



Pathology of Lower Female Genital Tract

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Vulvar Diseases- Topics

NON-NEOPLASTIC (MORE COMMON):

LICHEN SCLEROSUS

LICHEN SIMPLEX CHRONICUS

CONDYLOMA ACCUMINATUM

NEOPLASTIC (LESS COMMON):

DYSPLASIA (VIN)

VULVAR CANCER

Pathology of Lower Female Genital Tract

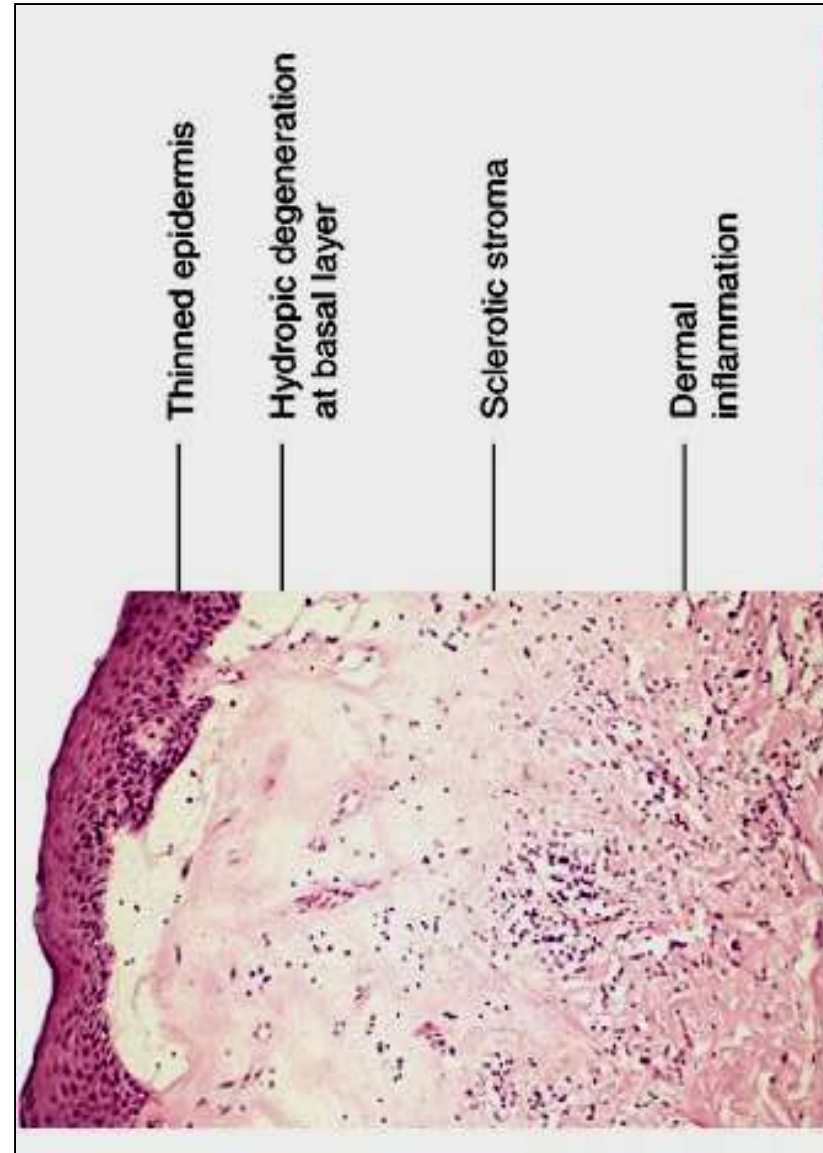
- **Vulvar Diseases:**
- Include non-neoplastic and neoplastic diseases.
- The neoplastic diseases are much less common.
- Of the neoplastic disorders, **squamous cell carcinoma is the most common.**

Non-neoplastic Vulvar Diseases

- **Lichen sclerosus**
- **Lichen Simplex Chronicus**
- **Condyloma accuminatum**

