Malignant lesions of vulva and vagina

Presented by:

Mohammad Qadourah

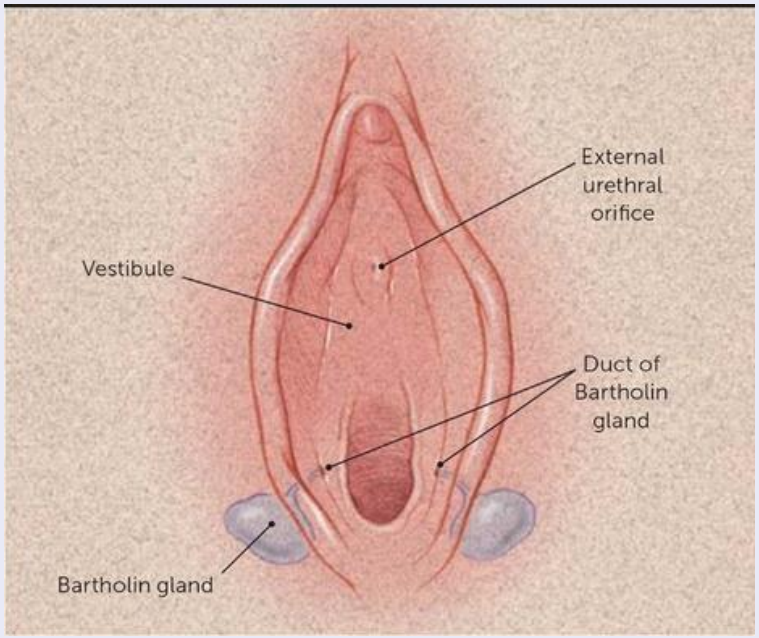
Sadeel Mokhles

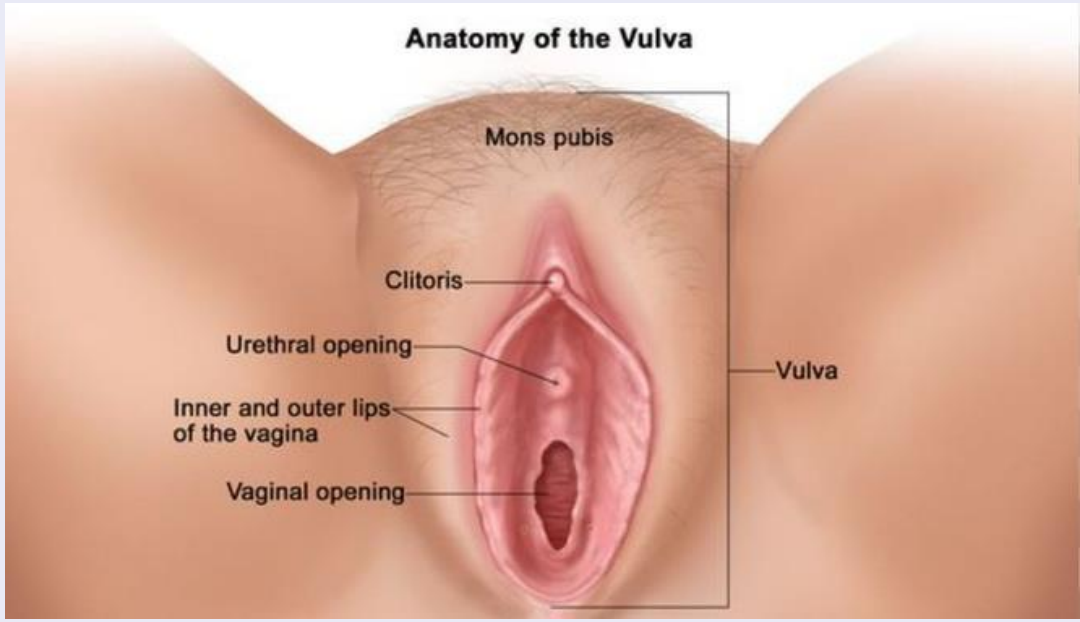
Jehad mohammed

Mohammad Obaidat

Introduction:

- Vulva: allofthestructuresthatmakethe female external genitalia





histology

- **Labia minora**
  - **Nonkeratinized stratified squamous epithelium • Rich in sebaceous glands**
- **Labia majora**
  - **Keratinized stratified squamous epithelium • Hair follicles • Eccrine, apocrine, and sebaceous glands**
- **Vestibule: nonkeratinized squamous epithelium with major** vestibular and minor vestibular glands
- **Urethra: columnar epithelium with minor vestibular glands**

Vulvar malignant lesions:

- **Epi**: rare, it makes up 0.7% of female cancers
    - The commonest effected age group is menopausal women
    - Occurs earlier if its HPV related

- **Etiology:**
    - HPV related: (35-65 yo)
        - High risk HPV: 16, 18, 31, 33

    - NON-HPV related: (55-58 yo)
        - Immunodefeciency
        - Infections : STDs
        - Smoking: co factor for HPV and VIN
        - Precursors lesions:
            - Vulvar epithelial neoplasia
            - Cervical epithelial neoplasia
        - Dermatoses:
            - Lichen sclerosis

Classifications:

- **Malignant lesions**
  - **Invasive:**
    - §Squamous cell carcinoma (SCC) and subtypes: > 80% of cases [1]
    - §Paget disease of the vulva: an adenocarcinoma characterized by localized pruritus and eczematous lesions (e.g., erythematous patches with white scaling, crusting, ulcerations)
    - §Basal cell carcinoma
    - § Melanoma
    - §Vulvar Sarcoma
  - **Other:**
    - § Bartholin
    - § verrocous

Clinical presentation:

- Maybe initiallyasymptomatic
- Burning sensation Pain
- Patches of discoloration
- Dysuria Dysparenuia
- Inguinal lymphadenopathy
-
-

oLocal Pruritis oPlaques
oMasses, lump oulcer
oBleeding (less frequent):

- hard and craggy and bleeds on Touch (highly specific for malignancy)

diagnosis

- History
- Physical:
    - Pelvic examination

  ●an assessment of the size of the lesion, ●its position on the vulva and its proximity to important midline structures,particularly the urethra and anus.
- Colposcope: biobsy

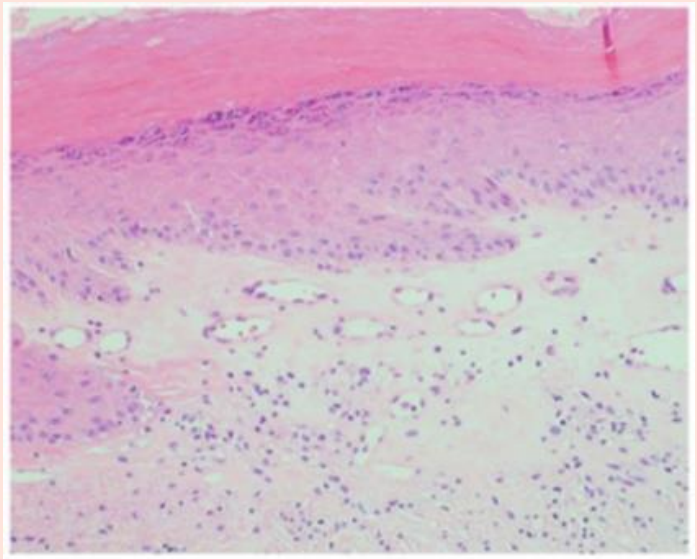
Prognosis:

- Women often present late embarrassment and reluctance to be examined
- Vulval tumours spread locally and metastasize first via the inguinofemoral lymph nodes, before involving pelvic lymph nodes. Haematogenous spread to liver and lungs is a late event.

Dermatoses (LICHEN SCLEROSIS)

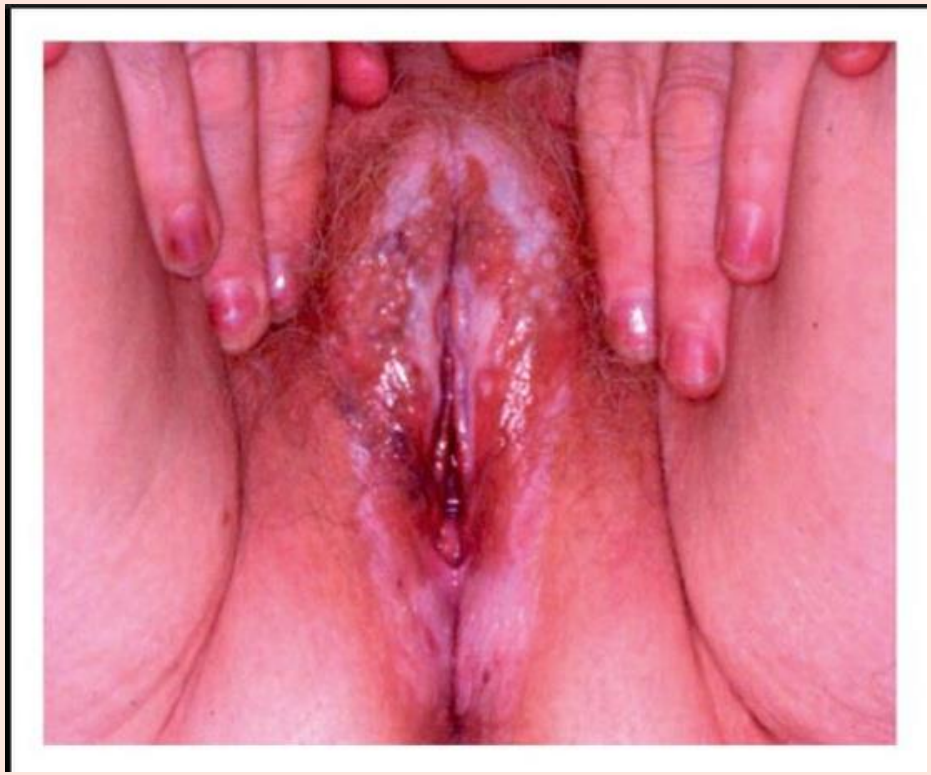
- Define:

  not precancerous but they do predispose risk for malignant (SCC) transformation.
- Epi: higher rates menopausal women
- Etiology:
  - Mainly unkown, Hormonal, immunological, and/or infectious factors are believed to play a role
- Patho-histology:
  - epidermal atrophy and loss of vulvar architecture localized hyperkeratosis,
  - degeneration of the basement membrane
  - Loss of collagenous and elastic connective tissue
  - Presence of an inflammatory infiltrate



