

Lecture 5

Topic:
Lower female genitalia
pathology

*Written according to section 3 recording
Anything added is written in italics*

The doctor almost didn't add anything worth mentioning in the lecture, she only read the slides

Pathology of the lower female genital tract

- **Vulvar Diseases:**

Vulva = female external genitals

- Can be divided to 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**
(warts)

*These are dermatosis
diseases (skin diseases)*

*After Infection by
HPV6/11*

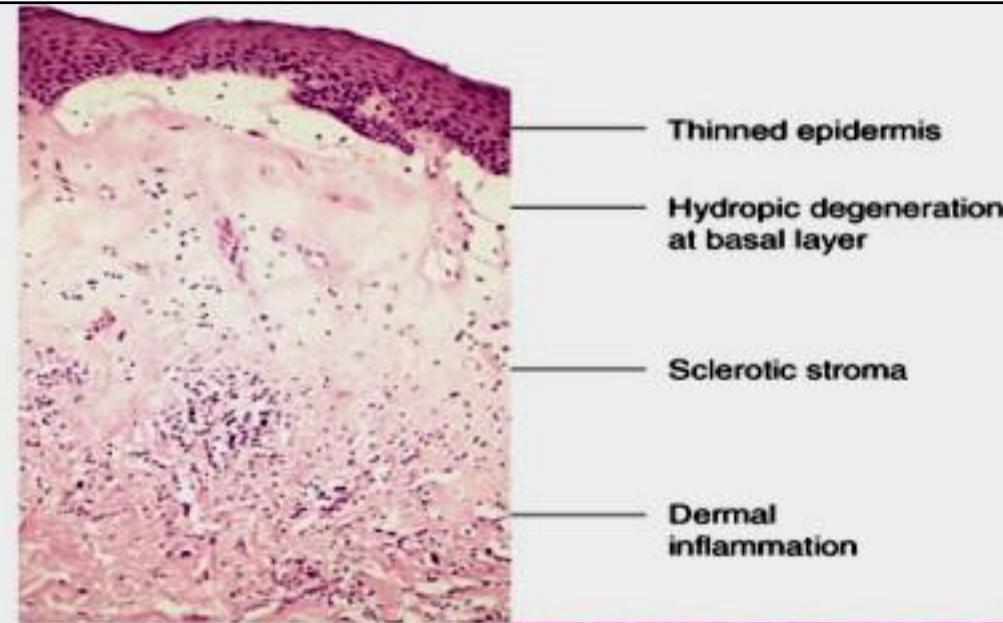
Lichen sclerosus

- postmenopausal women.
- smooth, white plaques; thinned out skin
- Microscopically: thinning of epidermis, disappearance of rete pegs, hydropic degeneration of basal cells
- pathogenesis: uncertain, (?)**autoimmune**
- lichen sclerosus is **not** pre-malignant by itself ,*but in clinical examination it might look like a pre-cancerous stage.*

These patients seek medical help because of 2 things:
1- they cause discomfort and cosmetic changes.
2-they might look like a pre-cancerous lesion.

Extra:
Rete pegs are epithelial extensions from the skin into the underlying connective tissue.

Lichen sclerosus

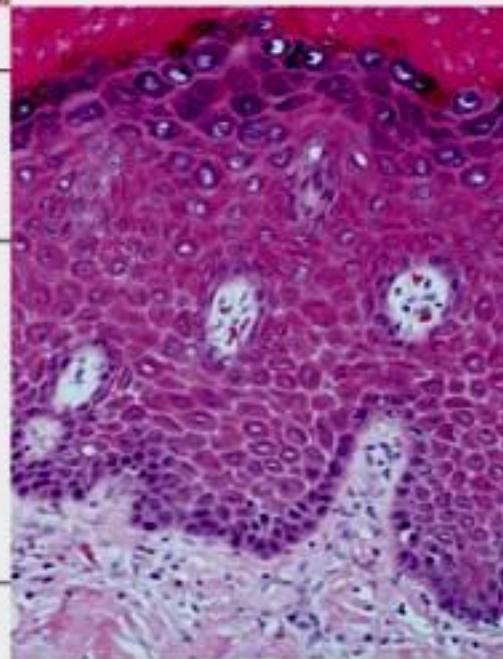


Hyperkeratosis

Thickened epidermis (acanthosis)

