

FEMALE GENITAL SYSTEM PATHOLOGY

The background is a solid blue color with a repeating pattern of white line-art icons. The icons include coffee beans, coffee cups with steam, coffee mugs, coffee filters, and speech bubbles containing the text "GOOD MORNING".

UTERINE CERVIX DISORDERS

CERVICITIS

- inflammation of the cervix (endo- + exocervix)

Etiopathogenesis :

- bacteria (Streptococcus, Staphylococcus, N. gonorrhoeae)
- viruses (Herpes simplex virus, Human papillomavirus)
- parasites

Either :

- sexually transmitted
- induced by lacerations of cervix
 - by foreign bodies
 - during childbirth

CERVICITIS

- Acute cervicitis

- Macroscopy :

- red, swollen cervix
 - copious pus “dripping” from the external os

- Microscopy :

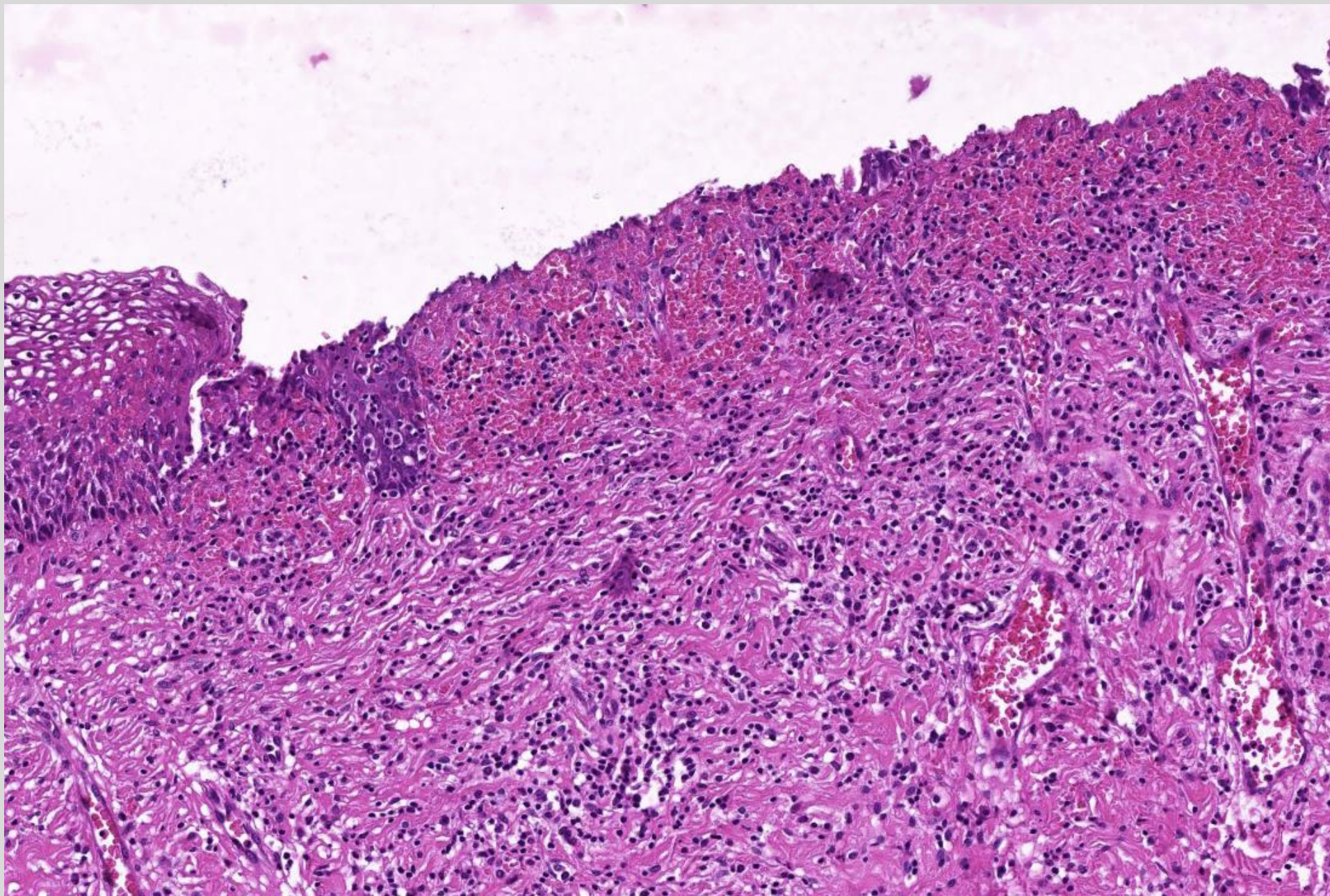
- extensive infiltrate of polymorphonuclear leukocytes
 - stromal edema



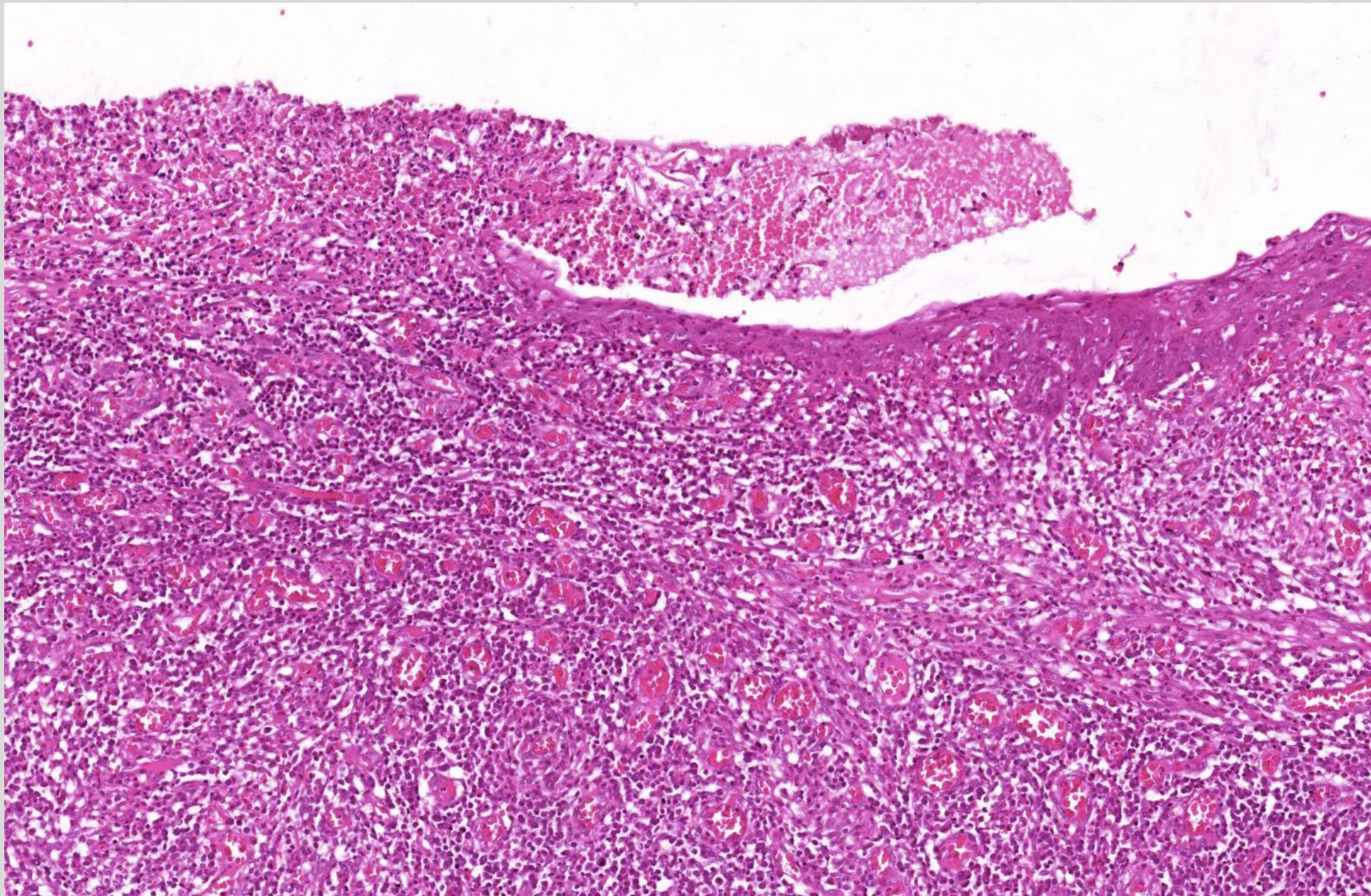
Cervicitis -
colposcopy

CERVICITIS

- Chronic cervicitis (*more common*)
 - **Macroscopy :**
 - hyperemic cervical mucosa
 - possible epithelial erosions
 - **Microscopy :**
 - loss of the epithelial lining
 - necrotic material, superficially
 - massive inflammatory infiltrate (+- lymphoid follicles)
 - proliferation of granulation tissue
 - numerous hyperemic new-formed capillaries



Chronic
cervicitis



Chronic
cervicitis

CERVICITIS

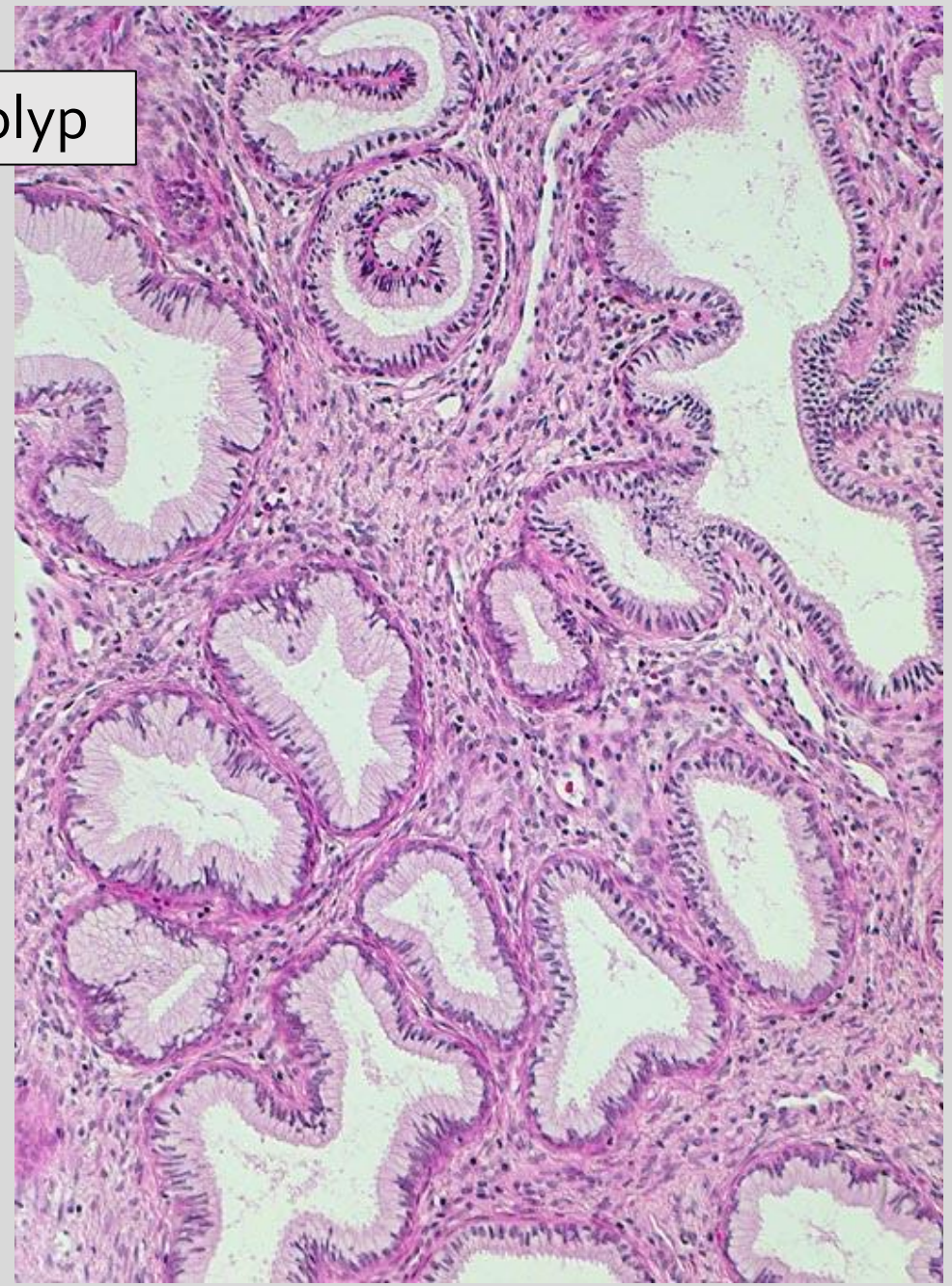
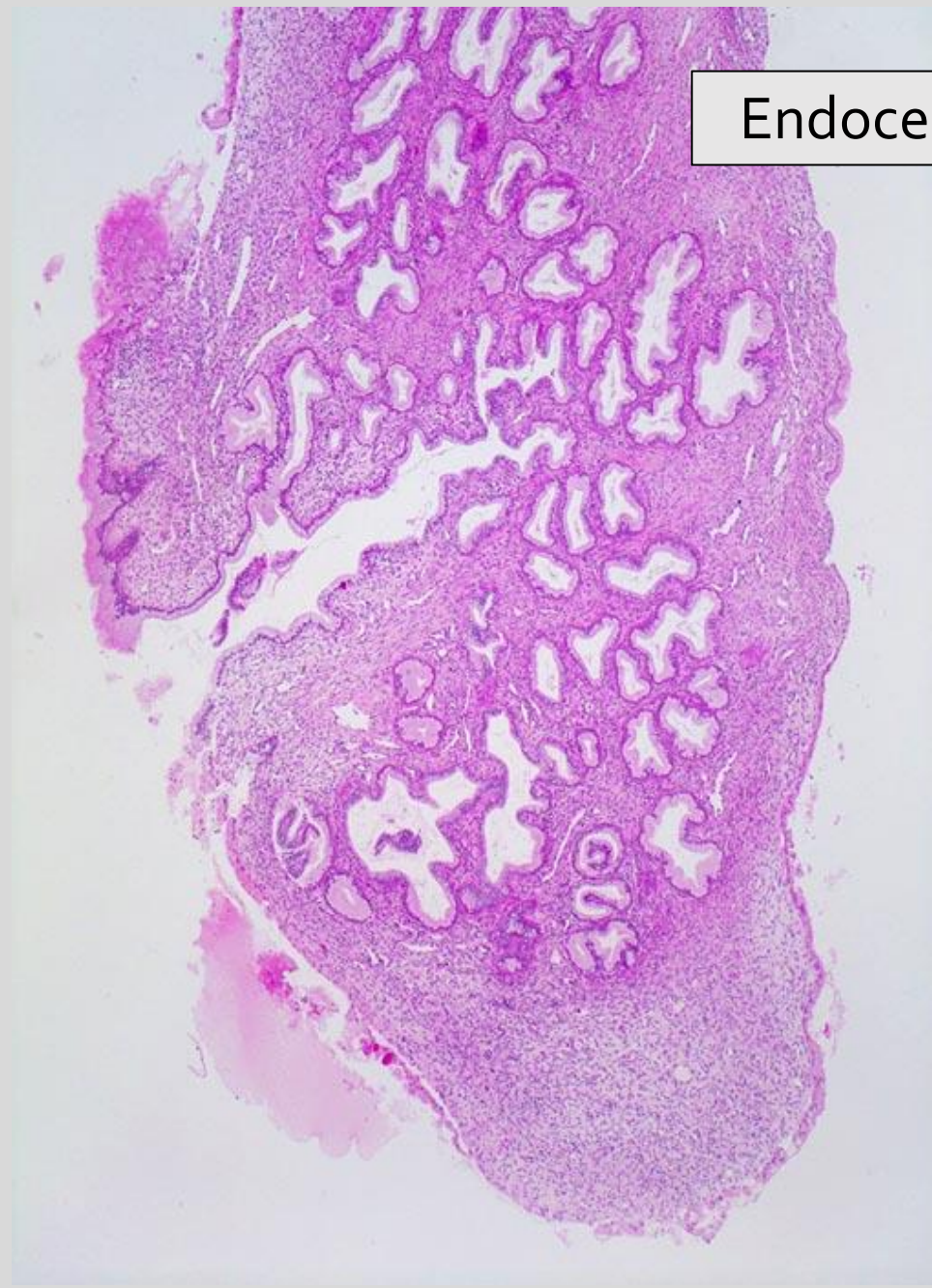
Human papillomavirus

