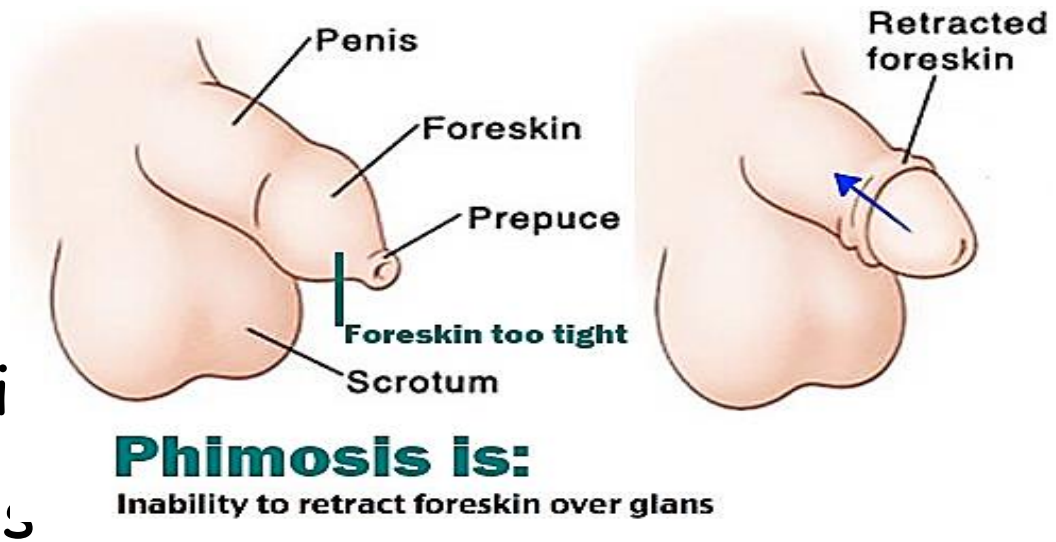
# Pathology

# Male genital system

# Congenital anomalies

## 1. Phimosis:

It is narrowing of the opening of the prepuce.



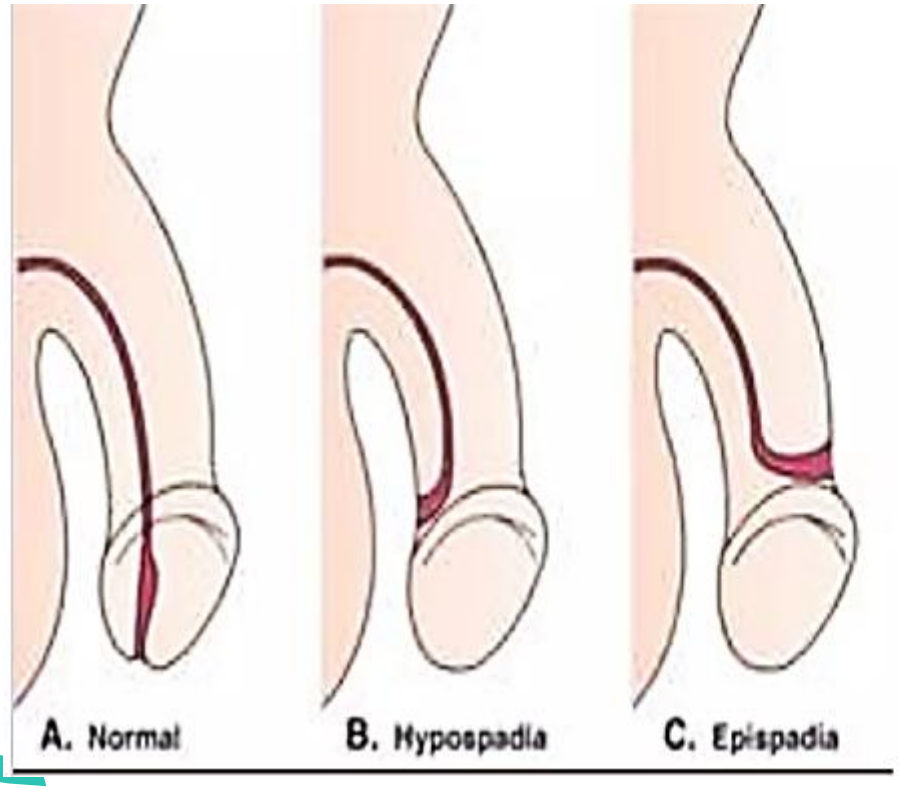

### Complications:

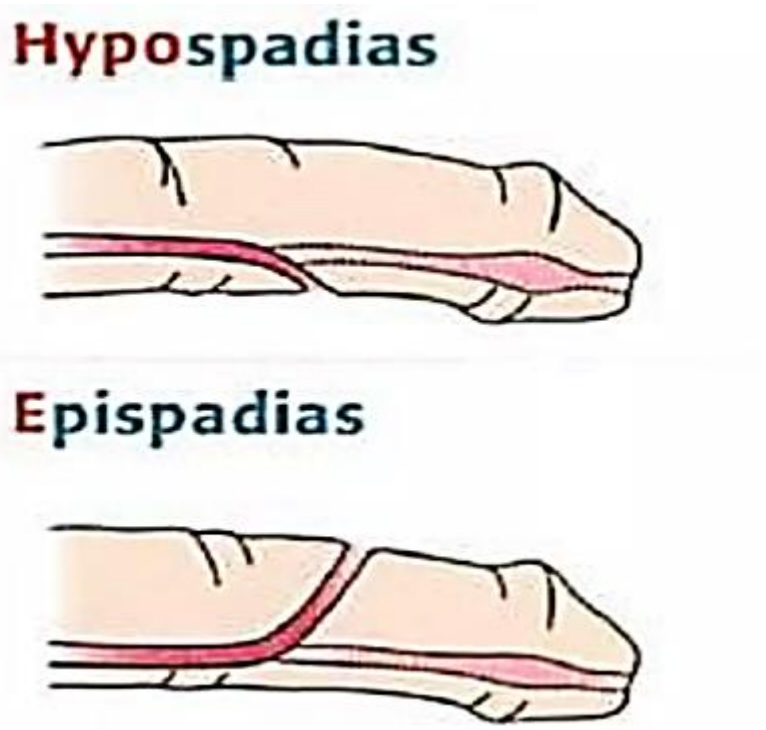
1. Balanitis: Inflammation of glans peni
2. Squamous cell carcinoma of the penis (due to accumulation of smegma that predispose to both infection and carcinoma).
3. Gradual urinary tract obstruction.

# Congenital anomalies

## 2. Hypospadias and epispadias of the penis

- Hypospadias: the urethra opens at ventral surface of the penis.
- Epispadias: the urethra opens at dorsal surface of the penis.



# Congenital anomalies

## 2. Hypospadias and epispadias of the penis

- Complications:

1. Urinary obstruction (as the urethral opening is often constricted).

2. Sterility (when the orifice is near the base of the penis).

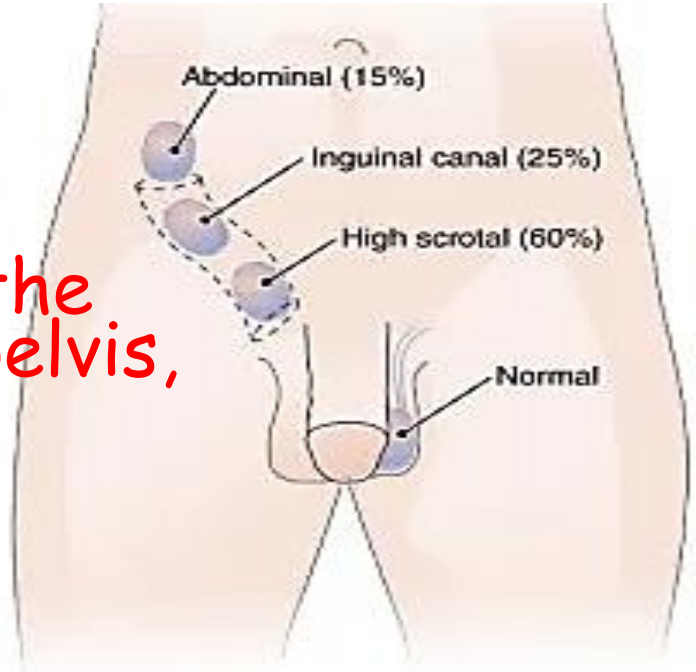
# Congenital anomalies

## 3.Cryptorchidism(undescended testis):

Most common congenital abnormality of the genitourinary tract

Def:

Failure of descent of one or both testis into the scrotum. The testis is found in the abdomen, pelvis, or in the inguinal canal.




## Causes:

1. Hormonal disturbances: Deficiency of gonadotrophic hormone of pituitary
2. Obstruction of the pathway: Organic obstruction prevents the descent.
3. Other defects: Short spermatic vessels or vas deferens or mal-development of the scrotum or cremaster muscle.

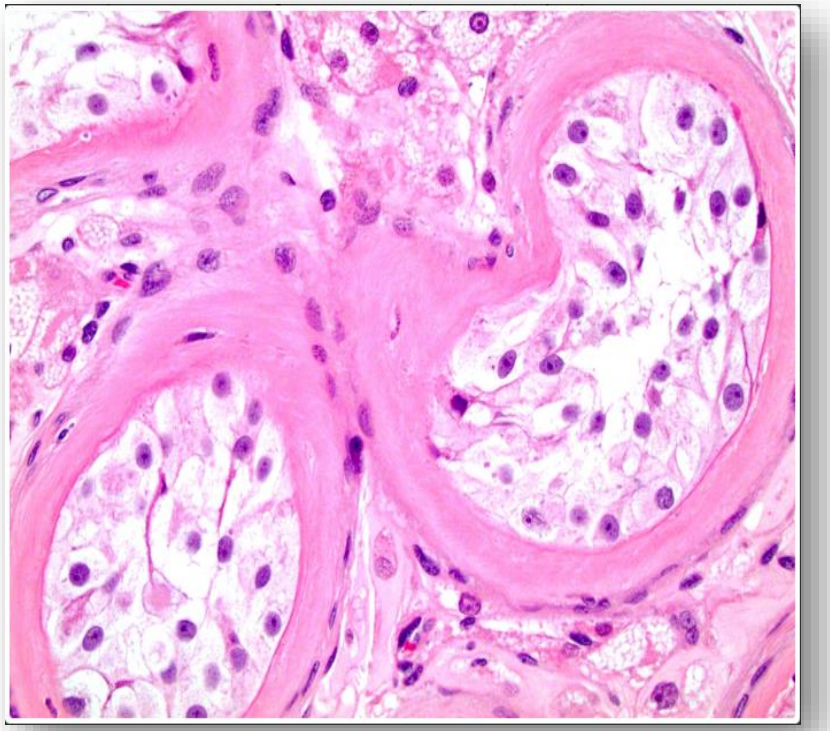
# Congenital anomalies

## 3.Cryptorchidism(undescended testis):

### ME:

-Atrophy of the seminiferous tubules with fibrosis.

-Germ cell neoplasia insitu which is likely a precursor of subsequent germ cell tumors



### Complications:

Infertility (in bilateral cases).

Malignancy (precancerous for seminoma).

# Inflammatory diseases

## Prostatitis

Inflammation of the prostate.

### Causes:

1. Organisms: E-coli, gonorrhea, staph. aureus, strept. pyogens…etc.
2. Routes of infection:

- Direct spread from cystitis, urethritis, urethral instrumentation.
- Blood borne infection

### Pathology:

1. Acute suppurative prostatitis which may form abscess.
2. Chronic nonspecific prostatitis follows acute.

# Inflammatory diseases

## Seminal vesiculitis:

Inflammation of seminal vesicles.

**Causes:**

It may be 2ry to prostatitis or blood borne.

## Funiculitis:

Inflammation of spermatic cord.

**Causes:**

1. Direct spread from epididymis.
2. Lymphatic spread from seminal vesicles.
3. Blood spread.

**Effect:** It leads to diffuse thickening of spermatic cord.

# Inflammatory diseases

## Orchitis:

Inflammation of testis.

Causes:

1. Bacterial orchitis:

Due to spread of infection from:

a) Epididymis directly

b) Spermatic cord by lymphatic or through vas deferens

c) Blood borne

Pathology: Acute inflammation with suppuration resulting in scarring and sterility.

2. Viral: mumps orchitis
3. Traumatic orchitis
4. Autoimmune orchitis

# Inflammatory diseases

Chronic specific inflammation of male genital system:

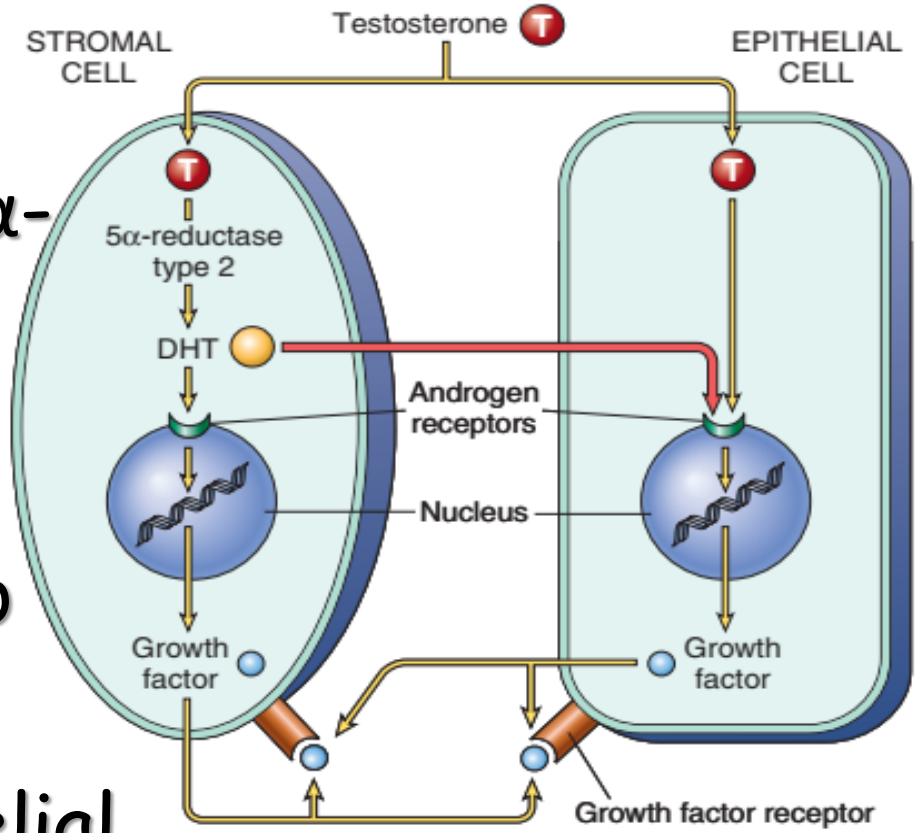
a) Tuberculosis.
b) Syphilis.
c) Filariasis
d) Bilharziasis.

# Benign(senile) prostatic hyperplasia

- Extremely common.
- ≈50% of men at 50 Years are affected, ≈95% are affected above 70 Years.
- Gradual onset with slow progression

## Pathogenesis:

- Hormonal changes with increase in 5 α-reductase enzyme in prostate that convert testosterone to dihydroxytestosterone (DHT)
- Accumulation of DHT(10 times more potent than androgens in combining to the androgen receptor and dissociate more slowly).
- Increasing the proliferation of epithelial & stromal cells and decreasing epithelial cells apoptosis.



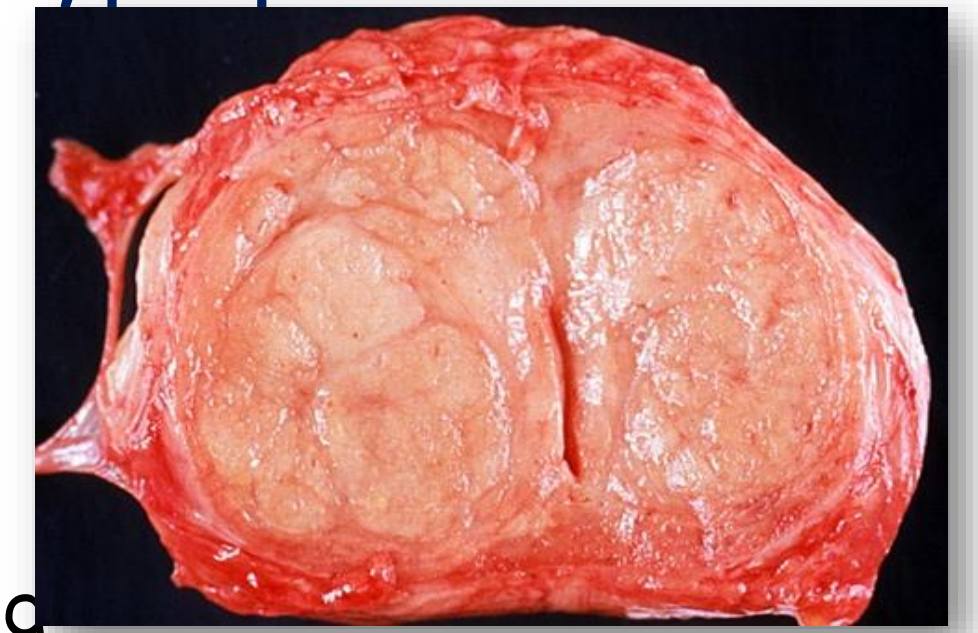
# Benign(senile) prostatic hyperplasia

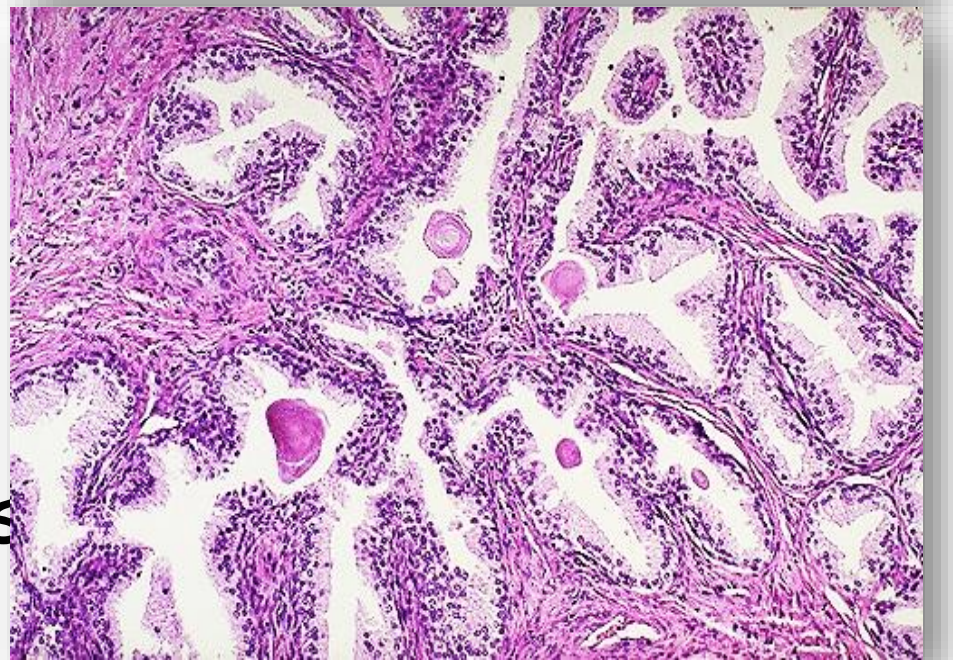
## Naked Eye:

- The gland is enlarged nodular, may show cystic change.
- Firm, rubbery in consistency.