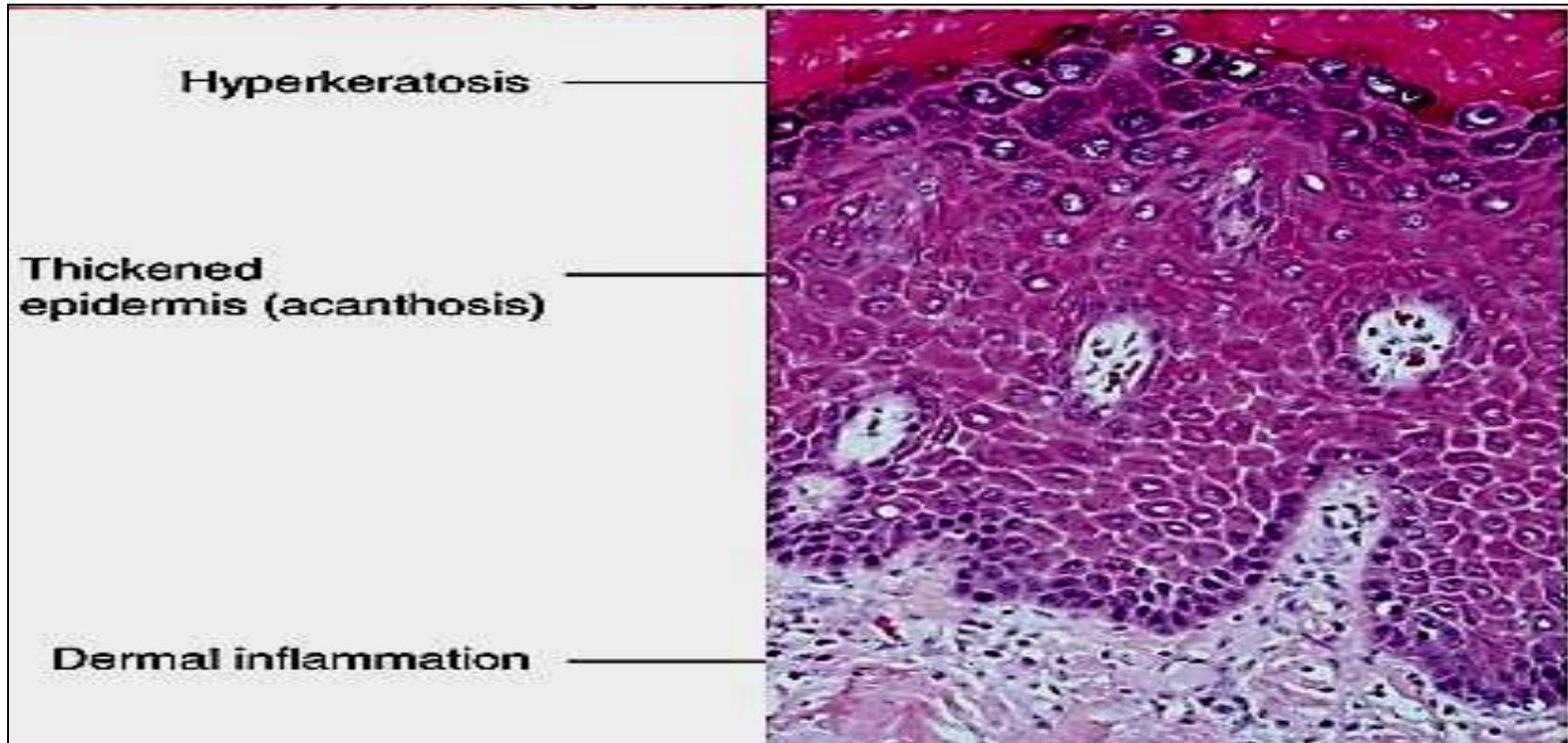
Lichen sclerosus

- **postmenopausal** women.
- white plaques; thinned out skin
- Microscopically: thinning of epidermis, disappearance of rete pegs, hydropic degeneration of basal cells
- pathogenesis: uncertain, (?)**autoimmune**
- is **not** pre-malignant by itself



