



# PATHOLOGY

- SHEET NO. 8
- WRITER : **Anas Ananzeh**
- CORRECTOR :
- DOCTOR : **Nisreen Abu Shahin**

# Pathology of Lower Female Genital Tract

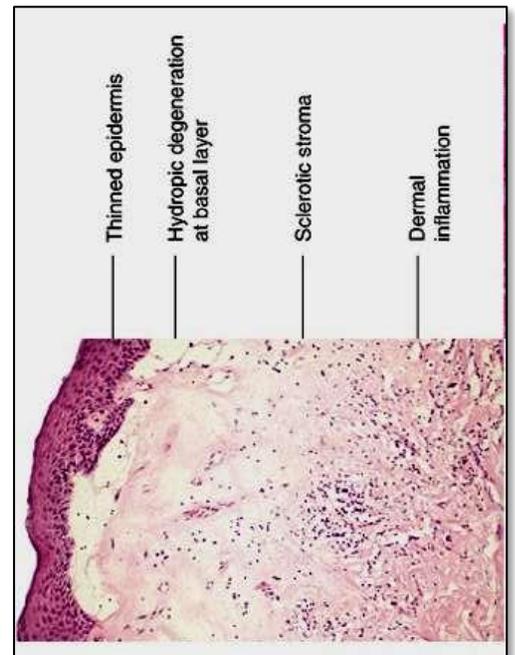
## ❖ Vulvar Diseases ❖

| NON-NEOPLASTIC ( <u>More common</u> ):   | NEOPLASTIC ( <u>Less common</u> ):   |
|--|--|
| <ol style="list-style-type: none"><li>1. LICHEN SCLEROSUS</li><li>2. LICHEN SIMPLEX CHRONICUS</li><li>3. CONDYLOMA ACCUMINATUM</li></ol> | <ol style="list-style-type: none"><li>1. DYSPLASIA</li><li>2. VULVAR CANCER</li></ol> <p><small>*Squamous cell carcinoma is the most common disorder</small></p> |

### → Non-Neoplastic diseases:

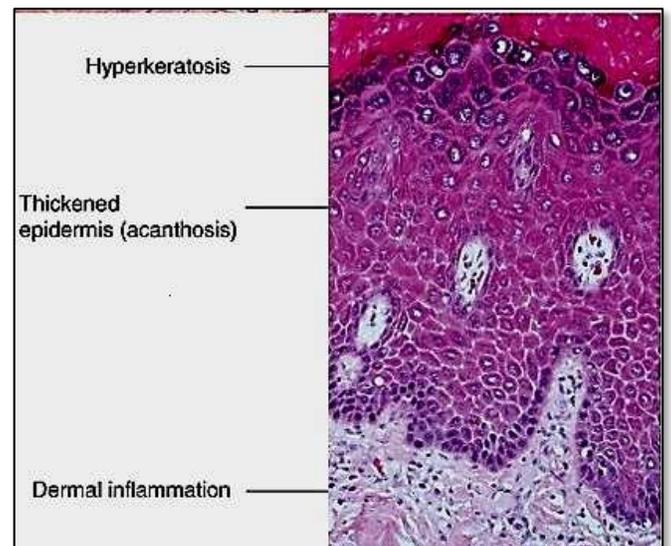
#### ★ Lichen Sclerosus:

- Mainly affects postmenopausal women
- Leads to production of white plaques, thinned out skin
- **It's not premalignant by itself** (it doesn't lead to cancer by itself)
- **Pathogenesis:**
  - Uncertain, but it might be an autoimmune process (related to inflammation)
- **Microscopically:**
  - thinning of epidermis,
  - disappearance of rete pegs,
  - hydropic degeneration of basal cells



#### ★ Lichen Simplex Chronicus:

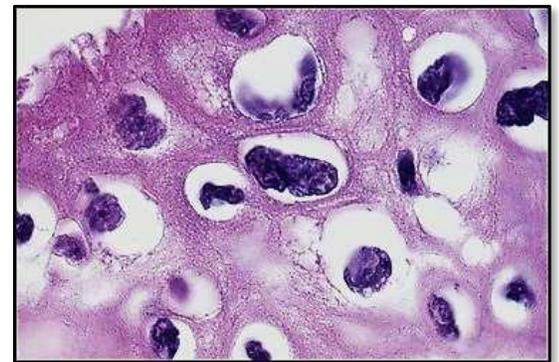
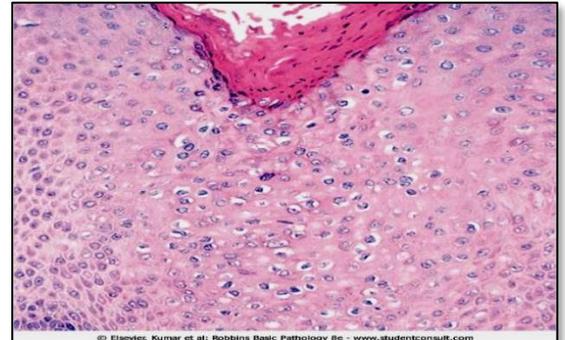
- End result of many inflammatory conditions
- Clinically, it's represented by **leukoplakia** (whitish plaque)
- **No increased predisposition to cancer (and it's not a cancer)**, however, maybe present at margins of adjacent cancer.