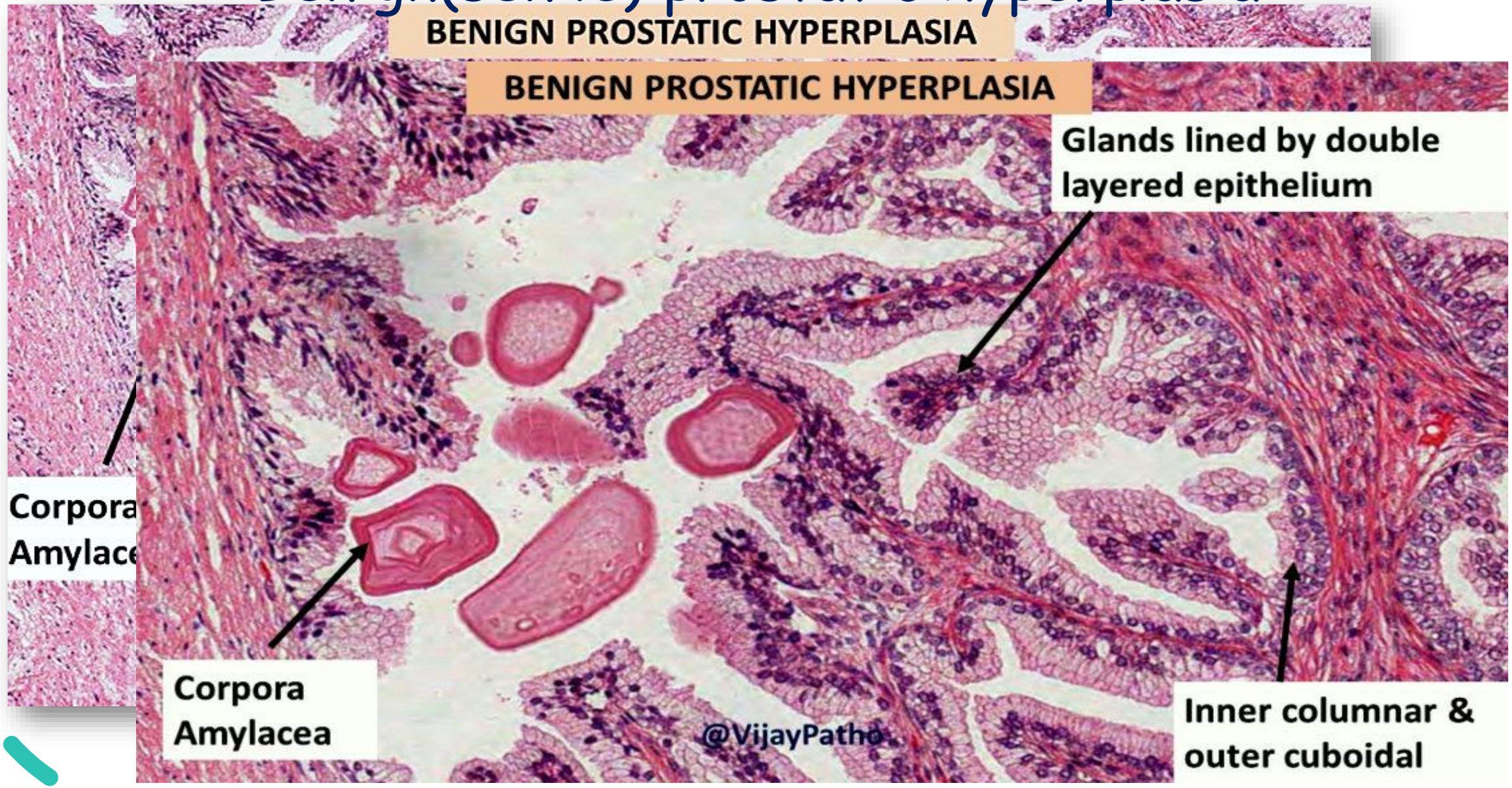
## Microscopic Examination:

- Hyperplasia of the acini which are larger than normal, variable in size and shape and lined by tall epithelium with frequent papillary projections.
- The acini may contain numerous corpora amylacea.
- Hyperplasia of the fibromuscular stroma with lymphocytes &plasma cells





# Benign(senile) prostatic hyperplasia



# Benign(senile) prostatic hyperplasia

## Clinical picture:

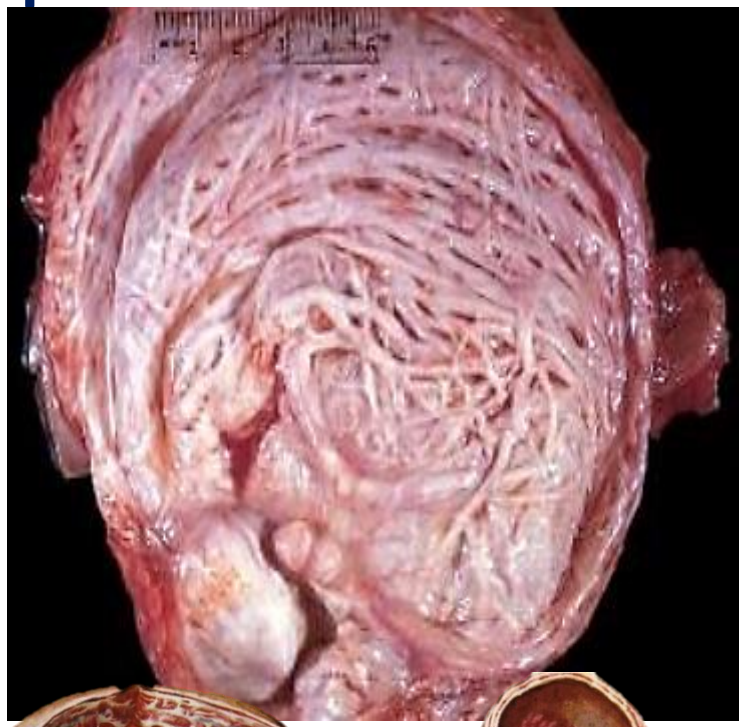
- Obstructive symptoms (Prostatism) due to compression on prostatic urethra and internal urethral meatus (interferes with the sphincter mechanism).

## Complications :

### Gradual urinary tract obstruction:

- Urethra: compressed as a slit.
- Urinary bladder: trabeculations, diverticulations, cystitis, stones.
- bilateral hydroureter, pyoureter.
- bilateral hydronephrosis, pyonephrosis.
- Chronic renal failure.

No relation to malignancy



# Prostatic Carcinoma

The most common malignant tumor in males >50 years

Predisposing factors :

- Racial factors- More common in African
- Endocrinologic factors- Androgens (so, Orchiectomy reduce the tumor size in Prostatic carcinoma patient).
- Environmental factors-high fat diet, exposur polycyclic aromatic hydrocarbons
- Genetic basis- familial cases (Chromosome No 1 and 10)


NE:

Affect the peripheral zone of the posterior lobe

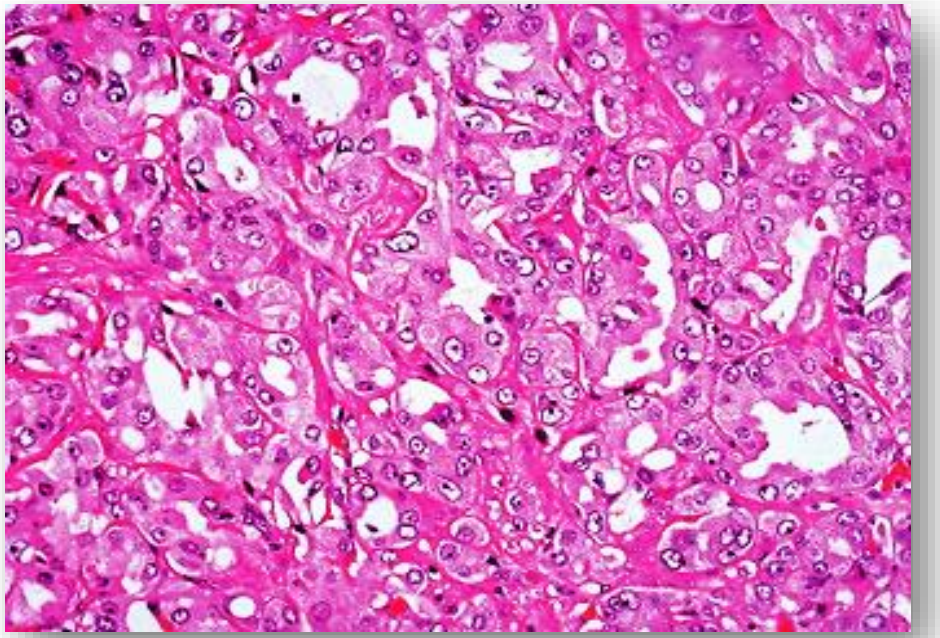
Uncapsulated mass palpable in rectal exam

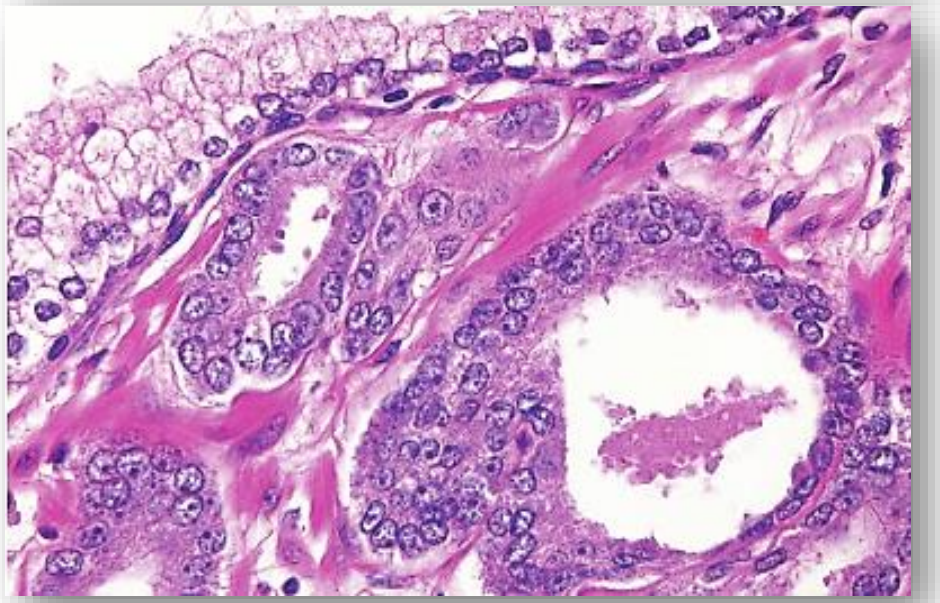
Multifocal, gritty and firm

# Prostatic Carcinoma

ME:

- **Adenocarcinoma;** malignant glands are lined cells having **prominent nucleoli.**
- Tumor cell produce **mucin** and **acid phasphatase**
- **Gleason Score:** is the system to grade the tumor based on the degree of differentiation among the cells.

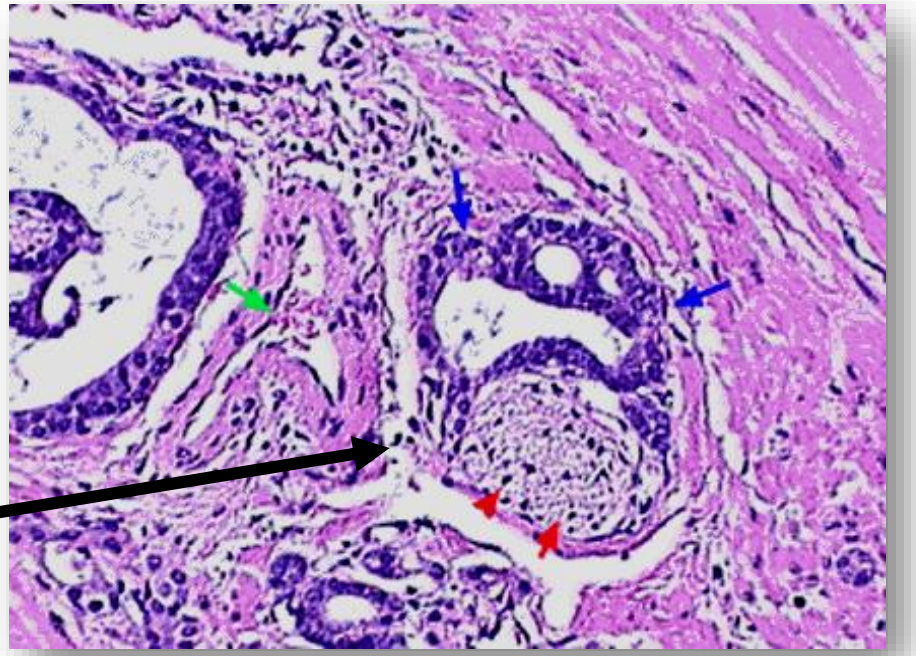




# Prostatic Carcinoma

## Spread:

- Local spread: to prostatic urethra , seminal vesicles, floor of urinary bladder and rectum
- Lymphatic spread: To para-aortic, iliac lymph nodes
- Perineural invasion
- Hematogenous metastases: bone(most often found in the vertebrae & sacrum), lung, liver
- Bony metastases are often osteoblastic & are associated with elevated serum **alkaline phosphatase**



# Prostatic Carcinoma

## Tumor markers:

- PSA :used as screening test and for assessing the response to treatment.
- CEA
- Prostatic acid phosphatase.
- Alkaline phosphatase in bone metastasis

# Testicular Tumors

## Germ Cell Tumor(90%):

- Seminoma.
- Non-seminoma:

- Teratoma.
- Yolk sac: Produce a fetoprotein
- Embryonal carcinoma.
- Choriocarcinoma: Produce HCG.

- Combined (e.g seminoma+ teratoma).

## Lymphoma (7%):

## Non-germ cells tumors(3%):

- Leydig cell tumor:

- Produce androgen (precocious puberty).

- Sertoli cell tumor:

- Produce estrogen ( feminizing characters as gynecomastia).

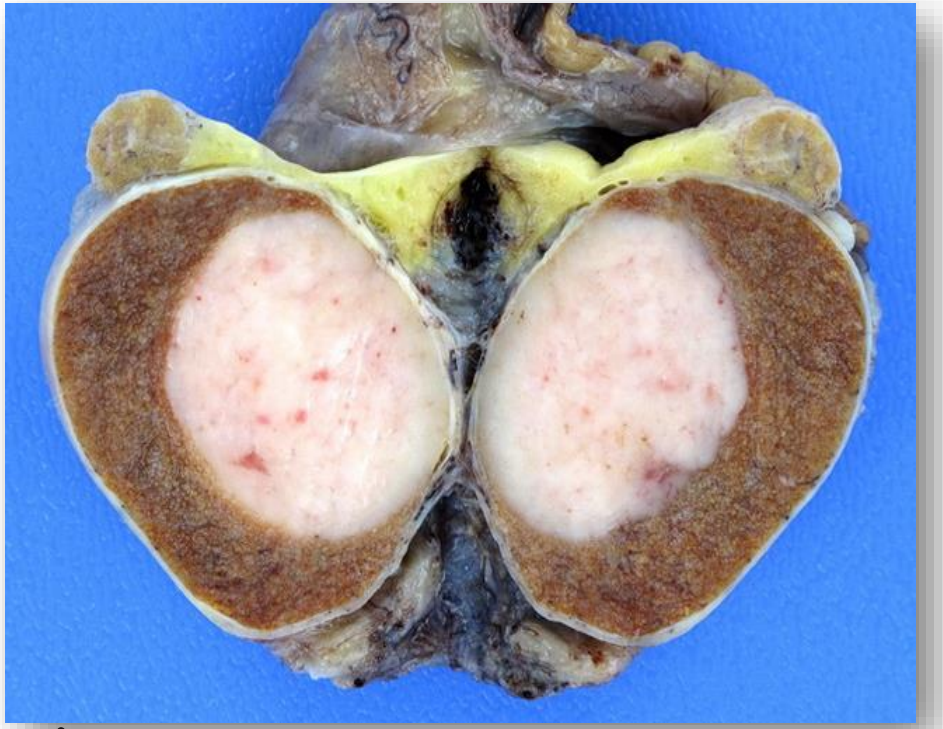
# Germ cell Tumors

## Seminoma

Most common germ cells with gonadal differentiation.