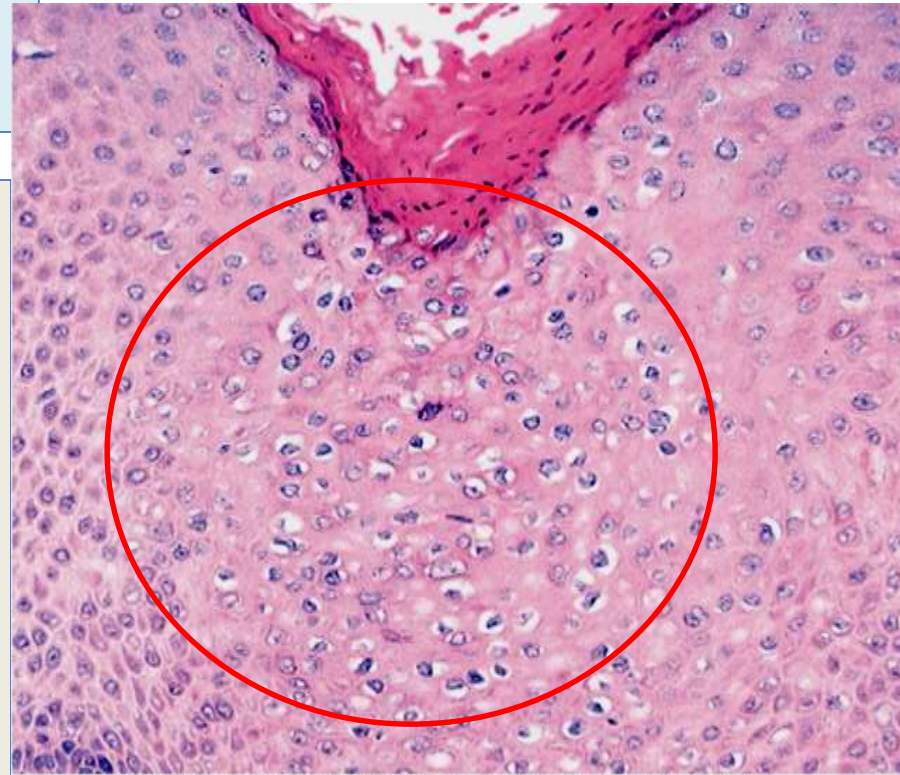
Lichen Simplex Chronicus

- end result of many inflammatory conditions
- **Clinical term: leukoplakia** (whitish plaque)
- epithelial thickening, hyperkeratosis, epithelium shows **no** atypia.
- **no increased predisposition to cancer**, however, maybe present at margins of adjacent cancer.

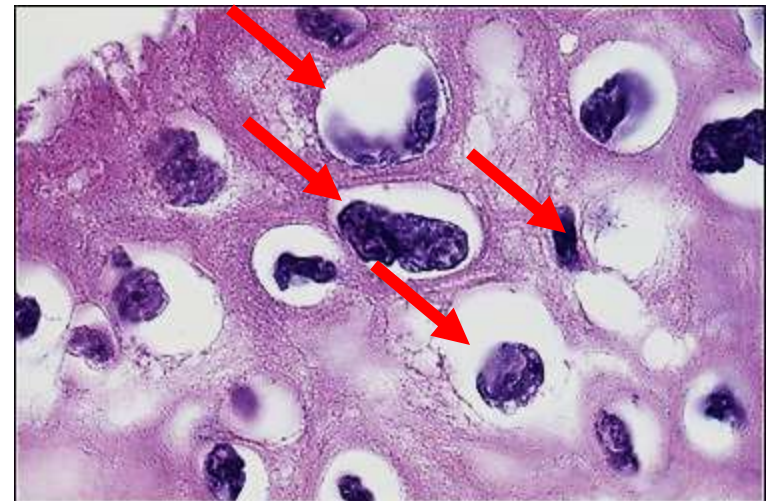


Condyloma

- Anogenital warts
- Infection by HPV (HPV type 6 and HPV type 11, mainly)
- **koilocytosis** (perinuclear cytoplasmic vacuolization + nuclear pleomorphism).
- HPV types isolated from cancers differ from those found in condylomas.
- Condyloma is **not** precancerous by itself.



