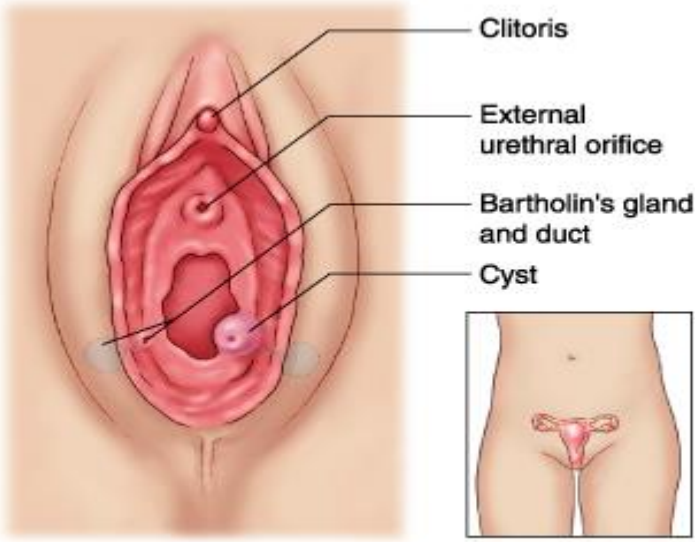
# Female genital tract

# Outline

- Vulva
- Vagina
- Cervix
- Body of uterus
- Fallopian tubes
- Ovaries
- Placenta – GTD

# Vulva

- Vulvitis
- Bartholin cyst
  - Obstruction of the excretory ducts of the gland
- Dermatologic disorders
- Non-specific epithelial disorders
- Tumors



# Tumors and tumor like lesions

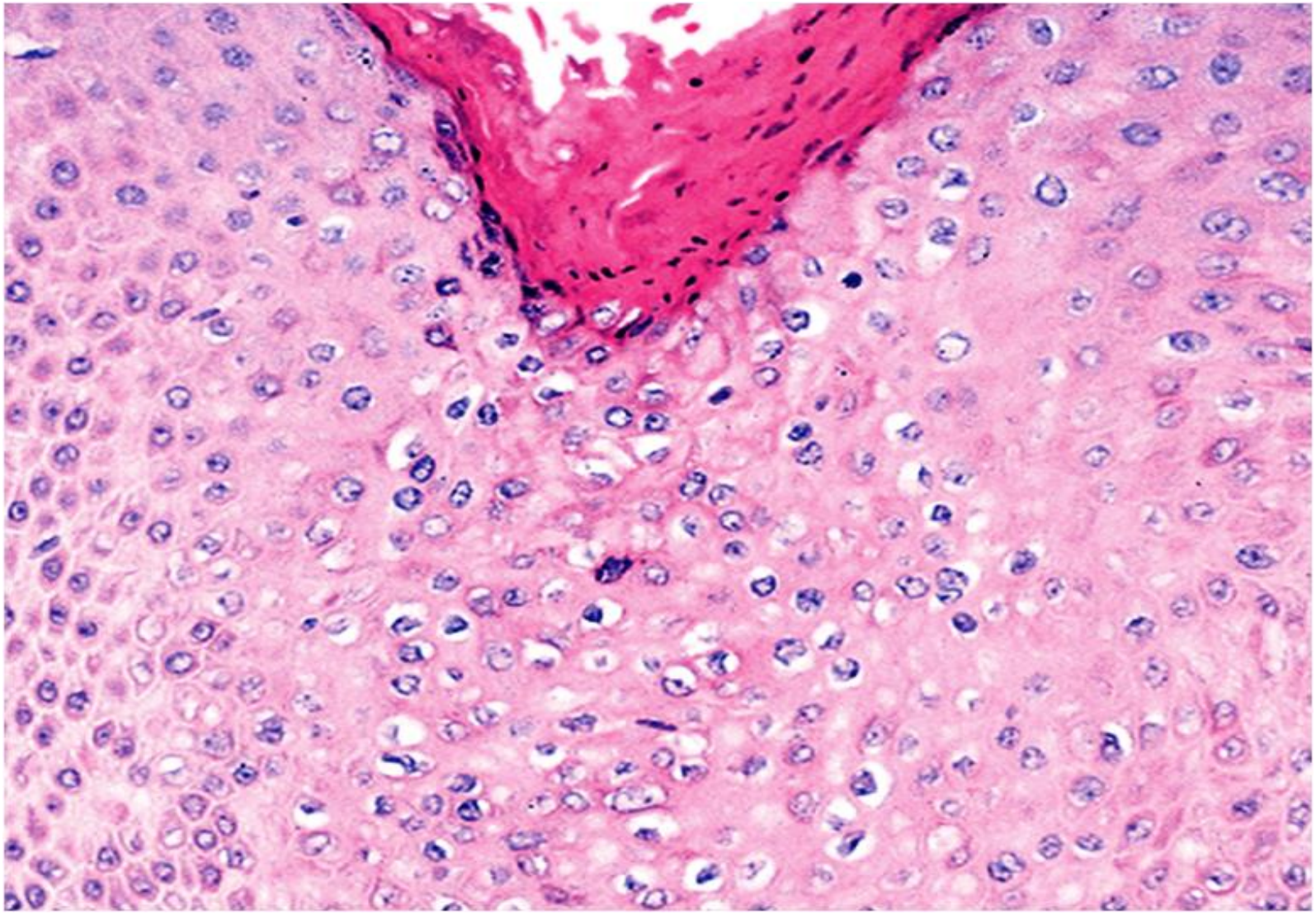
- Condyloma accuminatum
- Vulvar intraepithelial neoplasia (VIN)
- Carcinoma of the vulva

# Condyloma accuminatum

- Usually multiple lesions
- Associated with HPV 6 and HPV 11
- Not precancerous
- May coexist with foci of (VIN grade I)

# Numerous condylomas of the vulva

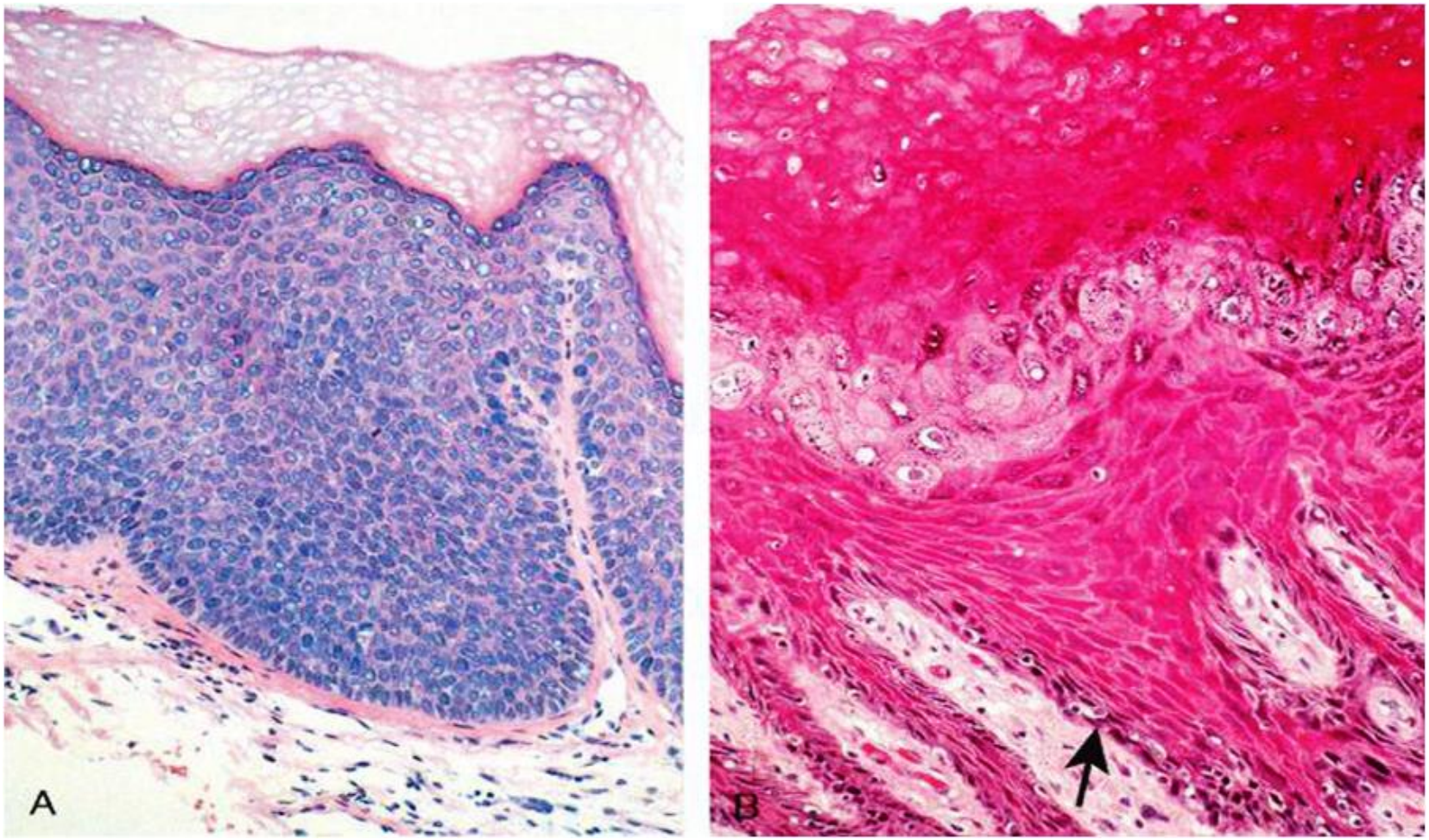
# Condyloma accuminatum



# Vulvar intraepithelial neoplasia (VIN)

| Classic VIN | Differentiated VIN |
| --- | --- |
| ▪Young patients (40–60 y)<br>▪HPV associated<br>▪Usually multiple | ▪Older women > 60 y<br>▪NOT HPV associated<br>▪P53 mutation |
| **low grade VIN (VINI)**<br>▪HPV 6, 11<br>▪NOT precancerous lesion<br>▪May coexist with conduloma accuminatum | |
| **High grade VIN**<br>**VIN II and VIN III (CIS)**<br>▪HPV 16, 18<br>▪May coexist with vaginal or cervical carcinoma | |

# VIN




A. Classic VIN, B. Differentiated VIN

# Vulvar carcinoma

- 3% of all genital tract cancers in women
- Squamous cell carcinoma 95%
- Adenocarcinoma
  - Bartholin gland CA
  - Eccrine gland CA
- Extramammary paget disease
- Melanoma
- Basal cell carcinoma (extremely rare)

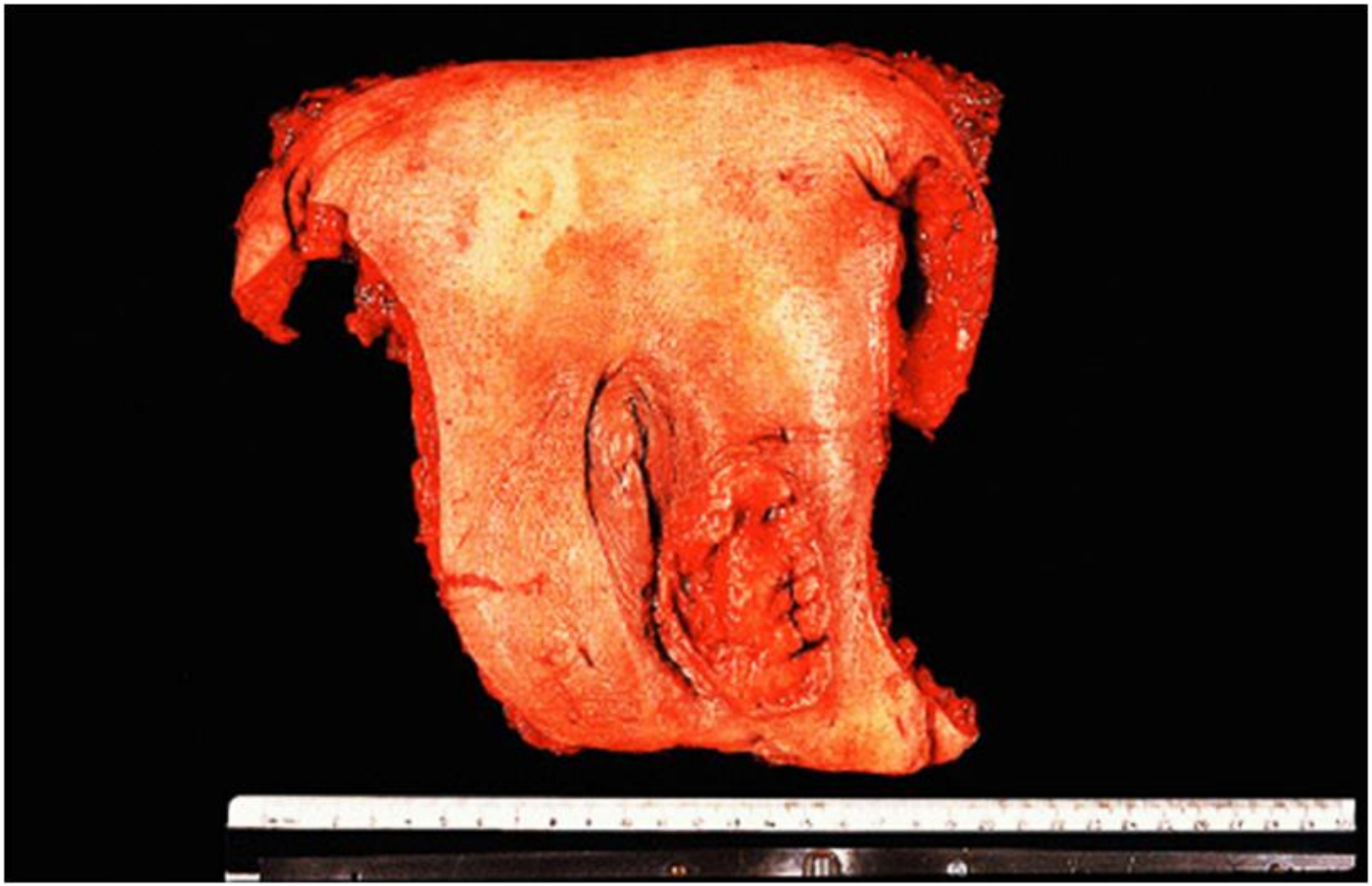
# Gross appearance

- Most common on labia majora
- VIN and early CA appear as **leukoplakia**
- Then **exophytic** or ulcerative **endophytic**