Age: 40-50y. Unknown before puberty.

Radiosensitive.



### Predisposing factors:

- Genetic factors
- Undescended testis
- Atrophic testis
- Venereal diseases (infections).

### NE:

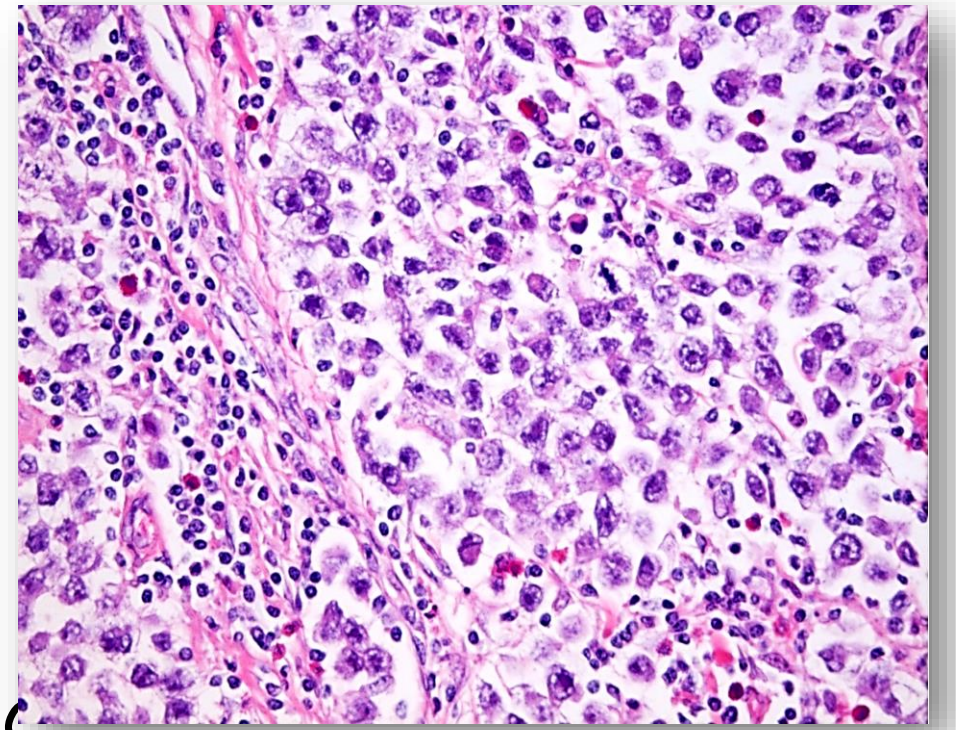
Well defined, fleshy, homogenous cut section (potato like).

# Germ cell Tumors

## Seminoma

**ME:**

- Nests and sheets of Spermatogenic cells with clear cytoplasm (due to glycogen content) with, large nucleus and prominent nucleolus.
- Tumour cells are separated by fibrous septa rich in lymphocytes and plasma cells



**Spread:**

- Local: tunica vaginalis, epididymis, spermatic cord and scrotal skin.
- Lymphatic: common iliac and pancreatic L.N. → mediastinal and supraclavicular L.N
- Blood: Lung, then brain and bones.

# Germ cell Tumors

## Non-seminoma

Less common germ cells with embryonic differentiation.
Age: 20y, may occur before puberty.
Radioresistant.
Teratoma formed of tissues derived from ectoderm, mesoderm and endoderm
Yolk sac : secretes Alpha fetoprotein.
Embryonal carcinoma.
Choriocarcinoma: secretes human chorionic gonadotrophins (HCG).
Combined (e.g seminoma+ teratoma).

# Non-germ cell Tumors

- Most of these are benign, representing 3% of testicular tumors and arise from non germinal cells (Leydig and sertoli cells). Called sex cord stromal tumors
- They include:

1. Leydig (interstitial) cell tumor: It produces androgens which leads to:

Before puberty it leads to sexual precocity.

After puberty, no body changes are detected.

2. Sertoli cell tumor: It produces estrogen leading to feminizing characters.

# Tunica Vaginalis

## Hydrocele

Collection of serous fluid within tunica vaginalis.

Types and causes:

a) Primary: unknown cause

b) Secondary due to:

1. Diseases of testis, epididymis and spermatic cord trauma, torsion of testis, inflammations and tumors.
2. Generalized oedema.

Effects:

Pressure atrophy of testis

2ry infection (pyocele).

## Haematocele

Collection of blood within tunica vaginalis.

Types and causes:

1. Primary: unknown cause
2. Secondary due to:
   - Trauma
   - Malignant tumors of testis.
   - Haemorrhagic blood diseases

Complications (effects):

- Pressure atrophy of testis.
- 2ry infection (pyocele).
- Organization & fibrosis.

## Chylocele

Accumulation of lymphatic fluid within tunica vaginalis.

Cause:

It is due to lymphatic obstruction e.g. in filariasis

# Varicocele

It is varicosity of the pampiniform plexus of veins in the spermatic cord.

**Causes:**

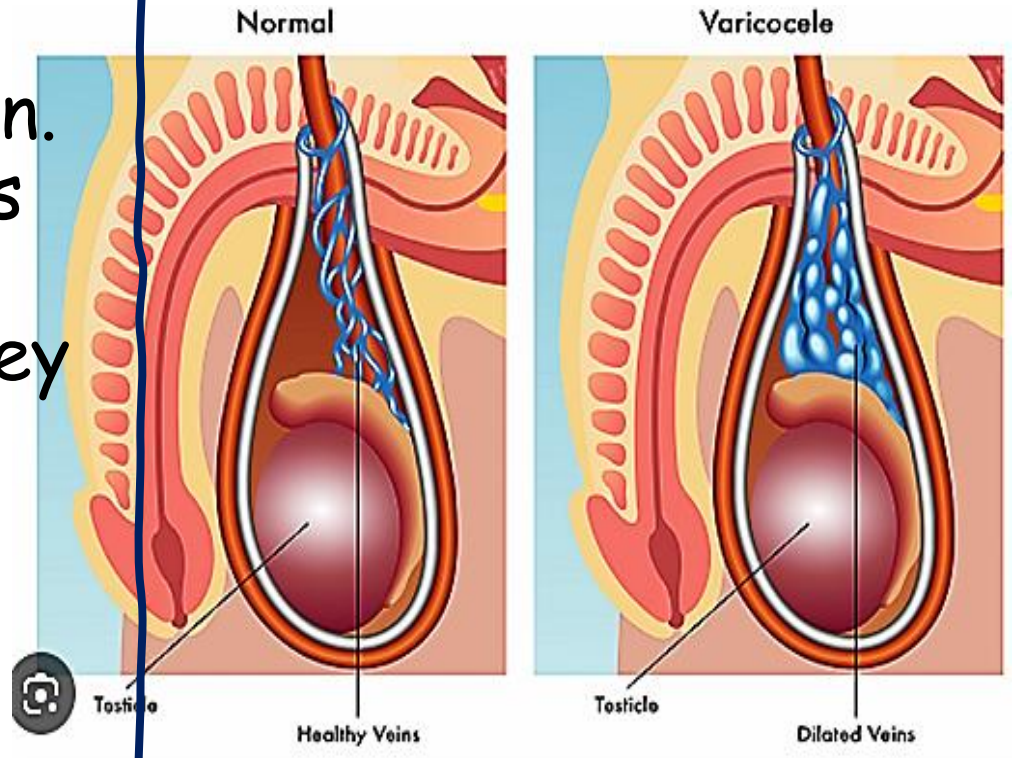
1. Primary: Occur in young unmarried men.
2. Secondary: Usually in middle age. It is due to:

- Pressure on the spermatic vein as kidney tumor
- Right side heart failure
- Venous thrombosis

**Pathology:**

a) Bag of warm like masses is felt in the scrotum

b) Defective spermatogenesis



Pathology

# Ovary and fallopian tube

# Ovarian Tumors

Ovarian cancer accounts for 3% of all cancers in females

- Benign tumors occur mostly in young women between (20-25 years old).
- Borderline tumors occur at slightly older ages.
- Malignant tumors are more common in older women (45-65 years old).

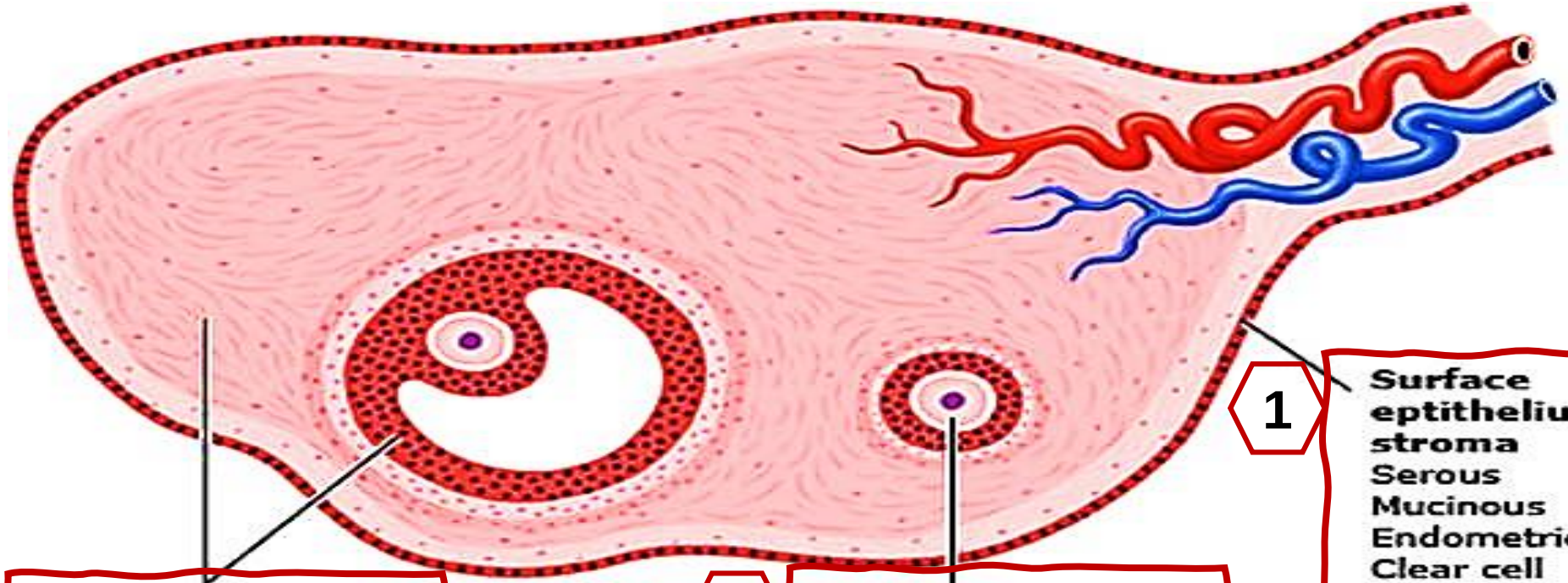
Risk factors:

- Nulliparity
- family history
- Germline mutations in certain tumor suppressor genes.

# Ovarian Tumors

## Origin:

Tumors of the ovary are remarkably varied as they may arise from any of the three cell types in the normal ovary:



1 **Surface eptithelium-stroma**
Serous
Mucinous
Endometrioid
Clear cell
Transitional cell

2 **Germ cells**
Dysgerminoma
Yolk sac
Embryonal carcinoma
Choriocarcinoma
Teratoma

3 **Sex cord-stroma**
Granulosa cell
Thecoma
Fibroma
Sertoli cell
Sertoli-Leydig
Steroid

# Ovarian Tumors

## 1. Surface epithelial tumors

- **Most common**, accounting for **>90%** of ovarian tumors.
- The most widely accepted theory for the origin of surface epithelial tumors is the transformation of coelomic epithelium. This view is based on the embryologic pathway by which the müllerian ducts are formed from the coelomic epithelium and evolve into serous (tubal), endometrioid (endometrial), and mucinous (cervical) epithelia present in the normal female genital tract.

Types:

A. Serous tumors
B. Mucinous tumors
C. Endometrioid tumors
D. Others

# Ovarian Tumors

## 1. Surface epithelial tumors

### A. Serous tumors:

- They account for 30% of all ovarian neoplasms.

**Age:** Benign lesions are usually between 30 and 40 years of age, and malignant serous tumors are more commonly seen between 45 and 65 years of age.

**Pathogenesis:** The low-grade tumors arising in serous borderline tumors with only rare mutations in p53(tumor suppressor gene). In contrast, the high-grade tumors have a high frequency of mutations in the p53 gene.

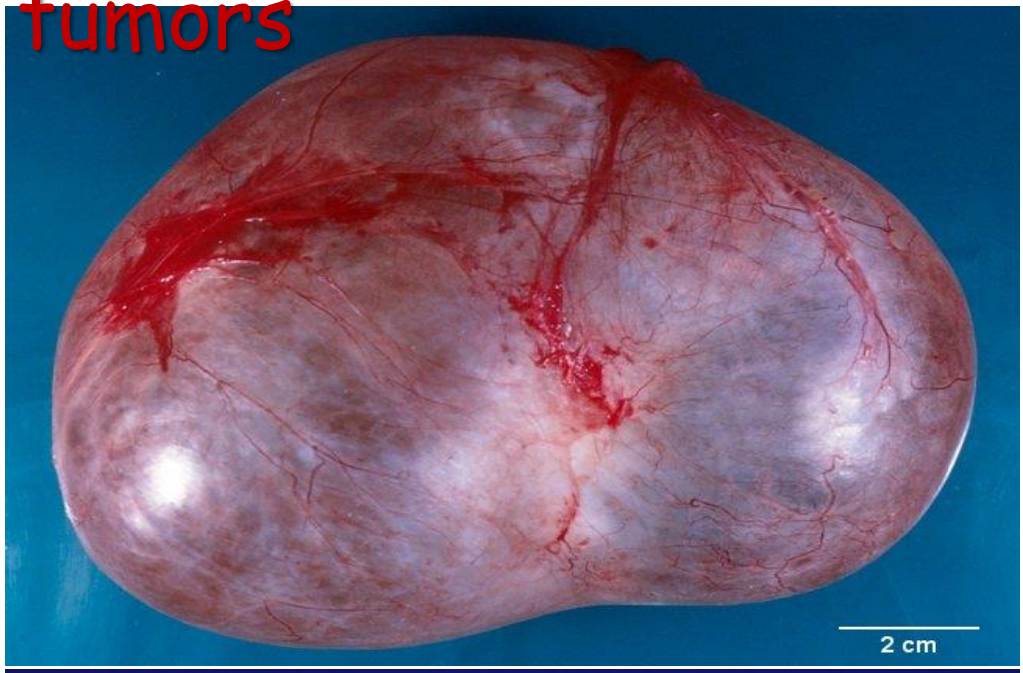
# Ovarian Tumors

## 1. Surface epithelial tumors

### A. Serous tumors:

N/E: They are cystic lesion (cystadenoma) with smooth surface and serous fluid contents. Intarcystic papillary projections may be present (papillary cystadenoma). The outer surface of cystadenocarcinomas may show, in addition, nodules and outward papillary projections.

- Bilaterality is common in serous tumors.



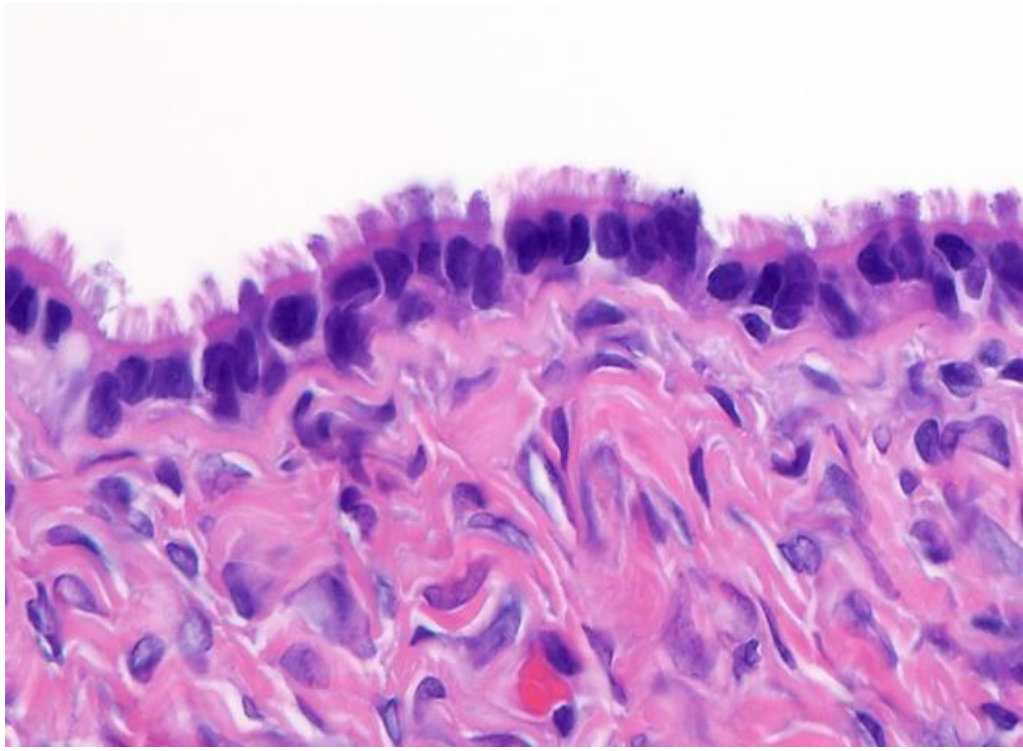

# Ovarian Tumors

## 1. Surface epithelial tumors

### A. Serous tumors:

**M/E:**

Benign tumors (serous cystadenoma) contain a single layer of columnar epithelial cells that line the cyst or cysts. The cells often are ciliated occasionally forming microscopic papillae.