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Neoplastic Vulvar Diseases

1- Vulvar Intraepithelial Neoplasia (VIN)

2- Invasive Carcinoma of Vulva:

- Types include:

Squamous Cell Carcinoma (most common);

adenocarcinomas; melanomas; basal cell carcinomas

HPV & Female Genital Diseases

- A common sexually transmitted infection of genital tract.
- Many different types of HPV including low risk and high risk types (risk here is for malignancy).
- Low risk HPV → anogenital warts (condylomas)
- High risk types → intraepithelial dysplasia and invasive cancers in all parts of lower female genital tract (vulva; vagina; and cervix) as well as male genital tract.
- Condylomas are similar in all these organs.
- Intraepithelial dysplasia and invasive cancers produced by HPV are similar in pathogenesis and morphology in all of these locations.

HPV & Female Genital Diseases

- **high-risk HPV types (16, 18, 45, and 31)** account for majority of precancerous lesions and invasive anogenital cancers
- peak age of **intraepithelial** neoplasia is about 30 years, whereas invasive cancer is about 45 years (progression to invasion needs 10-15 yr).
- HPV can be detected by molecular methods in nearly all precancerous lesions and invasive HPV-related anogenital neoplasms.

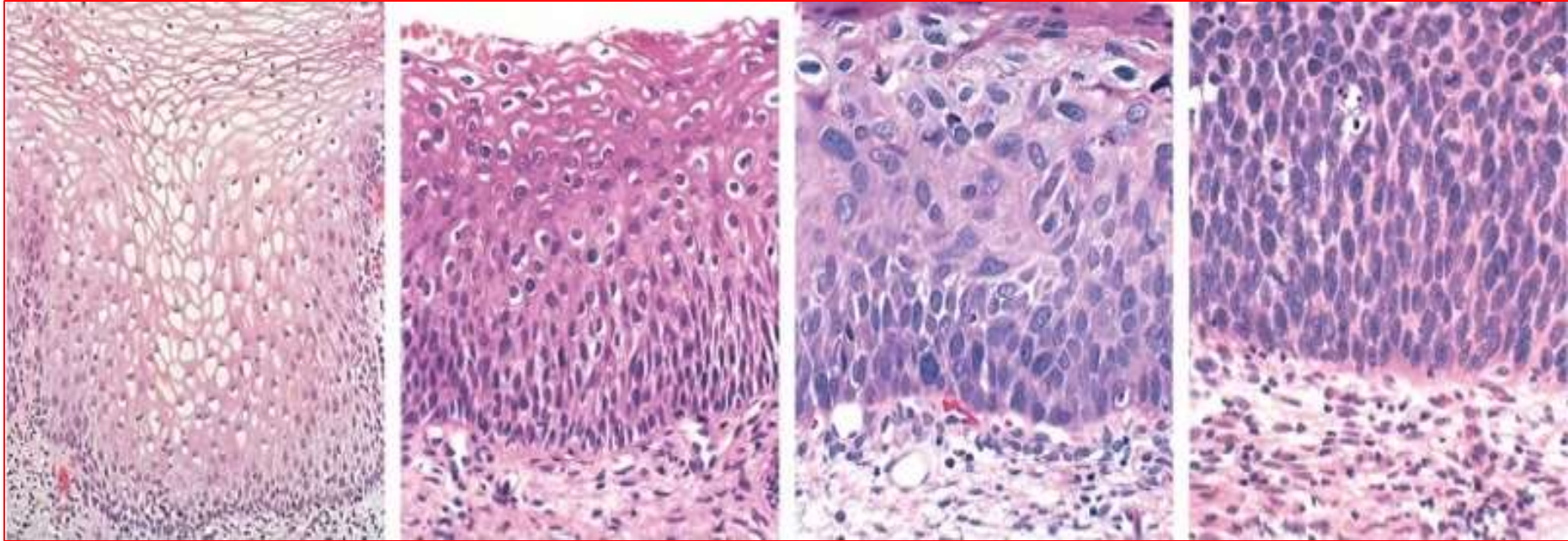
- **High** risk HPV (especially HPV 16 and 18) usually integrate into the host genome and express large amounts of certain viral proteins called E6 and E7 proteins, which block or inactivate tumor suppressor genes p53 and RB, respectively. → accumulation of **mutations** and **DNA damage** eventually leads to **malignancy**
- recently introduced HPV vaccine used in USA and Europe is effective in preventing HPV infections and hence cervical cancers and other anogenital HPV-related cancers.