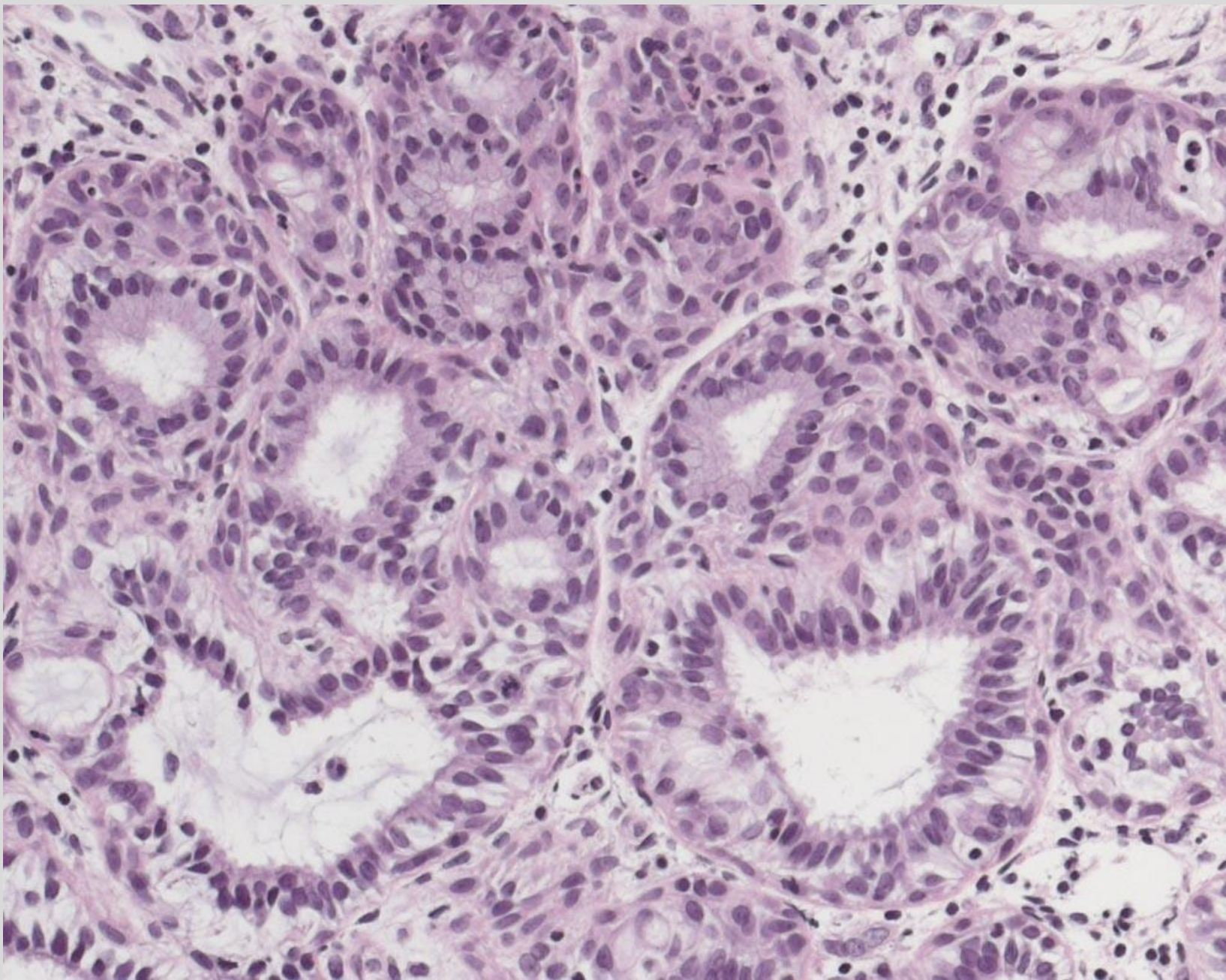
- benign genital warts (condylomata acuminata)
 - HPV 6, 11 – low risk
- macroscopy :
 - mostly multifocal, some solitary
- microscopy :
 - *koilocytic atypia* (nuclear enlargement, hyperchromasia, cytoplasmic perinuclear halo)

BENIGN TUMORS OF THE CERVIX

- Endocervical polyp
 - single, smooth or lobulated mass
 - mucinous superficial lining epithelium, with squamous metaplasia
- Microglandular hyperplasia
 - closely packed endocervical glands that lack intervening stroma
 - caused by progestin overstimulation
- Leiomyoma
 - symptomatic by bleeding or prolapsing

Endocervical polyp





Microglandular
hyperplasia

MALIGNANT TUMORS OF THE CERVIX

Intraepithelial and invasive squamous neoplasia

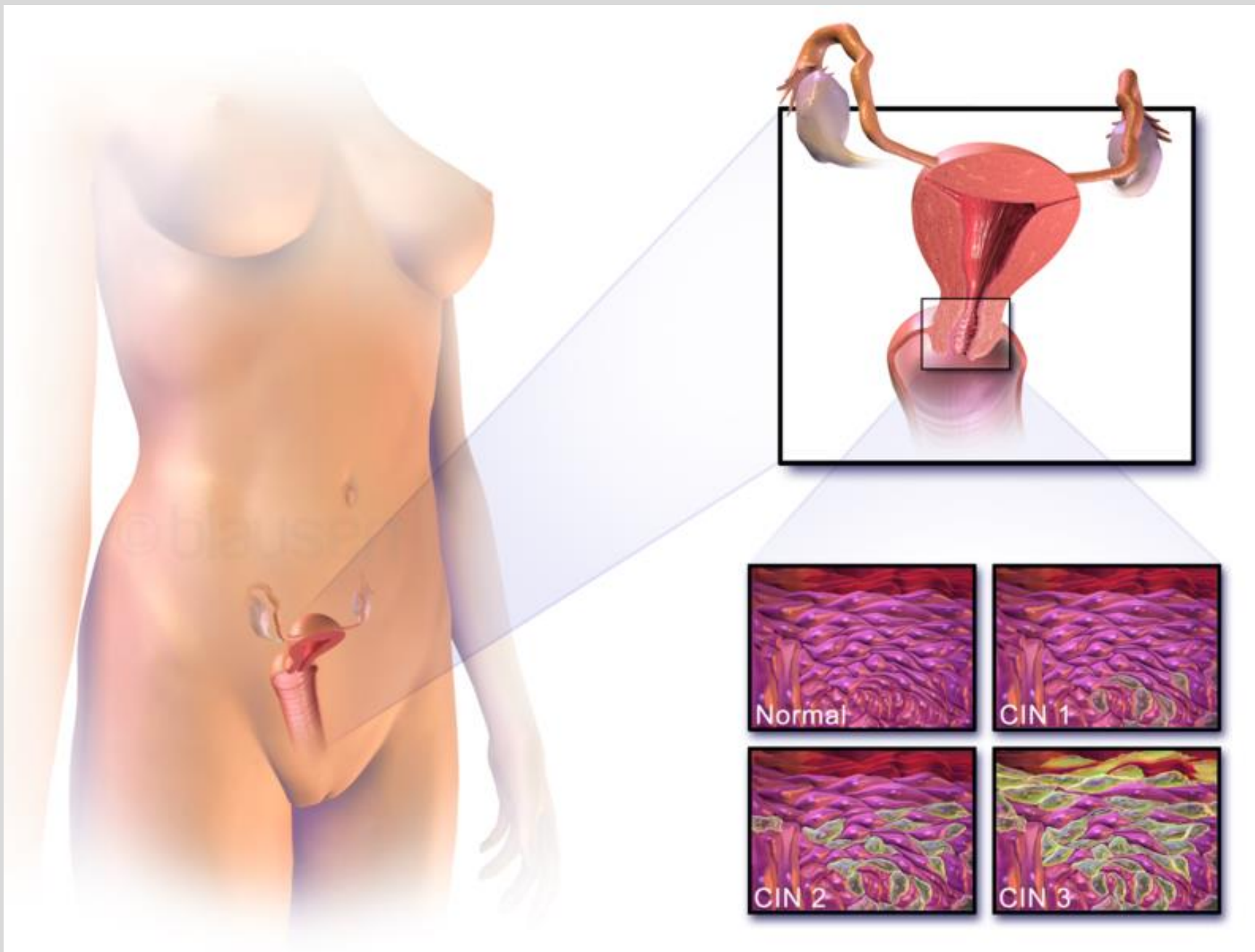
- broad spectrum of epithelial changes :
 - normal endocervix → hyperplasia → squamous metaplasia → dysplasia →
→ carcinoma in situ → superficially invasive carcinoma → invasive carcinoma
 - beginning at the squamocolumnar junction

Atypia (detected starting from *dysplasia* onwards)

- pleomorphic nuclei
- high nucleus/cytoplasm ratio
- mitoses
- loss of cellular polarity

Dysplasia

- CIN-1 : *mild dysplasia*
 - atypia in the basal 1/3 of the epithelium
 - upper 2/3 of the epithelium : normally matured
 - CIN-2 : *moderate dysplasia*
 - cells of the basal 2/3 of the epithelium : atypia
 - upper 1/3 of the epithelium : normal
 - CIN-3 : *severe dysplasia / carcinoma in situ*
 - malignant lesion involving the entire epithelium thickness
 - intact basement membrane
 - underlying stroma – not invaded
- } LSIL
- } HSIL



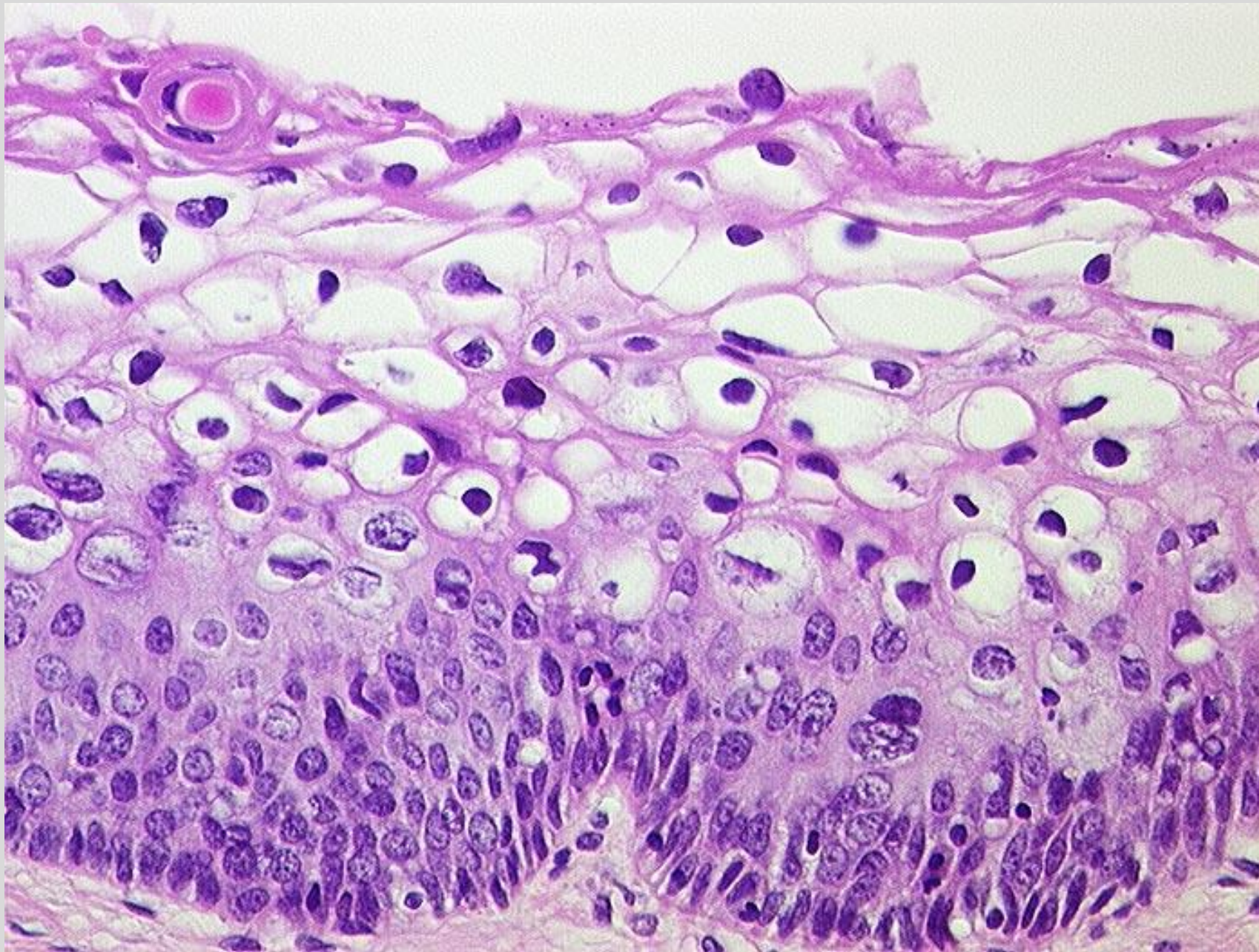
Cervical dysplasia

LSIL (CIN-1)

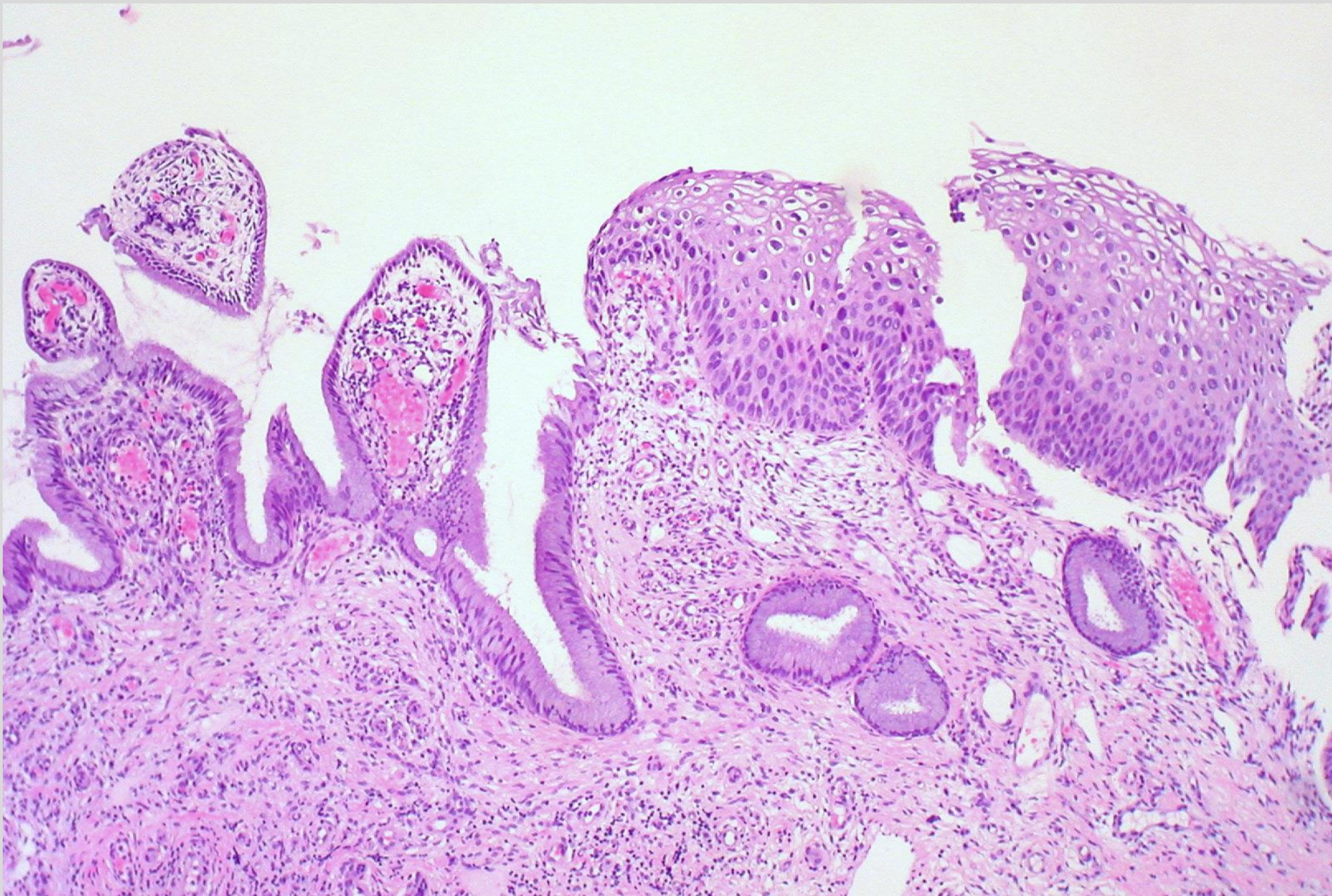
- 80% of the cases - associated with high-risk HPVs
- basal epithelium : atypia
- superficial epithelium : koilocytes
 - ballooned cytoplasm
 - irregular large nuclei

Evolution :

- 70% regress
- 6% progress to HSIL
- <1% become invasive cancer



Koilocytosis in a
low-grade
intraepithelial
neoplasia



LSIL – CIN-1

Human papillomavirus

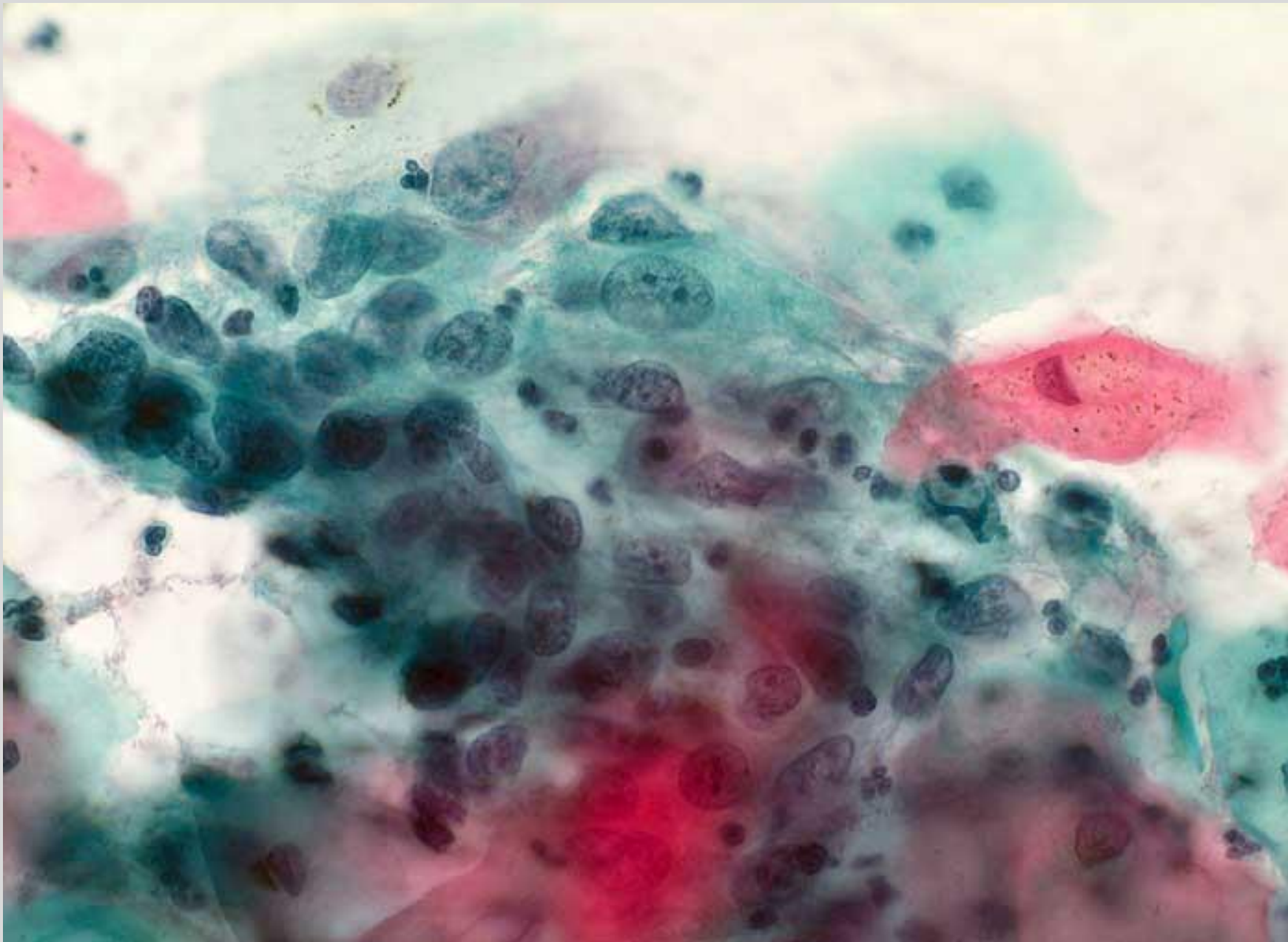
- high-grade CIN / invasive cancers
 - HPV 16, 18 – high risk
 - HPV 31,33,35 – intermediate risk

