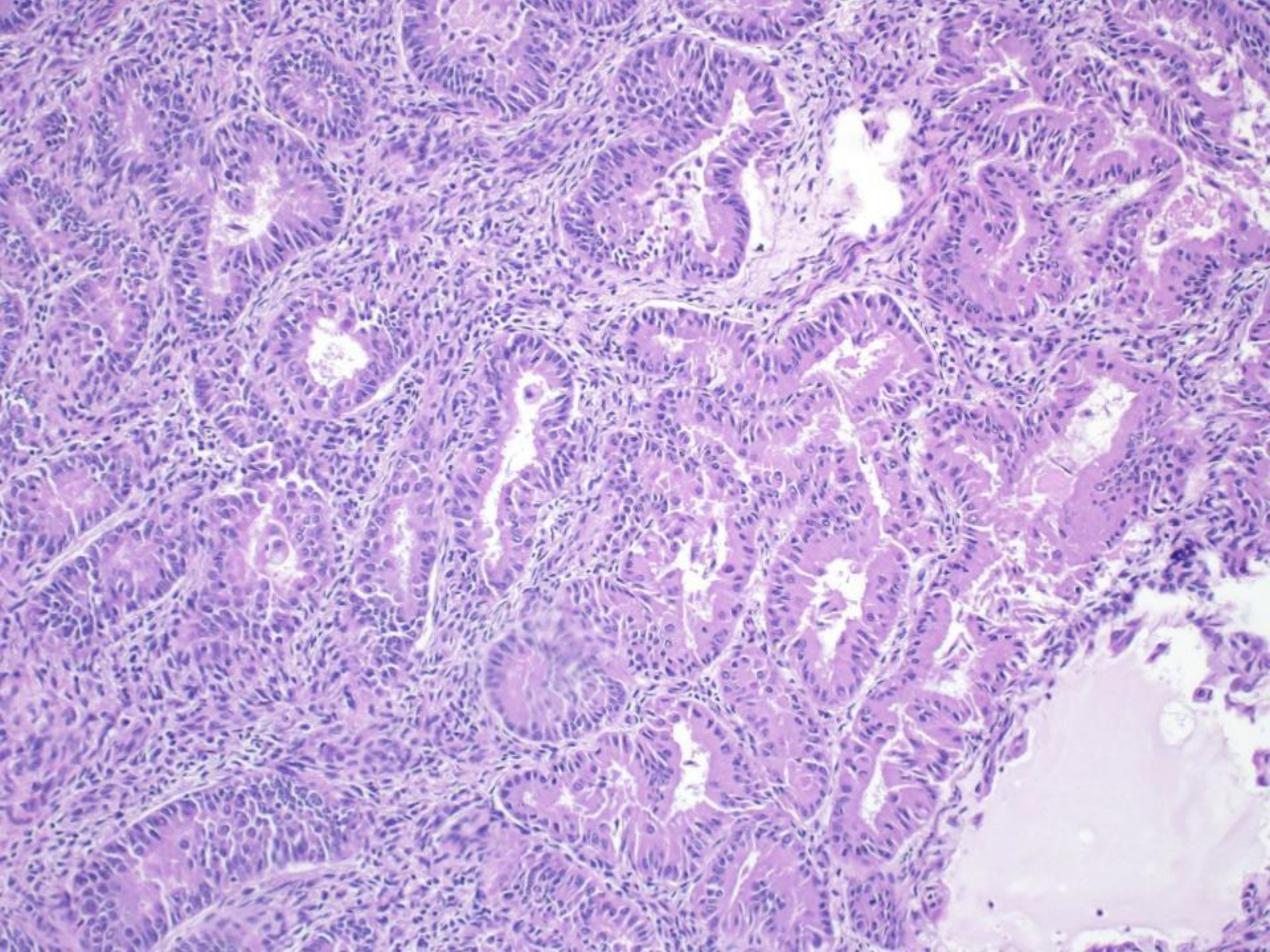


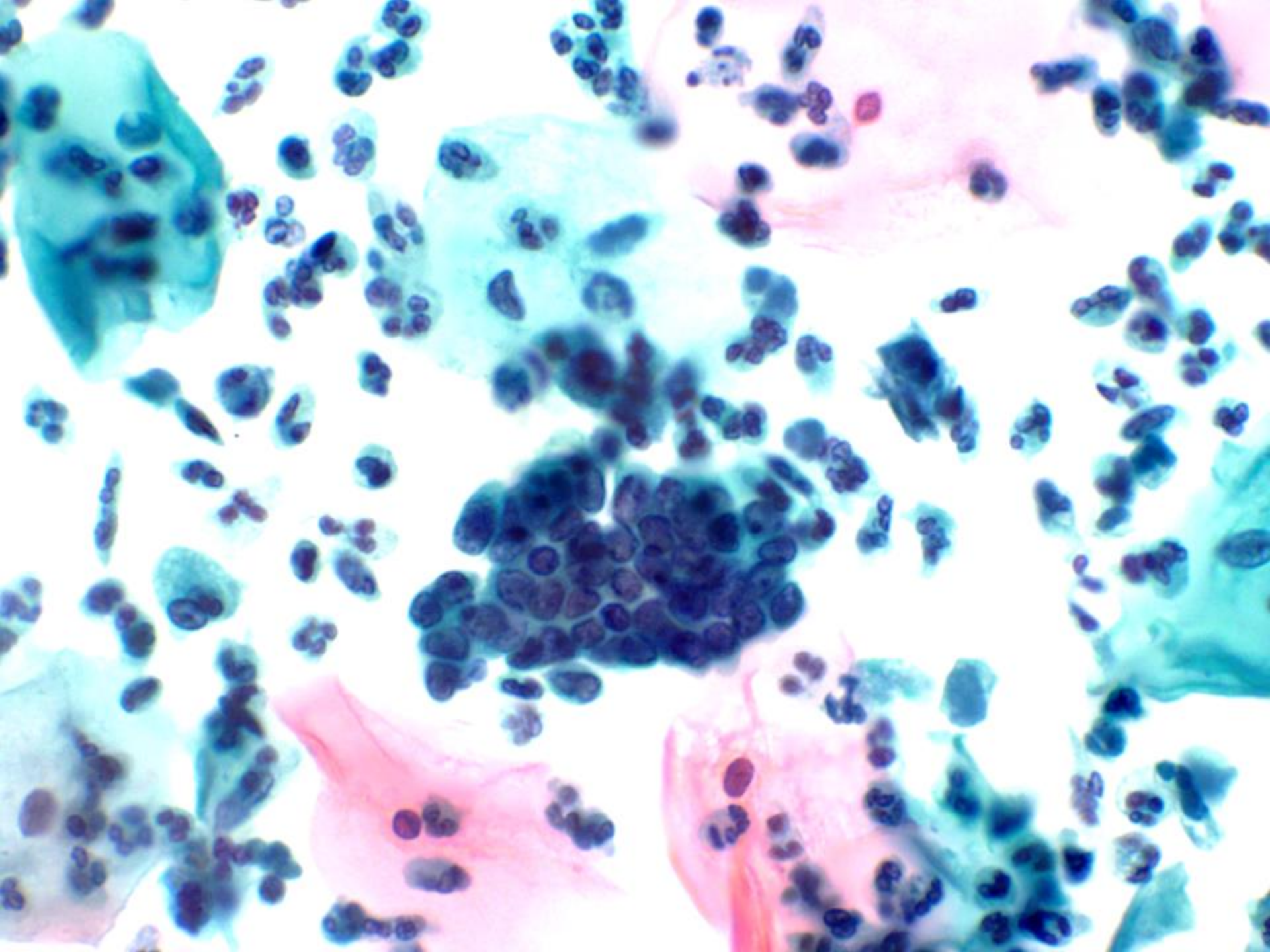


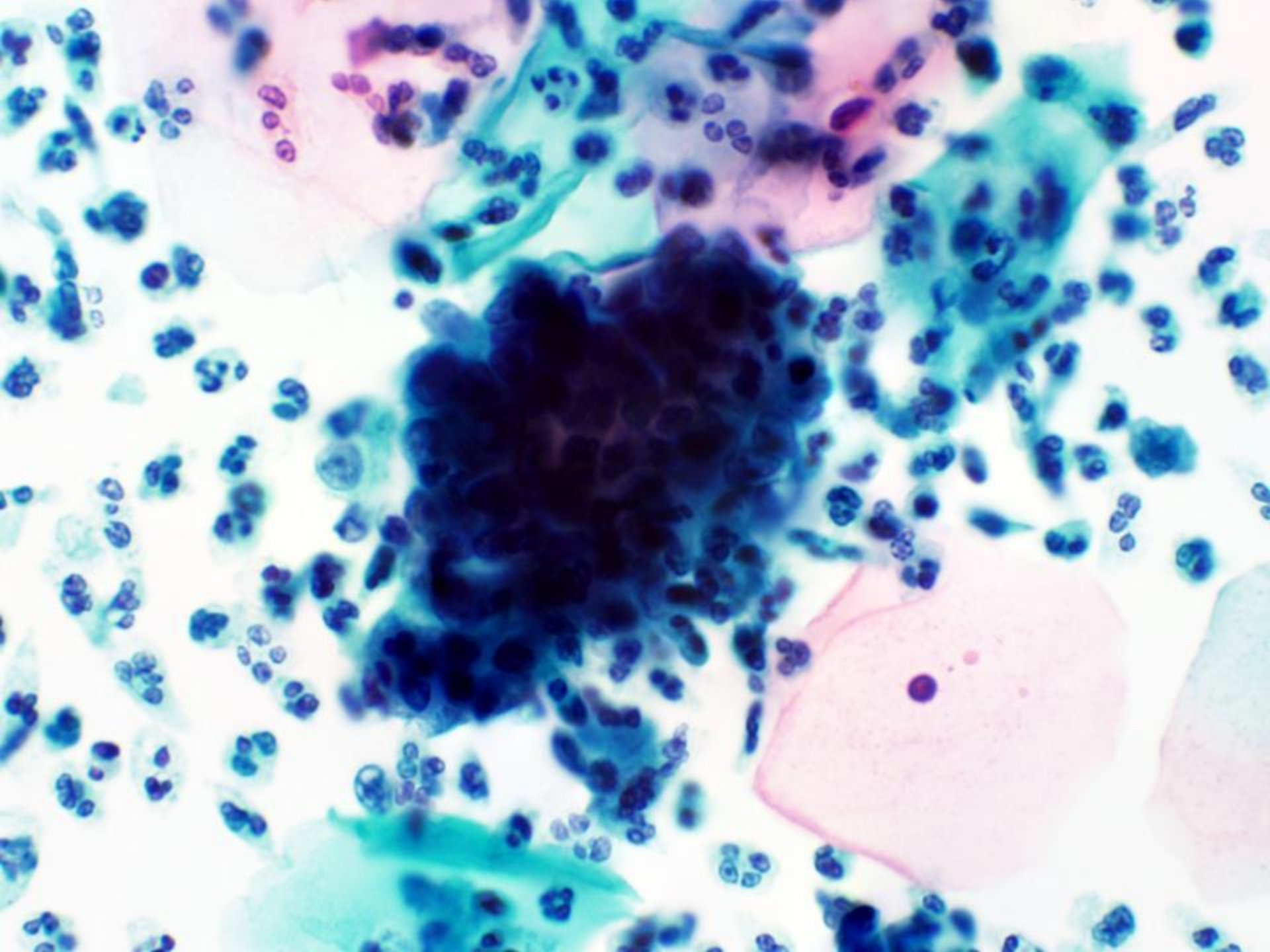