Dermal inflammation

Lichen simplex chronicus



Lichen Simplex Chronicus

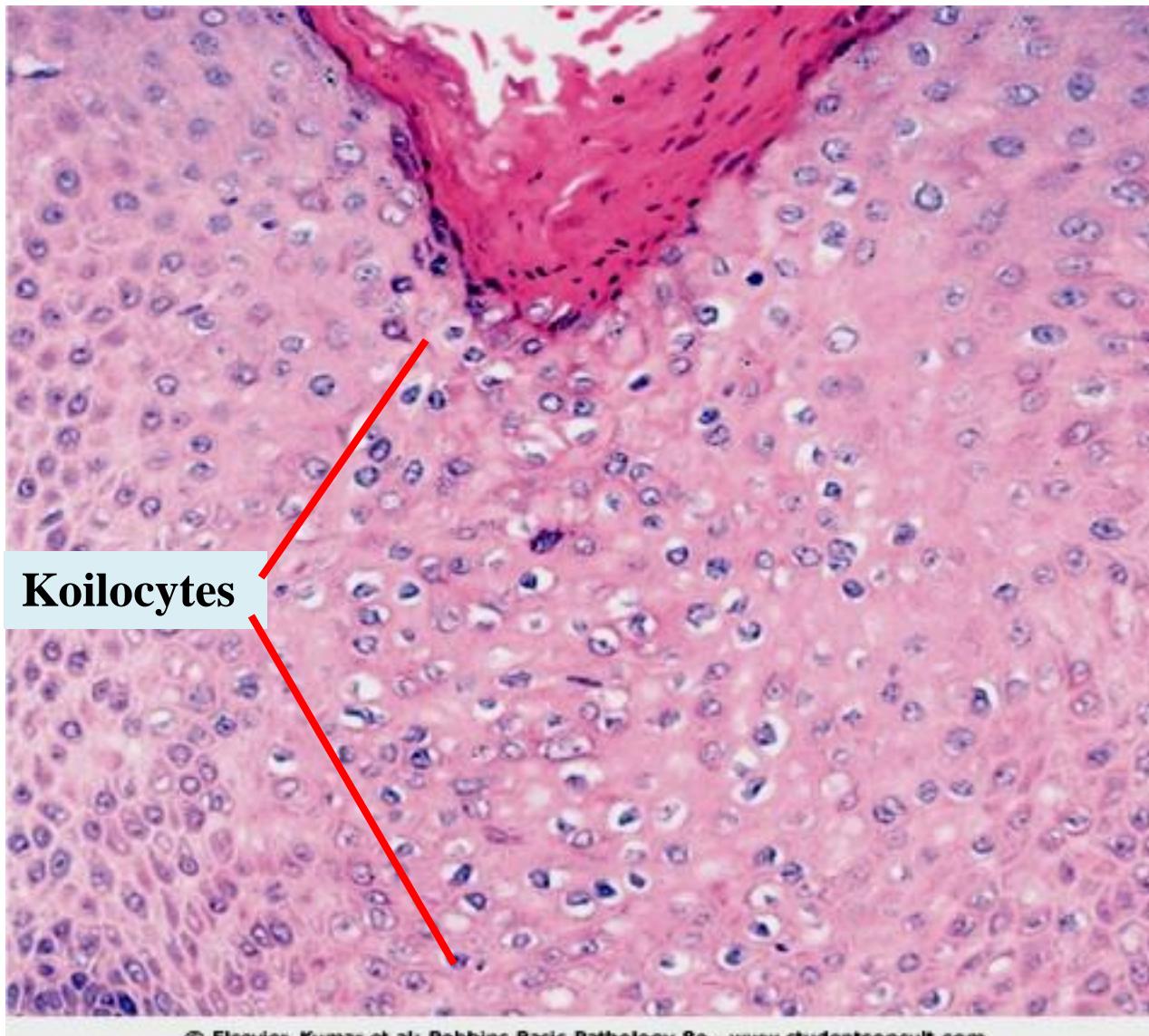
- *As you can relate from the name, this disease occurs due to a persistent chronic inflammation.*
- end result of many inflammatory conditions
- **Leukoplakia (*whitish plaques*)**.
The opposite to what happens in lichen sclerosis
- epithelial thickening, hyperkeratosis,
epithelium shows **no** atypia.
- **no increased predisposition to cancer**,
however, often present at the margins of adjacent cancer.

