Pathology of the lower female genital tract

- **Vulvar Diseases:**

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

Non-neoplastic vulvar diseases

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

skin disease that cause change in color and consistency of skin. usually manifest as enduration or change in color

Lichen sclerosus

- postmenopausal women.
- smooth, white plaques; thinned out skin

severe cases, prolonged condition patient will face atrophy, stenosis of the area.

- Microscopically: thinning of epidermis, disappearance of rete pegs, hydropic degeneration of basal cells

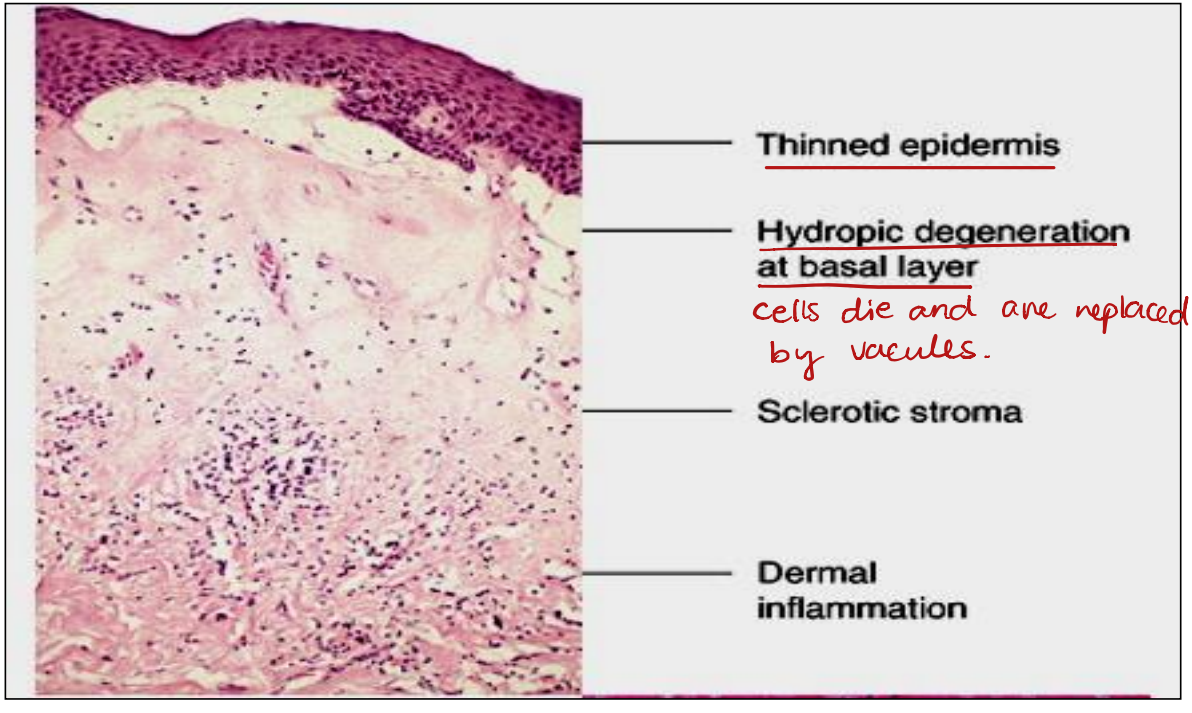
- pathogenesis: uncertain, (?)autoimmune