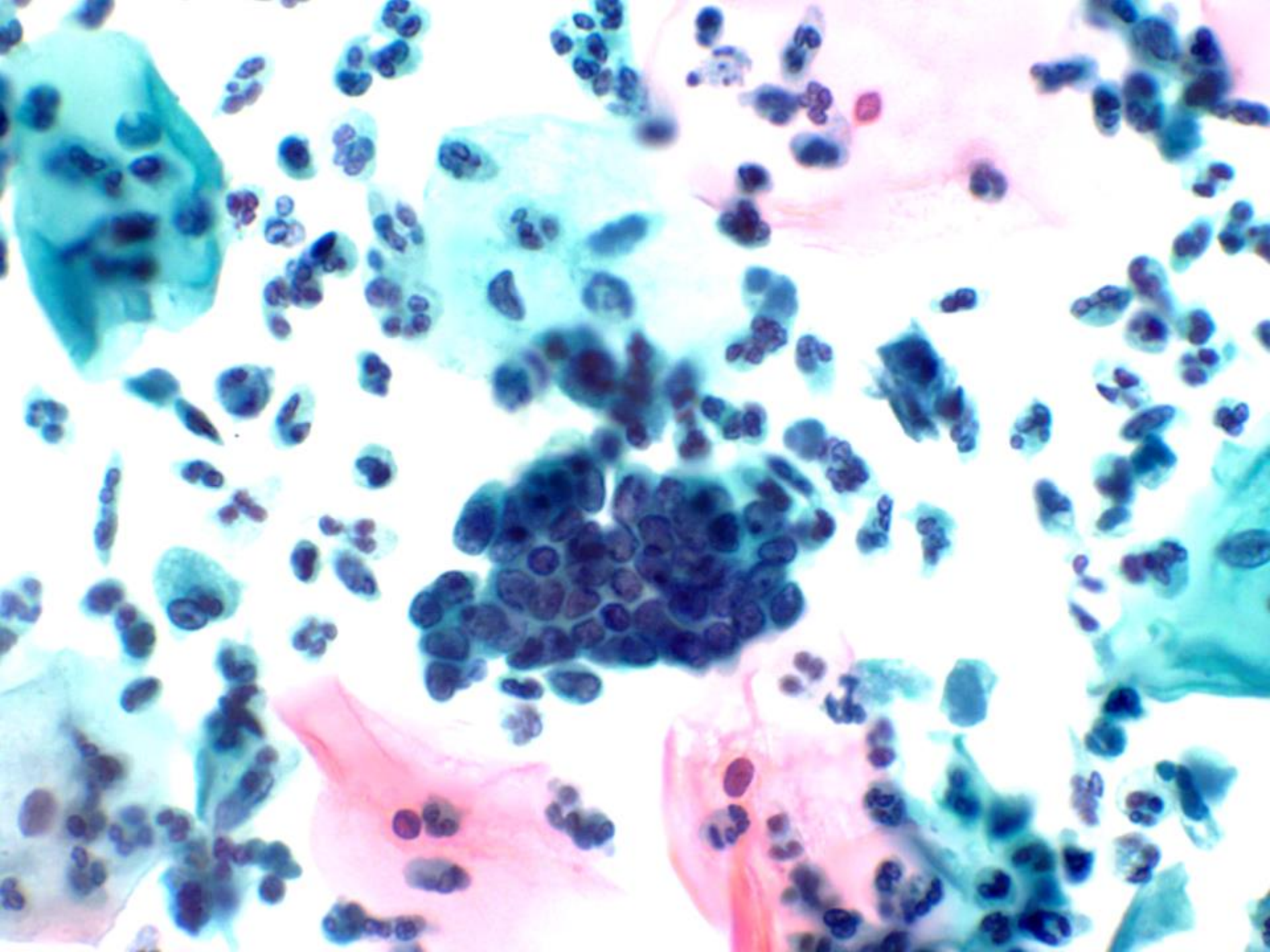


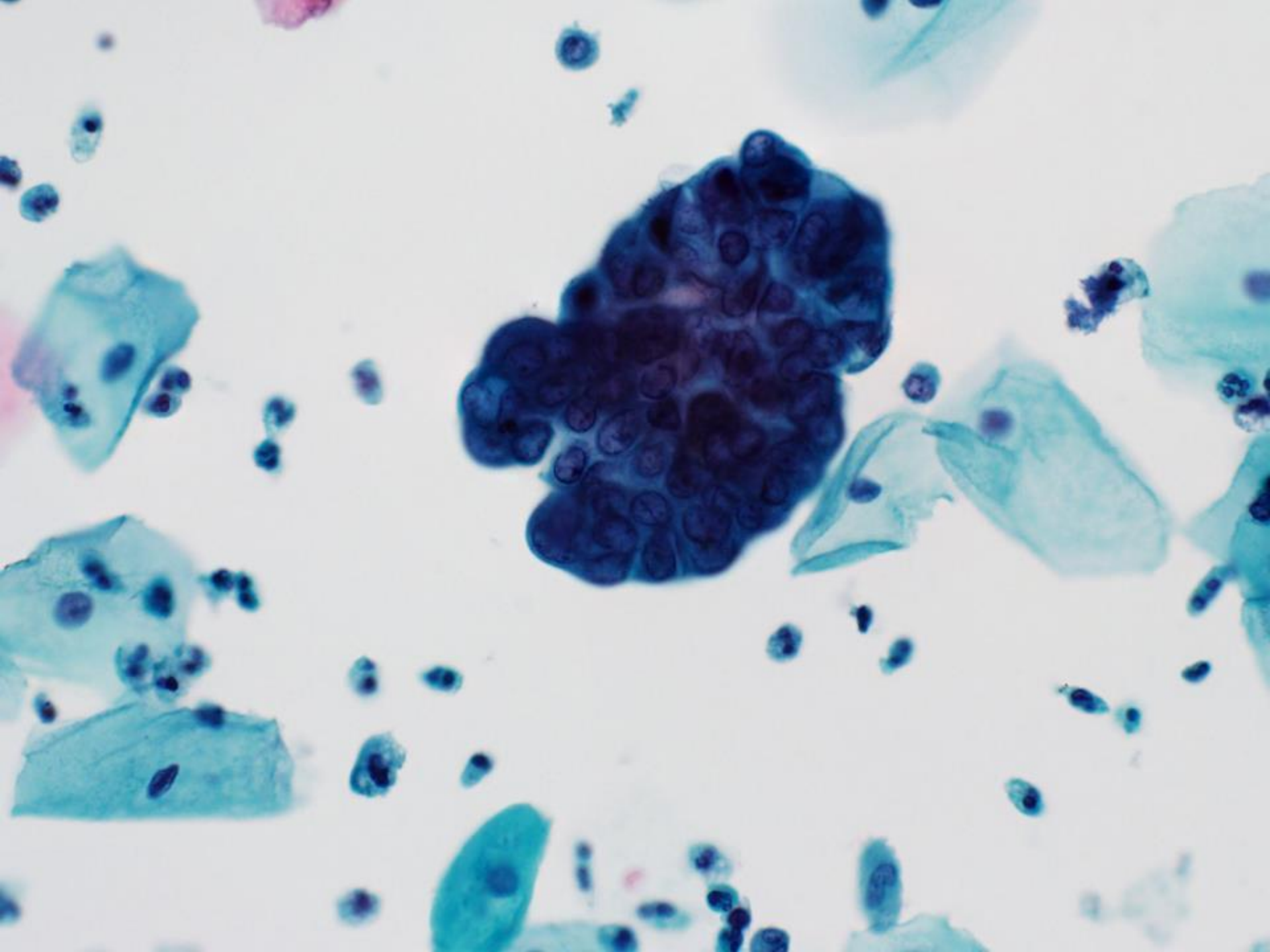






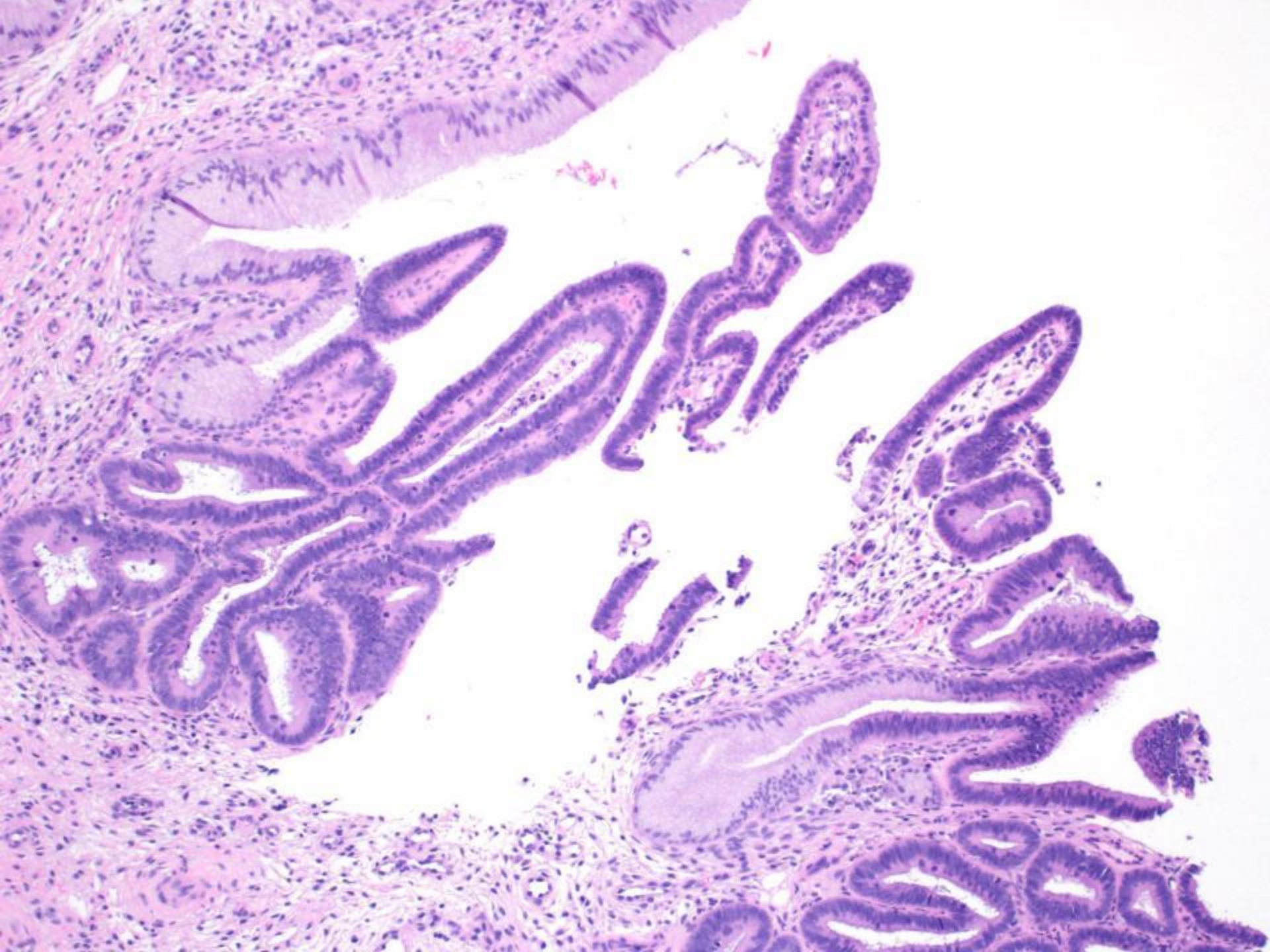






Assessment?