Condylomas

- Anogenital warts (HPV type 6 and HPV type 11)
- Hallmark (*microscopically*) = koilocytosis, *these are epidermal cells that are infected with the virus* (perinuclear cytoplasmic vacuolization (Halo) + nuclear pleomorphism).
- HPV types isolated from cancers differ from those found in condylomas.
- Condyloma is not precancerous by itself.

These types of HPV (6/11) are called low-risk types, because other types might result in a cancer (high-risk types)

Condyloma acuminatum



Neoplastic vulvar diseases

1 Vulvar Intraepithelial Neoplasia (VIN)

2 Invasive Carcinoma of Vulva:

**Squamous Cell Carcinoma (most common);
others:**

adenocarcinomas, melanomas, or basal
cell carcinomas

High-Grade Vulvar Intraepithelial Neoplasia

- -Here we have a dysplastic change in the cells, but the lesion is not invasive (considered a pre-malignant stage).
- high grade VIN (*vulvar intraepithelial neoplasia*) = **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.

*If the lesion is left without treatment, there is a high probability that cancer will develop.
(it's considered cancer if it invades across the basement membrane)*

Carcinoma of the Vulva

- 3% of all genital tract cancers in women.
- > 60 years (*elderly*).
- 90% → squamous cell carcinomas;
- remainder are: adenocarcinomas, melanomas, or basal cell carcinomas.
- **Squamous cell carcinoma SCC:** there are two biologic forms of vulvar SCC (*depending on the morphology of the neoplastic cells*):

1-basaloid or poorly differentiated type

2-well differentiated type

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

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

High risk types

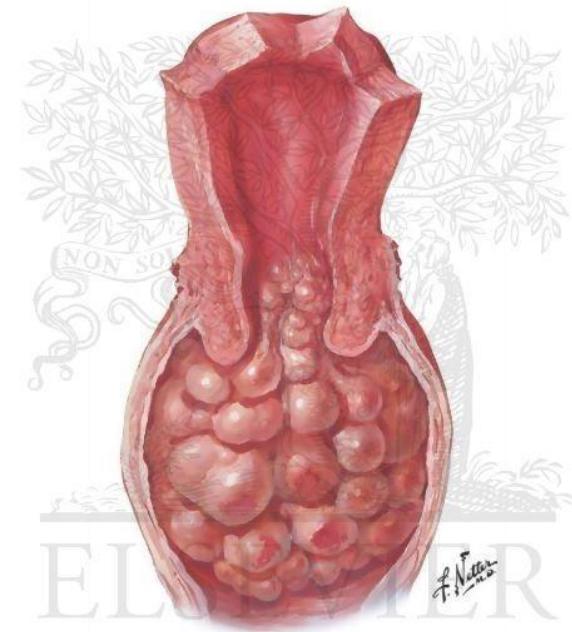
The second form of SCC (well-differentiated SCC):

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

Vaginal Neoplastic Diseases

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

*Sarcoma : so its of mesenchymal origin.
Rabdo : striated
Rhabdomyo : skeletal muscles*



Cervical pathology

- **Cervical carcinoma**
- Used to be the most frequent cancer in women *50 years ago, with high mortality, but it decreased in incidence because of the invention of Pap smear*
- Papanicolaou (Pap) smear → cervical cancer incidence dropped. It helped reduce cervical ca. mortality by 99%, ranking it 13th in cancer deaths for women recently because of the early detection of pre-invasive and early ca. .

