Vulva

Diseases of the vulva can also affect the male genitalia

Non-neoplastic disorders

Leukoplakia: A skin lesion that appears white may occur in both males and females, and it can affect the mucous membranes as well as other skin sites specially in the oral cavity

The most common lesion is leukoplakia, but we may also observe redness, hypopigmentation or hyperpigmentation; leukoplakia is not always present

Leukoplakia:- White patches or plaques are seen in a variety of conditions:

- Benign **dermatoses: psoriasis, lichen planus, Lichen sclerosus, lichen simplex chronicus**
- Malignant lesions of the vulva: SCC and cervical SIL
  "VIN and early vulvar carcinomas -> leukoplakia"
  "Exophytic or ulcerative endophytic tumours"

Biopsy and microscopic examination are often needed to differentiate these clinically similar-appearing lesions.

Bottom line:
Leukoplakia can affect both males and females.
Leukoplakia can present in many variety conditions like psoriasis, lichen plaques, or in malignant lesions like SCC in the vulva.
Since leukoplakia can appear in benign or malignant lesions, then biopsy and microscopic examination are often needed.
Leukoplakia could appear in different form, we may observe redness, hypo- or hyperpigmentation, so it does not always appear

Aspects	**Lichen Sclerosus**	**Lichen Simplex Chronicus (squamous cell hyperplasia)**
Nature	Benign but there is an increased risk of SCC 1% to 5% develop HPV-negative SCC of the vulva and VIN. So it is a precancerous lesion "Which one of them is precancerous?" Biopsy can provide a definitive diagnosis if there is diagnostic uncertainty and also rule out neoplasia. It can affect any part of the skin, such as the axilla or legs, but the most common site is the external genitalia	Benign No increased predisposition to cancer when lesions are isolated.----not a precancerous lesion Often is present at the margins of established vulvar cancer----suggesting some association with neoplastic disease So.. Biopsy if the diagnosis cannot be determined clinically or to exclude other dermatoses Careful search for other disorders is advised
Age	Most commonly postmenopausal at onset; it can rarely occur in children. But it can affect any age.	Any age, but mainly postmenopausal females

Aspects	Lichen Sclerosus	Lichen Simplex Chronicus (squamous cell hyperplasia)
	f>m	
Notes	Associated with other autoimmune disorders. such as Systemic Lupus Erythematosus (**SLE**), **Hashimoto**'s thyroiditis, and **Goodpasture**'s syndrome	
Pathogenesis	Autoimmune. the main theory - It can be familial/genetic etiology. Hormonal (low estrogen levels in postmenopausal women?) Immune-mediated chronic fibro-inflammatory condition of vulvar skin T cells in the subepidermis areas cell-mediated immune response with associated degenerative changes of the basal keratinocytes Secondary fibrosis of the superficial dermis, leading to a subepithelial hypocellular band of homogenous appearing collagen	Uncertain precise pathophysiology Persistence and progression correlate with scratching and rubbing (persistent itch/scratch cycle) It may be secondary to other dermatoses or neoplastic conditions. Could be due to irritant, infection (e.g. **candida**), or inflammatory conditions (**contact** dermatitis, **psoriasis**, etc.), or psychological causes (such as stress, and anxiety) "Which condition is associated with more severe itching?" "Which one of them is associated with malignancy as a secondary finding in biopsy?"
Treatment	Topical corticosteroids (first line), with topical calcineurin inhibitor therapy as second line Early diagnosis and treatment may prevent disease progression "Disease progression: before fibrosis and precancerous lesion"	Treat the underlying cause (Curable compared to LS) Topical steroids Topical immunomodulators Topical antipruritics
Appearance	Degenerative changes of the basal keratinocytes, Thinning of the epidermis (atrophy) Secondary fibrosis of the superficial dermis, leading to a subepithelial hypocellular band of homogenous appearing collagen Disappearance of rete ridges A bandlike (lichenoid) mononuclear inflammatory cell infiltrate.in subepithelial (dermis) A zone of acellular, homogenized, dermal fibrosis with displacement of inflammatory cells downward below the abnormal fibroid collagenous layer **basal layer** of epidermis → **thinning of epidermis** sclerosis of dermis & hydropic degeneration of rete pegs Dryness and sclerosis can lead to dyspareunia, which is painful intercourse, dysuria Sclerosis=fibrosis Intensely pruritic. Leukoplakia or papules/thin vulvar skin ----- vulvar skin, it can involve perianal skin.	Leukoplakia, excoriations, erythema and hyperpigmentation Epithelial thickening (hyperplasia, acanthosis) opposite to the LS where there is thinning More **purities** cycle than the LS Hyperkeratosis Hypergranulosis Increased mitotic activity is seen in the basal/suprabasal layers NO epithelial atypia WBCs infiltration of the dermis Dermal changes are less compared to LS The fibrosis is not band-like or homogeneous, as seen in lichen sclerosus

Aspects	Lichen Sclerosus	Lichen Simplex Chronicus (squamous cell hyperplasia)
	When the entire vulva is affected, the labia become atrophic and stiffened, and the vaginal orifice is constricted.	