HSIL vs. AIS

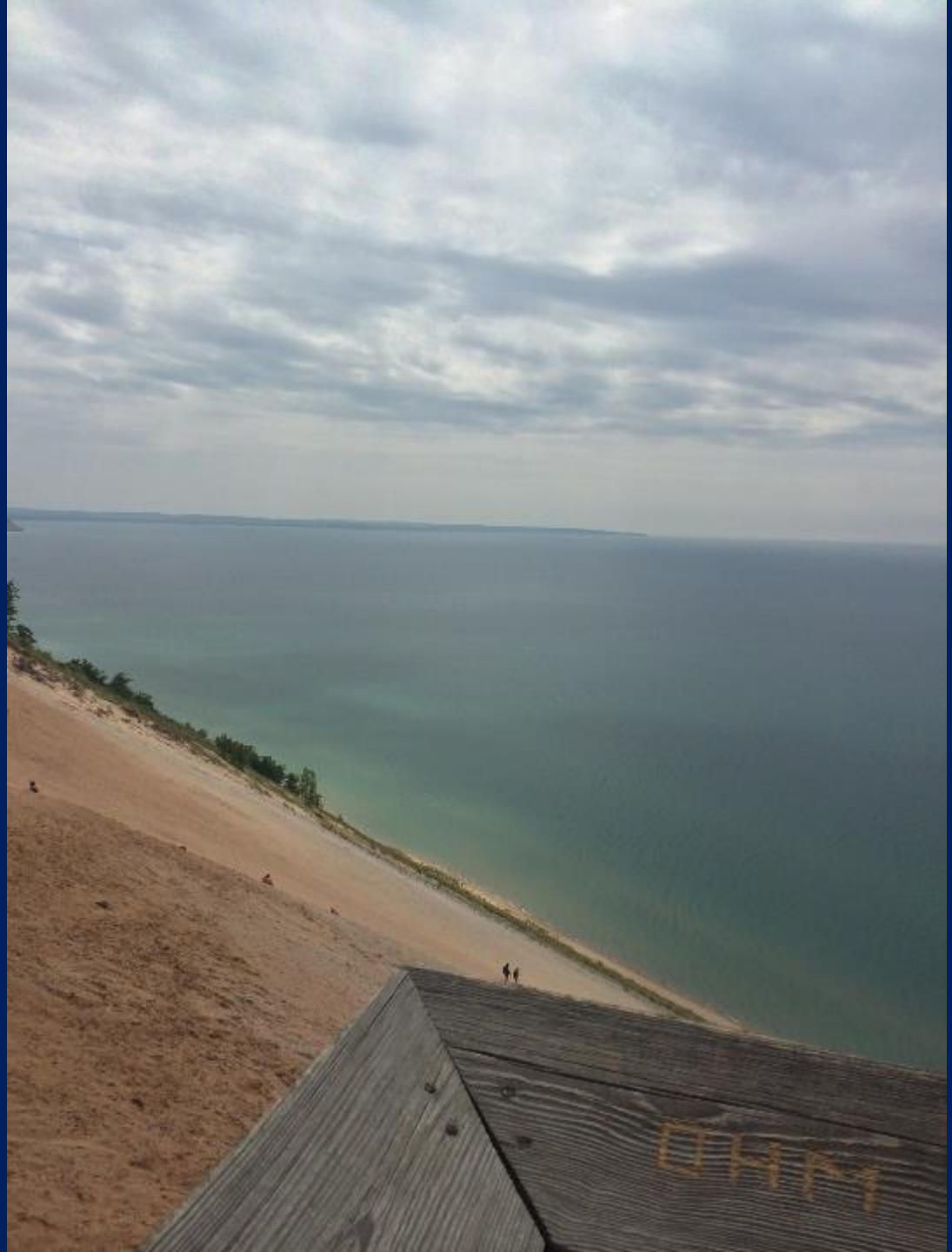


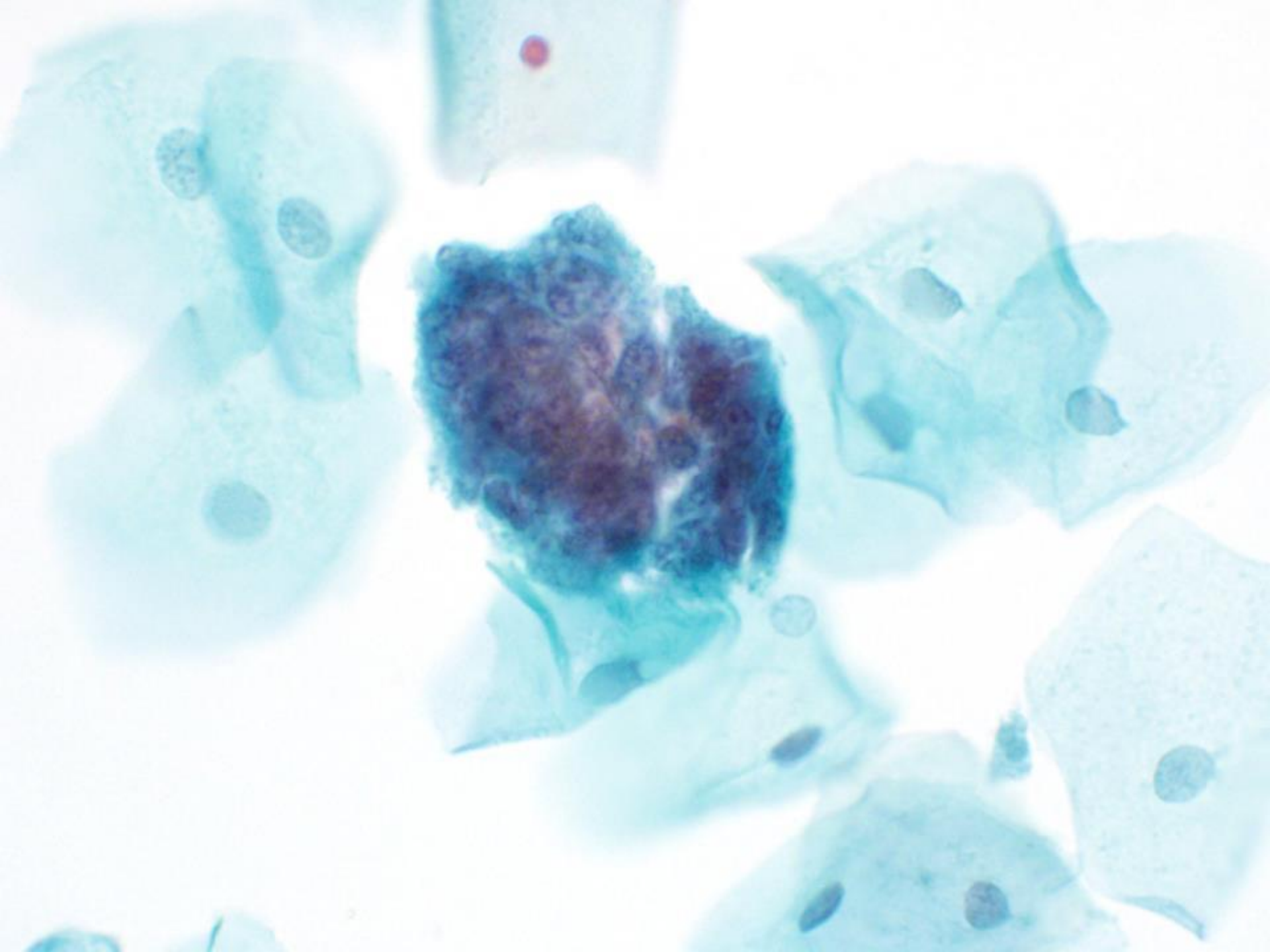
Adenocarcinoma in situ (AIS)

