NON-NEOPLASTIC DISORDERS OF THE LOWER FEMALE GENITAL TRACT (VULVA)

CATEGORY	LICHEN SCLEROSUS	LICHEN SIMPLEX CHRONICUS	CONDYLOMA ACCUMINATUM (ANOGENITAL WARTS)
DEMOGRAPHIC	• Postmenopausal women are mainly affected.	• Occurs as the end result of many inflammatory conditions that affect the vulva.	• Sexually transmitted infection (STI); affects sexually active individuals.
CLINICAL SYSTEMS & MANIFESTATIONS	• Grossly, white plaques; thinned out skin at the vulvar area.	• Clinical term: leukoplakia (whitish plaque) on gross examination.	• Affects the anogenital area. • Cauliflower-like lesion on gross examination is the hallmark of this disease.
MICROSCOPY	• Thinning of epidermis. • Disappearance of rete pegs (finger-like epithelial extensions at the epidermal-dermal junction). • Hydropic degeneration of basal cells. • Sclerotic stroma beneath the epidermis along with dermal inflammation.	• Epithelial thickening (acanthosis) unlike lichen sclerosus. • Hyperkeratosis (excessive keratin production). • Epithelium shows no atypia. • Dermal inflammation.	• Koilocytosis (infected keratinocytes showing perinuclear cytoplasmic vacuolization + nuclear pleomorphism; large irregularly outlined hyperchromatic nuclei).
PATHOGENICITY	• Pathogenesis: uncertain, (?) autoimmune. • Is not pre-malignant by itself.	• No increased predisposition to cancer, however, may be present at margins of adjacent vulvar cancer.	• Infection by HPV (HPV type 6 and HPV type 11, mainly). • HPV types isolated from anogenital cancers (high-risk types) differ from those found in condylomas (low-risk types). • Condyloma is **not** precancerous by itself.

NOTE: Lichen sclerosus and condyloma accuminatum are not pre-malignant by themselves.
Lichen simplex chronicus is not associated with an increased risk of cancer but may be present at the margins of adjacent vulvar cancer.

VULVAR NEOPLASMS – SUMMARY

1. VULVAR INTRAEPITHELIAL NEOPLASIA (VIN)

ETIOLOGY

Caused by high-risk HPV types: 16, 18, 45, and 31.

DEMOGRAPHIC

- Peak age: ~30 years.
- Can progress to invasive carcinoma after 10–15 years.

PATHOGENICITY & MOLECULAR BASIS

- HPV can be detected by molecular methods in all precancerous lesions.
- HPV integrates with the host genome and expresses large amounts of proteins, such as E6 and E7.
- **E6 protein:** blocks p53 tumor suppressor gene.
- **E7 protein:** blocks Rb (retinoblastoma) tumor suppressor gene.
- HPV vaccine helps reduce HPV infection and thus HPV-related cancers.

GRADING SYSTEM

GRADE	DYSPLASIA INVOLVES	ALSO KNOWN AS	BASEMENT MEMBRANE
VIN I	One-third of the epithelium	Mild dysplasia	Intact
VIN II	Two-thirds of the epithelium	Moderate dysplasia	Intact
VIN III	Three-thirds of the epithelium	Carcinoma in situ (severe dysplasia)	Intact

Same grading concepts are used in other lower genital tract organs (vagina, cervix, anus).

2. VULVAR SQUAMOUS CELL CARCINOMA (INVASIVE)

	POORLY DIFFERENTIATED SCC (HPV-RELATED)	WELL-DIFFERENTIATED SCC (NOT HPV-RELATED)
ETIOLOGY	• Associated with high-risk HPV, mainly types 16 and 18.	• Not associated with HPV.
MNEMONIC	"Young Women Are Messy" (Y = Young → younger age) (Messy → Poorly Differentiated)	Well-Differentiated → older women (clean, orderly)
DEMOGRAPHIC	• Relatively younger women. • More common.	• Older women (usually in their 60s–70s). • Less common.
CLINICAL SYSTEMS & MANIFESTATIONS	• May present as a vulvar mass, ulcer, pain, pruritus, bleeding, or discharge.	

KEY POINTS TO REMEMBER

- VIN is an intraepithelial (precancerous) lesion caused by high-risk HPV; graded I–III based on the extent of epithelial involvement.
- VIN III = carcinoma in situ (full-thickness dysplasia) with an intact basement membrane.
- HPV detected by molecular methods in all precancerous lesions.
- HPV E6 inhibits p53; E7 inhibits Rb → promotes uncontrolled cell proliferation.
- HPV vaccine reduces HPV infection and HPV-related cancers.
- Vulvar SCC:
  - Poorly differentiated → younger women, HPV 16/18 related, more common.
  - Well differentiated → older women (60s–70s), not HPV related, less common.

CERVICAL CARCINOMA – SUMMARY

ETIOLOGY

- More frequent; used to be the most frequent.
- Due to Pap smears, mortality has been reduced by 99%.

DEMOGRAPHIC

- Peak incidence at ~45 years.
- After 10–15 years from detection of precursors (typically ages 30–45).

PAP SMEAR CYTOLOGY & GRADING

- Pap smears detect precancerous changes.
- Grading is based on the size of the nucleus-to-cytoplasm (N:C) ratio and staining intensity:
  - Larger N:C ratio and darker stain indicate more severe dysplasia.

GRADE	DYSPLASIA INVOLVES	PAP SMEAR FEATURES
CIN I (Mild dysplasia)	One-third of the epithelium	Small N:C ratio, lighter stain
CIN II (Moderate dysplasia)	Two-thirds of the epithelium	Intermediate N:C ratio, moderate stain
CIN III (Severe dysplasia/ Carcinoma in situ)	Three-thirds of the epithelium	Large N:C ratio, dark stain

Grading reflects the extent of epithelial involvement; worse dysplasia has larger N:C ratio and darker staining.

STAGING (IMPORTANT PROGNOSTIC FACTOR)

- Staging refers to the extent of spread.
- Key stages:

STAGE	DESCRIPTION
Stage 1B (Early)	Cancer is confined to the cervix.
Stage 1B (Late)	Larger lesion but still confined to the cervix.
Stage 2B	Cancer extends beyond the cervix and involves the parametrium.

TREATMENT

- Precancerous lesions (CIN): laser ablation or cone biopsy.
- Invasive cancer: surgical excision is the main treatment.
- Advanced cases: radiotherapy and chemotherapy may be used.

PROGNOSIS

- Survival rates drop as stage increases.
- Early detection is critical for excellent outcomes.

KEY POINTS TO REMEMBER

- Cervical carcinoma is more frequent; used to be the most frequent, but mortality reduced by 99% due to Pap smears.
- Peak incidence at ~45 years; onset typically 10–15 years after detection of precursors (ages 30–45).
- Pap smear grading: larger N:C ratio and darker stain = more severe dysplasia.
- Staging is a key prognostic factor: early (Stage 1B) vs. late (Stage 1B) vs. Stage 2B (involves parametrium).
- Treatment: laser or cone biopsy for precancer; surgical excision for invasive cancer; radiotherapy/chemotherapy for advanced cases.
- Survival decreases with delayed detection; early detection is life-saving.