



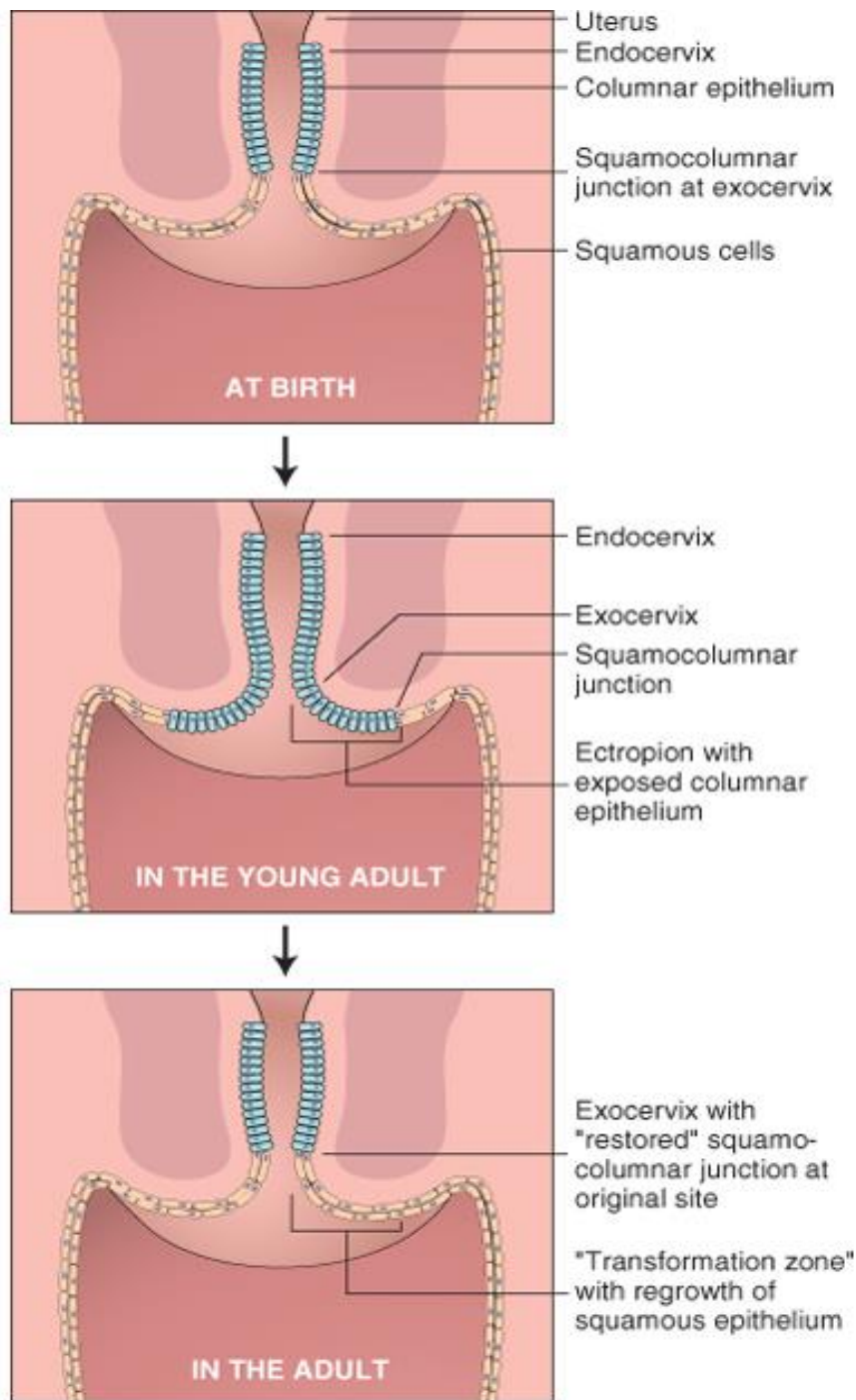
# Pathology

3<sup>rd</sup> Stage

Dr. Su'dud

## Female Reproductive System

### The Cervix



## Most cervical lesions are

1. inflammatory (cervicitis).
2. Carcinoma

## Cervicitis

Are associated with a mucopurulent or purulent vaginal discharge.