for injury of keratinocytes

- lichen sclerosus is not pre-malignant by itself

↳ Dysplasia → invasive cancer

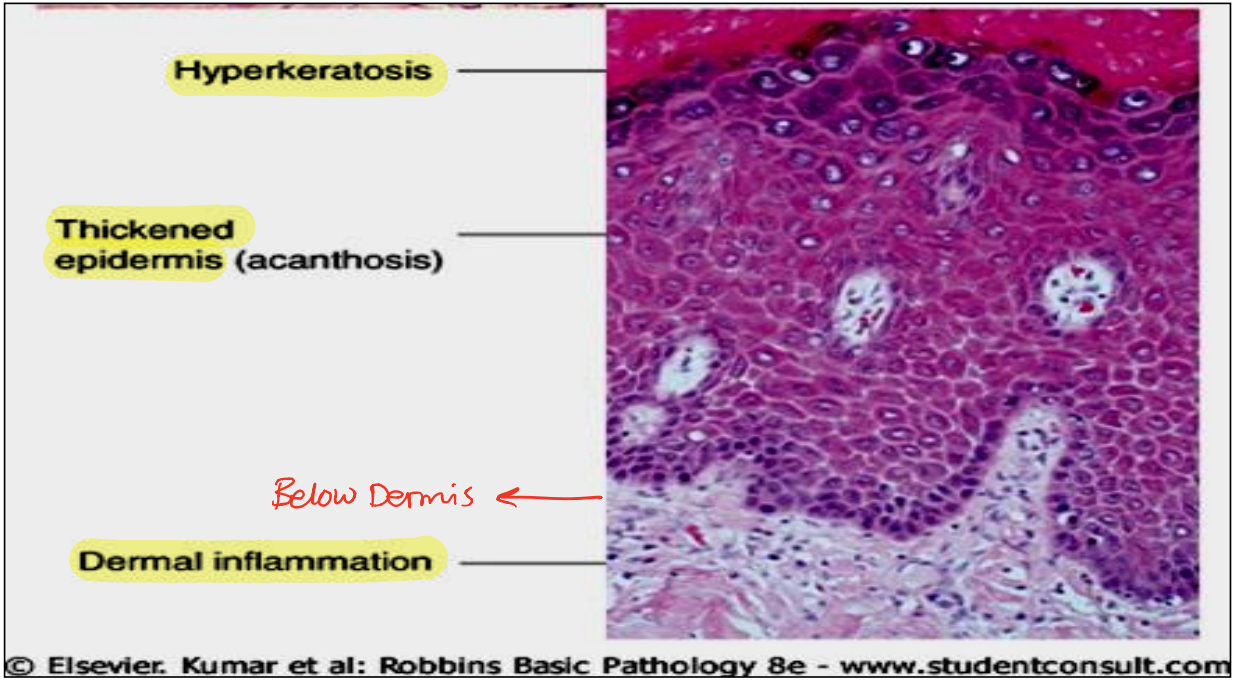
Lichen sclerosus



Lichen Simplex Chronicus

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

Lichen simplex chronicus



Condylomas

↳ Human Papilloma virus

- **Anogenital warts (HPV type 6 and HPV type11)**

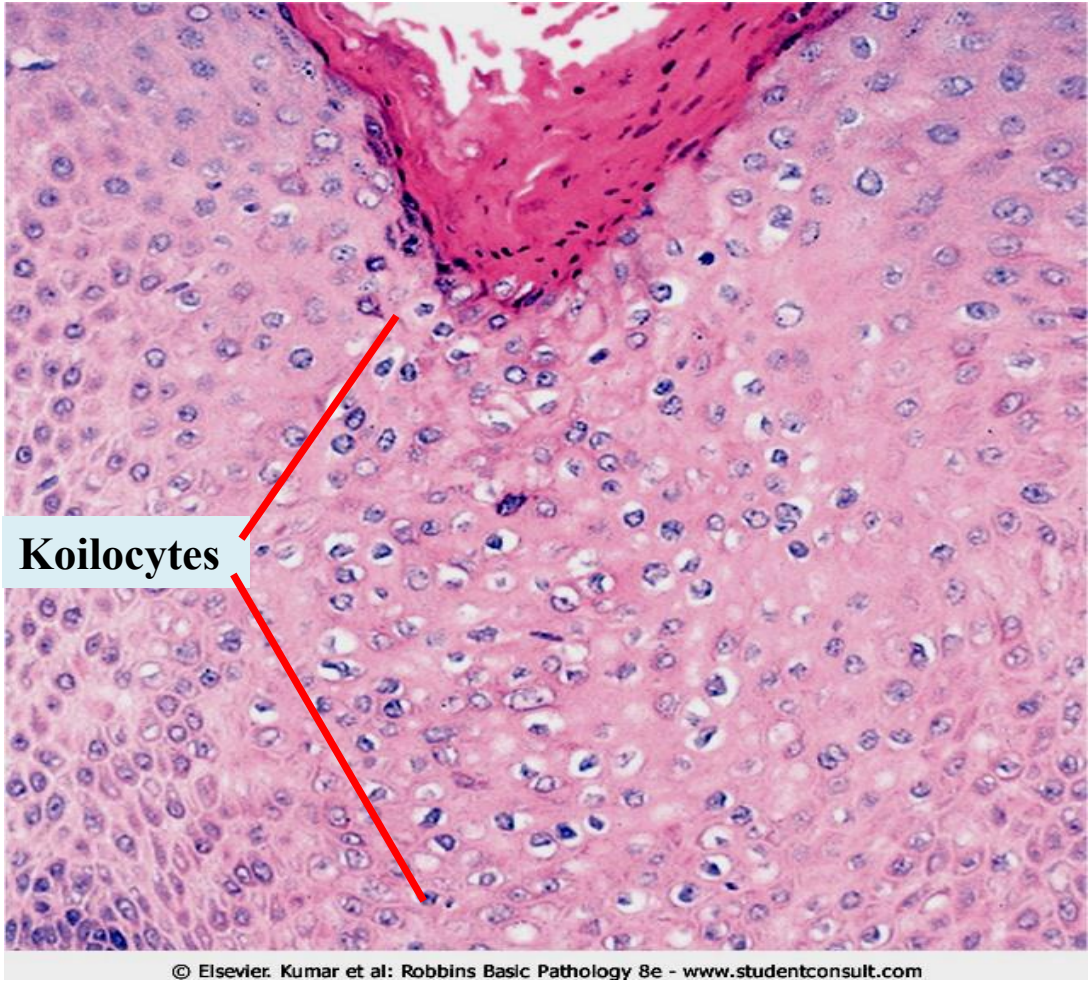
This virus is also responsible for much worse diseases, which are the cancers + precancers

- **Hallmark= koilocytosis (perinuclear cytoplasmic vacuolization + nuclear pleomorphism).**
- **HPV types isolated from cancers differ from those found in condylomas.** For cancer ↔ Low Risk : 6,11 → warts / High Risk: 16, 18
- **Condyloma is not precancerous by itself.**

Macroscopically / Grossly → Cauliflour Like / raised Lesions on skin