Clinical presentation:

- leukoplakia vulvar skin >>> Parchment-like, thin, shiny vulvar skin
- Loss of vulvar architecture
- Narrow, atrophic vaginal introitus resulting in dyspareunia



Treatment:

- Superpotent steriod cream if no cell atypia is found

- Excision if malignancy found

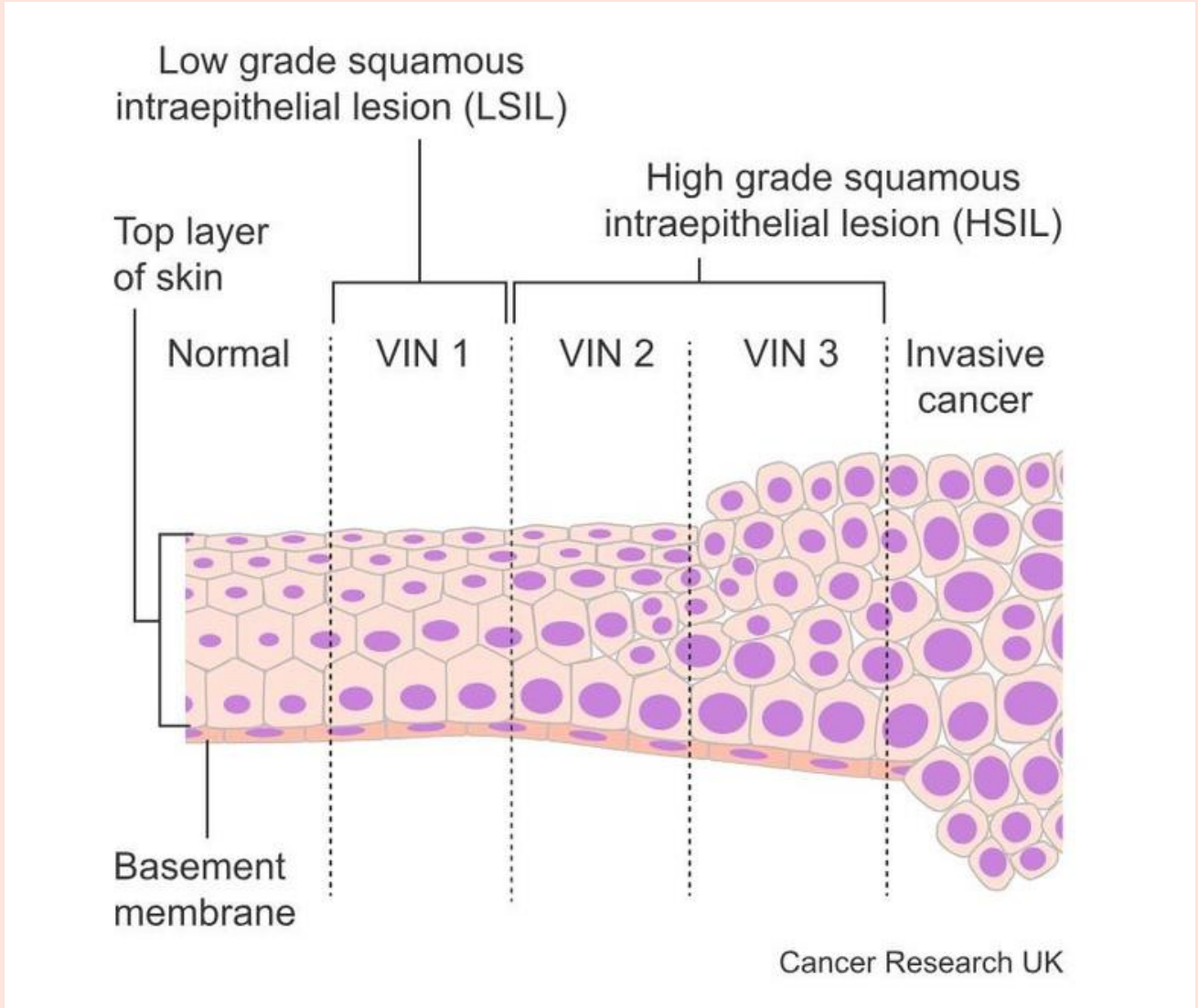
Precursor lesion of vulva (vulvar inter-epithelial neoplasia):

- Etiology: HPV dependent (more common), HPV non-dependent

Classification:

- VIN usual type which includes:
  - VIN1: now known as LSIL (low grade squamous interepithelial lesion): mild dysplasia and atypia, hyperplastic vulvar dystrophy
  - (high grade squamous interepithelial lesion) :moderatedysplasiaand atypia, hyperplastic vulvar dystrophy

- VIN (differentiated type, lichen sclerosis related): severe dysplasia and atypia, hyperplastic vulvar dystrophy


Low grade squamous intraepithelial lesion (LSIL)
High grade squamous intraepithelial lesion (HSIL)
Top layer of skin
Normal
VIN 1
VIN 2
VIN 3
Invasive cancer
Basement membrane
Cancer Research UK

Clinical features:

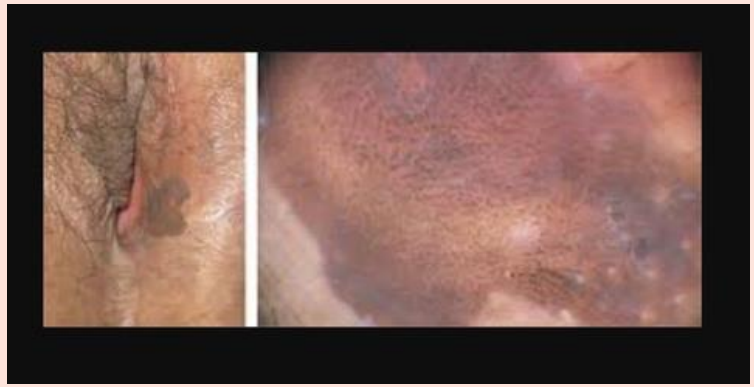
Clinically

: • Site:

- •Labia minor
- •Perinuim

• gross:

- •multifocal leukoplic, erythematous or pigmented lesion



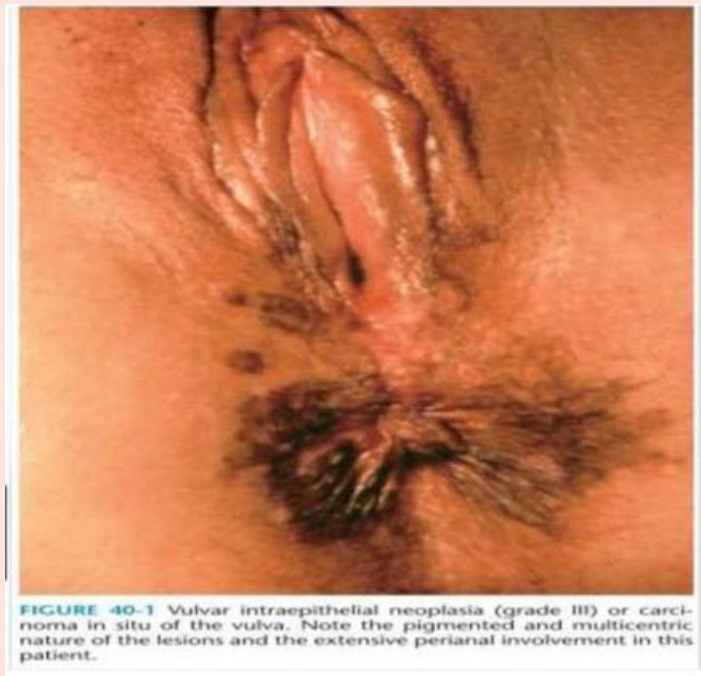


FIGURE 40-1 Vulvar intraepithelial neoplasia (grade III) or carcinoma in situ of the vulva. Note the pigmented and multicentric nature of the lesions and the extensive perianal involvement in this patient.

