

\* Pagets of Nipple  $\Rightarrow$  underlying cancer in breast  $\checkmark\checkmark$

Pagets of vulva  $\Rightarrow$  No underlying tumours anywhere

# Female Genital System

## PAGETS vs melanoma.

- written
- In Both these diseases, there is intraepithelial population of malignant cells.

### Melanoma.

- Starts in epidermis, & can invade dermis too.
- one of the uncommonst location of melanoma is vulva.
- so we have to distinguish

Pagets of vulva / is it carcinoma — PAS + , Keratin + , S100 -  
is it melanoma — PAS - , Keratin - , S100 +

melanoma  
IHC  $\downarrow$   
S100  
Melan A  
HMB-45

## V.V.V. Imppt

• Keratin  $\rightarrow$  It is an intermediary filament in epithelial cell.  
ie, if Keratin is present, it is epithelial  $\rightarrow$  carcinoma.  
there won't be Keratin  $\oplus$  in lipoma, melanoma etc.

• PAS - marks mucin  
only epithelial cells make mucin  
 $\hookrightarrow$  carcinoma

Vulva - skin & mucosa external to hymen - labia majora, minora, vestibule etc.

(low risk HPV)

lined by **squamous epithelium**.  
 ✓ stratified sq. - keratinized & non keratinized parts.

① B Bartholin's cyst

due to blockage of Bartholin's duct, due to infection etc.

\* unilateral  
 \* lower vestibule  
adjacent to vaginal canal. location? Based question.

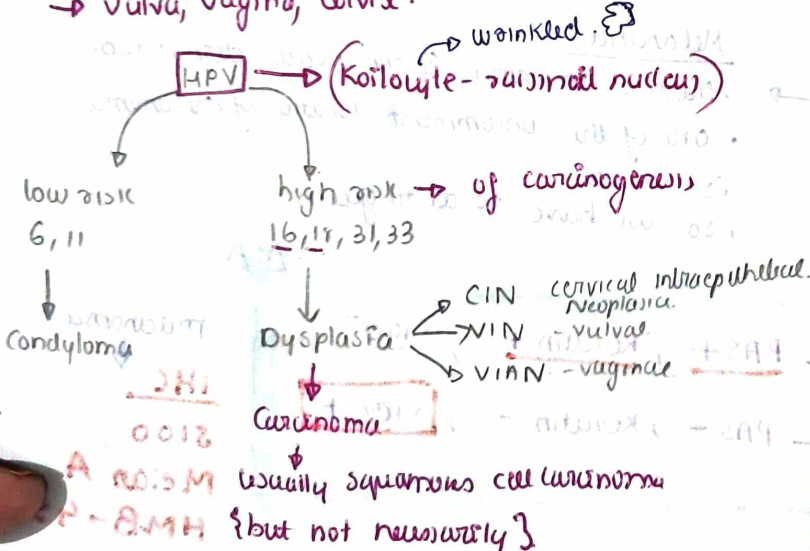
cystic dilation of Bartholin's gland.

\* usually in women of reproductive age

② Condyloma - HPV-6, 11

- warty neoplasm of vulvar skin, often large.
- most commonly due to HPV 6, 11.
- characterized by koilocytic change.
- Rarely progresses to carcinoma.

HPV infects lower female genital tract  
 → vulva, vagina, cervix.



③ Lichen (Sclerosis) (Thinning)

- thinning of epidermis and fibrosis of dermis.
- Leukoplakia with white plaque.
- parchment-like vulvar skin, paper thin.
- m/c → post menopausal women (like an atrophy change).
- Benign, associated with slightly increased risk of Squamous cell carcinoma.

④ Lichen Simplex chronicus (Thickening)

- Hyperplasia of vulvar squamous epithelium.
- Leukoplakia with thick leathery vulvar skin.
- associated with chronic irritation & scratching.
- Benign, no increased risk of sq. cell carcinoma.

HPV = warty low/high risk.

↓  
 Koilocytic change.

Etiology (2 pathways)

① HPV - 16, 18, 31, 33. related. 40s-50s

② Non HPV related  
 → long standing Lichen Simplex chronicus  
 postmenopausal. > 70 year old.

Vulvar Carcinoma.

- arises from squamous epithelium lining vulva.
- rare, account for only 5-11% of female genital cancer.
- presents as Leukoplakia → so now we have to differentiate between ca & Lichen sclerosis, simplex chronicus

How? → Biopsy

# ① Vulval Tumors. (Vulva = External FNs.)

- ① # Condyloma acuminatum / warts.
- ② # VIN / Bowen's disease → preinvasive.
- ③ # vulval carcinoma → Cancer.