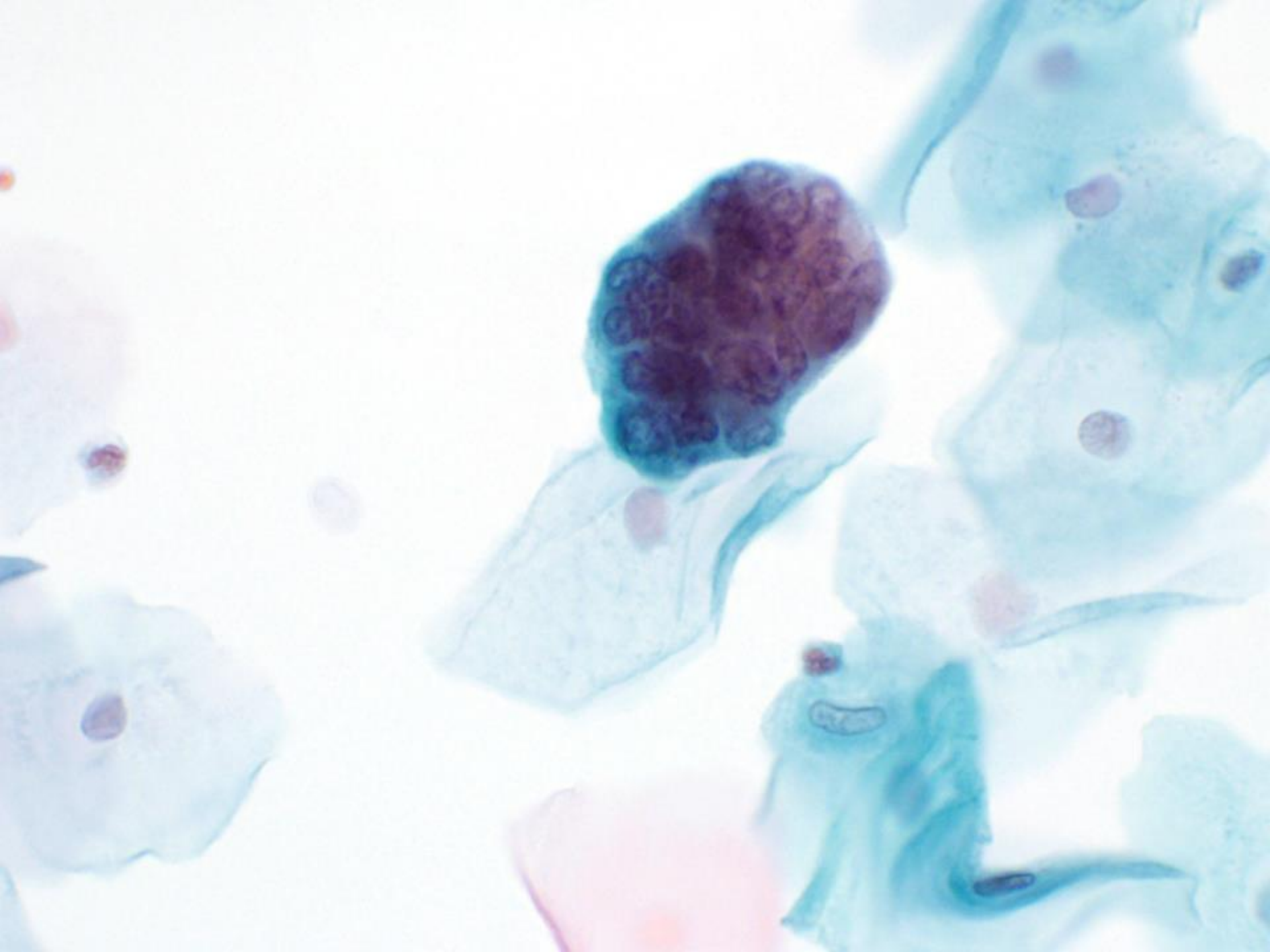
Table 2. Comparison of False-Negative Rates, Percentages of Reviews Concordant With Exact Interpretation, and Percentages of Slides With All Reviews Concordant With the Exact Interpretation*†

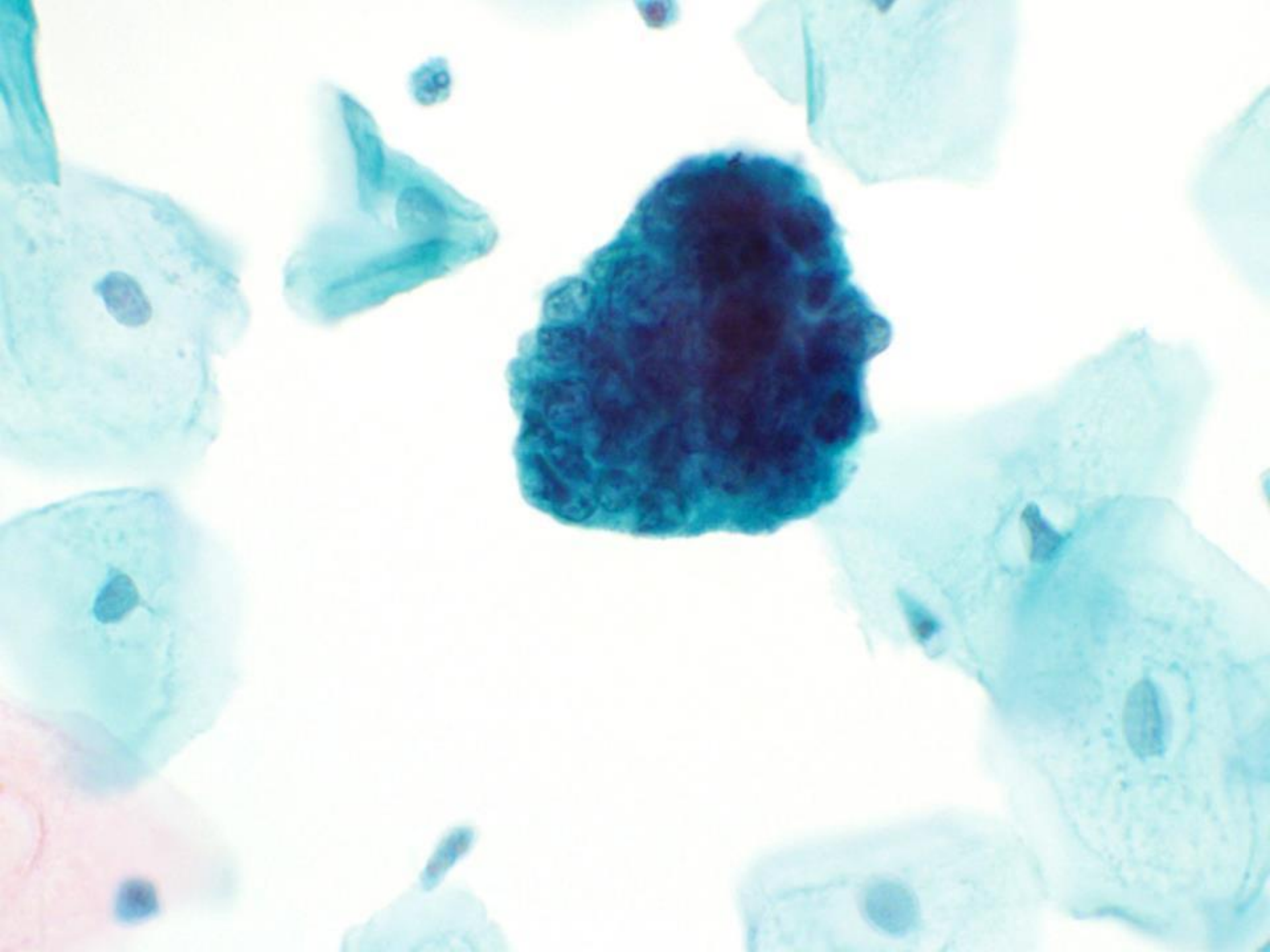
Reference Interpretation	A—False-Negative Rate/ Total Reviews (%)	B—Reviews With Exact Interpretation/ Total Reviews (%)		C—Slides With Exact Interpretation in All Reviews/Total Reviews (%)‡	
		226 Included	226 Excluded	226 Included	226 Excluded
AIS	25/213 (11.7)	99/213 (46.5)	99/213 (46.5)	0/20 (0.0)	0/20 (0.0)
ACA	251/2821 (8.9)	2036/2821 (72.2)	1873/2821 (66.4)	73/275 (26.5)	63/275 (22.9)
SCC	63/1886 (3.3)	1417/1886 (75.1)	1218/1886 (64.6)	68/189 (36.0)	41/189 (21.7)
HSIL	343/7535 (4.6)	5516/7535 (73.2)	4800/7535 (63.7)	196/763 (25.7)	115/763 (15.1)

Renshaw AA et al. Arch Pathol Lab Med 2004 128:153-7







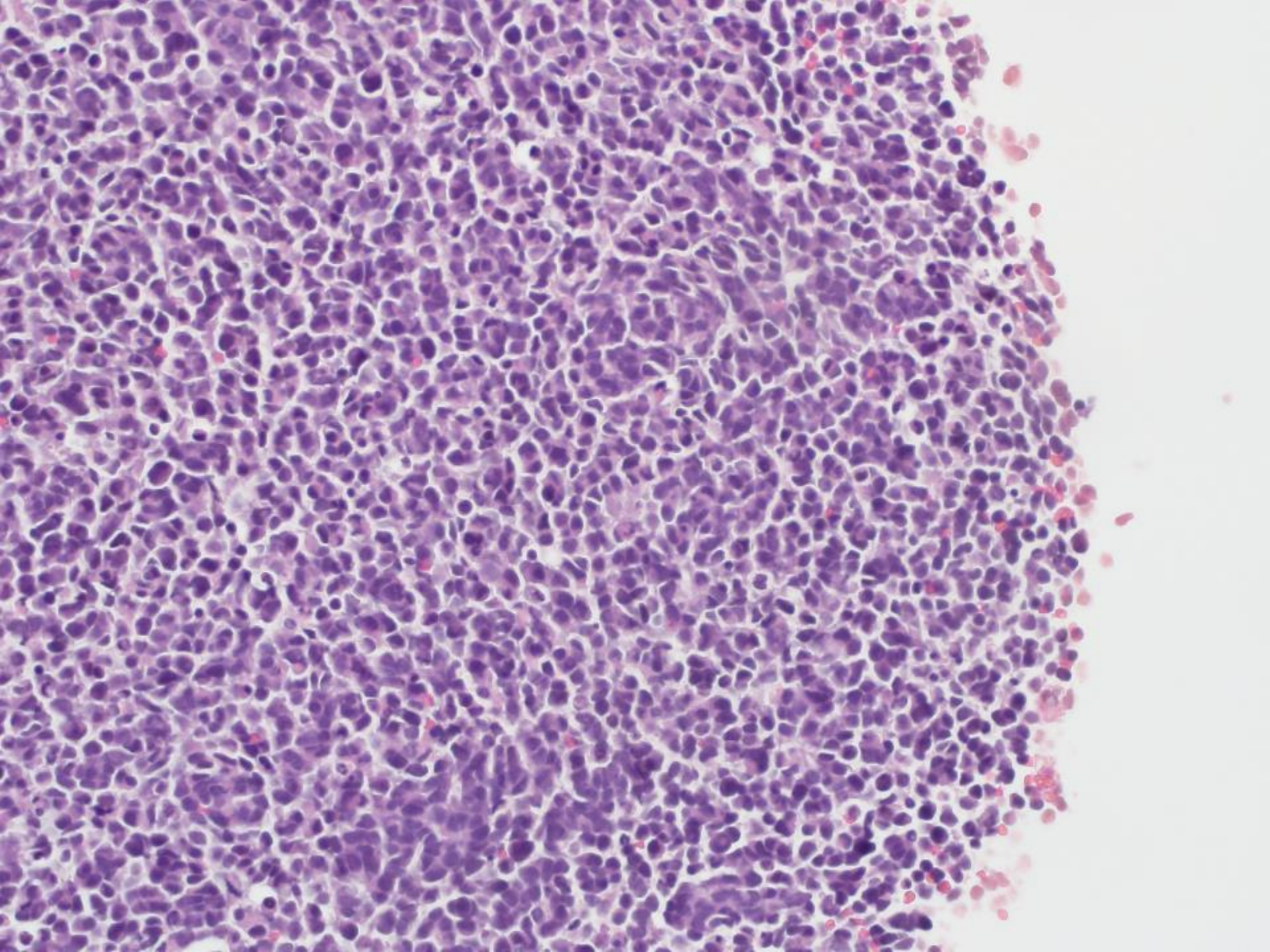


Assessment?