Intraepithelial Neoplasia (IN)- concepts:

- High risk HPV causes mutations in cells
- Dysplasia is graded depending on extent of epithelial involvement:
 - ***IN I:** Mild dysplasia (<third of full epithelial thickness)
 - ***IN II:** Moderate dysplasia (up to 2/3 of full epithelial thickness)
 - ***IN III:** Severe dysplasia in full epithelial thickness (is equivalent to **carcinoma in situ**)

Same concept and similar morphology in all lower genital tract organs.

Dysplasia = increased N/C ratio, nuclear enlargement, hyperchromasia, and abnormal nuclear membranes



Normal

IN 1

IN 2

IN 3

Vulvar dysplasia:

VIN 1

VIN 2

VIN 3

Vaginal dysplasia:

VaIN 1

VaIN 2

VaIN 3

Cervical dysplasia:

CIN 1

CIN 2

CIN 3

High-grade Intraepithelial Neoplasia and Carcinoma of **Ano-genital** Organs

- **high grade IN= IN II or IN III.**
- **IN III = carcinoma in situ**
- **may be multiple foci, or it may coexist with an invasive lesion.**
- **IN may be present for many years before progression to cancer.**
- **?genetic, immunologic, environmental influences (e.g., cigarette smoking or superinfection with new strains of HPV) determine the course.**

Vulvar Squamous cell carcinoma SCC

there are two biologic forms:

1- Basaloid or poorly differentiated SCC

- ❖ most common (90%)
- ❖ relatively younger
- ❖ HPV-related
- ❖ HPV lesions also in vagina and cervix.
- ❖ Poorly differentiated cells

2- Well-differentiated SCC

- ❖ Less common
- ❖ older women (60-70s).
- ❖ **Not** HPV-related
- ❖ Maybe found adjacent to lichen simplex or sclerosus
- ❖ well to moderately differentiated cells