- **Microscopically:**
  - ➔ Epithelial thickening,
  - ➔ Hyperkeratosis,
  - ➔ Epithelium doesn't show any atypia,
  - ➔ The underlying dermis shows mild to moderate inflammation

### ★ Condyloma:

- Anogenital warts
- STD infection by HPV (HPV type 6 and HPV type 11, mainly)
- **Condyloma is not precancerous by itself and it's not a cancer**
- HPV 6 & 11 are called low-risk types
- The whole mark of this skin lesion is the presence of **Koilocytes**
- **Koilocytosis:** the presence of abnormal morphology in the keratinocytes because the presence of virus inside it, also because of viral replication in the cytoplasm
- **Microscopically:**
  - ➔ **Koilocytosis:**
    - 1) perinuclear cytoplasmic vacuolization
    - 2) nuclear pleomorphism (abnormal shape of the nucleus and abnormal hollow surrounding the nucleus)



### 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 these locations.
- **high-risk HPV types (16, 18, 45, and 31)** account for majority of precancerous lesions and invasive anogenital cancers
- peak age of intraepithelial (preinvasive) 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 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.

### → Neoplastic diseases:

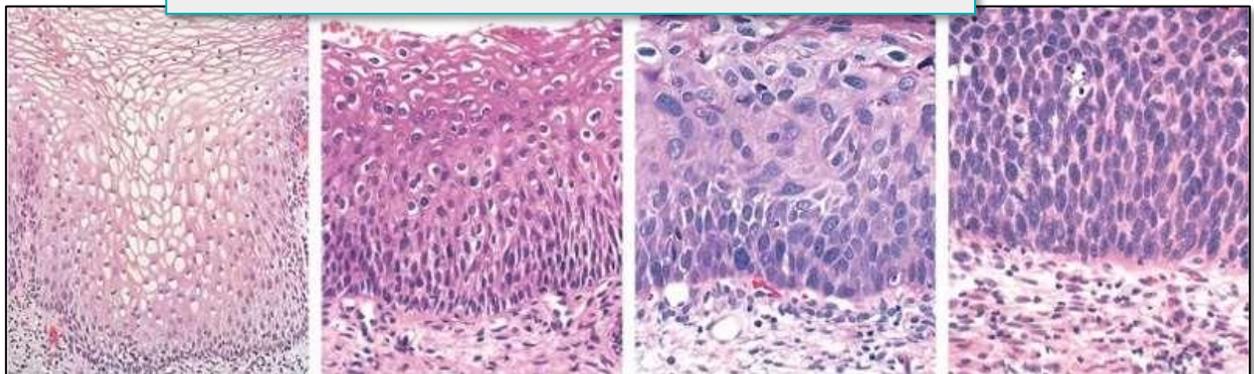
#### 1. Vulvar Intraepithelial Neoplasia (VIN)

2. **Invasive Carcinoma of Vulva:** types: Squamous cell carcinoma (most common), adenocarcinoma, melanomas, basal cell carcinoma

### ★ Intraepithelial Neoplasia (IN) - concepts:

- High risk HPV causes mutations in cells
- Dysplasia (which is a step before invasive cancer) is graded depending on extent of epithelial involvement:
  1. **IN I:** Mild dysplasia (<third of full epithelial thickness)
  2. **IN II:** Moderate dysplasia (up to 2/3 of full epithelial thickness)
  3. **IN III:** Severe dysplasia in full epithelial thickness (**is equivalent to carcinoma in situ**)
- **Intraepithelial Neoplasia concept applies to every place in anogenital tract that's infected by HPV (in the Vulvar, Vagina, Cervix & male genital tract)**
- **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
- So many factors, such as: genetic, immunologic, environmental influences (e.g., cigarette smoking or superinfection with new strains of HPV) determine the course.