## Cytological exam of the discharge

- ❖ white cells
- ❖ microorganism if possible
- ❖ inflammatory atypia of the shedded epithelial cells.

## Cervicitis could be

1. Non- specific (mixed bacteria)
2. Specific (*N. gonorrhoea*, herpes virus, *Chlamydia*, *trichomonas vaginalis* and human papilloma virus (HPV))

Preinflammatory diseases of the cervix (CIN)

## Squamous cell carcinoma

usually arise over a number of years, probably 10-15 years, from an epithelium which shows progressive abnormality (CIN).

## Cervical intra - epithelial neoplasia (CIN)

What is CIN: (cervical dysplasia)

- ❖ it is a pre malignant stage characterized by the presence of atypical cells within the squamous epithelium of the cervix which show
  - pleomorphism,
  - ↑ mitotic figures
  - ↑ NIC ratio
  - hyper chromasia
- ❖ peak age incidence is 30 years.
- ❖ Squamo – columnar junction (transformation zone) is the commonest site of involvement.
- ❖ HPV (Human Papilloma Virus) can be detected in nearly all pre – cancerous lesions.

## **CIN are graded as Follows:**

1. **CIN I (mild dysplasia)**  
Atypical cells are confined to the lower 1/3 of the epithelium
2. **CIN II (moderate dysplasia)**  
Atypical cells extends into the middle 1/3 of epithelium
3. **CIN III**
  - sever dysplasia  
Atypical cells involved 75% of the epithelium
  - Ca in situ  
atypical cells involved the whole thickness of epithelium

## **Bethesda system** (other system for grading)

- ✓ Lowgrade squamous Intra epithelial lesions (LSIL) → CIN1
- ✓ High grade squamous Intra epithelial lesions (HSIL) → CIN II, CIN III

## **CIN may**

1. progress to invasive cancer
2. many persist without change or
3. regress

The higher grade of CIN the greater risk of progression into invasive ca

## **Epidemiology and pathogenesis**

Risk factors for CIN and invasive squamous Ca are:

- ✚ early marriage
- ✚ multiple pregnancies (multiparous).
- ✚ low socio – economic status
- ✚ persistent infections with high risk human papilloma virus type16, 18, 31 and 32

## **Invasive cervical Ca**

peak age incidence is about 40ys

commonest site (region of transformation zone)

## Morphological Features

### Gross

1. fungating (exophytic)
2. Infiltrative (no definite mass) endophytic (barrel shaped).
3. ulcerative

### Histological features

1. Sq. cell Ca 75%
2. adeno. Ca 20%  
Common in nullipara, mostly is seen in endocervix & in young girls exposed prenatally to diethylstilbestrol
3. Adeno-squamous carcinoma 5%

## Diagnosis

- pap cervical smear
  - early diagnosis
  - for screening (higher risk ♀)
  - for follow up
- colposcopic examination after application of diluted acetic acid (appears white area). (schiller test).
- biopsy

## Body of the uterus

### A. Endometrium

The endometrium is that part of the uterine lining above the level of the internal os consists of a basal layer, which is insensitive to hormonal stimulation & a superficial functional layer which is markedly sensitive to ovarian hormones.

# Endometritis

## 1. Acute endometritis

### Causes:

- ❖ intrauterine trauma from instrumentation
- ❖ intrauterine contraceptive device
- ❖ post - partum retention of placental fragments.

The causative agents may be streptococcus, *staphylo coccus aureus*, *N. gonorrhoea*, *Trichomonus vaginalis* and *Chlamydia*

### Histological features

Biopsy by diagnostic curettage (D&C).

1. odema
2. congestion
3. infiltration with acute inflammatory cells and small intra luminal abscess (abscess inside the glands).

## 2. Chronic Endometritis

### a. Non-Specific

May follow

1. acute endometritis
2. abortion
3. childbirth
4. ICD (intra uterine contraceptive device)
5. chronic salpingitis.

### Histologically

chronic inflammatory cells infiltrate the stroma mainly (lymphocytes with predominance of plasma cells) with some fibroblastic and vascular proliferation

### b. Specific Endometritis

Tuberculous endometitis.

The patient is usually presented with **infertility** caused by the associated tuberculous salpingitis

## Histological features

Few small scattered tubercles with little or no caseation

The tubercles are fully developed in the premenses stage so diagnostic curettage should be performed at this stage.