Microscopically → Hallmark. (koilocytosis) infection of the keratinocytes

Condyloma acuminatum



Neoplastic vulvar diseases

1- Vulvar Intraepithelial Neoplasia (VIN)

if persists, transforms into

2- Invasive Carcinoma of Vulva:

Squamous Cell Carcinoma (most common);

adenocarcinomas, melanomas, or basal cell carcinomas

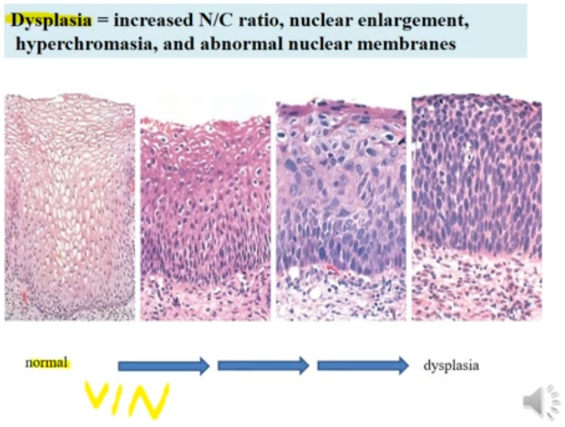
High-Grade Vulvar Intraepithelial Neoplasia and Carcinoma of the Vulva

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

The doctor gave extra details about Vulvar intraepithelium neoplasia which i couldnt fit into the previous page:

Similar lesions to the VIN could be also found in different places like the vagina, cervix (CIN) or even the male genital tract; with the same concept and morphology of lesions.