Cervical cancer

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

So there is a time lapse between the cancer and the pre-cancerous lesion (i.e. between CIN and cervical cancer → 10 to 15 years), so if we detect the CIN and treat it, cervical cancer wont develop. :O

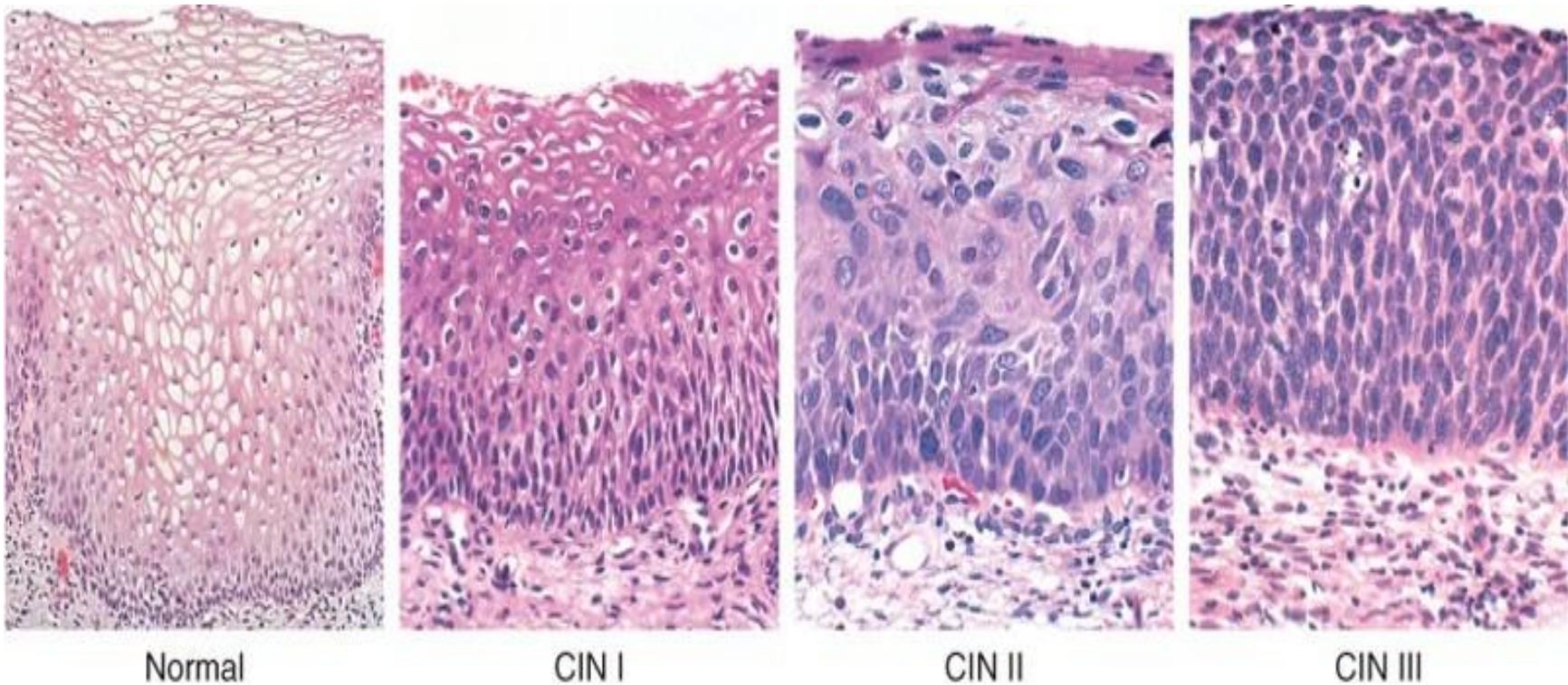
Cervical intraepithelial neoplasia (CIN)

- 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)



Similar to VIN III

In Dysplasia *the higher the grade the higher/more the :*
**Nuclear/Cytoplasmic (N/C) ratio, nuclear enlargement,
hyperchromasia, *extent of epithelial involvement* and
abnormal nuclear membranes**