HSIL (CIN-2 / CIN-3)

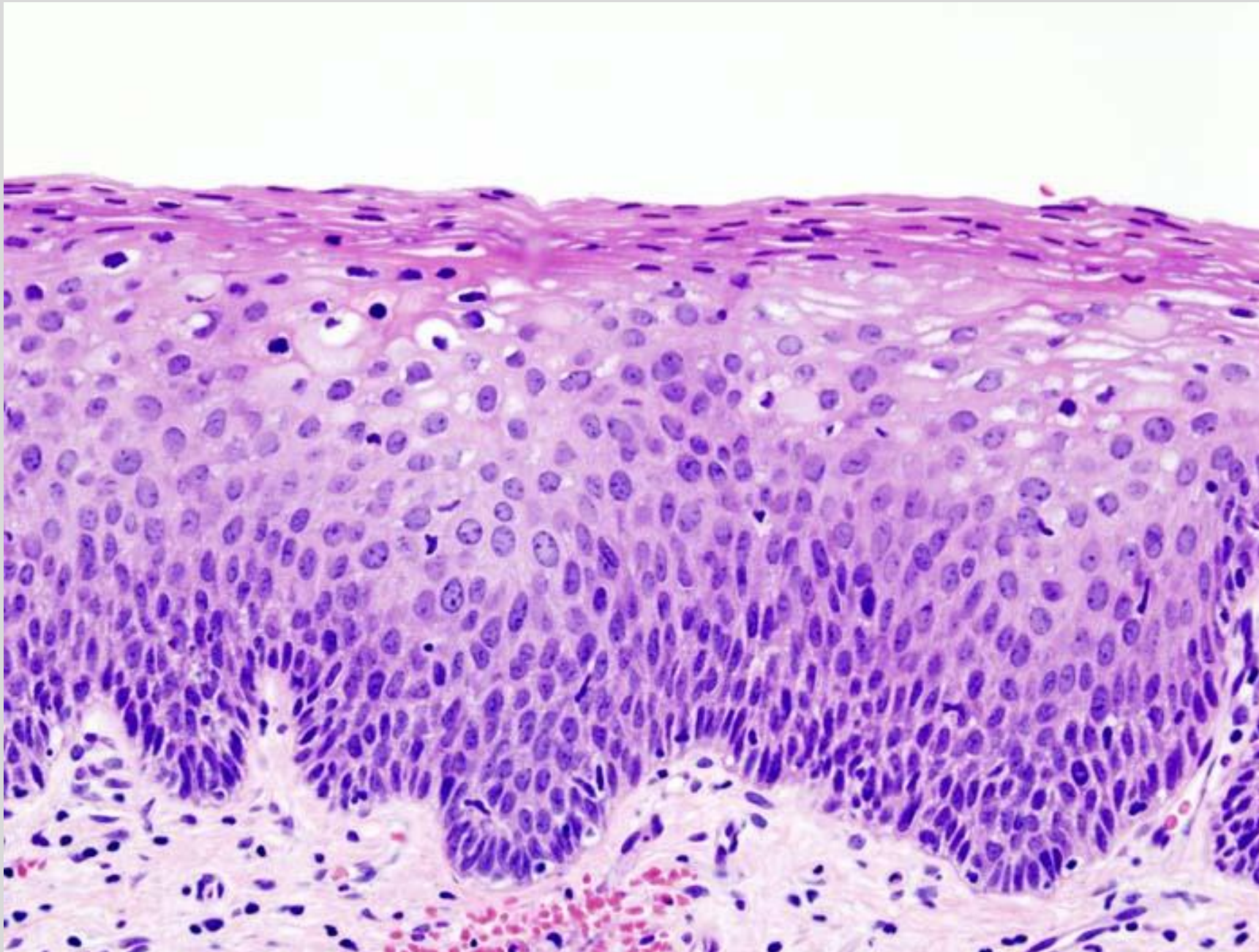
- 100% of the cases - associated with high-risk HPVs
- basal epithelium : prominent atypia
 - disorganization of basal cell alignment
 - nuclear changes upward in the epithelium
- superficial epithelium : koilocytes
 - ballooned cytoplasm
 - irregular large nuclei

Evolution :

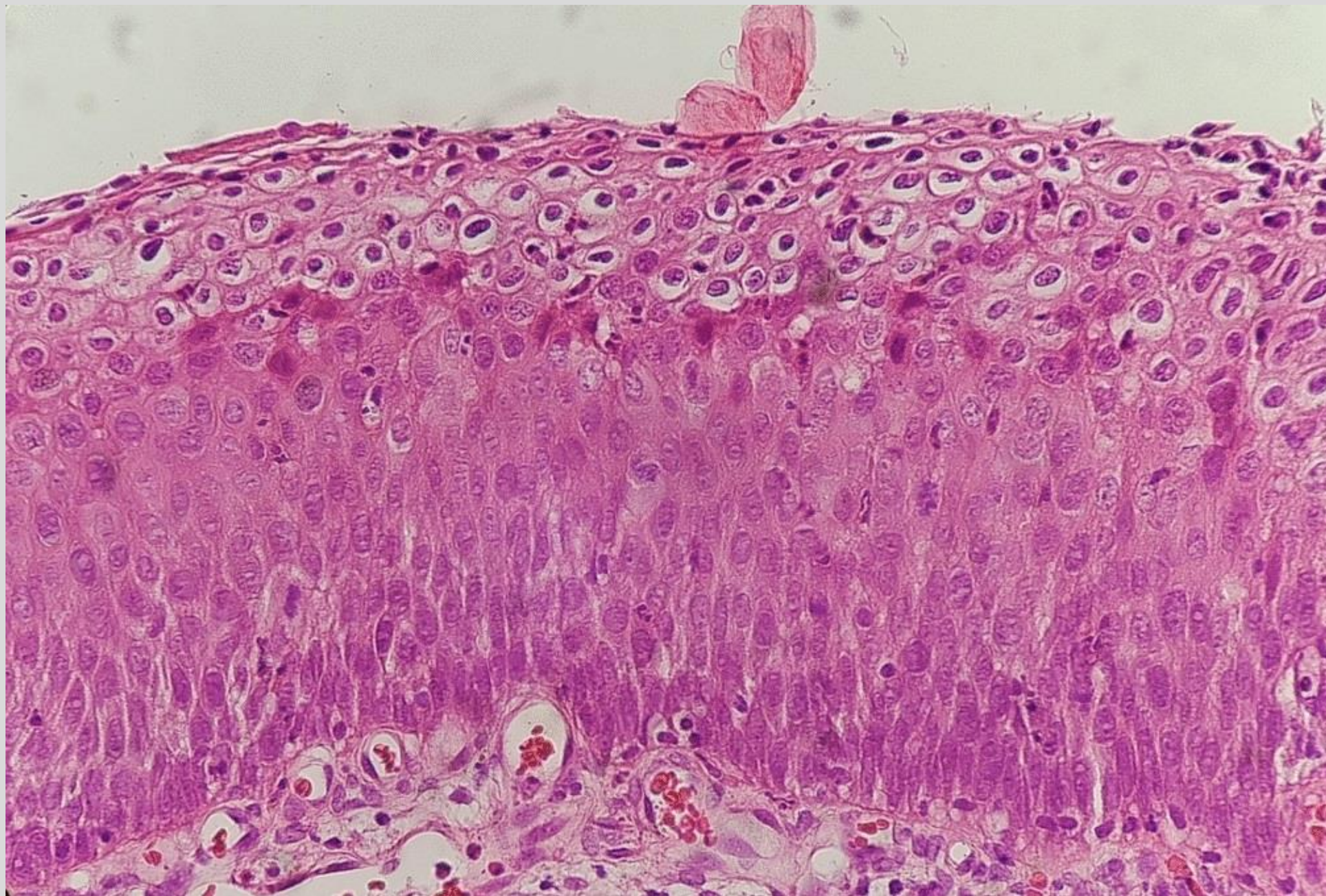
- 10-20% become invasive carcinoma
 - over a shorter interval, compared to LSIL



Pap smear –
moderate dysplasia
(HSIL)



HSIL – CIN 2



HSIL- CIN-3

Management of intraepithelial neoplasia

Papanicolaou smear (Pap)

- cervical screening smear
- detecting intraepithelial changes long before invasion occurs

Biopsy

- when SIL is discovered on Pap smear

LEEP (wired “loop” electrosurgical excision procedure)

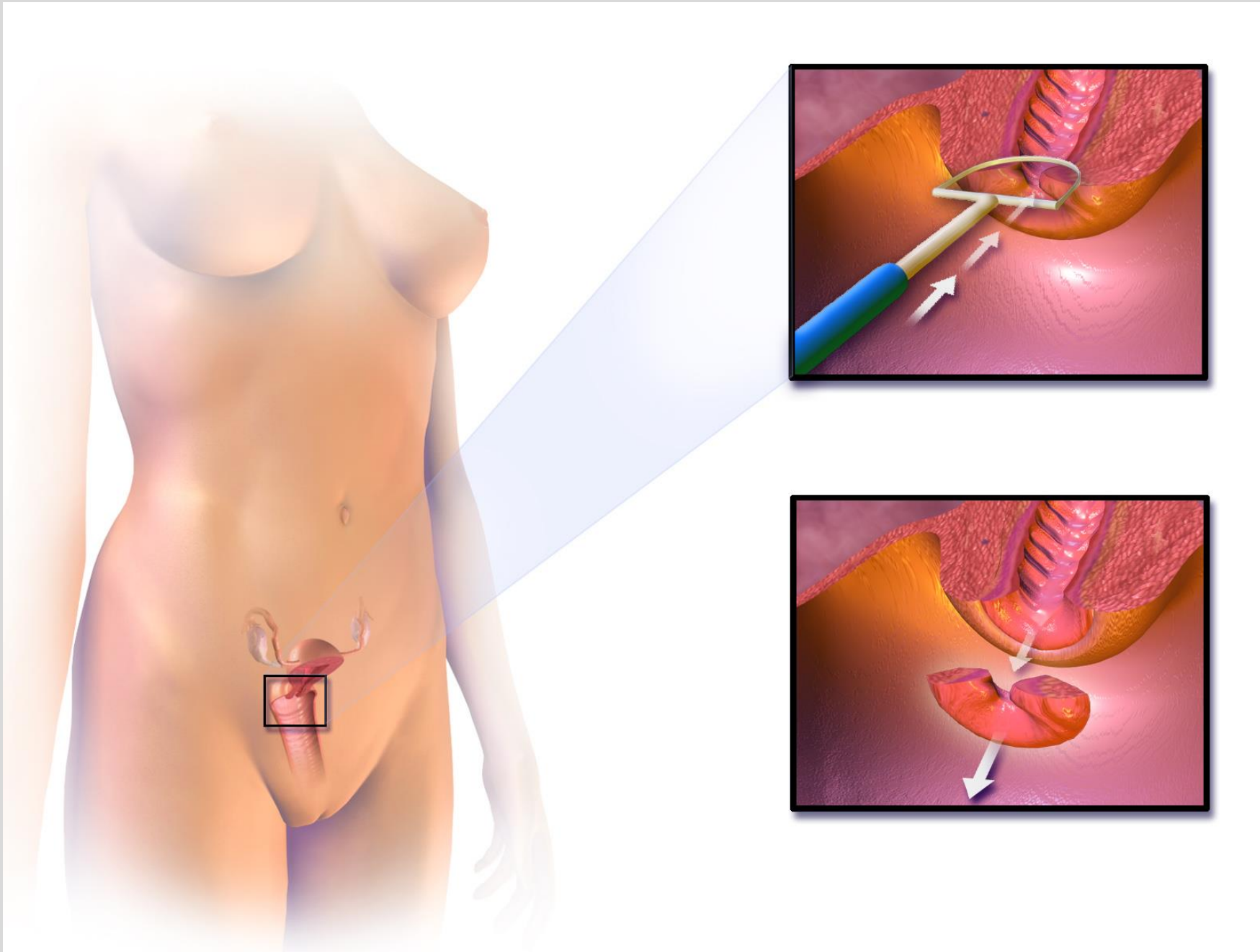
- treating high-grade lesions

Conization

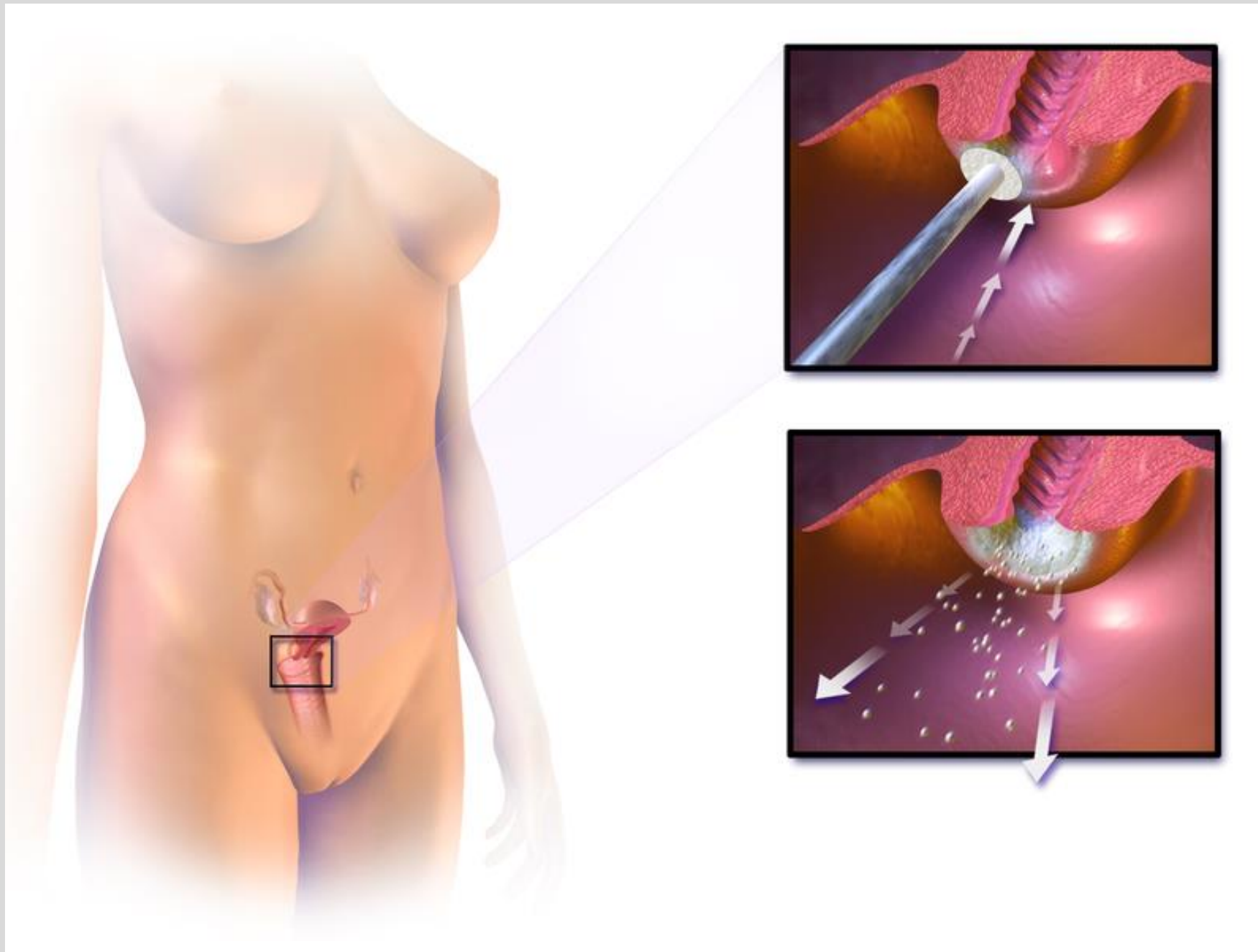
- removal of a cone of tissue around the external os)

