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# Pathology of the vulva and uterus

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# Pathology of the vulva

## Inflammation

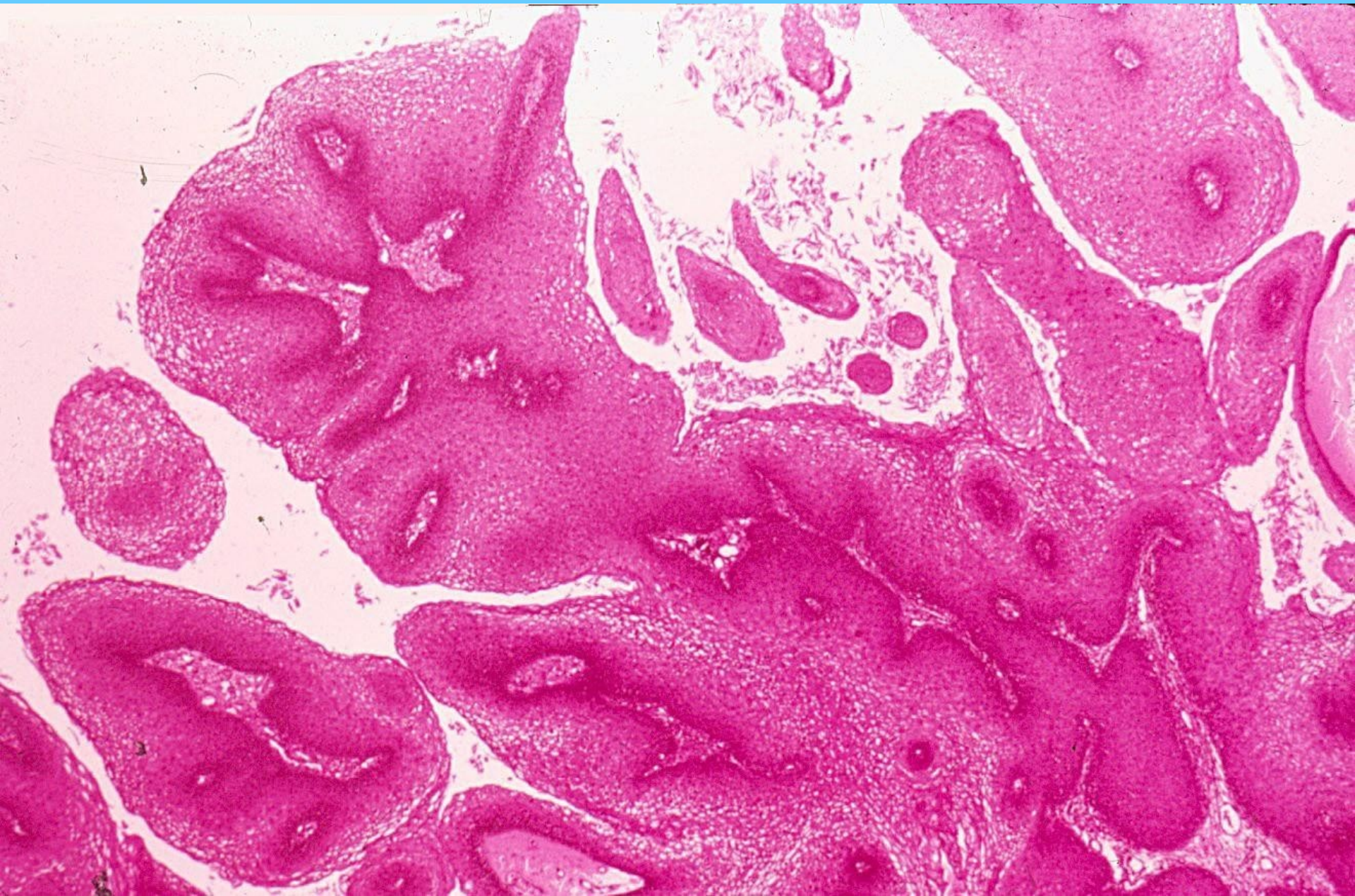
- Noninfectious – contact dermatitis, atopic dermatitis, psoriasis..
  - Infectious – Viral – HPV (condyloma acc. / squamous ca), HSV
    - Bacterial – Syphilis (ulcus durum, condylomata lata)
      - Neisseria gonorrhoeae, granuloma inguinale, lymphogranuloma venereum, ulcus molle
    - Mycotic – candida, dermatophytes
    - Parasitic – rare – enterobius vermicularis
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# Pathology of the vulva

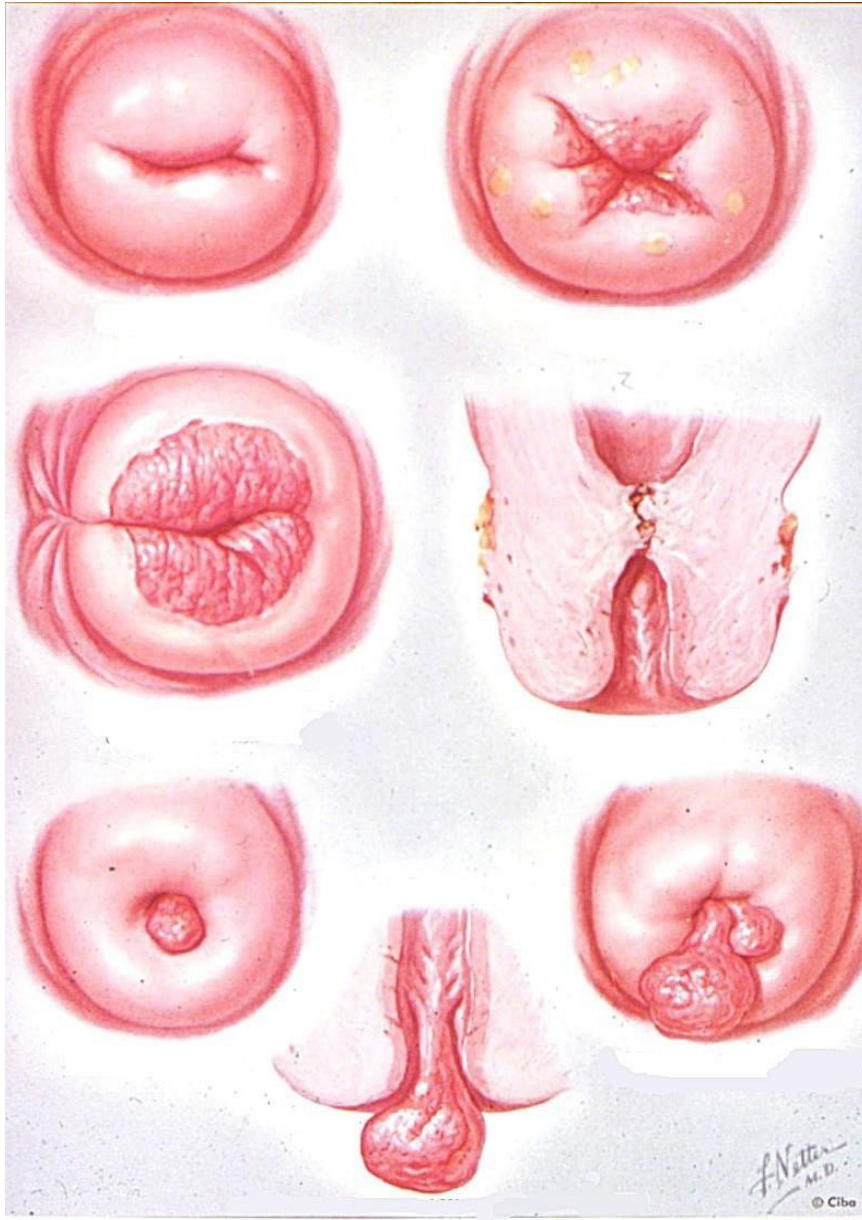
## Tumors

- Squamous cell carcinoma – HPV associated / independent
- Precursor lesions – uVIN – HPV associated
  - dVIN – associated with chronic diseases on vulva
- Basal cell carcinoma
- Extramammary paget disease – intraepithelial spread of carcinoma
- Melanoma

## 4. Condyloma accuminatum

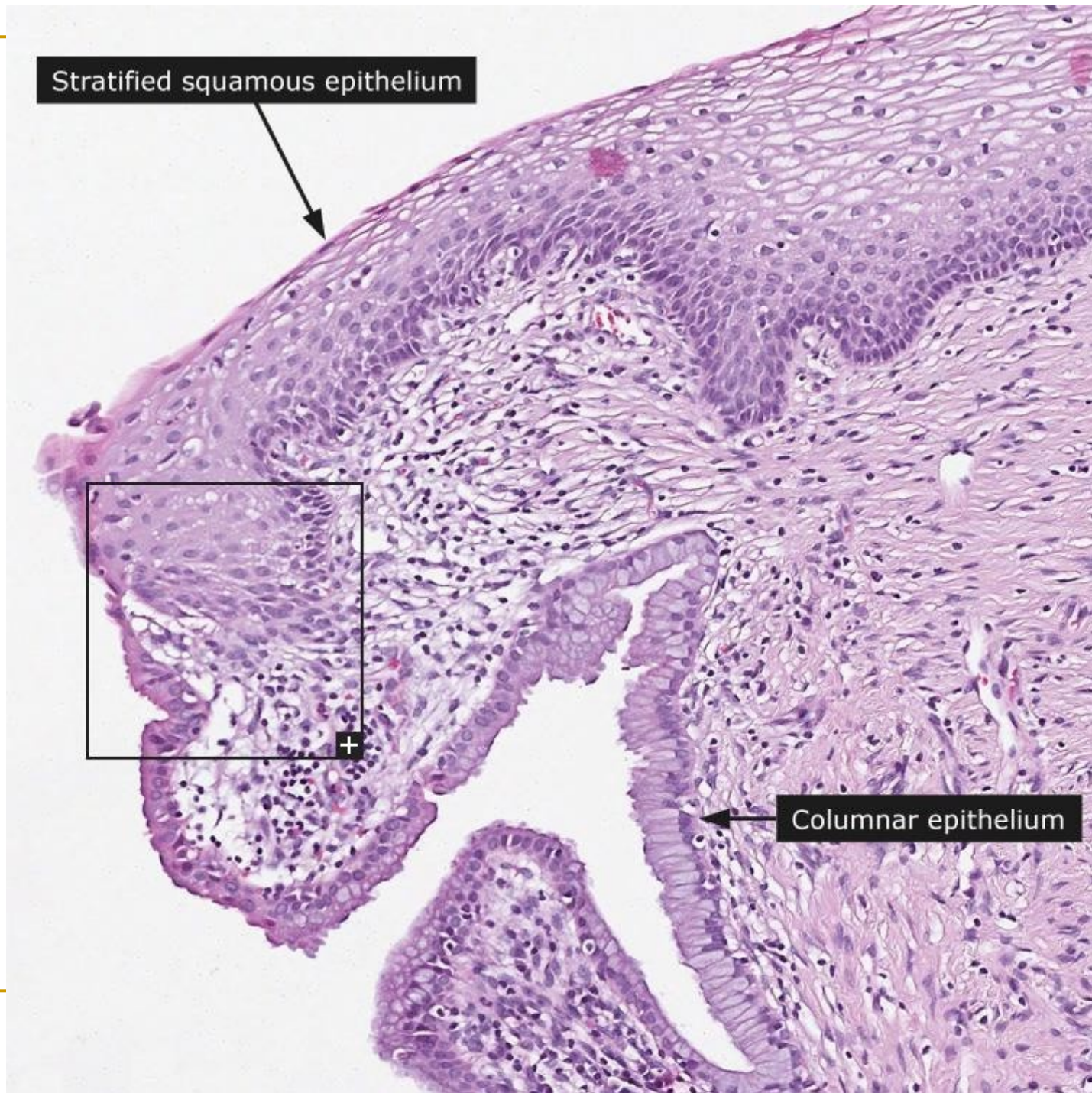






- **Cervical ectropion** (or **cervical eversion**) is a condition in which the central (endocervical) columnar epithelium protrudes out through the external os of the cervix and onto the vaginal portion of the cervix , undergoes squamous metaplasia , and transforms to stratified squamous epithelium.
- **Endocervical polyps** are benign exophytic growths that occur in 2% to 5% of adult women. Most polyps arise within the endocervical canal and vary from small and sessile to large, 5-cm masses that may protrude through the cervical os. All are soft, almost mucoid, lesions composed of a loose fibromyxomatous stroma harboring dilated, mucus-secreting endocervical glands, often accompanied by inflammation.

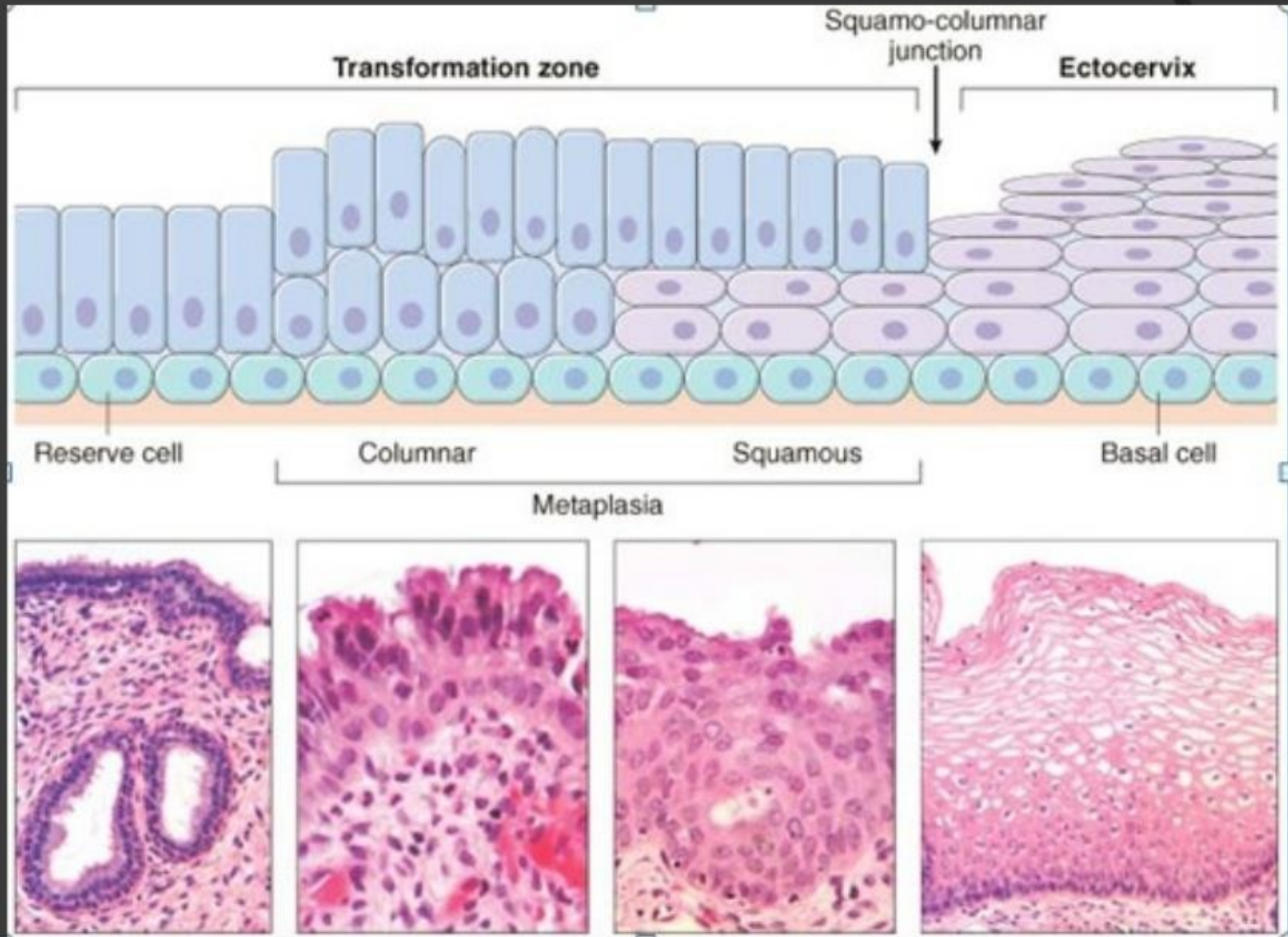
Stratified squamous epithelium



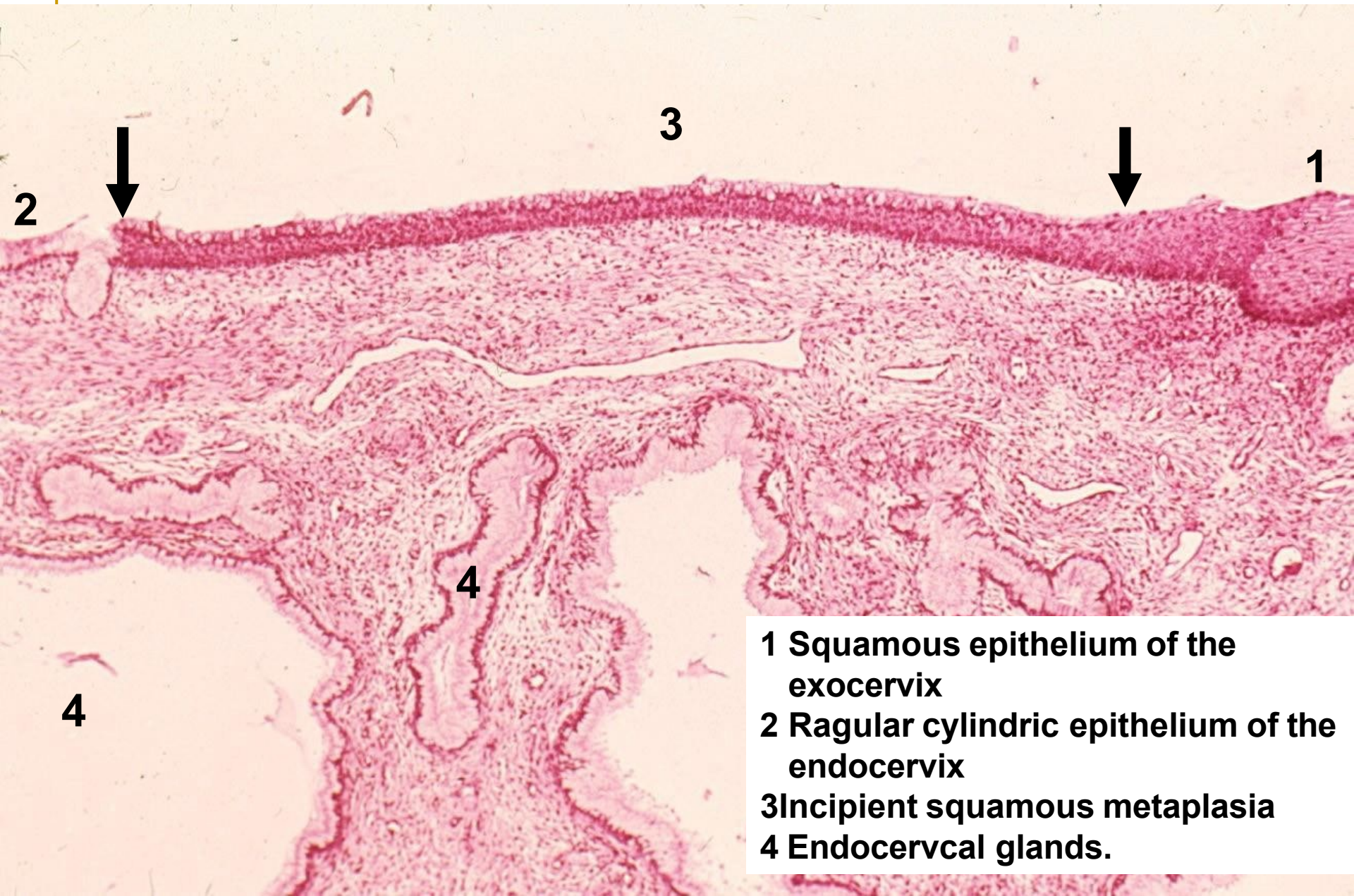
Columnar epithelium



# SCJ & T zone Histologically:



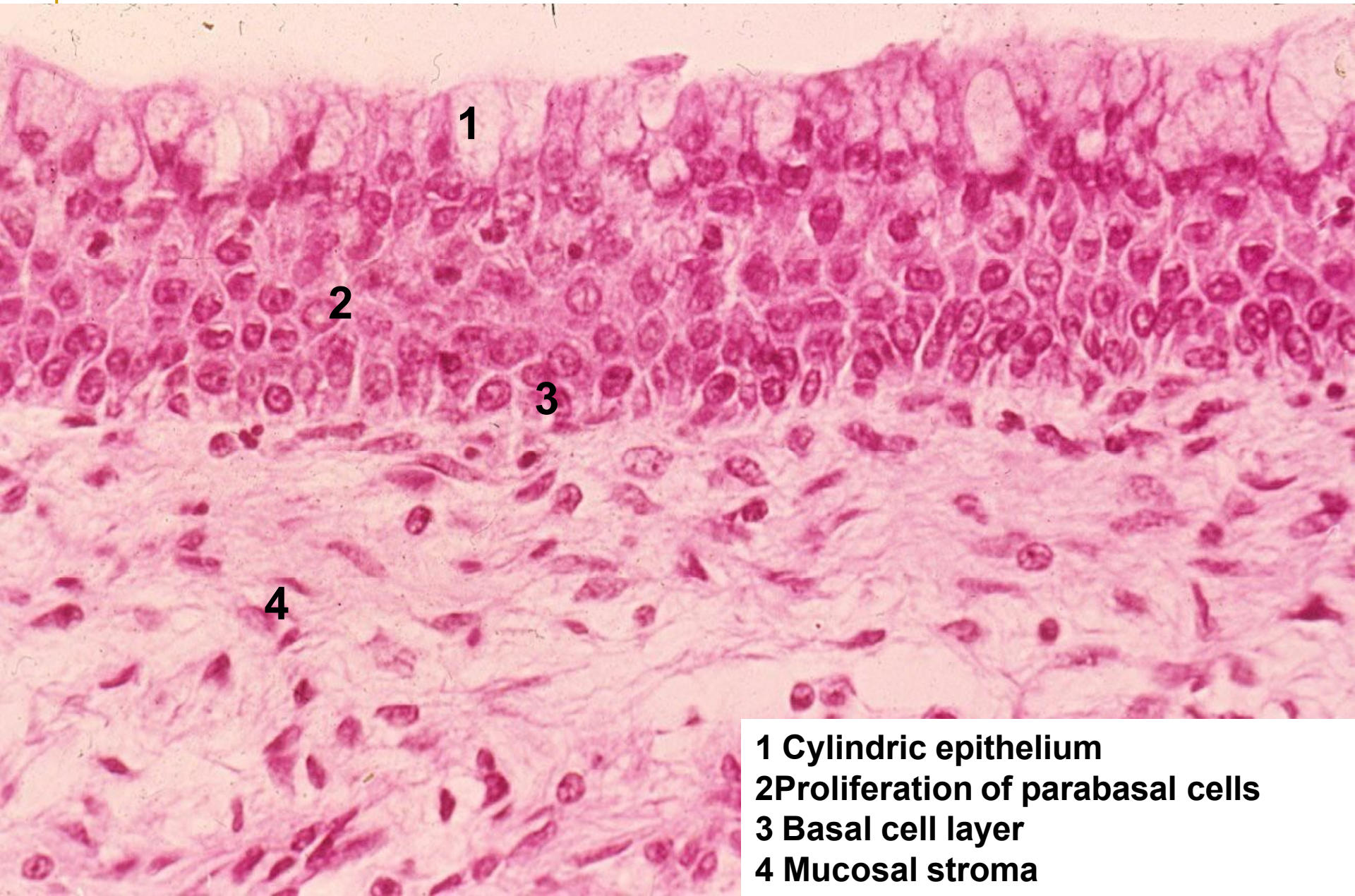
# Incipient squamous metaplasia.