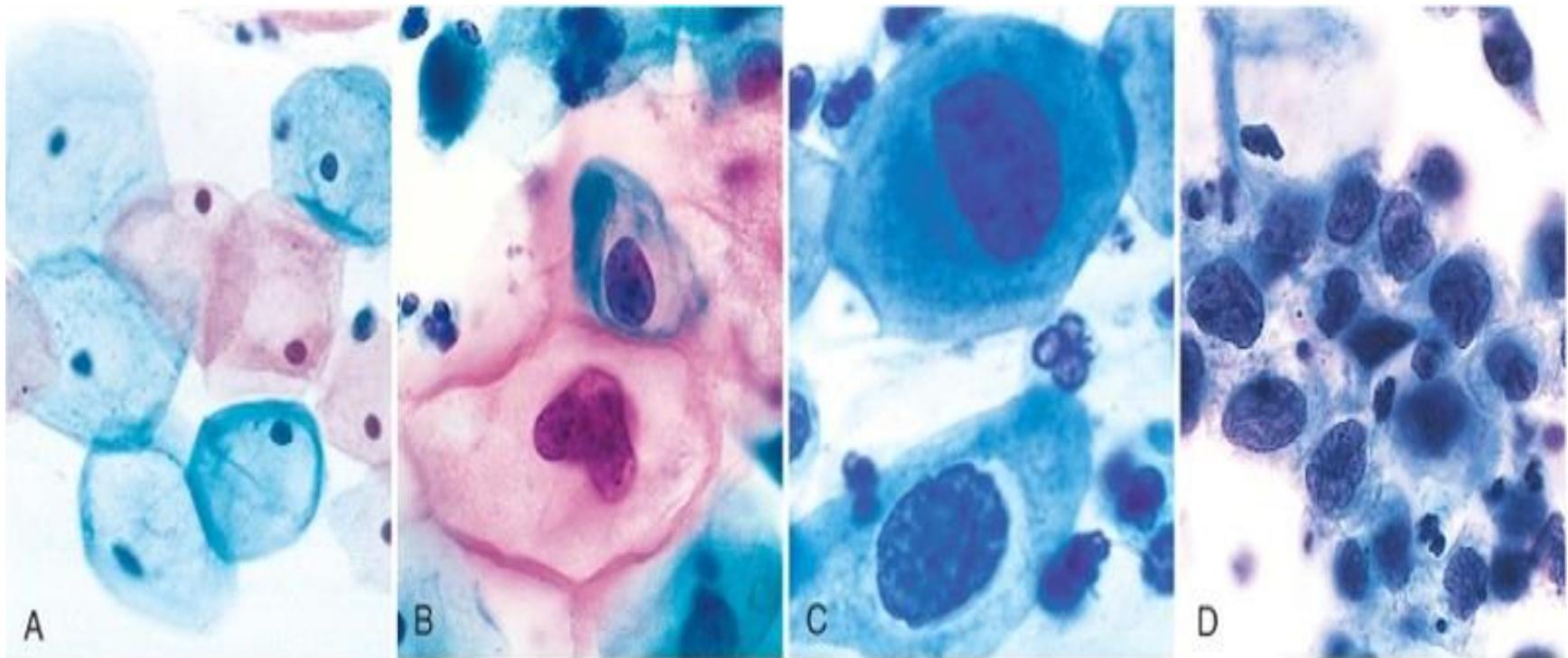
Normal

CIN I

CIN II

CIN III

Pap smear pictures



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Normal

CIN I

CIN II

CIN III

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 (*mainly these two*), 45, and 31), account for majority of cervical ca

- HPV 16 and 18 usually integrate into the host genome and express large amounts of *viral proteins* : **E6 and E7 proteins, which block or inactivate tumor suppressor genes p53 and RB, respectively, so loss of the regulation of the cell cycle occurs → higher risk of tumorigensis and more mutation .**
- recently introduced **HPV vaccine given to teenagers** in USA and Europe is effective in preventing HPV infections and hence cervical cancers.

Not discussed (Doesn't mean its not included)

Clinical Aspects Of Cervical Cancers

- symptoms:(vaginal bleeding; leukorrhea; dyspareunia; dysuria)
- CIN: treatment by **laser or cone biopsy**
- 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