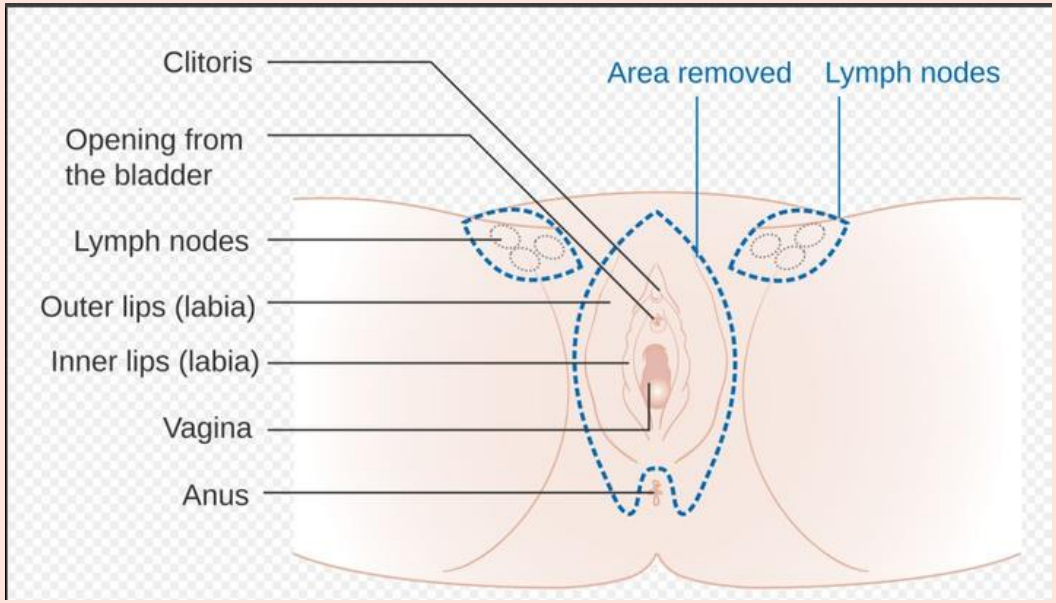
Diagnosis:

- Physicalexamination alone isn't sufficient to achieve diagnosis, bc There is no pathognomic appearance, hence the need for a biopsy of any abnormal vulvar lesion. Different patterns may be present in the same patient

- Colposcopy:
    - Biobsy

Treatment:

- observation:
  - Low grade lesions
- Medical:
  - High grade lesions
    - Emiquimod cream
- Surgical:



⇨ dVIN is associated with lichen sclerosis and invasive disease (specifically, SCC of the vulva).[15] Recurrence rates for dVIN are much higher than those for uVIN.[16] Treatment of these lesions should include surgical excision with a scalpel, LEEP, or laser. Wide local excision is preferable as the initial treatment.:

  - Wide local excision
  - Vulvectomy
  - CO2 Laser Ablation
  - Simple excision with 5mm safety margin
- Long term follow up

prognosis

- Lessthan 10% chance of turning malignant despite treatment, and its higher in immunocompromised patents

- And 80% if without treatment

Invasive valvular cancer

1. **Squamous cellcarcinoma(the most common90%)**
2. Malignant melanoma (second most common)
3. Basal cell carcinoma (rare) Vulvar sarcoma (1%
4. of vulvar malignancies)

Squamous cell carcinoma

Epidemiology

• Most common vulvar malignancy : Accounts for ~90% of all vulval cancers .

• Typically affects postmenopausal women , especially age >60 .

• Increasing incidence in younger women due to HPV-associated disease (especially HPV type 16).

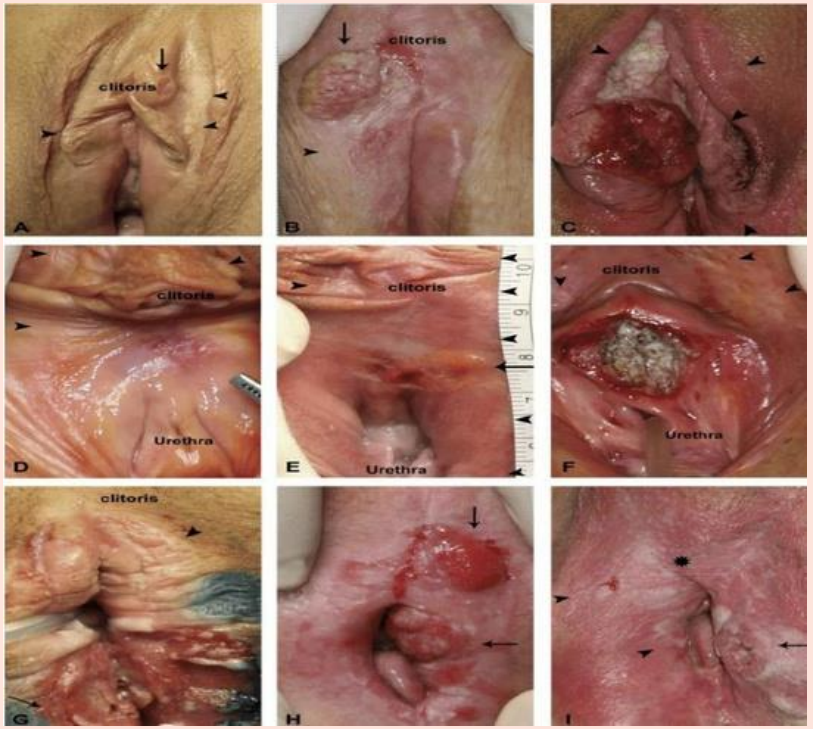
Squamous cell carcinoma

Common Sites of Involvement

- Labia majora – **most frequent site.**
- Labia minora – second most common.

Less common:

- Clitoris
- Perineum



Pathogenesis

- Pathway 1: HPV-Associated(HPV+)

•Incidence: 95%
•Risk Factors:
- HPV infection
- Smoking
- Immunosuppression (HIV, transplant)
- Sexual practices (# of partners)

•Clinical Features:
- Age: 20–40 years
- Multifocal, Multicentric

•Progression Rate: 5% over ~6–7 years

•Speed: SLOW
•Prognosis: Good

•Outcome: Warty/Basaloid VSCC
•Accounts for 40% of VSCCs

- Pathway2:HPV-Independent (HPV−, via dVIN)

•Incidence: 5%
•Risk Factors:
- Age
- Irritation
- Inflammation, oxidative stress Ischemic
- stress Associated with Lichen sclerosus

•Clinical Features:
- •Age: 60–80 years
- Unifocal, Unicentric

•Progression Rate: 90% within ~1–2 years
•Speed: FAST
•Prognosis: Poor
•Outcome: Keratinizing VSCC

- Accounts for 60% of VSCCs

Why does HPV related VSCC have a better prognosis?

- Occurs in younger women (20–40 yrs) → better treatment tolerance.
- Slow progression from uVIN (5% over ~6–7 years) → early detection possible.
- Less aggressive behavior → lower risk of deep invasion/metastasis.
- More immunogenic → better response to treatment like radiation.
- Fewer genetic mutations (vs. TP53 mutations in HPV-negative) → less aggressive biology.

Subtypes

- Verrucous carcinoma Bas
- aloid carcinoma
- Keratinizing carcinoma

Clinical features

- May initially be asymptomatic
- Local pruritus, possibly with burning sensation and pain
- Plaques, growth of various shapes, often wart-like lesions or ulcers
- Patches of discoloration (reddish, blackish, or whitish)
- Vulvar bleeding or discharge (less common)
- Dysuria, dyspareunia
- Inguinal lymphadenopathy

General Principles of Vulvar Cancer Evaluation

1. Initial assessment includes:

• A pelvic exam and vulvoscopy.

• Most importantly, biopsy of all suspicious lesions is mandatory.

• This allows histological confirmation and tumor grading.

2. Evaluate for comorbid conditions, like HPV or HIV. (Transition) "Once the diagnosis is confirmed, we move on to staging the disease."

Methods of Spread

1. Local (Direct) Extension

- Spreads to adjacent structures, including:
- Vagina
- Urethra
- Anus

2. Lymphatic Spread (30%)

- Most commonly involves **inguinofemoral** lymph nodes.
- **Lymph node status** is the most important prognostic factor.

3. Hematogenous Spread

- Occurs in advanced stages.
- Common distant metastasis sites include:
- **Lungs**
- **Liver**
- **Bones**

Staging Workup for Vulvar Cancer

- **Biopsy and Histology**

- **MRI of the pelvis :**
  - Primary tumor size
  - Local spread (e.g., urethra, vagina, bladder mucosa) •Assess distant spread

- **Lymph node evaluation**

- **Staging classification:**

- Either **FIGO** or **TNM** systems are used.