Assessment?

HCG's with high N/C ratios
Clean background
Pleomorphic nuclei
Considerations:

- HSIL
- AIS
- Adenocarcinoma NOS



Uterine MMMT

Table I. Clinical and Cytological Features in SurePath™ Cervical Samples in Eight Cases of Uterine MMMT

No.	*Age*	*Clinical features*	*Cellularity*	*Epi:Sarc elements*	*Background*	*Endocervical involvement*	*Myometrial infiltration*
1	67	Persistent vaginal bleeding	+++	1:2	Atrophic	Not involved	Not involved
2	63	Weight loss, pelvic mass	++	1:0	Atrophic	NA[a]	NA[a]
3	82	H/O breast carcinoma on tamoxifen	+++	3:1	Atrophic	Local recurrence involving cervix	<50%
4	65	Vaginal bleeding for 6 weeks	+++	3:1	Atrophic	Involved	>50%
5	62	Suspicious endometrial polyp with dilated vessels	++	1:0	Estrogenized	Not involved	>50%
6	60	PMB; huge endometrial polyp	++	1:0	Estrogenized	Not involved	<50%
7	65	Polypoid endometrium 6 cm	++	1:0	Atrophic	Cervical tissue not involved but polypoid tumor extends to external os	<50%
8	60	PMB; round mass in cavity	+	1:0	Estrogenized	Not involved	Not involved

[a]PMB, postmenopausal bleeding; NA, not available.

Smith J et al. Diagn Cytopathol 2012 42:165-169

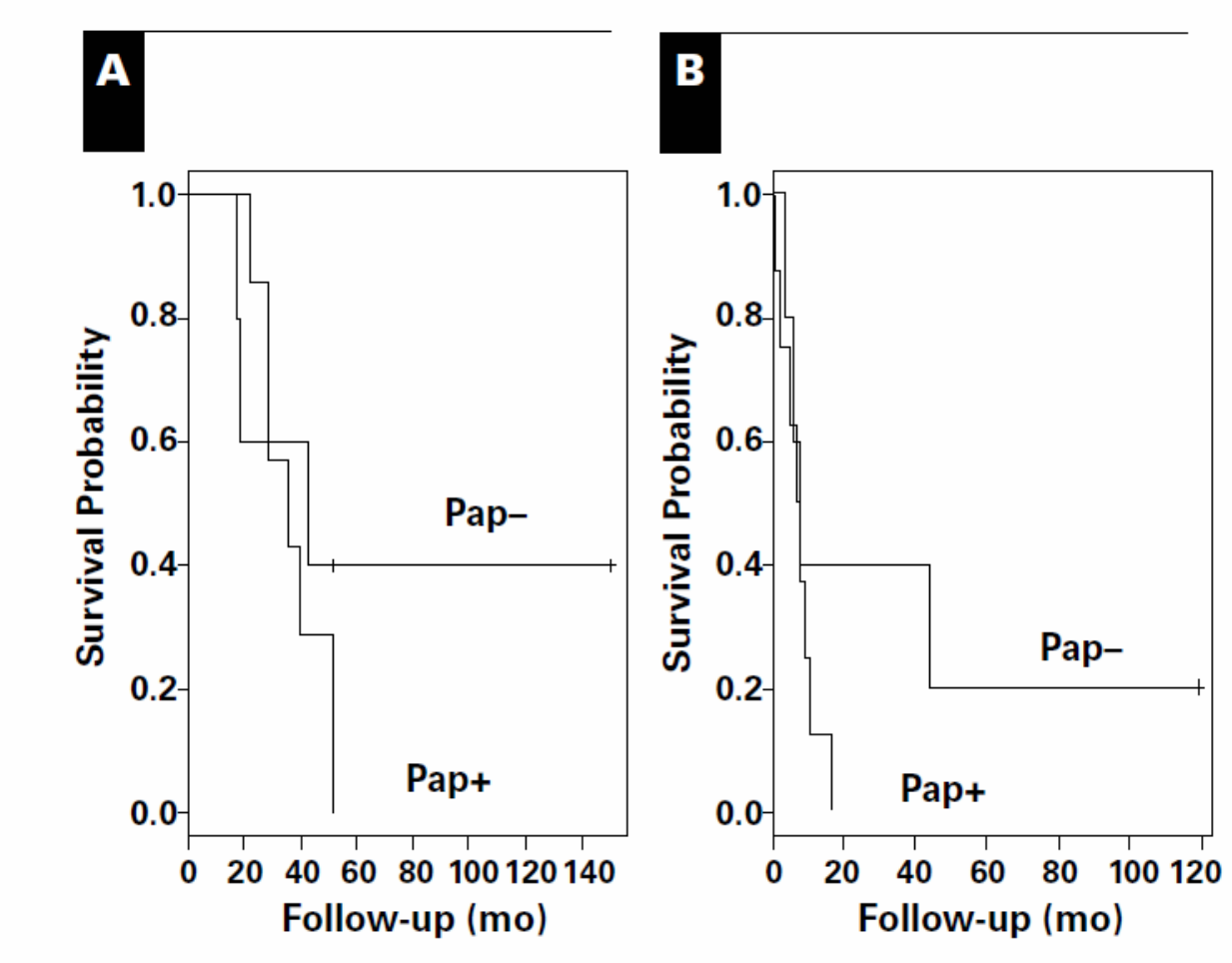
Uterine MMMT

Summary of Papanicolaou Smear and Histologic Data

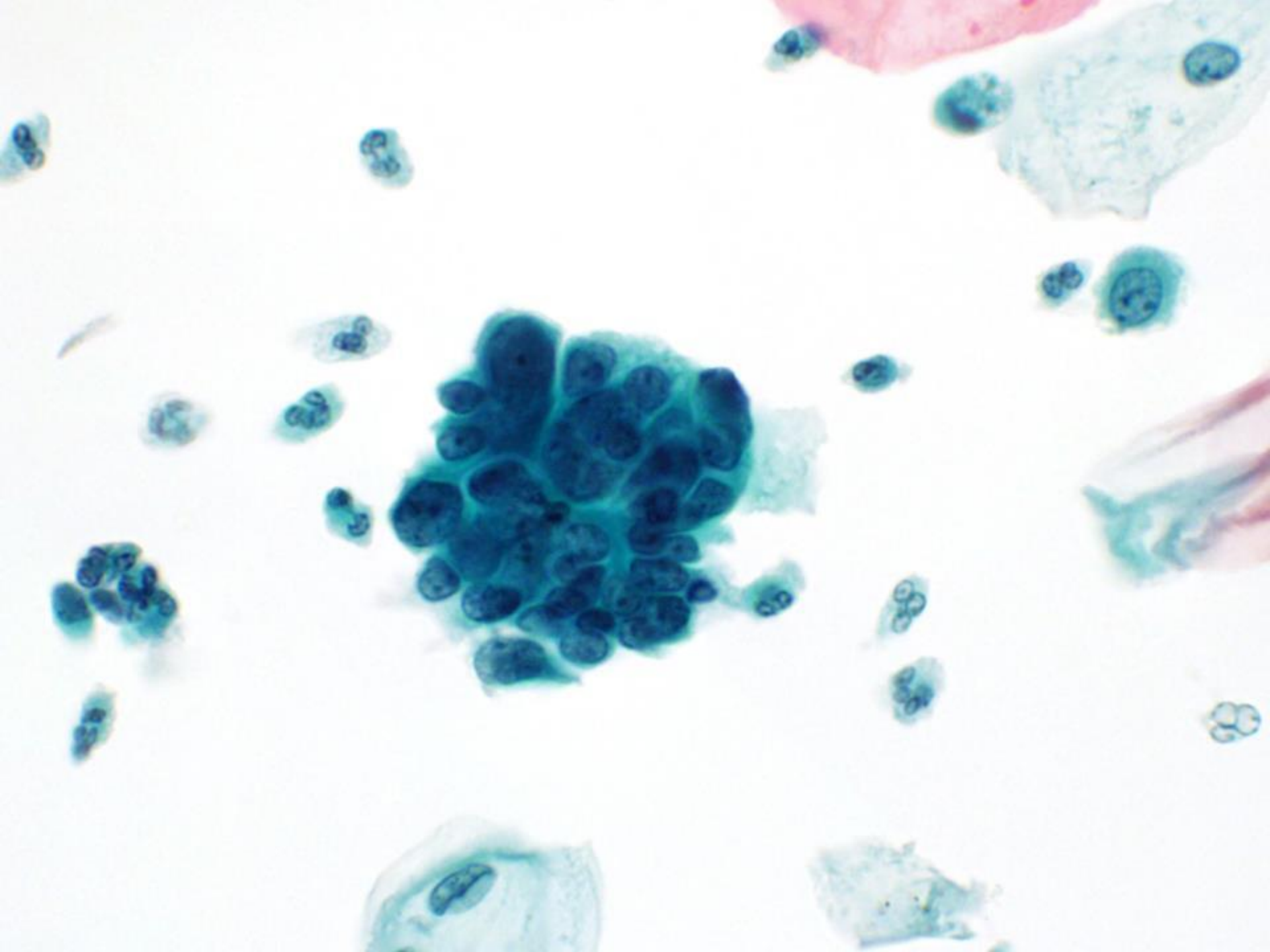
Original/Review Diagnosis/Case No.*	Diathesis	Carcinoma†	Sarcoma†	Metastasis	Cervix Involvement	Myometrial Invasion‡	Lymphatic or Vascular Invasion
Diagnostic/diagnostic							
1	No	E, 50	U, 40; R, 10	NK	—	—	—
2	Yes	E, 60; CC, 4; M, 1	C, 20; U, 15	Yes	Yes	Yes, O	Yes
3	No	S, 75; E, 10	U, 14; R, 1	No	No	Yes, Su	No
4	Yes	E, 90	U, 10	Yes	No	Yes, O	Yes
5	No	E, 70	C, 30	No	No	Yes, I	Yes
6	Yes	E, 5	U, 80; R, 15	NK	—	—	—
7	Yes	E, 30	U, 50; C, 20	No	Yes	No	No
Atypical/diagnostic							
8	Yes	E, 5	U, 95	NK	—	—	—
Atypical/atypical							
9	No	E, 40	U, 60	NK	—	—	—
10	No	E, 5	R, 50; U, 25; L, 20	No	Yes	Yes, O	No
11	No	E, 95	U, 5	No	No	Yes, Su	No
Negative/atypical							
12	No	E, 80	U, 20	Yes	No	Yes, O	Yes
13	No	S, 50	U, 50	No	No	No	No
14	No	E, 20	U, 45; R, 30; U, 5	No	Yes	Yes, O	No
15	No	E, 50	U, 50	NK	—	—	—
Negative/negative							
16	No	E, 50	U, 50	Yes	No	No	No
17	No	S, 60; CC, 30	U, 9; C, 1	Yes	No	Yes, Su	No
18	No	E, 35	U, 60; R, 5	No	No	Yes, Su	No
19	No	E, 70	U, 30	Yes	No	Yes, O	No
20	No	S, 5	U, 95	No	No	No	No
21	No	E, 35; Sq, 20	U, 40; R, 3; C, 2	No	No	Yes, I	No
22	No	E, 10	U, 85; C, 5	No	No	Yes, Su	No
23	No	E, 65; CC, 5	U, 30	No	No	Yes, Su	Yes
24	No	S, 25; Sq, 20; E, 5	U, 40; C, 5; L, 5	No	No	No	No
25	No	E, 80	U, 20	Yes	Yes	Yes, O	Yes