- **HPV-positive tumors**
  More often multifocal and appear warty

- **HPV-negative tumors**
  Usually unifocal

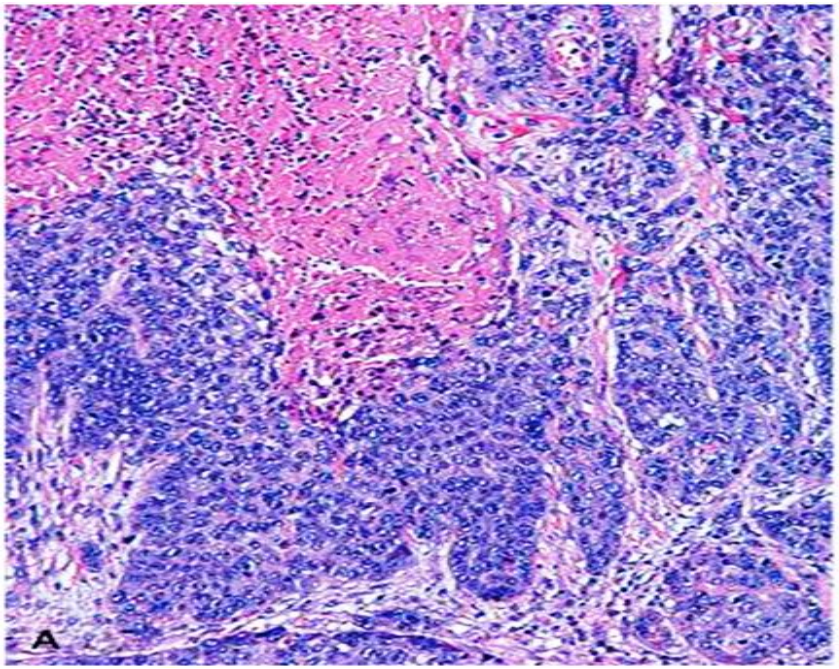
# Vulvar carcinoma

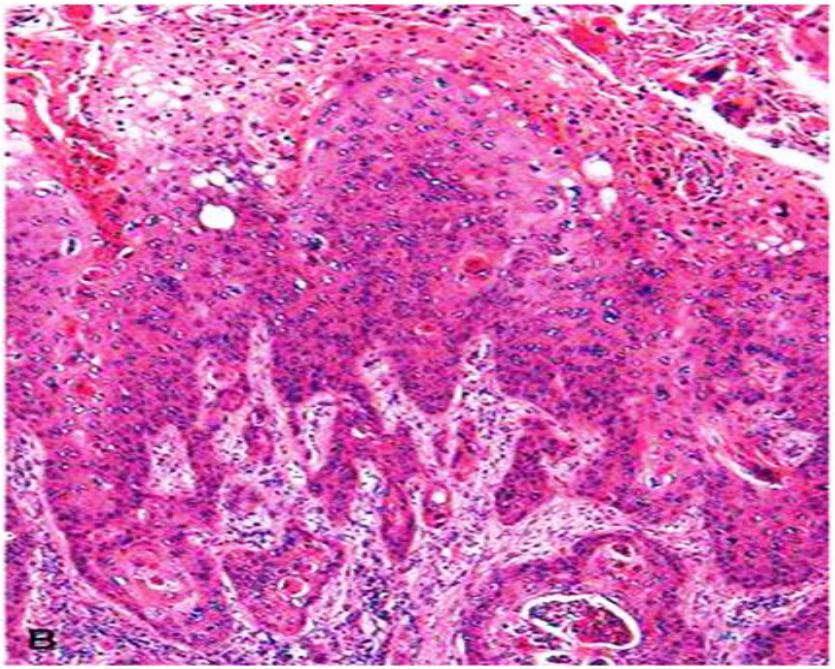


Tumor of labia majora

# Histologic subtypes

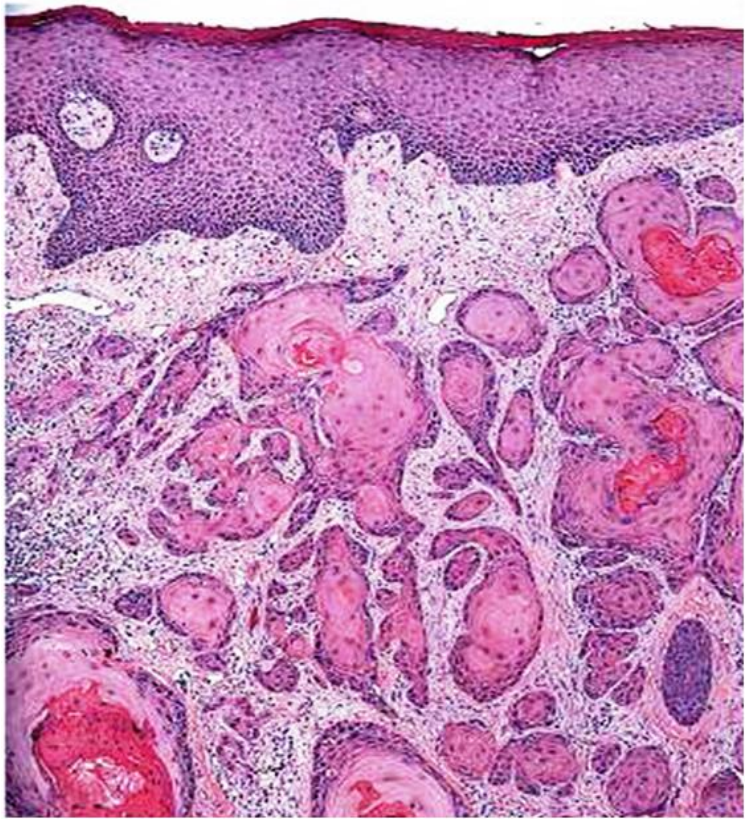
- **HPV associated vulvar SCC**
- Begin as classic VIN
- Young patients
- Poorly differentiated (basaloid) SCC



# Histologic subtypes

- **HPV negative vulvar SCC**
- Old patients
- Associated with lichen sclerosus, lichen simplex chronicus, or differentiated VIN
- Well-differentiated (keratinizing) SCC



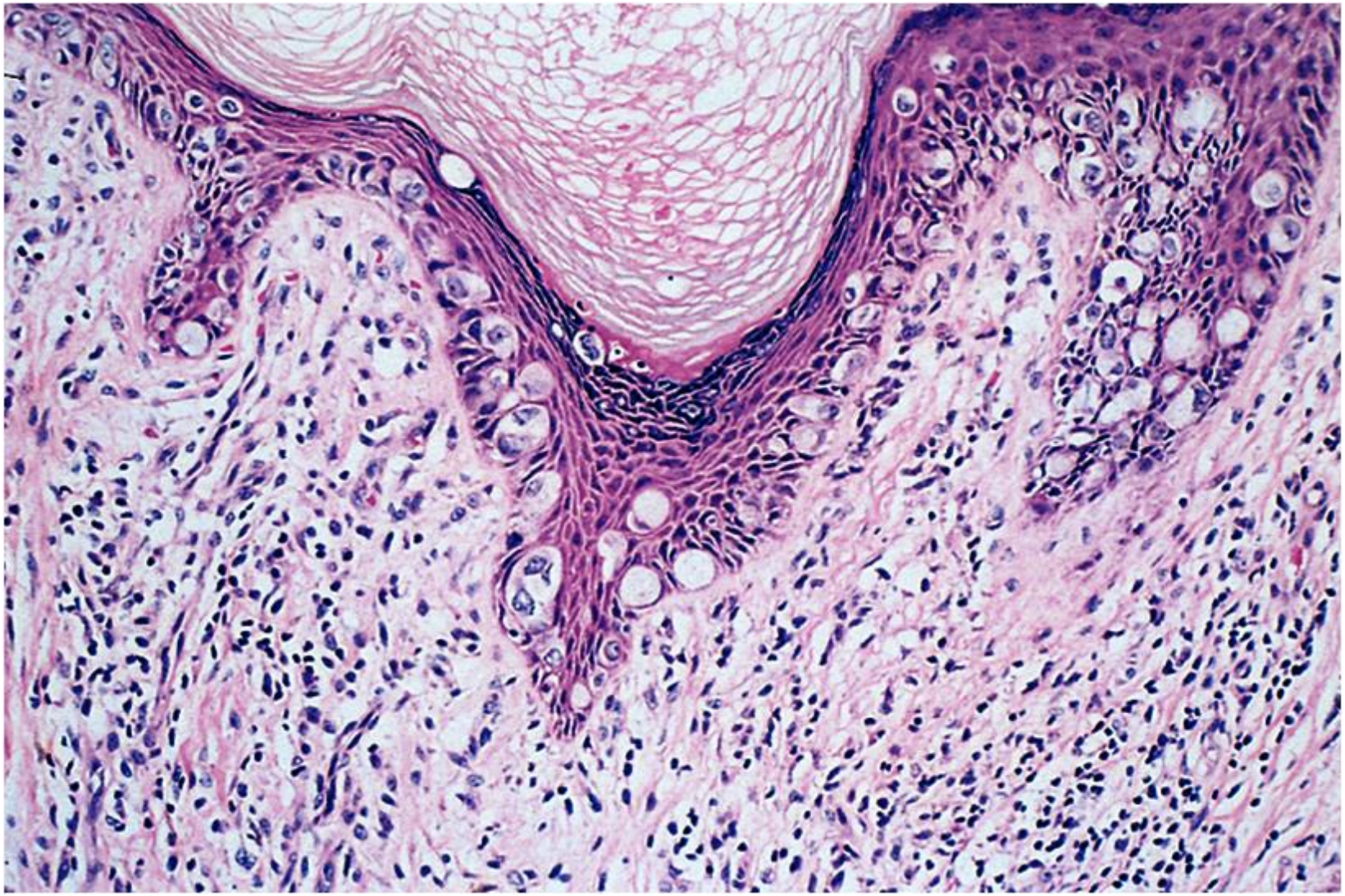
# Tumor spread

- All patterns tend to remain confined to the vulva for a few years
- Direct invasion
- Involvement of regional nodes
- Hematogenous spread
- Prognosis depends on the stage:
  - The size of the tumor (< 2 cm good)
  - The depth of invasion
  - LN involvement

# Extramammary Paget Disease

- A form of intraepithelial carcinoma
- The majority of vulvar Paget have NO underlying carcinoma
  - Arise from epithelial proginator cells
- Occasionally an underlying carcinoma of sweat gland may be present
  - May invade locally and metastasize

# Paget disease of the vulva



# VAGINA

- Primary diseases are rare:
- Congenital anomalies
- Vaginitis
- Primary tumors

- Vagina is more often secondarily involved in the spread of cancer or infections arising in cervix, vulva, bladder or rectum

# Vaginal tumors and precursor lesions

- Vaginal intraepithelial neoplasia (VAIN)
- Squamous cell carcinoma

- Vaginal adenosis
- Vaginal clear cell carcinoma

- Sarcoma botryoid

# VAIN and SCC

- Uncommon, old women, HPV associated

- Low grade VAIN
- VAIN I (flat condyloma)

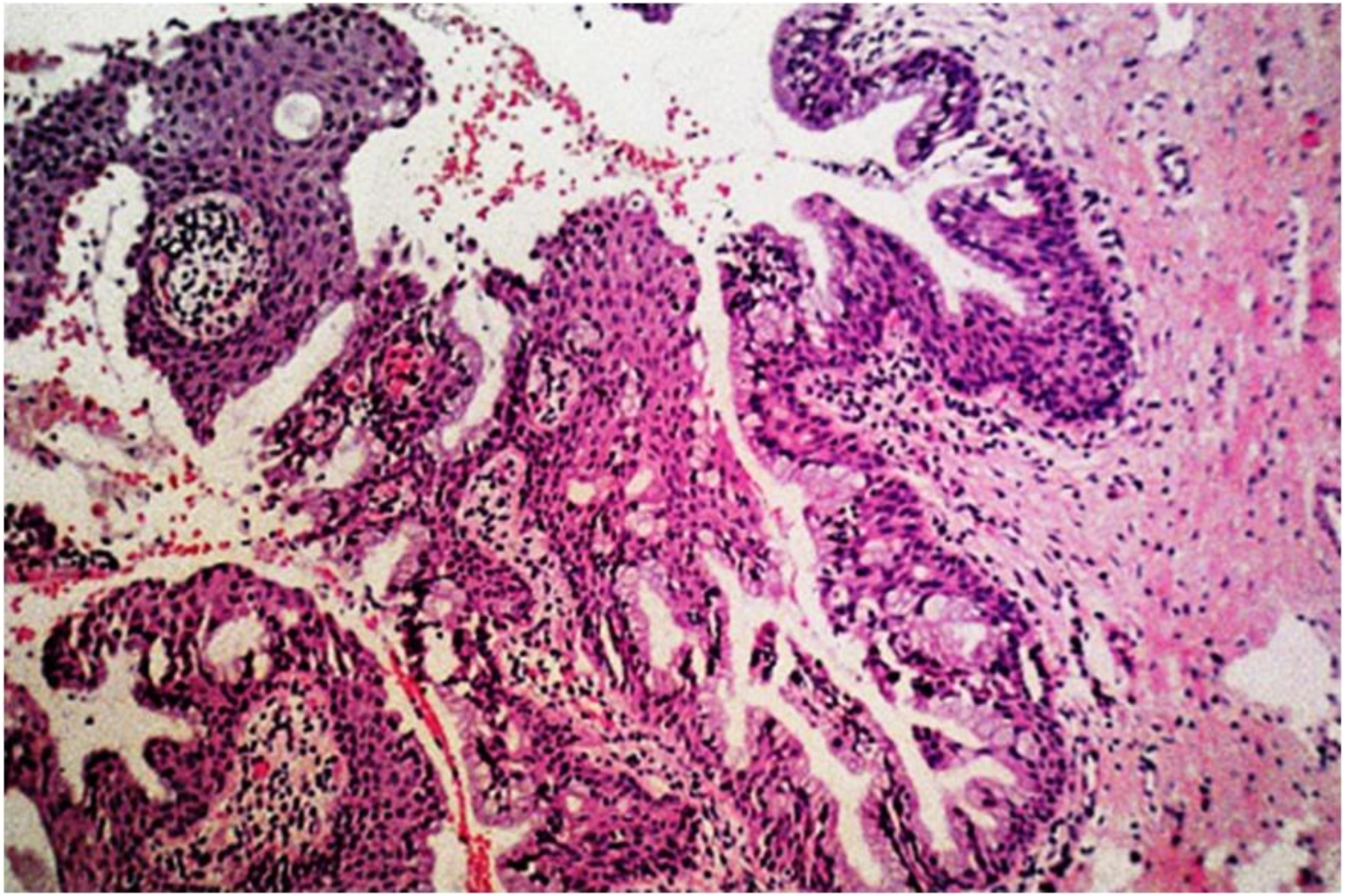
- High grade VAIN
- VAIN II, VAIN III

# Vaginal adenosis

- **Definition:**
- The presence of Mullerian type epithelium in the vagina
  - Endocervical type, most common
  - Tuboendometrioid