Cryosurgery

Hysterectomy



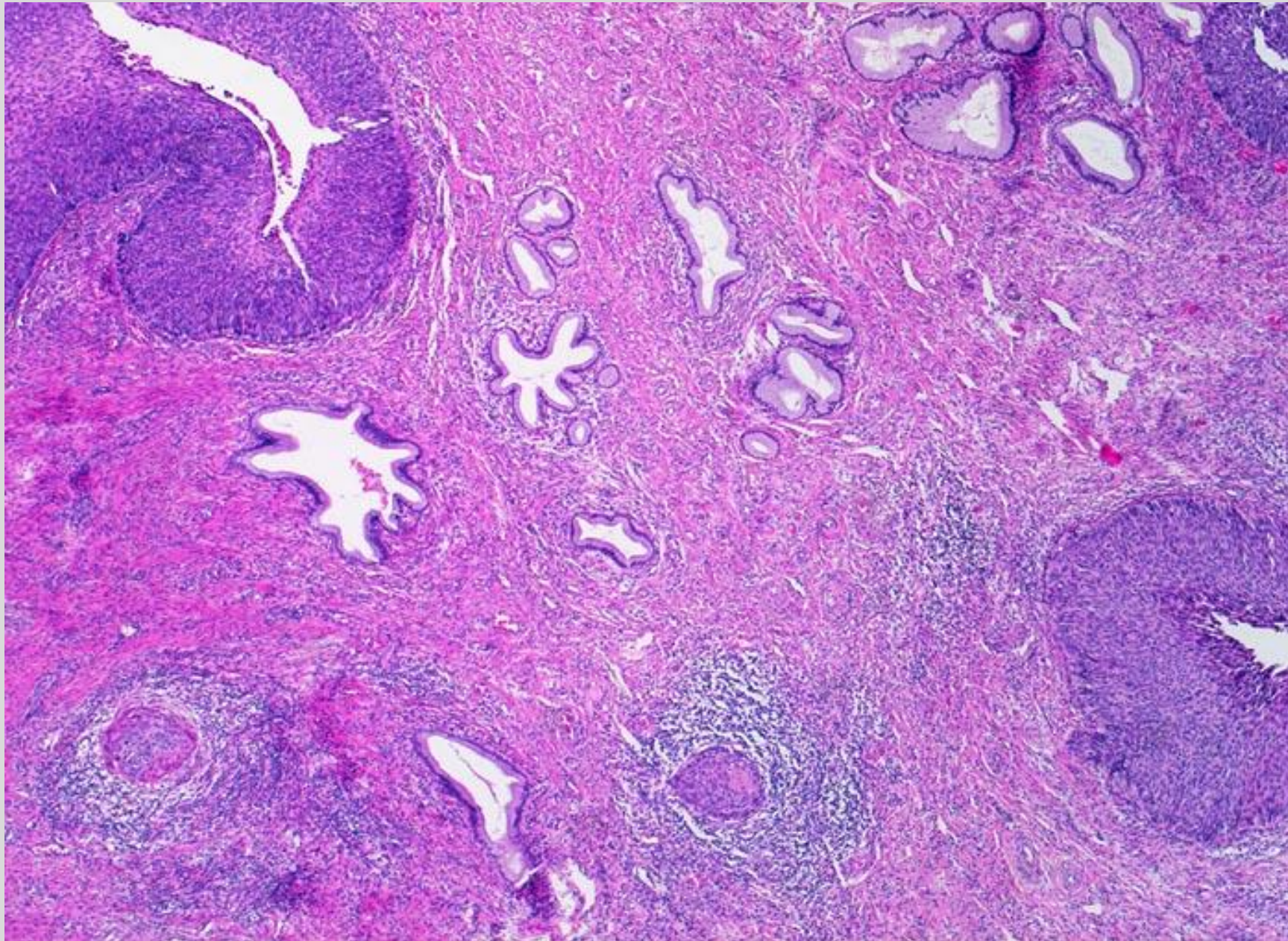
LEEP (wired “loop”
electrosurgical
excision procedure)



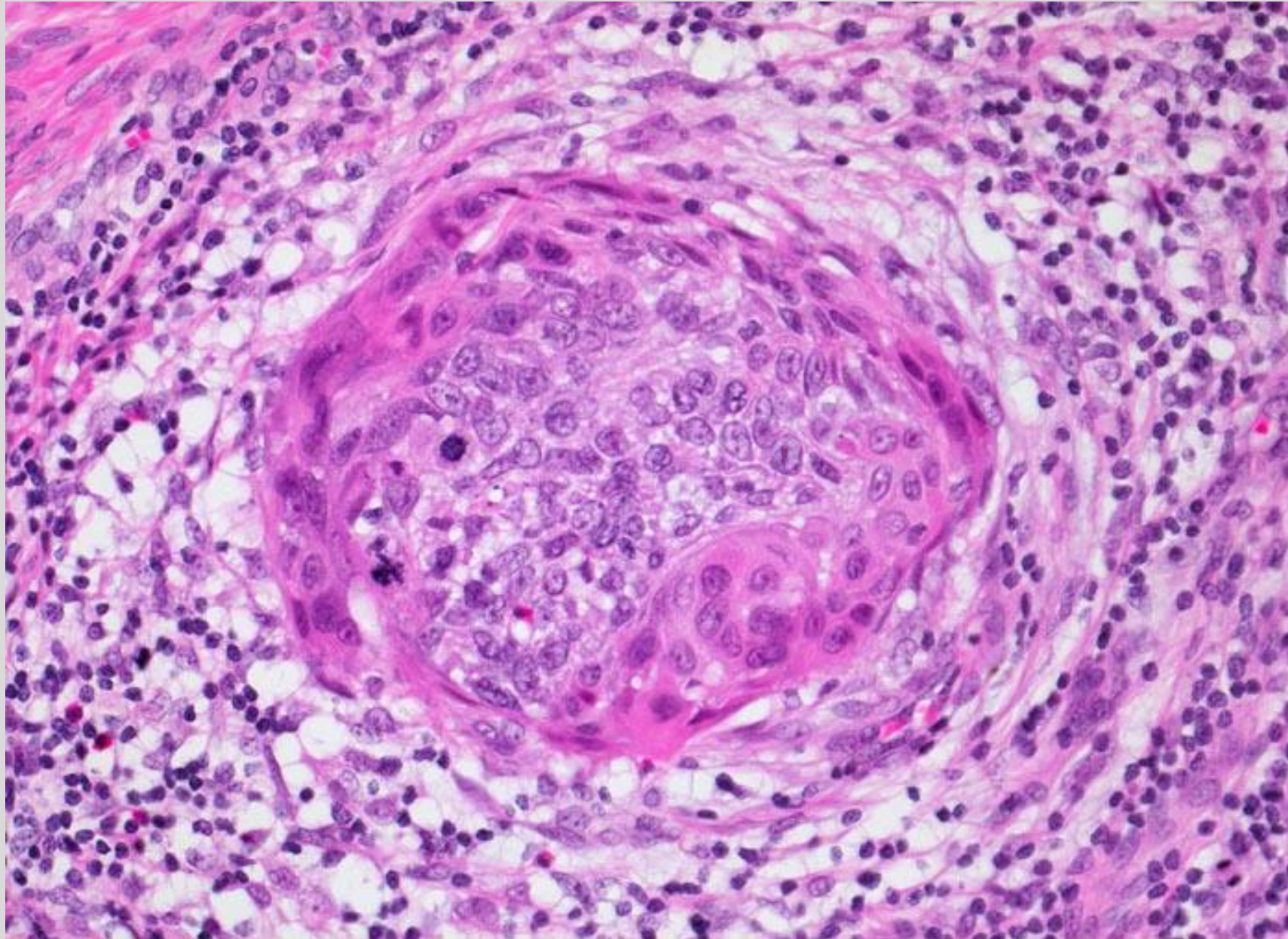
Cervical cryotherapy

Superficially invasive squamous cell carcinoma

- formerly known as microinvasive carcinoma
- **minimal invasion** of the stroma by neoplastic cells
 - depth of invasion **< 3mm** from the basement membrane
 - width of invasion **≤ 7mm** maximum lateral extension
- *absence* of vascular invasion
- *absence* of lymph node metastases
 - does not affect the prognosis of HSIL
 - similar treatment



Superficially invasive
squamous cell
carcinoma



Superficially invasive
squamous cell
carcinoma

Invasive squamous cell carcinoma

- most common type of cervical cancer
- carcinomatous cells found **over 3mm** below the basement membrane
- spreading by direct extension or lymphatics

Macroscopy :

- **ulcerating pattern** : poorly defined, granular and eroded lesion
- **fungating pattern** : exophytic mass
- **infiltrative pattern** : endophytic mass

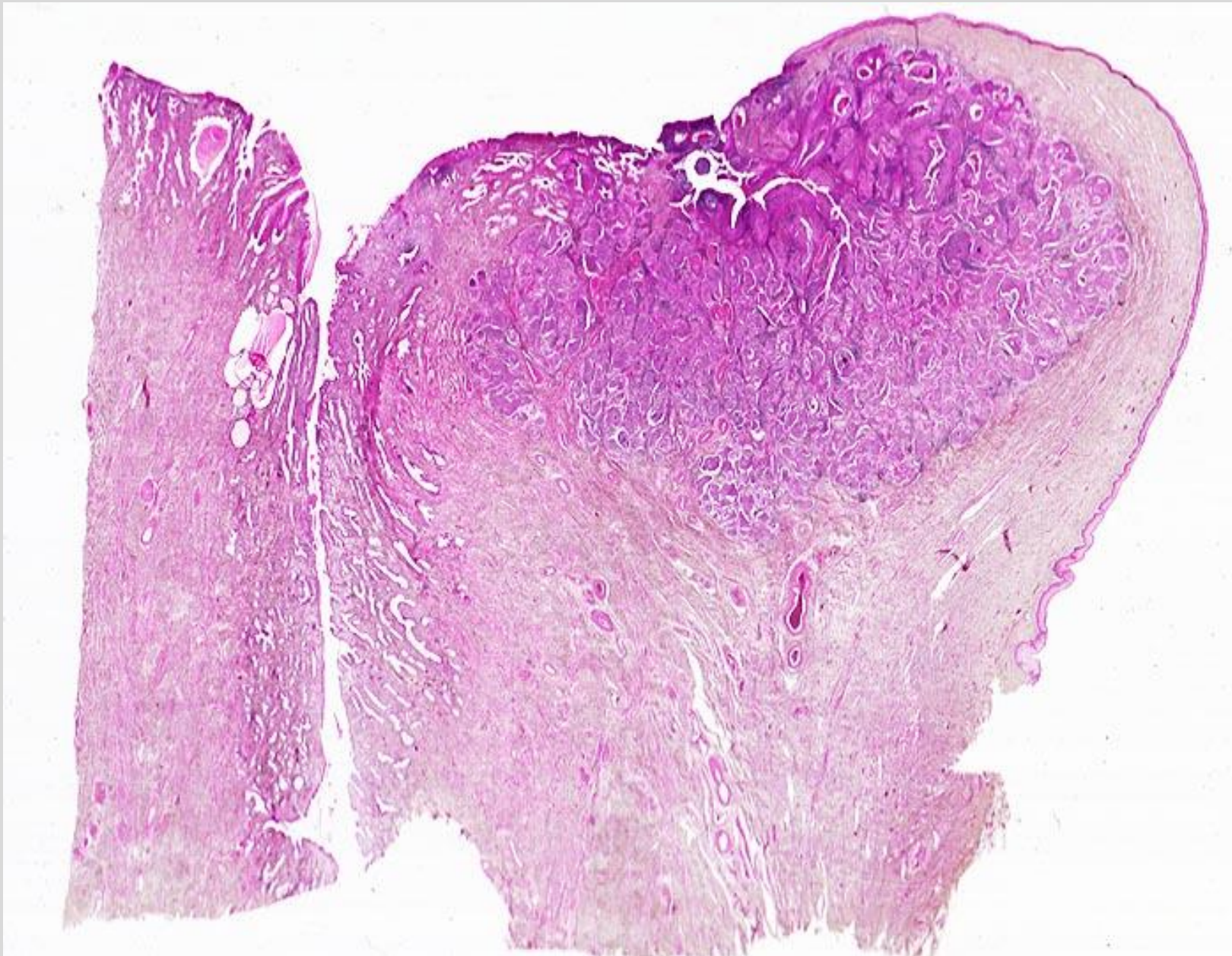
Invasive squamous-cell carcinoma



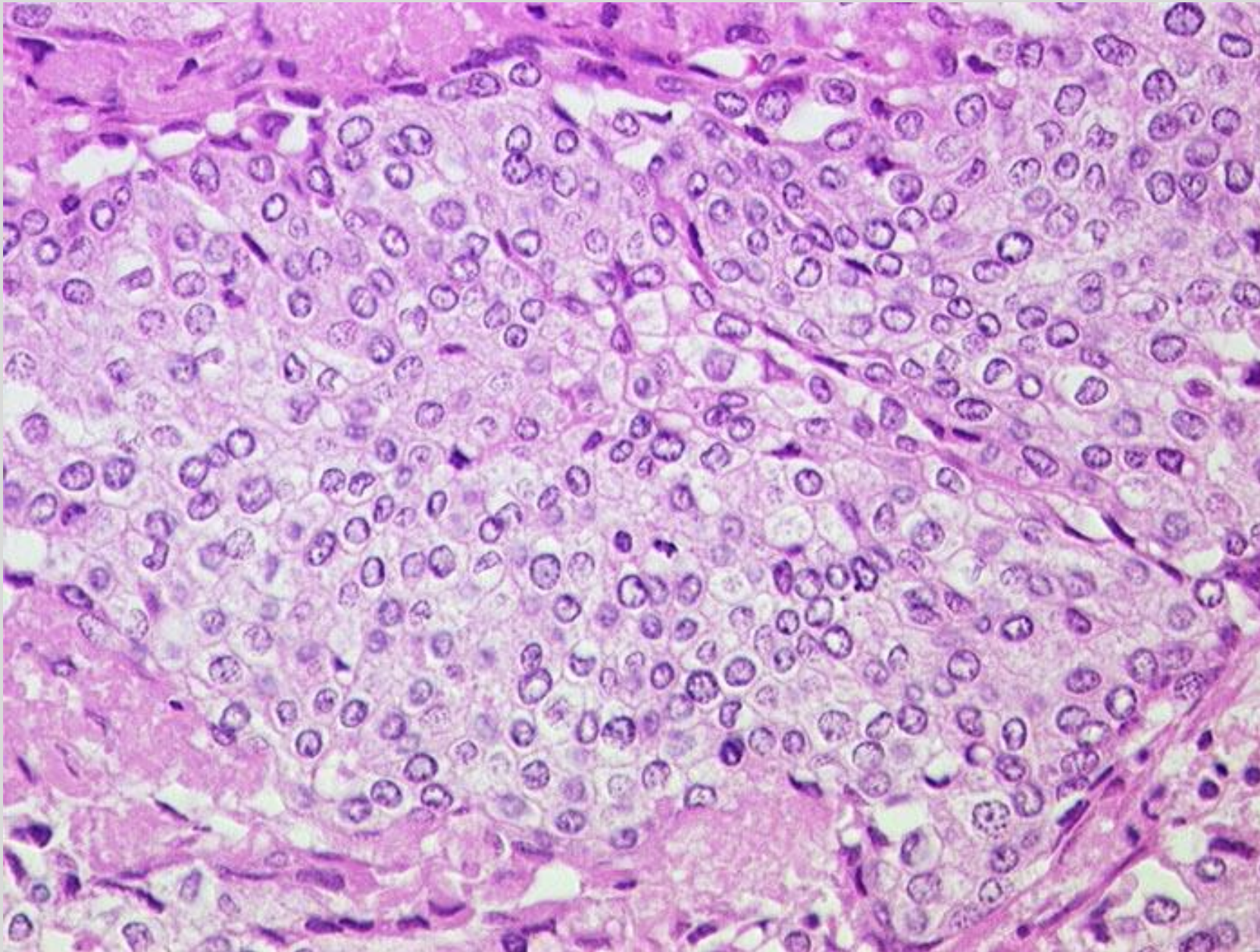
Invasive squamous cell carcinoma

Microscopy :

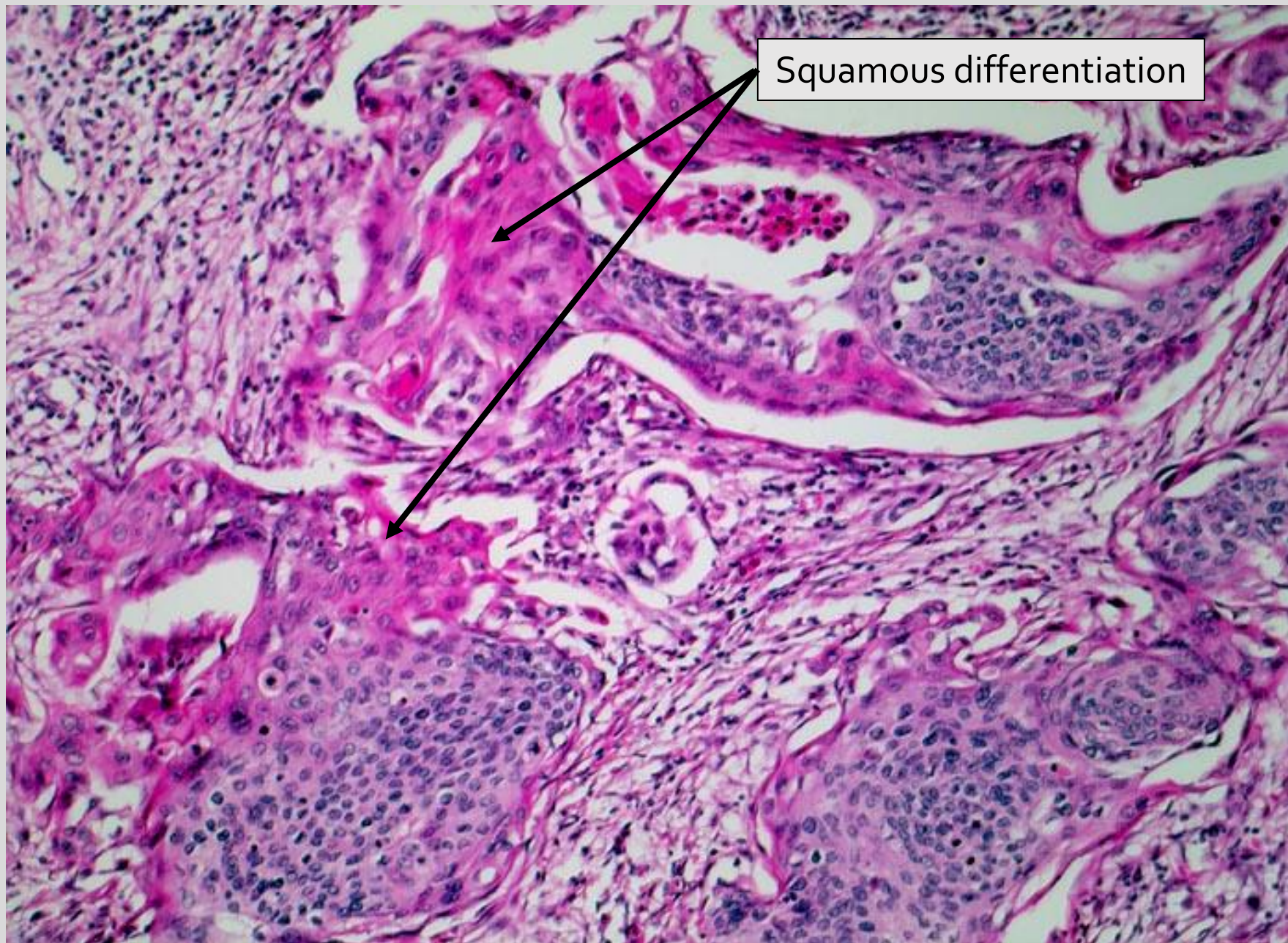
- nonkeratinizing pattern (moderately differentiated)
 - solid nests of large malignant squamous cells
 - no keratinization
- keratinizing pattern (well differentiated)
 - "keratin pearls" – nests of keratinizing cells in concentric whirls
- small cell carcinoma
 - infiltrating masses of small, cohesive, malignant cells
 - no keratinization
 - *neuroendocrine differentiation* (chromogranin +, synaptophysin +)