- 1 Squamous epithelium of the exocervix
- 2 Regular cylindric epithelium of the endocervix
- 3 Incipient squamous metaplasia
- 4 Endocervical glands.



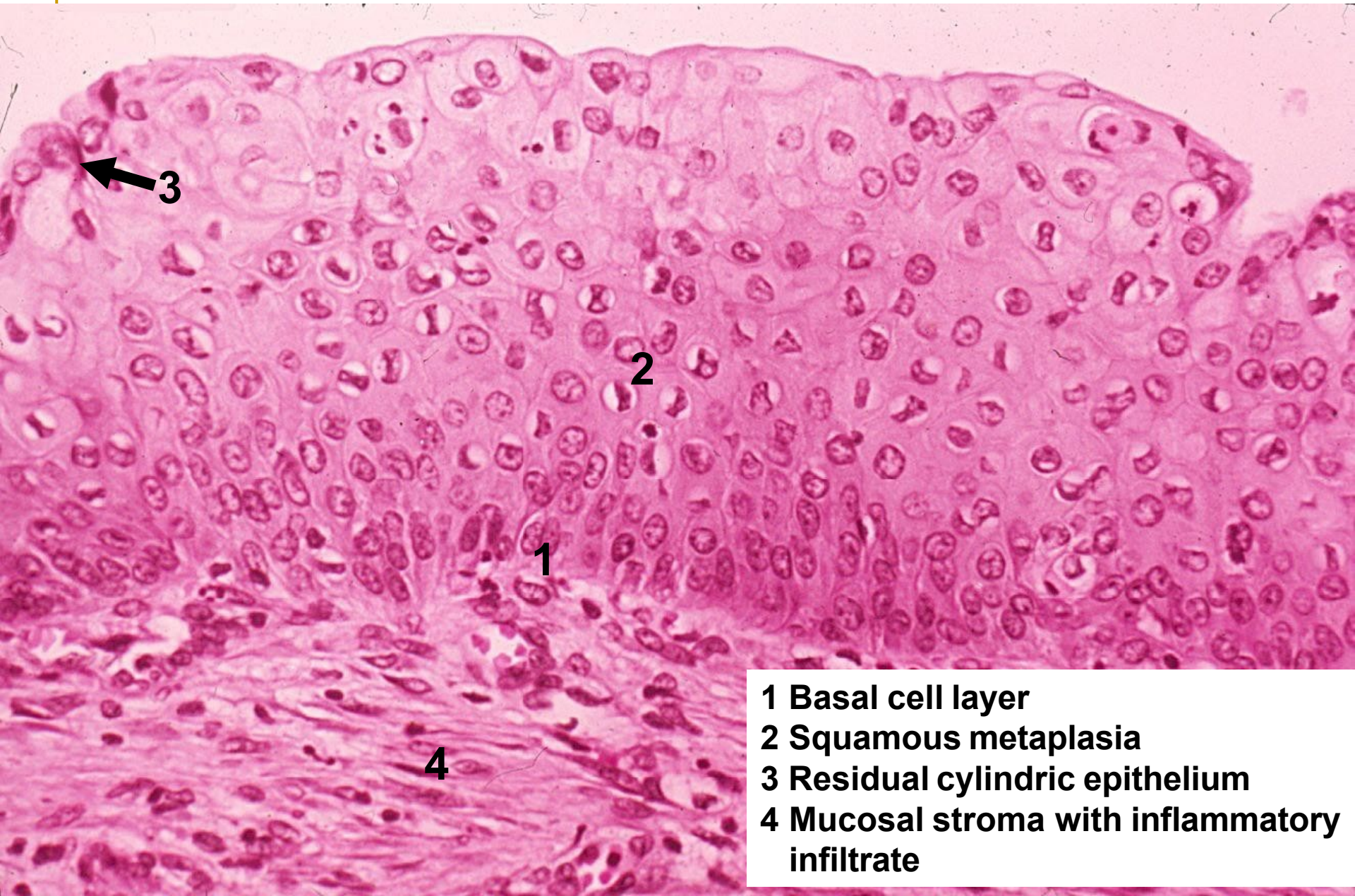
# Incipient squamous metaplasia - detail



- 1 Cylindric epithelium**
- 2 Proliferation of parabasal cells**
- 3 Basal cell layer**
- 4 Mucosal stroma**



# Squamous metaplasia



# Pathology of the uterine cervix

## dysplasias and malignancies of uterine cervix

- HPVs infect immature basal cells of the squamous epithelium in areas of epithelial breaks, or immature metaplastic squamous cells present at the squamocolumnar junction
- Although the virus can *infect* only the immature squamous cells, *replication* of HPV occurs in the maturing squamous cells and results in a cytopathic effect, “*koilocytic atypia*,” consisting of nuclear atypia and a cytoplasmic perinuclear halo
- HPV low risk / high risk (16,18,31,33,45)

# Pathology of the uterine cervix

## dysplasias and malignancies of uterine cervix

- oldest classification system - mild dysplasia on one end and severe dysplasia/carcinoma in situ on the other
- followed by *cervical intraepithelial neoplasia* (CIN) classification, with mild dysplasia termed *CIN I*, moderate dysplasia *CIN II*, and severe dysplasia termed *CIN III*
- nowadays a two-tiered system, with CIN I renamed low-grade squamous intraepithelial lesion (LSIL) and CIN II and CIN III combined into one category referred to as high-grade squamous intraepithelial lesion (HSIL)

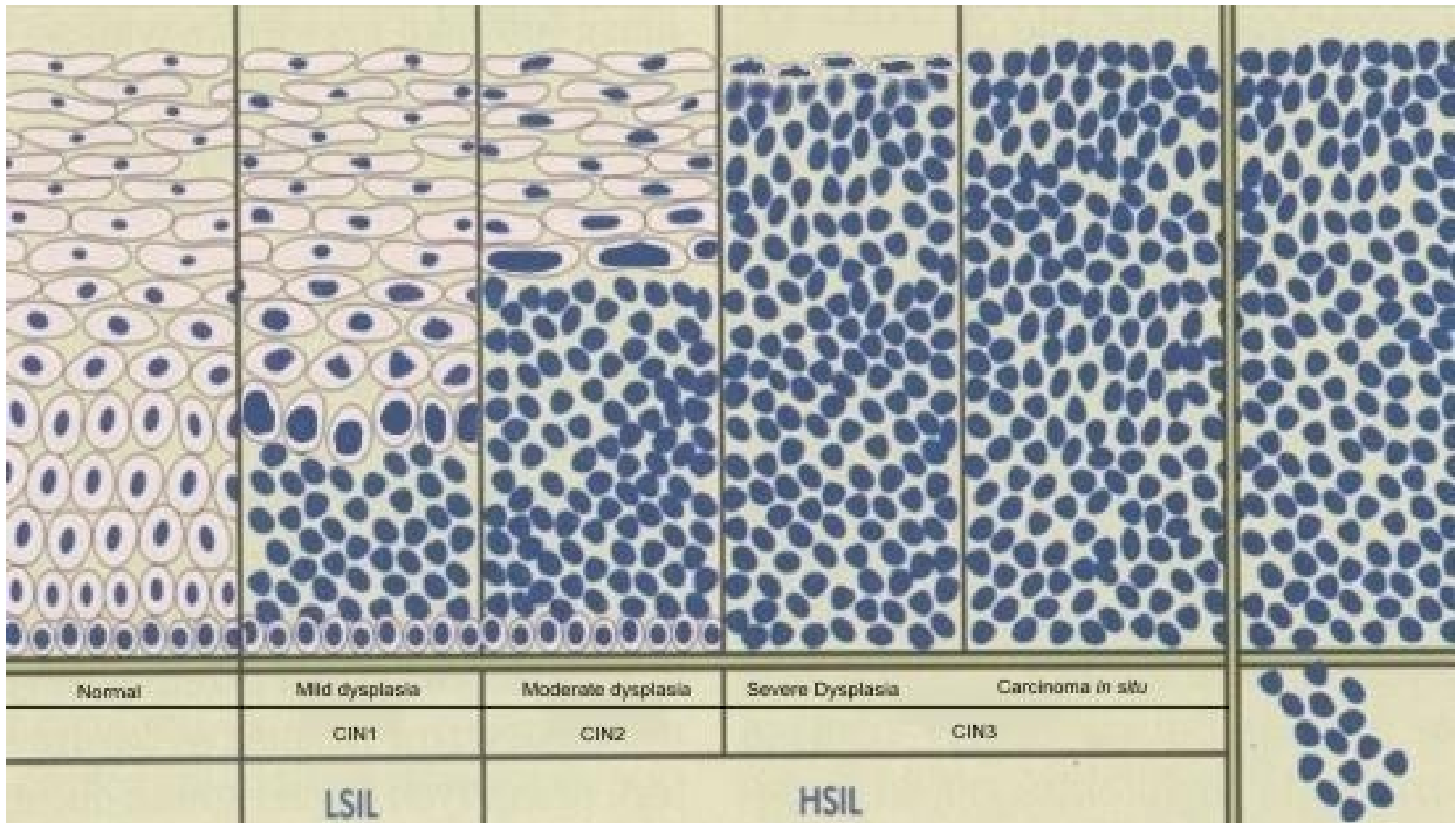


# Pathology of the uterine cervix

## dysplasias and malignancies of uterine cervix

- SIL - nuclear atypia: nuclear enlargement, hyperchromasia (dark staining), presence of coarse chromatin granules, and variation of nuclear sizes and shapes
- Nuclear changes may be accompanied by cytoplasmic halos - nuclear alterations and perinuclear halo are termed *koilocytic atypia*.
- The grading of SIL : expansion of the immature cell layer from its normal, basal location. If the atypical, immature squamous cells are confined to the lower one third of the epithelium, the lesion is graded as LSIL; if they expand to two thirds of the epithelial thickness, it is graded as HSIL.

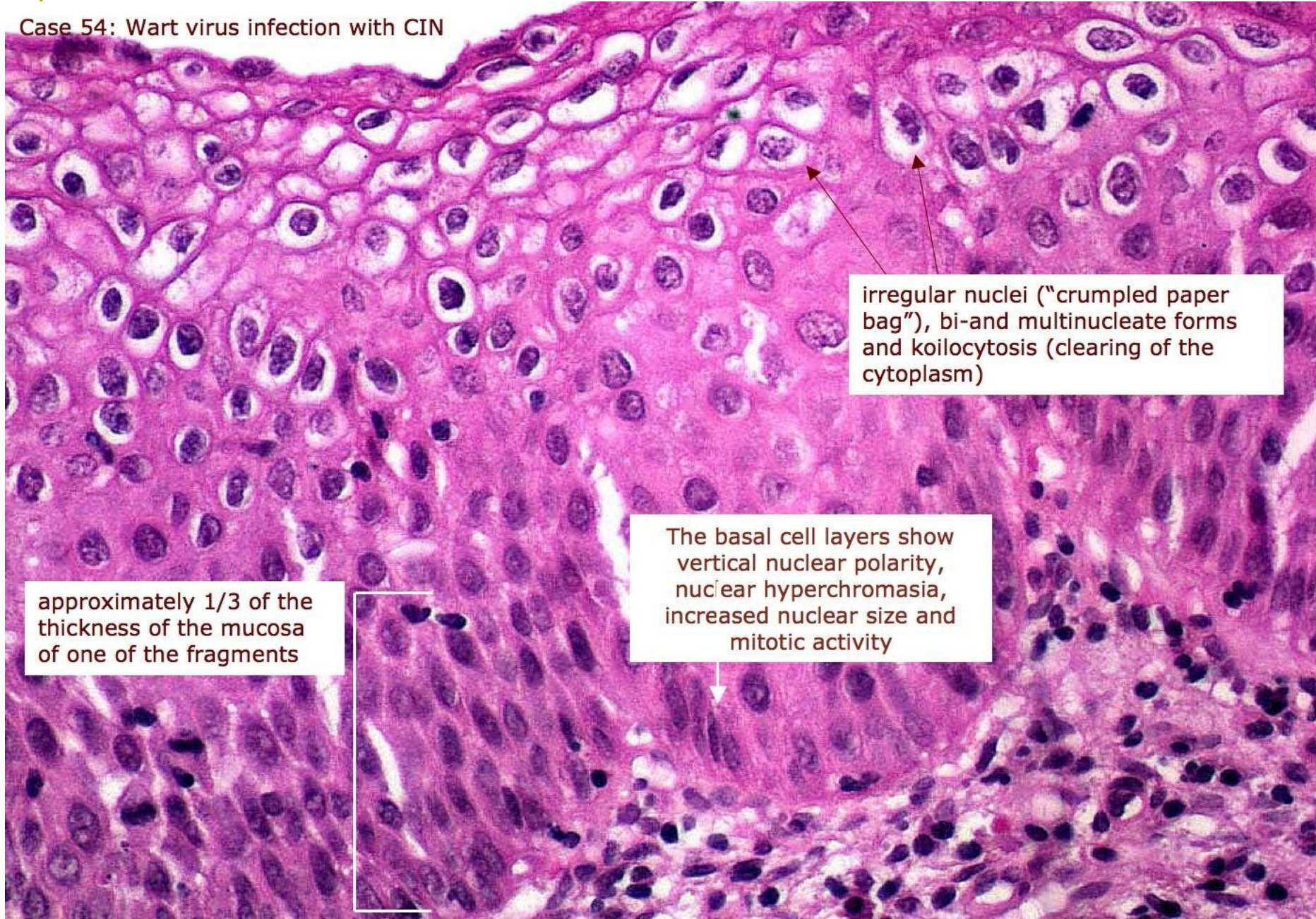
# Dysplasia of uterine cervix





# LSIL / CIN I

Case 54: Wart virus infection with CIN

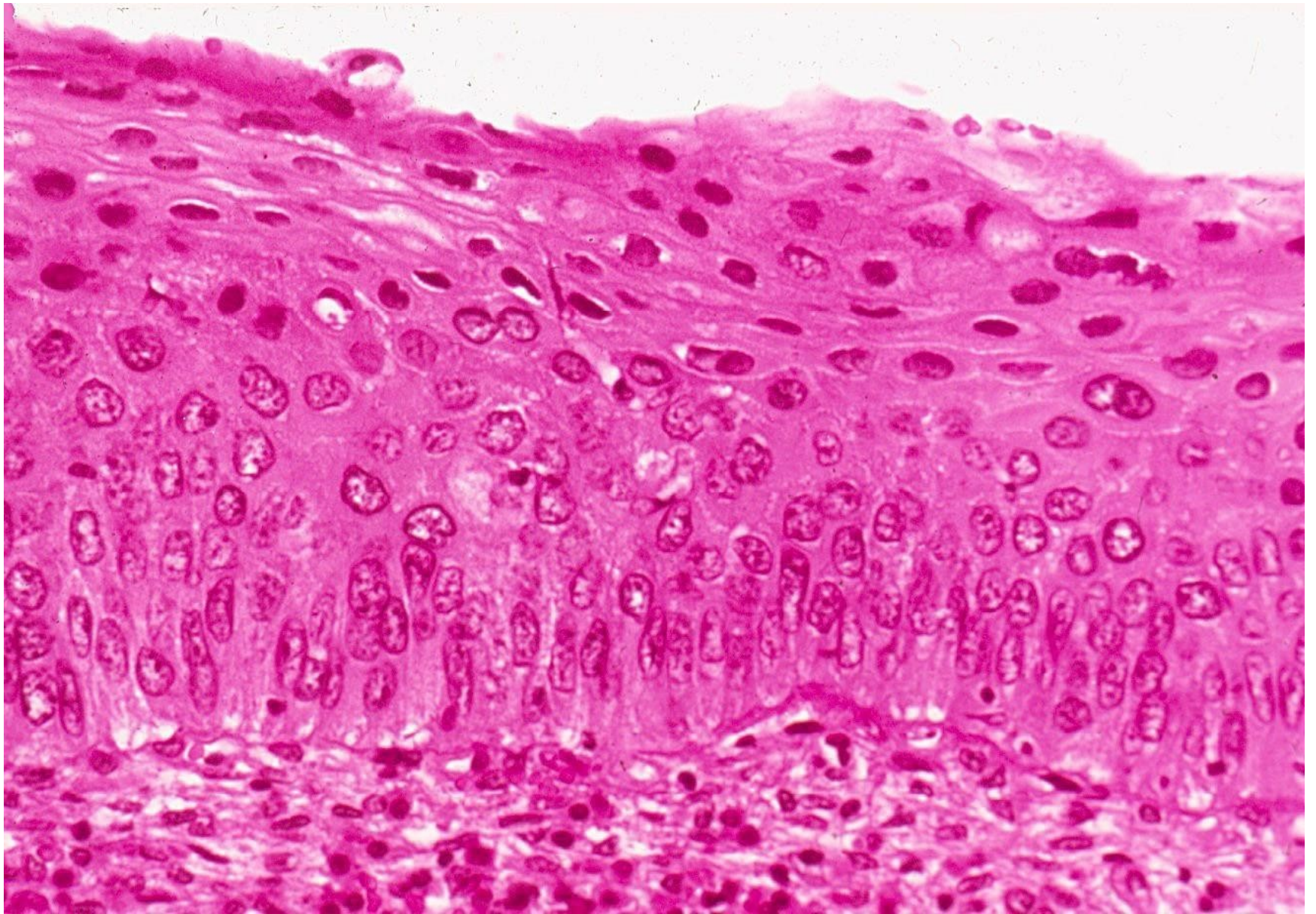


irregular nuclei ("crumpled paper bag"), bi- and multinucleate forms and koilocytosis (clearing of the cytoplasm)

The basal cell layers show vertical nuclear polarity, nuclear hyperchromasia, increased nuclear size and mitotic activity