It is an infection due to a high risk HPV which causes changes in the DNA of the cell by giving it the characteristic of a malignant cell. It has the capacity to integrate itself into the genome of the host cell and every replication causes replication of the viral genome. This virus has many special viral proteins which promote cell division/DNA replication, most important ones are the E6, and E7 which inhibit the regulators of the cell cycle retinoblastoma (RB) and p53 **respectively**. their presence is important to maintain the normal DNA and prevent transformation into something malignant, once inhibited the cell cycle becomes autonomous which means it would start at anytime without an initiator, leading to high and abnormal replication even if the DNA needs repair. This cell is under high risk of mutations, so with time cells will accumulate mutations and will transform into something malignant. if left untreated, it will transform to an invasive cancer.



Here is a picture from the video, the cells here as we move right are gaining changes recognized as dysplasia, the numbers change moving to the right (more severe) as the number increases it indicates the higher level of severity;
VIN I —> less then 1/3 dysplastic cells
VIN II—> more than 1/2 dysplastic cells
VIN III —> full thickness dysplastic tissue, worst degree of dysplasia

VIN III is equivalent to carcinoma in situ which means it is malignant but is still not invasive. **The average age for the peak incidence of this lesion is 30.** So the only difference between cancer and this lesion is the invasion.
Not all lesions are transformed into cancer, some of them regress, stay the same or transform into invasive cancer. The risk factors related to the fate of the lesions is not very clear, some people say that we have genetic or immunologic or environmental factors.
The average age for the peak incidence of the invasive cancer is 45. We can detect the lesion before invasion which help in early detection and treatment of pre-cancers.

Carcinoma of the Vulva

- 3% of all genital tract cancers in women.
- > 60 years.
- 90% →squamous cell carcinomas;
- **Squamous cell carcinoma SCC:** there are two biologic forms of vulvar SCC:

First type of SCC (basaloid or poorly differentiated SCC):

- most common (75% to 90%)
- relatively younger
- HPV-related (types 16 & 18) → DNA of virus in the cancer.
- HPV lesions also in vagina and cervix.
- Poorly differentiated cells

The second form of SCC (well-differentiated SCC):

- older women (60-70s).
- **Not** HPV-related
- Less common
- well to moderately differentiated
- Maybe found adjacent to lichen simplex or sclerosus → still not pre-cancerous.

Vaginal Neoplastic Diseases

- **Sarcoma botryoides (embryonal rhabdomyosarcoma):**
- Rare sarcoma of **skeletal** muscle type
- infants and **children** <5 years.
- soft polypoid masses (botryoides= grape-like).
- Primitive cells (**rhabdomyoblasts**)

Cervical pathology

- **Cervical carcinoma**
- Used to be the most frequent cancer in women
- Papanicolaou (Pap) smear → cervical cancer incidence dropped (early detection of pre-invasive and early ca). It helped reduce cervical ca mortality by 99%, ranking it 13th in cancer deaths for women recently.