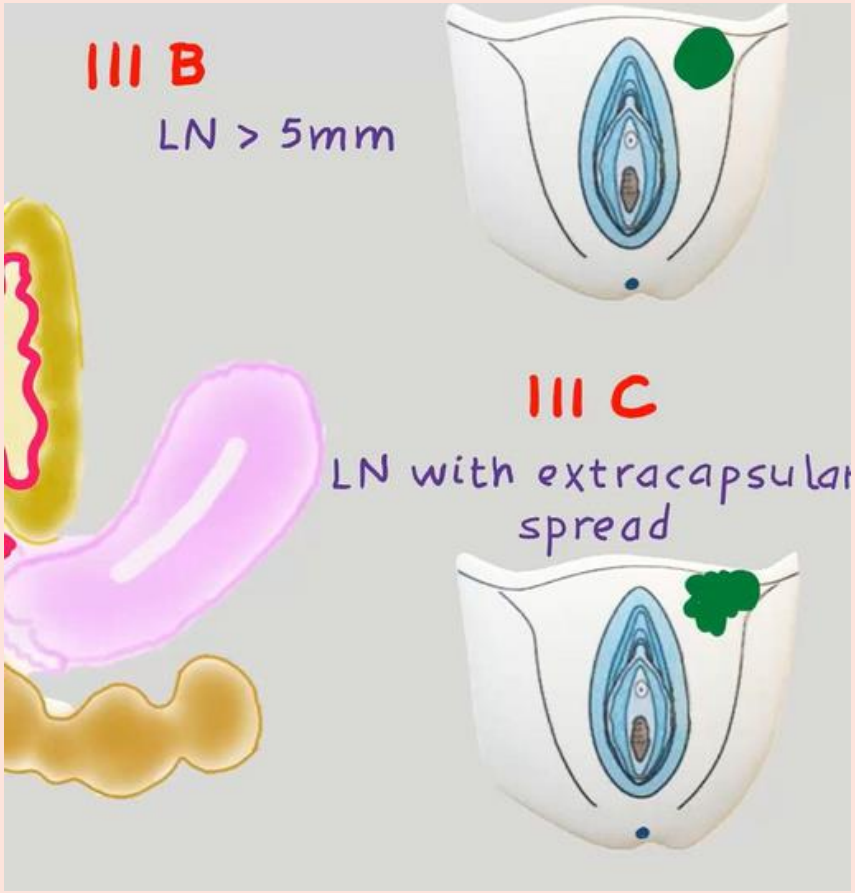
- These help in prognostication and guiding treatment decisions.

Carcinoma of Vulva FIGO* staging

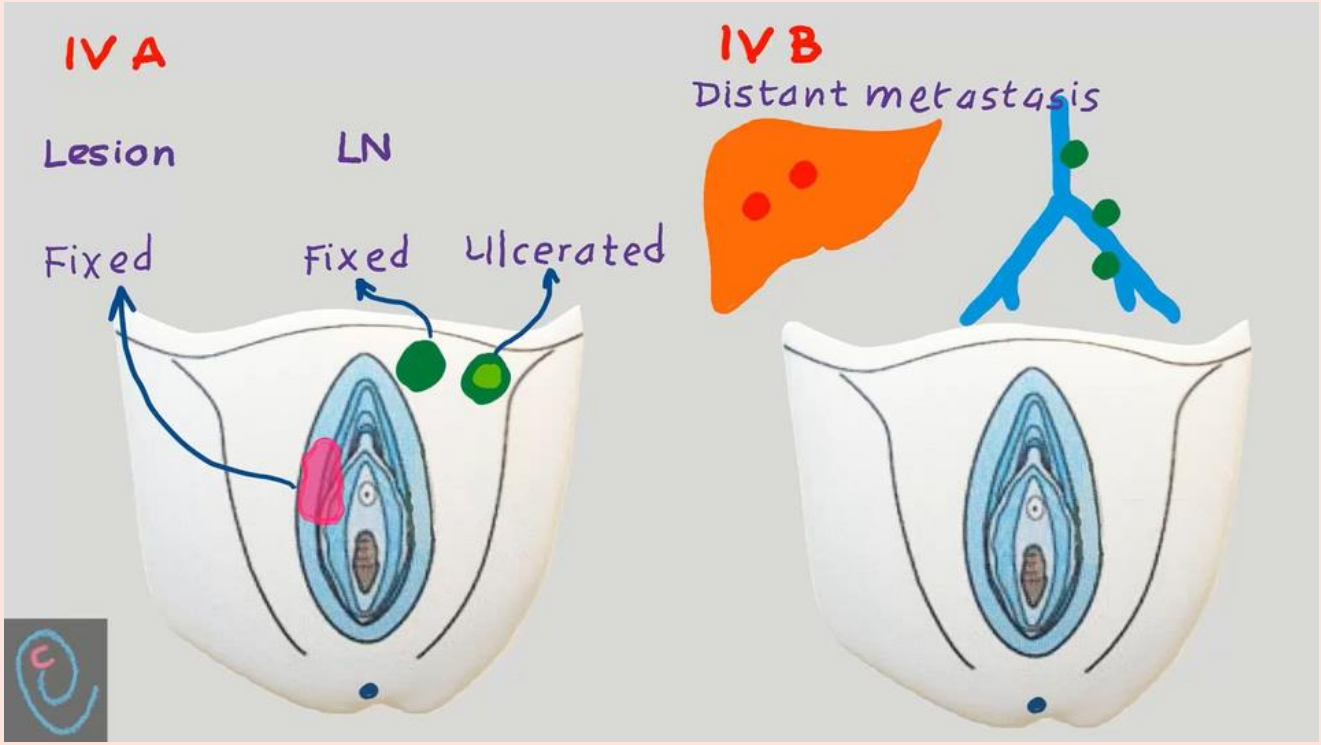
FIGO: International Federation of Gynecology and Obstetrics*

Carcinoma Of Vulva FIGO staging

Carcinoma Of Vulva FIGO staging



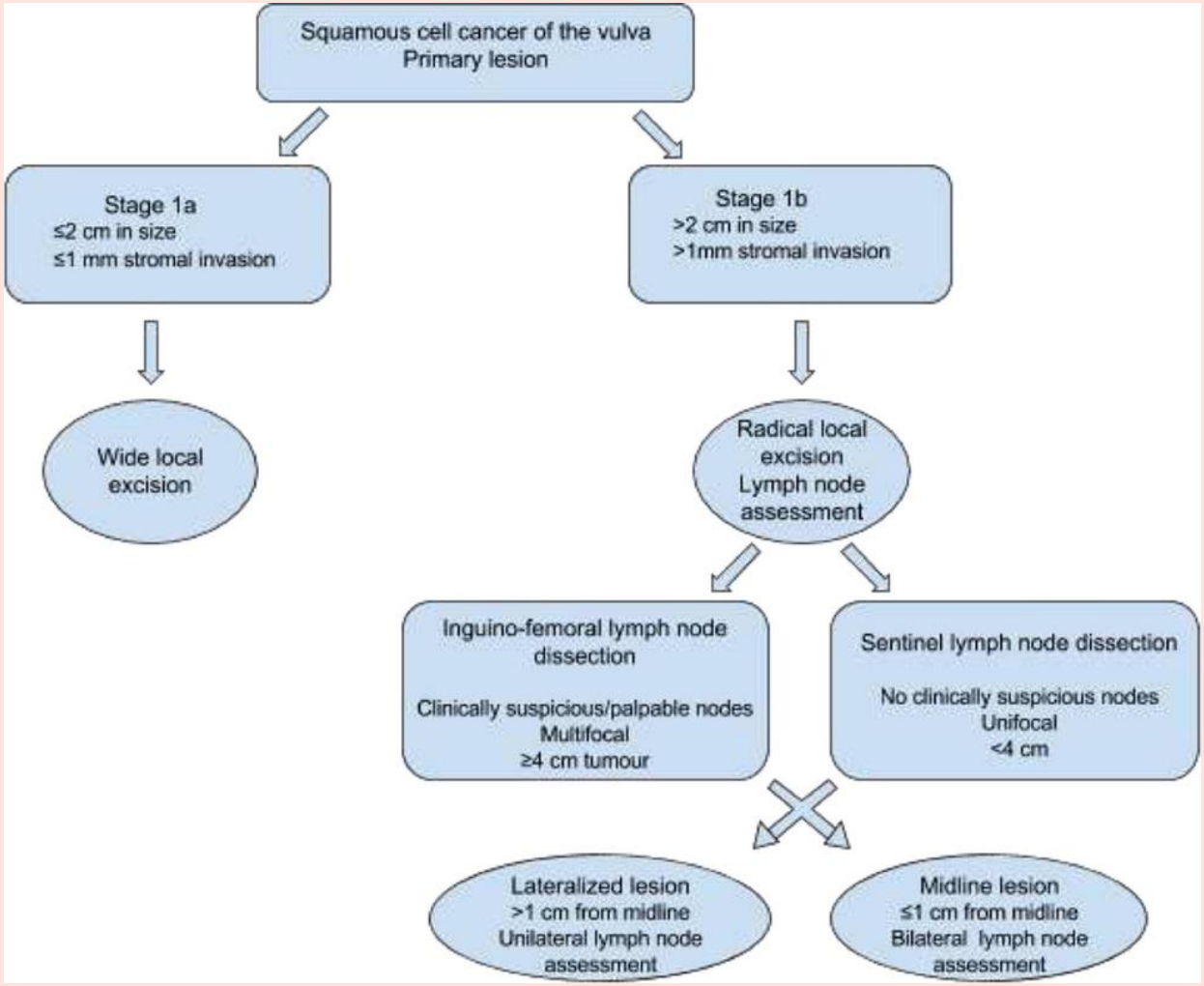
Carcinoma Of Vulva FIGO staging



Stage	Description
I	Tumor confined to the vulva
IA	Tumor size ≤ 2 cm and stromal invasion ≤ 1 mm [a]
IB	Tumor size > 2 cm or stromal invasion > 1 mm [a]
II	Tumor of any size with extension to lower one-third of the urethra, lower one-th of the vagina, lower one-third of the anus with negative nodes
III	Tumor of any size with extension to the upper part of adjacent perineal structures, with any number of non-fixed, non-ulcerated lymph nodes
IIIA	Tumor of any size with disease extension to the upper two-thirds of the urethra, upper two-thirds of the vagina, bladder mucosa, rectal mucosa, or regional lymp node metastases ≤ 5 mm
IIIB	Regional [b] lymph node metastases > 5 mm
IIIC	Regional [b] lymph node metastases with extracapsular spread
IV	Tumors of any size fixed to bone, or fixed, ulcerated lymph node metastases, or distant metastases
IVA	Disease fixed to pelvic bone or fixed or ulcerated regional [b] lymph node metasta
IVB	Distant metastases

[a] Depth of invasion is measured from the basement membrane of the deepest, adjacent, dysplastic, tumor-fre ridge (or nearest dysplastic rete peg) to the deepest point of invasion. [b] Regional refers to inguinal and fer lymph nodes.