• HPV affects: squamous cells  
and vulva is made of

↓  
Squamous cells

• all HPV infections are characterized by { high & low risk }

↓  
KOILOCYTE

• dark blue, oval nucleus  
weird nucleus

+ surrounded by perinuclear halo.

Koilocyte = oval nucleus + perinuclear halo.

↓  
characteristic of HPV infection.

## ④ # Extramammary Paget's disease.

• paget's is also seen in breast  
↓  
that is called mammary p.d.

→ the one occurring in vulva  
is called → Extramammary paget's disease.

monomorphic.

benign = low risk.

benign - Caused by HPV - 6, 11 (small number)

HPV - 16, 18 : high risk = high numbers of HPV.

V - vulval  
I - intraepithelial  
N - Neoplasm.

In paget's disease there is underlying tumours in deeper tissue.

↓  
and small tumours (cells) from large tumours goes to epidermis

↓  
seen as lighter cells in epidermis.

↓  
so the patient has red, pruritic lesion

• paget's cells are pale cells.

↓  
+ PAS  
+ mucicarm.  
CK7 +

• malignant epithelial cell in epidermis of vulva, nipple.

→ presents as - erythematous, pruritic, ulcerated skin.

→ represents carcinoma in situ, usually no underlying carcinoma.

## 2 Vaginal Tumors

1 Squamous cell carcinoma → of course; due to HPV

2 clear cell adenocarcinoma → clear cell adenocarcinoma occurs due to

3 Sarcoma botryoides/  
Embryonal Rhabdomyosarcoma.

DES diethylstilbestrol

given to mother

causes clear cell carcinoma in daughter

DES → daughter

all clear cell carcinoma

of F6 tract is due to

DES

give to mother

causes in daughter

Embryonal → in children

Rhabdomyo → skeletal muscle.

Sarcoma → malignant.

It is skeletal muscle tumour in vagina occurring in children.

• botryoides ⇒ bunch of grapes.

• this tumour cells looks like

Bunch of grapes

MICROSCOPY

• Cambium layers (cells) ++  
• below it - cell - hypocellular.

They'll use which connect has Cambium layer.

SB / ERMS

## 3 CERVICAL CANCER

RISK factors

- HPV { cause there is sq. cells in cervix }
- Smoking
- Immuno deficiency
- OCP.

• premalignant lesion

Cervical Intraepithelial Neoplasia (CIN)

CIN - I, II, III

CIN I - lowe 1/3rd dysplastic cells in epithelium.

CIN II - lower 2/3rd dysplastic cell

CIN III - 3/3 or almost full thickness

100% carcinoma - Full thickness affected in epithelium

invasive - full thick + basement membrane breach.

CIN - I, II, III, carcinoma

Bm is intact

invasive → Bm breached

posible sm. special stain

PTAH

Rms (skeletal muscle)

phospho tungstic acid Hematoxylin.

IHC for all sm  
→ Desmin +  
→ myoD1 +  
→ myogenin +

P4Q

Newer name.

# CIN I → **LSIL**

# CIN II, III, C-insitu → **HSIL**

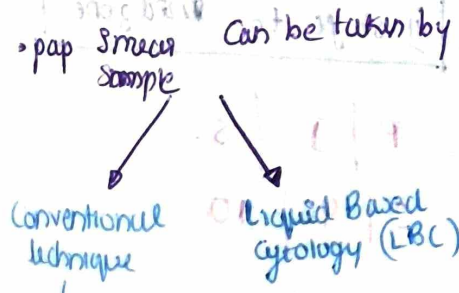
• low grade squamous intraepithelial lesion - LSIL

• High grade squamous intraepithelial lesion.

Screening for Cervical Cancer.

↓  
**PAP Smear.**

• pap - papinicalou.

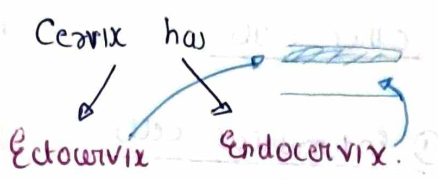


• after taking sample from ecto & Endocervix using Ayre's spatula

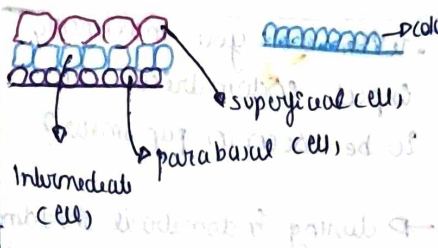
↓  
paint it on a slide.