- Exposure to diethylstilbestrol (DES) in utero
- Precursor to vaginal clear cell carcinoma

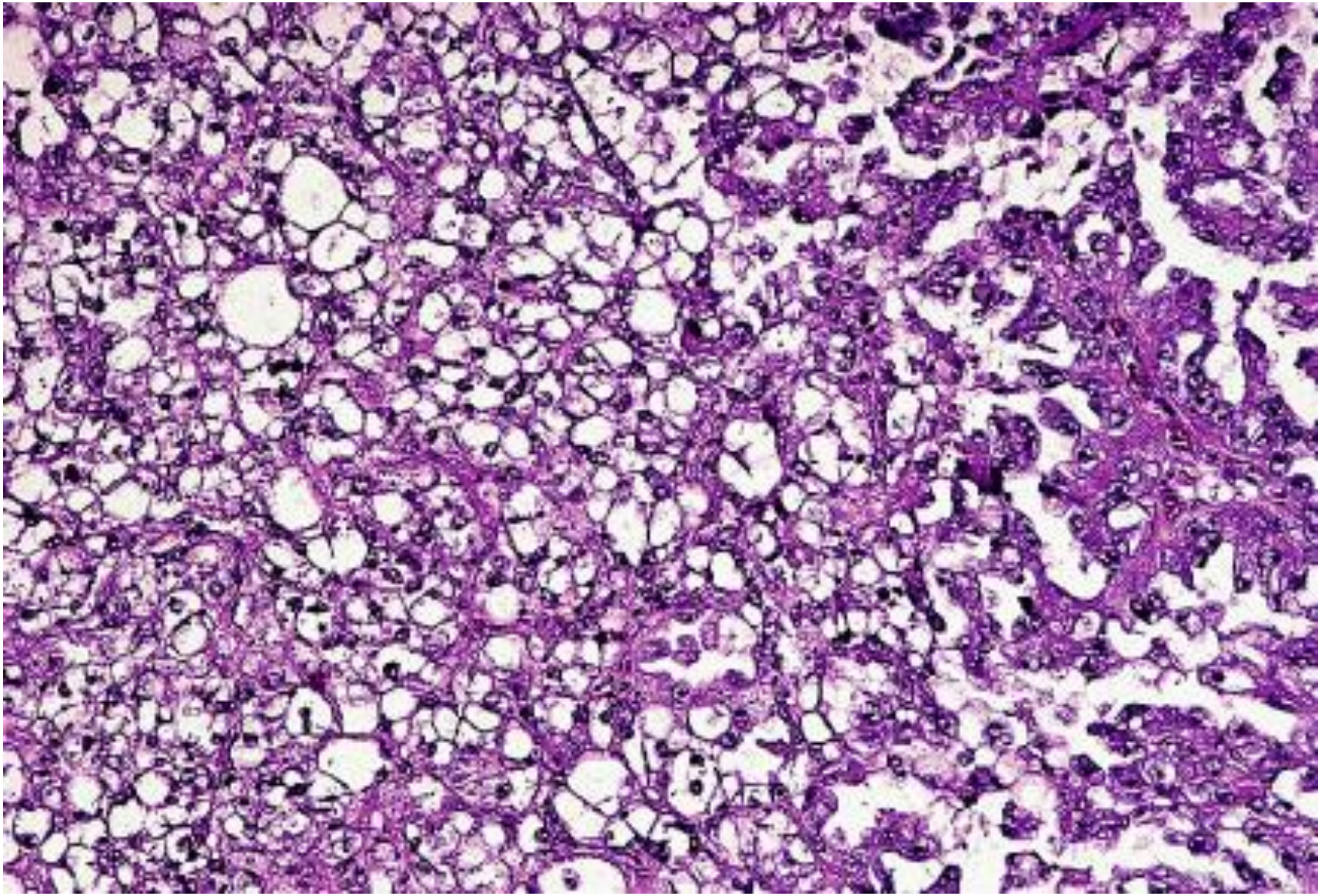
# Vaginal adenosis



# Clear cell carcinoma

- Young women in their late teens to early 20s
- Exposure to DES in utero in 2/3 of cases
- The overall risk is < 1:1000
- In 2/3 the tumor arises in the vagina
- In 1/3 the tumor arises in the cervix
- Tumor cells contain glycogen
- Relatively good prognosis

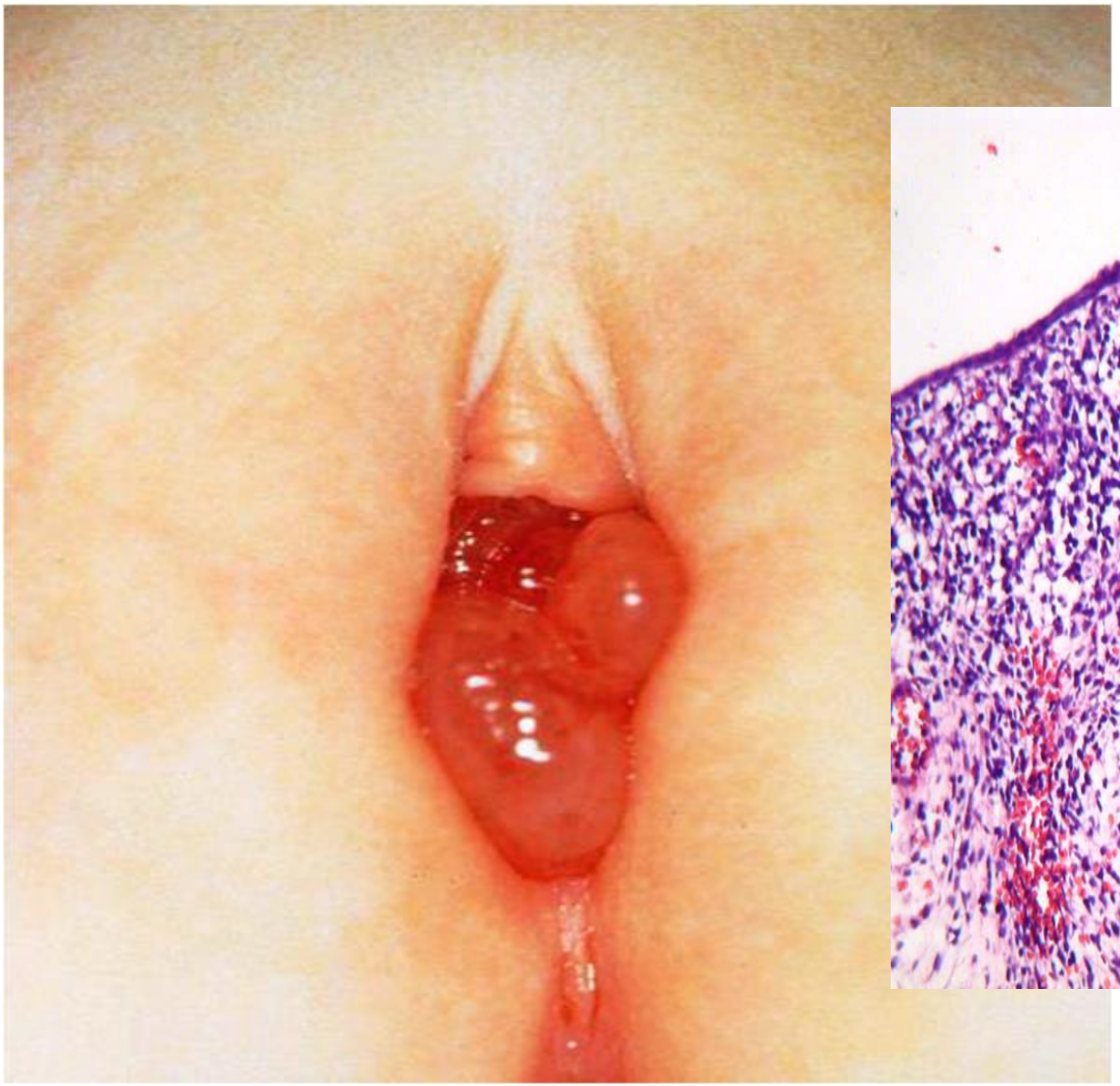
# Clear cell adenocarcinoma of the vagina

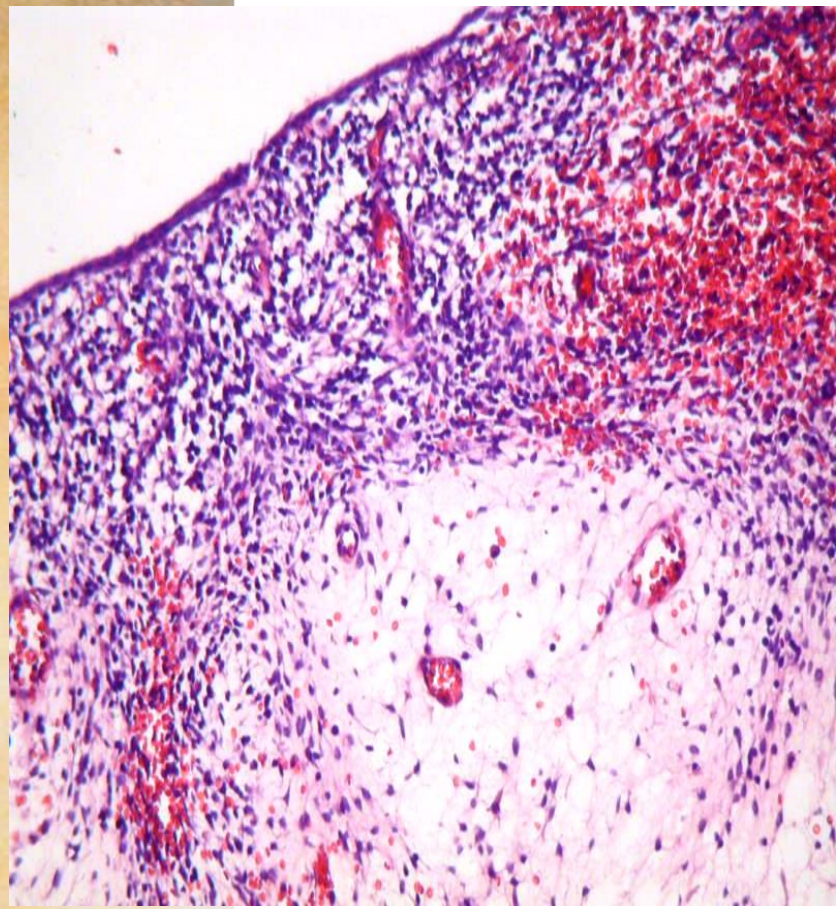


# SARCOMA BOTRYOIDES

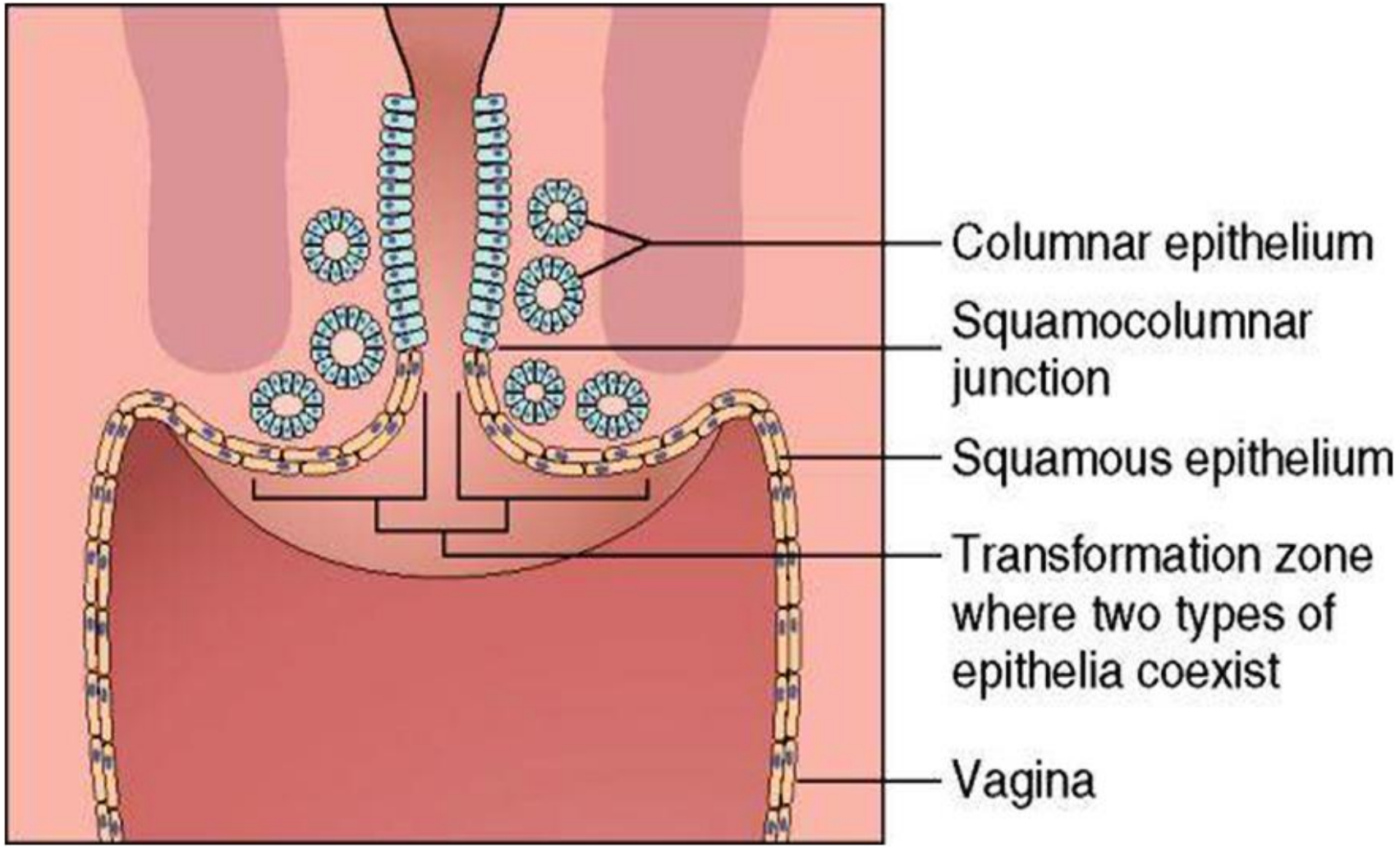
- A rare vaginal tumor
- Most frequent in infants &children < 5 years
- Soft polypoid masses "punch of grapes"
- A subtype of embryonal rhabdomyosarcoma
- Treatment is CTX and surgery &/or RTH