Neoplastic disorders - Tumours of the vulva:

Condyloma acuminatum
Genital warts.
Occur on the anogenital surface.
Single or multiple lesions.
Range from a few millimetres to many centimetres in diameter.
Red-pink to pink-brown.
STI-----Low-risk HPV subtypes 6 and 11----- do not commonly progress to cancer.
Risk of having other HPV-related lesions in the vagina and cervix.
Koilocytosis.

Carcinoma of the vuvla (Inflammation>Carcinoma)
Represents about 3% of all female genital tract cancers. Not common.
Squamous cell carcinomas (90%). First most common - Not only in vulva.
Adenocarcinomas. Second.
Basal cell carcinoma. Third.

Two distinct forms of vulvar squamous cell carcinomas that differ in pathogenesis and course:

Note: The morphology opposite of the prognosis.

Aspect	HPV-positive carcinoma	HPV-negative carcinoma
HPV Related	High-risk HPV strains (especially HPV type 16).	Not related to HPV.
Age Usually seen in postmenopausal females	Middle-aged women.	Older women.
Preceded by	Usual vulvar intraepithelial neoplasia (uVIN): Includes **LSIL (low-grade squamous intraepithelial lesion)** and **HSIL (high-grade)** Shows **koilocytic changes** (hallmark of HPV cytopathic effect)	Differentiated VIN (dVIN): HPV unrelated precancerous lesions (HPV-, atypia in basal cell layer) dVIN has a higher potential to become invasive than HPV-

Aspect	HPV-positive carcinoma	HPV-negative carcinoma
	LSIL and HSIL (warty/basaloid)----HPV related precancerous lesions (HPV+, koilocytic change)	associated uVIN. Are diagnosed later (due to lack of early symptoms)
Risk factors	Cigarette smoking and immunodeficiency (e.g.HIV)	History of lichen sclerosus
Appearance	Multifocal Poorly differentiated non-keratinizing squamous cell carcinomas	Unifocal Well-differentiated keratinizing squamous cell carcinomas
Prognosis	The outcome of HPV-associated vulvar squamous cell carcinoma (VSCC) is favourable compared to HPV-independent VSCC.	The prognosis is less favourable
Pathogenesis	HPV oncoproteins E6 and E7 inhibit p53 and RB (tumour supressor genes)---resulting in the overexpression of p16 (+ by IHC)	Somatic mutation: like p53 mutations
Notes	Tend to remain confined to their site of origin for a few years. Ultimately invade and spread-----first to regional lymph nodes	Tend to remain confined to their site of origin for a few years. Ultimately invade and spread-----first to regional lymph nodes
Treatment	Surgical, radiotherapy, chemotherapy	Surgical, radiotherapy, chemotherapy

- Stage (depth of invasion and LN status)
  a. The risk of metastasis correlates with the depth of invasion
    i. The outcome is dependent on the tumour stage (size/depth)
    1. The overall 5-year survival is 70% to 93% with -LNM but 25% to 41% in +LNM

(Lymph node metastasis=LMN)

Mammary Paget disease
Breast/nipple.
Always associated with an underlying carcinoma.
Always malignant.

Extramammary Paget disease
It may affect either males or females. When it involves the vulva, it is named accordingly, and when it affects the penis, it is referred to as penile extramammary Paget’s disease.
Vulva or penis.
Manifests as a red, scaly, crusted plaque that may mimic the appearance of inflammatory dermatitis
Pruritus, erythema, crusting, ulcers in vulva.
Rare.
Intraepithelial adenocarcinoma.
May persist for years or even decades without evidence of invasion.

Extramammary Paget disease
Carcinoma in situ, low risk of underlying carcinoma (vs Paget disease of the breast, which is always associated with underlying carcinoma).
Paget disease is an intraepidermal proliferation of epithelial cells. Good if the sec cancer is early but bad if its late
Most commonly appears to arise from epidermal progenitor cells (primary). Good unless invasion of the dermis
Only a minority of cases have an underlying tumour (secondary).
The Paget cells are large cells with abundant pale polygonal, finely granular cytoplasm and occasional cytoplasmic vacuoles infiltrate the epidermis, singly and in groups.
The Paget cells may invade locally and ultimately metastasize.
The Paget cells are (+) for mucin stain (PAS)
After metastasis occurs, the prognosis is poor.
So, may be benign or malignant