• Smear has debris - mucus, blood etc.

• also, since it is randomly painted, they have to view all fields from corner to corner.



↓ Squamous epithelium      ↓ Columnar epithelium



LBC - It's a machine.

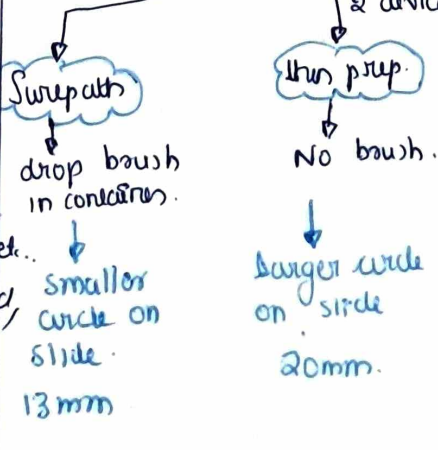
• It is going to remove all debris

• Since it is uniform throughout → saves time

a) we don't have to view everything from corner to corner.

- take sample using brush  
↓  
then put into container having a liquid which is alcohol.

LBC from 2 devices.



PAP stain Components

• whenever we get a slide, we first to do fixation ①

↓  
95% ethanol

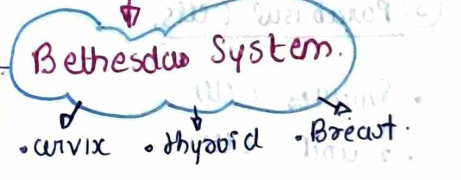
• then we do staining ②

**PAP stain:**

- H - Hematoxylin
- O - Orange green (G6)
- P - pap stain
- E - Eosin Azure 50 (EA 50)

Reporting ③

• for reporting we use,



Adequacy for reporting of PAP Smear. **prev. data**

① Conventional PAP Smear.

- Endocervical cells ≥ 10 well preserved
- 8000 - 12000 / ectocervical cells per 10hpf.

② Liquid Based cytology

- Endocervical cells ≥ 10 well preserved
- 5000 cells/hpf - Ectocervical cells

How do these cells actually look like in PAP smear?

① Superficial cells.

- P - polygonal.
- P - Pink
- P - Pyknotic nucleus. {dot like nucleus}

② Intermediate cells.

- B - Blue
- B - Bigger nucleus {compared to superficial cells}

③ Parabasal cells.

- Smaller cells
- round cells
- in clusters

round cells in cluster.

Endocervical cells.

- they are columnar cells.
- lateral view  
↓  
Picket fence butterfly on fence appearance.
- Top view  
↓  
Honeycomb appearance.

Other cells.

① Endometrial cells.

- 3D - Ball like clusters.
- dark blue.

• when do you maximally expect endometrial cells to be seen in pap smear?

→ during endometrial shedding

→ during menstruation

day 1-5

↓  
during active bleeding, we see proper endometrial cells.

But from day 6-10

↓  
even when there is no active bleeding, we see remnant cells

↓  
Exodus cells **Exodus Bull**

• duct bull  
↓  
thick bull inside, surrounded by thin bull.

Maturation Index.

say, count 100 cells on slide.

• write in sequence

**P/I/S** always

• analyze which cells are majority.

**I. shift to right.**

P/I/S  
0/10/90

lot of Pink.

Estrogen predominance.

**II. shift to mid zone.**

P/I/S  
0/90/10

progesterone predominance.

**III. shift to left.**

P/I/S  
100/0/0

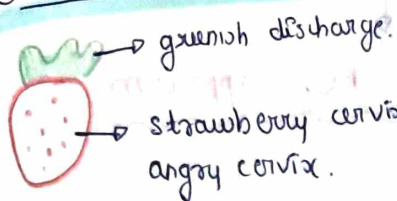
Atrophic Smear/

post-menopausal female smears.

# INFECTIONS.

## ① Trichomonus infection.

①



Smear

- pear shaped / kite shaped  
Trichomonas, flagellated.

\* Trichomonus " often seen with

Leptothrix



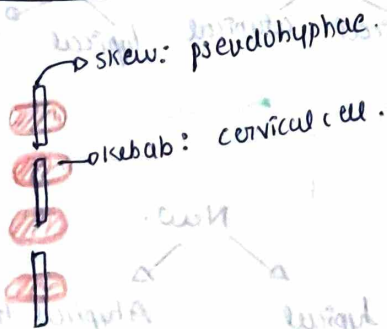
## ② CANDIDA infection.