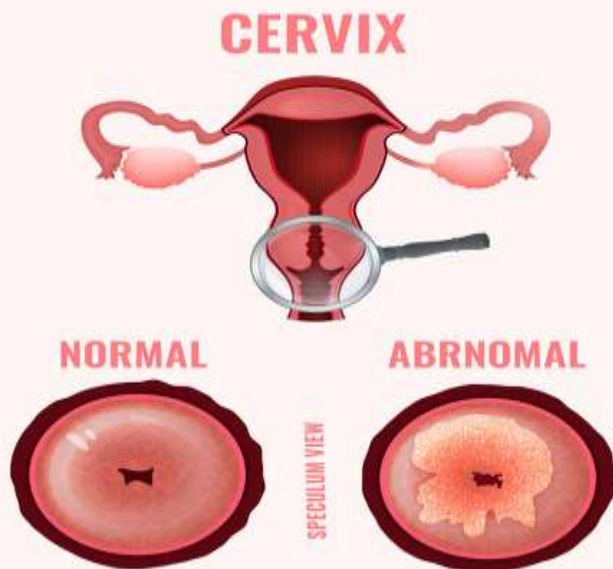
Cervical Diseases

PAP SMEAR TEST

CERVICAL CANCER

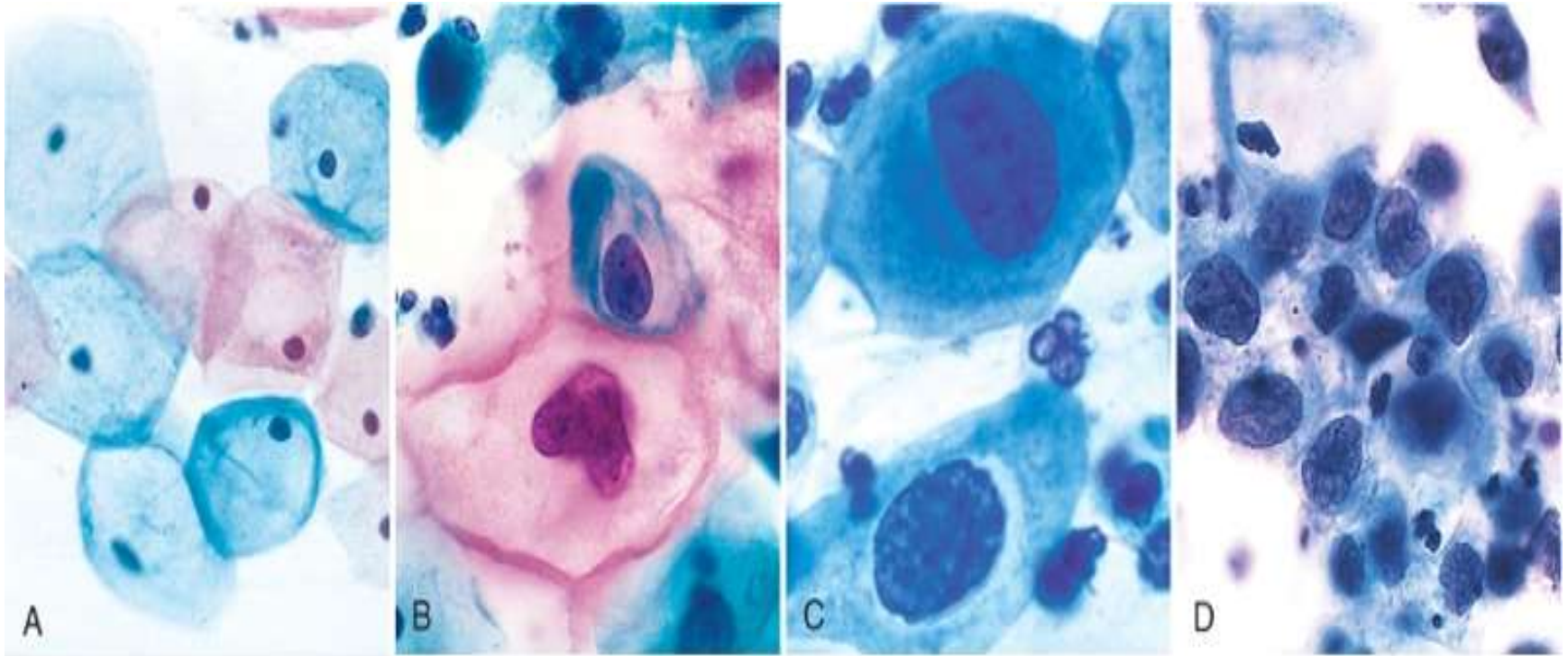
Cervical Carcinoma

- Used to be the most frequent cancer in women
- Papanicolaou (Pap) cervical smear: a screening test for detection of HPV related lesions of the uterine cervix.
- Cervical cancer incidence dropped (early detection of pre-invasive and early cancer). It helped reduce cervical ca mortality by 99%.