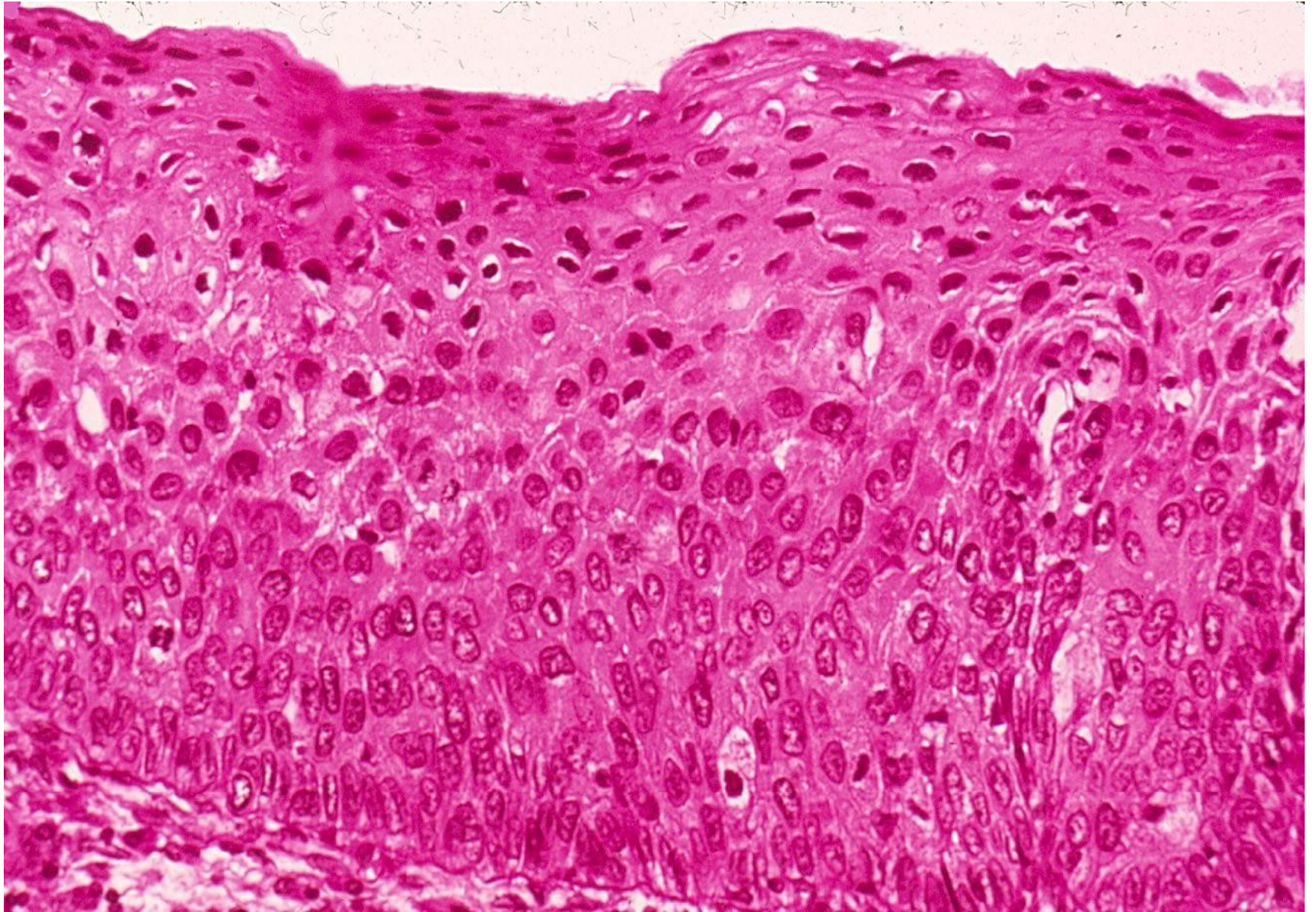
approximately 1/3 of the thickness of the mucosa of one of the fragments