# Ovarian Tumors

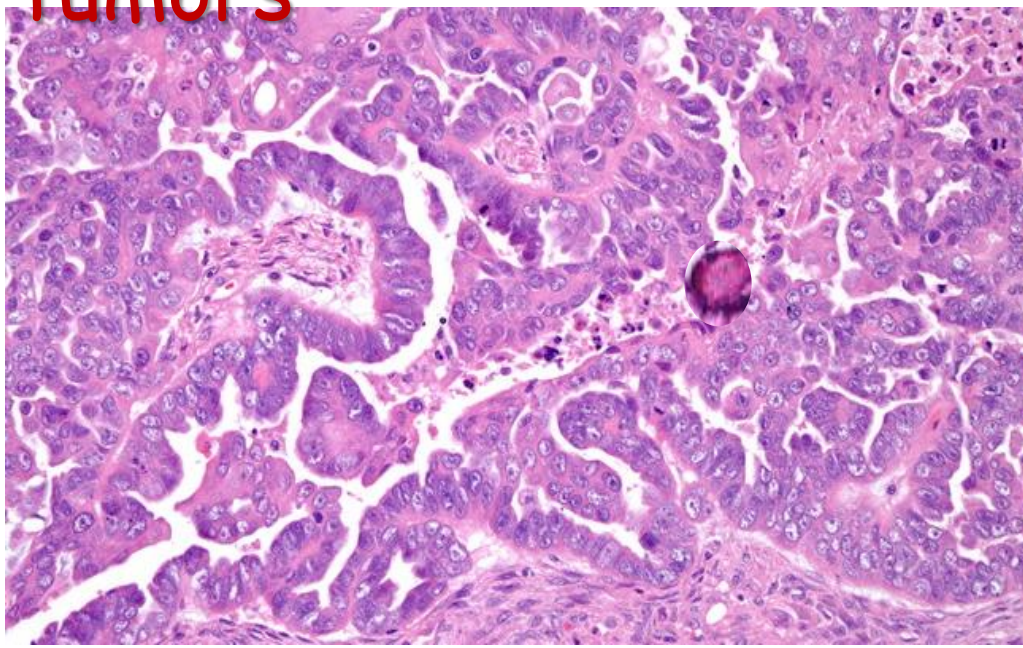
## 1. Surface epithelial tumors

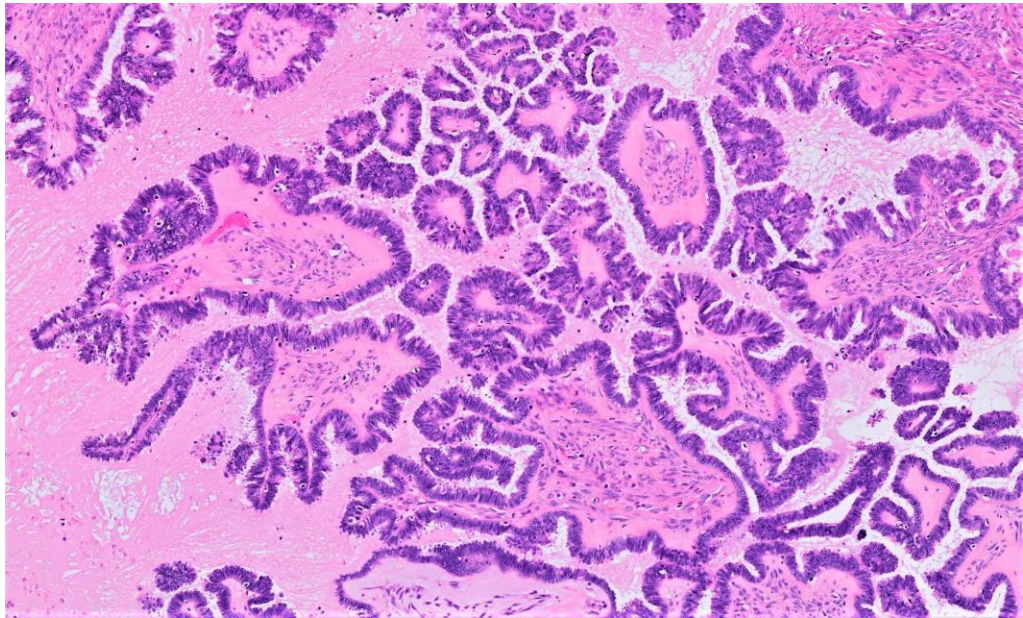
### A. Serous tumors:

**M/E:**

Malignant tumors have multilayered epithelium with many papillae, solid areas and stromal invasion. Psammoma bodies (concentrically laminated calcified concretions) are commonly present.

Borderline tumors show some of features of carcinomas but without stromal invasion.





# Ovarian Tumors

## 1. Surface epithelial tumors

### B. Mucinous tumors:

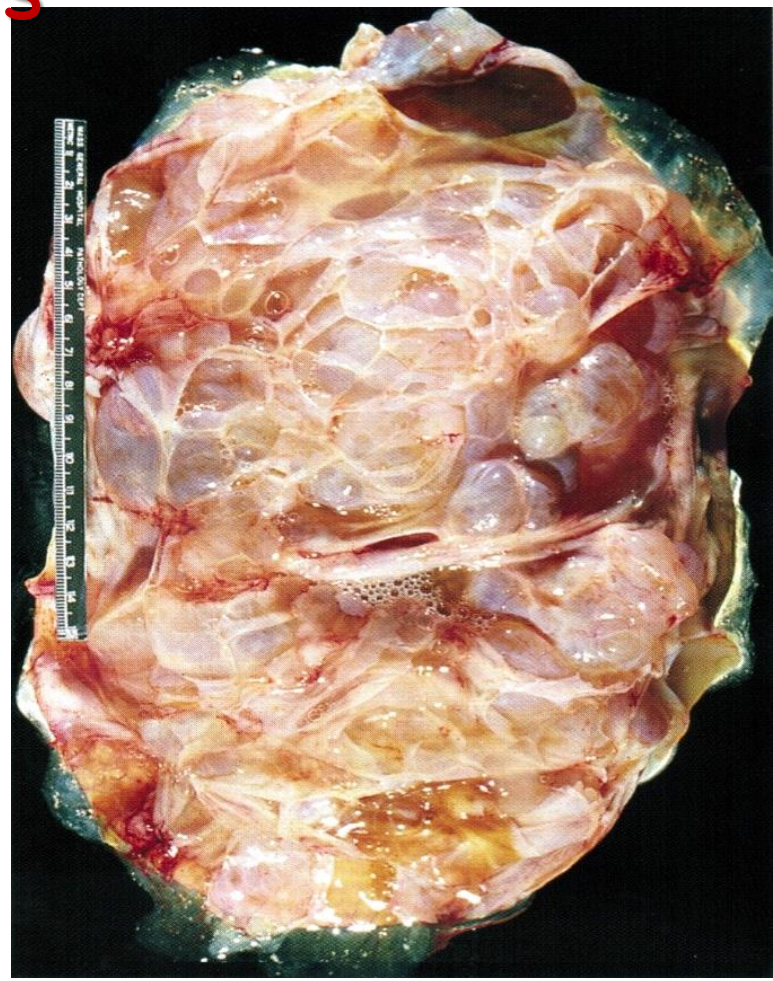
- They account for 25% of all ovarian neoplasms.
- Only 10% of mucinous tumors are malignant; another 10% are borderline, and 80% are benign.
- wide age range with a **mean age** at diagnosis of **50 years**.
- symptoms include **abdominal pain, distension, pelvic mass**.

# Ovarian Tumors
## 1. Surface epithelial tumors

### B. Mucinous tumors:

NE:

- Mucinous neplasms tends more to be unilateral and larger. They appear as multiloculated cystic tumors (mucinous cystadenoma) filled with sticky, gelatinous fluid.
- Rupture of the cyst may lead to pseudomyxoma peritonii, in most cases, this disorder is caused by metastatic spread of tumors in the gastrointestinal tract, primarily the appendix



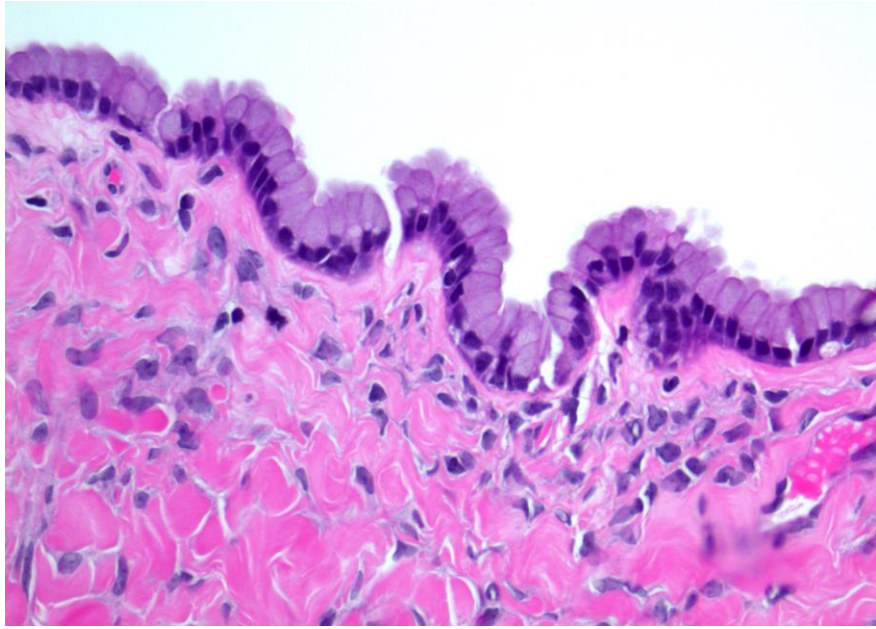
# Ovarian Tumors

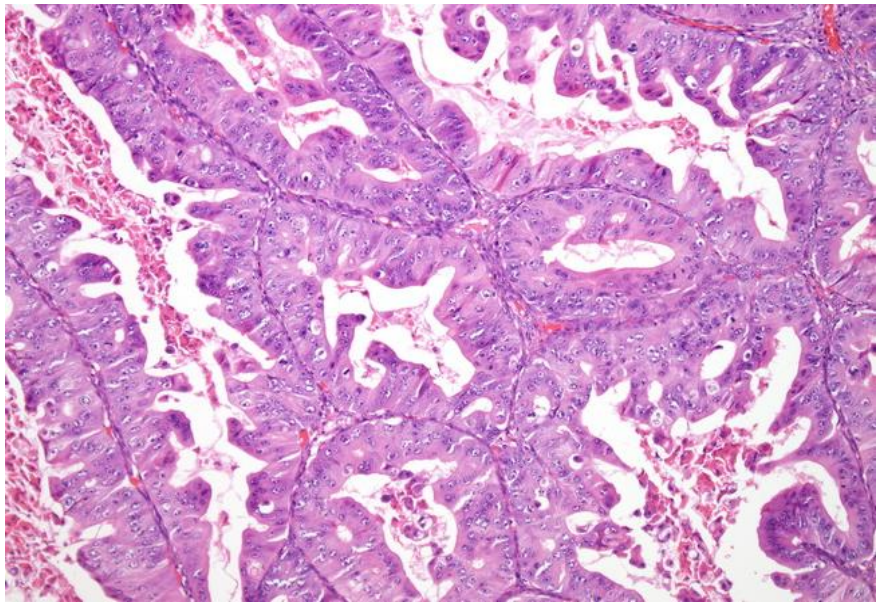
## 1. Surface epithelial tumors

### B. Mucinous tumors:

**M/E:**

- Benign lesions are lined by tall columnar non ciliated epithelium with apical mucin similar to intestinal or cervical epithelium.
- Malignant tumors usually show solid areas, necrosis and stromal invasion.
- Borderline tumors show some of features of carcinomas but without stromal invasion





# Ovarian Tumors
## 1. Surface epithelial tumors

### C. Other tumors:

- **Endometrioid tumors**

Most are malignant.

Many cases occur in the setting of concurrent endometriosis.

- **Clear cell adenocarcinoma:**

Uncommon, show cells with clear cytoplasm.

- **Brenner's tumor:** Most are benign. They consist of rounded islands of transitional epithelium embedded in dense fibrous stroma.

# Ovarian Tumors
## 2. Sex cord stromal tumors

- Normally, the ovarian stroma, which is derived from the sex cords of the embryonic gonad differentiate into Sertoli and Leydig in male and granulosa and theca in female gonads, tumors resembling all of these cell types can be identified in the ovary.
- Moreover, because some of these cells normally secrete estrogens (granulosa and theca cells) or androgens (Leydig cells), their corresponding tumors may be either feminizing (granulosa–theca cell tumors) or masculinizing (Leydig cell tumors).

# Ovarian Tumors
## 2. Sex cord stromal tumors

### A. Granulosa cell tumor:

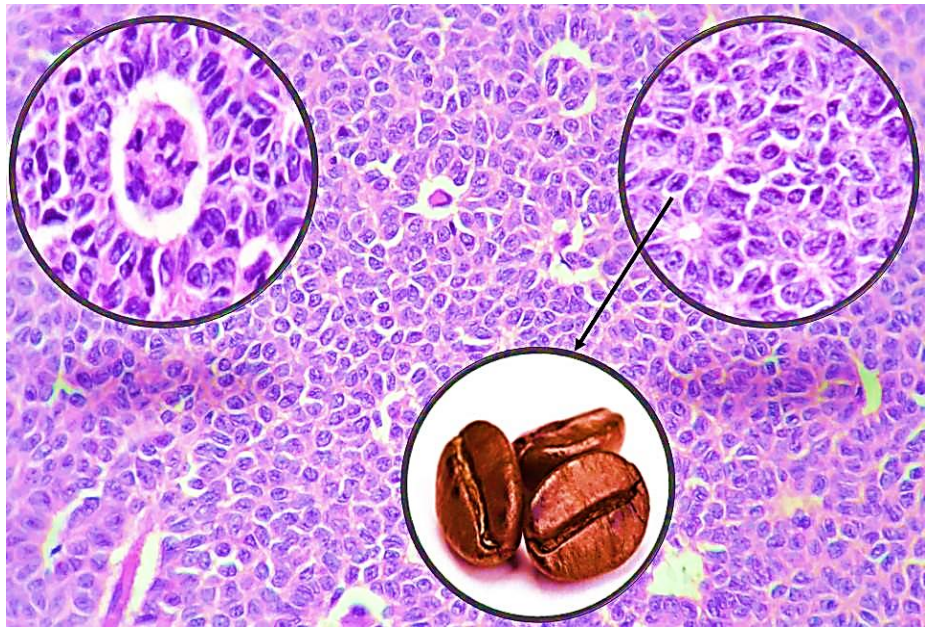

90% of all ovarian sex cord stromal tumors of low grade malignancy.

Age: Menopausal women.

C/P: Hyperestrogenism, associated endometrial hyperplasia and bleeding.

NE: Well circumscribed mass with solid and cystic areas, hemorrhage and necrosis

M/E: Uniform ovoid cells with cleaved nucleus arranged in diffuse, trabecular or microfollicular pattern



# Ovarian Tumors
## 2. Sex cord stromal tumors

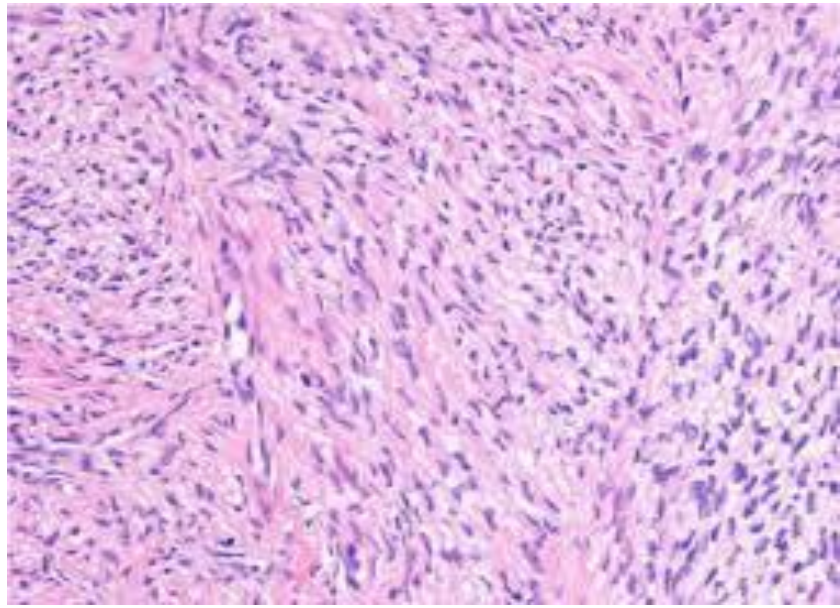
### B. Thecoma-fibroma:

Theca cell tumor (thecoma): benign tumor, mostly mixed with fibroma (fibrothecoma). Mostly are hormonally inactive but, may secrete estrogen

NE: Solid yellow lobulated mass.

M/E: Ovoid to spindle cells with cytoplasmic lipid vacuoles.

Meig's syndrome: Ovarian fibroma with hydrothorax and ascitis.



