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
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
Lichen sclerosus

- Thinned epidermis
- Hydropic degeneration at basal layer
- Sclerotic stroma
- Dermal inflammation
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

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

Koilocytes
Neoplastic vulvar diseases

1- Vulvar Intraepithelial Neoplasia (VIN)

2- Invasive Carcinoma of Vulva:
Squamous Cell Carcinoma (most common);
adenocarcinomas, melanomas, or basal cell carcinomas
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<th>High-Grade Vulvar Intraepithelial Neoplasia and Carcinoma of the Vulva</th>
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- 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.
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)
- 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
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.
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
Pap smear pictures

Normal

CIN I

CIN II

CIN III
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.

• 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
• Invasive cancer: surgical excision
• 5-year survival: preinvasive $\rightarrow$ 100%; stage 1 $\rightarrow$ 90%; stage 2 $\rightarrow$ 82%; stage 3 $\rightarrow$ 35%; and stage 4 $\rightarrow$ 10%.
• Radiotherapy and Chemotherapy in advanced cases