CIN II





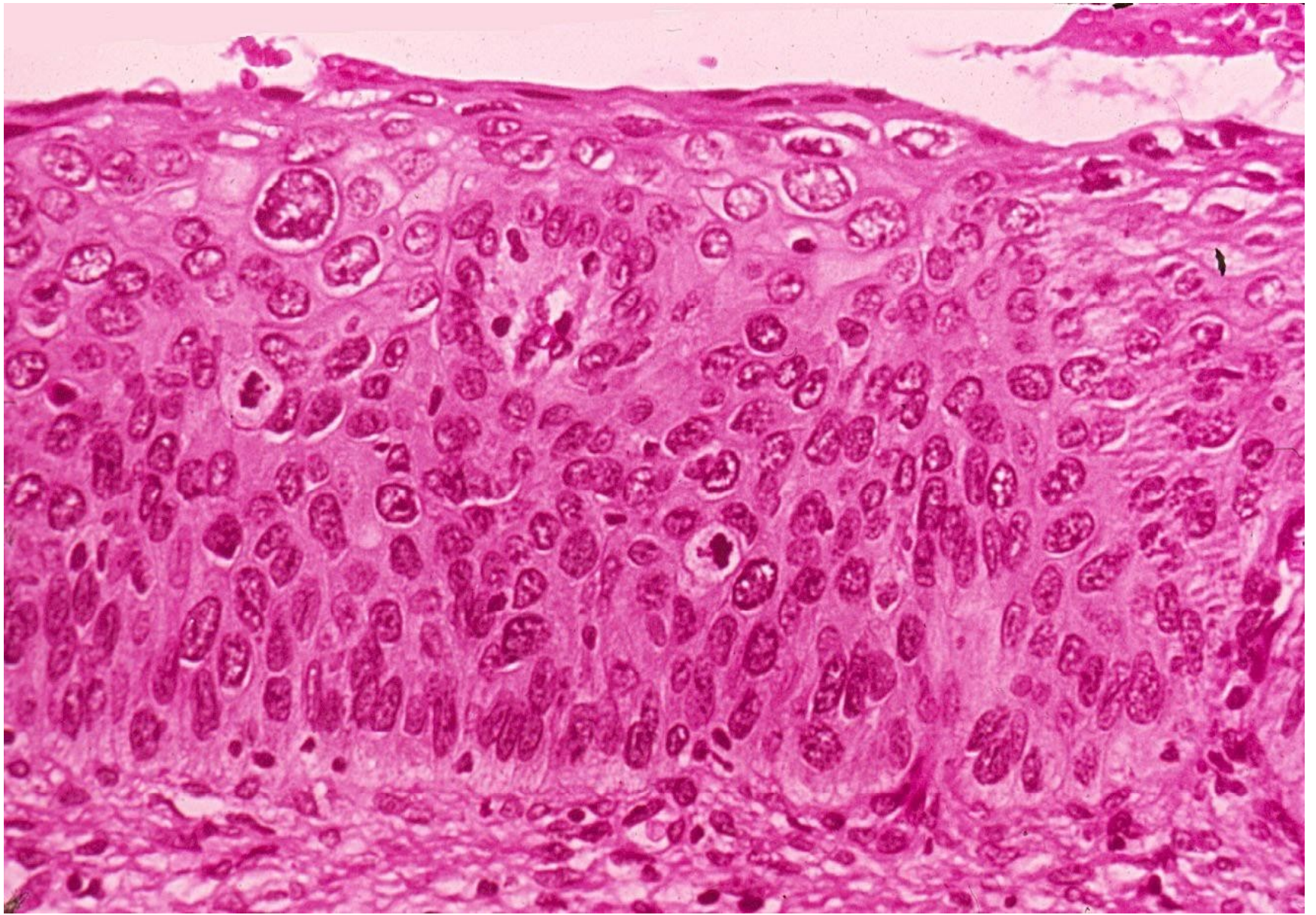
CIN II





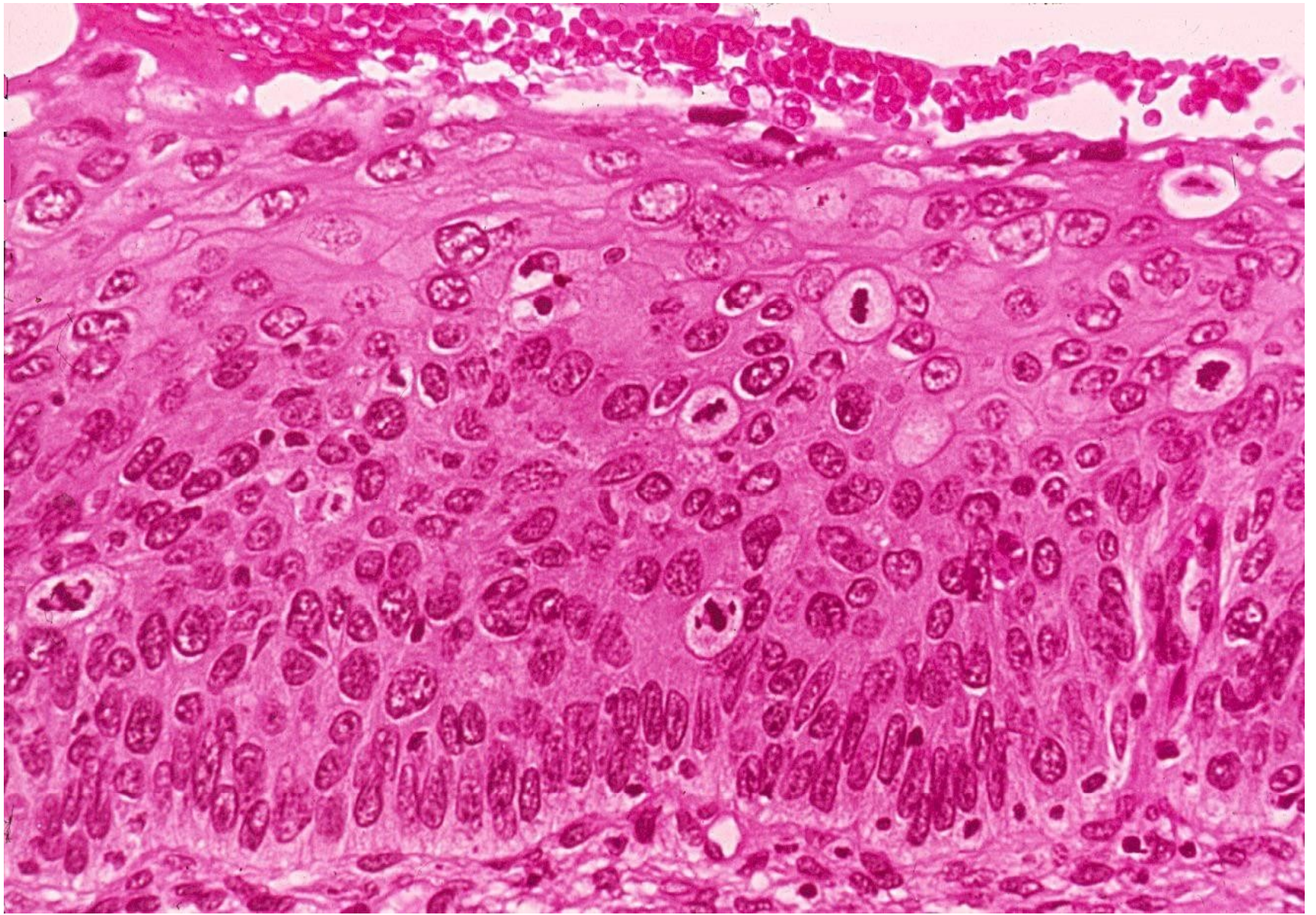
CIN III - koilocytes





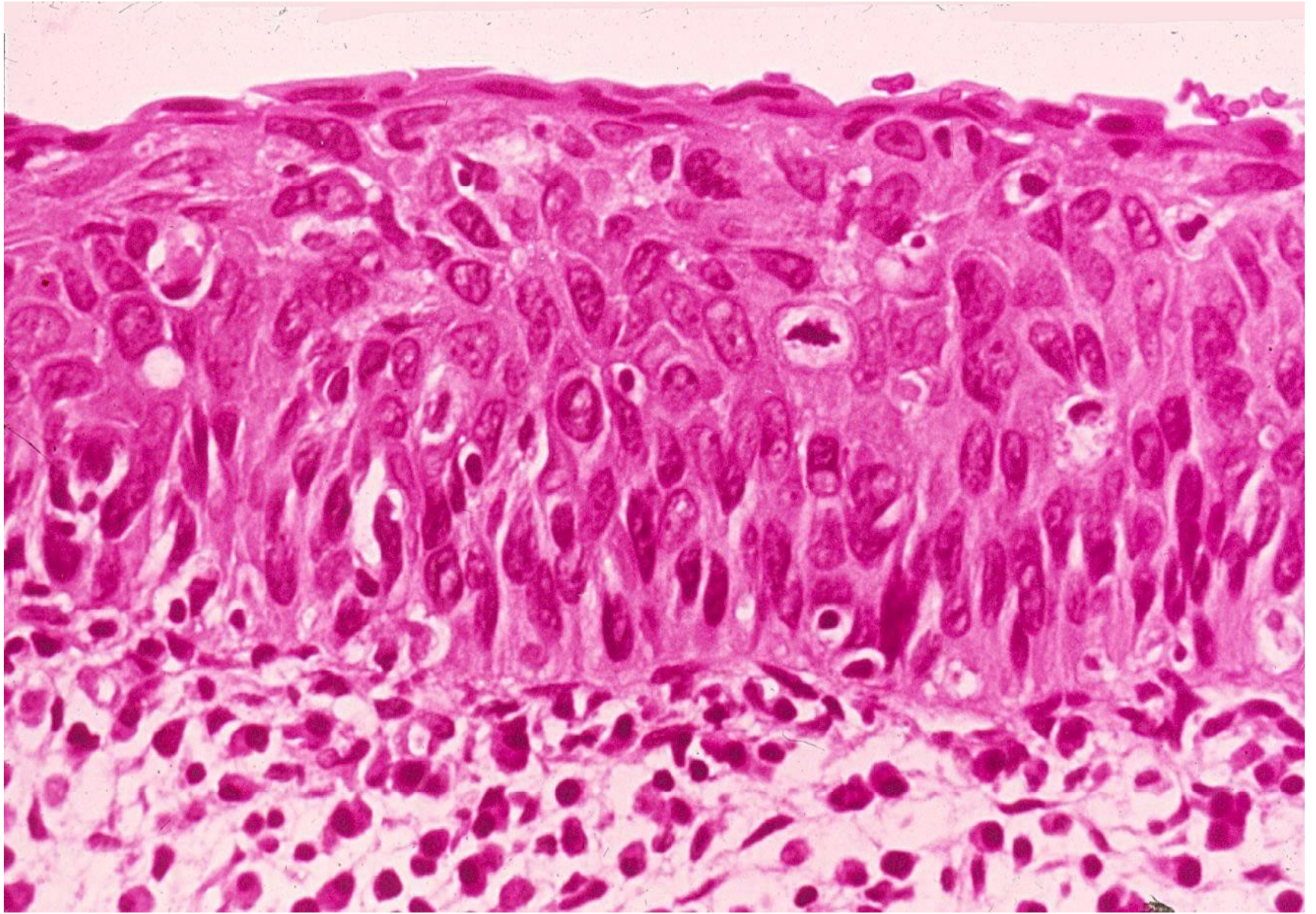
CIN III – atypias, mitoses





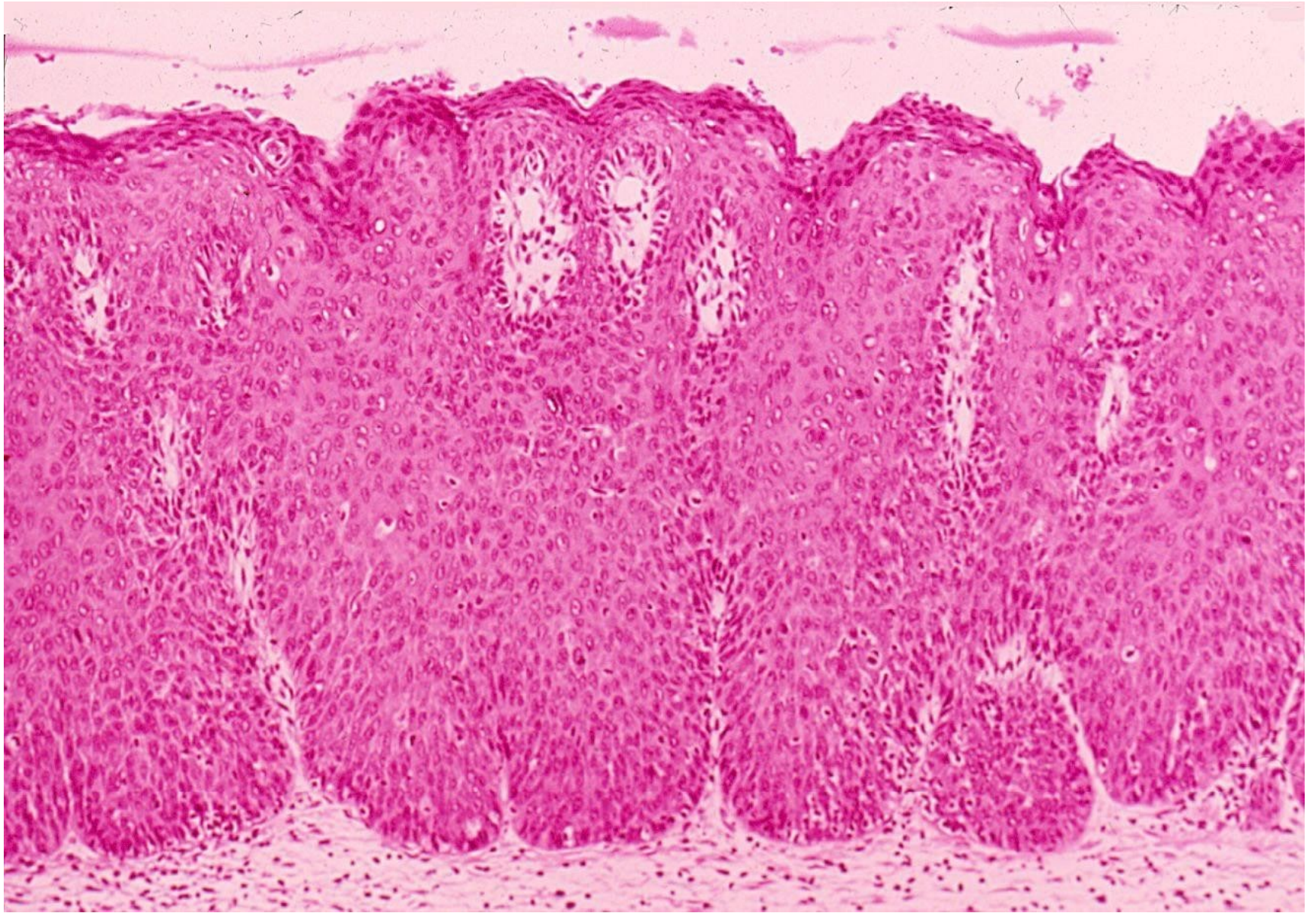
CIN III – atypias, mitoses





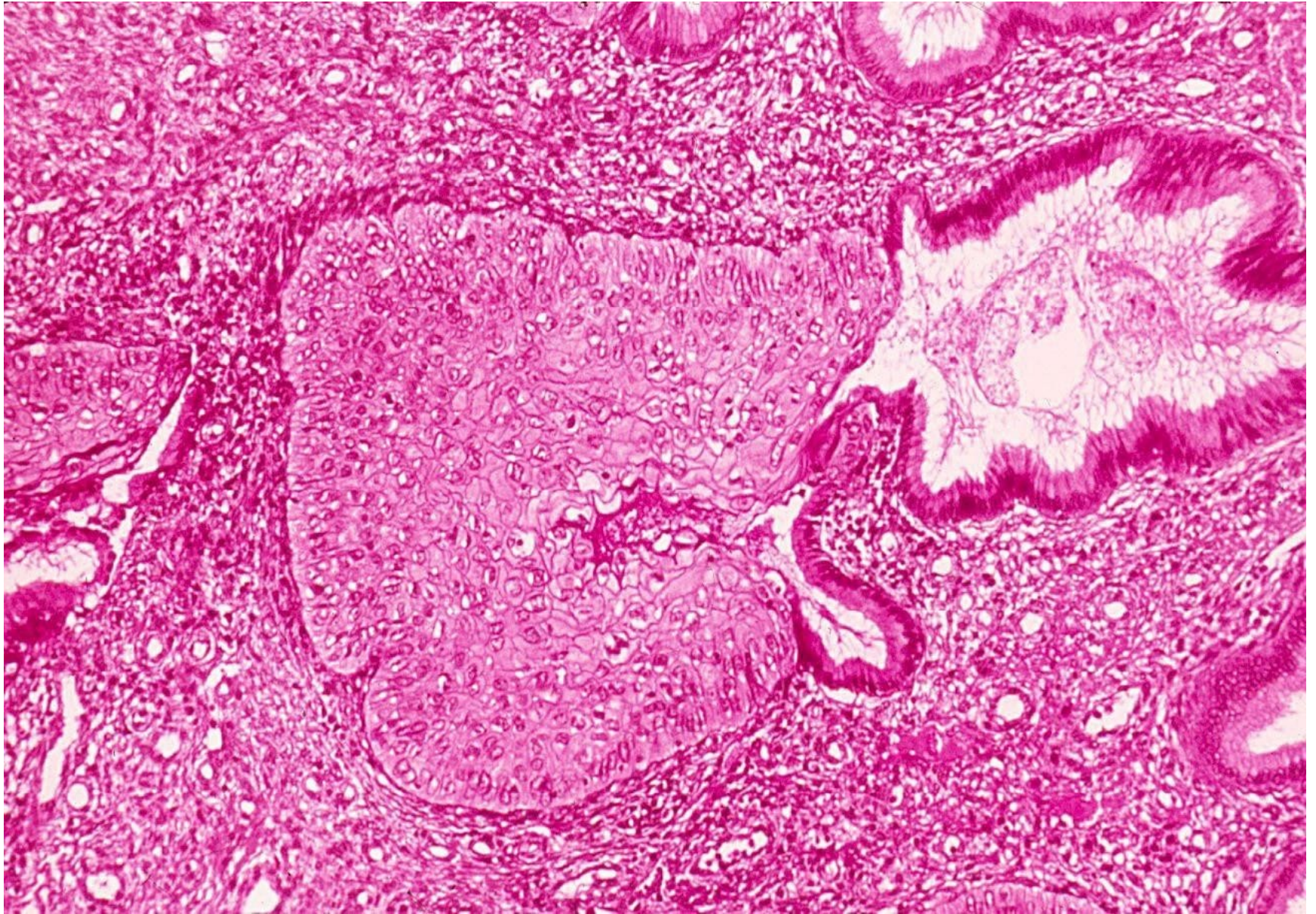
CIN III





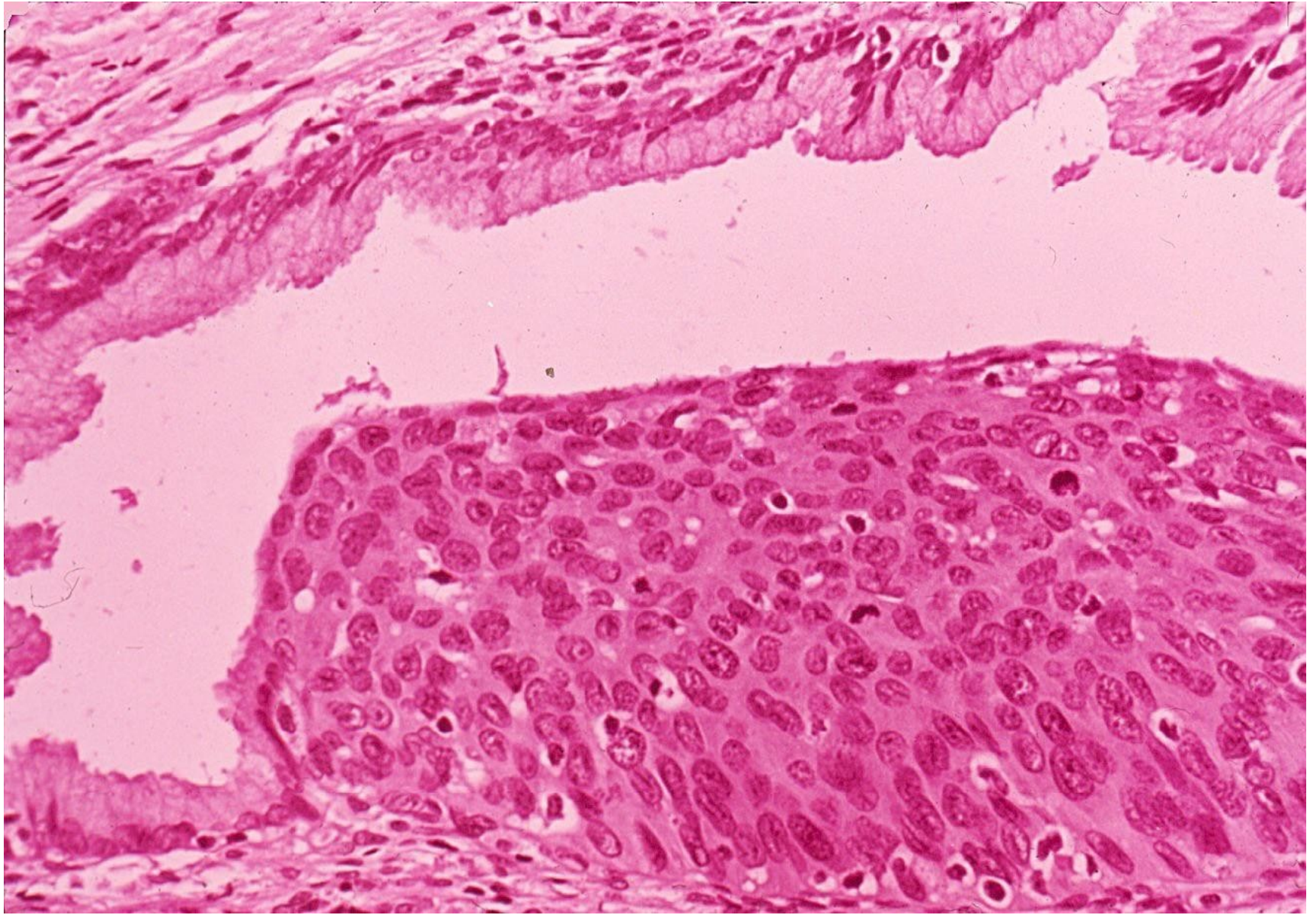
carcinoma in situ





endocervical gland with metaplasia and dysplastic changes

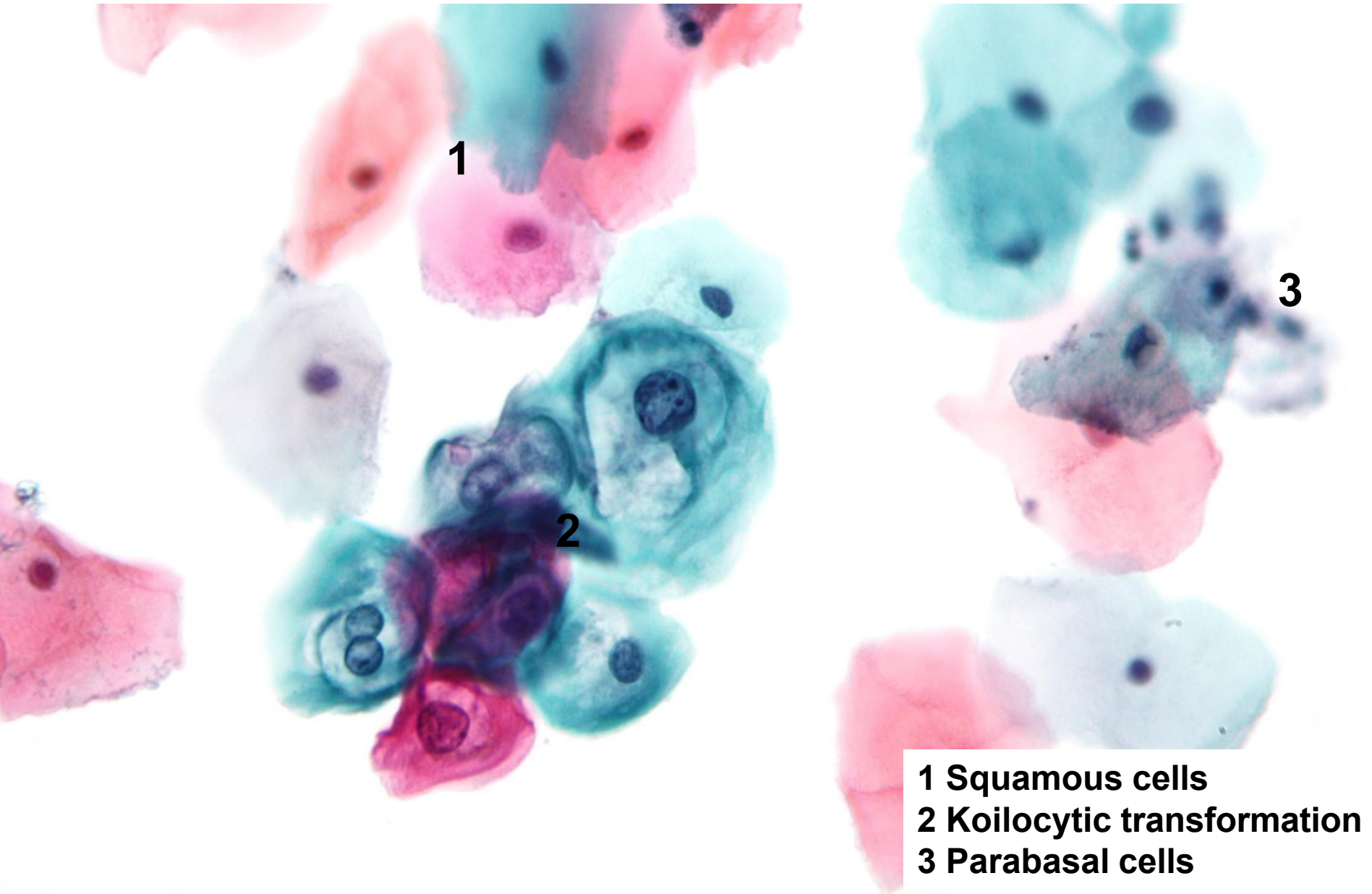




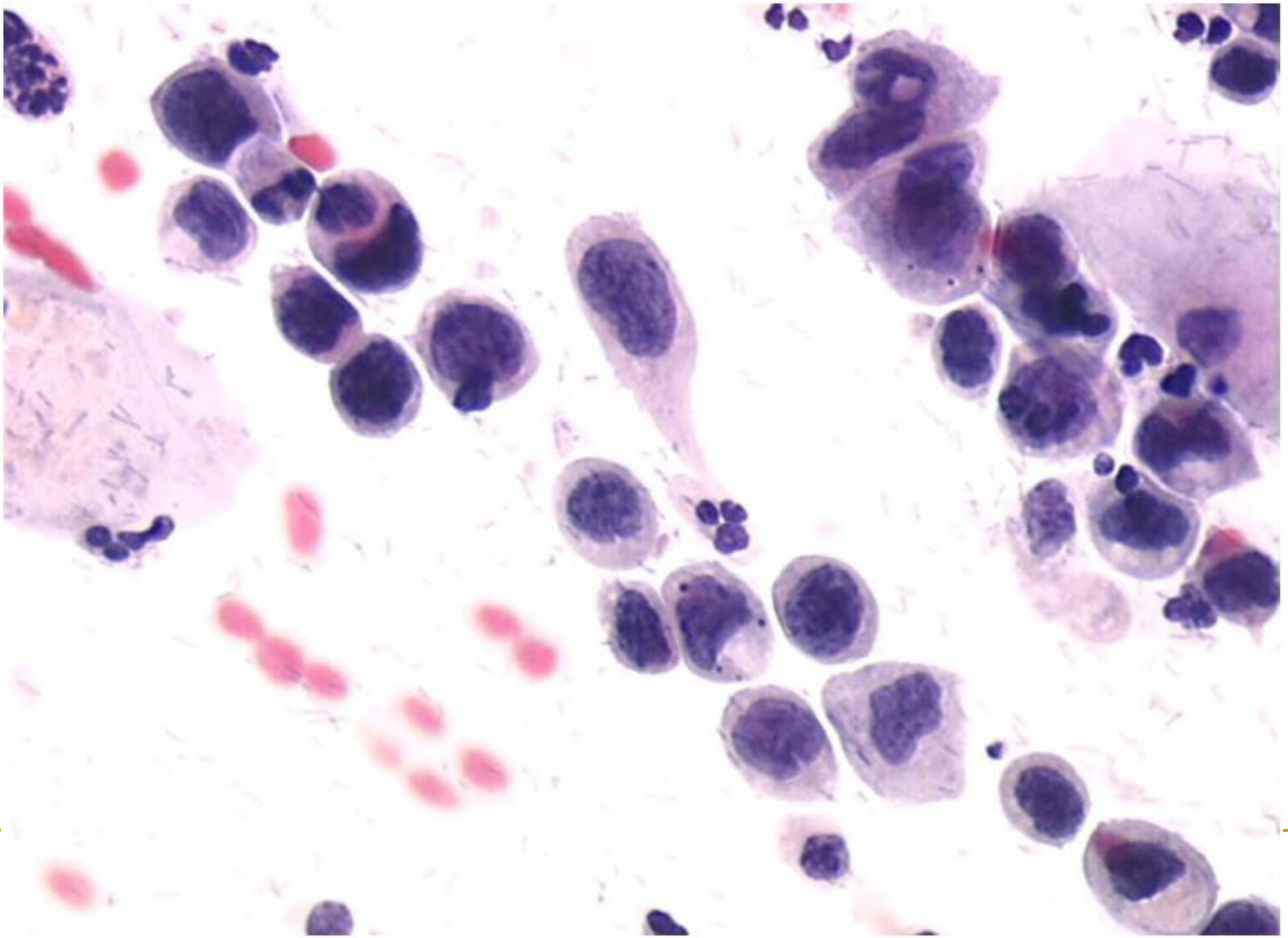
endocervical gland with high grade dysplasia



# Pap smear - LSIL

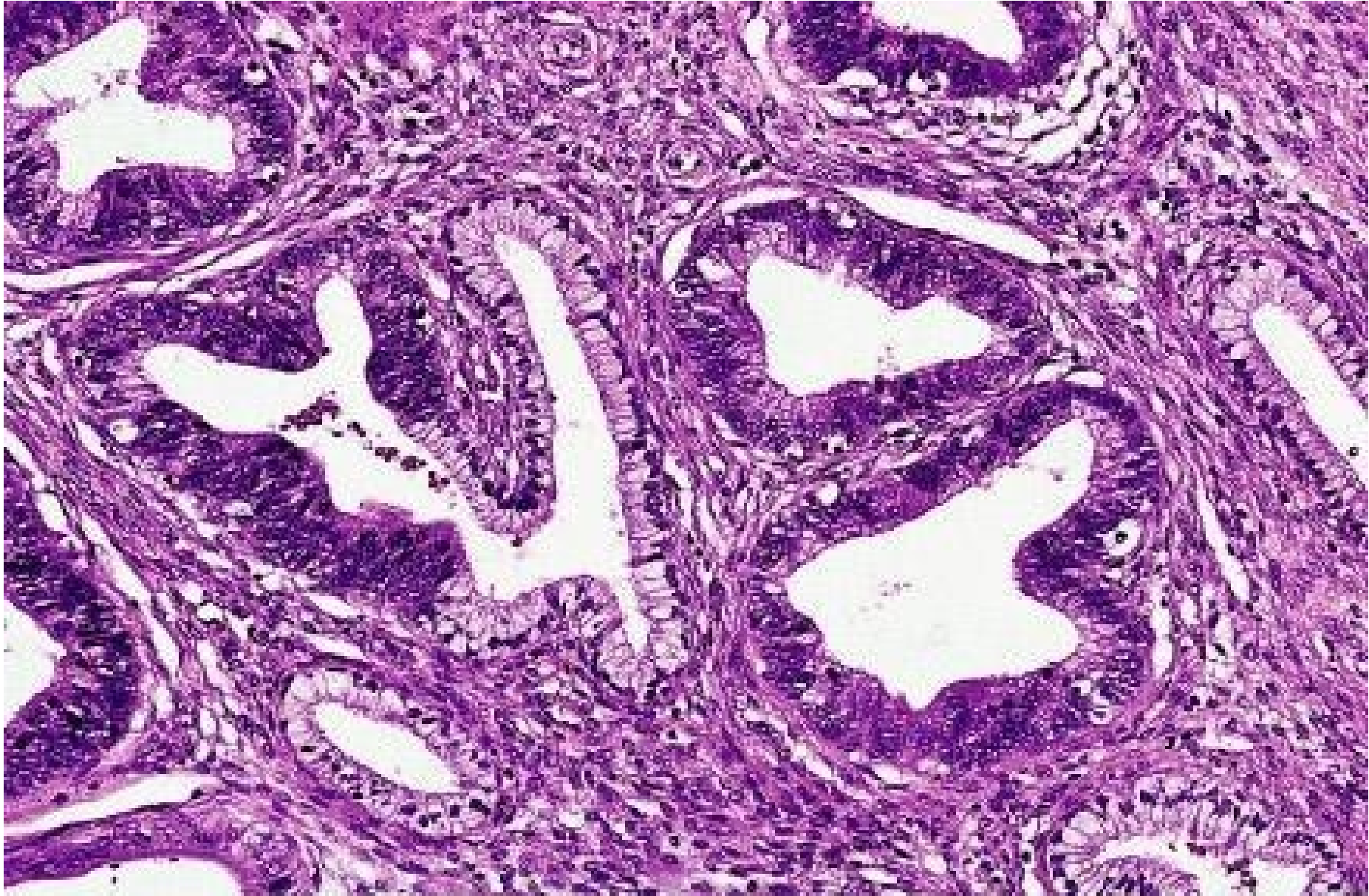


## Pap smear- HSIL

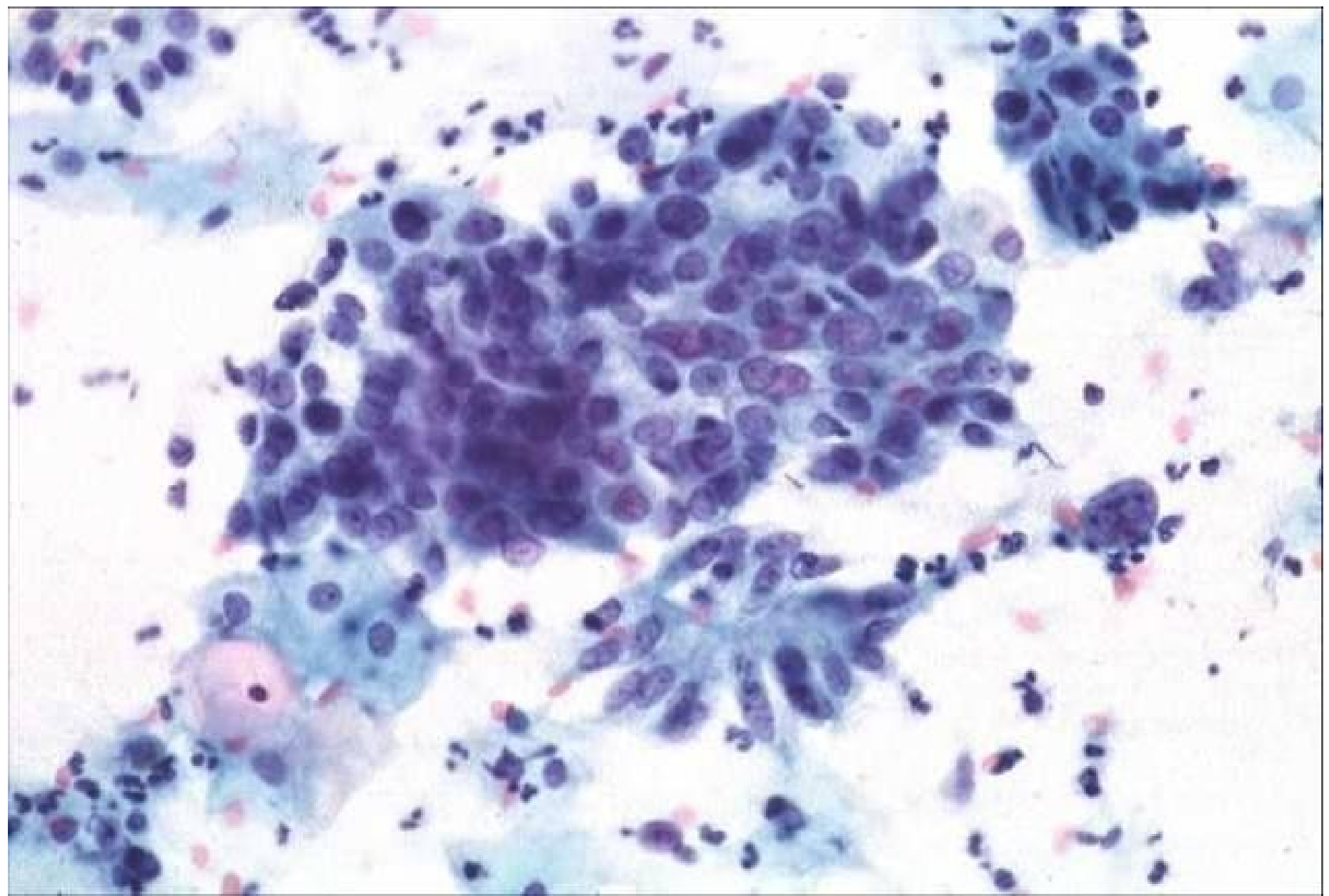




# Adenocarcinoma in situ – derived from glandular epithelium



## Pap smear – AIS





# Pathology of the uterine cervix

## dysplasias and malignancies of uterine cervix

- Squamous cell carcinoma is the most common histologic subtype of cervical cancer, 80% of cases. HSIL is an immediate precursor of cervical squamous cell carcinoma.
- The second most common tumor type is cervical adenocarcinoma, 15% of cervical cancer cases, develops from a precursor lesion called adenocarcinoma in situ.
- Adenosquamous and neuroendocrine carcinomas - remaining 5% of cases.
- All of the above tumor types are caused by high oncogenic risk HPVs.

# Pathology of the uterine cervix

dysplasias and malignancies of uterine cervix

- Invasive cervical carcinoma may manifest as either fungating (exophytic) or infiltrative cancers.
- On histologic examination, squamous cell carcinomas are composed of nests and tongues of malignant squamous epithelium, either keratinizing or nonkeratinizing, invading the underlying cervical stroma.