# Ovarian Tumors
## 2. Sex cord stromal tumors

### C. Other Tumors:

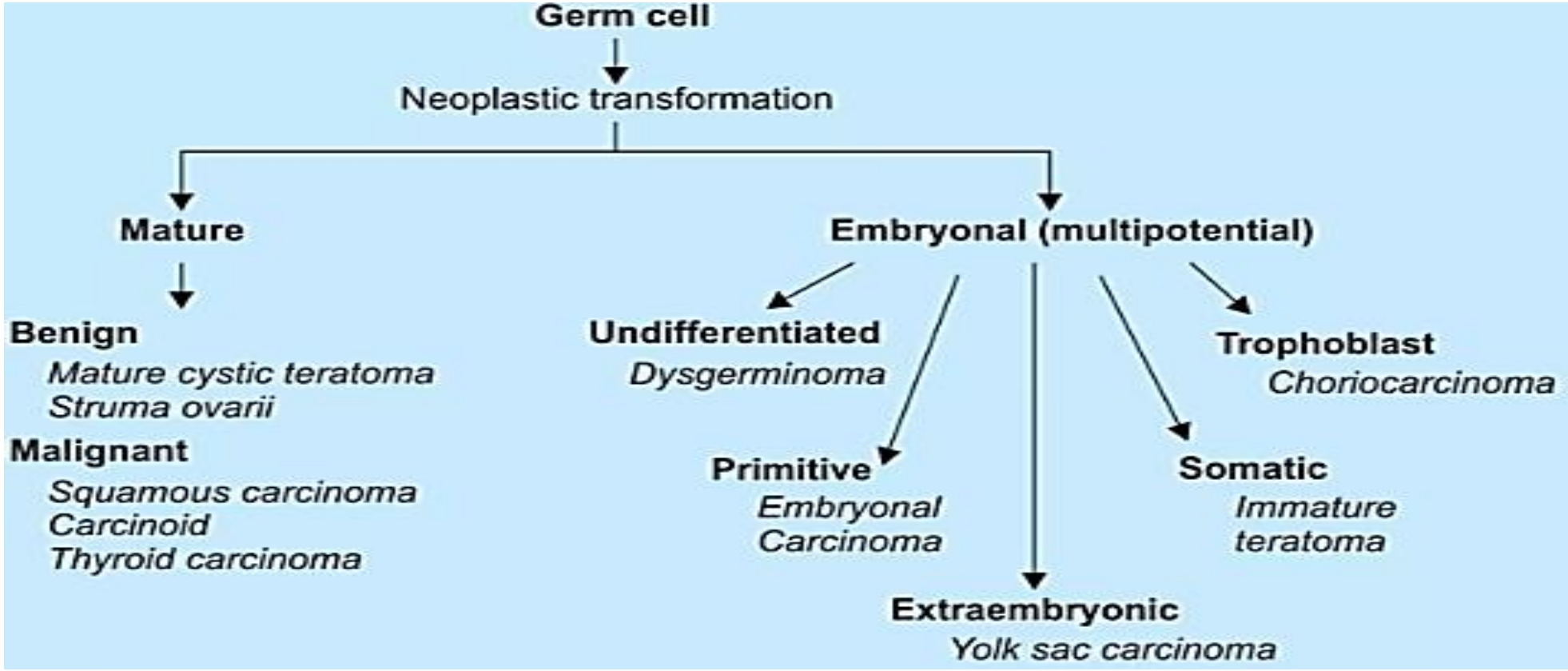
These may be sertoli cell tumor (secretes estrogen), leydig cell tumor (secrets androgen) or combination of them. The majority are benign.

- Mixed male and female differentiation (Gynandroblastoma):

Contain elements of granulosa, theca, sertoli and leydig tumors. It produces both hormones

# Ovarian Tumors
## 3. Germ cell tumors

- 30% of all primary ovarian neoplasms.
- >90% of ovarian GCT are mature cystic teratomas which are benign tumors. Remaining 5% are malignant.



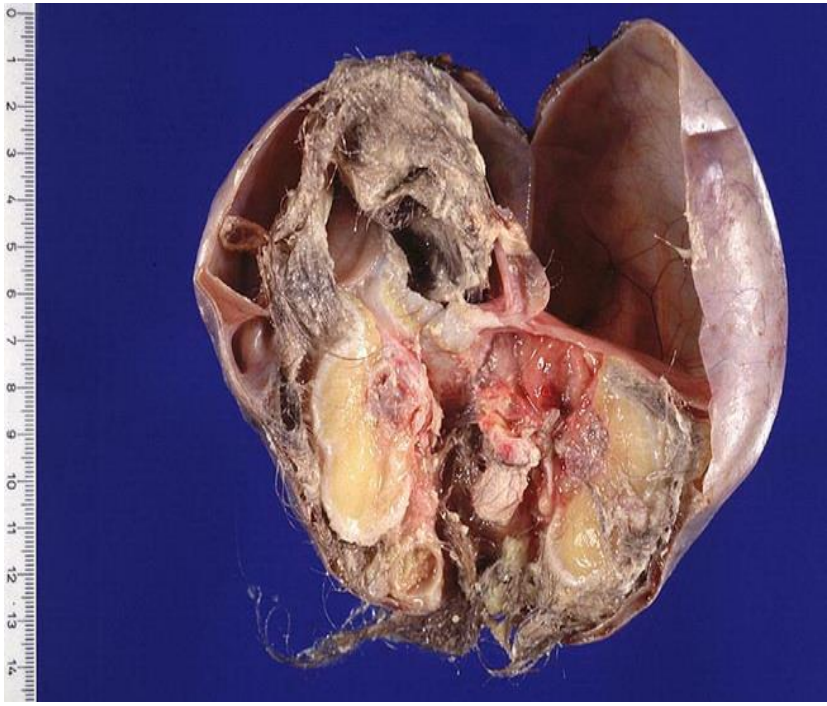
# Ovarian Tumors
## 3. Germ cell tumors

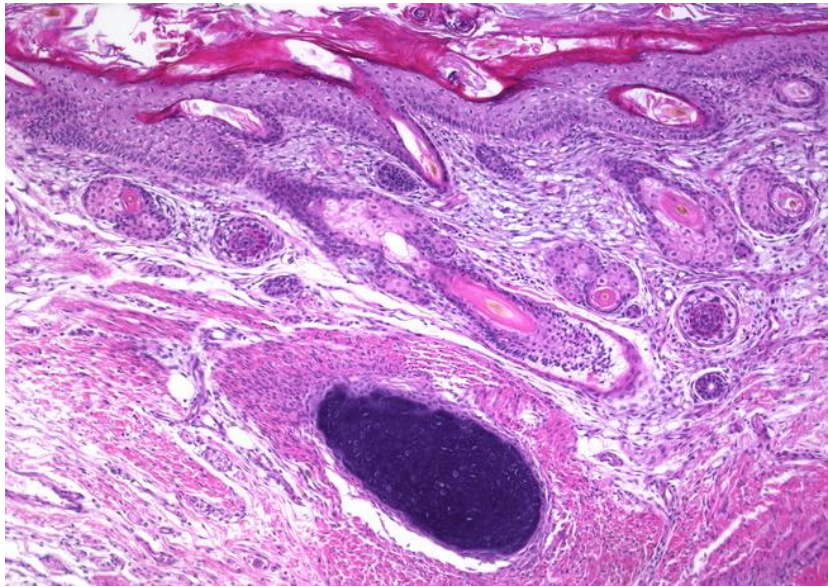
### A. Teratoma:

1) Mature teratoma: It is usually cystic (dermoid cyst) and benign.

2) Immature teratoma: It is predominantly solid and malignant.

3) Monodermal teratoma: Characterized by one sided development. Examples are struma ovarii (only thyroid tissue) and some cases of mucinous cystadenoma (G.I.T. epithelium).





# Ovarian Tumors
## 3. Germ cell tumors

### B. Other tumors:

- **Dysgerminoma**
- Uncommon malignant non functioning neoplasm occurs in children and young adults. Microscopically, it is similar to seminoma of testis (Sheets or cords of large clear cells, Stroma may contain lymphocytes).
- **Choriocarcinoma:** Differentiation towards trophoblasts. It secretes HCG hormones
- **Yolk sac tumor :**occur in children, adolescent and young adult, secretes alpha fetoprotein

# Ovarian Tumors

## 4. Unclassified tumors

Lymphomas, Hemangiomas, Lipomas, Leiomyomas,...etc...

## 5. Metastatic tumors

- These tumours are usually bilateral. They reach both ovaries by transcoelomic spread, blood spread, retrograde lymphatic spread or direct spread. Site of primaries include uterus, G.I.T, gall bladder, pancreas, and lung.

- Krukenberg tumor is bilateral ovarian secondaries showing signet ring cells scattered in fibrous stroma. The primary is present in G.I.T, mainly stomach.

# Non Neoplastic Cysts of the Ovary

1- Follicular cysts: Extremely common finding. They are <2cm, lined by follicular cells, and filled with clear fluid. They commonly originate in unruptured graafian follicles.

2- Corpus luteum cysts: Dilatation of degenerated corpus luteum. Usually single and filled with blood.

3- Polycystic ovary (stein- leventhal syndrome): Affects women in reproductive age and is in the form of bilateral multiple small cystic follicles with cortical fibrosis.

Oligomenorrhea, hirsutism and infertility are presenting symptoms. The condition is related to disturbance in androgen synthesis

N.B:- Sometimes these cysts rupture, producing intraperitoneal bleeding and peritoneal symptoms (acute abdomen).

# Fallopian tubes

- Suppurative salpingitis, gonococcus accounts for more than 60% of cases. These tubal infections are a part of pelvic inflammatory disease.
- Tuberculous salpingitis is an important cause of infertility.
- Tumors of the fallopian tube are uncommon. Primary adenocarcinoma of the fallopian tubes is rare.
- Serous tubal intraepithelial carcinoma considered as a precursor lesion to most of high grade serous tumors.

# Pathology

# Uterine Corpus and Gestational Trophoblastic Diseases.

# Abnormal Uterine Bleeding (AUB)

Definition: Any deviation from a normal menstrual cycle pattern.

The key characteristics are regularity, frequency, heaviness of flow, and duration of flow.

The **causes** of abnormal bleeding may be:

Organic (Structural) abnormality, such as chronic endometritis, submucosal leiomyomas, endometrial polyp or endometrial neoplasms.

Functional disturbances (dysfunctional uterine bleeding) as a result of abnormalities in the menstrual cycle or systemic diseases.

# Dysfunctional uterine bleeding

Nonstructural" causes of abnormal uterine bleeding (AUB)

(1) Disorders of endometrial origin (disturbances of the molecular mechanisms responsible for regulation of the volume of blood lost at menstruation);

(2) Disorders of the hypothalamic-pituitary-ovarian axis

(3) Disorders of hemostasis (the "coagulopathies").

# Endometritis

Inflammation of the endometrial lining of the uterus. is classified as acute or chronic

Acute Endometritis-It is uncommon, may progress to puerperal sepsis

Puerperal sepsis:

It is endometrial infection during puerperium (after labour or abortion), caused by strept. H., staph. Aureus, E. coli, pseudomonas

Predisposing causes:

1- Uterine retention of products of conception and blood clots provide a culture medium for bacteria.

2-Traumatic lacerations during childbirth.

# Endometritis

## Puerperal sepsis:

**N/E:**

1- Uterus is bulky (subinvoluted), soft and flabby.

2- Uterine cavity contains septic necrotic material, remnants of placenta and pus.

3- Endometrium is hyperemic, edematous with necrosis and ulceration.

4- Myometrium show:

Septic inflammation which may form abscesses.

Myometrial veins contain septic thrombi.


# Endometritis

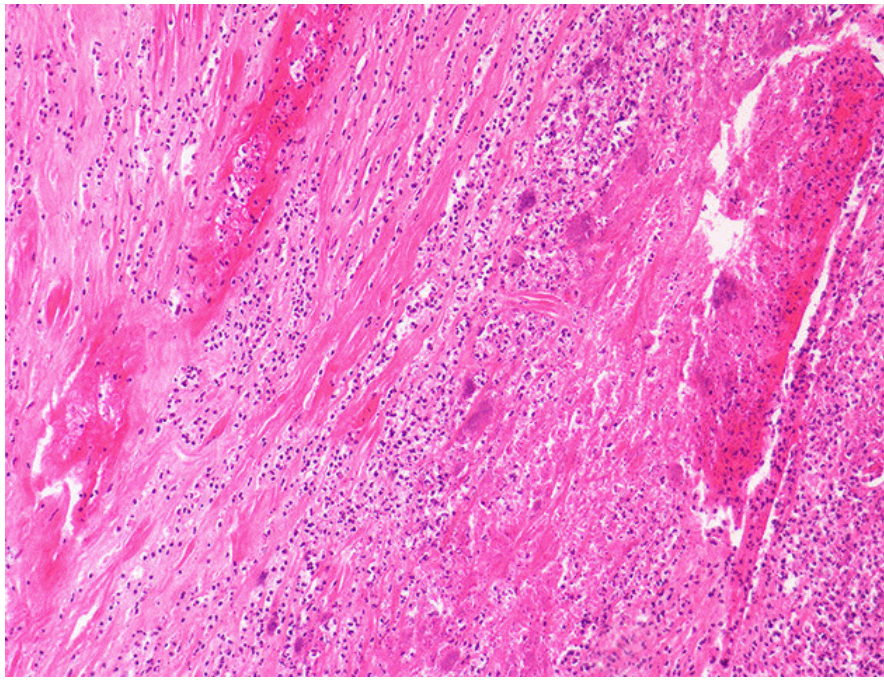
## Puerperal sepsis:

## M/E:

1- Uterine cavity contains septic material and pus.

2- Endometrium show:
Ulceration of surface epithelium with acute suppurative inflammation.

3- Myometrium show:
Suppurative myometritis which may lead to myometrial abscesses.
Myometrial veins contain septic thrombi.



## Complications:

- Direct spread to pelvic structures
- Blood spread: - Pyeamia (septic thrombo phlebitis), Septicaemia.
- Severe toxemia.

# Endometritis

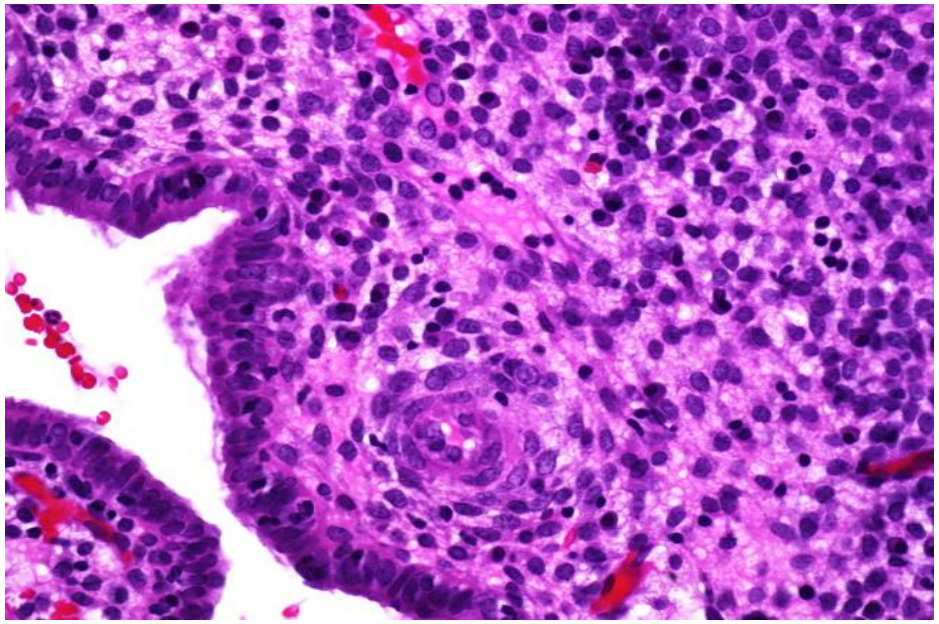
## Chronic Endometritis:

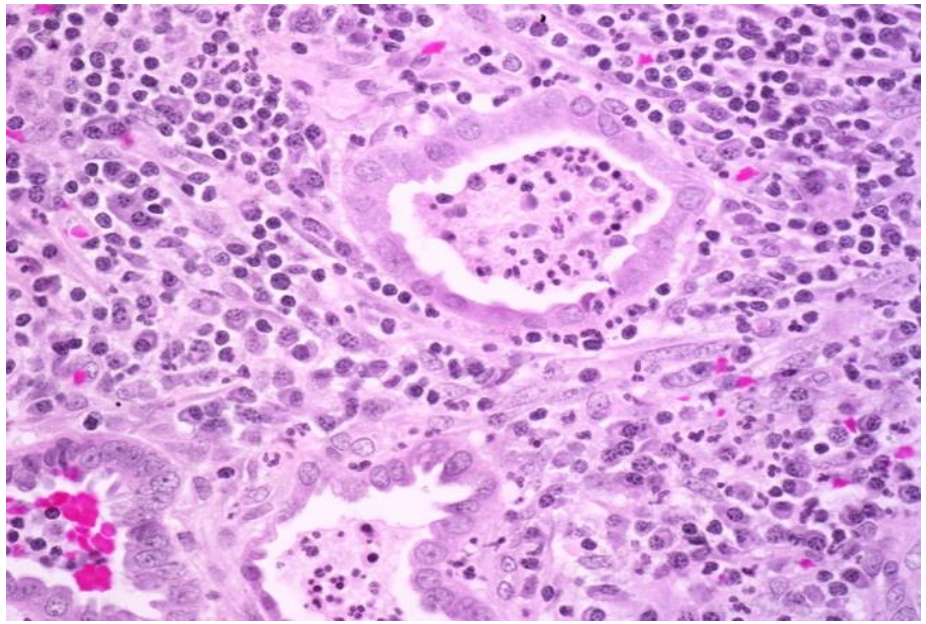
Presented with bleeding, pain, discharge and infertility.