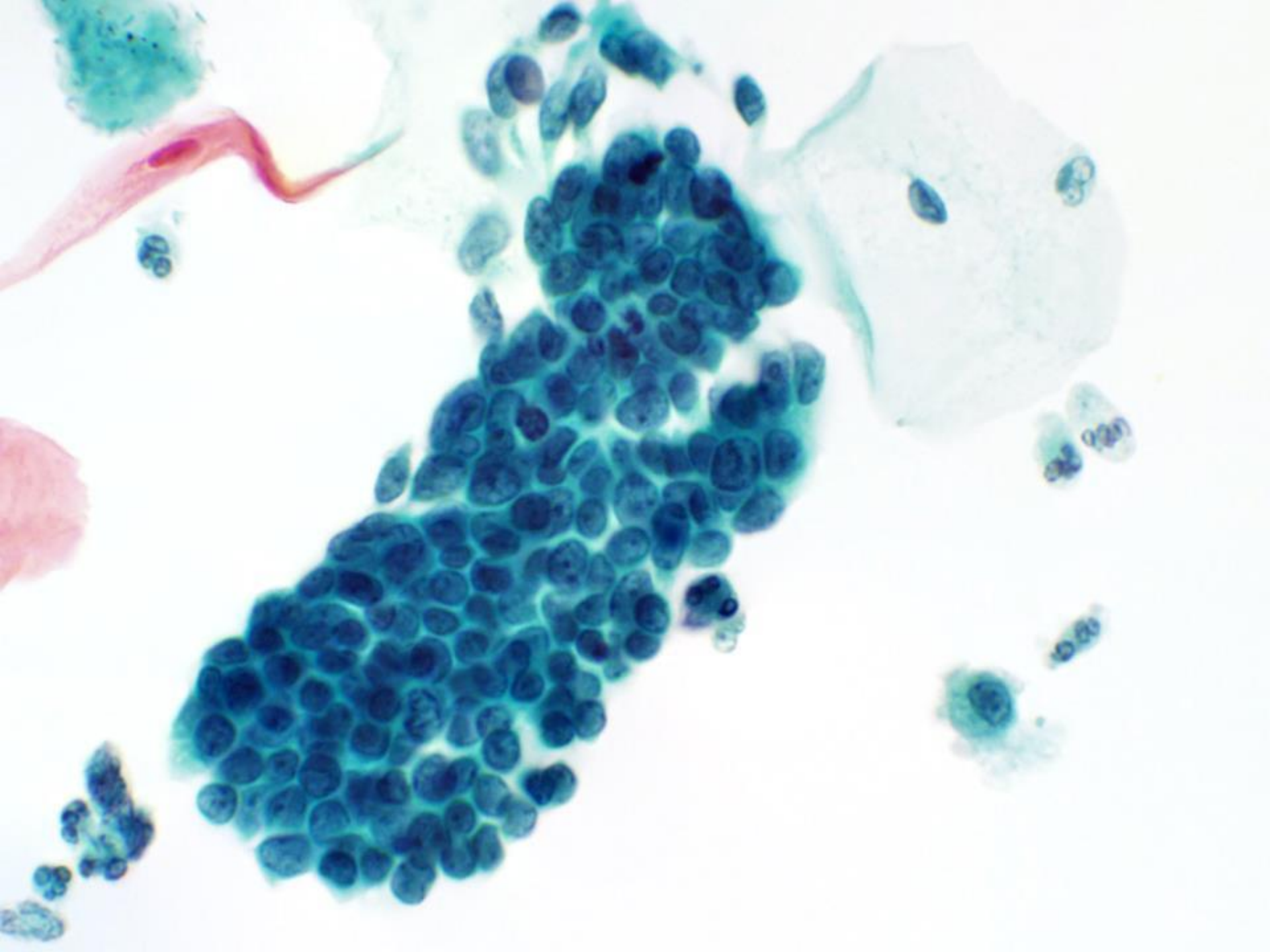
Snyder MJ et al. Am J Clin Pathol 2004 122:434