Swab from cervix at transformation zone.
it is placed in a solution and viewed under light microscope.
↳ Liquidate cytologic examination.
You will observe the shape of the nucleus, cytoplasm and N/C ratio. and decide whether cells are normal / abnormal

Cervical cancer

- 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 intraepithelial neoplasia (CIN)

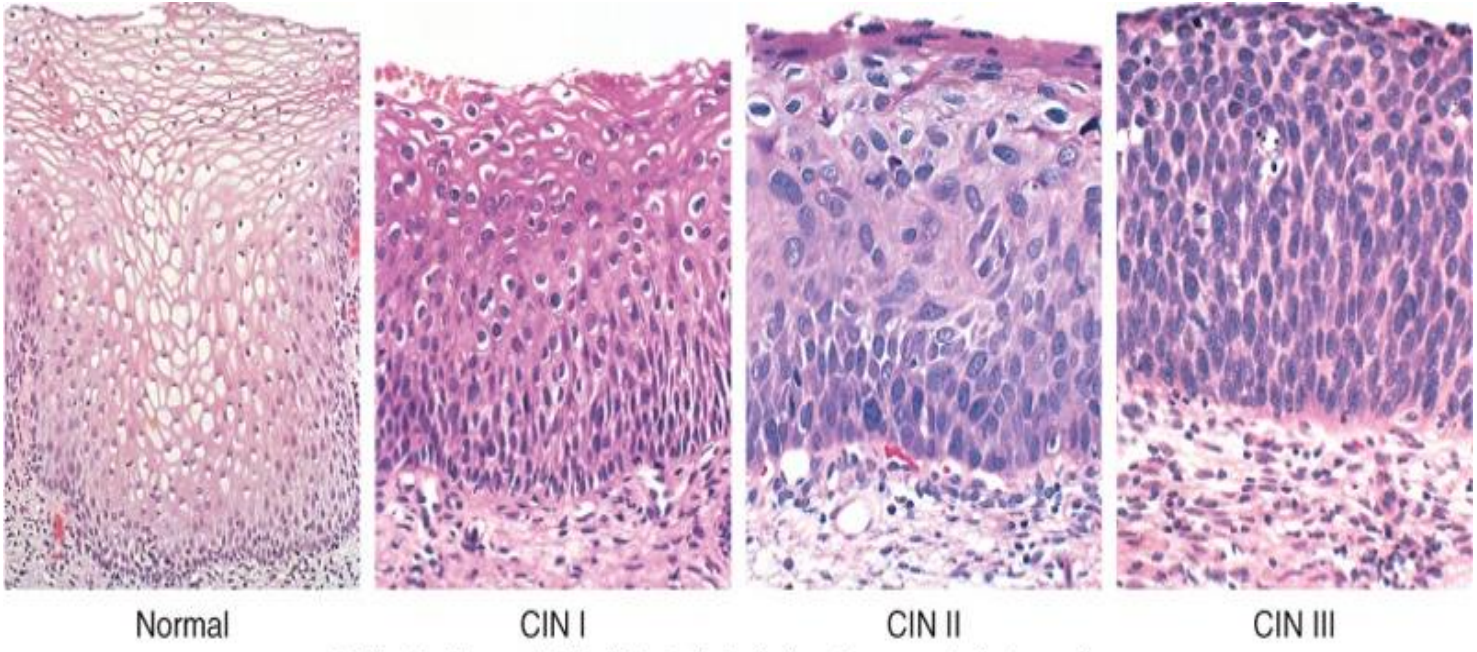
- Dysplasia graded depending on the extent of epithelial involvement:

*__CIN I__: Mild dysplasia (<third of full epithelial thickness)

*__CIN II__: Moderate dysplasia (up to 2/3 of full epithelial thickness)

*__CIN III__: Severe dysplasia in full epithelial thickness (carcinoma in situ)