# Sarcoma botryoides





# CERVIX


Columnar epithelium
Squamocolumnar junction
Squamous epithelium
Transformation zone where two types of epithelia coexist
Vagina

# Transformation zone

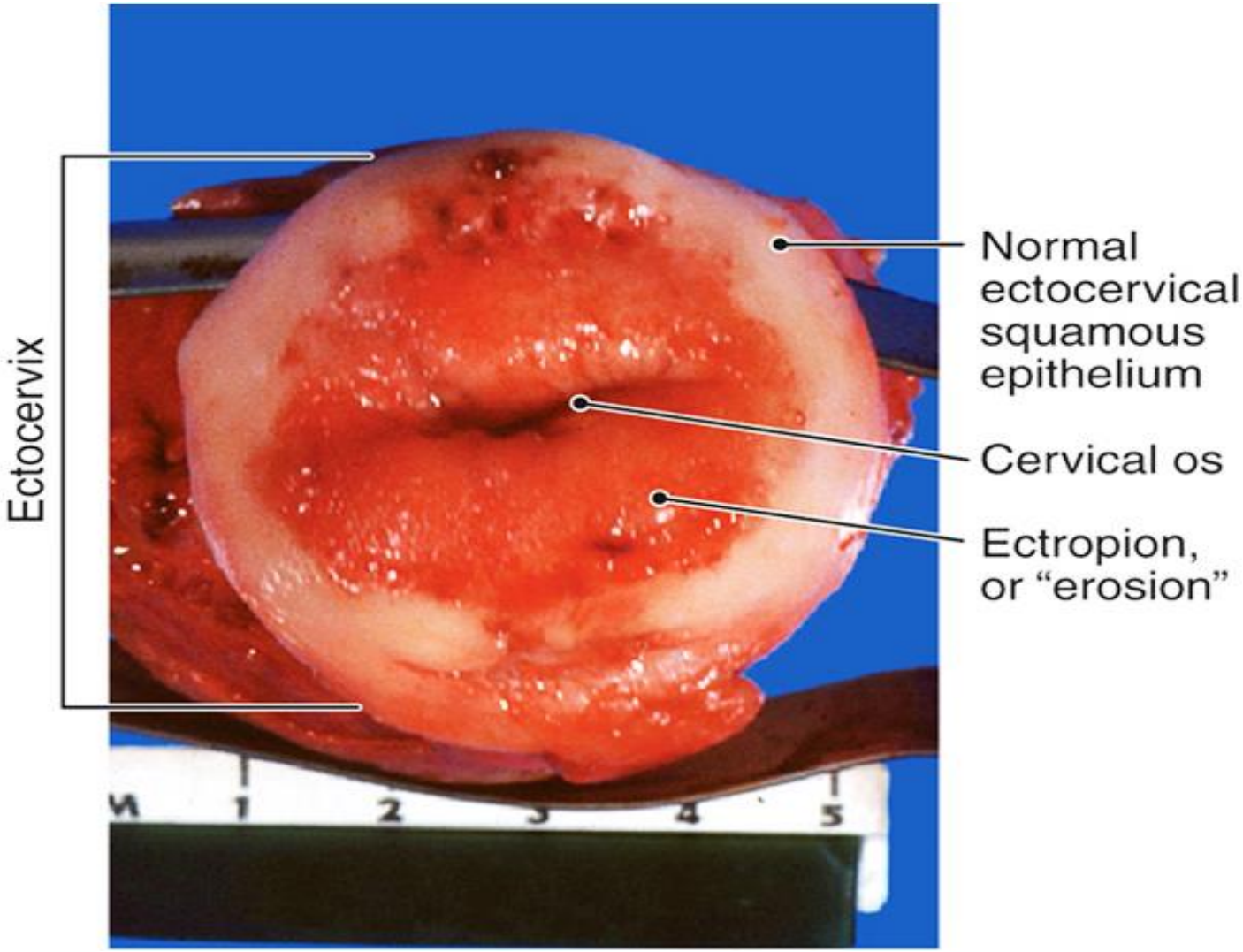
- Zone of squamo-columnar junction
- Dynamic, changes location in response to woman's hormonal status
- Unstable region in which replacement of one epithelia for another repeat (fight of epithelia)
- In young it is located on the ectocervix

# Ectropion (erosion)

- The portion of endocervical mucosa that extend beyond the external os to cover the ectocervix

- Physiological change
- Appear red and moist

# Ectropion (erosion)



# CERVICITIS

"Inflammations of the cervix"

- Extremely common and associated with a mucopurulent to purulent vaginal discharge

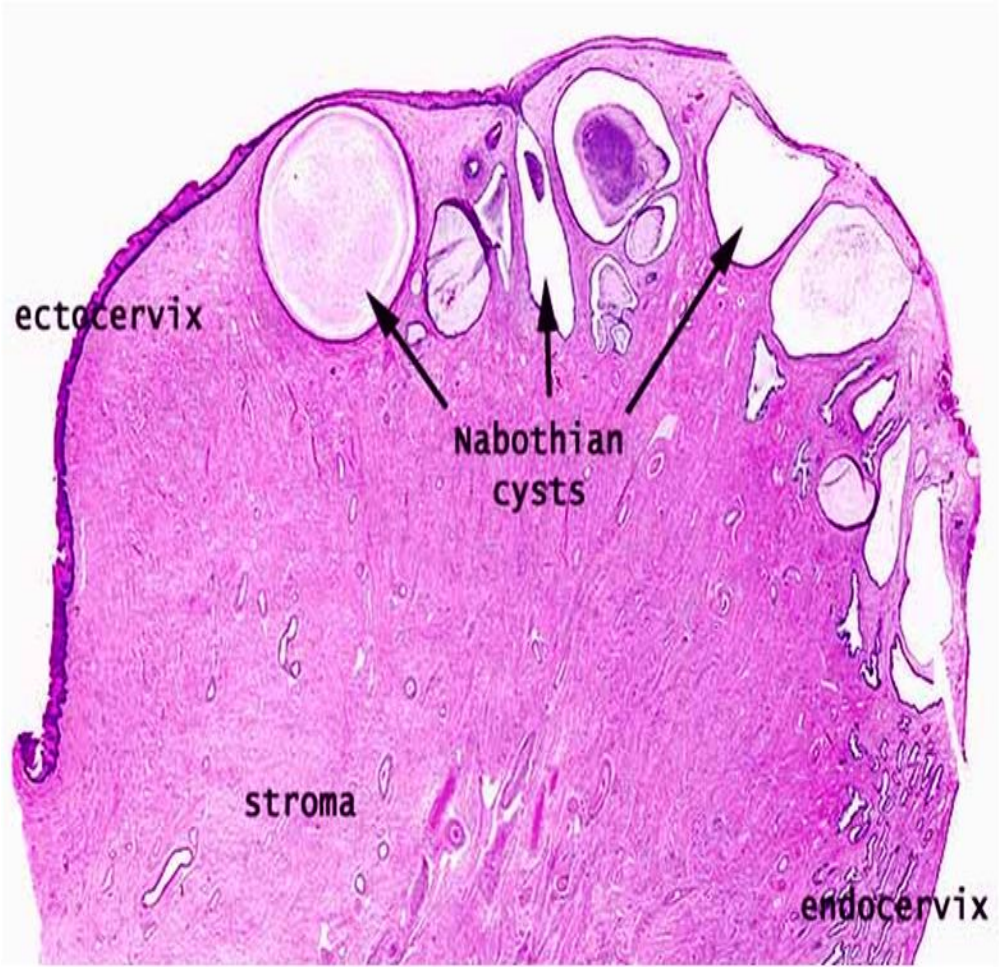
- **Noninfectious (non-specific) cervicitis**
- Vaginal aerobes and anaerobes, streptococci, staphylococci, enterococci, and E.coli.

- **Infectious (specific) cervicitis - STD**
- Chlamydia trachomatis is the most common, 40% of STD clinics

# Nabothian cyst

- Cyst in the cervix lined by columnar mucus-secreting cells and associated with inflammatory cells
- **Pathogenesis:**
- Inflammation lead to squamous metaplasia
- Overgrowth of the regenerating squamous epithelium blocks the orifices of endocervical glands in the transformation zone

# Nabothian cyst

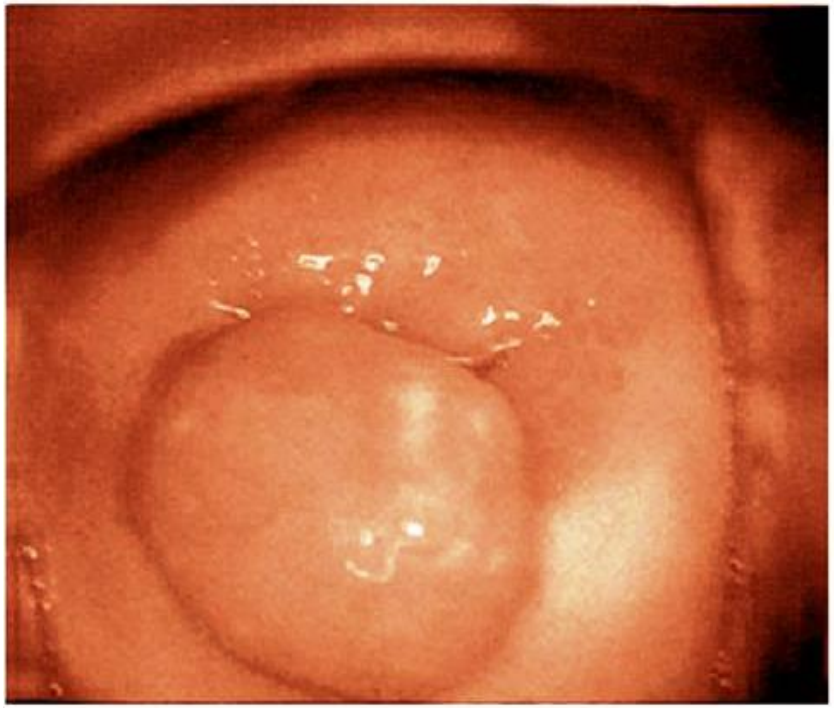


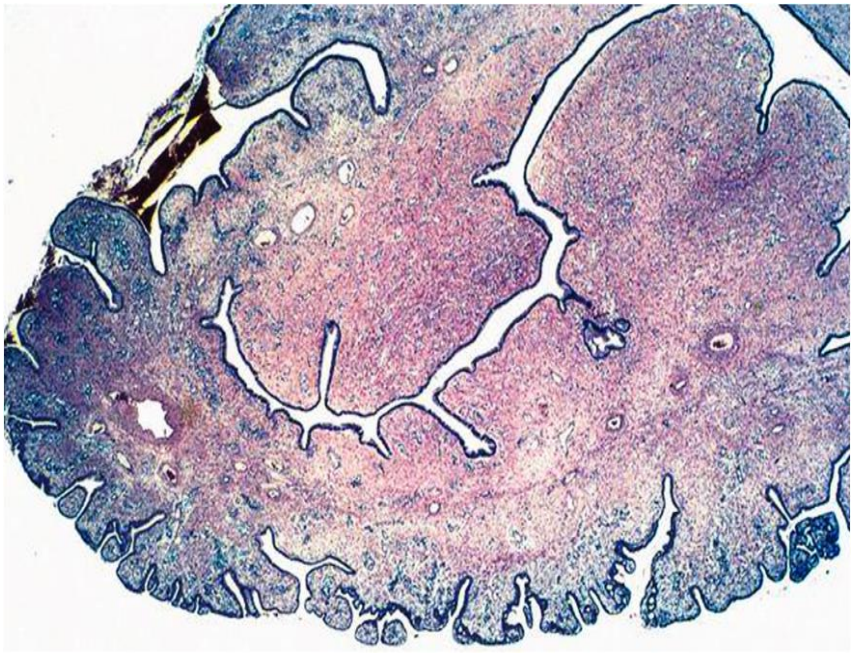
# Endocervical polyp

- Common, 2-5% of all adult woman
- Inflammatory in origin, NOT premalignant
- Lead to vaginal spotting

- **Morphology:**
- Most arise in endocervical canal
- Loose fibromyxoid stroma
- Dilated endocervical glands
- Inflammation + squamous metaplasia