Treatment


Squamous cell cancer of the vulva
Primary lesion
Stage 1a
≤2 cm in size
≤1 mm stromal invasion
Stage 1b
>2 cm in size
>1mm stromal invasion
Wide local excision
Radical local excision
Lymph node assessment
Inguino-femoral lymph node dissection
Clinically suspicious/palpable nodes
Multifocal
≥4 cm tumour
Sentinel lymph node dissection
No clinically suspicious nodes
Unifocal
<4 cm
Lateralized lesion
>1 cm from midline
Unilateral lymph node assessment
Midline lesion
≤1 cm from midline
Bilateral lymph node assessment

Treatment

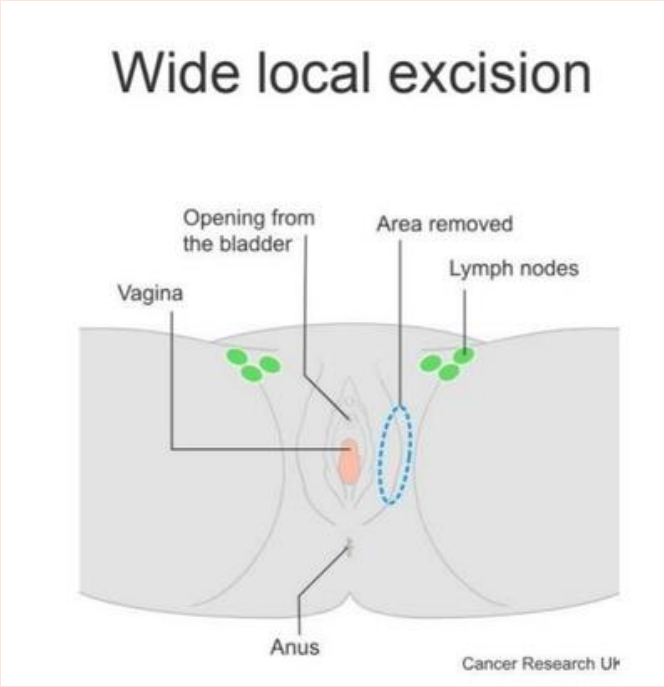
1. Stage 1a

•Criteria: Lesion is ≤2 cm in size and ≤1 mm of stromal invasion.

•Treatment:

• Wide local excision (no lymph node assessment needed due to low risk of spread).

• A tumor-free margin of ≥1 cm is required



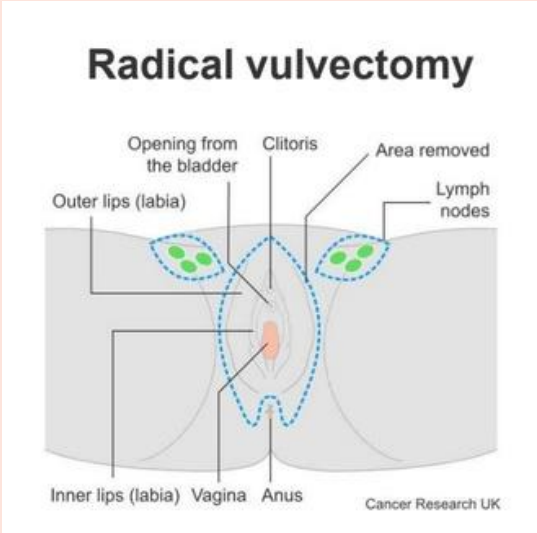
Treatment

2. Stage 1b

•**Criteria**: Lesion is >2 cm or >1 mm stromal invasion.
•**Treatment:**
• Radical local excision.
• Lymph node assessment is required, which depends on additional tumor features:

•**Sentinel lymph node biopsy:**
•**Appropriate if:**
•No clinically suspicious lymph nodes
•Unifocal lesion
•Tumor size <4 cm

•**Inguino-femoral lymph node dissection:**
•Indicated when there are:
•Multifocal tumors
•Tumor size ≥4 cm
•Positive sentinel lymph node biopsy



Laterality of Lesion Determines Side of Node Assessment:

•**Lateralized lesion** (>1 cm from midline):
• Unilateral lymph node assessment
•**Midline lesion** (≤1 cm from midline):
• Bilateral lymph node assessment

Treatment

3. Stage 2;
Radical excision + Sentinel lymph node biopsy

4. Stage 3;
Radical excision + Inguino-femoral lymph node dissection + adjuvant radiotherapy ± chemo

5. Stage 4;
Palliative chemo/radiotherapy, supportive care

Prognosis

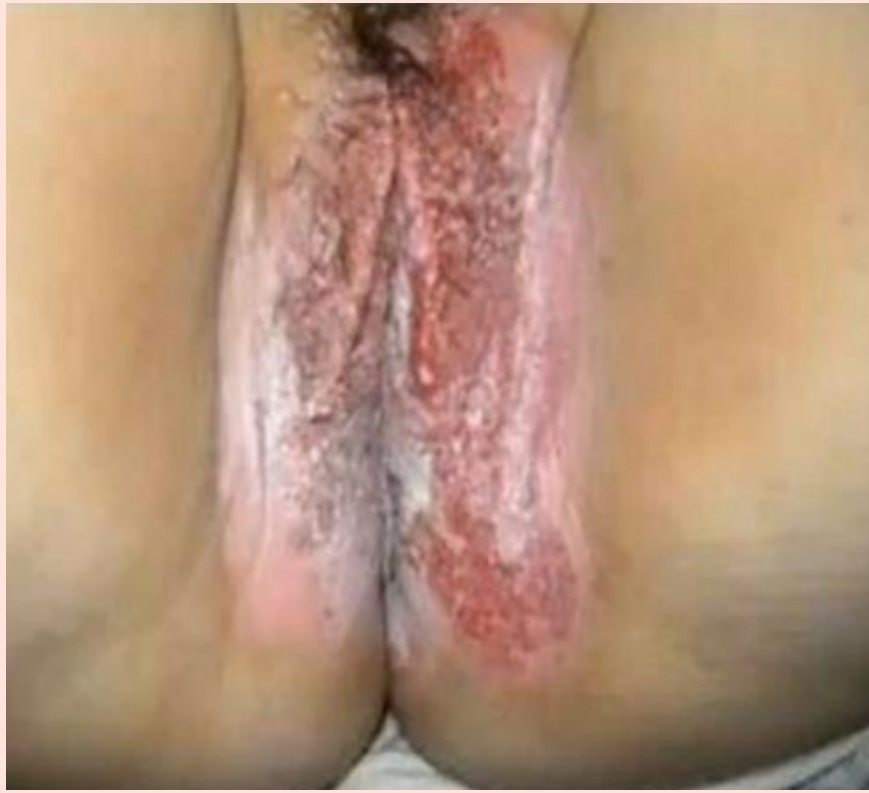
Prognosis:

- the overall survival rate for vulvar CA >> 70%
- The most important prognostic factor is the status of the LN
- Negative LN >> 5 y survival rate 90%
- Positive LN >> 5 y survival rate 50%

Paget disease of the vulva

An **adenocarcinoma in situ** Low risk **(< 15%)** of underlying invasive Paget disease/invasive adenocarcinoma

C**haracterized** by localized pruritus and eczematous lesions (e.g., **erythematous patches with white scaling, crusting, ulcerations**)



Paget disease of the vulva

Main Treatment Approach: for noninvasive

- Local superficial excision with 5- to 10-mm margins

Colonoscopy should be undertaken to exclude an underlying rectal cancer.

Cystoscopy should be performed to exclude an underlying urothelial cancer.

- If an underlying invasive carcinoma is present, the treatment should be the same as for other invasive vulvar cancers.