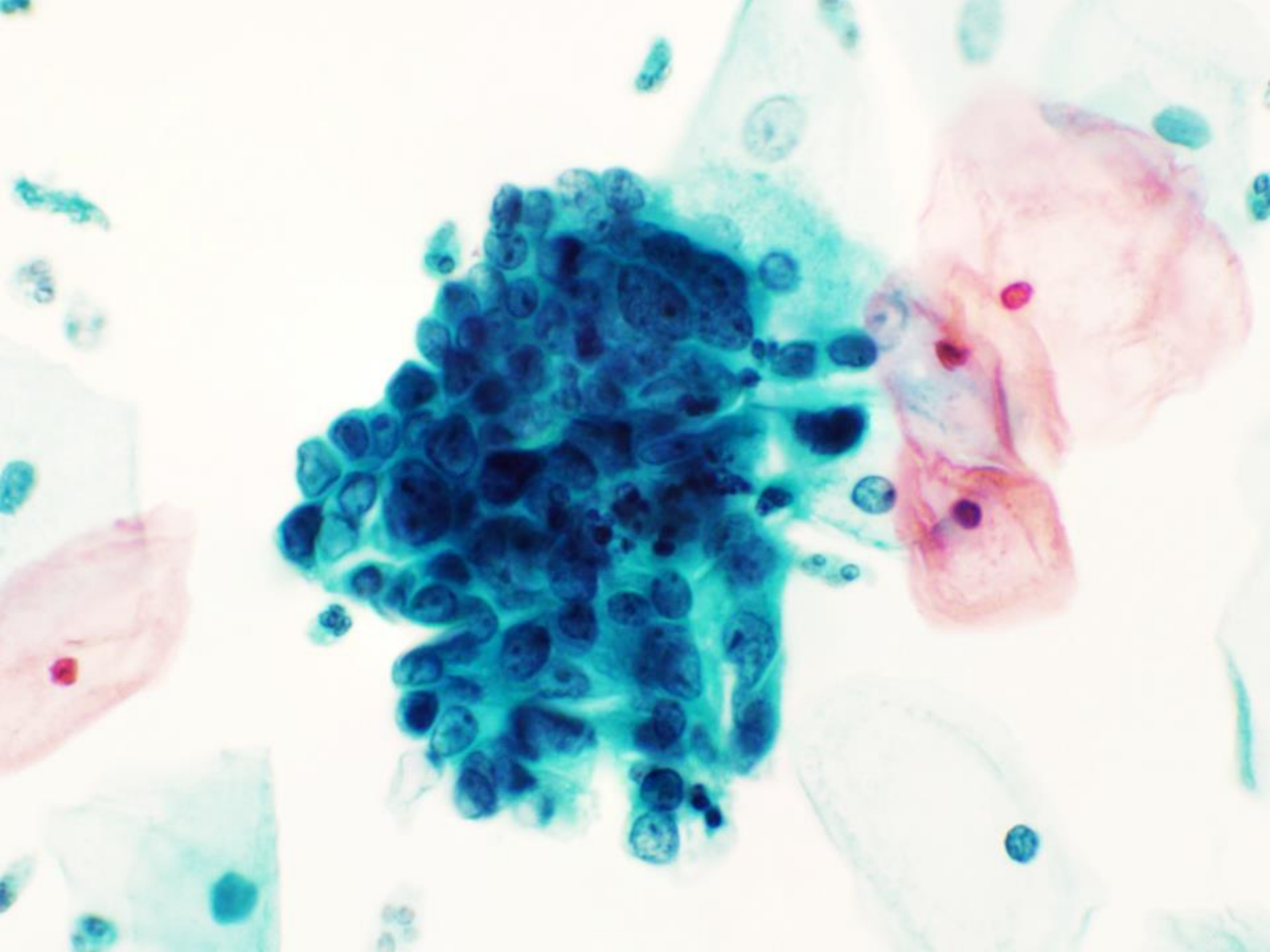
Uterine MMMT

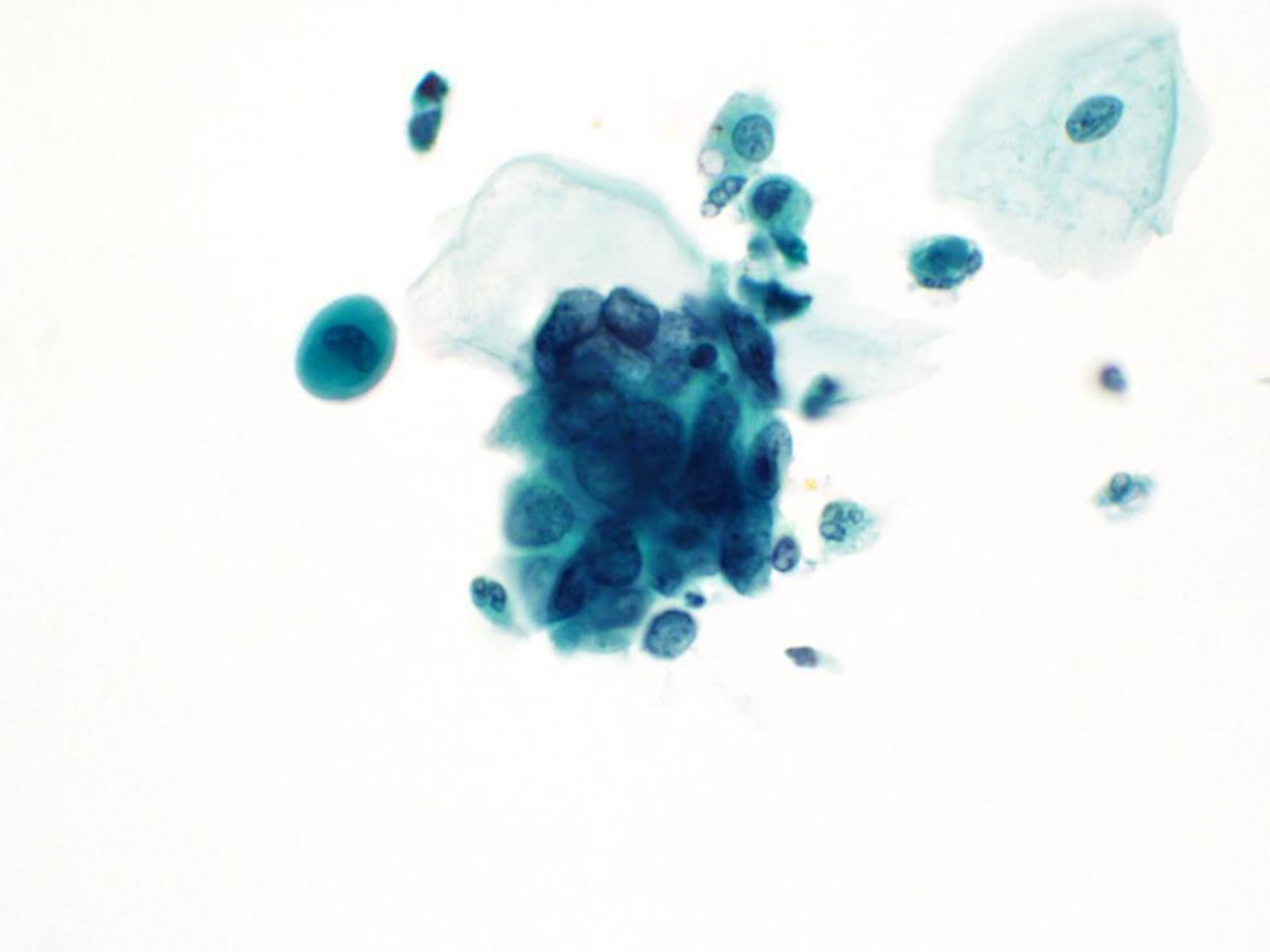


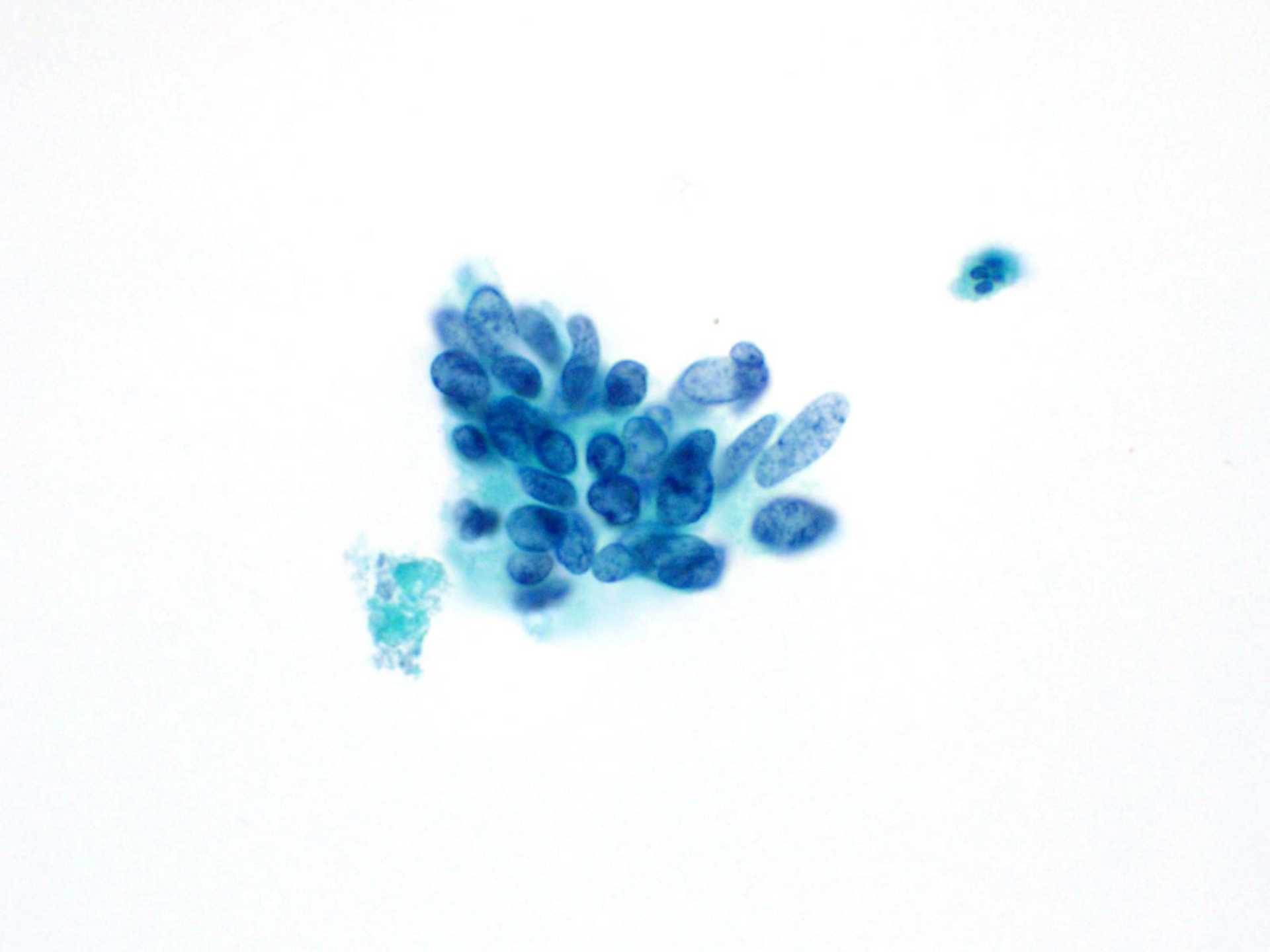
Snyder MJ et al. Am J Clin Pathol 2004 122:434