Invasive squamous
cell carcinoma



Non-keratinizing
squamous cell carcinoma



Squamous differentiation

Keratinizing squamous
cell carcinoma

Adenocarcinoma

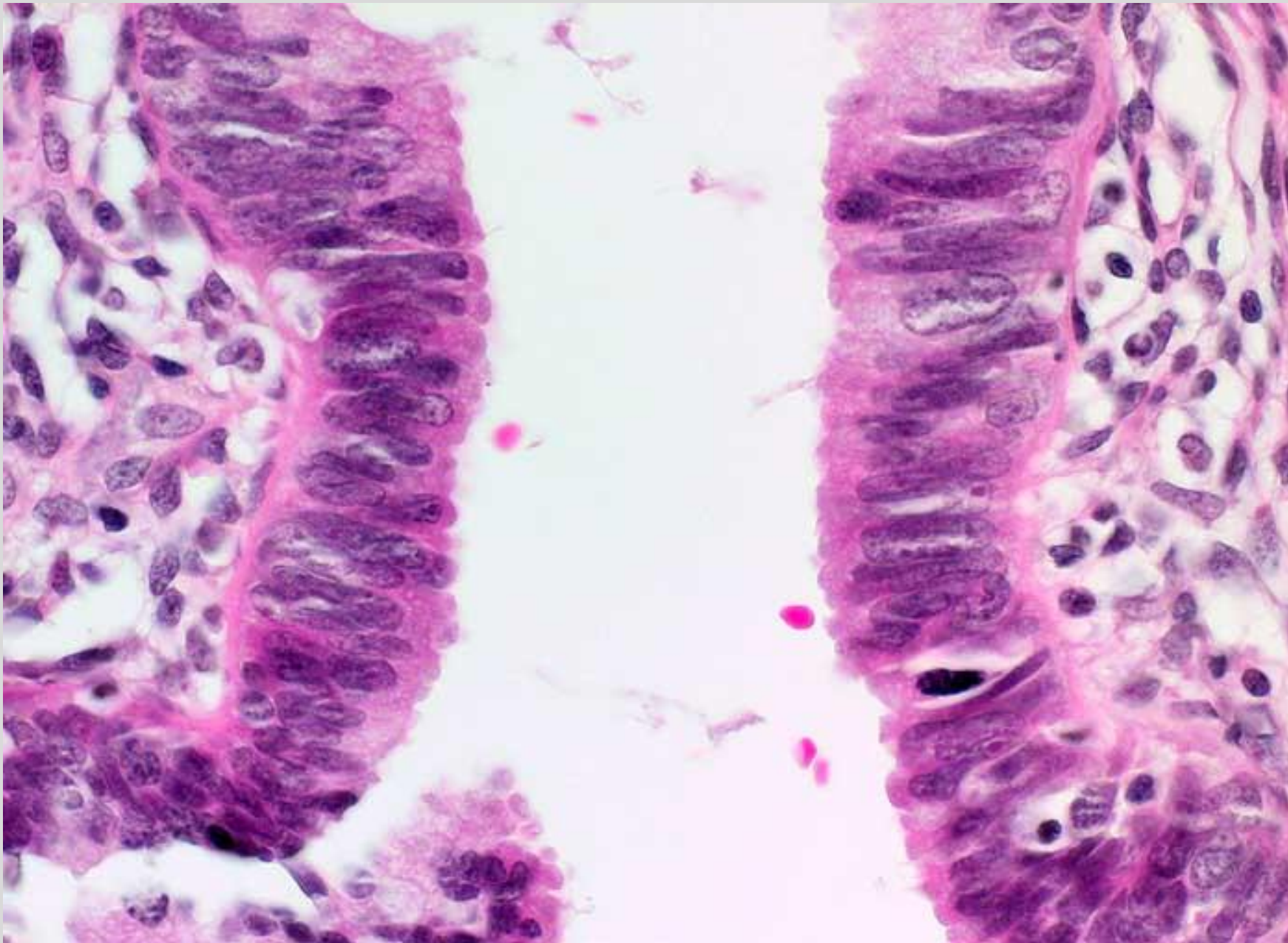
- mostly originated in endocervical glands => mucinous type
- forms : *in situ* and *invasive*

Adenocarcinoma in situ

- generally arises at the squamocolumnar junction
- extending into the endocervical canal
- **intraepithelial**

Microscopy :

- tall columnar cells with eosinophilic or mucinous cytoplasm
 - sometimes resembling goblet cells
 - showing variable atypia



Adenocarcinoma
in situ

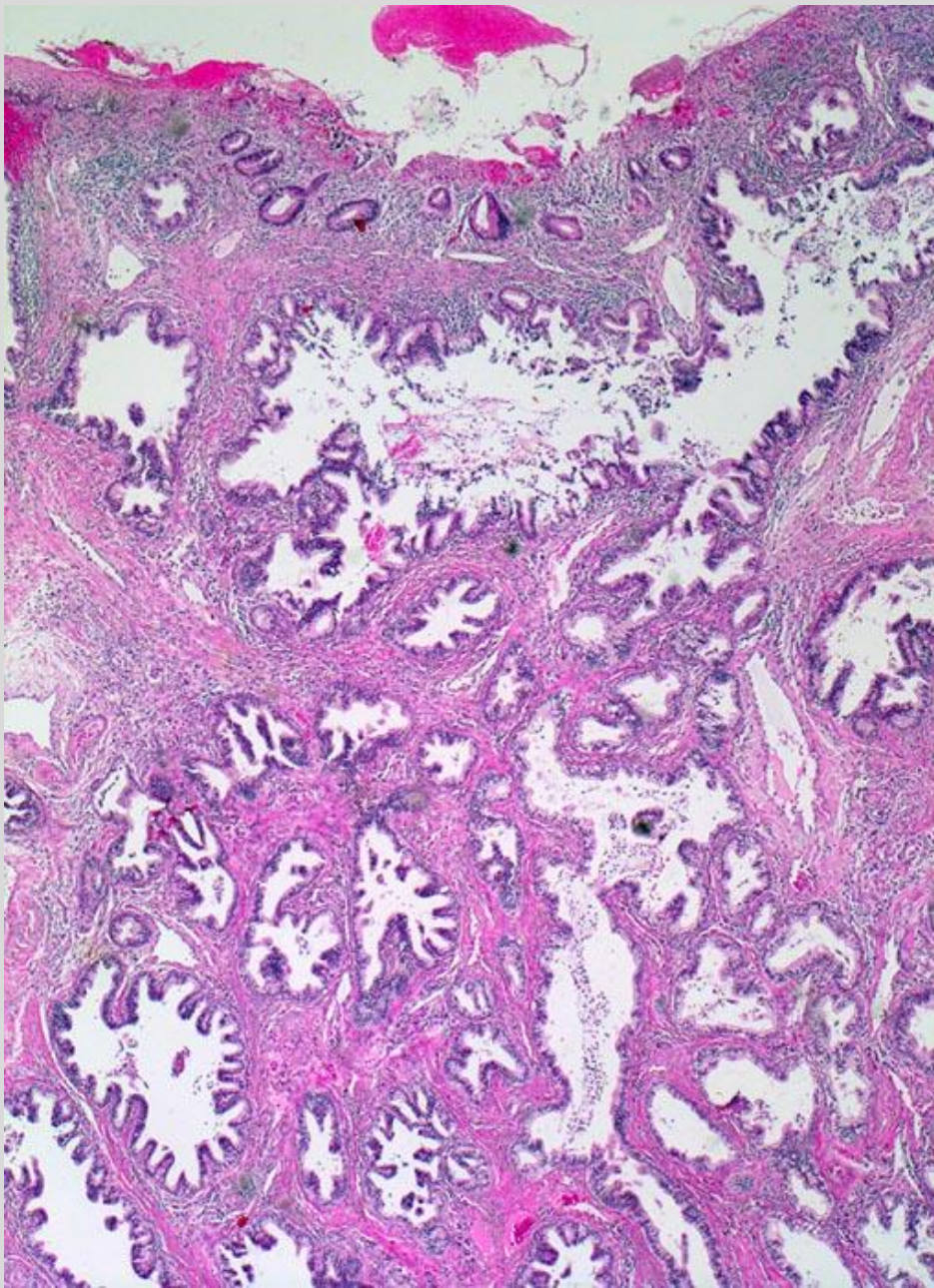
Invasive adenocarcinoma

Macroscopy :

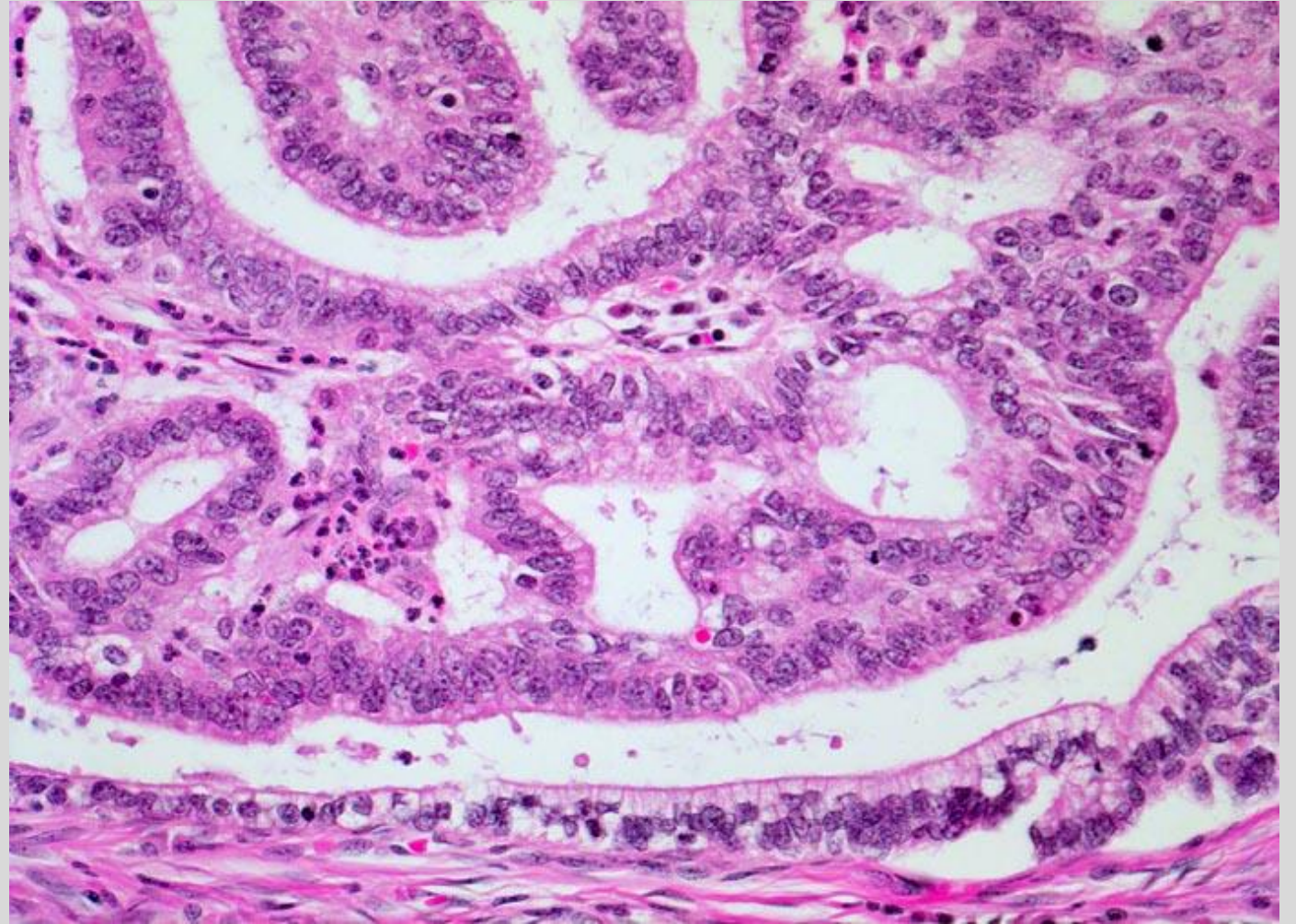
- fungating polypoid or papillary mass

Microscopy :

- papillary pattern:
 - exophytic tumors
- tubular or glandular pattern:
 - endophytic tumors
- poorly differentiated:
 - solid sheets of cells



Invasive cervical adenocarcinoma:
tubular – glandular pattern



Staging of cervical invasive carcinomas

Stage I :

- confined to the cervix
 - A – microscopic invasion (≤ 3 mm deep and ≤ 7 mm wide)
 - B – clinically visible or dimensions greater than IA

Stage II :

- invading beyond the uterus, but not to the pelvic wall or lower 1/3 of the vagina

Stage III :

- extending to the pelvic wall and/or lower third of the vagina
- and/or causing hydronephrosis or non-functioning kidney

Stage IV :

- involves mucosa of the bladder or rectum, and/or extends beyond the pelvis

Prognosis and treatment of invasive carcinomas

- depending on the stage
- 5 year survival rate :
 - 100% for superficially invasive carcinomas
 - <50% for tumors extending beyond the pelvis
 - very poor for small-cell neuroendocrine tumors

Non-advanced stages :

- surgical resection

Advanced stages :

- combined chemotherapy and radiotherapy



UTERINE BODY DISORDERS

ENDOMETRITIS

- inflammation of the endometrium
- must be distinguished from :
 - polymorphonuclear leukocytes – *during menstruation*
 - mild lymphocytic infiltrate – *at other times*
- variants :
 - acute endometritis
 - chronic endometritis

Acute endometritis

- always associated with parturition and septic abortion
- most cases result from an ascending infection
- mixed bacterial flora
- **curettage** – diagnostic and often curative

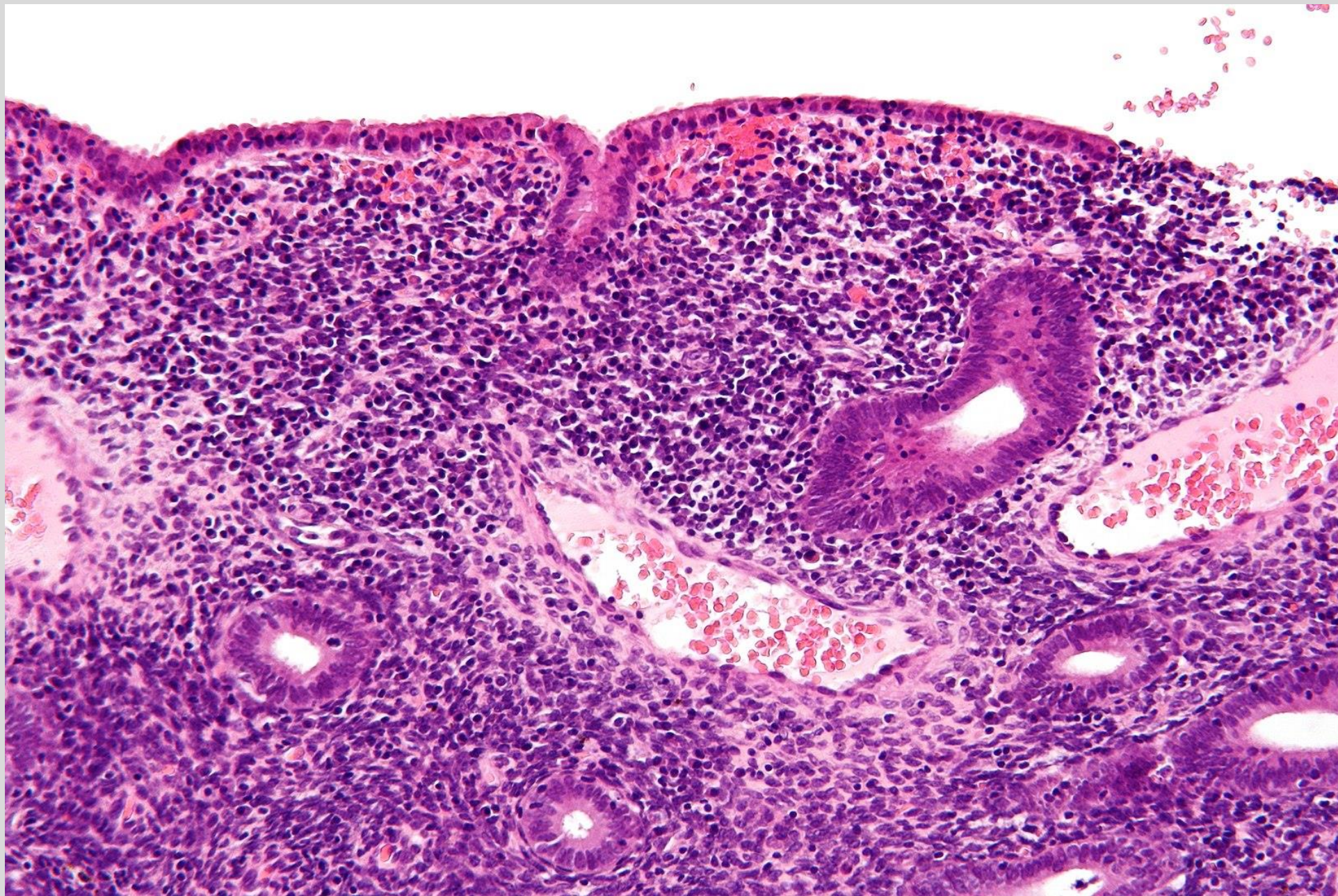
Complications :

- puerperal sepsis
- myometritis
- parametritis with iliac venous thrombosis
- salpingitis with infertility
- peritonitis