2)Malignant Melanoma

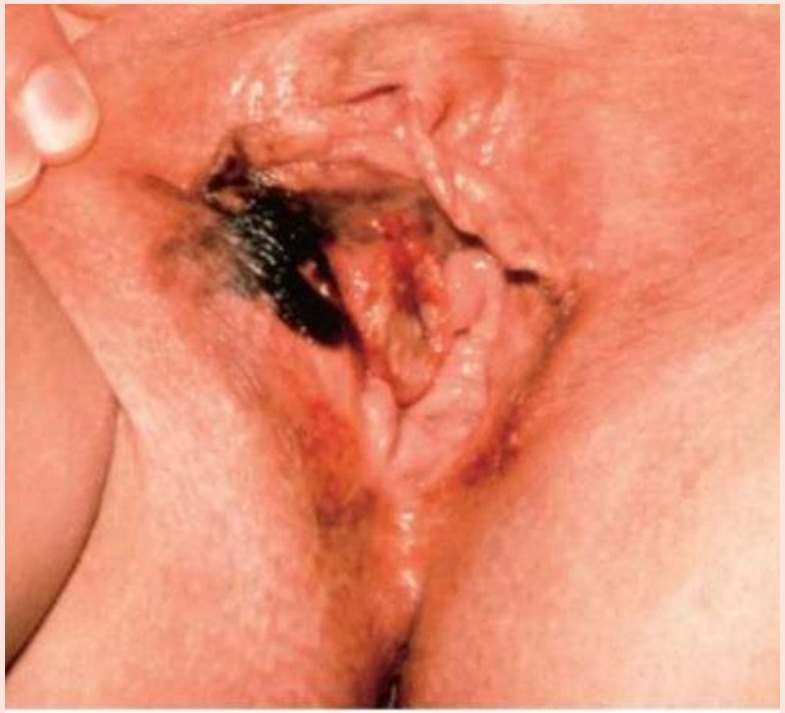
Is the second most common type of vulvar cancer

- **De novo / from pre-existing junctional or compound nevus**
- **occur in post menopausal white women**
- **Positive for S100 immune stain**

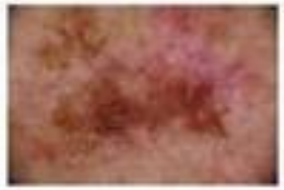
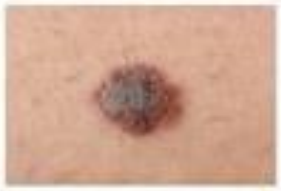
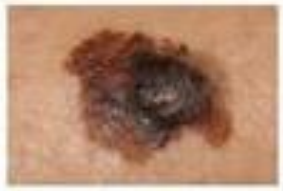
Malignant Melanoma

Clinical Features:

- **New pigmented lesion**
- **Histologic diagnosis •**
- **Usually <1 mm in depth • Or less than granular layer of theepidermis**



40-5 Malignant melanoma arising from the rig

	Benign		Malignant	
Symmetrical		A Asymmetry		Assymetrical (the two sides do no match)
Borders are even		B Border		Borders are uneven
One color		C Color		Two or more colors
Smaller than 6 mm (1/4 inch)		D Diameter		Larger than 6 mm (1/4 inch)
Ordinary mole		E Evolution		Changing in size, shape, color, or another trait

Management

- Less than 1 mm in depth Radical local
- excision with 1 cm safety margin More
- than 1 mm in depth Radical local
- excision with lymphadenectomy Prognosis: The overall 5-year survival
- rate for vulvar melanomas is approximately 30%

- **3) Bartholin gland carcinoma**

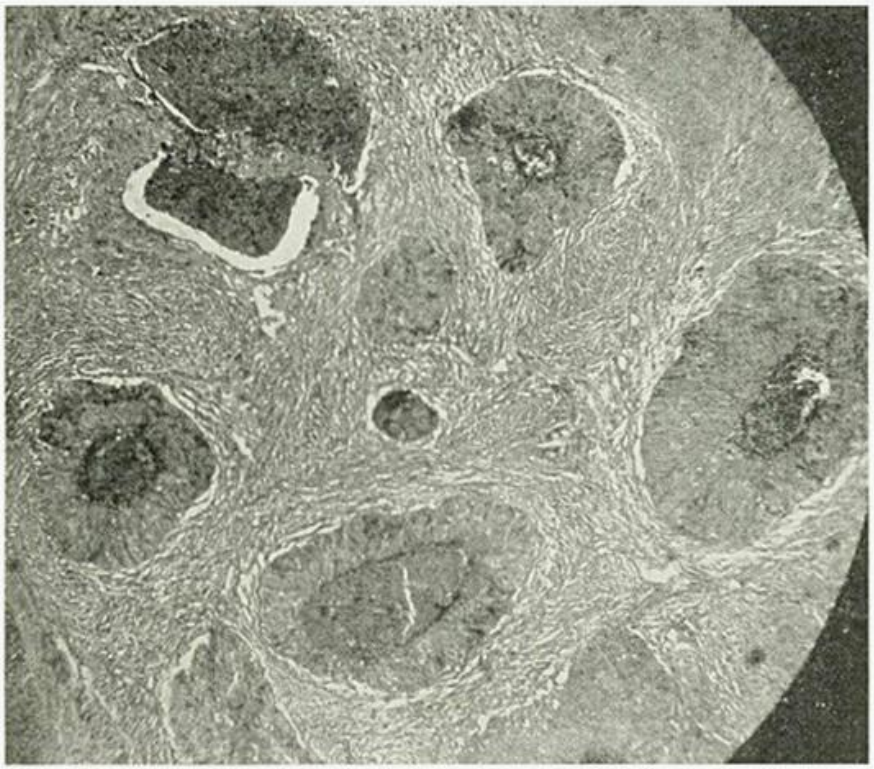
is a type of cancer of the vulva arising in the Bartholin gland.

It typically presents with a painless mass at one side of the vaginal opening in a female of middle- age and older, and can appear similar to a Bartholin cyst.

The mass may be big or small, may be deep under skin or appear nearer the surface .with overlying ulceration

- **Management**

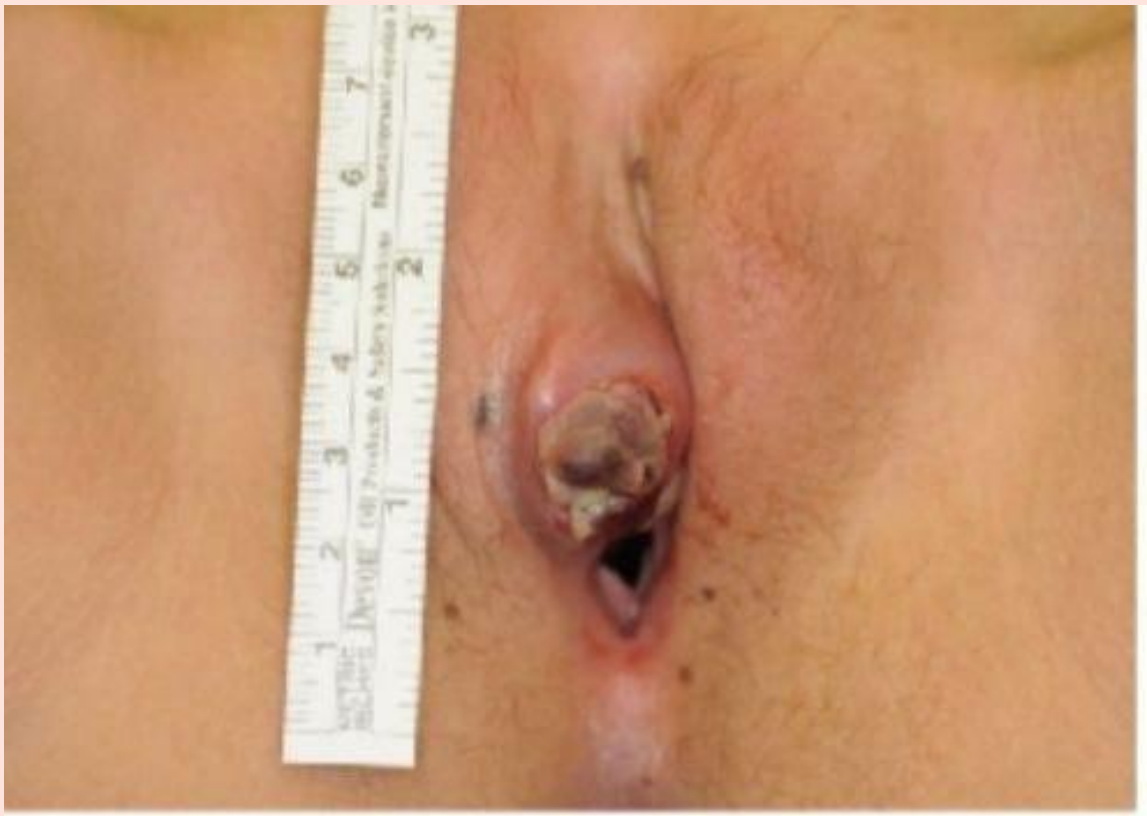
hemivulvectomy and radiation



Barthlin carcinoma tissue cross section

4) vulvar sarcoma

Vulvar cancer commonly forms as a lump or sore on the vulva that often causes itching. Though it can happen at any age, vulvar cancer is usually diagnosed in older adults.