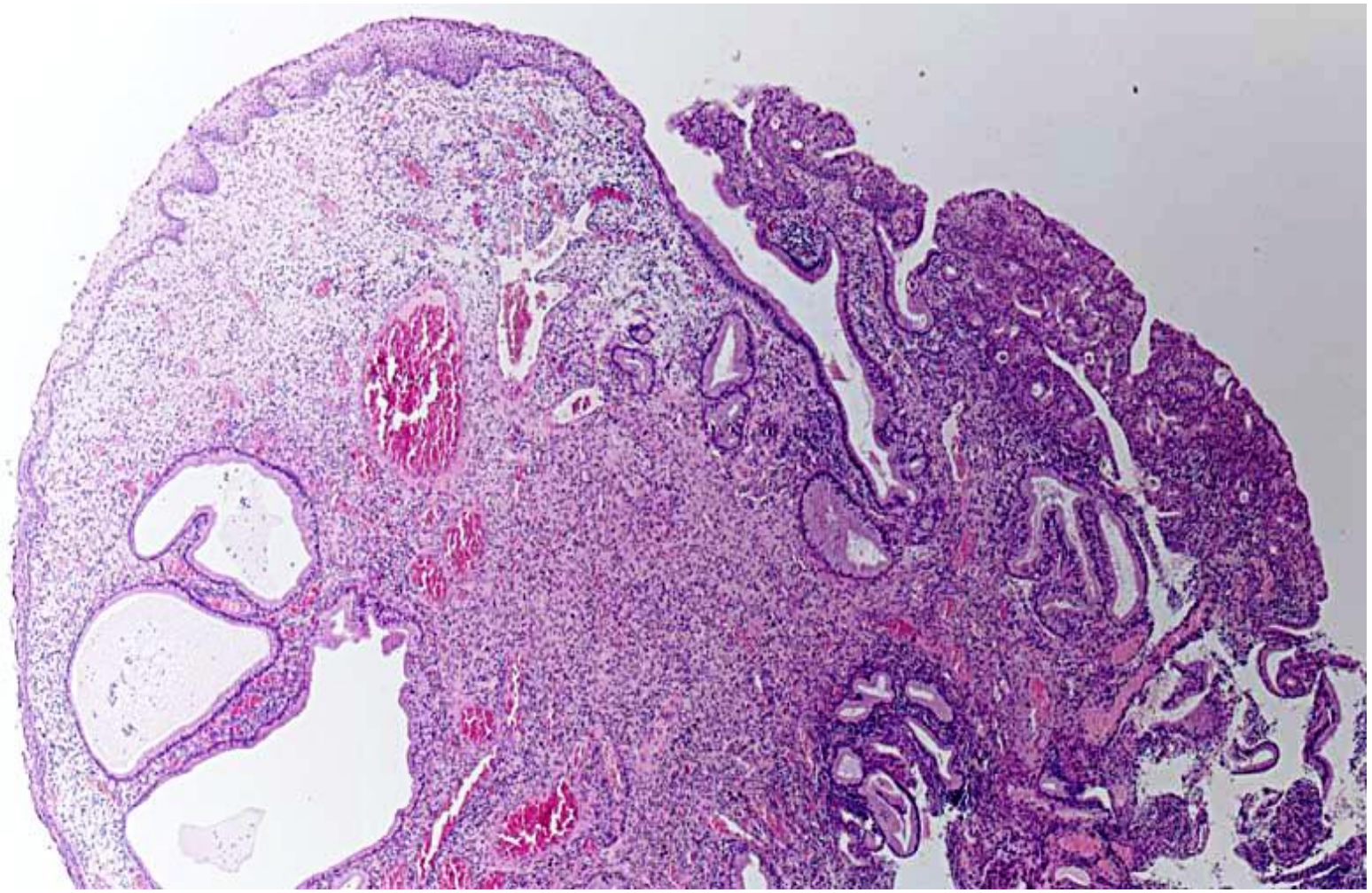
# Endocervical polyp





Microscopic: Fibrous stroma covered with endocervical columnar epithelium

# Endocervical polyp



Poylpoid lesion composed of endocervical glands and squamous epithelium

# TUMORS OF THE CERVIX

- **Cervical Intraepithelial Neoplasia (CIN)**
- **Squamous Cell Carcinoma**

- Nearly all invasive cervical SCC arise from precursor epithelial changes (CIN)

- Not all cases of CIN progress to invasive cancer, many persist without change or even regress

# CIN and cervical carcinoma

- Cervical CA is major cause of cancer-related deaths in females, particularly in the developing world

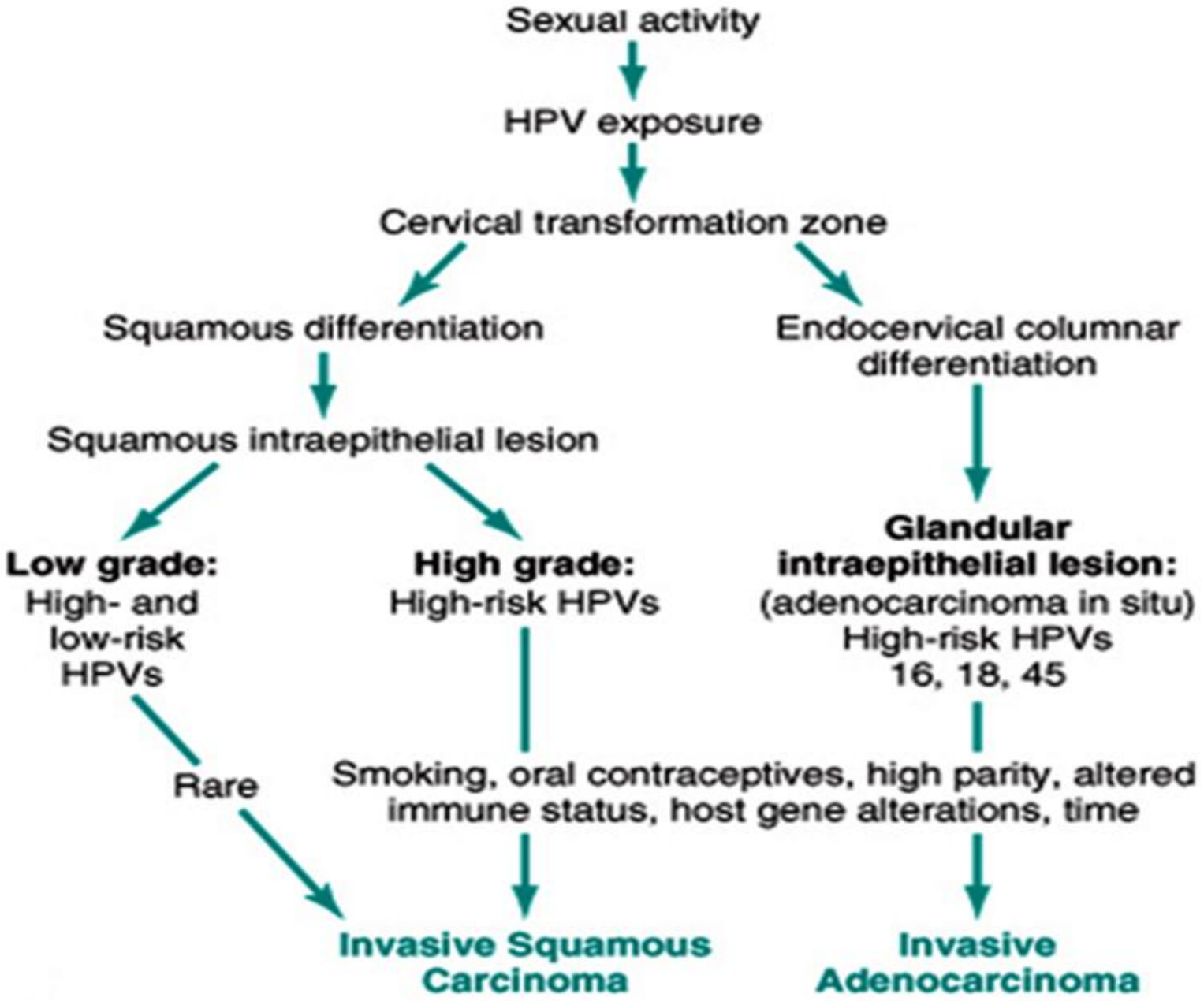
- The Pap smear is the most successful cancer screening test ever developed
  - Increased detection of preinvasive and potentially curable early cancers

# Pathogenesis

- The peak age incidence of CIN is 30 years
- The peak age incidence of CA is 45 years
- Sexual transmitted disease caused by HPV
  - HPV can be detected in nearly all precancerous lesions and invasive CA
  - High-risk HPV: 16, 18, 45, and 31
- low-risk HPV: 6, 11, 42, and 44
  - Condyloma accuminatum, not precancerous

## Risk factors of CIN and invasive carcinoma

- Early age at first intercourse
- Multiple sexual partners
- A male partner with multiple sexual partners
- Persistent infection by "high-risk" HPV
- Low socioeconomic class
- Increased parity
- ?? Exposure to OCPs and nicotine
- Genital infections (as clamydia trachomatis)
- Immunodeficiency as HIV


Sexual activity
HPV exposure
Cervical transformation zone
Squamous differentiation
Endocervical columnar differentiation
Squamous intraepithelial lesion
Low grade:
High- and low-risk HPVs
High grade:
High-risk HPVs
Glandular intraepithelial lesion:
(adenocarcinoma in situ)
High-risk HPVs
16, 18, 45
Rare
Smoking, oral contraceptives, high parity, altered immune status, host gene alterations, time
Invasive Squamous Carcinoma
Invasive Adenocarcinoma

# Cervical Intraepithelial Neoplasia

- May begin as low-grade CIN and progress to higher grade or may begin as high-grade CIN

- **On the basis of histology:**
- CIN I: Mild dysplasia (flat condyloma)
- CIN II: Moderate dysplasia
- CIN III: Severe dysplasia and carcinoma in situ

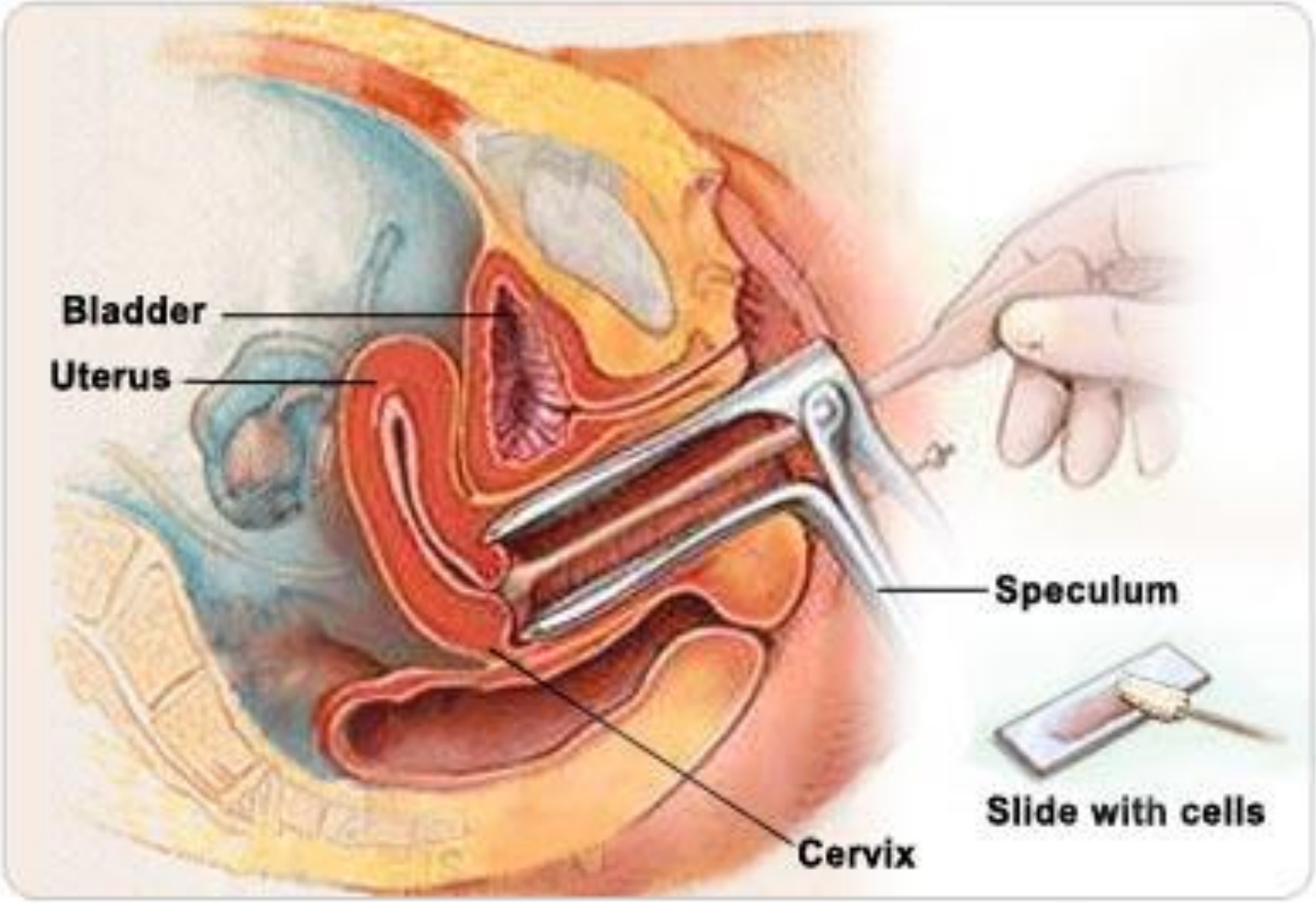
# Terminology and progression

| Abnormality | CIN | Bethesda system (current system in cytology) |
|---|---|---|
| Condyloma acuminatum | | Low grade SIL (LSIL) |
| Mild dysplasia | CIN I | Low grade SIL (LSIL) |
| Moderate dysplasia | CIN II | High grade SIL (HSIL) |
| Severe dysplasia/ CIS | CIN III | High grade SIL (HSIL) |

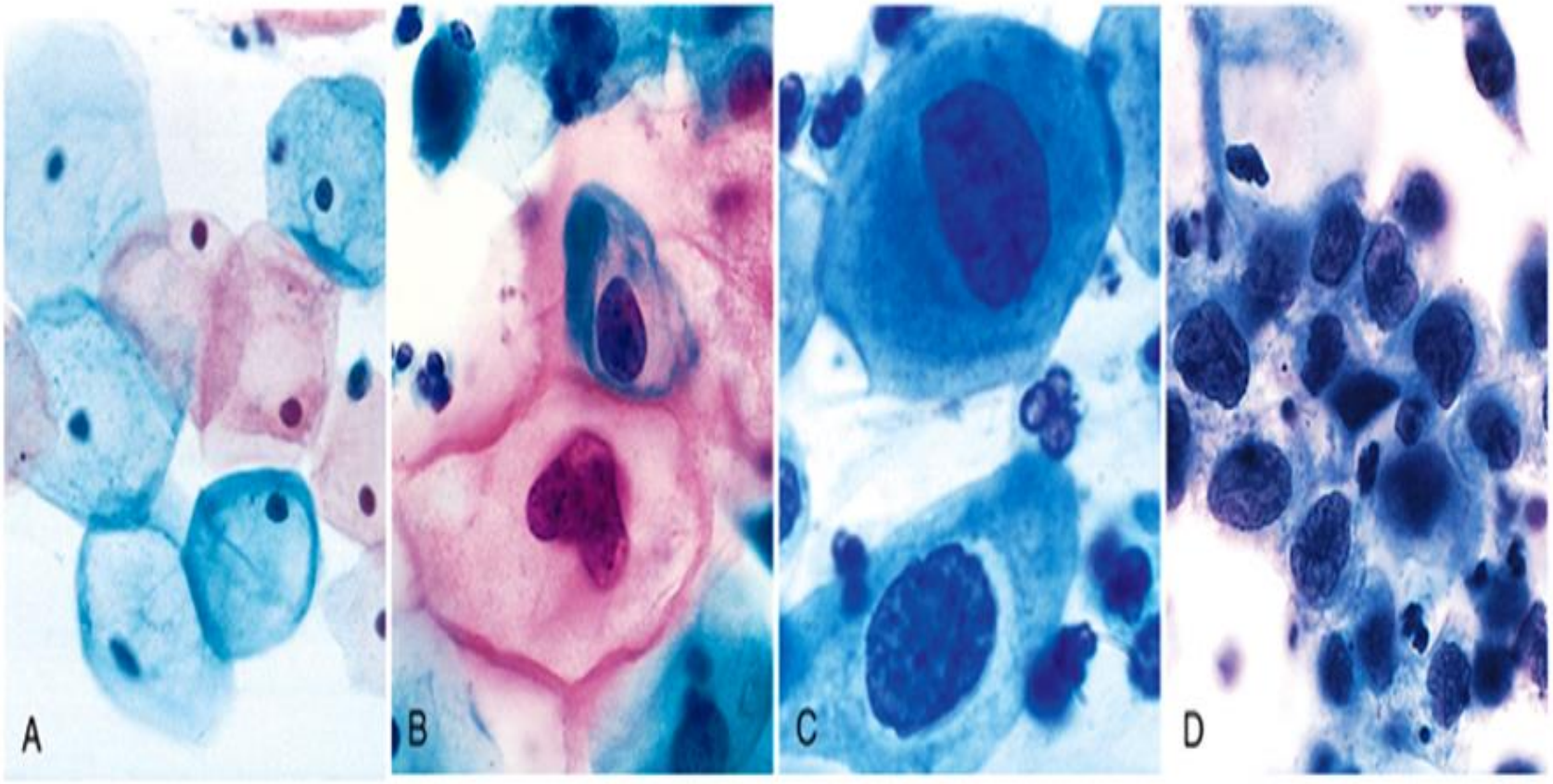
CIN, cervical intraepithelial neoplasia
SIL, squamous intraepithelial lesion

| Lesion | Regress | Persist | Progress |
|---|---|---|---|
| LSIL | 60% | 30% | 10% to HSIL<br>1–5% to CA |
| HSIL | 30% | 60% | 10% to CA |