**M/E:** infiltration by plasma cells.

**Causes:**

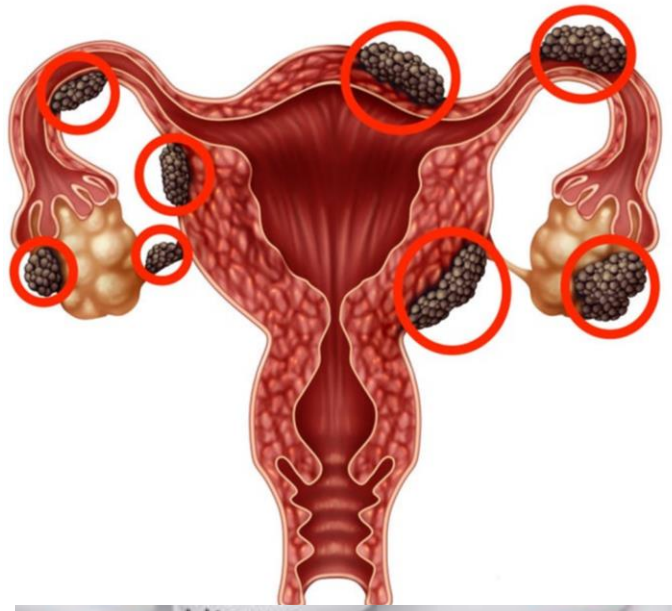
- Pelvic inflammatory disease (PID), in postpartum or post-abortion patients with retained gestational tissue.
- Women with intrauterine contraceptive devices
- Women with tuberculosis, Syphilis (rare).





# Endometriosis

- Endometriosis is the presence of endometrial tissue (glands and stroma) in a location outside the uterus.
- It responds to ovarian hormones as the uterine endometrium.

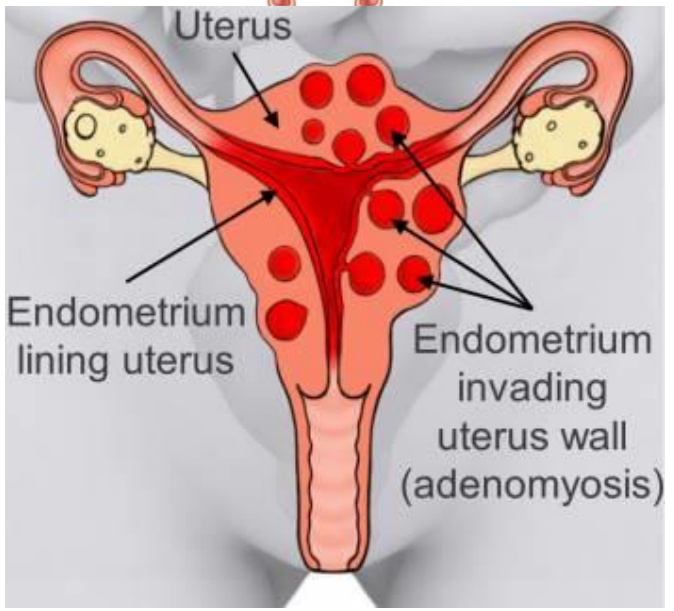


## External Endometriosis

- Presence of endometrial tissue (glands and intervening stroma) outside the uterus.
- Frequently is multifocal and often involves pelvic structures (ovaries, Douglas pouch, uterine ligaments, tubes, and rectovaginal septum)

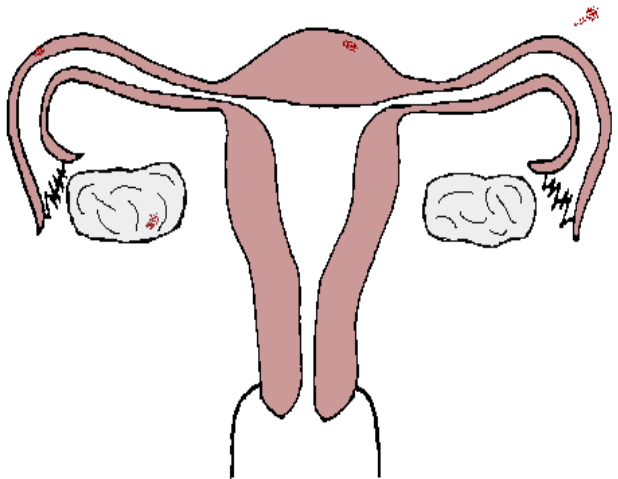
## Internal Endometriosis (adenomyosis)

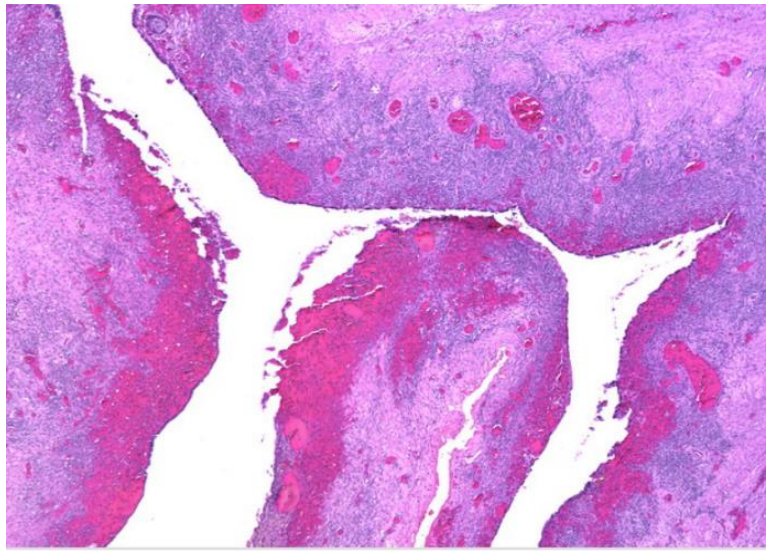
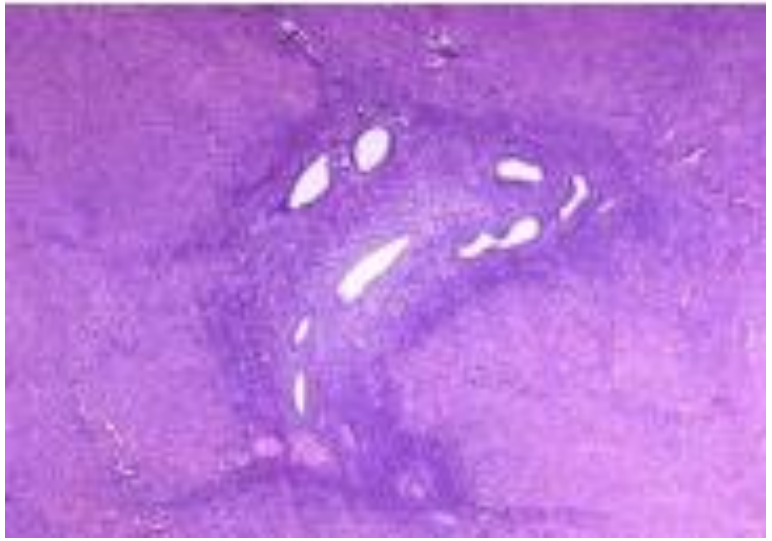
- Presence of endometrial tissue (glands and stroma) in the myometrium of uterine wall.



| | External Endometriosis | Internal Endometriosis |
|---|---|---|
| Site | Outside the myometrium | Myometrium of body of uterus called **Adenomyosis** |
| Pathogenesis | 1. The regurgitation theory: during menstruation, viable endometrial fragments pass via fallopian tube to implant on the peritoneum<br>2. Metaplasia of serosal cells leads to peritoneal lesions.<br>3. Vascular and lymphatic dissemination theory. | **Abnormal growth activity of the endometrium**, the basal zone of endometrium dips into the adjacent myometrium. |

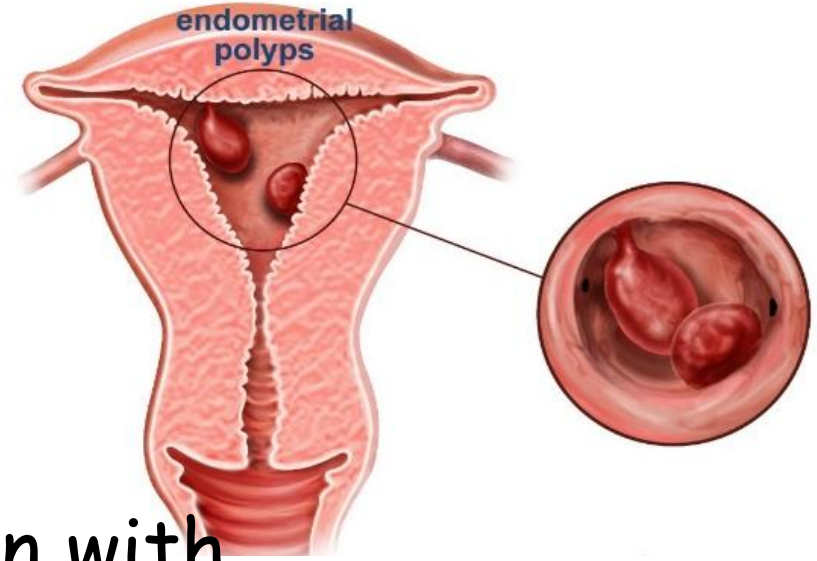
| | External Endometriosis | Internal Endometrisis |
|---|---|---|
| N/E | Hemorrhagic lesions (as the endometrial tissue undergoes cyclic menstrual bleeding).<br>It excites excessive fibrous tissue around them<br>•Ovarian endometriosis (chocolate cysts): cyst with dark red brown altered blood content.<br>• Fibrous adhesion with surroundings. | • The uterus is symmetrically enlarged<br>• The uterine wall is thickened<br>• The lesions form dark red foci |



| | External Endometrisis | Internal Endometrisis |
|---|---|---|
| M/E | • Lesion consists of endometrial glands and stroma with hemosiderin.<br>• fibrosis and hemosiderin laden macrophage.<br>  | • Nests of endometrial glands and stroma in myometrium between muscle bundles<br>  |

# Endometrial polyp

- Endometrial polyps are sessile masses of that project into the endometrial cavity.
- They may be single or multiple




**Effect:**

It may cause abnormal bleeding.

**Types:**

1.Functional endometrium,
2.Hyperplastic endometrium, in association with endometrial hyperplasia
3.Endometrial polyps in association with the administration of tamoxifen, an antiestrogen therapy of breast cancer.

# Endometrial Hyperplasia

## Definition:

Increased proliferation of the endometrial glands relative to the stroma, resulting in an increased gland-to-stroma ratio when compared with normal proliferative endometrium.

## Effect:

Abnormal uterine bleeding.

## Causes:

prolonged unopposed **estrogen** stimulation:
1.Repeated anovulatory menstrual cycles,
2.Obesity. 3.Estrogen secreting tumors
4.Polycystic ovarian disease.


## N/E:

Endometrial hyperplasia appears as increased endometrial thickness

# Endometrial Hyperplasia

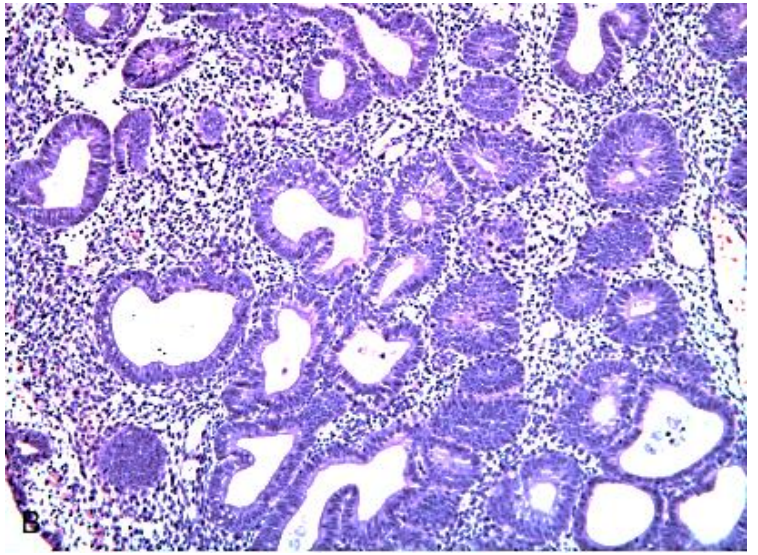
ME:

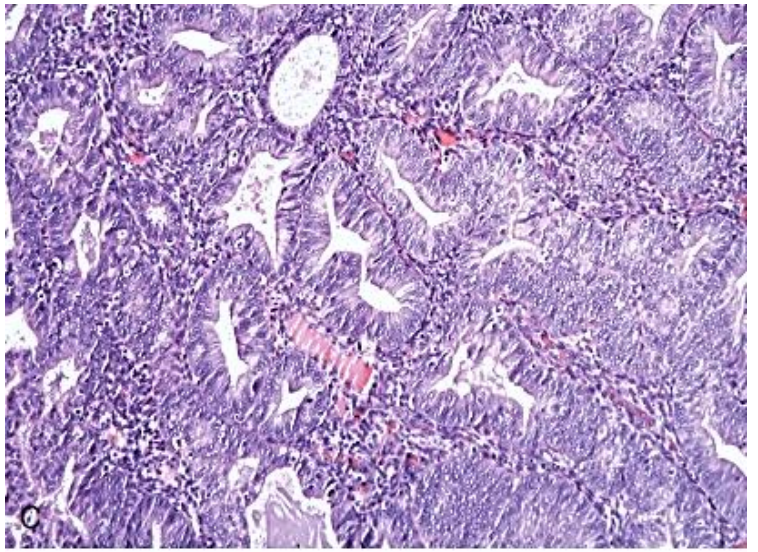
-Charcterized by glandular proliferation and crowding

-Increased gland to stromal ratio

-Endometrial hyperplasia is placed in two categories based on the presence of cytologic atypia:

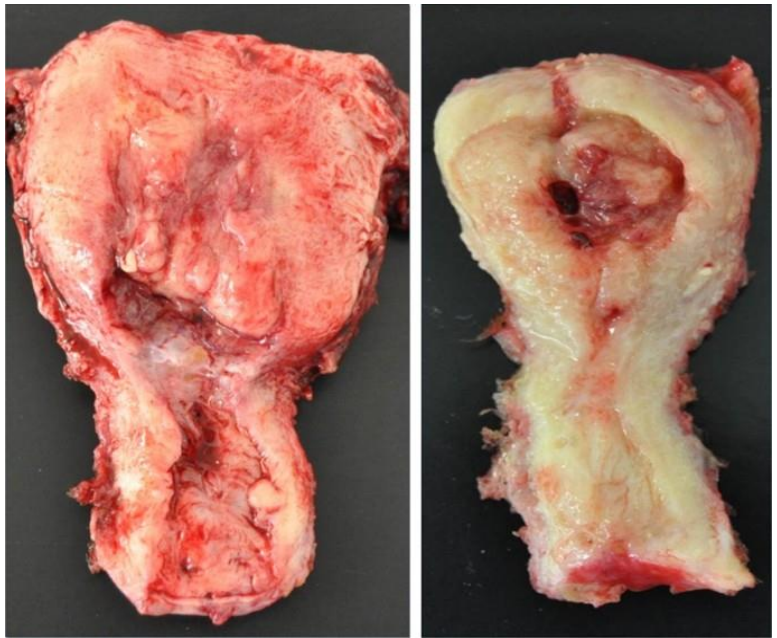
- Hyperplasia without atypia carries a low risk (between 1% and 3%) for progression to endometrial carcinoma.
- Hyperplasia with atypia, also called endometrial intraepithelial neoplasia (EIN), is associated with a much higher risk (20%–50%).

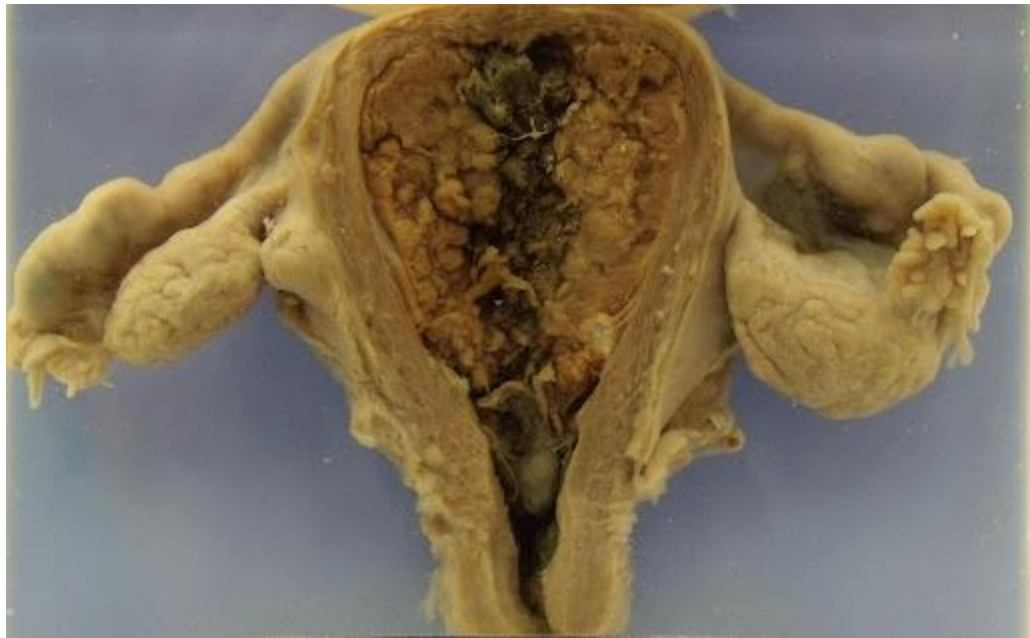




# Endometrial Tumors

1. Endometrial Carcinoma
2. Carcinosarcoma (Malignant Mixed Mullarian Tumor)
3. Endometrial Stromal Tumours
   - Benign: Stomal nodule
   - Malignant: Endometrial Stromal Sarcoma (ESS)





# Endometrial Carcinoma

- Endometrial carcinoma (EC)is the most common cancer of the female genital tract
- Endometrial carcinoma has two broad categories,
  - type I: Endometroid carcinoma (about 80% of cases)
  - type II: Serous carcinoma (about 20% of cases).