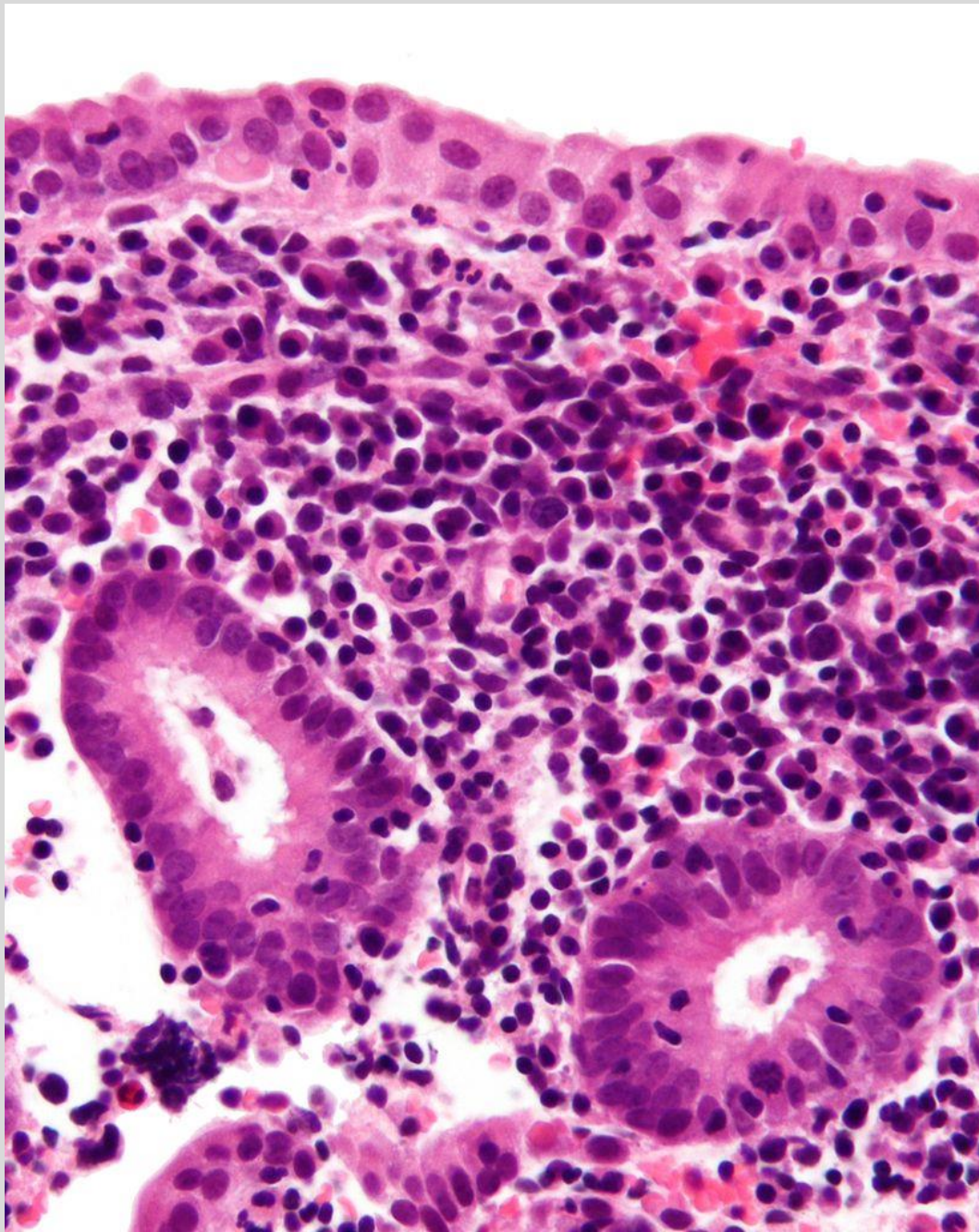
seldom, due to
**antibiotic
therapy**

Chronic endometritis

- associated with :
 - IUDs (intrauterine devices)
 - pelvic inflammatory disease
 - retained products of conception
- diagnosis based on :
 - plasma cells presence in the endometrium
- usually self-limited



Chronic
endometritis



Chronic endometritis – numerous
plasma cells in endometrium
interstitium / stroma / chorion

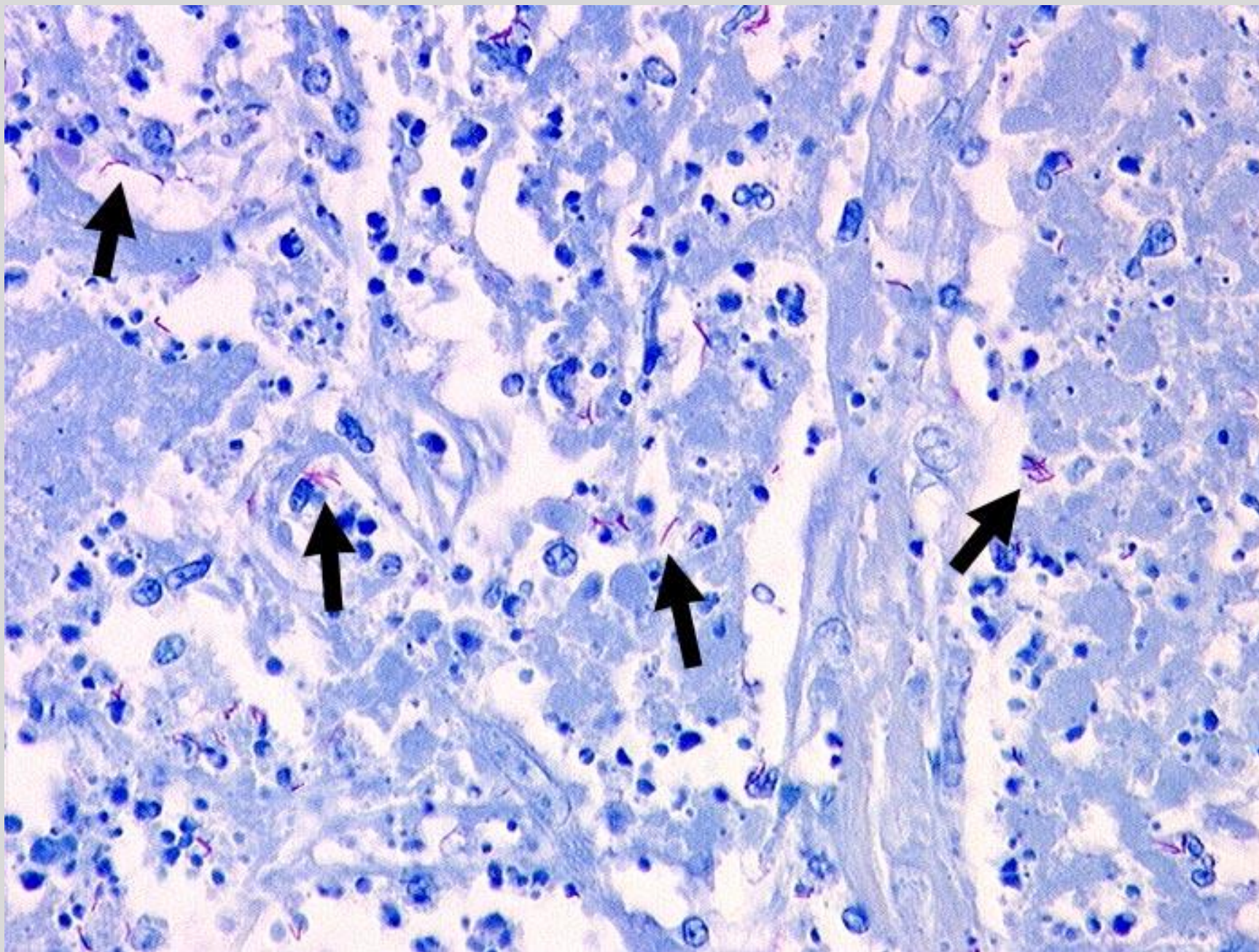
Chronic endometritis

Tuberculous endometritis – particular variant

- bacillary infestation spreading from :
 - the fallopian tubes
 - the bloodstream (less common, in generalized miliary)

Microscopy:

- tubercles are shed each month, if the woman is still menstruating
- caseation if menstruation ceases



Tuberculous
endometritis –
Ziehl-Neelsen stain

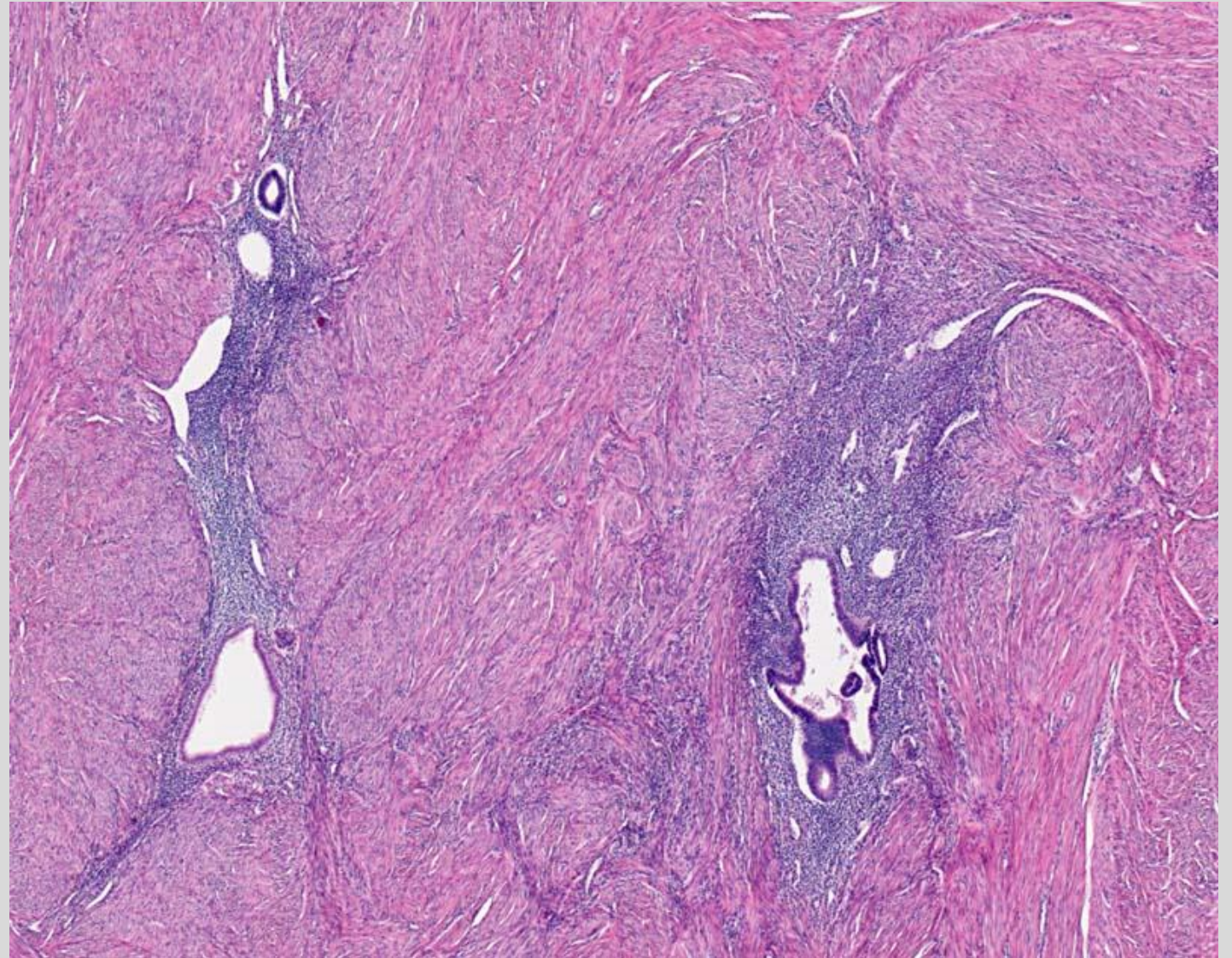
Adenomyosis

- presence of endometrial glands and stroma within the myometrium

Symptoms :

- pain
 - occurs as foci of adenomyosis enlarge when blood is entrapped during menses
- dysmenorrhea or menorrhagia are correlated
 - if glands are 1 mm or more deeply into the myometrium

Adenomyosis



Endometriosis

- presence of benign endometrial glands and stroma outside of the uterus
- usually found in ovaries, uterine ligaments, pouch of Douglas, pelvic peritoneum, but also vagina, lungs, etc.
- often participating in the menstrual cycle

Pathogenesis :

- **menstrual implantation** – regurgitated foci through the fallopian tubes
- **intraoperative implantation** – following hysterotomy / episiotomy
- **lymphatic and hematogenous dissemination**

Endometriosis

Gross :

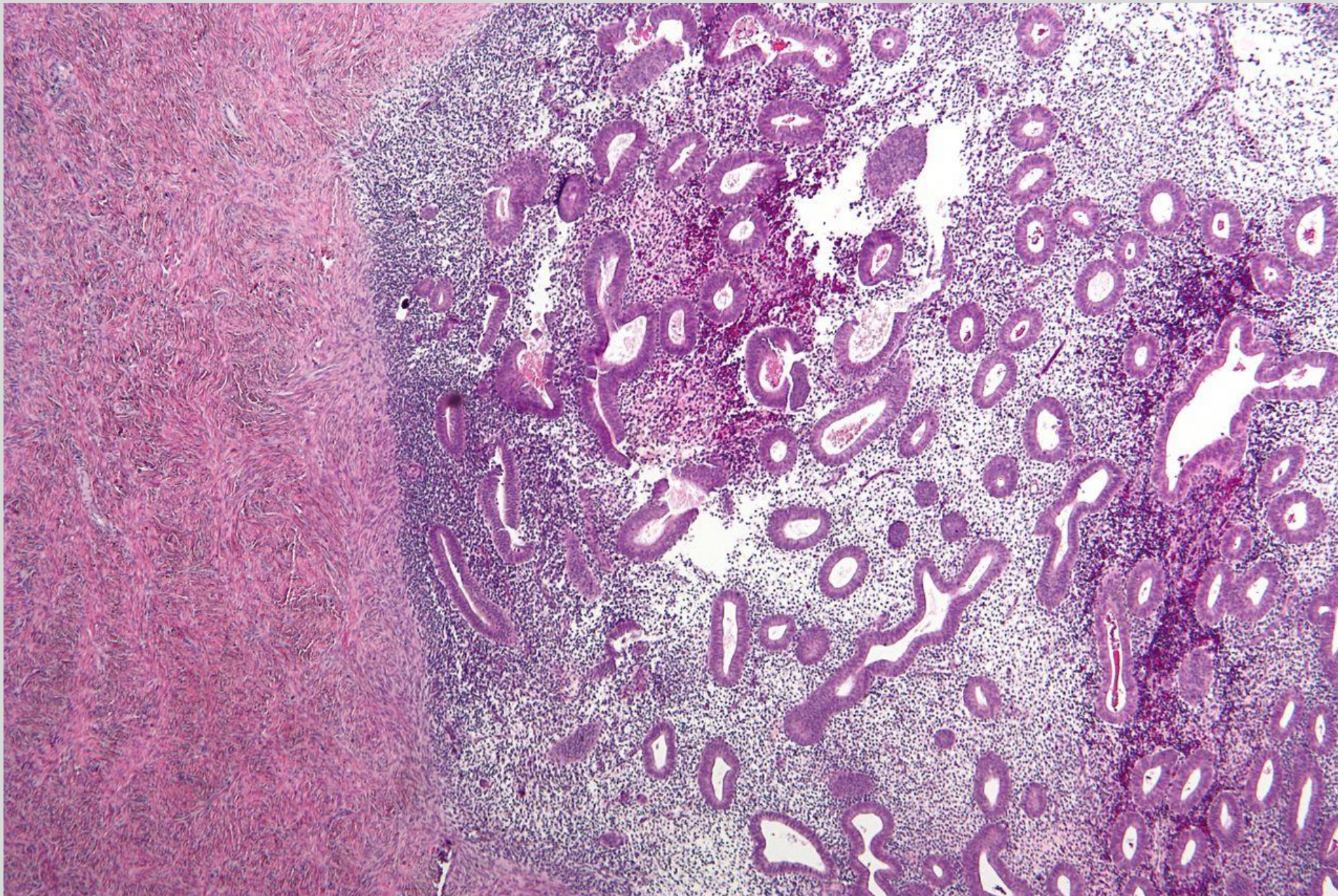
- red to bluish nodules, varying from 1 to 5 mm
- brown discoloration – deposition of hemosiderin through bleeding

Microscopic findings :

- ectopic endometrial glands and stroma
- fibrous tissue and hemosiderin-laden macrophages (*healed foci*)



Endometriosis –
abdominal fatty tissue



Endometriosis -
ovary

ENDOMETRIAL HYPERPLASIA AND ENDOMETRIAL CARCINOMA

- broad spectrum of proliferative disease, constituting a **continuum**
- the lesion progresses from the mildest hyperplasia to invasive cancer
- closely related to **prolonged estrogenic stimulation of the endometrium**, due to :
 - anovulation
 - increased production from endogenous sources
 - exogenous estrogen

Endometrial hyperplasia

- increased proliferation of the endometrial glands, relative to the stroma
- important cause of abnormal uterine bleeding
- classified in **non-atypical** and **atypical** variants

Associated conditions (**high levels of estrogen**) :