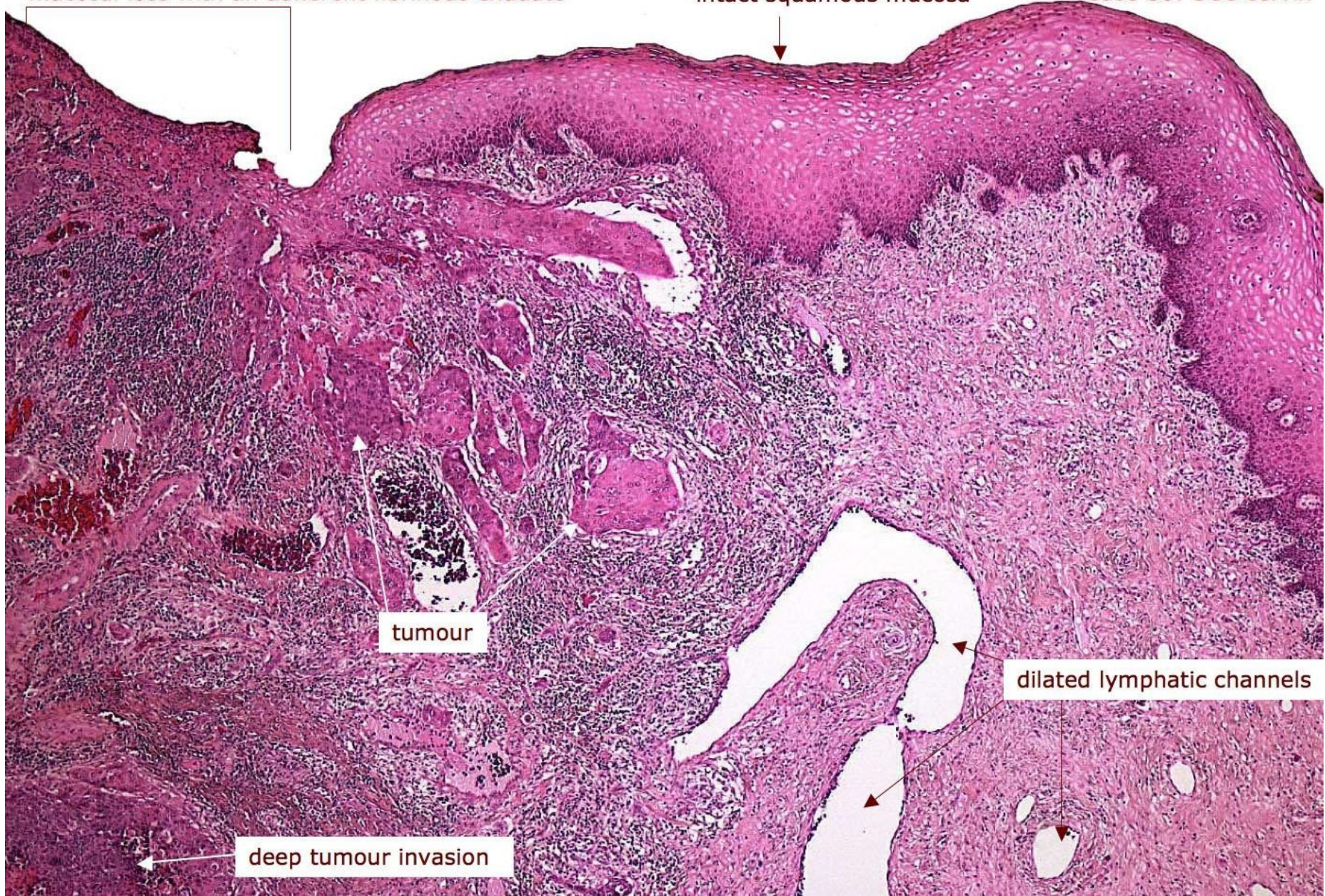


# Squamous cell carcinoma

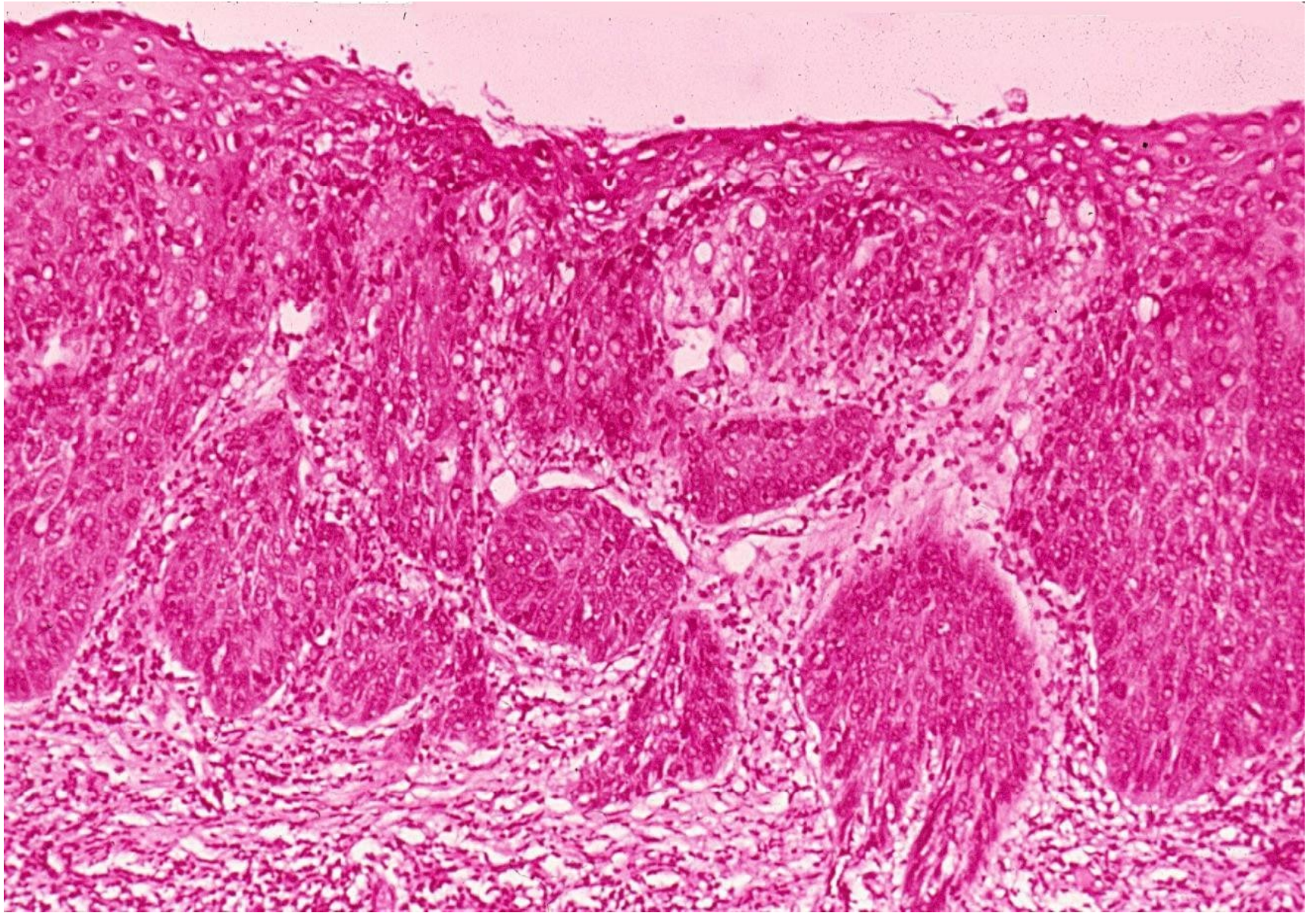
mucosal loss with an adherent fibrinous exudate

intact squamous mucosa

Case 56: SCC cervix

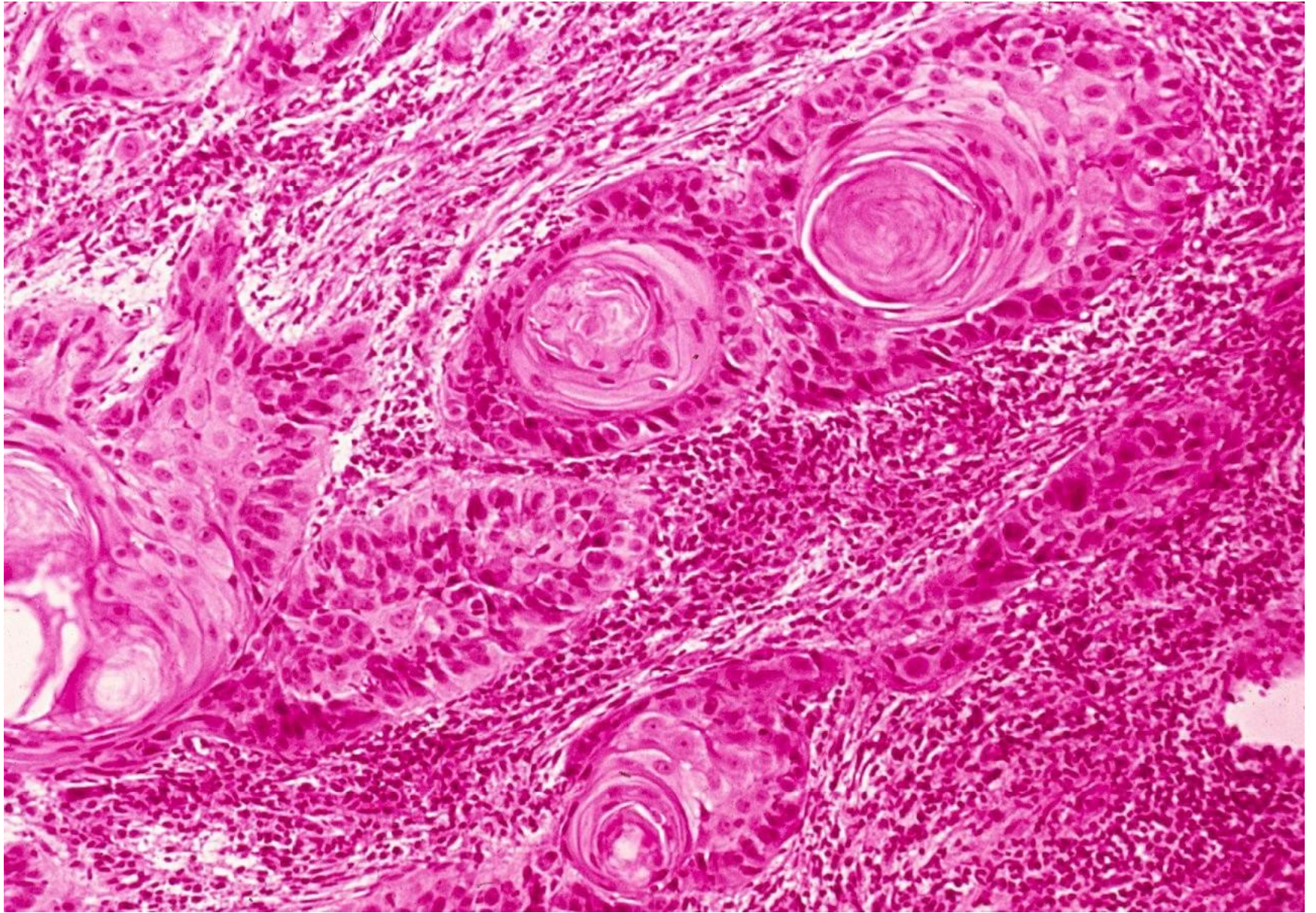






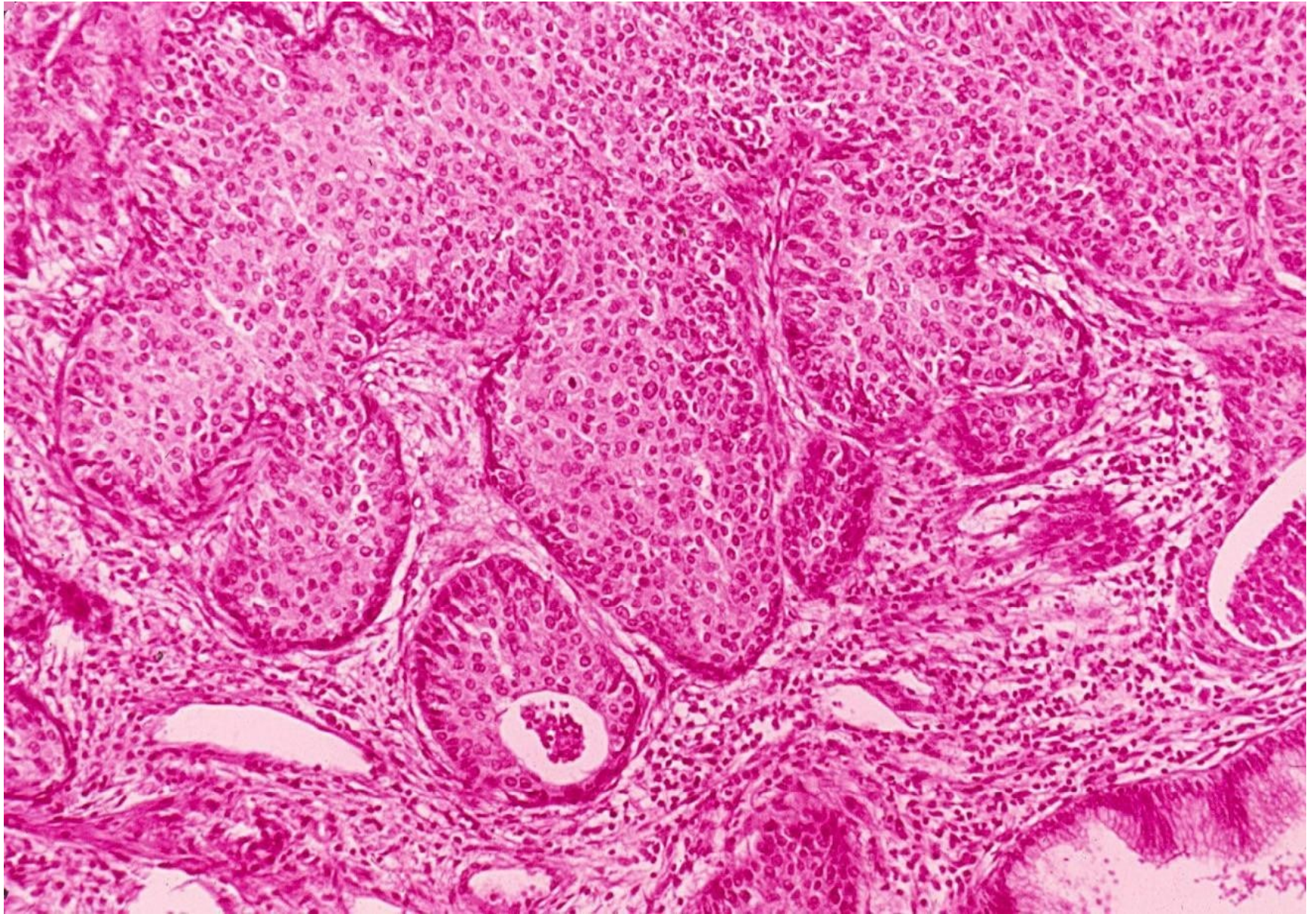
early invasive squamous cell carcinoma





Squamous cell carcinoma





nonkeratinizing squamous cell carcinoma

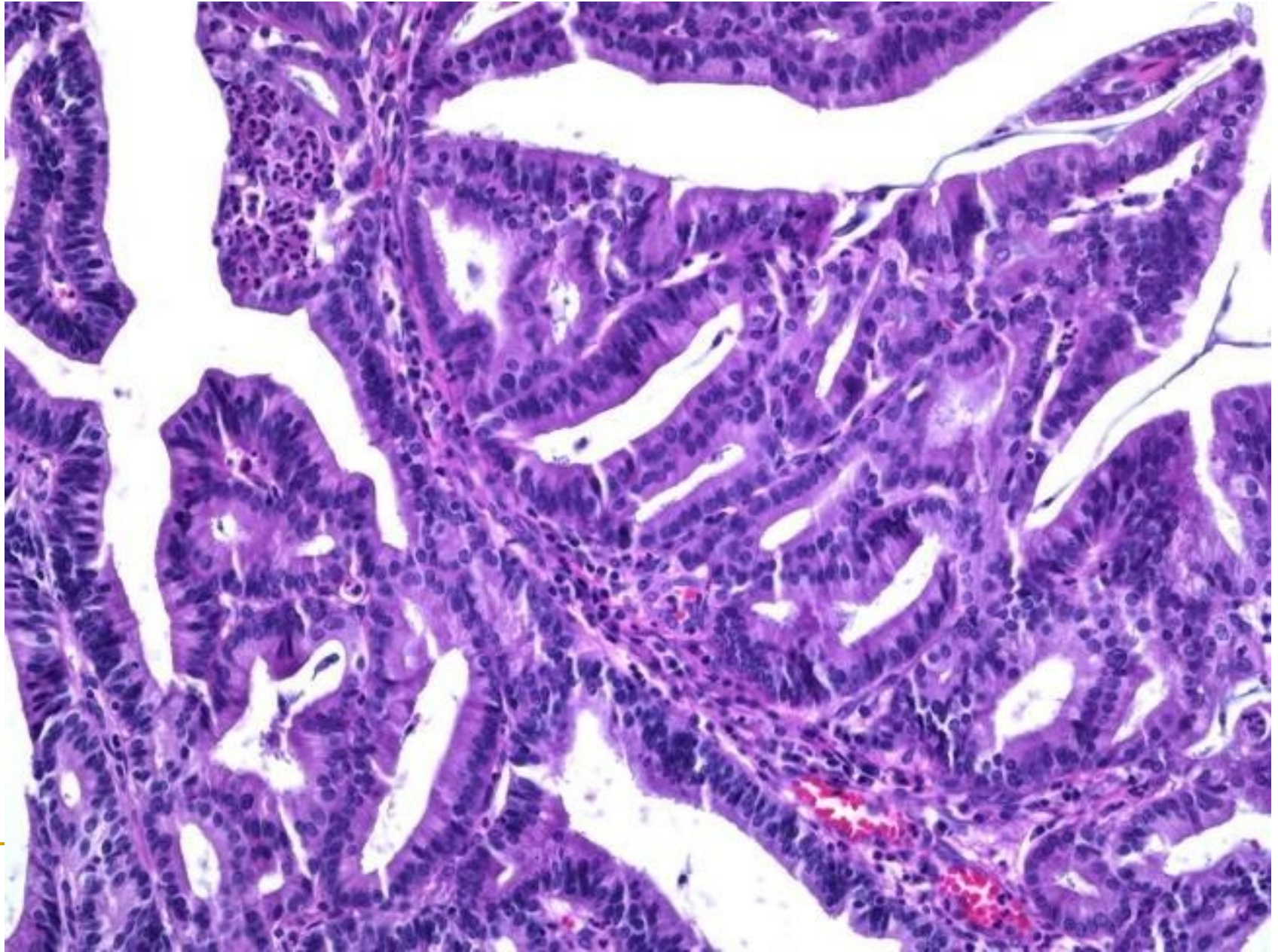


# Pathology of the uterine cervix

## dysplasias and malignancies of uterine cervix

- Adenocarcinomas are characterized by proliferation of glandular epithelium composed of malignant endocervical cells with large, hyperchromatic nuclei and relatively mucin-depleted cytoplasm, resulting in dark appearance of the glands, as compared with the normal endocervical epithelium
- HPV associated (85%), HPV independent

# Invasive adenocarcinoma







endometrial histology in the menstrual cycle

# Pathology of the Uterus

functional endometrial disorders (dysfunctional uterine bleeding)

- In most instances, dysfunctional bleeding is due to the occurrence of an **anovulatory cycle**. Anovulation results in excessive and prolonged estrogenic stimulation without the counteractive effect of the progestational phase that regularly follows ovulation.
- Failure of ovulation results in prolonged, excessive endometrial stimulation by estrogens. Under these circumstances the endometrial glands undergo mild architectural changes, cystic dilation etc, ... Unscheduled breakdown of the stroma may also occur (“**anovulatory menstruation**”), with no evidence of endometrial secretory activity



# Pathology of the Uterus

functional endometrial disorders (dysfunctional uterine bleeding)

- **Inadequate luteal phase**
- Inadequate corpus luteum function resulting in low progesterone output, with subsequent early menses.
- The condition often manifests clinically as infertility, with either increased bleeding or amenorrhea. Endometrial biopsy shows secretory endometrium, which, however, lags in its secretory characteristics expected at that date.