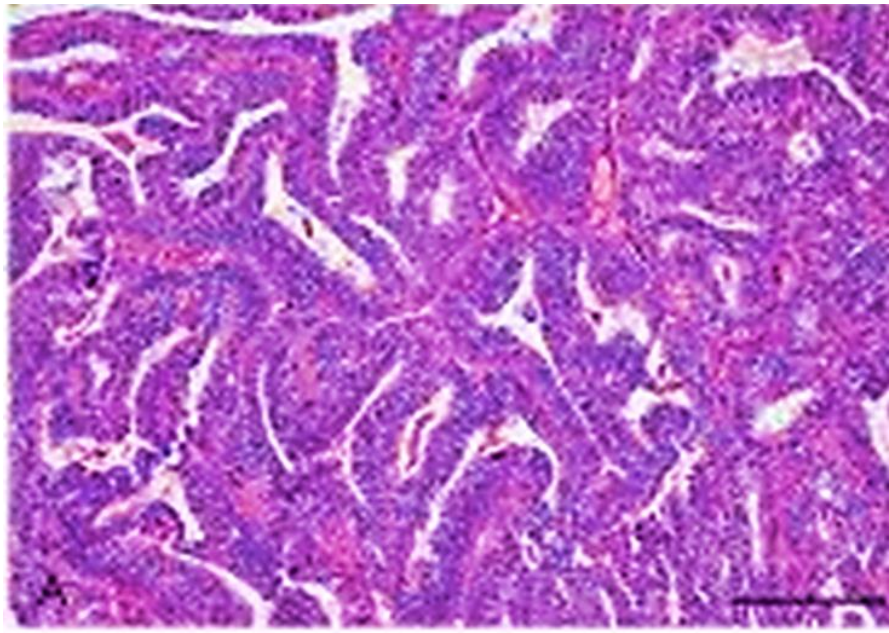
**Precursor (precancerous, preneoplastic) lesions:**

- Type I carcinoma: atypical endometrial hyperplasia (also known as endometrioid intraepithelial neoplasia, EIN)
- Type II carcinoma: a surface endometrial lesion is called Endometrial intraepithelial carcinoma, EIC

# Endometrial Carcinoma

## NE:

It may be polypoid or infiltrative.
Type II tends to be more bulky and diffuse.

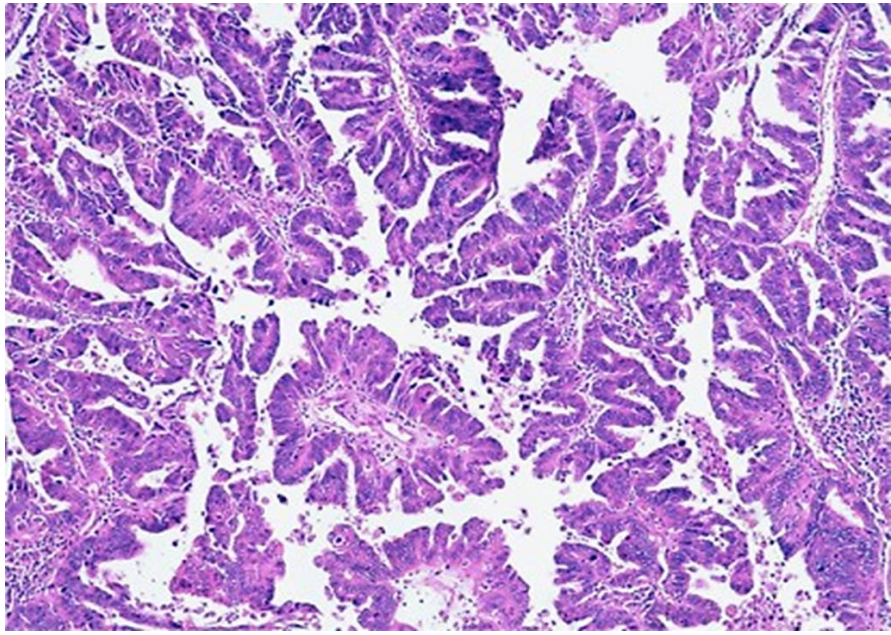


## ME:

Type I: resembling endometrial glands.

- According to the degree of glandular differentiation, endometrioid carcinoma is graded into GI, GII and GIII.

Type II
usually of serous histology (simulating tubal epithelial lining).

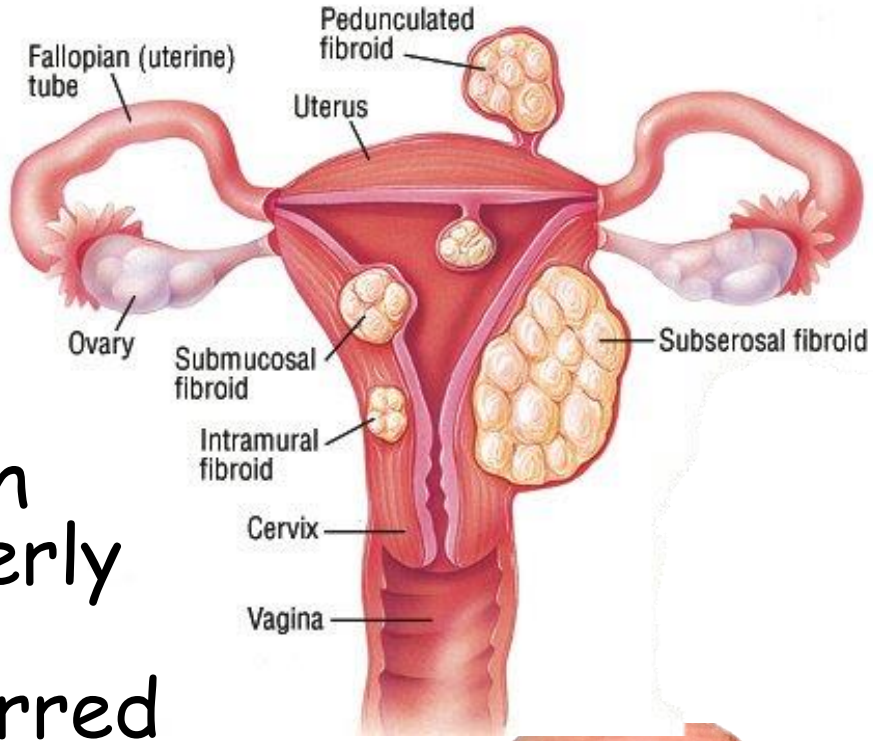


# Endometrial Carcinoma

| Characteristics | Type I | Type II |
|---|---|---|
| Age | 55–65 years | 65–75 years |
| Risk factors and Clinical settings | Unopposed estrogen<br>Obesity<br>Hypertension<br>Diabetes | Atrophy<br>Thin patients |
| Morphology | Endometrioid | Serous<br>Clear cell |
| Precursor | Atypical endeomtrial hyperplasia<br>Endometrioid intraepithelial neoplasia (EIN) | Endometrial intraepithelial carcinoma (EIC) |
| Molecular genetics | *PTEN* | *p53* |
| Behavior | Indolent<br>Spreads via lymphatics | Aggressive<br>Intraperitoneal and lymphatic spread |

# Tumors of Myometrium

- Benign:
  Leiomyoma
- Maliganat:
  Leiomyosarcoma




## Leiomyoma

Benign tumors that arise from the smooth muscle cells in the myometrium are properly termed leiomyomas, but
because of their firmness often are referred to clinically as **fibroids**
-Leiomyomas are the most common benign tumor in females, affecting 30% to 50% of women of reproductive age.

### Etiology:

Associated with prolonged hyperestrinism.

# Leiomyoma

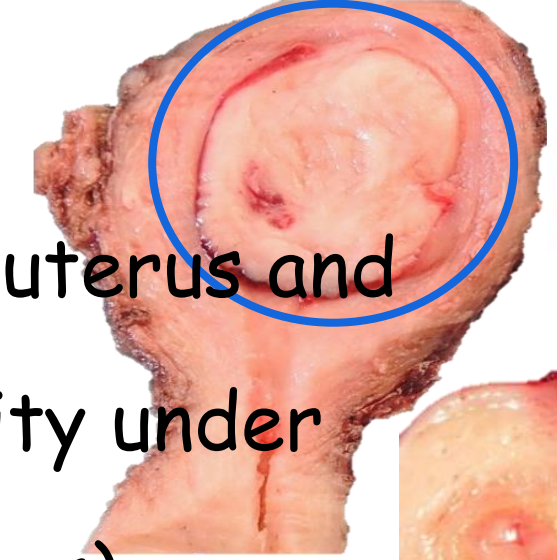
NE:

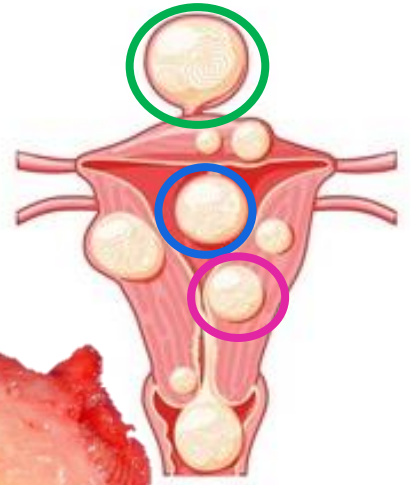
- Site: Commonly arises in the body of uterus and cervix.

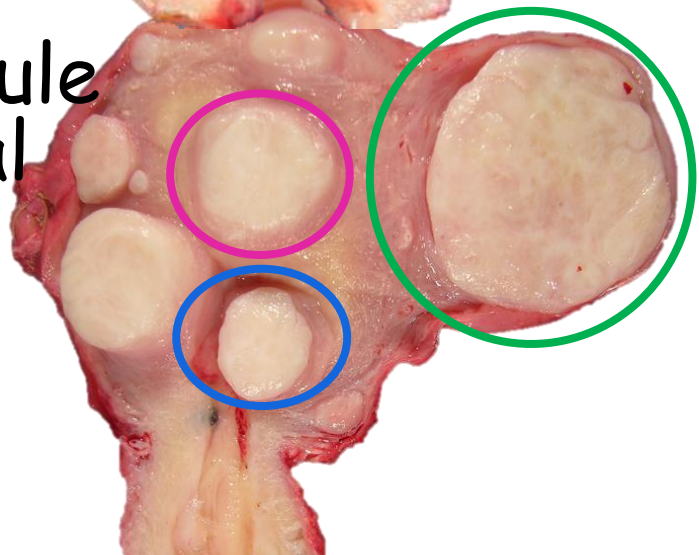
Submucous (project in the uterine cavity under the endometrium

Intramural (within the wall of the uterus)

Subserous (projects to outside under the peritoneum)







- Rounded masses, surrounded by pseudo-capsule of compressed uterine muscle and interstitial tissue.
- Cut surface: whorly appearance
  firm in consistency

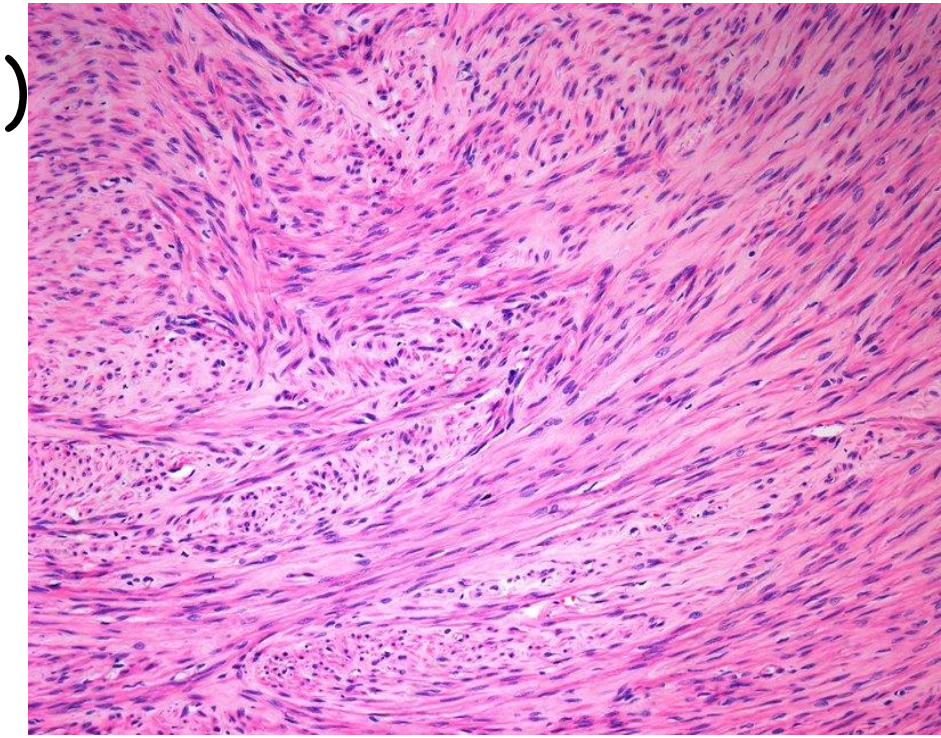
# Leiomyoma

**ME:**

Interlacing bundles of: smooth muscle cells & fibroblasts.

Secondary changes: e.g. hyaline degeneration, cysts, necrosis and calcification.

Red degeneration(hemorrhagic infarction) occurs particularly during pregnancy.



**Complications:**

1- Abnormal uterine bleeding.

2- Infertility due to prevention of implantation of fertilized ovum.

3- Risk of abortion.

4- Interfere with child birth.

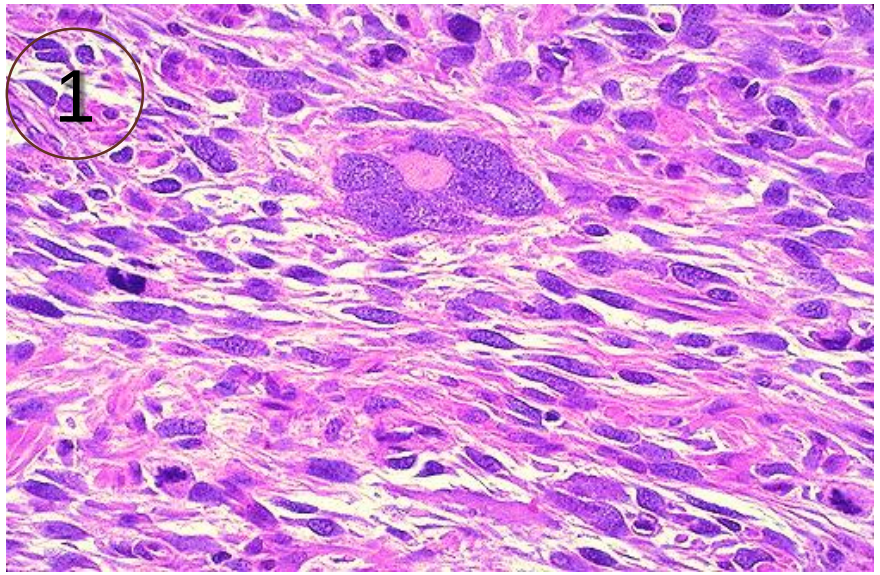
5- Iron deficiency anemia

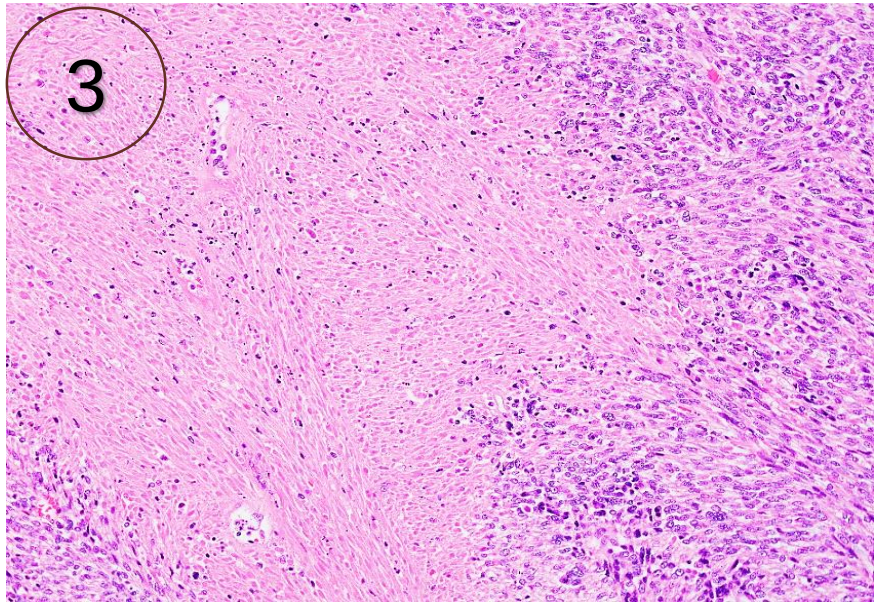
6- Malignant transformation to Leiomyosarcoma (rare, 1%).