# Pap smear

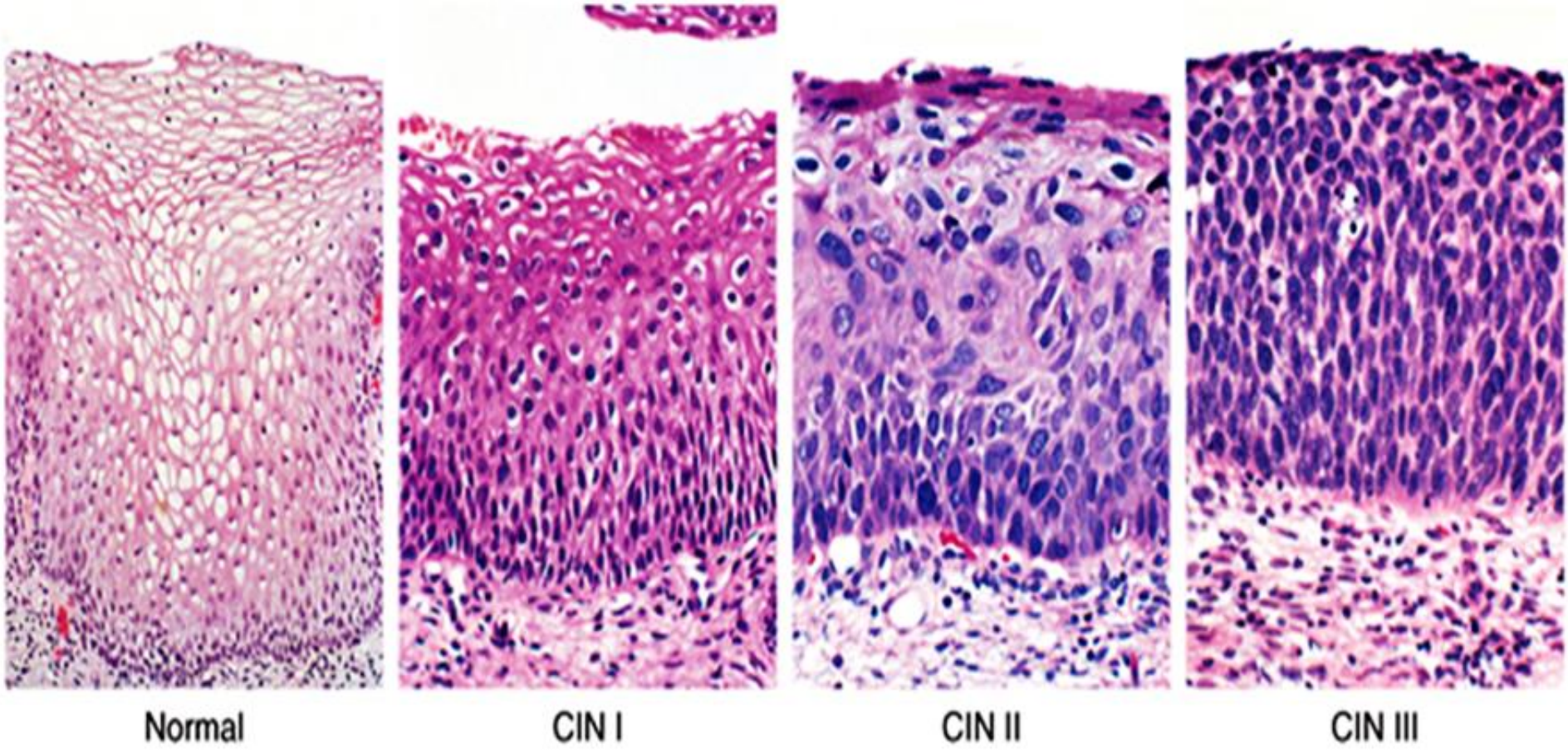


# Pap smear




A. normal, B. CIN I, C. CIN II, D. CINIII

# Histopathology



# Invasive Carcinoma of the Cervix

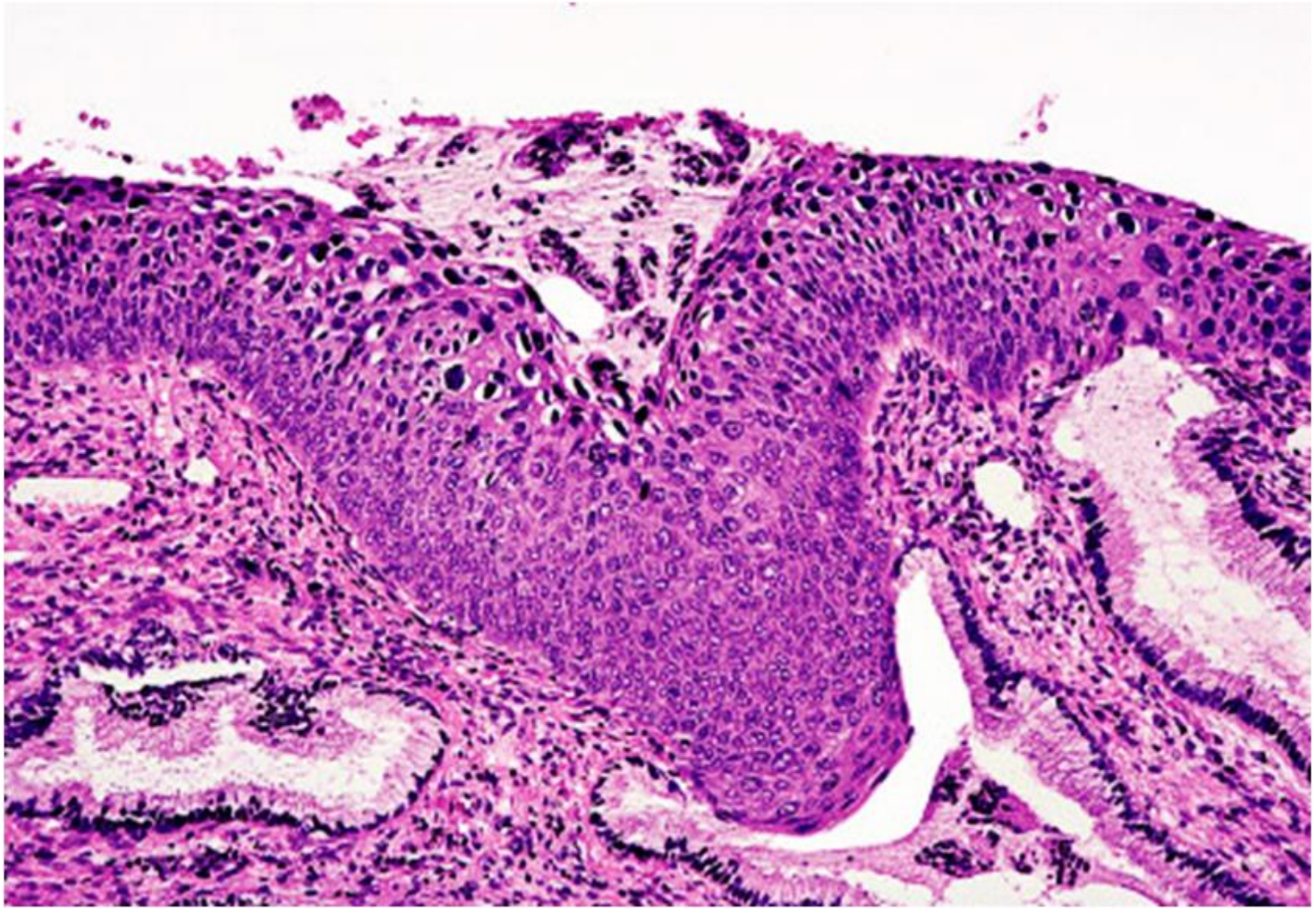
- The most common cervical carcinomas are squamous cell carcinomas (75%)
- Adenocarcinomas
- Adenosquamous carcinomas
- Small-cell neuroendocrine carcinomas (<5%)

# Morphology of cervical carcinoma

- Carcinomas of the cervix develop in TZ
- Range from microscopic foci of early stromal invasion to grossly conspicuous tumors