cervical smear

Cervical Pap smear pictures



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Normal

CIN I

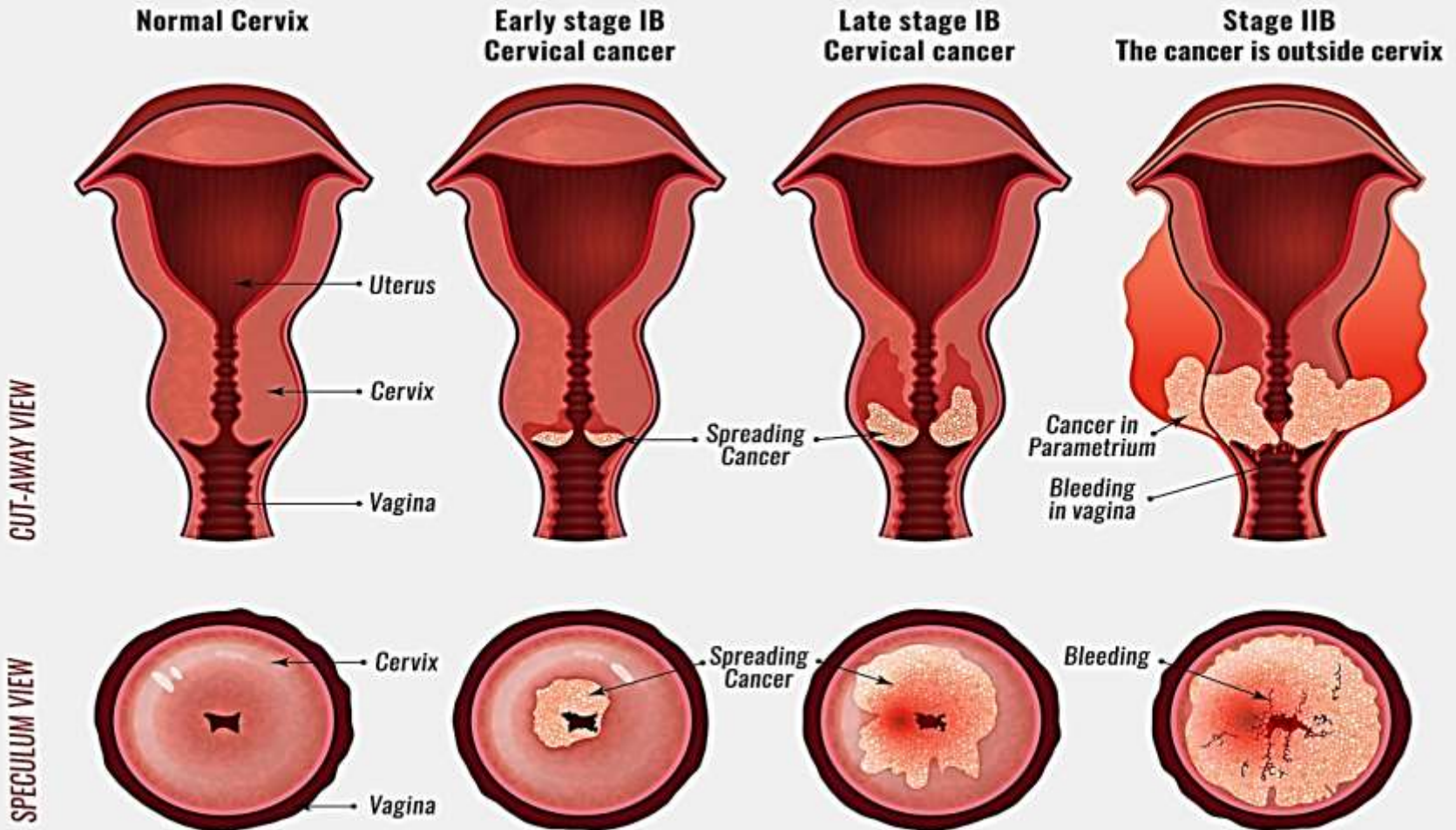
CIN II

CIN III

Cervical Cancer

- Types: most common are SCC (75%), followed by adenocarcinomas and adenosquamous carcinomas (20%), and neuroendocrine carcinomas (<5%).
- SCC now has peak incidence at 45 years, almost **10 to 15 years after detection of their precursors: cervical intraepithelial neoplasia (CIN)**

Cervical cancer stage is one of the most important prognostic factors



Clinical Aspects of Cervical Cancers

- CIN: treatment by **laser or cone biopsy**
- Invasive cancer: surgical excision
- 5-year survival drops with increased stage:
 - Pre-invasive (CIN)→ 100%;
 - stage 1→ 90%;
 - stage 2→82%;
 - stage 3→ 35%;
 - and stage 4→ 10%.
- Radiotherapy and Chemotherapy in advanced cases