## Endometrial hyperplasia

- ✓ Endometrial hyperplasia is related to an abnormally high, prolonged level of estrogenic stimulation with diminished or absence of progestational activity.
- ✓ It is one of the causes of abnormal uterine bleeding
- ✓ hyperplasia occurs most commonly around menopause or in association with persistent anovulation in younger women

## Causes

- ✚ Failure of ovulation (around menopause),
- ✚ prolonged administration of estrogenic steroid (oral contraceptive pills).
- ✚ estrogen producing ovarian lesions such as polycystic ovary and granulosa cell tumor
- ✚ Obesity.

## Types

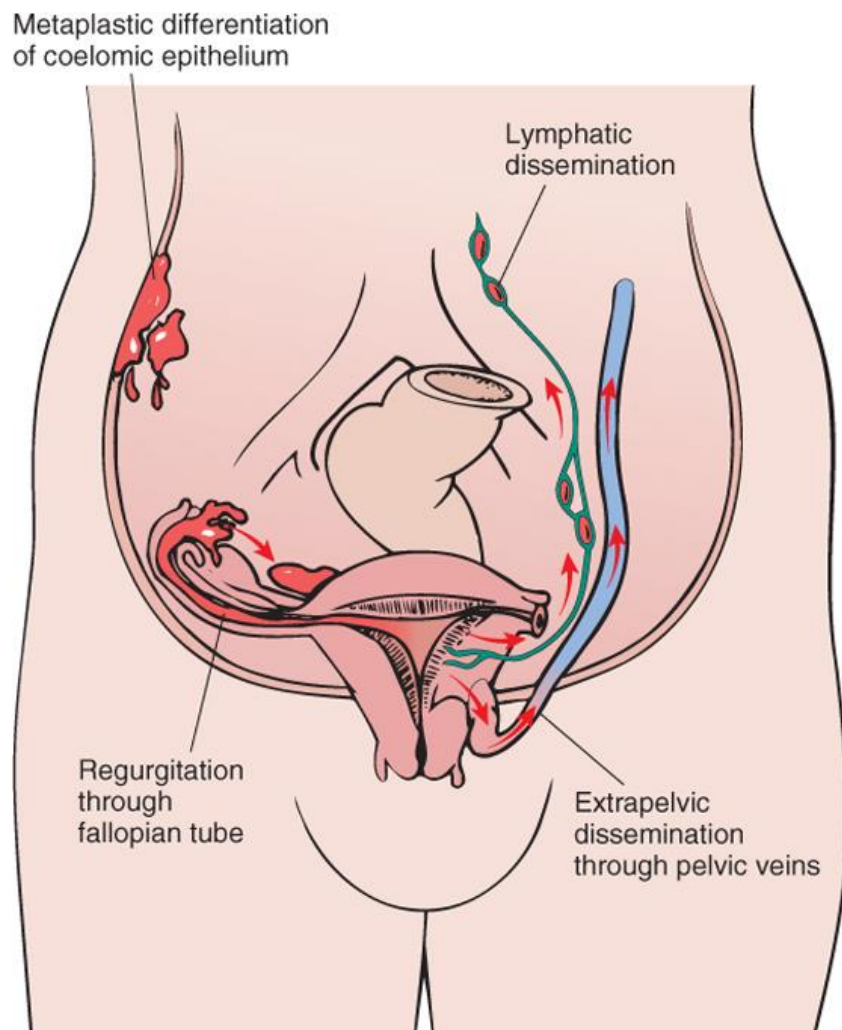
1. **Simple Cystic glandular hyperplasia** (simple hyperplasia)
  - The glands are cystically dilated with variable sizes
  - Lined by normal epithelium.
  - The stroma is oedematous.
  - No or very little tendency for carcinoma.
2. **Complex hyperplasia without atypia**
  - ↑ in no. of glands.
  - It is lined by hyperplastic stratified tall columnar epithelium with multilayerings and without atypia
  - There is abundant mitotic figures
  - < 5% tendency to malignancy.
3. **Complex hyperplasia with atypia**
  - Same as above + Atypia which could be mild, moderate or severe.
  - With high risk of malignancy

## Endometriosis

- ☒ Refers to presence of endometrial glands and stroma outside the uterus
- ☒ may involve ovaries, fallopian tube, peritoneum, bowel, umbilicus, and broad ligament
- ☒ it occurs in about half of women with infertility
- ☒ the ectopic endometrium undergoes, cyclical bleeding and is a common cause of dysamenorrhoea and pelvic pain.