# CIN III gross

# CIN III

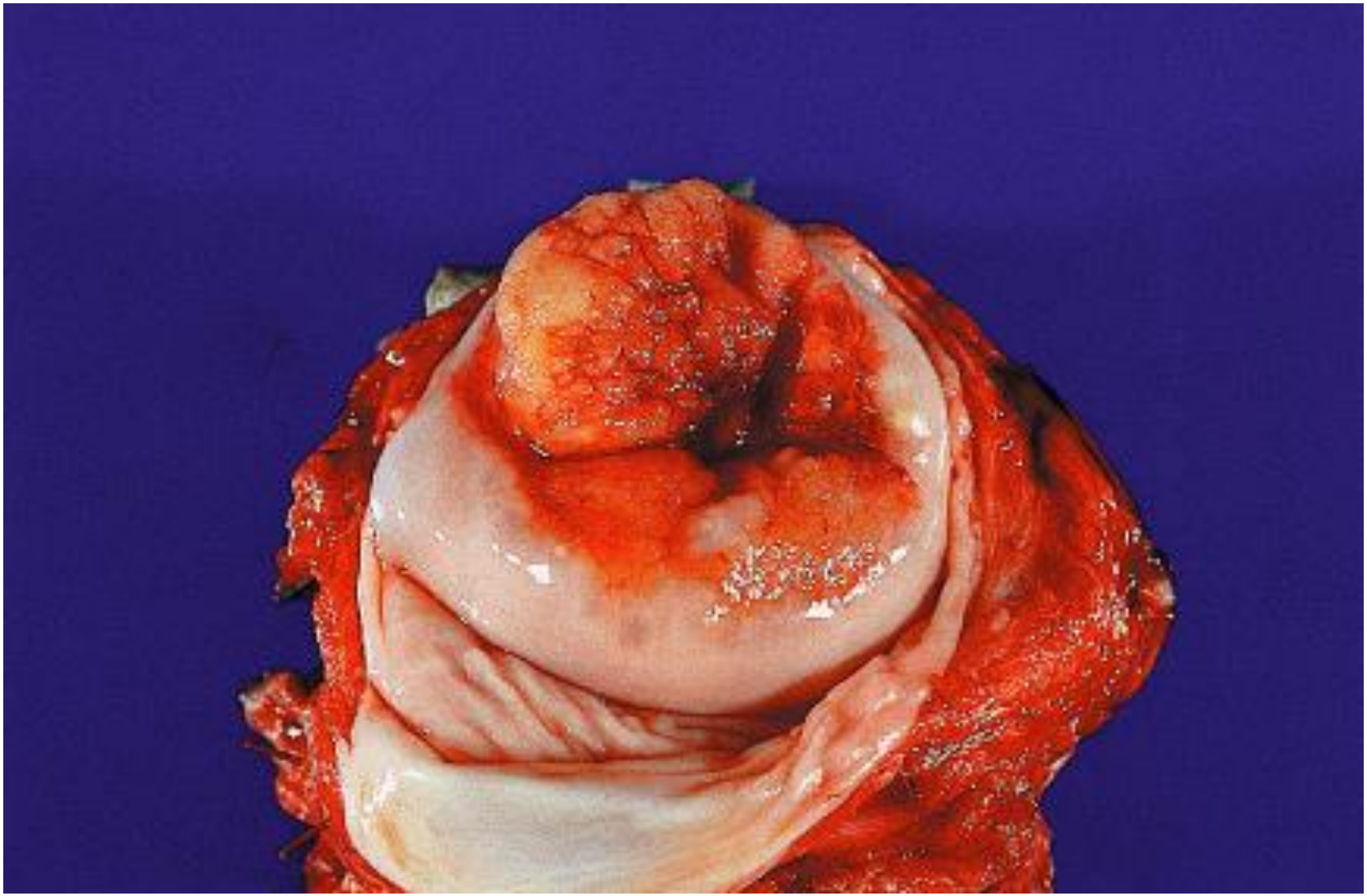


Extensive involvement of the surface epithelium and the glands

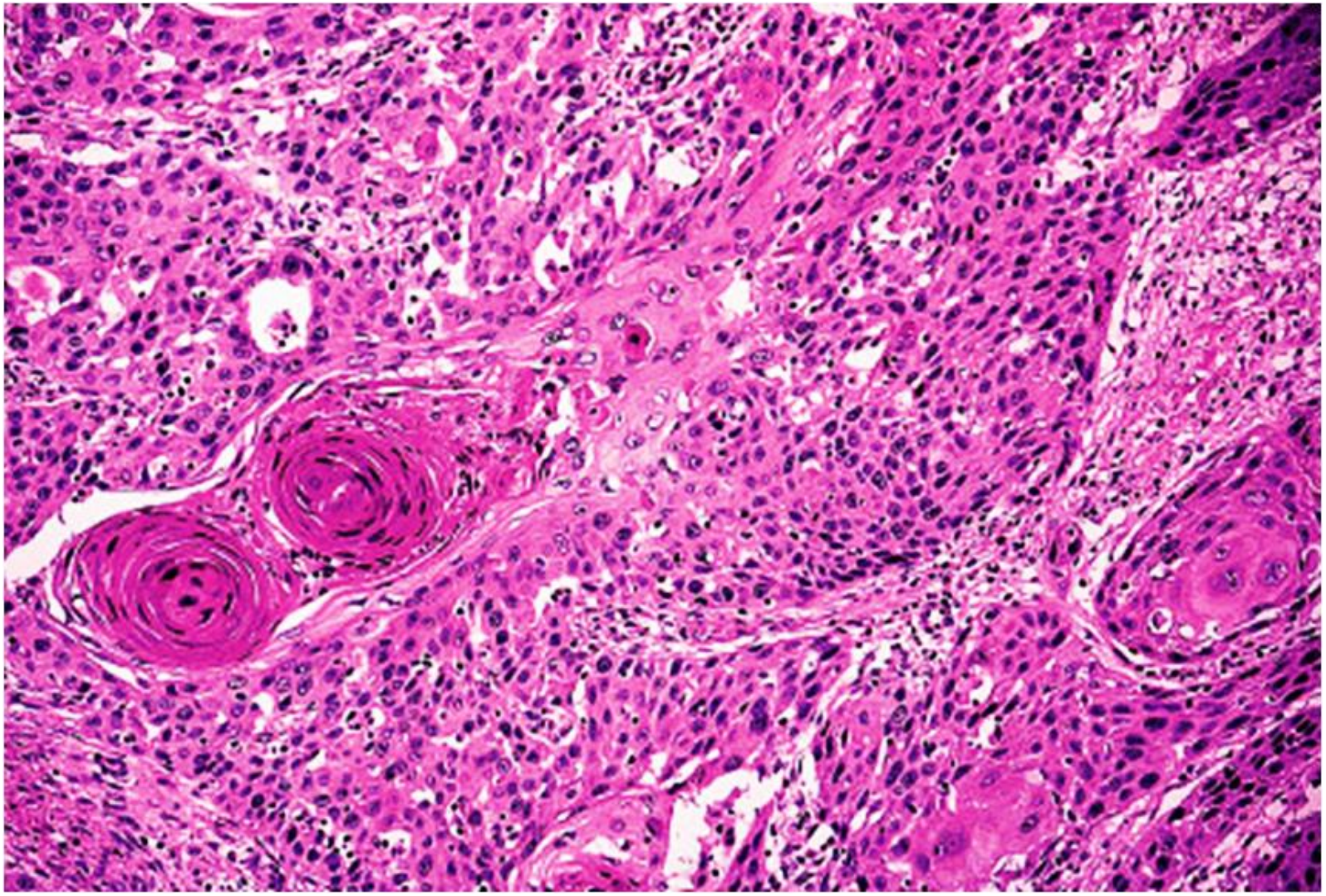
# Grossly visible tumors

- May be exophytic, or
- Encircling the cervix and penetrating into the underlying stroma "barrel cervix"

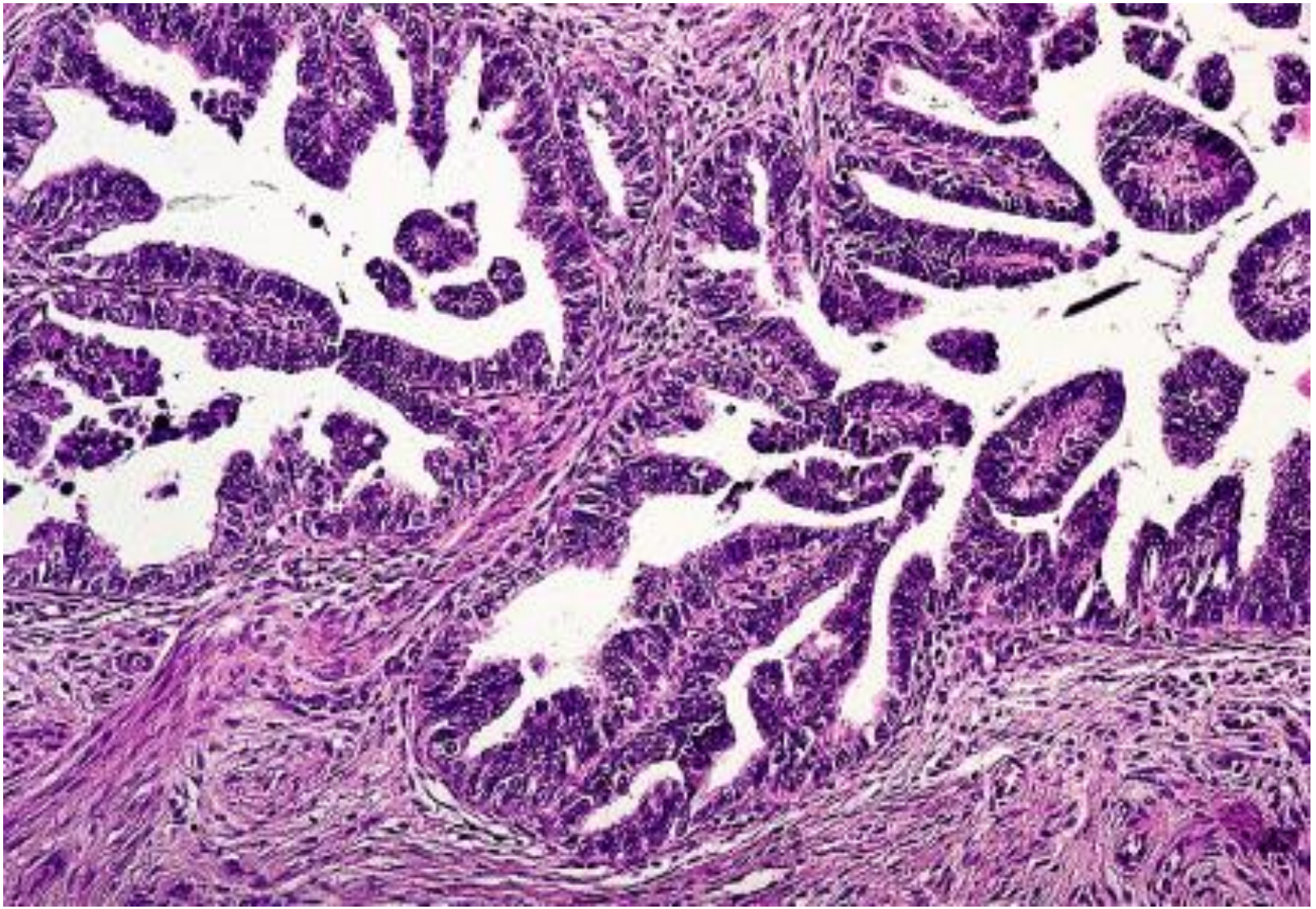
# Cervical cancer



# Invasive squamous cell carcinoma



# Invasive adenocarcinoma



# Tumor spread

- Extension into the parametrial soft tissues
- Extension to bladder and rectum
- Spread to pelvic lymph nodes depends on:
- Tumor depth and the presence of LVI
- Distant metastases occur late including:
- Para-aortic LNs and other organs
- **Tumor stage** is the most important prognostic factor.

Pelvic exentration specimen. Extension to the bladder and rectum

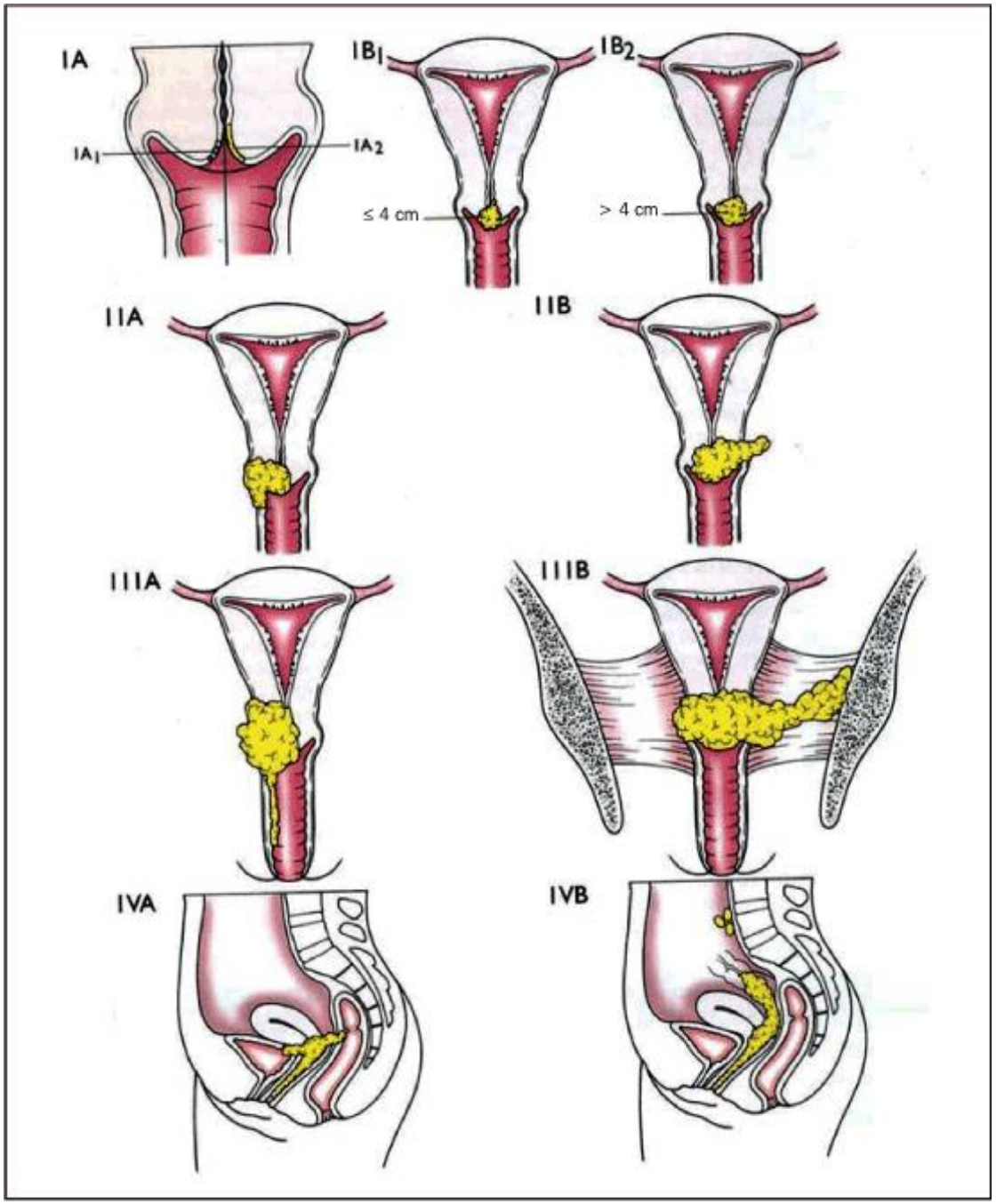
# Clinical Course

- The vast majority of cervical neoplasms are diagnosed in the preinvasive phase.
- More advanced cases are symptomatic:
- Vaginal bleeding, leukorrhea, painful coitus (dyspareunia), and dysuria
- Most common cause of death is renal failure

# FIGO staging system

| FIGO | Extent | 5 year survival |
|---|---|---|
| Stage I | Cervical carcinoma confined to uterus | 90% |
| Stage II | Tumor invades beyond the uterus but not to pelvic wall or to lower third of vagina | 82% |
| Stage III | ▪Tumor extends to the pelvic wall and/or<br>▪Involves the lower third of the vagina and/or<br>▪Hydronephrosis or non-functioning kidney | 35% |
| Stage IV | ▪Tumor invades the bladder or rectum and/or extends beyond true pelvis<br>▪Distant metastasis | 10% |

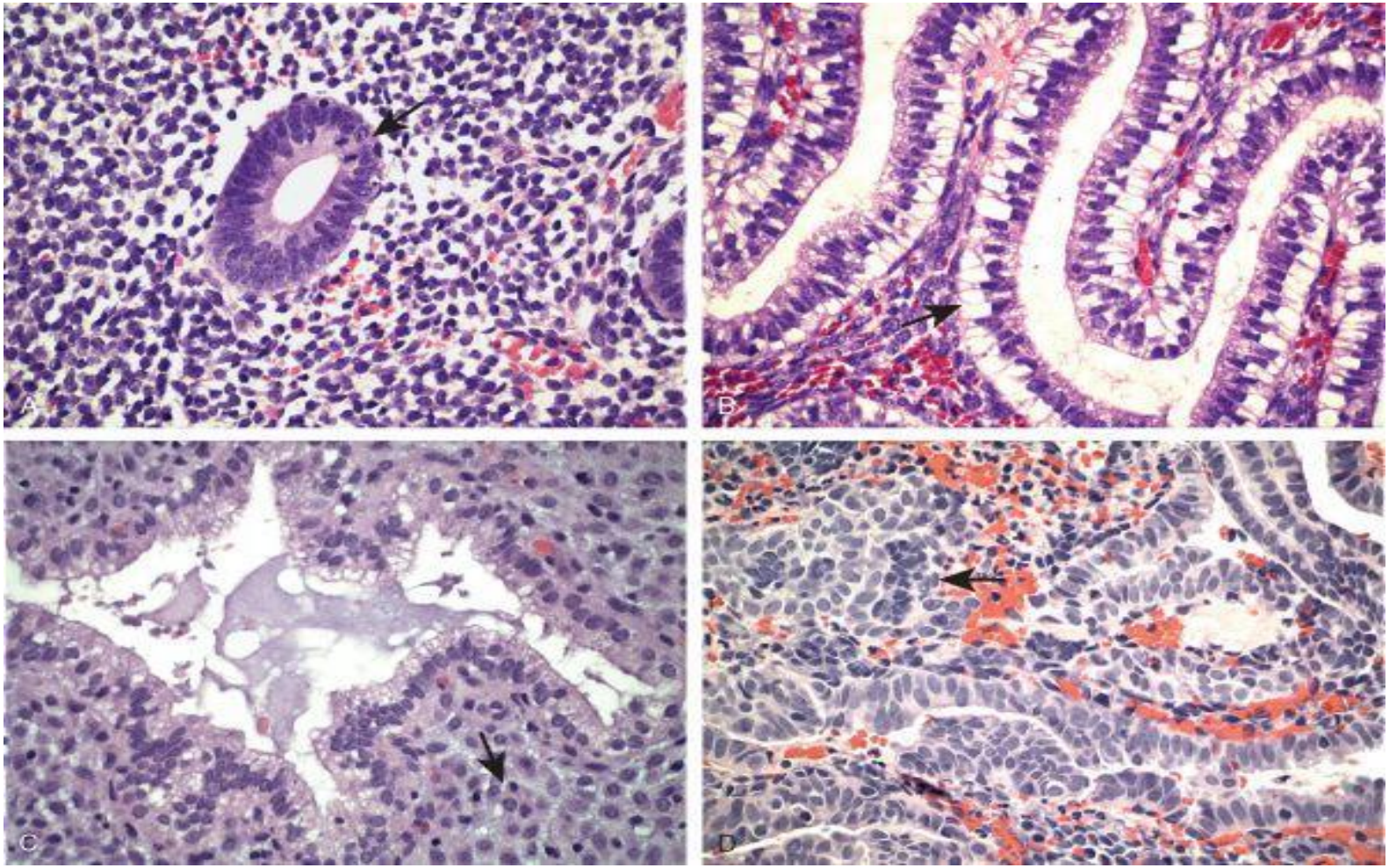
# FIGO staging system



# BODY OF UTERUS

- Endometritis
- Adenomyosis
- Endometriosis
- Abnormal uterine bleeding (AUB)
- Endometrial hyperplasia
- Tumors
  - Endometrial polyps
  - Endometrial carcinomas
  - Smooth muscle tumors