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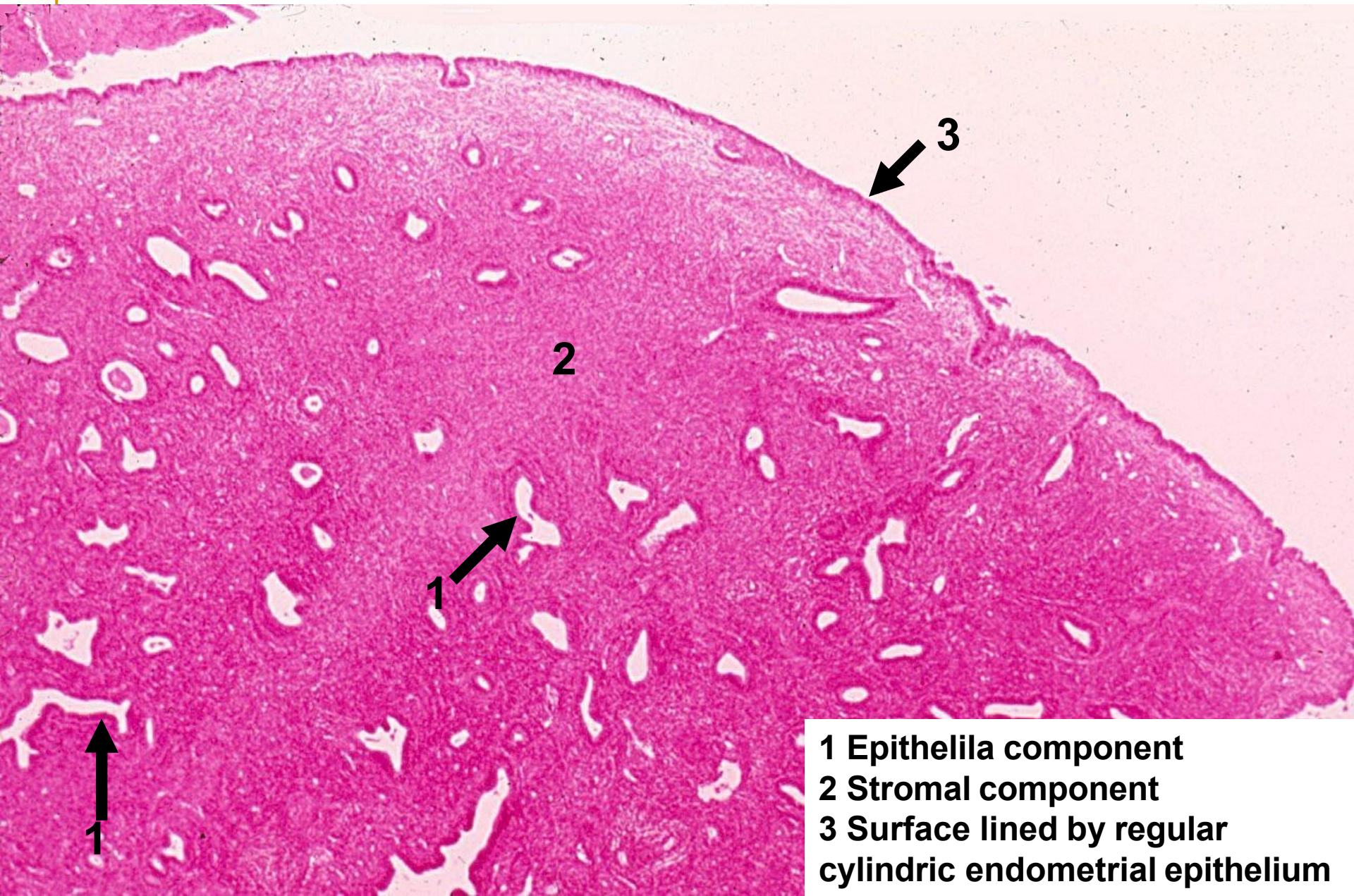
# Pathology of the Uterus

## endometrial polyp

- Hyperplastic protrusion of endometrium
  - Present as abnormal uterine bleeding
  - Benign condition
  - Microscopically: cystically dilated glands, stromal fibrosis, thick walled blood vessels
-



# Endometrial polyp



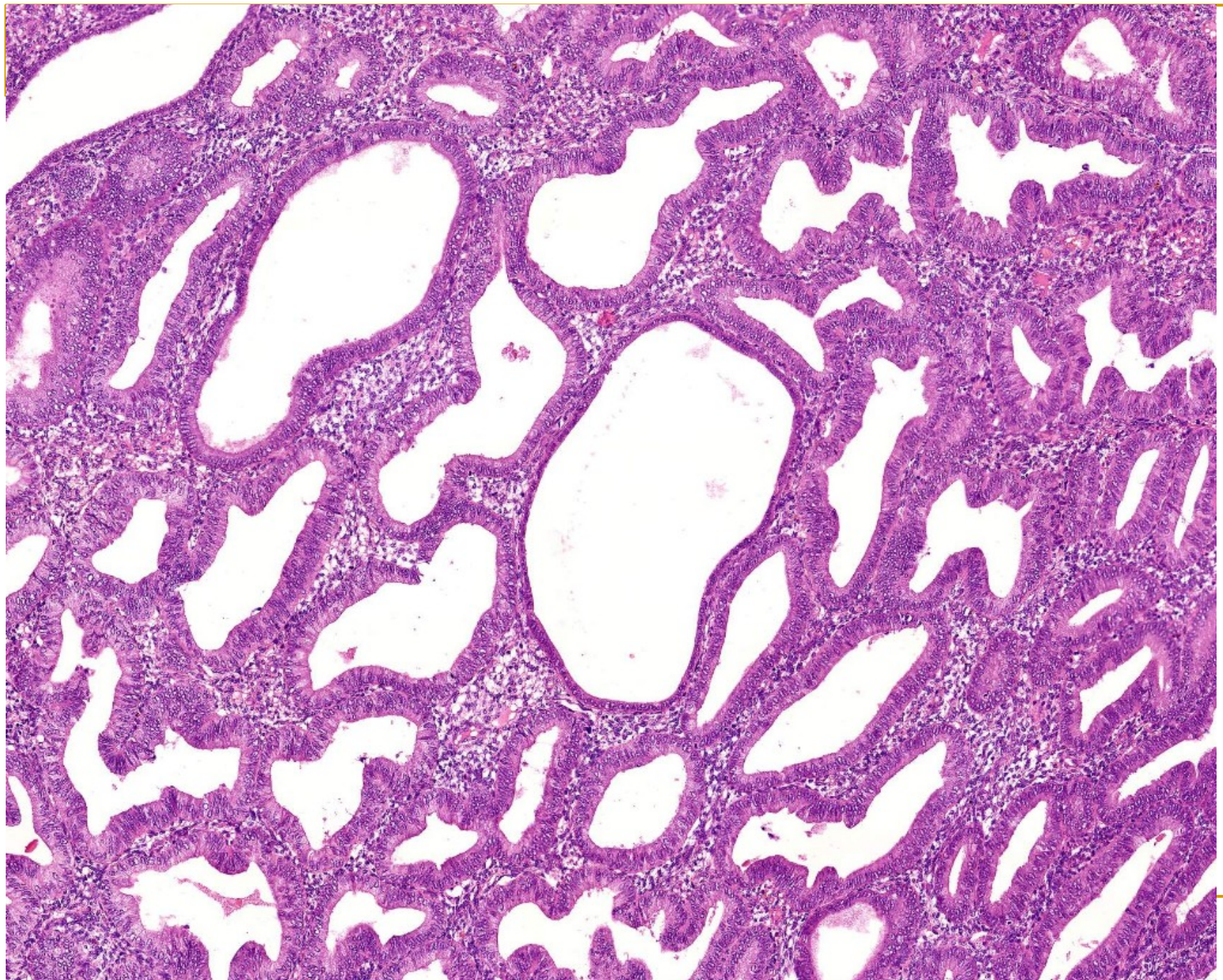
- 1 Epithelial component
- 2 Stromal component
- 3 Surface lined by regular cylindric endometrial epithelium

# Pathology of the Uterus

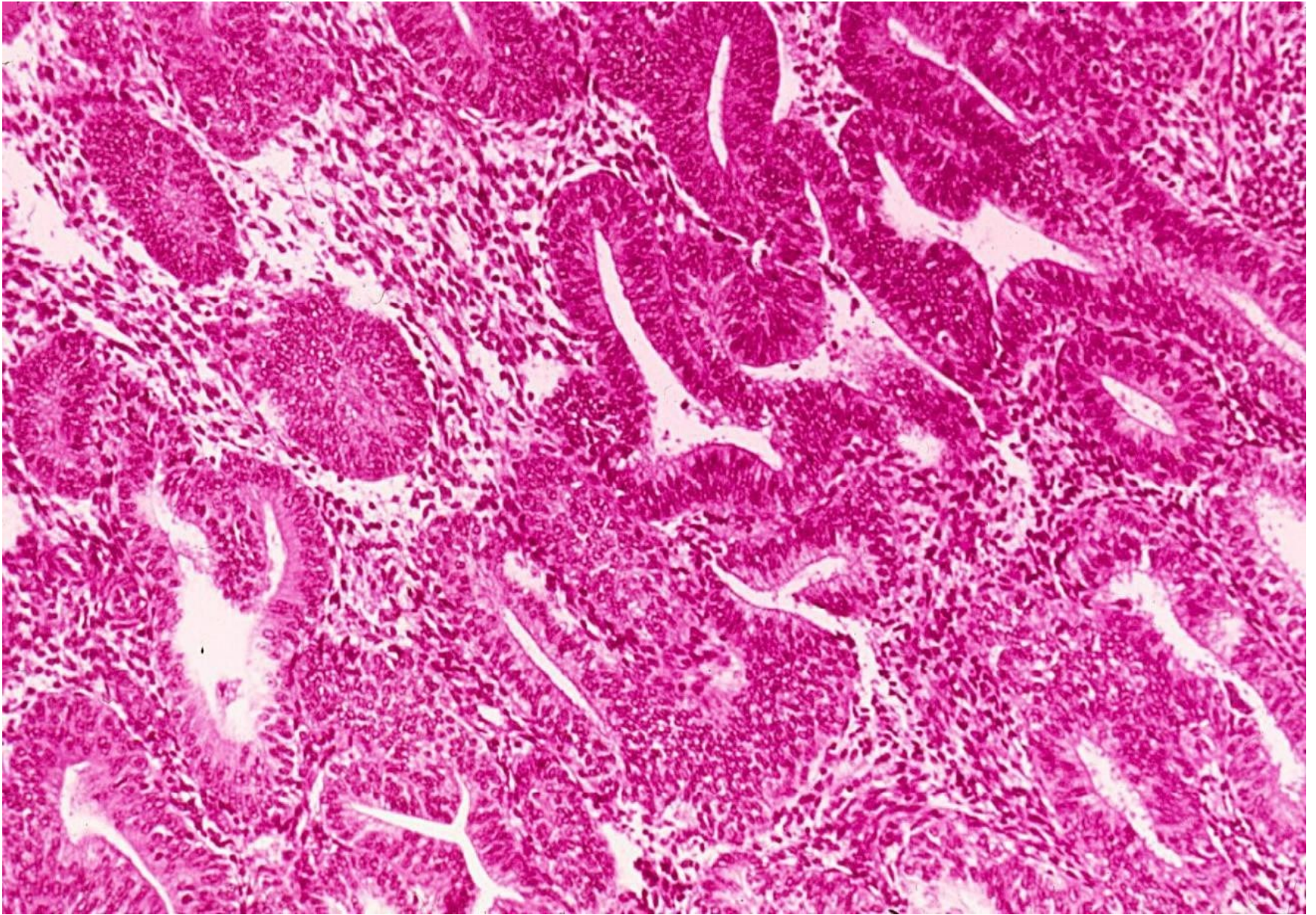
## endometrial hyperplasia

- Endometrial hyperplasia (an important cause of abnormal bleeding) - increased proliferation of the endometrial glands relative to the stroma, resulting in an increased gland-to-stroma ratio when compared with normal proliferative endometrium.
- Endometrial hyperplasia deserves special attention because of its *relationship with endometrial carcinoma*. Endometrial hyperplasia is associated with *prolonged estrogen stimulation of the endometrium*, which can be due to anovulation, increased estrogen production from endogenous sources, or exogenous estrogen.









endometrium - complex hyperplasia with atypia



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# Pathology of the Uterus

malignant tumors of the endometrium

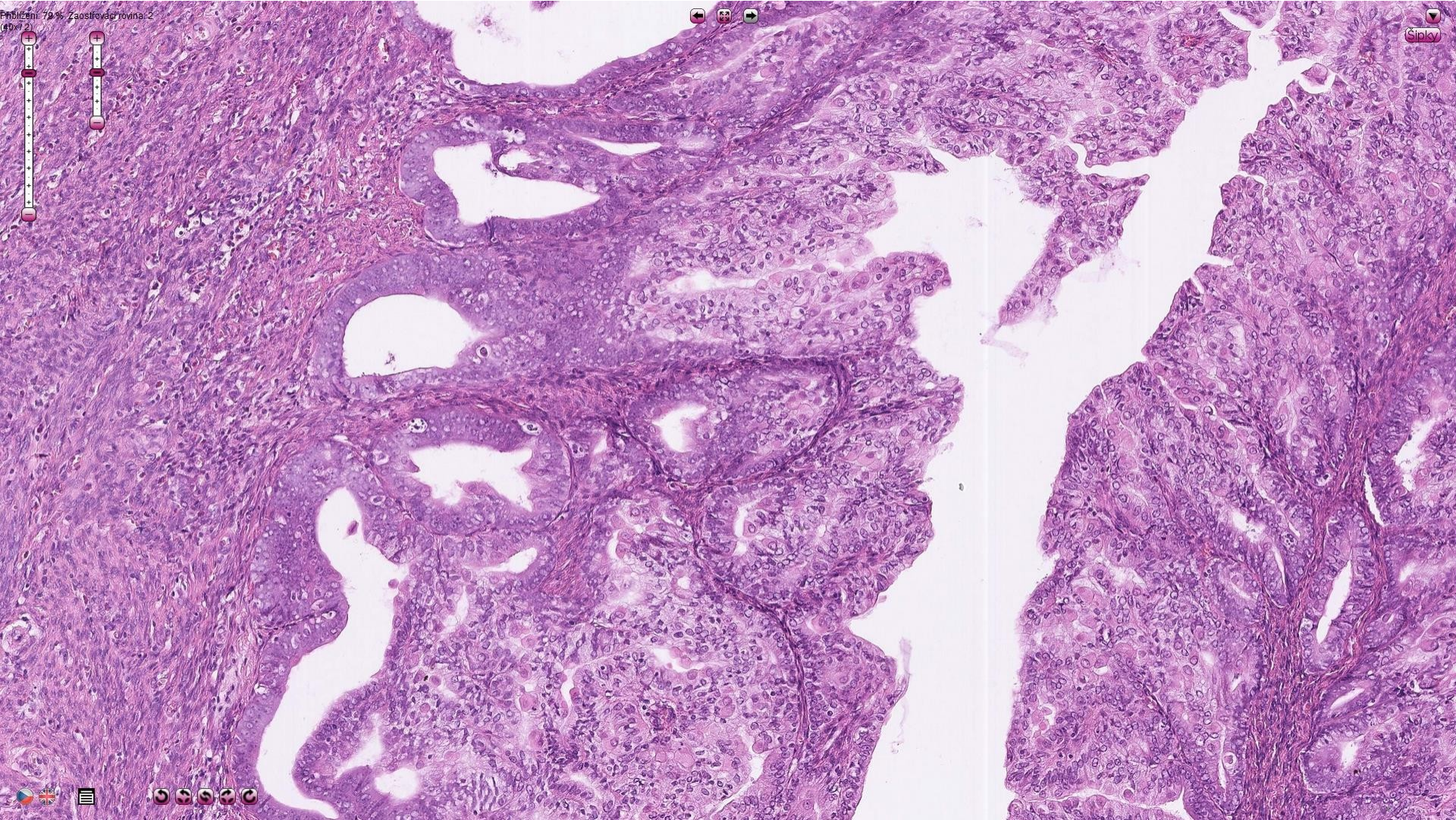
- *Endometrial carcinoma is the most common invasive cancer of the female genital tract and accounts for 7% of all invasive cancer in women, excluding skin cancer.*
  - Carcinoma of the endometrium is uncommon in women younger than 40 years of age. The peak incidence is in 55- to 65-year-old women.
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# Pathology of the Uterus

## malignant tumors of the endometrium

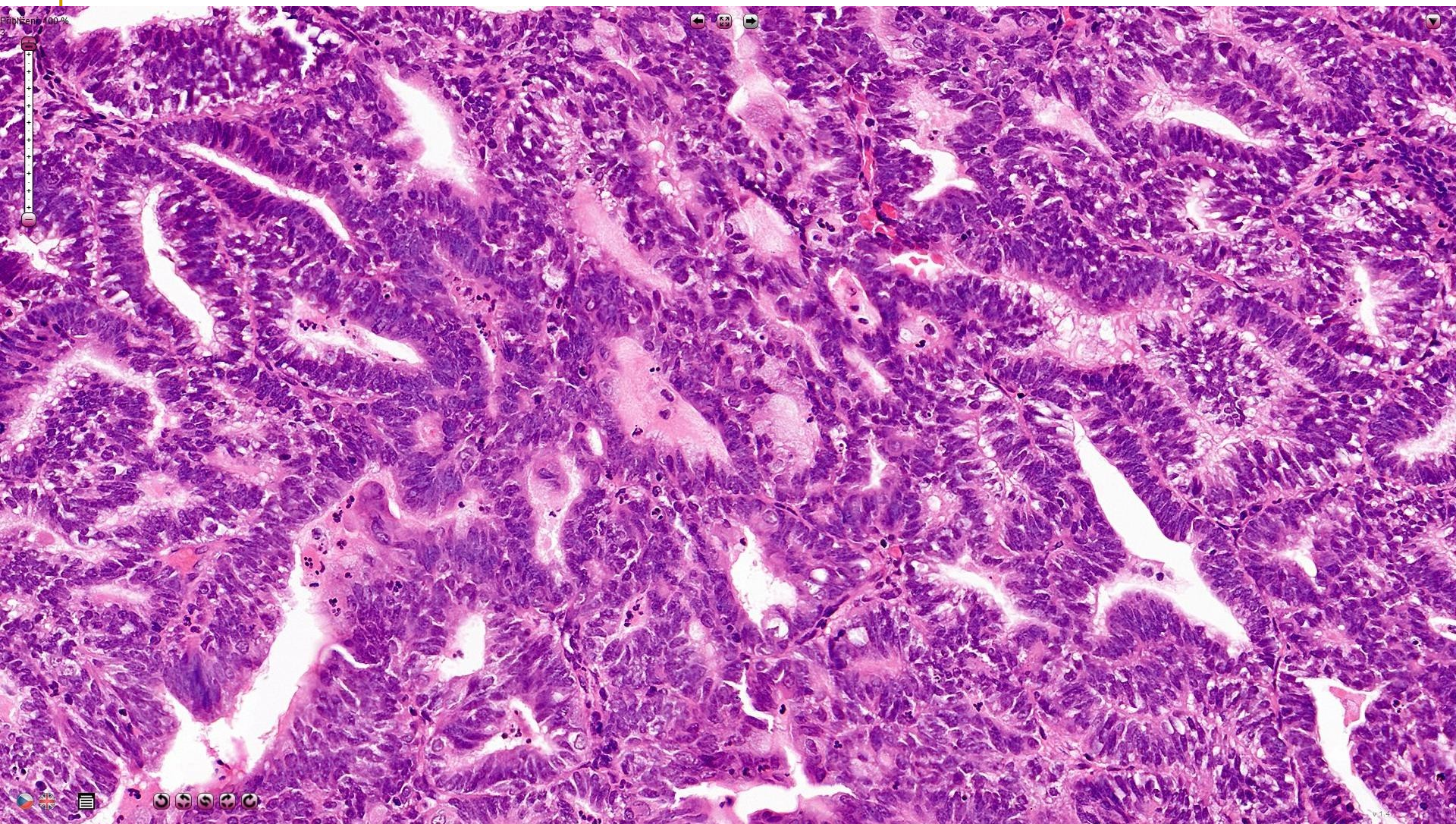
- **Type I carcinomas.**
- The most common type, accounting for greater than 80% of all cases. The majority are well differentiated and mimic proliferative endometrial glands and, as such, are referred to as *endometrioid carcinoma*.
- They typically arise in the setting of endometrial hyperplasia and are associated with:
  - ❑ obesity
  - ❑ diabetes (abnormal glucose tolerance is found in more than 60%)
  - ❑ hypertension
  - ❑ infertility
  - ❑ and unopposed estrogen stimulation.