### Three theories explain the origin of endometriosis

- ❖ The **regurgitation theory**, retrograde menstruation through the fallopian tubes, which mediate spread of endometrial tissue to the peritoneal cavity.
- ❖ The **metaplastic theory** proposes endometrial differentiation of coelomic epithelium which is the origin of the endometrium
- ❖ The **vascular or lymphatic dissemination theory**, this theory would explain the presence of endometriotic lesion in the lungs or lymph nodes.



## Grossly

- ✓ pelvic endometriosis is seen as small bluish nodules with surrounding fibrosis.
- ✓ in the ovaries the lesions are commonly cystic & contain altered blood (chocolate cyst).

## "Chocolate" cyst

### Histological features

- ✚ In all sites depends on finding two of the followings three features :
- ✚ endometrial gland
- ✚ stroma.
- ✚ hemosiderin laden macrophage

## Endometrial polyps

- ☒ It is focal over growth of the endometrium which protrudes in to the uterine cavity.
- ☒ Such polyps may be pedunculated or sessile & are pink & fleshy with a smooth surface. Malignant change is extremely uncommon.

## Endometrial carcinoma

Appears most frequently between the ages of 55 and 65 years.

### Risk factors for endometrial Ca

- ❖ Obesity.
- ❖ Diabetes
- ❖ Hypertension
- ❖ Infertility: nulliparous,.
- ❖ Family history of breast Ca.

Excess estrogens as in

1. prolonged estrogen replacement (contra ceptive pills)
2. estrogen -secreting ovarian tumors.

Such as granulosa cell tumor of the ovary.



## Pathological features

### Gross

- ✓ localized as nodule.
- ✓ diffuse through the wall

### Histological features

- ✓ Adenocarcinoma (most common)
- ✓ Adenosquamous

## The myometrium

The myometrium is the thick muscular wall of the uterus & is capable of marked alterations in size, capacity & contractility, during pregnancy & labour.

## Adenomyosis

- ✚ Is the growth of the basal endometrium down into the myometrium, unlike endometriosis there is no cyclical changes
- ✚ It may produce menorrhagia, dys amenorrhea and pelvic pain before the onset of menstruation.
- ✚ It is seen in about 15-20 % of hysterectomy specimens.
- ✚ **Grossly**  
It appears as pink nodules with cystic changes
- ✚ **Histological features**  
Nests of endometrial stroma, glands, or both are found between muscle bundles of myometrium.

## Tumors of Myometrium

### Benign: Leio myomas (Fibroids)

- ☒ Benign tumor arise from the smooth muscle of the uterus.
- ☒ They are firm (fibrous tissue) that is called fibroids.
- ☒ Estrogen and contraceptive pills and pregnancy stimulate their growth.
- ☒ They shrink post-menopausally
- ☒ Chromosomal abnormalities found in 40% of cases.

## Pathological Features

### Gross

- ❖ Firm, grey-white masses, sharply demarcated from surrounding tissue by (false capsule)
- ❖ Cut section shows characteristics whorling appearance.
- ❖ May be single, but most often multiples.

### Types

1. Within the myometrium (intramural)
2. Beneath the endometrium (sub mucosal)
3. Beneath the serosa (subserosal)

### Histological Features

interlacing muscle bundles running in different directions (whorling) with foci of fibrosis, calcification, haemorrhage, and necrosis

### Complications

- ✓ Degenerative, hyaline changes and calcification.
- ✓ Infection with suppuration
- ✓ Torsion of pedunculated fibroids (sub serosal).
- ✓ Red degeneration (specific form of ischaemic necrosis occurs particularly in pregnancy (dull beefy red appearance))
- ✓ In cases of sub mucosal may fill the cavity causing infertility.