②

Candida - Curdy - Kebab.

- curdy white discharge.

- Shish Kebab.



## ③ Bacterial Vaginosis.

③

• caused by: *Gardnerella vaginalis*

• 2 criteria for diagnosis

→ Amsel's criteria,  
Nugent's criteria.

Smear.

① Cocci bacilli stuck to cells

↓  
clue cells



② coccobacilli in background.

fuzzy background.

## ④ Adenomycosis.

④

H/O IUCD !

→ cotton ball / woolly ball / sunray /  
dust bunnies / Gupta bodies.

## ⑤ HPV.

⑤

→ koilocyte. → dirty, dark, shrivelled nucleus.

→ perinuclear halo.

## ⑥ HSV.

⑥

3 M  
M → Multinucleation  
M → moulding  
M → margination.  
{dark periphery}



Squamous cell carcinoma

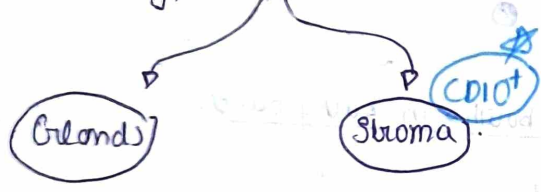
\* Tadpole cells



UTERUS

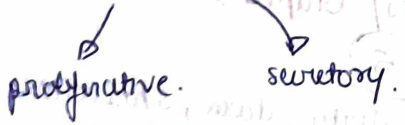
ENDOMETRIUM

Normally, Endometrium has.



- they show variation with cycle.
- Stroma is CD10+

Phases:



① proliferative.

Glands - uniform, round  
 Stroma - closely packed / compact.  
 {not white space in btwn}

Secretory Endometrium.

early SE → subnuclear vacuolations.  
 ↓  
Piano Key appearance.

late sec. Endo → secretion into lumen.

Glands - tortuous, random shape.  
 Stroma - loose, edematous.  
 {white space in between}

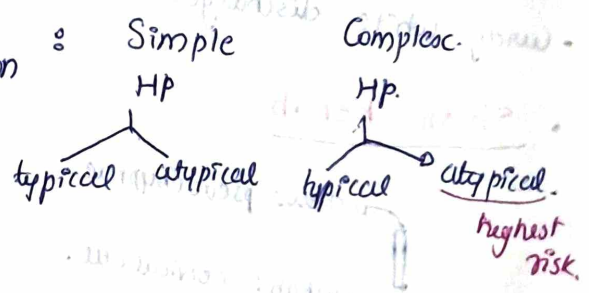
Endometrial hyperplasia - premalignant

Hyperplasia - ↑ in number of cells.

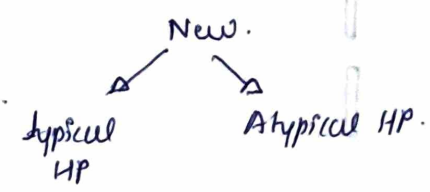
↓  
 due to Estrogen.

can progress to  
Endometrial cancer.

Earlier classification



Newer classification



# ENDOMETRIOSIS

## DEFINITION

Endometrial glands, stroma, Hemosiderin outside uterus.

## SITES

ovary, broad ligament, Intestine, lung, POD, Scars.

## Endometriosis in ovary

→ presents with → pelvic pain, infertility

## GROSS

chocolate cyst  
↓  
due to old blood  
Brown.

## MICROSCOPY

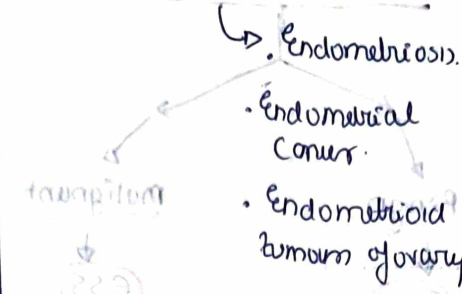
Glands, stroma, Hemosiderin (Brown).

## Hypothesis theories?

- 1) retrograde menstruation Sampson's theory (menstrual blood occurs into ovary)
- 2) theory of metaplasia
- 3) stem cell theory
- 4) ARID1A, PTEN genes

chr 10  
LOWDEN

# PTEN



# ADENOMYOSIS

## DEFINITION

Endometrial Glands, stroma in myometrium.

It should be at least  $\geq 2.5$  mm away from endometrial-myometrial junction.

## GROSS

uterus - like ball.  
Bleeding from myometrium

## HMC

glands, stroma in btw muscle layer.