VAGINAL INTRAEPITHELIAL NEOPLASA(VAIN)

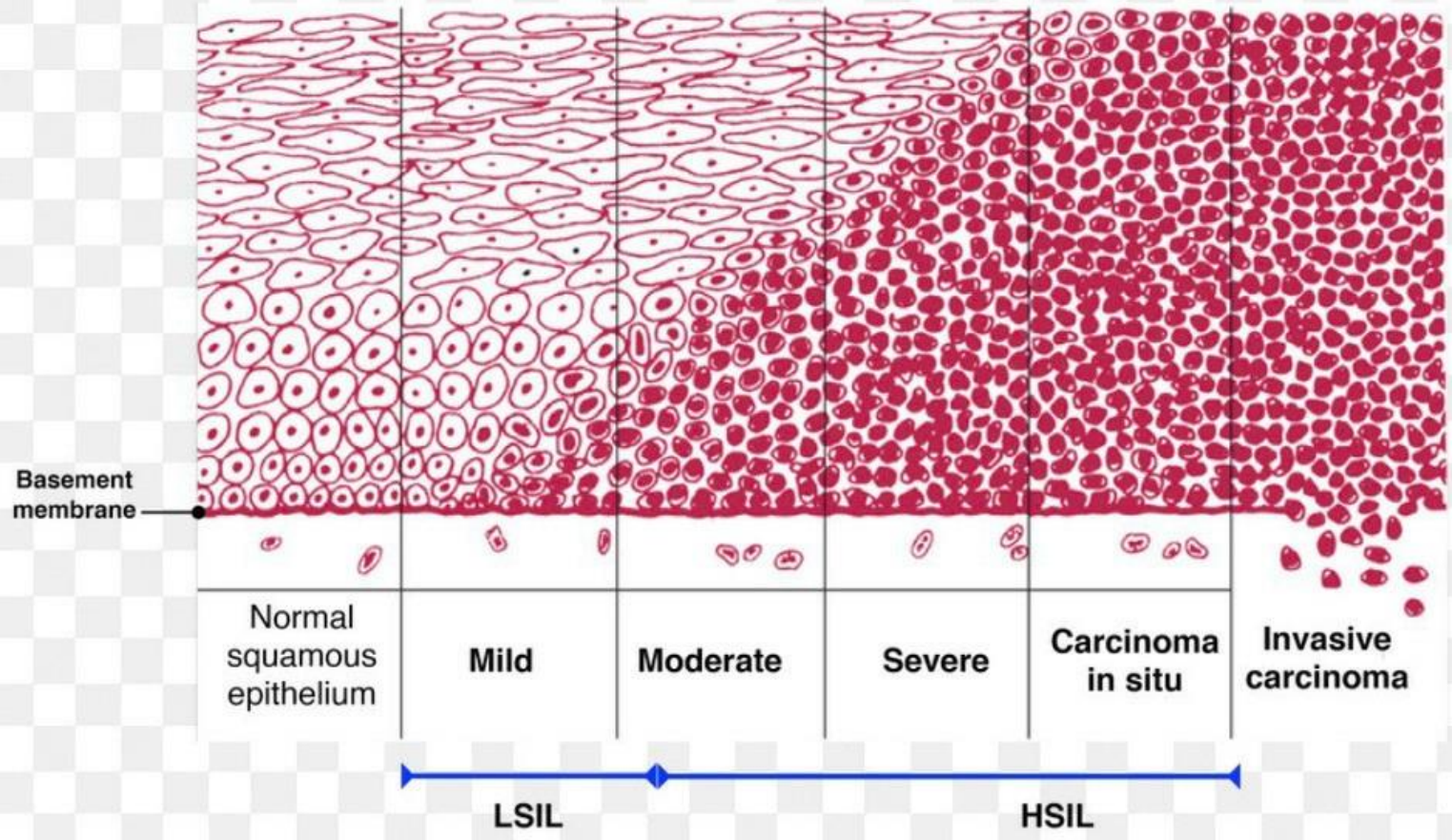
- Carcinomain situ ofthe vagina(vaginal intraepithelial neoplasia [VAIN]) Is
- much less common than its counterparts on the cervix or vulva.
- Most lesions occur in the upper third of the vagina The patients are usually
- asymptomatic.

- **RISK FACTORS**
  - 1- HPV INFECTION
  - 2-PATIENTS WITH A PAST HISTORY OF IN SITU OR INVASIVE CARCINOMA OFTHE CERVIX OR VULVA
  - 3-PATIENTS WHO RECEIVEDIRRADIATIO N FOR CERVICAL CANCER

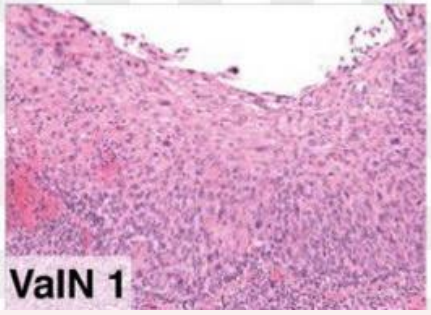
vaginal intraepithelial neoplasia (VAIN)can be classified into three types:

- **VAIN I involves the basal epithelial layers**
- **VAIN 2 involves up to two-thirds of the vaginal epithelium**
- **VAIN 3 involves most of the vaginal epithelium (carcinoma in situ)**

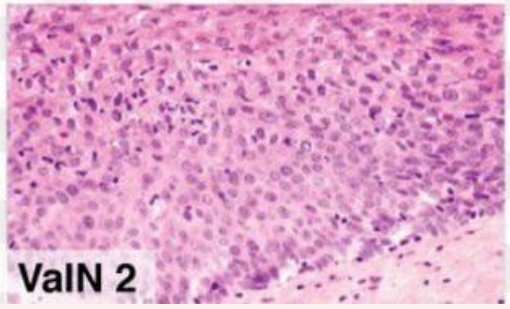
Vaginal Intraepithelial Neoplasia



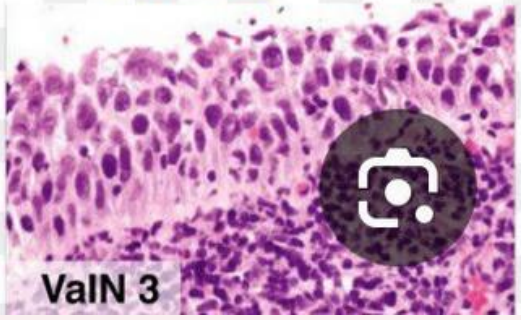
- Mild dysplasia
- Abnormal cells can be found in 1/3 of the vaginal epithelium



- Moderate dysplasia
- Abnormal cells can be found in 2/3 of the vaginal epithelium



- Severe dysplasia
- Abnormal cells can be found in more than 2/3 of the vaginal epithelium and up to the full thickness of the lining



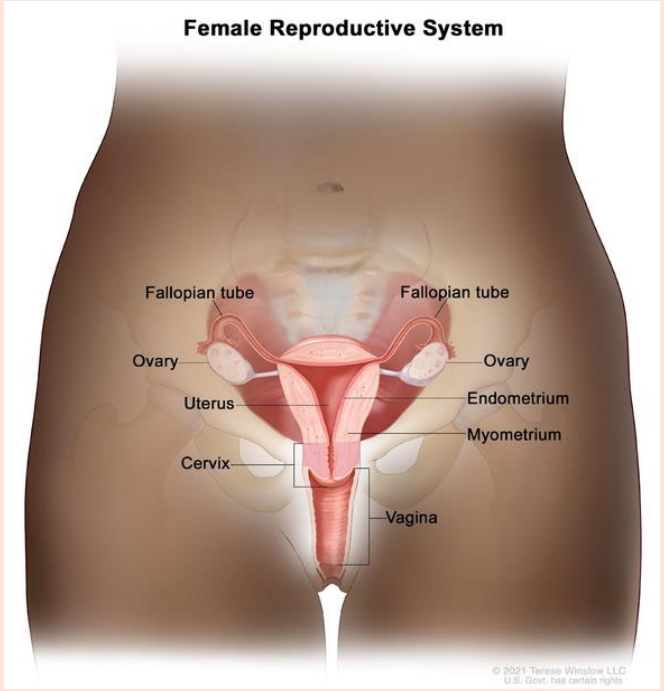
DIAGNOSIS

- **DIAGNOSIS–Definitive diagnosis by vaginal biopsy with directed colposcopy**

TREATMENT

- Patients with VAIN I and II can be monitored and typically will not require therapy
- The goals of treatment of VAIN III are ablation of the intraepithelial lesion while preserving vaginal depth, caliber, and
- sexual function Treatment modalities
- include:
- 1-laser ablation
- 2-exicision
- 3-5-flourouracil
  4-partial or total vaginectomy

Vaginal Cancer



In General: Incidence

Vaginal cancer is rare, accounting for just 1–2% of gynecological malignancies. Most vaginal tumors arise from metastatic spread from the endometrium or cervix. Primary cancers of the vagina: Squamous cell carcinoma (SCC) accounts for approximately 80% to 90% of vaginal cancer cases and adenocarcinoma accounts for 5% to 10%.

Rarely, melanomas (often nonpigmented), sarcomas, small-cell carcinomas, lymphomas, or carcinoid tumors have been described as primary vaginal cancers.

Distant hematogenous metastases occur most commonly in the lungs, and, less frequently, in the liver, bone, or other sites.

Risk Factors

Increasing age: >60. Human papillomavirus (HPV) infection (types 16 & 18). Smoking Diethylstilbestrol (DES) exposure in utero. (Rare now) Precancerous lesions: vulvar squamous intraepithelial lesions (SIL).

History of hysterectomy; orbenign,premalignant,ormalignantdisease.

Clinical Features

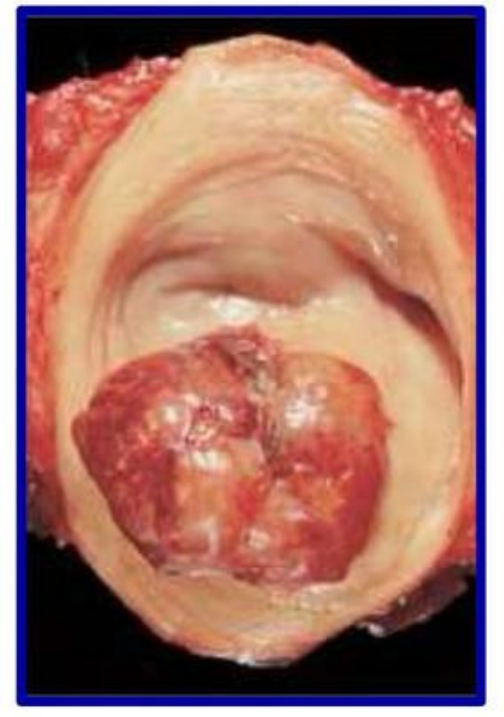
- Although early vaginal cancer may not cause noticeable signs or symptoms, possible signs and symptoms of vaginal cancer include:
- Abnormal bleeding or blood-stained vaginal discharge is the most common presenting complaint.
- Dyspareunia. Pelvic pain. Vaginal mass. Dysuria. Constipation.