Malignant tumors (RARE) leiomyosarcoma

### Questions

#### Define

- ✚ Endometrial hyperplasia
- ✚ Adenomyosis
- ✚ Endometriosis

#### T & F

- ✚ Endometrial ca is common in multiparous
- ✚ malignant transformation is the Commonest complications of leiomyoma uterus
- ✚ Tuberculous endometritis is associated with infertility

## Ovaries

### Non -neoplastic ovarian cysts

Cysts: are fluid filled cavities lined by epithelium.

Ovarian cysts are most common cause of enlargement of the ovary.

### Types

#### 1. follicular cyst

- Are singles or Multiples
- Found in the cortex
- Represent an unruptured graffian follicles.
- 1.5 cm in diameter.
- Containing clear fluid and lined by flattened granulosa cells.
- Secrete estrogen → inhibit FSH → anovulatory cycles → infertility.

#### 2. Luteal Cysts

- Usually solitary
- Seldom more than 5 cm in diameter
- Lined by flattened luteinized cells,.
- Contains clear amber or blood stained fluid

#### 3- Chocolate Cyst (endometriosis)

#### 4- Poly Cystic Ovaries (stein leventhal syndrom)

- Ovaries contain numerous follicular cysts, with superficial fibrosis.
- These follicles secrete excessive estrogens and androgens.
- patient have oligamenorrhea, infertility, obesity and hirsutism.

### Poly-cystic ovarian disease (Stein-Leventhal syndrome)

- ☒ 5% Prevalence
- ☒ Anovulation
- ☒ Oligomenorrhea
- ☒ Obesity
- ☒ Hirsutism

## Ovarian Tumors

1. Surface epithelial tumors (70%)
2. Sex-cord stromal tumors
3. Germ cell tumors
4. Metastatic tumors

### Surface Epithelial Tumors

Derived from Coelomic epithelium thus differentiate into variety of tissues.

1. Serous tumors → (tubal differentiation)
2. Mucinous = → (endocervical)
3. endometrioid → (endometrial diff.)
4. Brenner tumors → (transitional =)

#### 1. Serous Ovarian Tumors

- Most common ovarian tumors
- It is unilateral, but could be bilateral.
- It is unilocular cyst, filled with serous fluid.
- measured up to 40 cm in diameter

#### Classification of serous tumors

##### a. benign serous cyst adenoma

- Occurs as cysts usually unilocular with papillary projection into the lumen.
- Lined by tubal like epithelium contains serous fluid.

##### b. Borderline serous cyst adenomas

- there is stratification of the epithelium ?(more than one layer).
- lined by atypical cells.
- No invasion (similar to Ca in situ)

##### c. Malignant serous cyst adenocarcinoma

- Cystic and solid in some areas .
- Atypical cells.
- With invasion.

## 2. Mucinous Ovarian Tumors

- Uni or bilateral, lined by endo cervical like epithelium.
- Cystic, pedunculated, multilocular, filled with sticky, gelatinous fluid
- **Classification.**
  - Benign → Mucinous cyst adenomas.
  - Borderline → Borderline=
  - Malignant → mucinous cyst adeno Ca.
- This type may undergoes torsion of the pedicle or may rupture into peritonealcavity→ (pseudo myxoma peritonea)

## 3. Endometrioid Tumors

- it is a malignant tumor.
- it looks like epithelium of endometrium.

## 4. Brenner's Tumor

- it shows transitional cell differentiation.
- Could be benign , borderline or malignant (rare).

## Sex – Cord stromal Tumors

1. Fibroma when associated with asites and hydrothorax - (Meig syndrom)
2. Thecoma majority benign and secretes estrogen
3. Granulosa cell tumor
4. Sertoli – leyding cell tumor (Androblastoma)Very uncommon benign tumor and secrets androgen

## Granulosa cell Tumor

- ❖ Derived from granulosa cell of ovarian follicle
- ❖ Secrete estrogen
  - Precocious puberty
  - Endometrial hyperplasia
  - Invasive endometrial Ca
- ❖ small follicles filled with eosinophilic secretion) → (Call Exner bodies)

## “Germ cell” tumors

- ✓ Teratomas(commonest)
- ✓ Dysgerminoma (look exactly like the testicular seminoma), malignant
- ✓ Endodermal Sinus (Yolk Sac), malignant, Just like testicular
- ✓ Choriocarcinoma, malignant, just like testicular