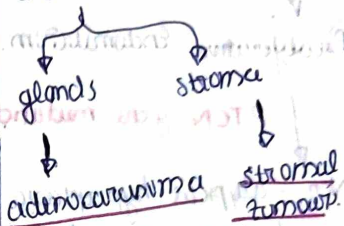
MMMT - malignant mixed Mullerian tumour

SIEC - serous intraepithelial carcinoma

# Uterine Tumours

- Endometrial tumours
- myometrial tumours

## Endometrial tumours



## Endometrial Carcinoma

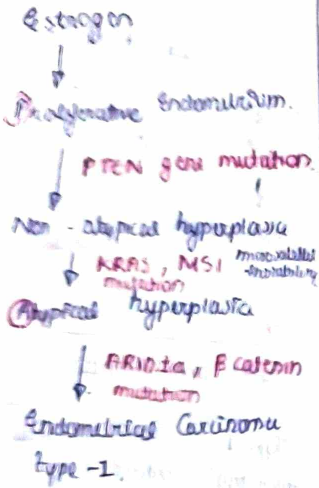
Types and Genetics.

Type I Endometrial Ca	Type II Endometrial Ca	features
50-65y	65-75	age
estrogen excess	atrophy	Hormonal status
Endometrioid Endometrial Ca	serous cell, clear cell, MMMT variety.	Morphology
Hyperplasia	SIEC	Prognosis
	aggressive	

Indolent  
{better prognosis?}

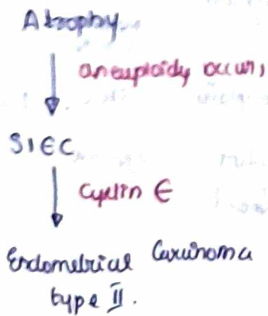
(Genetic)

**Type - I**

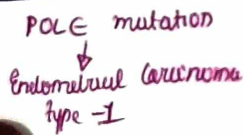


Non ⇒ Kabhi Nahi KRA)

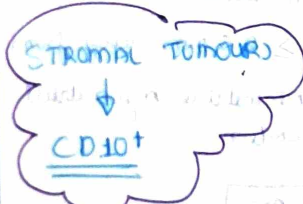
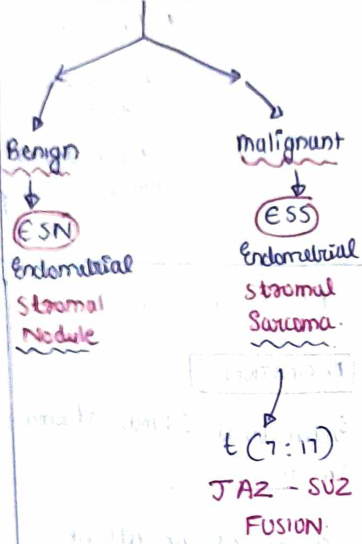
**Type - II**



Update: ROBBINS 10th ed.



**Endometrial Stromal Tumours**



Gross & yellow appearance  
IHC - CD10+

**MYOMETRIAL TUMOUR**

- Smooth Muscle tumour
- ↓
- LEIO MYO**
- Leiomyoma (benign)
- STUMP (in-brain)
- Leiomyosarcoma (malignant)

**LEIOMYOMA / FIBROIDS**

- benign - smooth muscle tumour.
- in uterus
- ↓ AKA
- Fibroids.

Genetic - MED 12 gene mut  
Chr, 12, 6, rearrangement

- MED 12 gene mutations:
- fibroids
  - fibroadenoma breast
  - phyllodes tum - breast

**SITES**

- 1) Submucosal (close to cavity) leiomyoma.
- 2) Intramural L (deep in muscle)
- 3) Subserosal L.

**GROSS**

- whorling
- white

**MC**

- Whorling, fascicles
  - ↓
  - circle shaped nuclei
- IHC: SMA+
- Smooth muscle actin.
- cell showing cyto nucle → any cell smooth muscle related leiomyoma, leiomyosarcoma

**DEGENERATION**

- 1) Hyaline degeneration. (mc - pink)
  - 2) Calcific degeneration
  - 3) Red degeneration
- ↓  
Begy red colour  
↓  
associated with pregnancy.
- preserts with → fever, abd pain.

**Types**

- Cellular Leiomyoma - cells + ++
- Symplastic - Atypa-some have there.
- Metastasizing leiomyoma
- leiomyoma present in lung, is thought to be metastasized from uterus.
- Mind it! It's benign.
- It's just a theory.