Types of Vaginal cancer

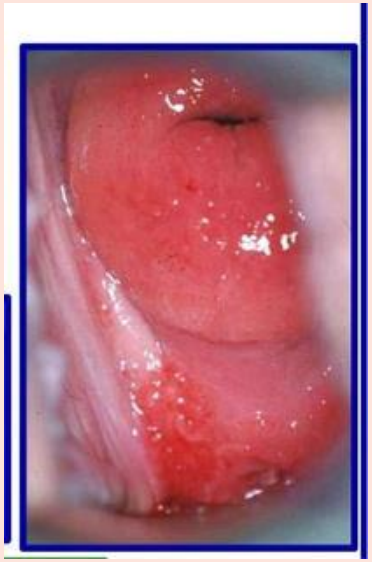
1. Squamous cell carcinoma. 2. Adenocarcinoma ; (clear cell adenocarcinomas). 3. Melanoma. 4. Sarcoma (Sarcoma Botryoides).

1. Squamous cell carcinoma.

- Mostcommon type of vaginal cancers.
- Develops from the squamous cells lining the vagin al.
- Prevelance of occupation: Upper vagina; the posterior wall.
- Diagnosis is confirmed by biopsy.
- An examination under anaesthetic, cystoscopy and sigmoidoscopy defines local spread.
- An MRI scan of the pelvis confirms findings and a (CT) scan of the thorax and abdomen establishes whether distant metastases are present.



2. Adenocarcinoma & Diethylstilbestrol (DES) exposure in utero.



- Develops from the glandular cells on the surface of the vagina.
- It was linked to vaginal adenocarcinoma clear cell
- Seen in daughters of women who received diethylstilbestrol during pregnancy.
- This association was mainly applicable to vaginal cancersdiagnosed in younger women since adenocarcinomas that are not associated with DES exposure occur primarily during postmenopausal years.

3. Melanoma

- Develops in the pigment producing cells (melanocytes)
- Occur mostly in post menopausal women
- Most frequent location : distal vagina (lower third of the anterior wall)
- Radical surgical treatment as well as local excision, with post operative radiotherapy, have been shown to obtain similar results.
- poor prognosis with a 5 years survival rates around 5 - 10 %.

4. Sarcoma Botryoides (Grape - Like)

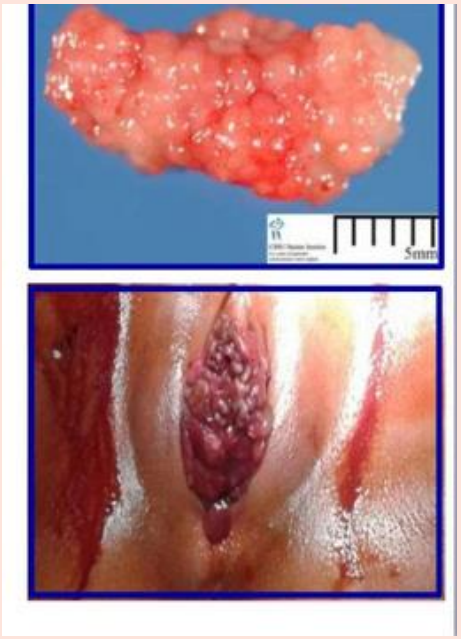
Develops in theconnectivetissuecellsormusclescellsinthewallsofthe vagina.

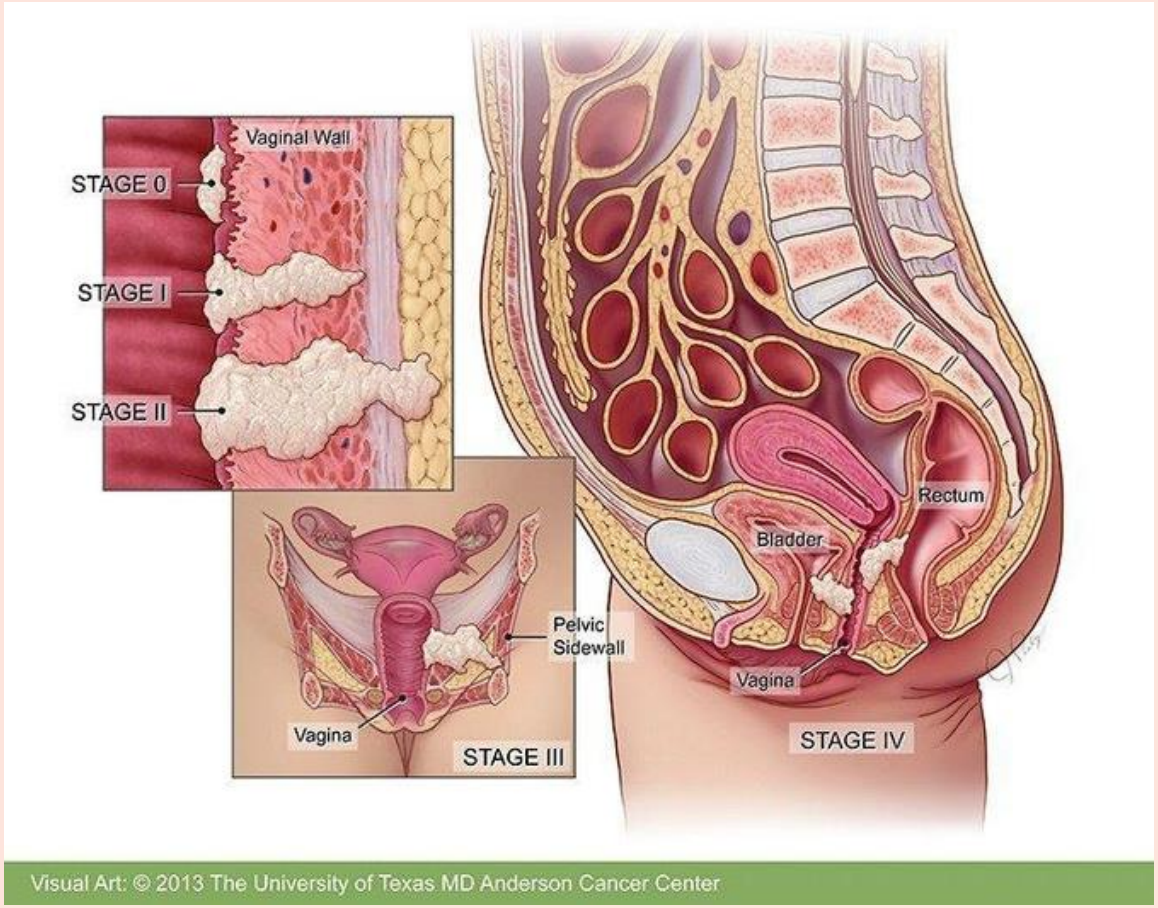
It is a form of embryonal rhabdomyosarcoma

Affecting the paediatric population (mean : 2-3 years old)

The mass is highly malignant

The treatment regimes range from excision of the tumor to radical hysterectomy with adjuvant chemotherapy and / or radiotherapy.





Staging of vaginal cancer uses the FIGO system:

FIGO Nomenclature	
Stage I	The carcinoma is limited to the vaginal wall.
Stage II	The carcinoma has involved the subvaginal tissue but has not extended to the pelvic wall.
Stage III	The carcinoma has extended to the pelvic wall.
Stage IV	The carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum; bullous edemas as such does not permit a case to be allotted to stage IV.
	IVa - Tumor invades bladder and/or rectal mucosa and/or direct extension beyond the true pelvis.
	IVb - Spread to distant organs.

Diagnostic Evaluation

- History and physical examination. • Pelvic examination. • Cervical cytology (Pap smear). • HPV testing. • Colposcopy. • Biopsy. If the cervix is intact, biopsies are mandatory to rule out a primary carcinoma of the cervix.

Carcinoma of the vulva should also be ruled out

Treatment

Stage I	Stage II, III, IVa
For lesions < 0.5 cm thick: - Radiation therapy (Wide local excision) - Surgery (radical vaginectomy with reconstruction) For lesions > 0.5 cm thick: - Surgery (Radicalvaginectomy with pelvic lymphadenectomy for upper vaginal lesions, inguinal lymphadenectomy for lower third) - Radiation therapy	- Radiation therapy (Radical vaginectomy orpelvic exenteration with/without radiation) - Chemoradiation

أحمد بن يوسف السيِّد
t.me/alsayed_ah

حاول أن تعمل -**كل يوم**- شيئاً لإخوانك في غزة، ولا تنتظر النتائج الكبرى من عملك، فلو كفلت عائلة أو سددت فاقة أرملة أو جاهدت بمالك أو بلسانك أو استمر قلبك ولسانك في الدعاء الخاشع لله بتفريج الكربة وتحقيق النصر؛ أو حرضت غيرك ممن له قدرة أعلى من قدرتك؛ فكل ذلك خير.

المهم ألا تفتر أو تنسى..

ودعك ممن همه تخذيل الناس عن هذه الخطوات، ممن لم يفعل شيئا لا كبيرا ولا صغيرا لإخوانه سوى التثبيط والنقد.