## Teratomas

1. **Mature cystic teratomas** (Dermoid cysts) (commonest)
  - Benign
  - Cyst lined by stratified Sq. epithelium containing sebaceous glands, hair, nervous tissue, sebaceous material and teeth, (mature tissues)
2. **Solid immature teratomas**
  - Seen in adolescents
  - Solid with primitive tissues (immature tissues).
  - Malignant
3. **Strumma Ovarii** (Monodermal) or specialized
  - Shows one line of differentiation.
  - usually contains thyroid tissue.
  - May cause hyperthyrodism

## Metastatic Ovarian tumor

Krukenburg tumor

(Secondary mostly from GIT) due to transcoelmic spread

## Fallopian Tubes

- ✚ Inflammation (salpingitis)
- ✚ Mostly caused by *streptococci*, *staphylococcus* but could be due to (gonococcal, chlamydia, Mycoplasma and tuberculosis)

## Complications

- ☒ Pyosalpinx
- ☒ Peritonitis
- ☒ Tubo-ovarian adhesions
- ☒ Infertility ectopic pregnancy

## Tubal neoplasms

- ❖ Adenocarcinomas
- ❖ Leiomyomas

Diseases of pregnancy

## Ectopic Pregnancy

- ✓ Chiefly tubal, but ovarian or abdominal rare
- ✓ 1% of normal women
- ✓ 35%-50% of women with previous salpingitis/PID
- ✓ + HCG, Abdominal pain, 1<sup>st</sup> trimester, ultrasound

**Placental Neoplasms**, i.e. gestational trophoblastic disease

- ✚ Benign: moles (Hydatidiform moles)
- ✚ Malignant: choriocarcinoma
- ✚ Both are associated with increased or persistent levels of the placental hormone HCG

## Hydatidiform mole

- Hydatidiform– drop of water
- mole – shapeless mass

## Types

### 1. Non - invasive mole

#### a. Complete (classic) mole

- Appear in 4<sup>th</sup> - 6<sup>th</sup> month of pregnancy.
- Uterine size is larger than expected date of gestation
- vaginal bleeding
- On palpation: uterus, has doughy feeling with no fetal parts.
- U/S no fetus
- Sonicaid (no fetal heart sound).
- Lab → high HCG level (human chorionic gonado tropin in serum or urine)
- 10% will progress into invasive mole, 2% into chorio Ca).

- **Grossly**  
the uterus is filled with grape – like vesicles up to 3 cm in  $\varnothing$  contains clear watery fluid.
- **Histology**
  - Villi are large and edematous
  - Villous blood vessels are absent
  - Trophoblastic cell proliferation (cyto and syncytio trophoblast)

#### b. Partial Mole

- Uterus contains some cystic villi , while the rest are normal placental villi.
- A fetus with multiple malformations is often present.

## 2. Invasive Mole

- there is penetration of the myometrium by molar tissue .
- Rarely trophoblastic tissues spread through blood vessels and reach the lungs.
- It is benign.
- persistent elevation of HCG

## Etiology

- ☒ For complete mole (it is due to fertilization of abnormal ova by 2 sperms (diploid karyotype)
- ☒ for incomplete mole → fertilization of normal ova by 2 sperms → tetraploidy karyotype.

The main thing differentiating benign from malignant from worrisome trophoblastic neoplasms is invasiveness of the trophoblast



## **Chorio Carcinoma**

- ❖ highly malignant tumor
- ❖ 50% follow H.mole
- ❖ 50% may follow abortion,normal pregnancy or ectopic pregnancy.
- ❖ High level of HCG
- ❖ Wide spread to lungs (cannon ball appearance on X-ray)
- ❖ **Grossly**  
The tumor appears as hemorrhagic soft and fleshy mass
- ❖ **Histology**
  - Most important ----- No villi are present.
  - Atypical changes in both cyto and syncytiotrophoblasts.
  - Hemorrhage and necrosis.

## **Questions**

### **Define**

- ✓ Meigs syndrome
- ✓ Stein leventhal syndrome
- ✓ Chocolate cyst

### **T & F**

- ✓ Dermoid cyst is the commonest malignant germ cell tumor
- ✓ Invasive mole is a malignant trophoblastic tumor
- ✓ common site of ectopic pregnancy is the ovary