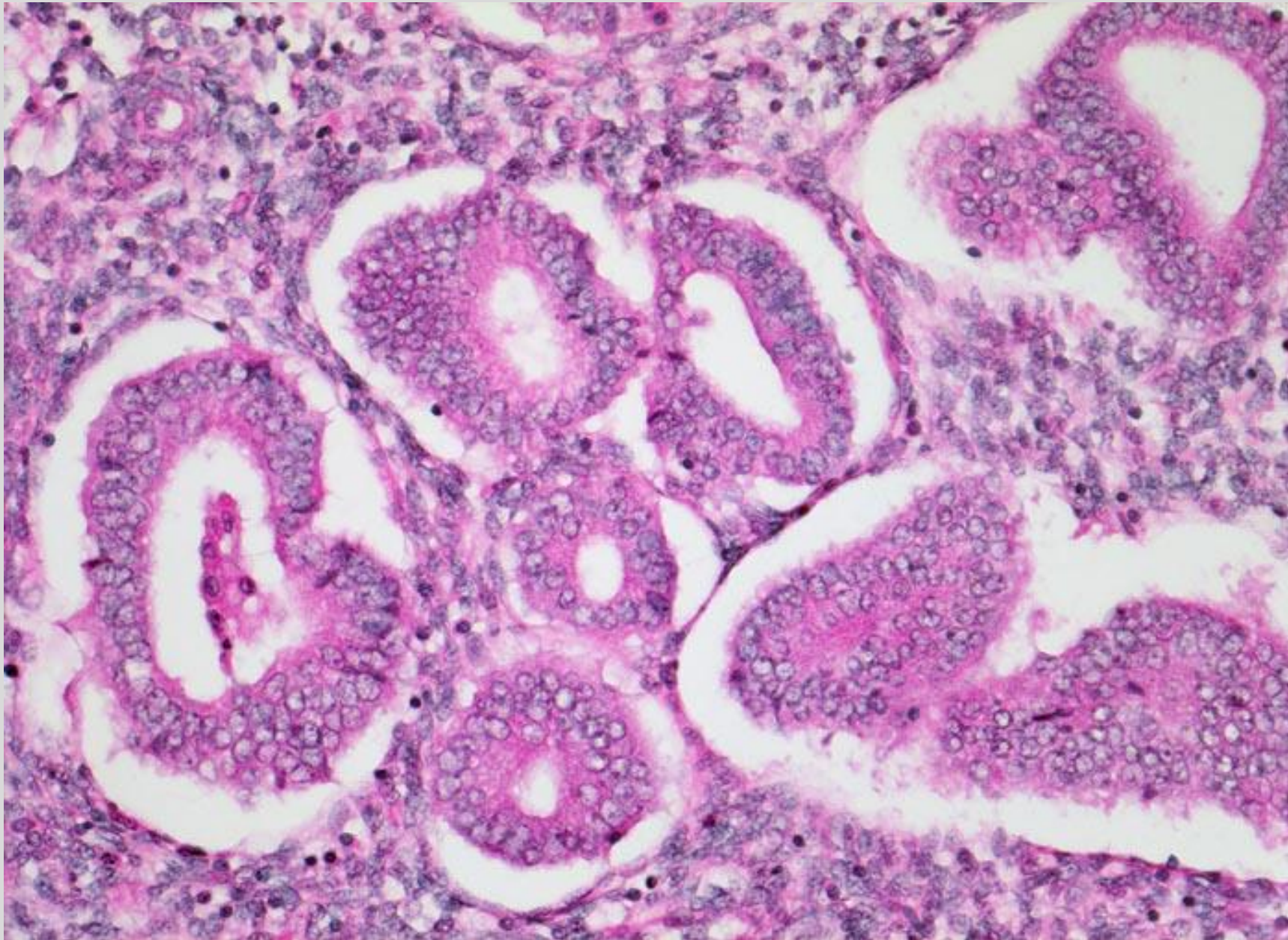
- obesity
- menopause and estrogen replacement therapy
- polycystic ovarian syndrome
- functioning granulosa cell tumors of the ovary
- excessive ovarian cortical function
- prolonged administration of estrogenic substances

Non-atypical endometrial hyperplasia

- increased gland-to-stroma ratio
- rarely progresses to adenocarcinoma (1-3%)
- may evolve into *cystic atrophy* if estrogen is withdrawn\

Microscopy :

- glands with variation in size and shape
 - lined by tall, tightly packed cells
 - **no cytological atypia**
- intervening stroma – retained
- focally – *back-to-back glands*



Non-atypical
endometrial hyperplasia

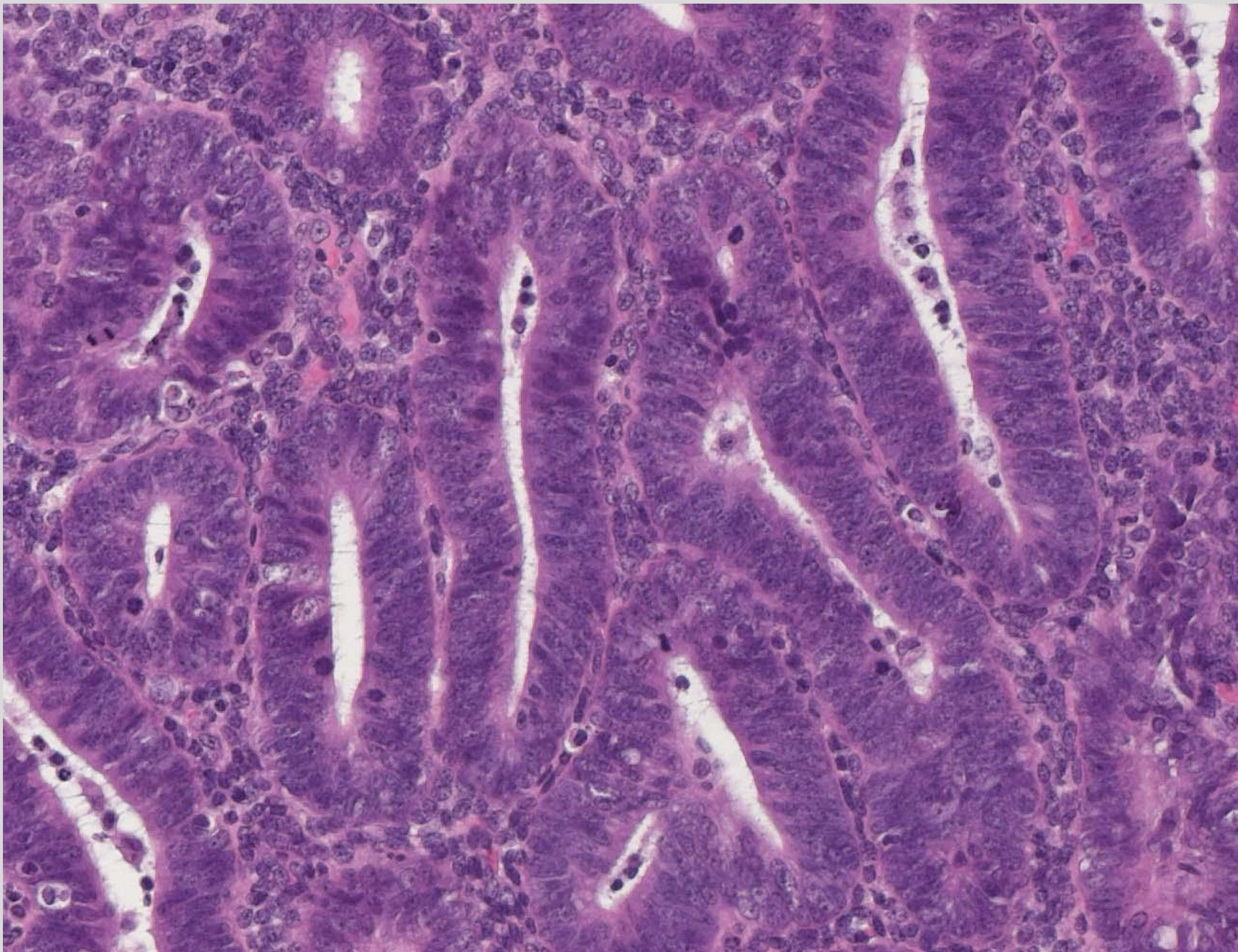
Atypical endometrial hyperplasia

(endometrial intraepithelial neoplasia)

- 30-40% chance of developing endometrial cancer within one year
- usually managed by hysterectomy

Microscopy :

- complex patterns of proliferating glands
 - commonly *back-to-back*
 - lined by **atypical rounded cells**
 - losing the perpendicular orientation to the basement membrane (cell polarity)
 - conspicuous nucleoli
 - open, vesicular chromatin



Atypical hyperplasia:
crowded (back-to-back)
glands, loss of cell
polarity, overlapping
cells, atypical mitoses.

Endometrial carcinoma

- most common in peri- or postmenopausal women
- usually presenting as non-specific *abnormal vaginal bleeding*

Gross: - diffuse or a localized polypoid growing pattern

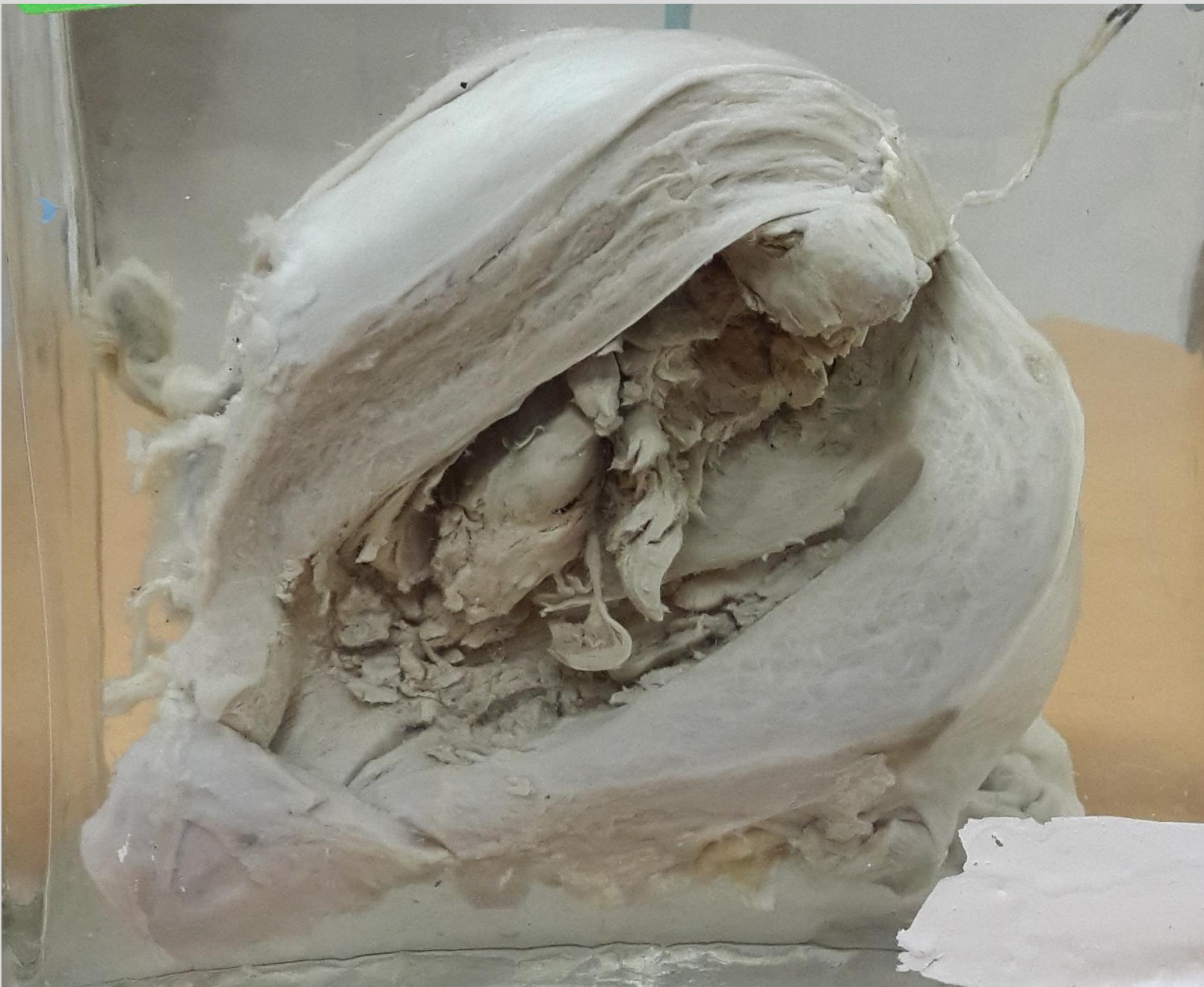
- areas of necrosis and hemorrhage
- spread occurs by direct continuity: invasion of myometrium

Two histologic types :

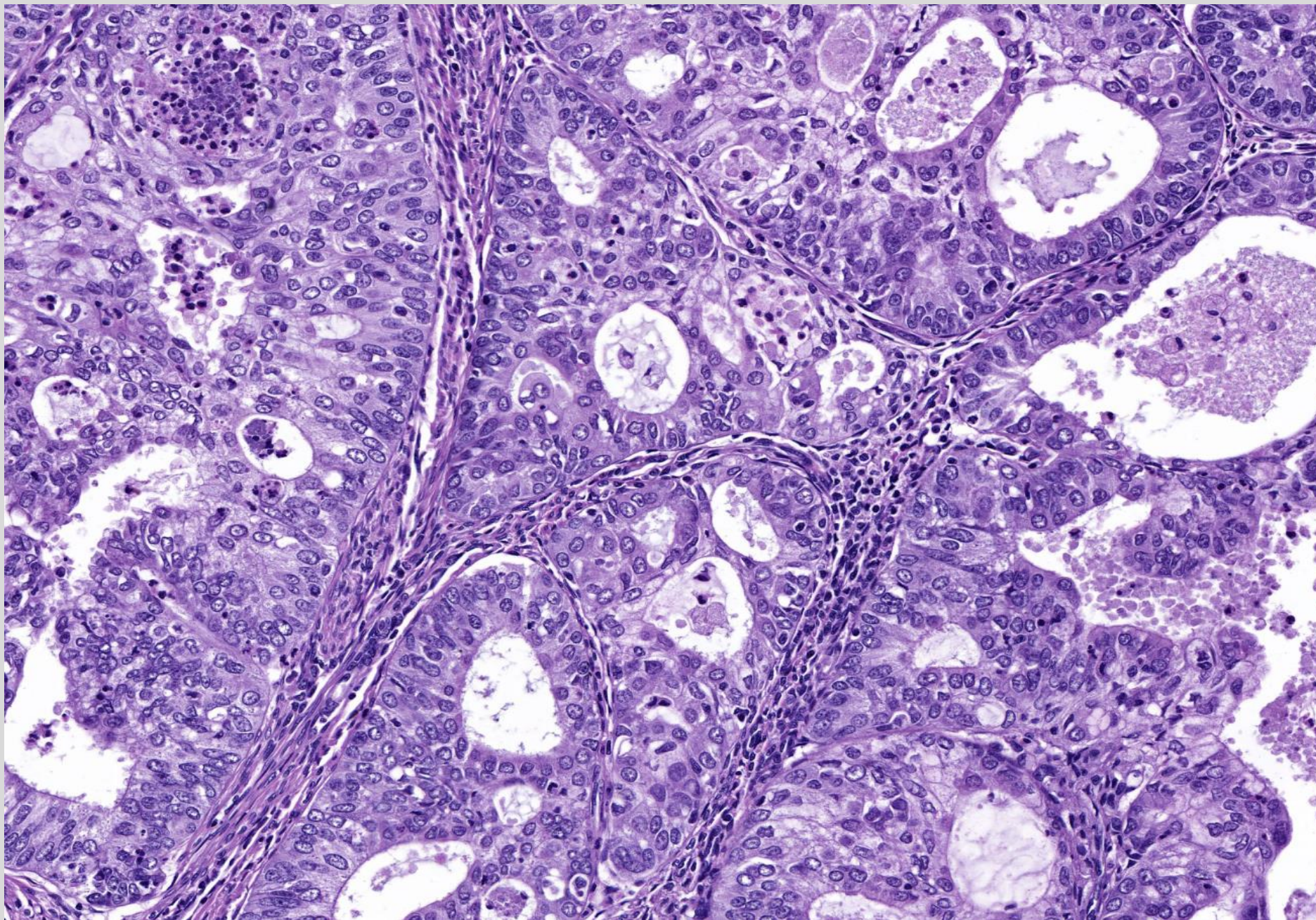
- **endometrioid** (type I) – 80-85%
 - associated with estrogenic stimulation
 - often arise from atypical endometrial hyperplasia
 - favorable prognosis
- **non-endometrioid** (type II) – 15%
 - mostly *papillary serous carcinomas*
 - not associated with estrogenic stimulation or endometrial hyperplasia
 - highly lethal

Endometrioid carcinoma (type I) :

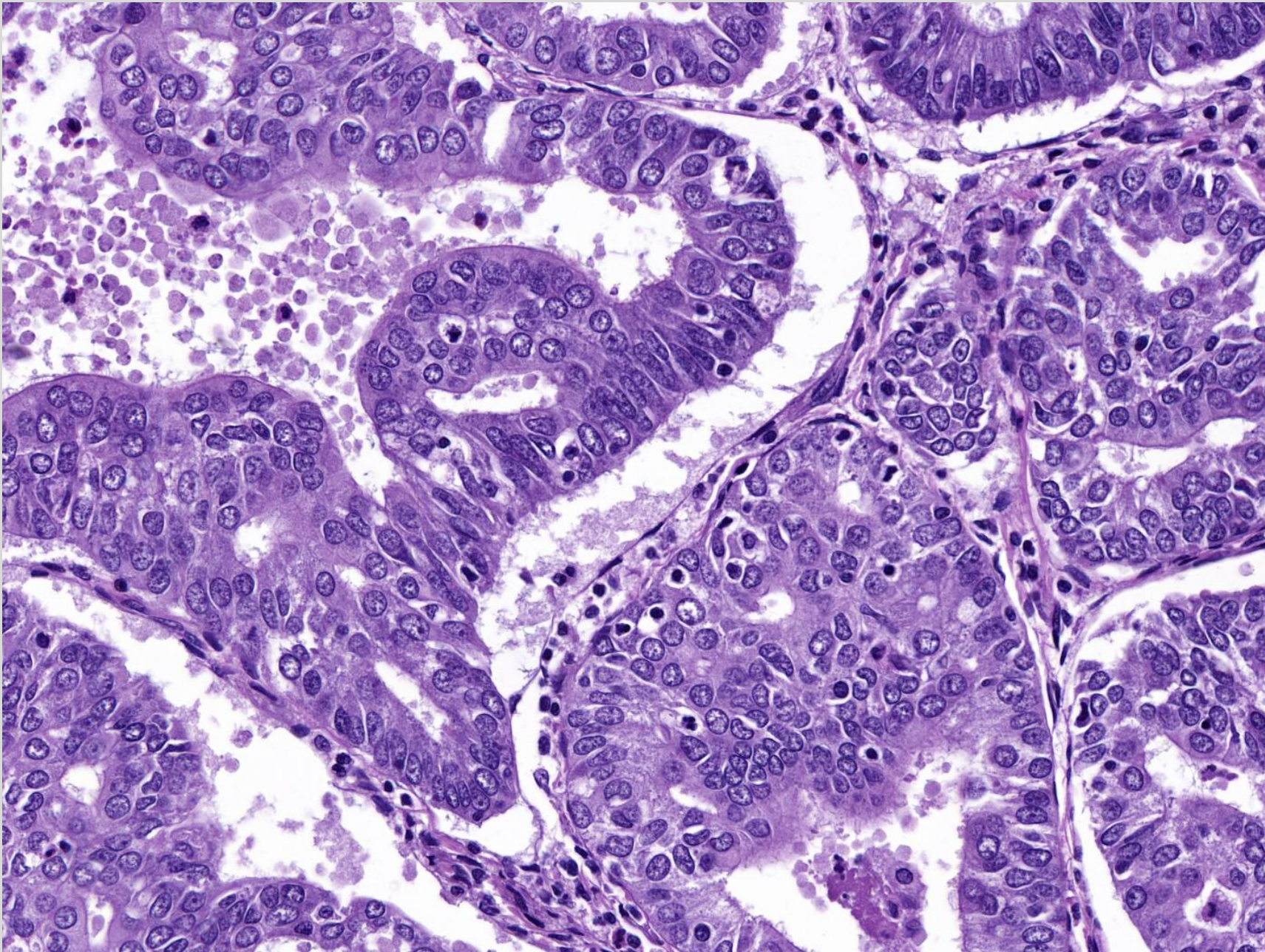
- divided into three grades, based on the ratio of glandular to solid elements :
 - Grade 1 (well differentiated)
 - mostly neoplastic glands
 - minimal (<5%) solid areas
 - Grade 2 (moderately differentiated)
 - 5%-50% of malignant cells form solid areas
 - Grade 3 (poorly differentiated)
 - >50% areas of solid tumor