## ★ Vulvar squamous cell carcinoma SCC:

- The most common type of invasive carcinoma
- There are two biologic forms:

### 1. Basaloid or poorly differentiated SCC

- The most common (90%)
- Patients are relatively younger
- HPV-related (High risk HPV)
- HPV lesions also in vagina and cervix.
- Poorly differentiated cells

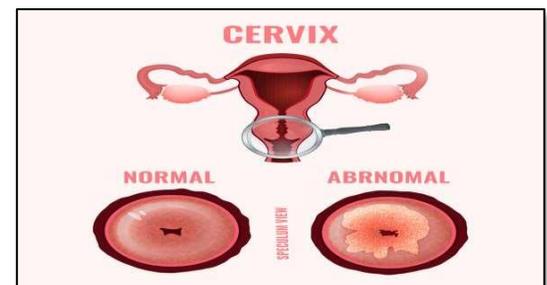
### 2. Well-differentiated SCC

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

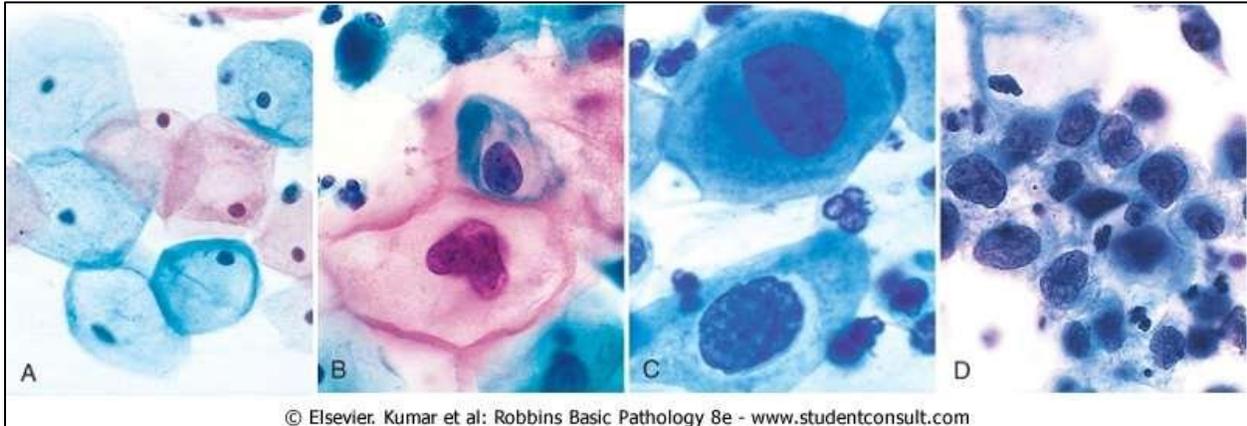
## ❖ Cervical Diseases ❖

### ★ Cervical carcinoma:

- **Used** to be the most frequent cancer in women
- Also it was one of the most common cancers to cause death
- But everything changed when the screening test (Pap) was produced
- Papanicolaou (Pap) cervical smear : مسحة عنق الرحم : a screening test for detection of HPV related lesions of the uterine cervix.
- The area that the swab is taken from is a transitional zone (between endocervical glands and squamous epithelium)
- The doctor who invented this method, took a swab from the transitional zone, and screened it under microscope, then he saw cells (squamous epithelium/keratinocytes), and by comparing different slides he invented a grading system with different stages.
- Cervical cancer incidence dropped (**early detection of preinvasive and early cancer**). It helped reduce cervical ca mortality by 99%.



## Cervical Pap smear pictures



Normal

CIN I

CIN II

CIN III

N/C ratio increases as we increase the stage

Nucleus gets more irregular, darker (hyperchromatic) & larger as we increase the stage

What does a larger nucleus mean? It means the DNA is more active, and the cell is replicating more

- **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**
- **Treatment:**
  - **CIN: Treatment by laser or cone biopsy**
  - **Invasive cancer: Surgical excision**
  - **Advanced cases: Radiotherapy and chemotherapy**
- **5 Year survival drops with increased stage:**
  - Pre-invasive (CIN) → 100%;
  - stage 1 → 90%;
  - stage 2 → 82%;
  - stage 3 → 35%;
  - and stage 4 → 10%.

### Past Papers

1- ONE is correct regarding human papilloma virus (HPV) associated disorders in the female genital tract :

- a. Condyloma accuminatum is caused by HPV type 18 infection
- b. Progression from dysplasia to invasive cancer is the role in all cases
- c. Dysplasia of the lower third of cervical mucosa is equivalent to CIN3
- d. Infection and related lesions of HPV can only affect the cervix
- e. HPV type 16 leads to human cell dysplasia through viral proteins E6 and E7

2-The major differences between the dysplastic cells in cervical dysplasia (CIN) and the normal cervical epithelial cells include all of the following except :

- a. nuclear contour irregularities
- b. size of nuclei
- c. High N/C ratio (nuclear/ cytoplasmic ratio)
- d. number of nuclei per cell
- e. nuclear hyperchromasia

3-The grade of the cervical condition to involve the full thickness of epithelium is:

- a. CIN I
- b. CIN II
- c. CIN III
- d. None of the above

Answers:

1. E
2. D
3. C