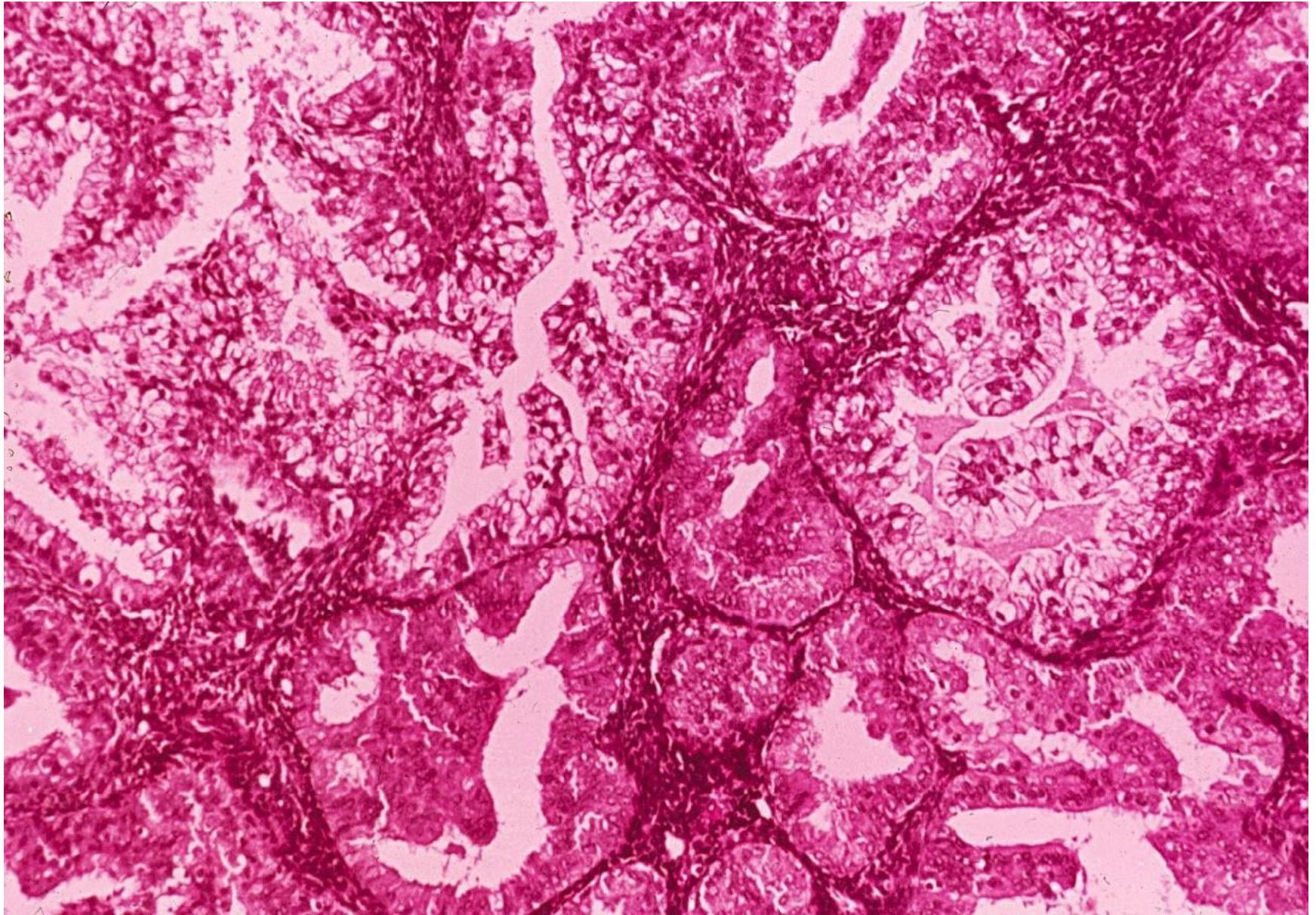
endometrium – endometrioid adenocarcinoma





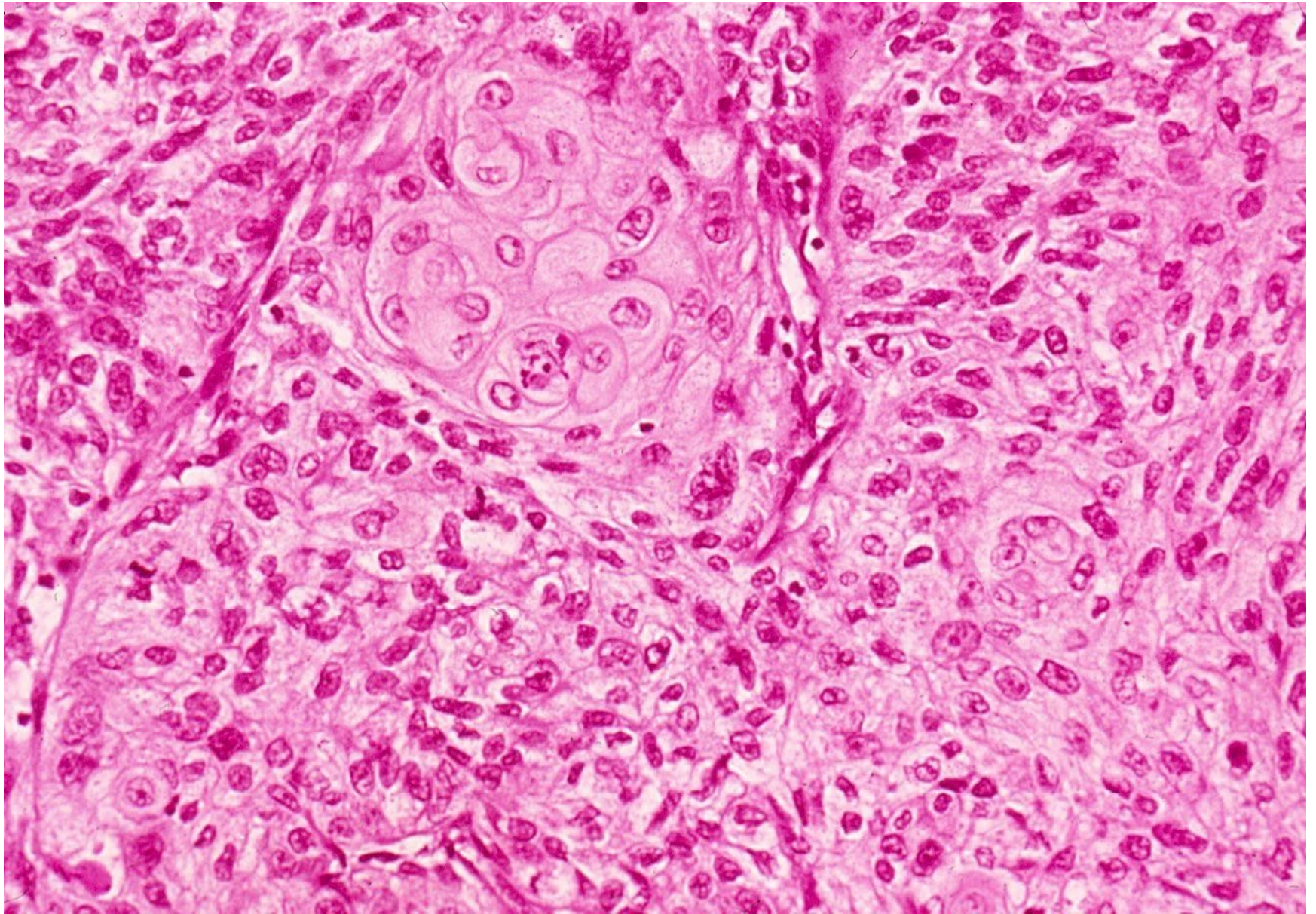
endometrium - endometrioid adenocarcinoma - detail





endometrium - endometrioid adenocarcinoma with  
mucinus component





up to 20% of endometrioid carcinomas contain foci of squamous differentiation



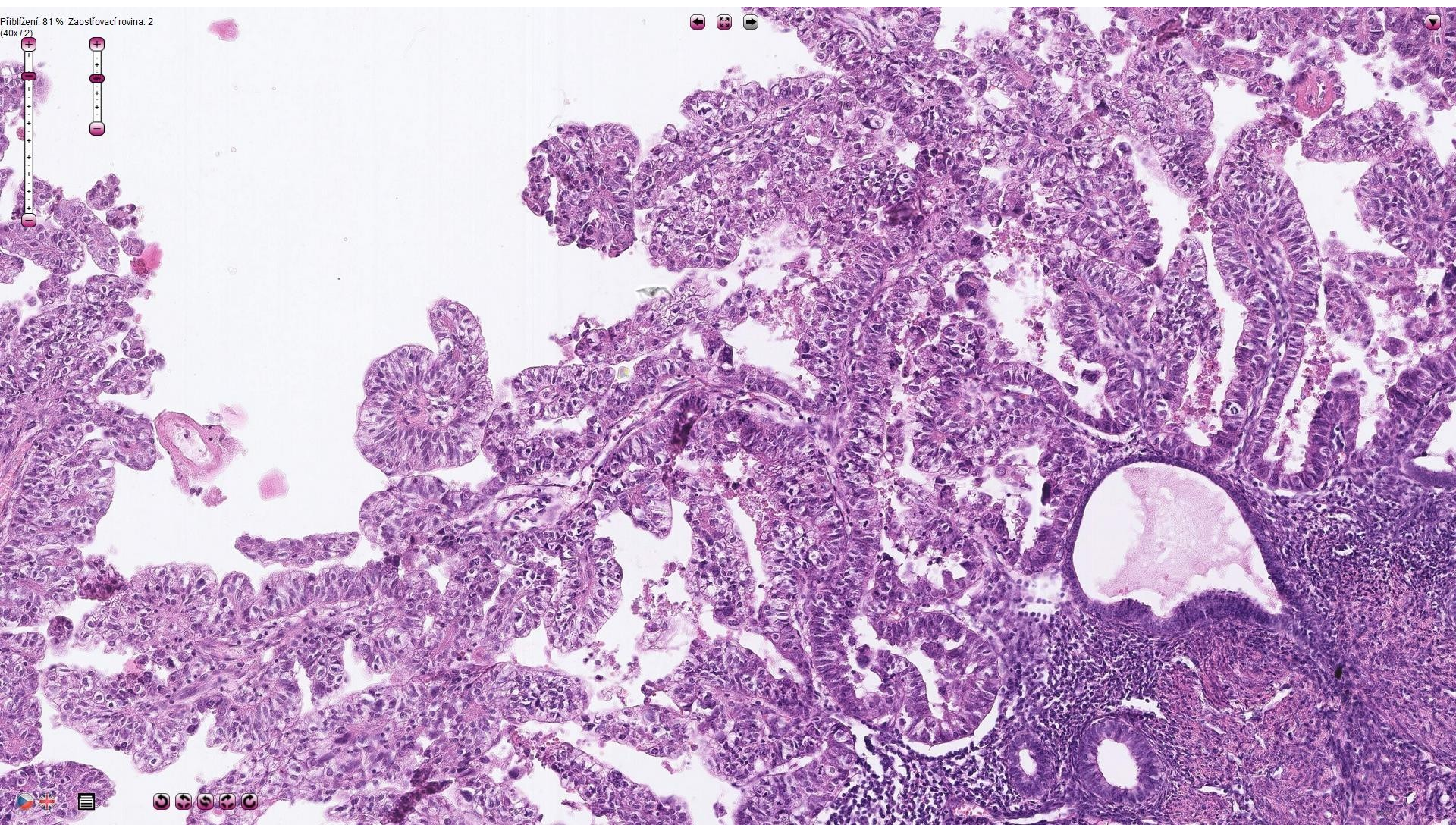
# Pathology of the Uterus

## malignant tumors of the endometrium

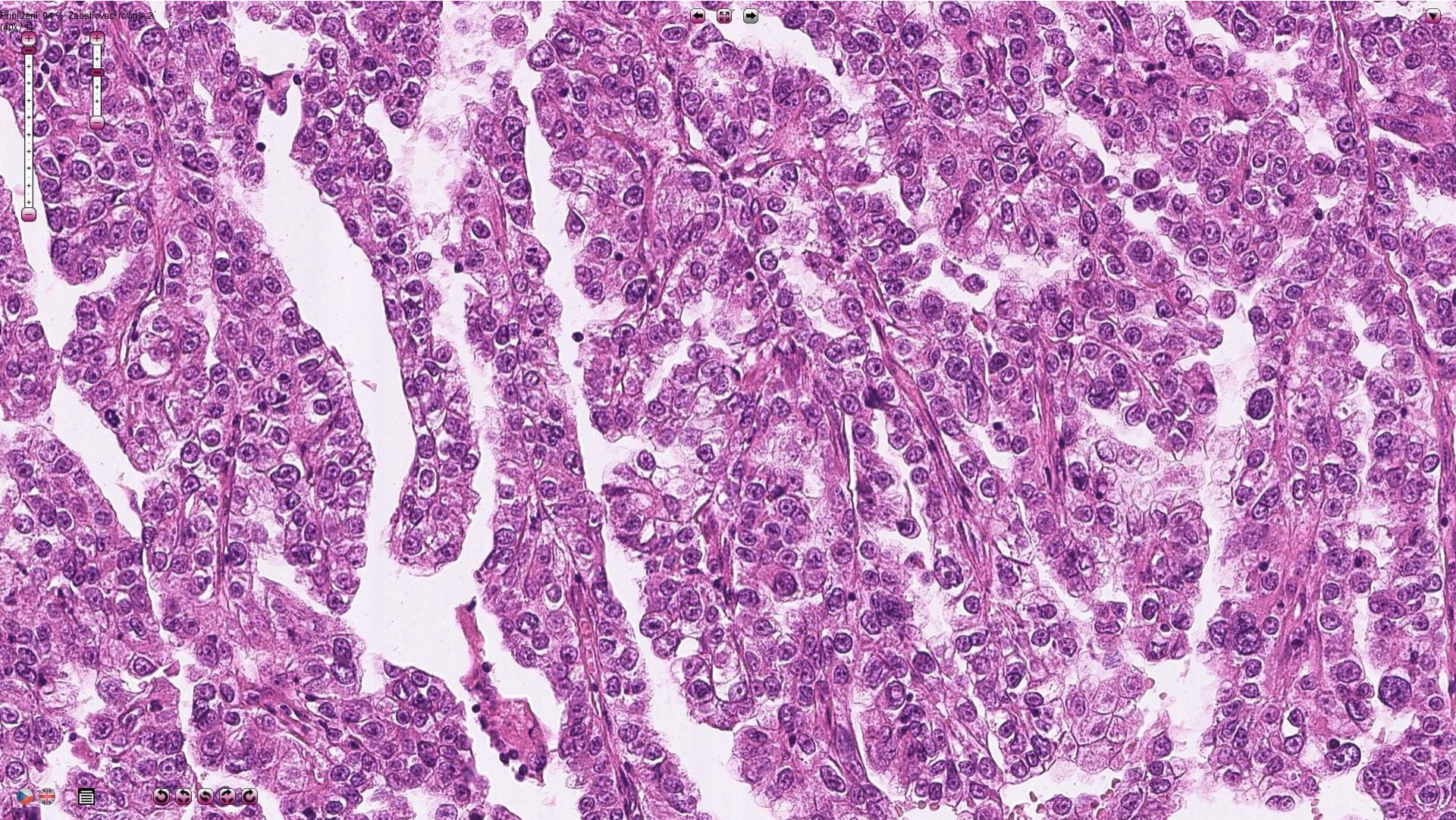
- **Type II carcinomas.**
- These generally occur in women a decade later than type I carcinoma, and in contrast to type I carcinoma they *usually arise in the setting of endometrial atrophy*
- Type II tumors are by definition *poorly differentiated (grade 3)* tumors and account for approximately 15% of cases of endometrial carcinoma.
- The most common subtype is *serous carcinoma*, referred to as such because of morphologic and biologic overlap with ovarian serous carcinoma.
- Less common histologic subtypes :clear cell carcinoma and malignant mixed müllerian tumor



# Serous adenocarcinoma







endometrium – clear cell carcinoma



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# Pathology of the Uterus

tumors of the endometrium molecular classification

- **POLE mutated – good prognosis**
  - **MMR deficient – may be associated with Lynch sy.**
  - **P53 mutated - aggressive**
  - **Non specific molecular profile**
-



# Pathology of the Uterus

tumors of the endometrium with stromal differentiation

- **Adenosarcomas**

- Adenosarcomas present most commonly as large broad-based endometrial polypoid growths that may prolapse through the cervical os. The diagnosis is based on malignant-appearing stroma, which coexists with benign but abnormally shaped endometrial glands.

- **Stromal Tumors**

- The endometrial stroma occasionally gives rise to neoplasms that may resemble normal stromal cells. Similar to most neoplasms, they may be well or poorly differentiated. Stromal neoplasms are divided into two categories: (1) benign stromal nodules and (2) endometrial stromal sarcomas.



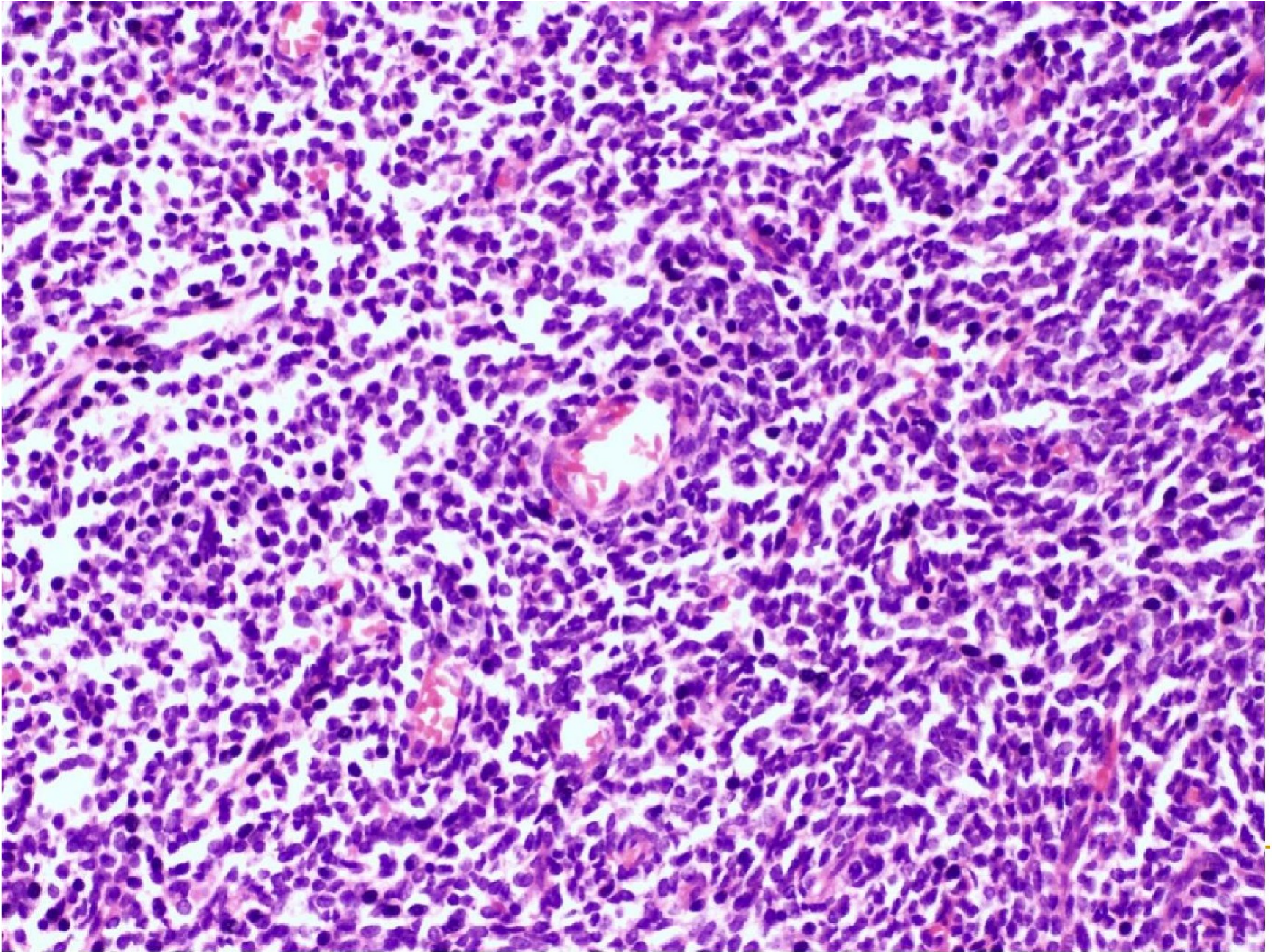
# Pathology of the Uterus

tumors of the endometrium with stromal differentiation

- **Stromal nodule** is a well-circumscribed aggregate of endometrial stromal cells in the endometrium that does not penetrate the myometrium and is of little consequence.
- **Stromal sarcoma** consists of neoplastic endometrial stroma lying between muscle bundles of the myometrium and is distinguished from stromal nodules by either diffuse infiltration of myometrial tissue or the invasion of lymphatic channels (previously termed **endolymphatic stromal myosis**).