# Endometrium



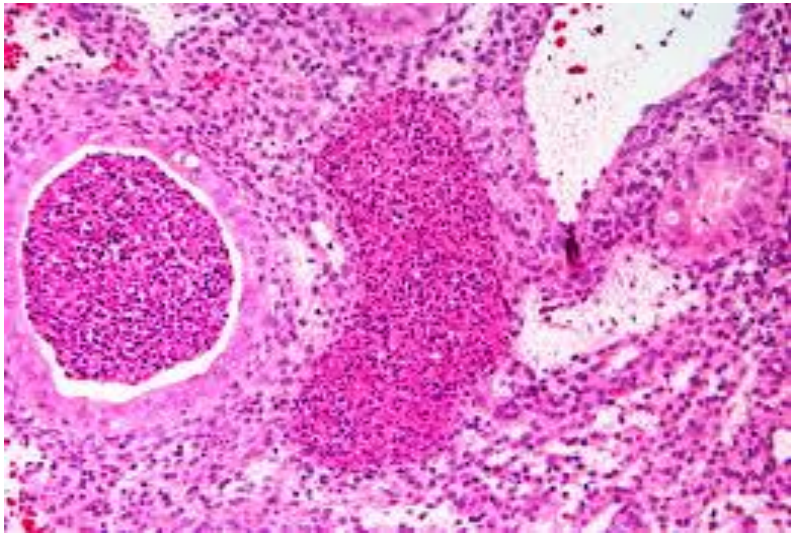
A, Proliferative phase with mitoses B, Early secretory phase with subnuclear vacuoles. C, Late secretory exhaustion and predecidual changes . D, Menstrual endometrium with stromal breakdown

# ENDOMETRITIS

- "Inflammation of the endometrium"
- **Etiology:**
- Pelvic inflammatory disease (PID)
  - Gonoccoci , chlamydia, enteric bacteria
- Retained products of conception
  - Streptococci and staphylococci
- Foreign body as IUCD
- Tuberculosis usually due to spread from tuberculous salpingitis

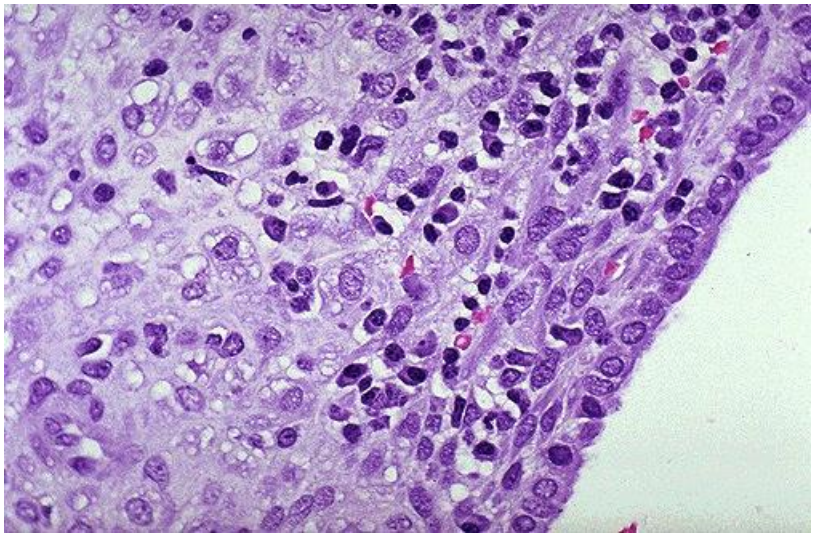
# Morphology

- **Acute endometritis**
- Rarely seen by pathologists
- Neutrophilic infiltration of superficial epithelium and endometrial glands



# Morphology

- **Chronic endometritis**
- Lymphoplasmacytic infiltrate
- Plasma cells are essential for diagnosis
- TB … granulomatous endometritis



# Clinical picture

- Fever
- Abdominal pain
- Menstrual abnormalities (AUB)
- Infertility and ectopic pregnancy due to damage to the fallopian tubes

# ADENOMYOSIS

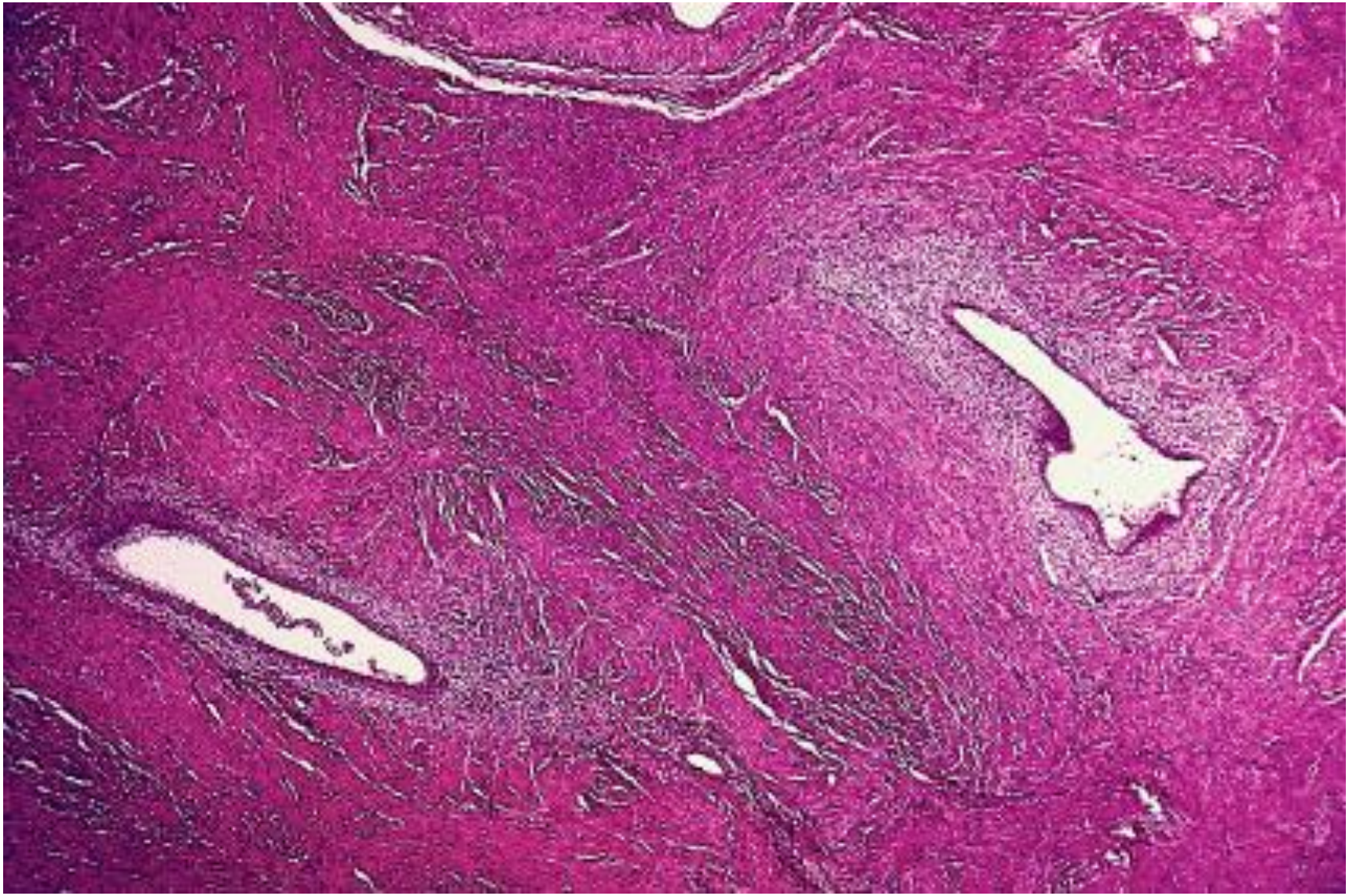
- **Definition:**
- The growth of the basal (non-functional) layer of the endometrium down into the myometrium

- The uterine wall is thickened due to Reactive hypertrophy of the myometrium
- The uterus is enlarged and globular

- C/P: Menorrhagia, dysmenorrhea,& pelvic pain

# Adenomyosis

# Adenomyosis



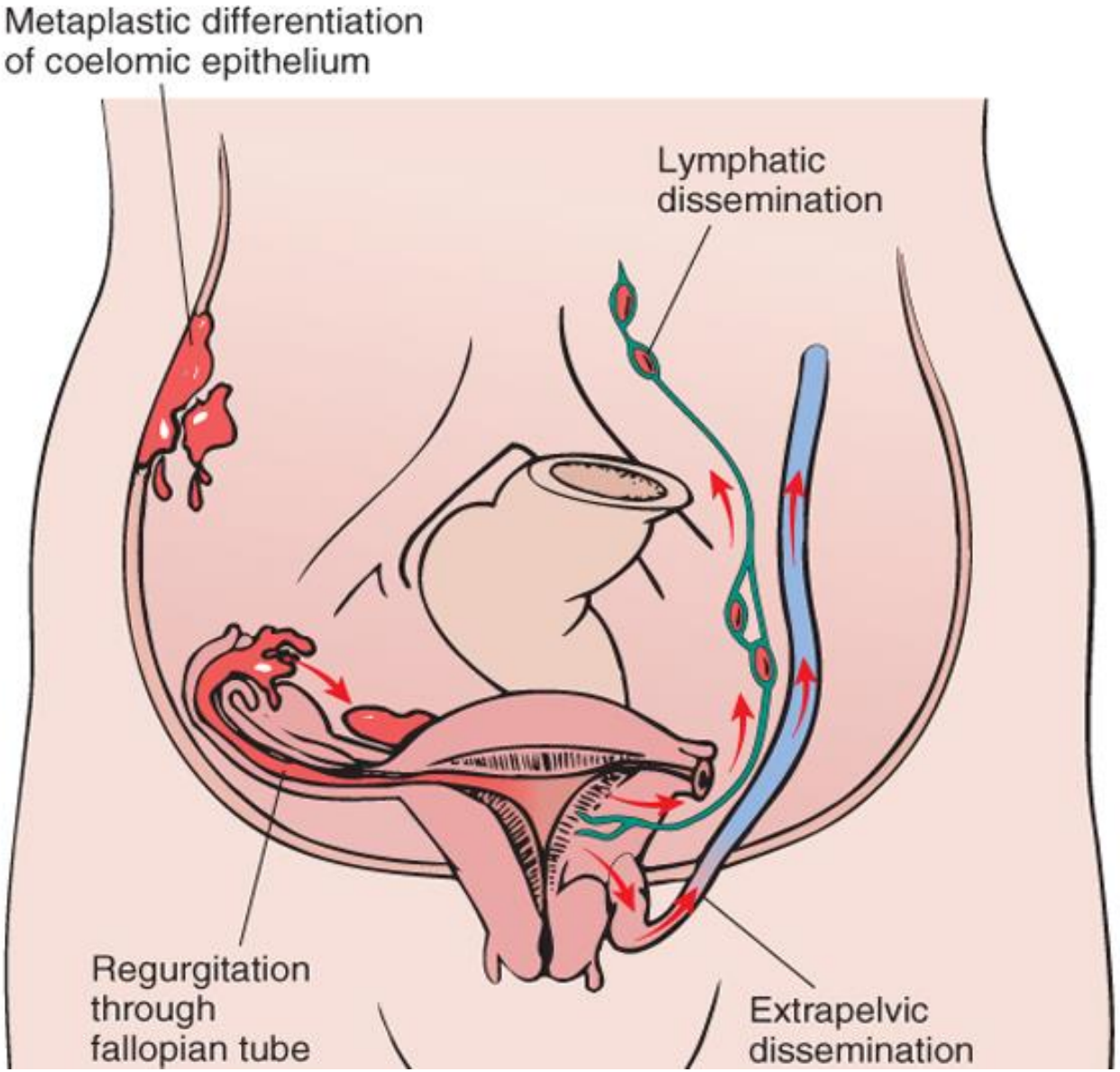
# ENDOMETRIOSIS

- **Definition:**
- The presence of endometrial glands and stroma outside the endomyometrium
- 10% of women in their reproductive years
- 50% of women with infertility
- **Clinical picture**
- Dysmenorrhea and pelvic pain
- Pelvic mass filled with blood as chocolate cyst
- Infertility

# Site

- Frequently multifocal
- Ovaries, the most common site
- Pouch of Douglas
- Uterine ligaments
- Fallopian tubes
- Rectovaginal septum
- Pelvic peritoneum
- Vulva and vagina
- Laparotomy scars
- Umbilicus, lymph nodes, lungs

# Pathogenesis



# Morphology

- Functioning endometrium, which undergoes cyclic bleeding

- **Gross appearance:**
- Red-blue to brown nodules or implants
- lie on or just under the serosal surface
- In ovaries, the lesions may form large blood-filled cysts **(chocolate cysts)**

# Choclate cyst

# Morphology

- **Microscopic examination:**
- Finding two out of three features: Endometrial glands, endometrial stroma, or hemosiderin pigment

- **Complications:**
- Organization of the blood leads to fibrosis
- Adherence of pelvic structures, sealing of the tubal ends, and distortion of the ovaries
- (frozen pelvis)

# Endometriosis