Polypoid endometrial
carcinoma



Endometrioid
carcinoma



Endometrioid
carcinoma

Non-endometrioid carcinoma (type II) :

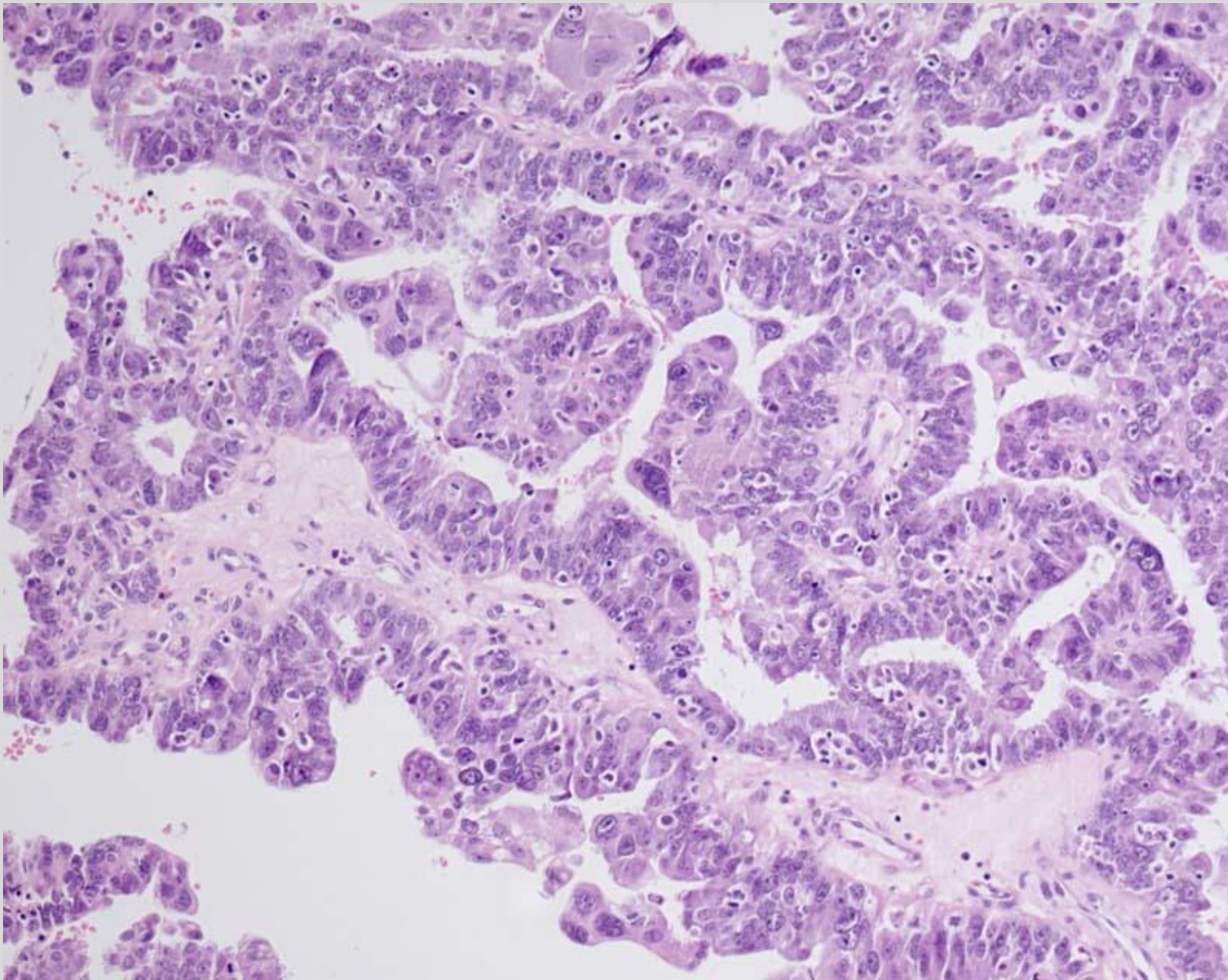
- usually arise in the setting of *endometrial atrophy*
- poorly differentiated (grade 3) – by definition

Variants :

- serous carcinoma
 - most common subtype
 - biologic overlap with ovarian serous carcinoma
- clear cell carcinoma
- malignant mixed müllerian tumor



Serous
adenocarcinoma -
uterus



Serous papillary
adenocarcinoma -
uterus

Staging and management of endometrial carcinoma

Staging (both type I and II) :

- **stage I** : confined to the corpus uteri itself
- **stage II** : involving the corpus and the cervix
- **stage III** : extending outside the uterus, but not outside of the true pelvis
- **stage IV** : extending outside the true pelvis, or involving the mucosa of the bladder or the rectum

Treatment :

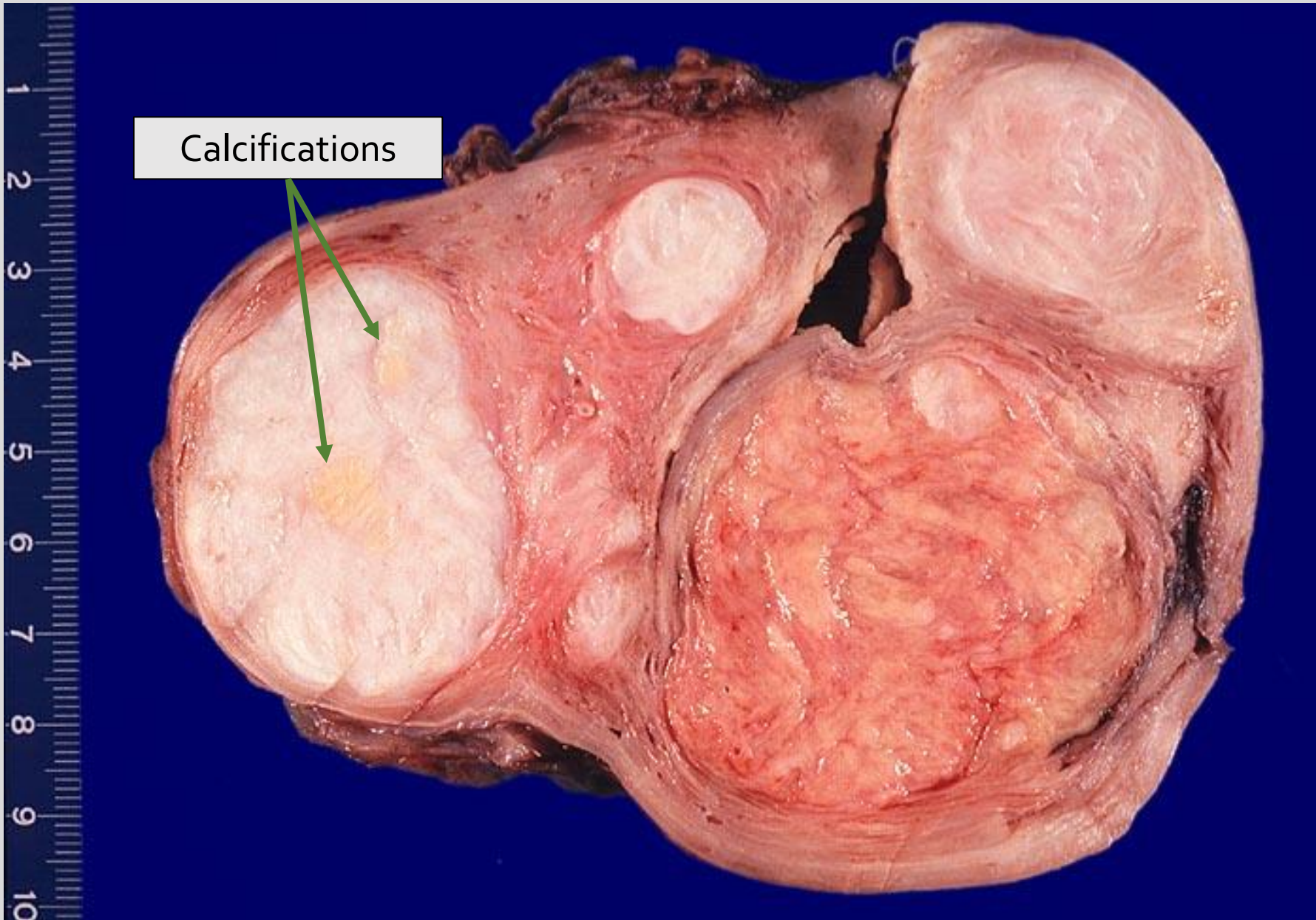
- **hysterectomy** : well-differentiated tumors, confined to the endometrium
- **hysterectomy + postoperative radiation** : otherwise

LEIOMYOMA

- benign tumor of smooth muscle origin
- most common tumor of the female genital tract

Grossly :

- hard, round
- white, pale gray
- encapsulated
- whorled appearance on the cut surface
- 1 mm to >30 cm
- most are intramural

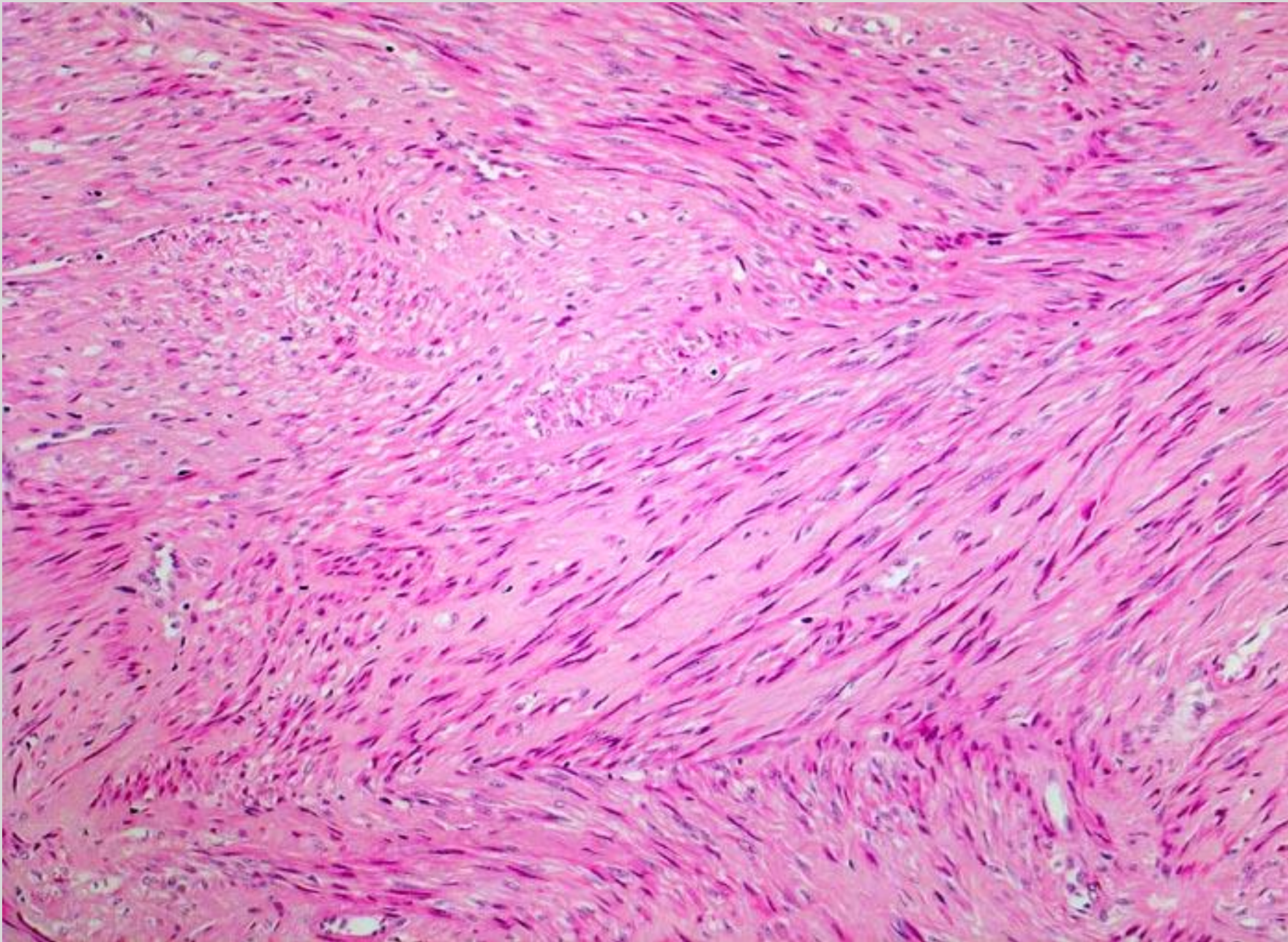


Multiple leiomyomas
- uterus

LEIOMYOMA

Microscopically :

- interlacing fascicles of
 - uniform spindle cells
 - elongated nuclei
 - blunt ends
 - abundant, eosinophilic and fibrillar cytoplasm



Leiomyoma - uterus

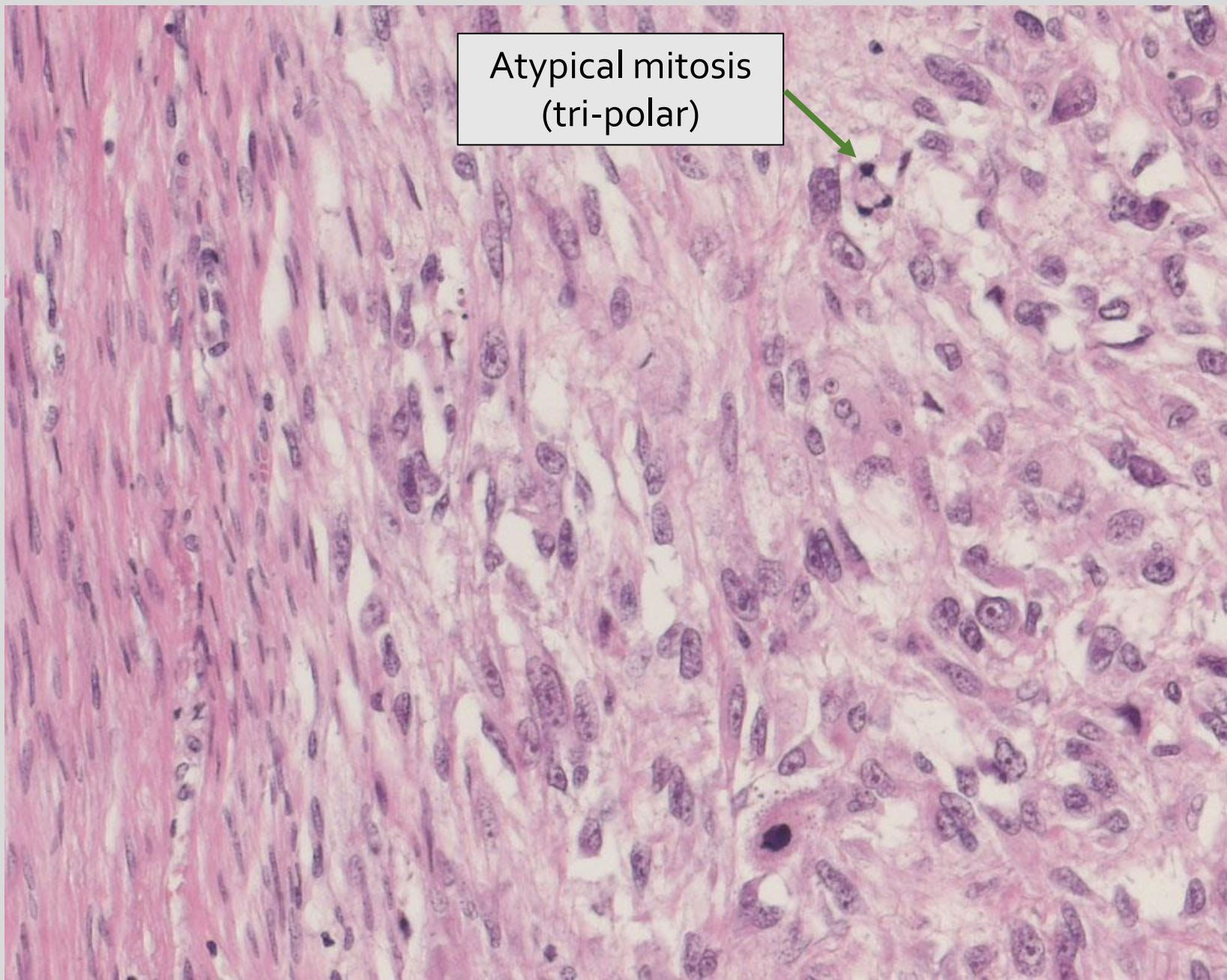
LEIOMYOMA

Complications :

- hyaline or mucoid degeneration +/- calcification
- necrosis and hemorrhage (*submucous* variant)
- torsion (*subserous* variant)
- malignant transformation – leiomyosarcoma
 - nuclear atypia
 - >4 mitoses / 10 high-power microscope fields



Leiomyosarcoma



Leiomyosarcoma