## endometrium – low grade stromal sarcoma



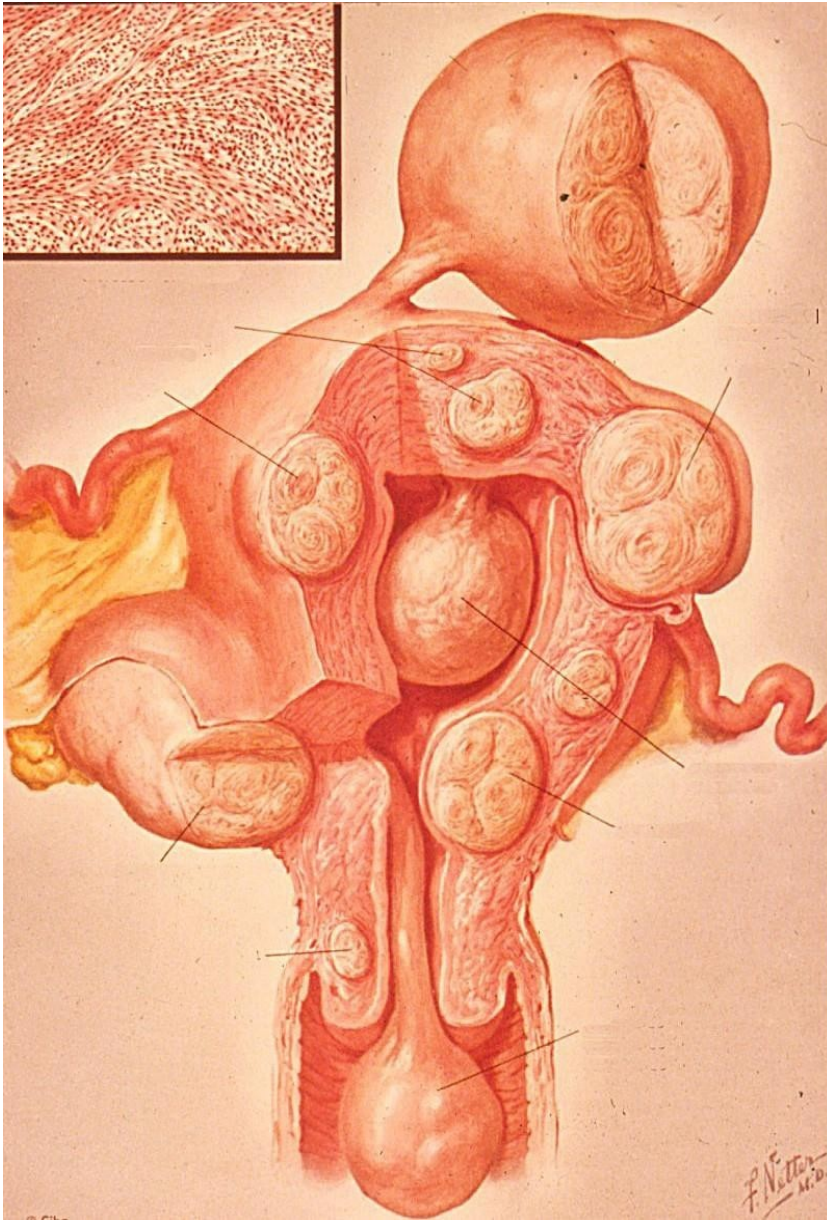


# Pathology of the Uterus

## tumors of the myometrium

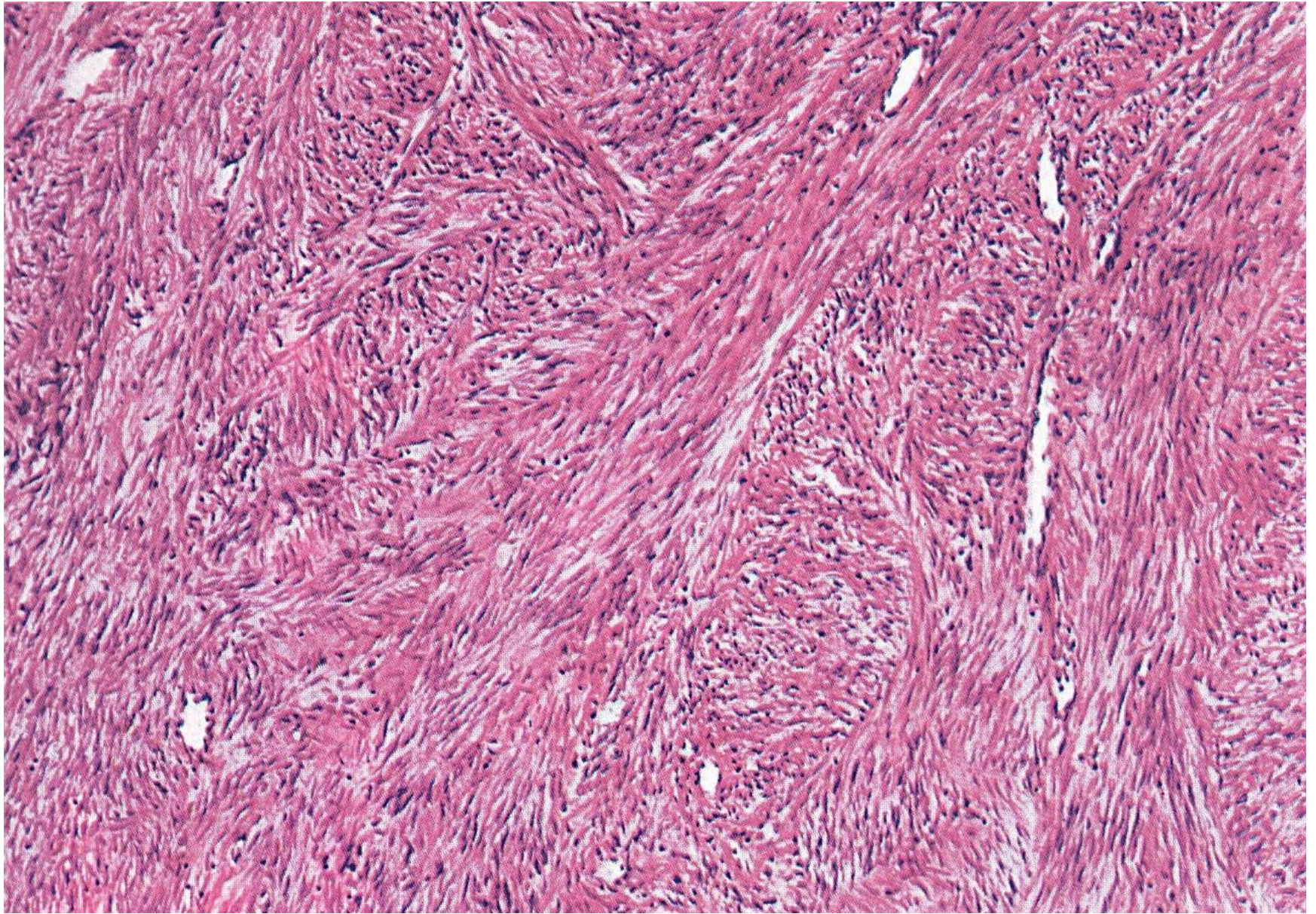
- Uterine leiomyomas are perhaps the most common tumor in women. They are benign smooth muscle neoplasms that may occur singly, but most often are multiple.
- Micro: the leiomyoma is composed of whorled bundles of smooth muscle cells that resemble the uninvolved myometrium. Benign variants of leiomyoma :
  - ❑ atypical or bizarre (symplastic) tumors with nuclear atypia and giant cells
  - ❑ cellular leiomyomas.





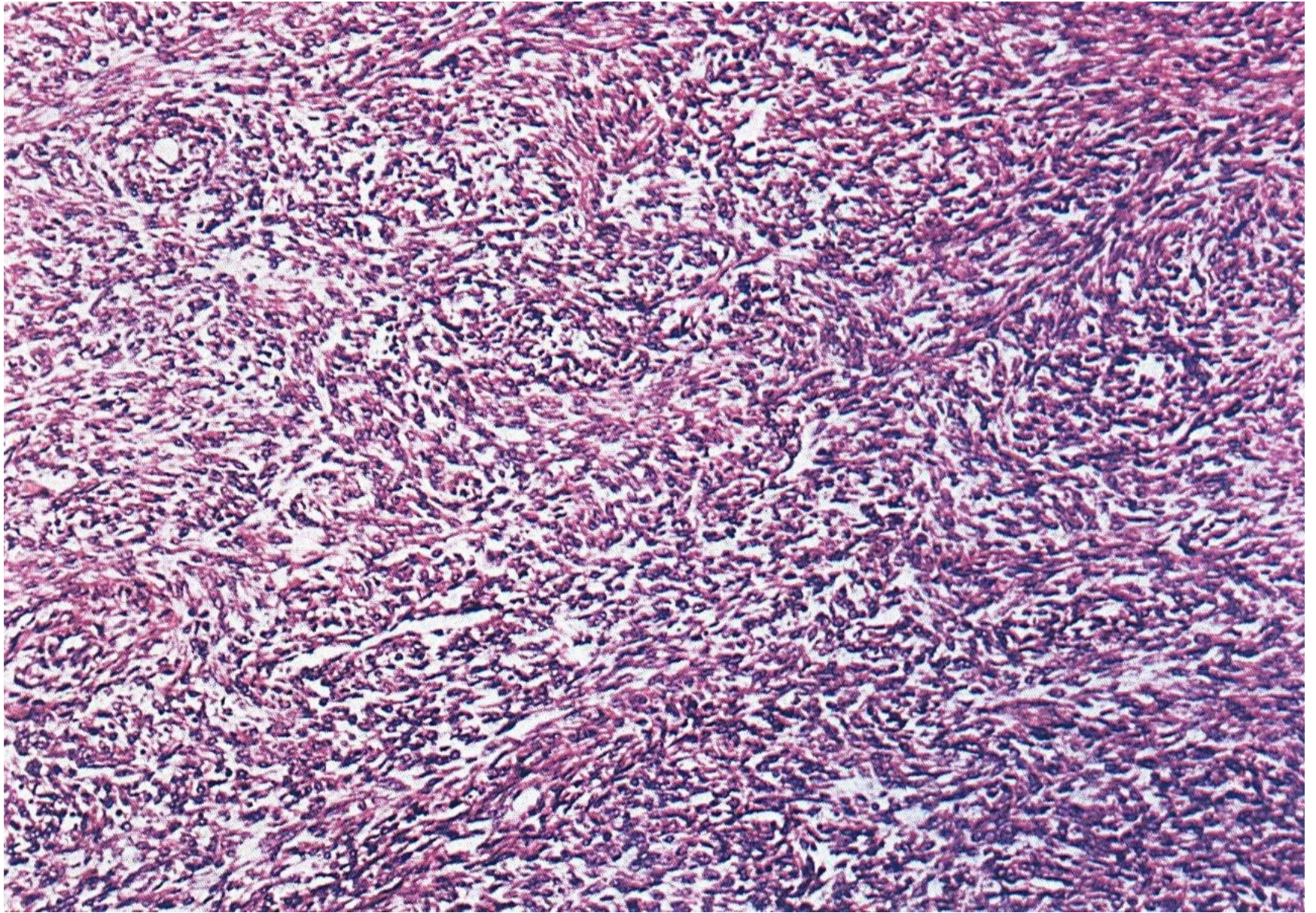
- Leiomyomas are sharply circumscribed, discrete, round, firm, gray-white tumors varying in size from small, barely visible nodules to massive tumors that fill the pelvis.
- They can occur within the myometrium (intramural), just beneath the endometrium (submucosal) , or beneath the serosa (subserosal).





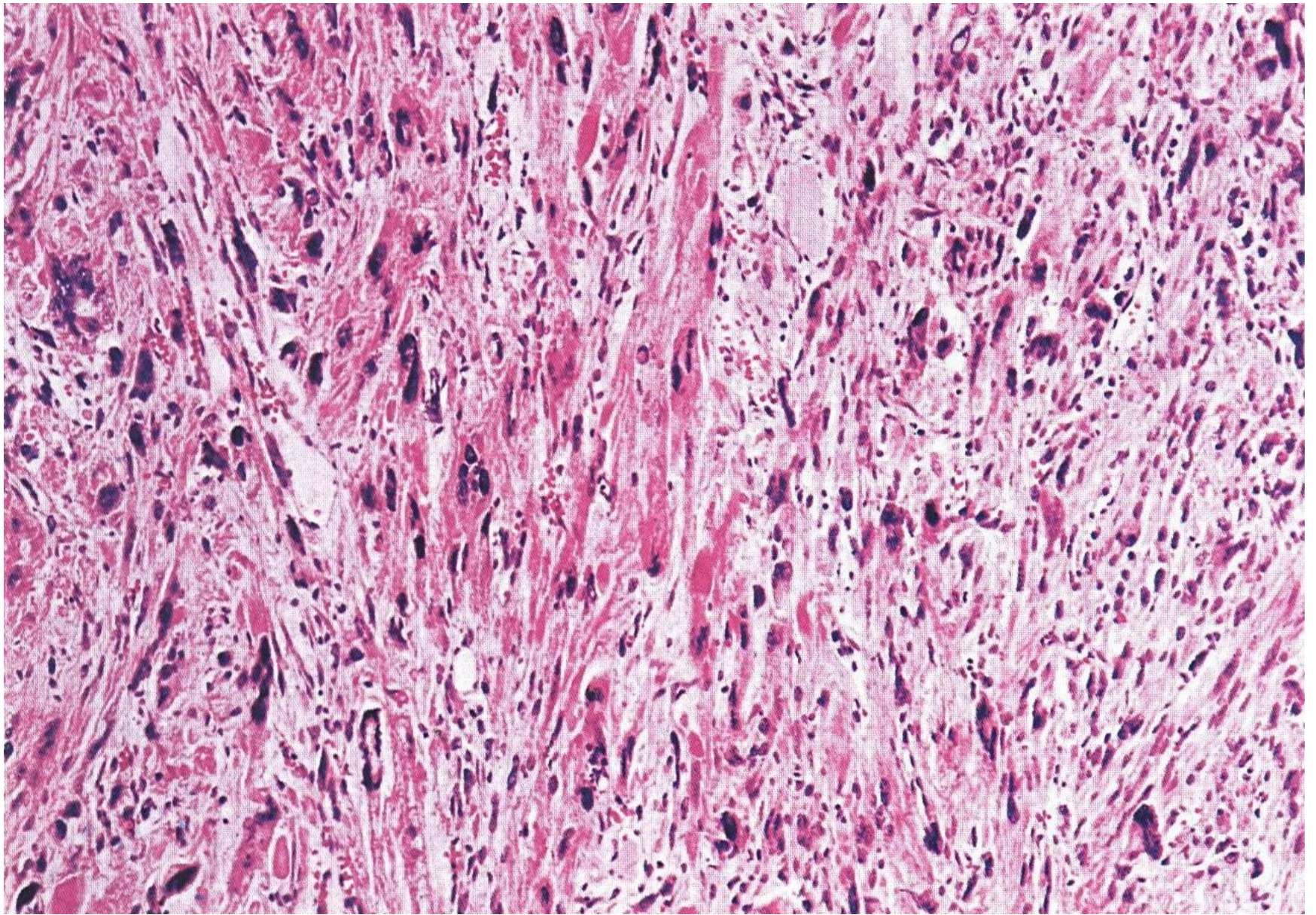
myometrium – leiomyoma





myometrium – cellular leiomyoma





myometrium – bizarre leiomyoma

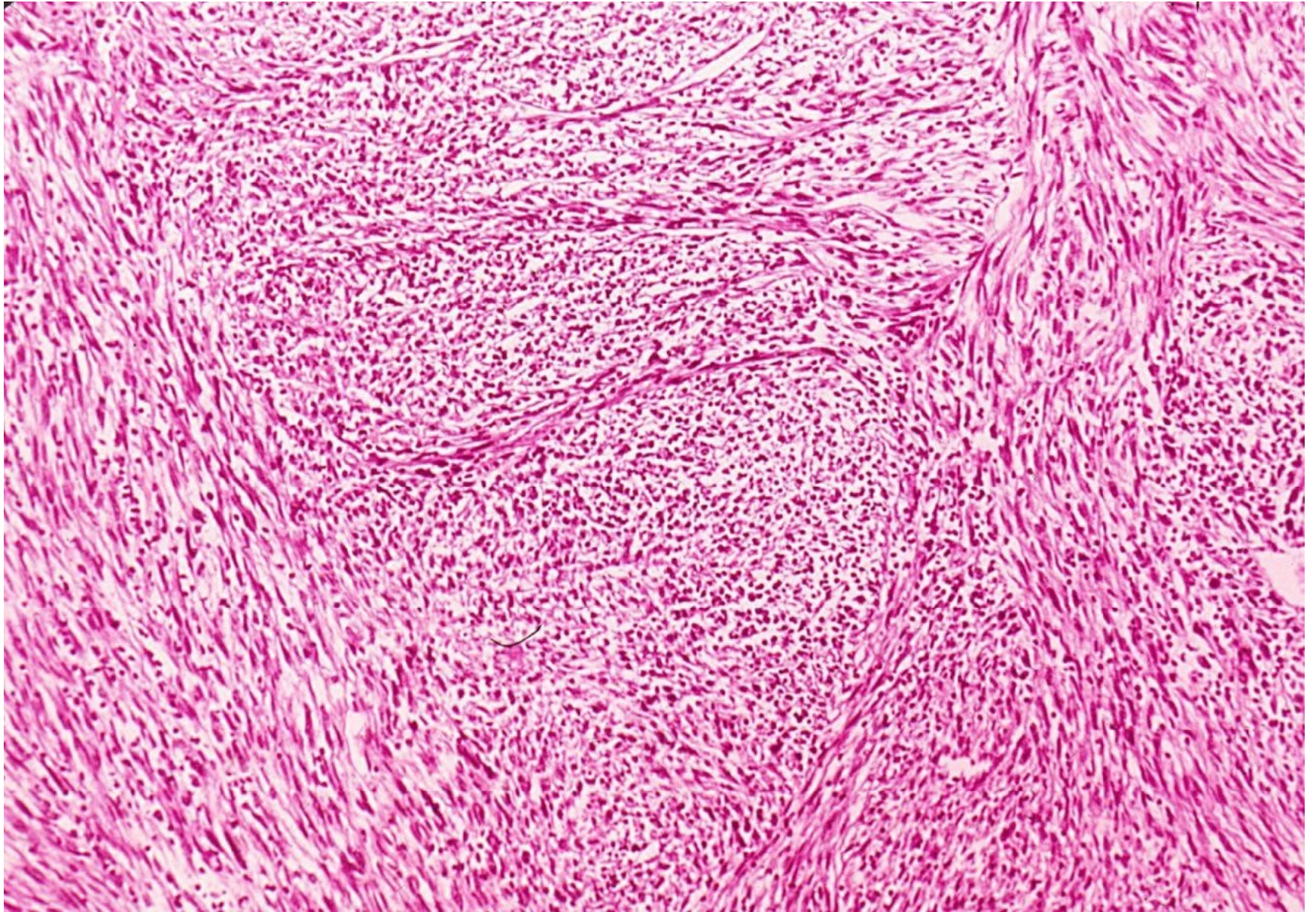


# Pathology of the Uterus

## tumors of the myometrium

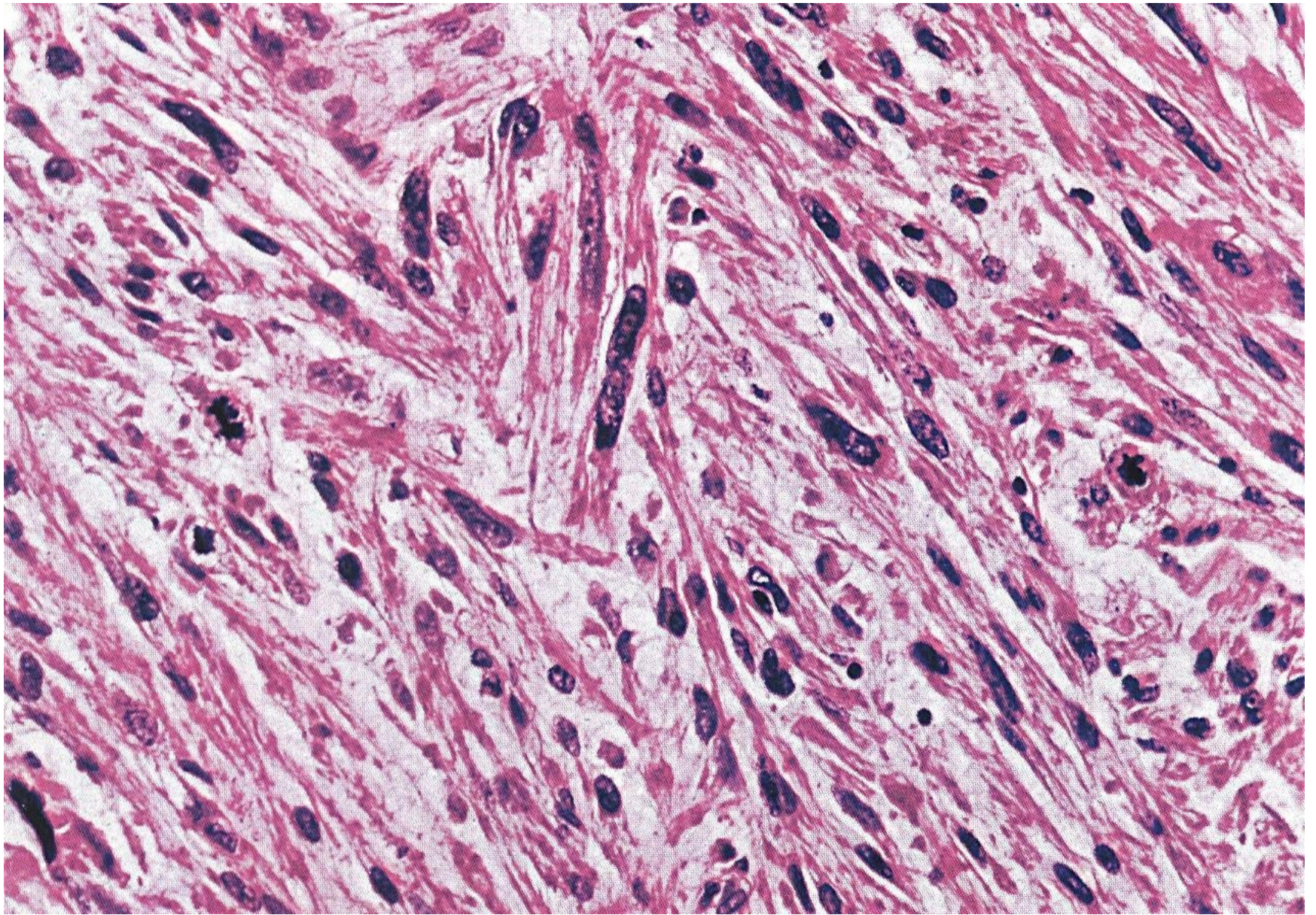
- **Leiomyosarcomas**
- These uncommon malignant neoplasms arise de novo from the myometrium or endometrial stromal precursor cells.
- On histologic examination, they contain a wide range of atypia, from those that are extremely well differentiated to highly anaplastic, pleomorphic lesions. The distinction from leiomyomas is based on nuclear atypia, mitotic index, and zonal necrosis.





myometrium – leiomyosarcoma





myometrium – leiomyosarcoma – detail