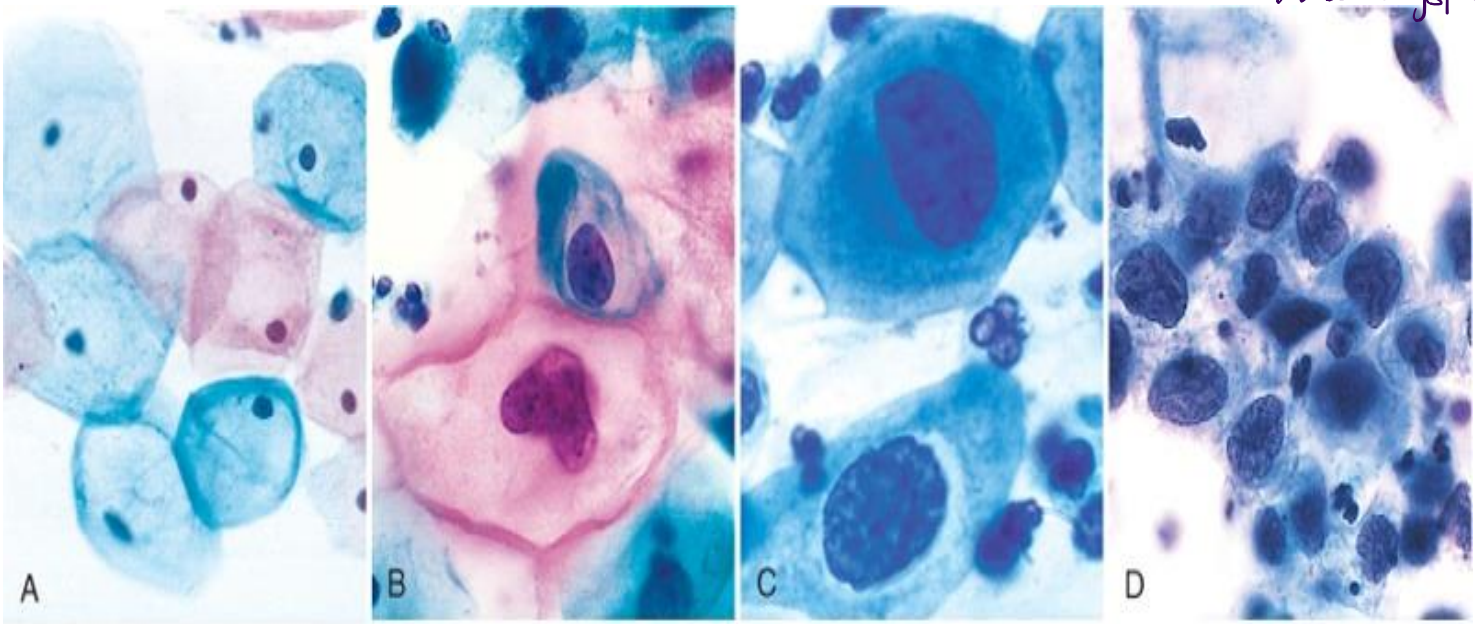
Dysplasia = increased N/C ratio, nuclear enlargement, hyperchromasia, and abnormal nuclear membranes



going to the right → hyperchromatic cells, larger nucleus, DNA is high/abnormal.
→ less differentiated. → N/C ratio is increasing → Abnormal cells.

Pap smear pictures

full thickness dysplasia



Normal **CIN I** **CIN II** **CIN III**

↓

Can detect as early as this stage.

Carcinoma in situ.

CIN-Epidemiology and Pathogenesis

- peak age of CIN is 30 years, whereas invasive cancer is about 45 years.
- HPV can be detected by molecular methods in nearly all precancerous lesions and invasive neoplasms.
- high-risk HPV types (16, 18, 45, and 31), account for majority of cervical ca

- HPV 16 and 18 usually integrate into the host genome and express large amounts of **E6 and E7 proteins, which block or inactivate tumor suppressor genes *p53* and *RB*, respectively**. (discussed previously)

- recently introduced **HPV vaccine** used in USA and Europe is effective in preventing HPV infections and hence cervical cancers.

Clinical Aspects Of Cervical Cancers

- CIN: treatment by **laser or cone biopsy** in gyne clinic
- Invasive cancer: surgical excision
- 5-year survival: preinvasive→ 100%; stage 1→ 90%; stage 2→82%; stage 3→ 35%; and stage 4→ 10%.
- Radiotherapy and Chemotherapy in advanced cases