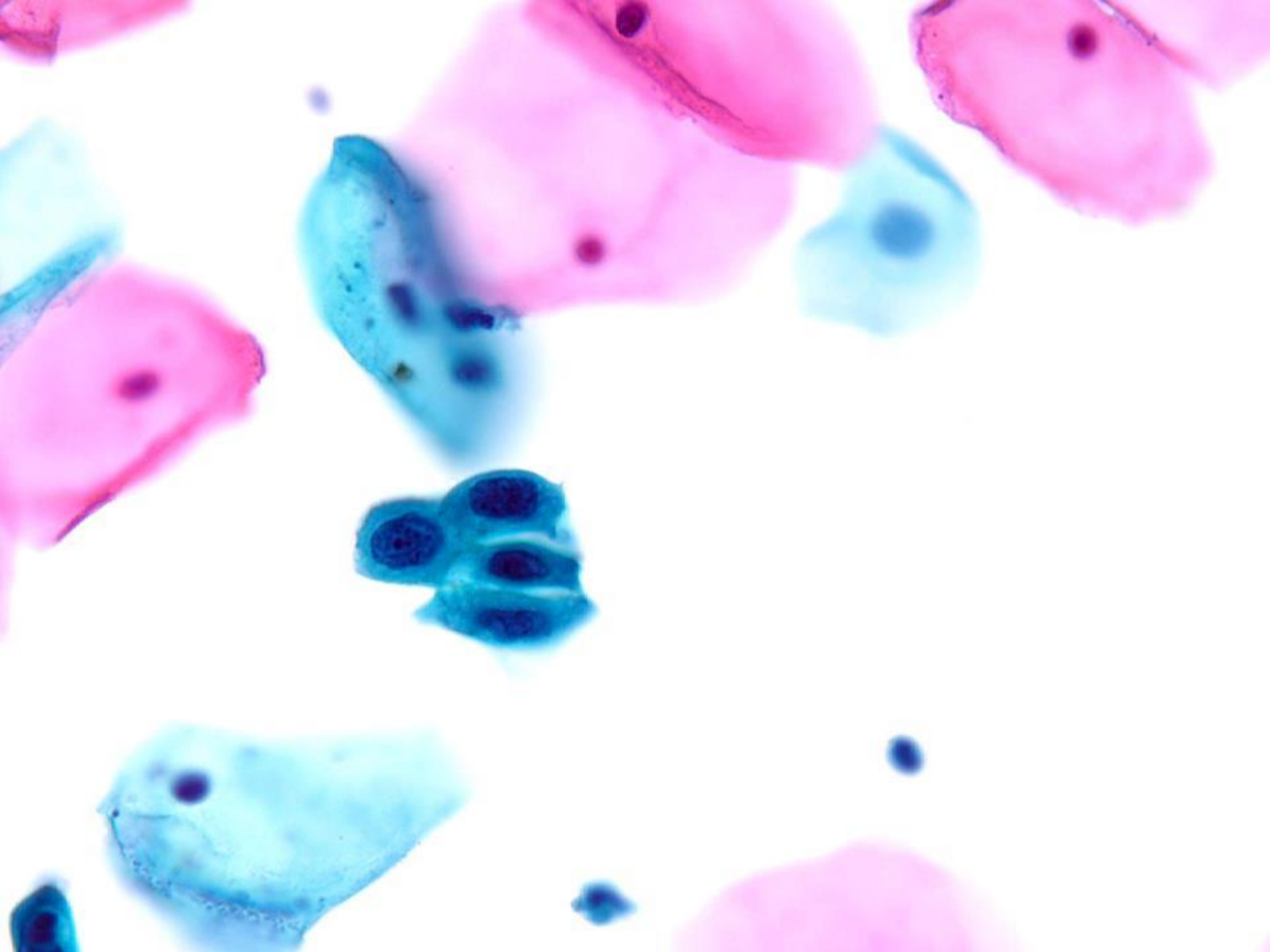






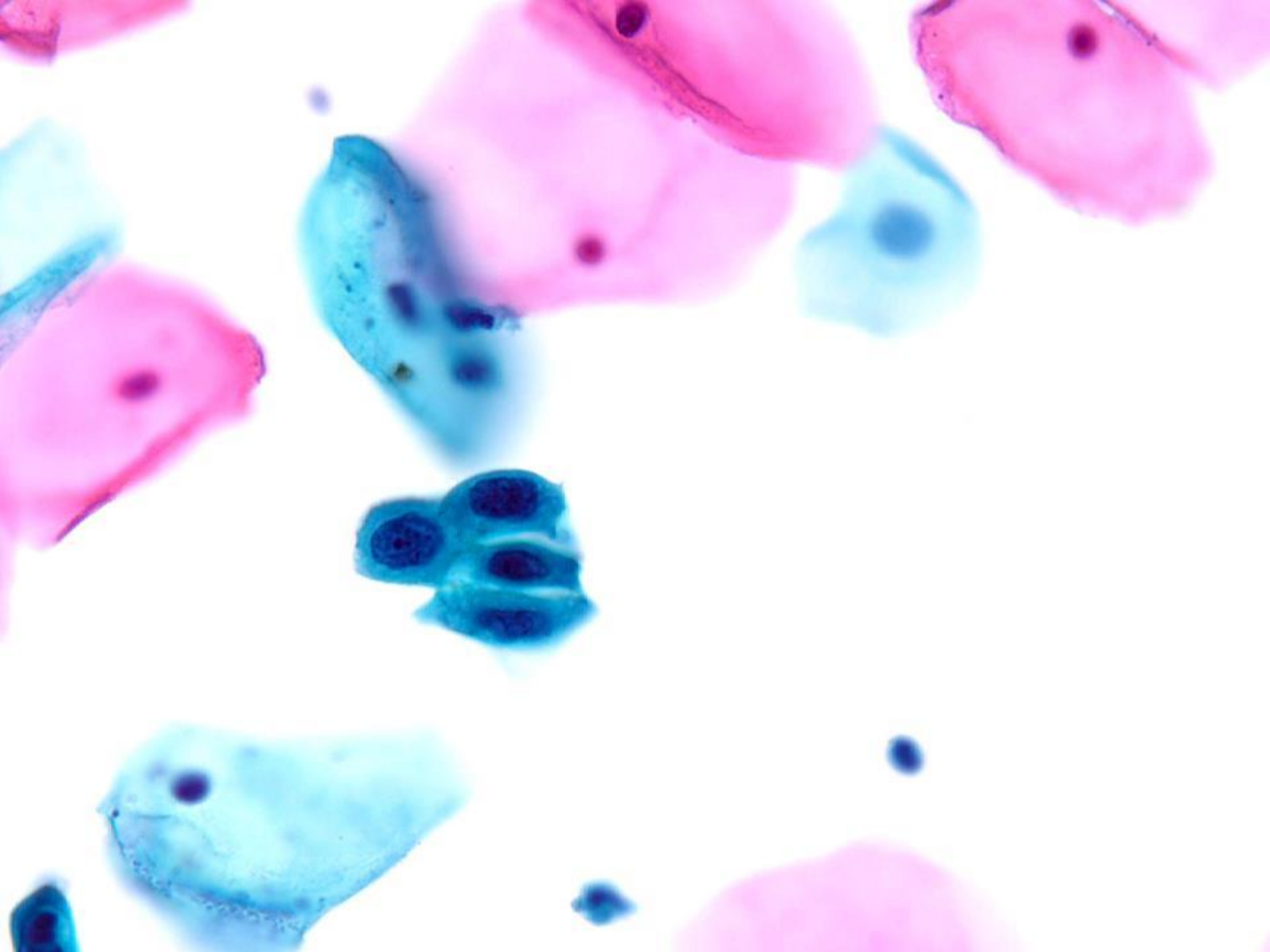


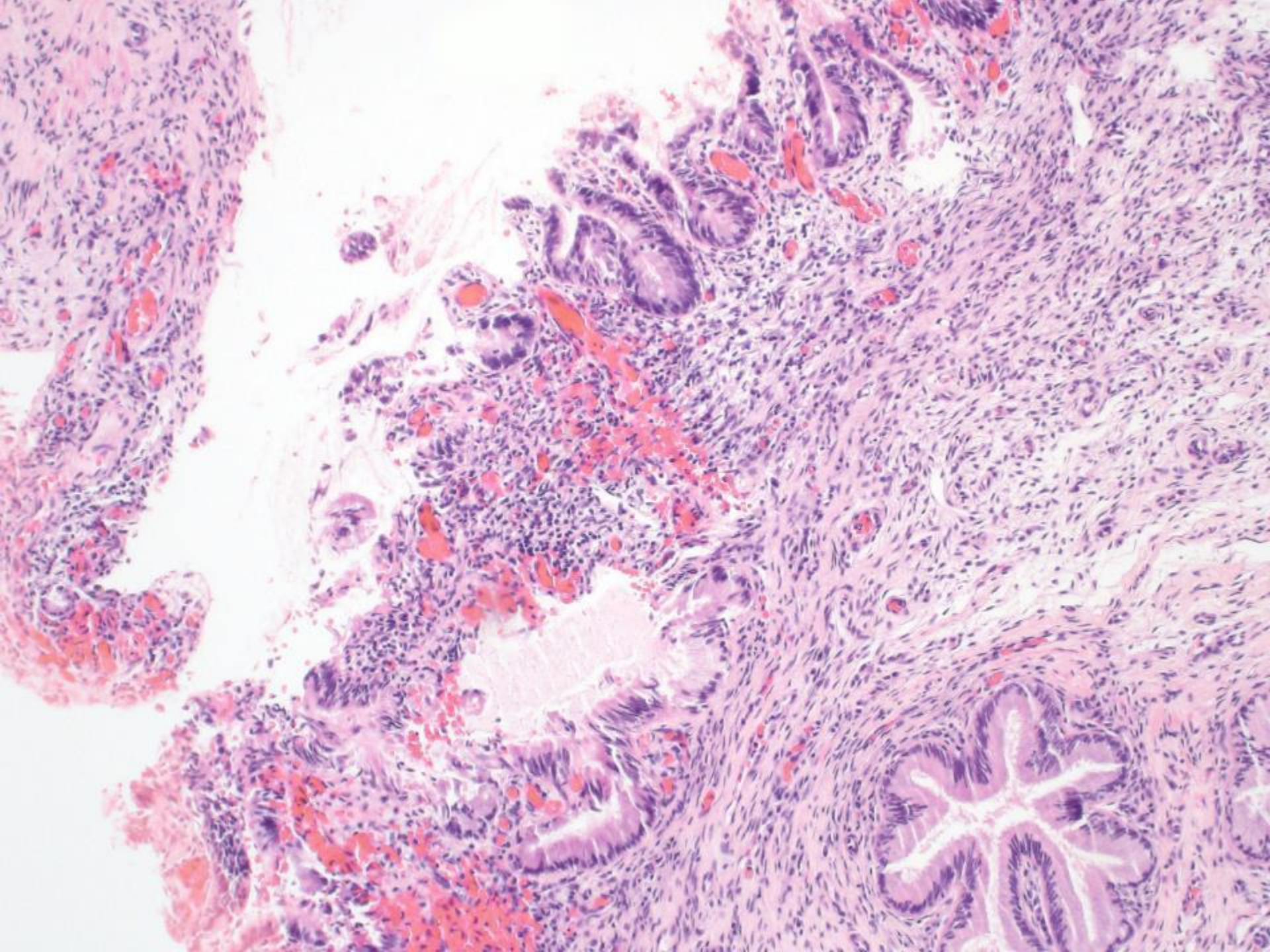
Assessment?

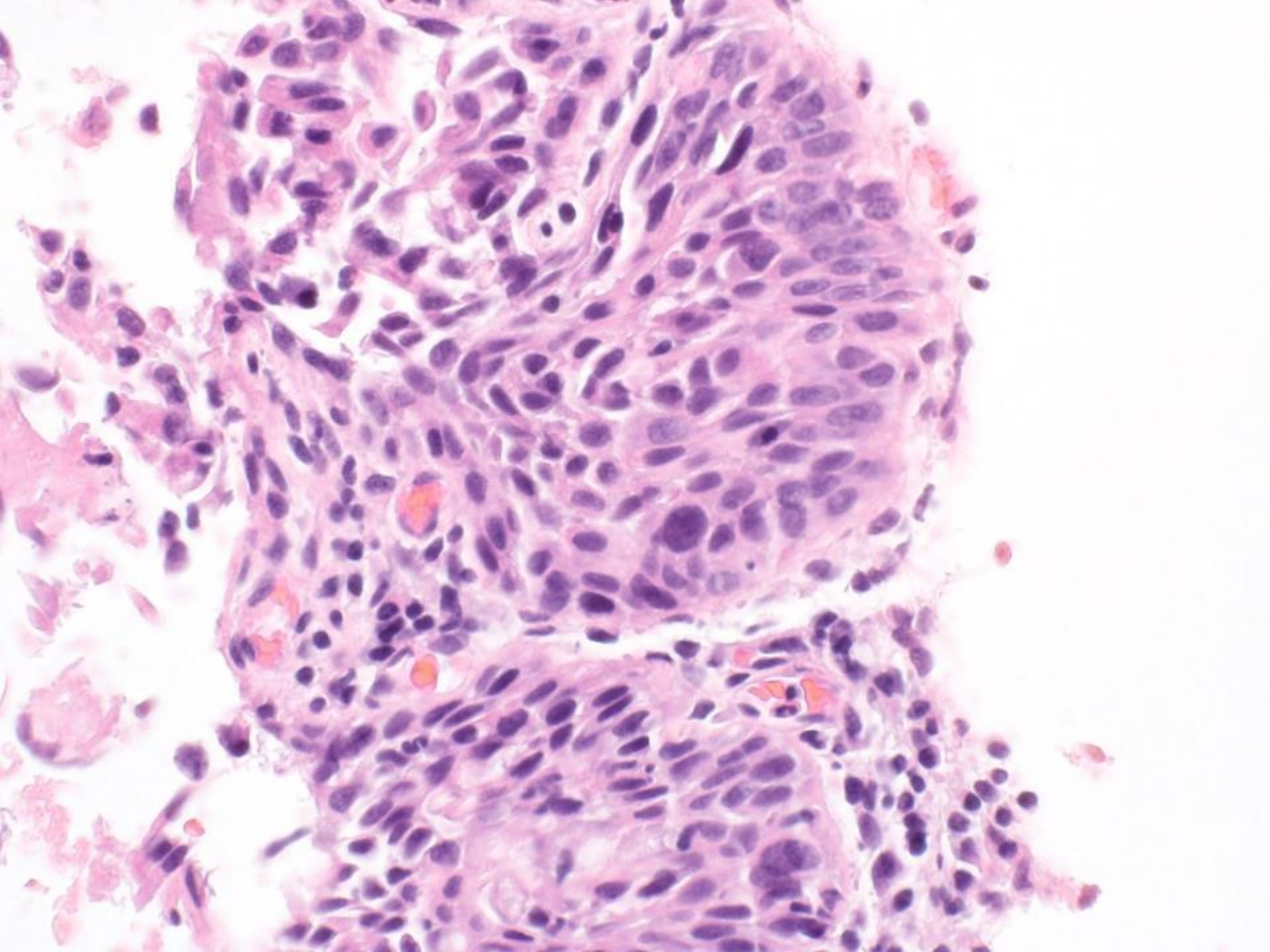


Assessment?

Post-Completion Error







Concomitant Glandular & Squamous Lesions

- Complicating factors:
  - The differential of HCG's includes squamous and glandular lesions
  - Colposcopic sampling may not adequately sample glandular (endocervical) regions
  - Both lesions are positive for HR-HPV
- Possible solutions – Be proactive!
  - Do not become passive regarding AGC
  - Evaluate ECC/bx adequacy for glandular component
  - Re-review Pap tests in select cases
  - Follow up (HPV, Pap test, etc.)

Post-Completion Errors

- All may be present:
  - Infectious organisms
  - Low grade lesion (LSIL)
  - High grade lesion (HSIL) / ASC-H
  - Atypical glandular cells (AGC)
  - Normal / atypical endometrial cells
  - Carcinoma
- When does it happen?

CAFE
HEINZ