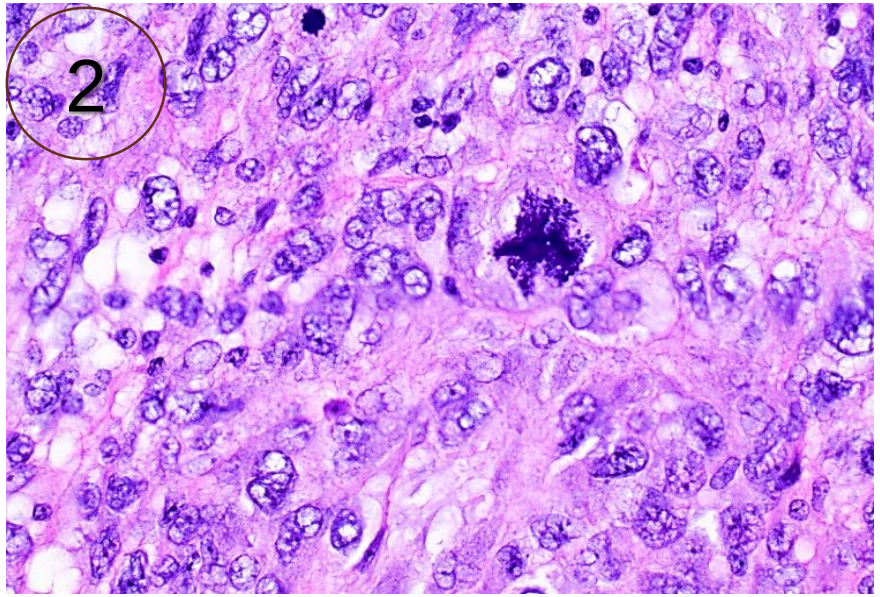
# Leiomyosarcoma

## On microscopic examination:

1. Atypia,
2. Increased mitotic figures
3. Coagulative necrosis.



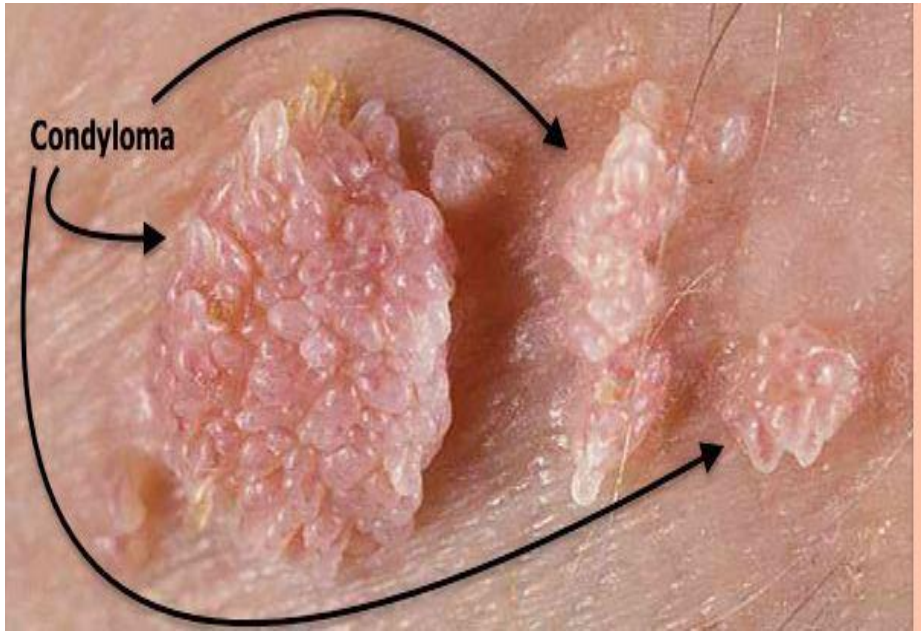
# Pathology

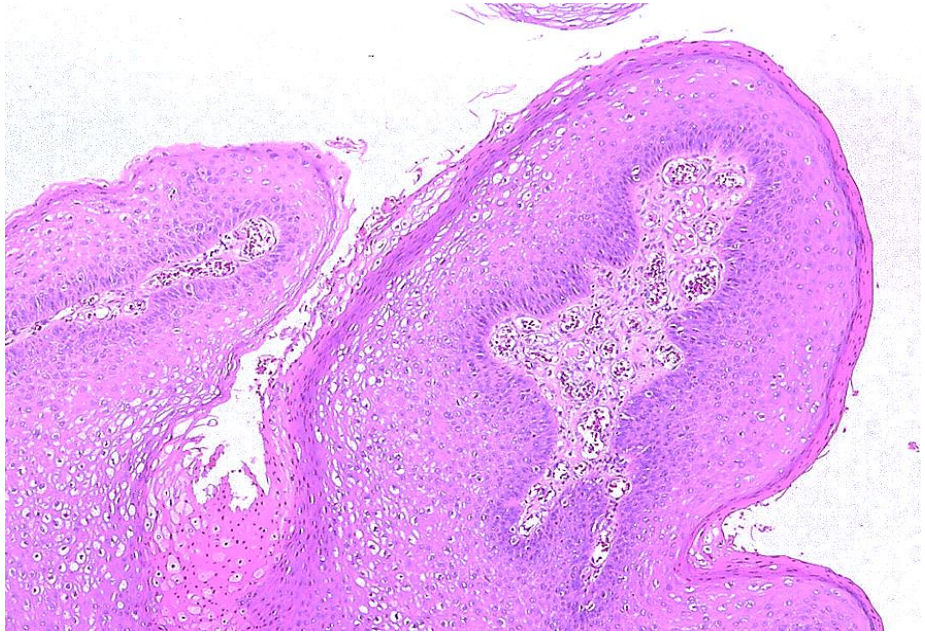
# Vulva, vagina, cervix

# Vulva

## Benign lesions of the vulva

- Condyloma Accuminata which is virus related (low risk HPV).
- Squamous cell papilloma is not of viral origin.
- Hidraadenoma papilliferum.



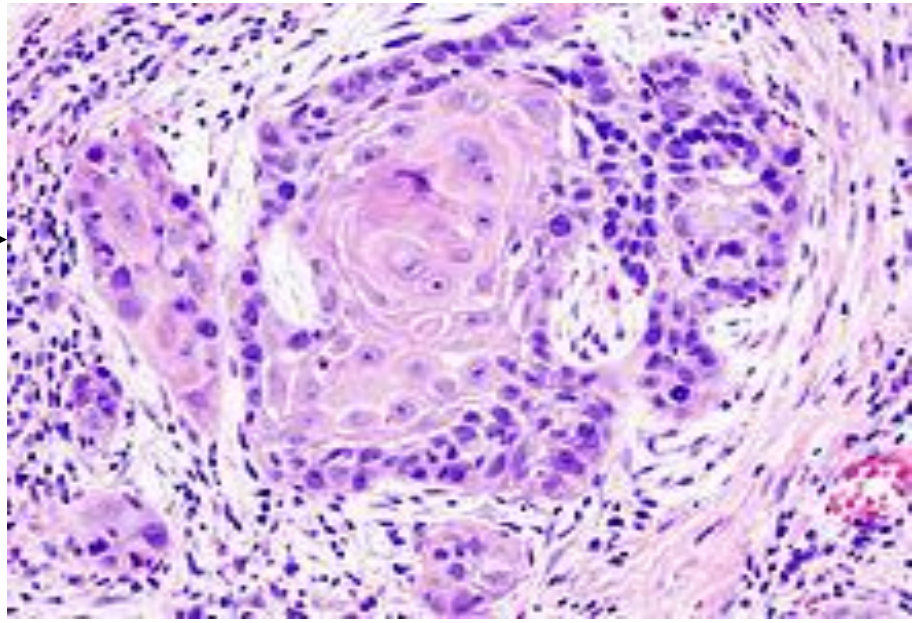



# Vulva

## Carcinomas:

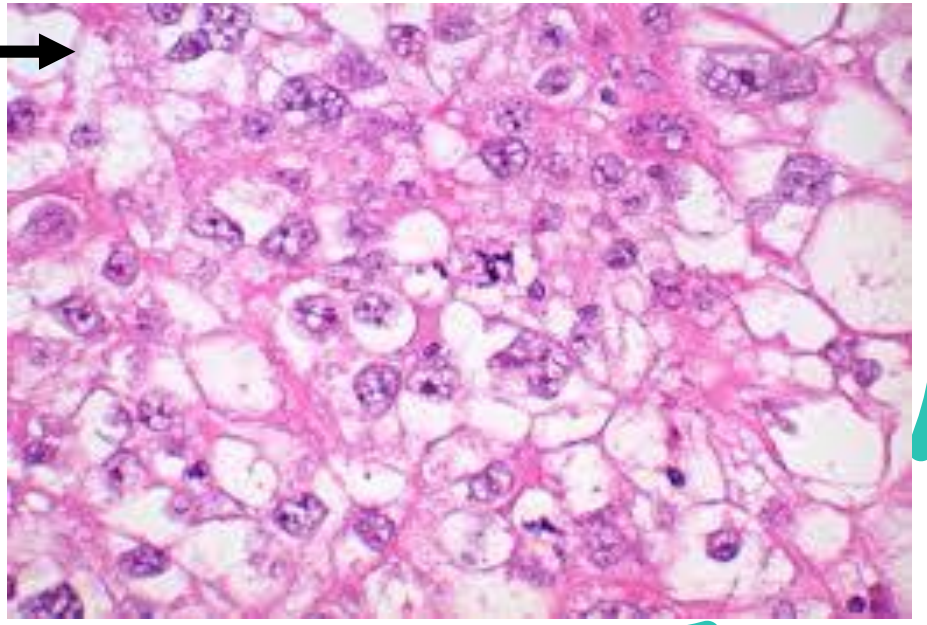
**Squamous cell carcinoma:**

Squmous cell carcinomas are, in a proportion of cases, related to (high risk HPV). They are preceded by a precursor lesion (*vulvar intraepithelial neoplasia, VIN*).



**Clear cell carcinoma:**

A variant of adenocarcinoma. It is preceded by a precursor lesion (vaginal adenosis). The condition is uncommon but is seen in up to 90% of patients exposed in utero to DES.



# Vagina

**Vaginitis:** Caused by:

-Monilia - trichomonas vaginalis

-Gonorrhea -Staph.

-Herpes simplex ... etc.

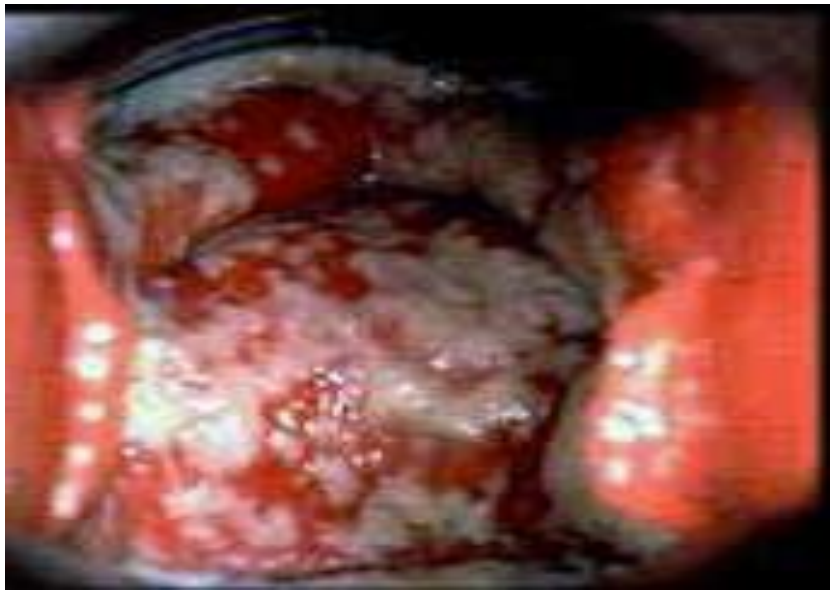
It occurs in :

-Infants and young women (high glycogen content of vaginal epithelium.)

-Pre-pubertal and postmenopausal women (lack of oestrogen)

-Diabetic women

-In case of prolonged loop application.



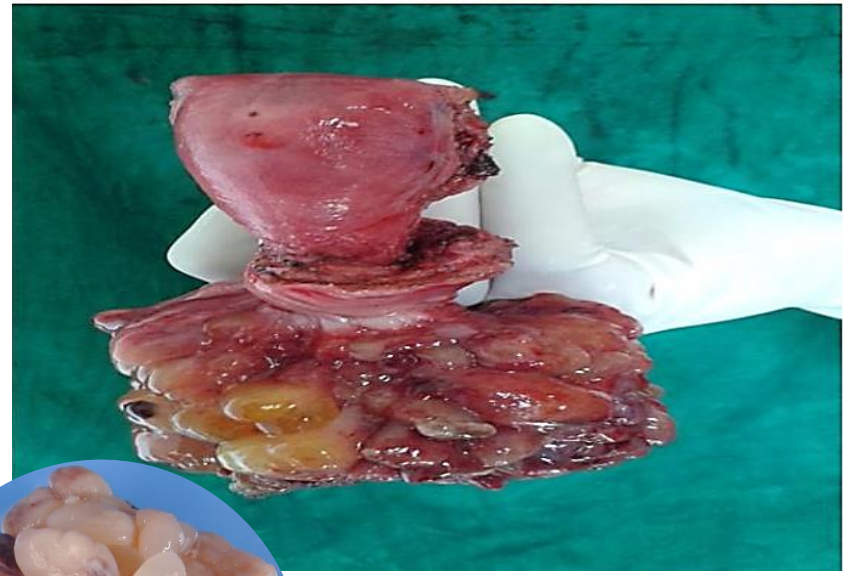
# Vagina

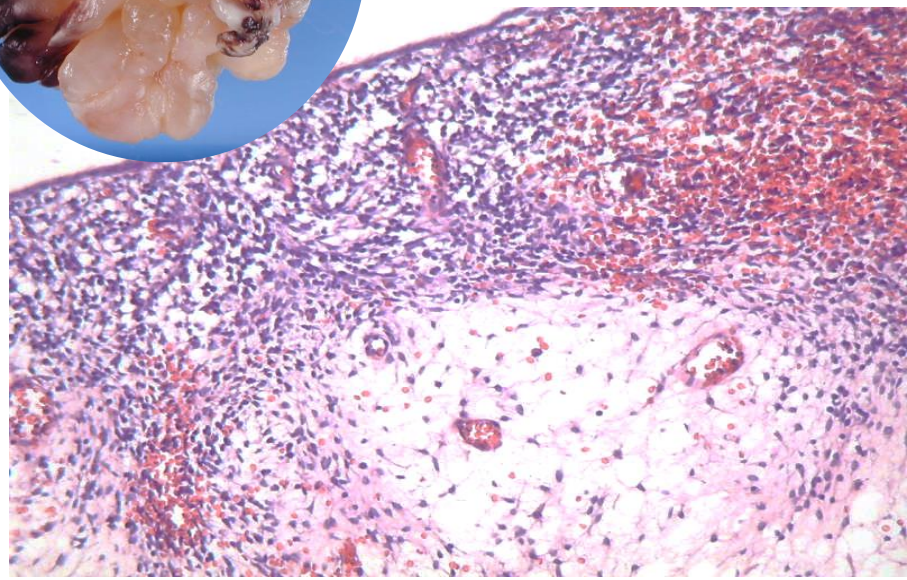
## *Embryonal rhabdomyosarcoma* (Sarcoma botryoides):

This tumor is uncommon occurring chiefly in girls from birth to adolescence (90% of cases occur under 5 years of age).

Grossly, appears as a large polypoid (grapes-like) , reddish, soft mass .

Microscopically, it consists of malignant embryonal cells (small round to oval cells with hyperchromatic nuclei and scanty cytoplasm) in a myxoid stroma with rhabdomyoblastic differentiation.





# Cervix

## Cervicitis

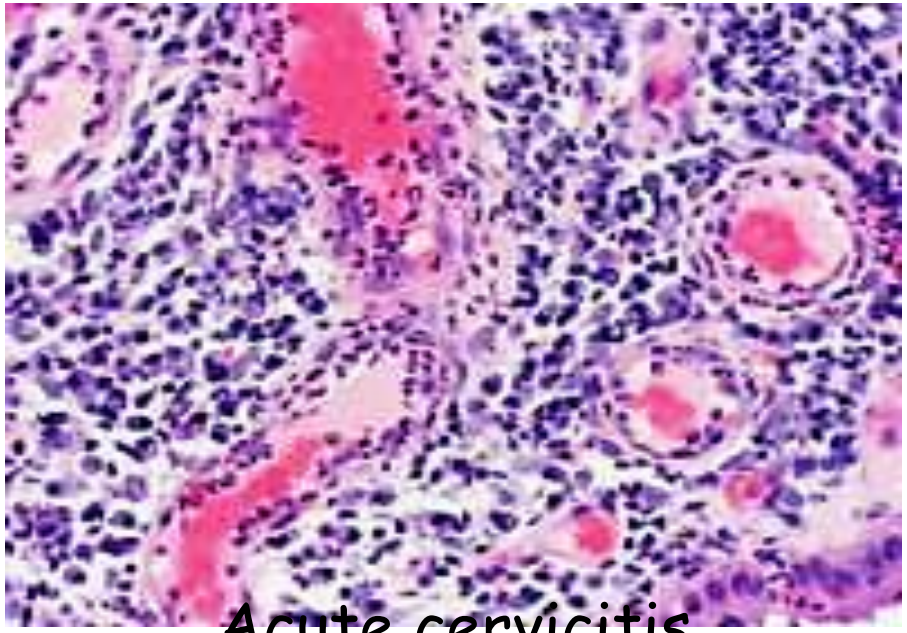
- Some degree of cervical inflammation may be found with no or little clinical consequence.

Cause: E. coli, staph, strept. H. gonococci, chlamydiae, mycoplasmas, trichomonas vaginalis and herpes simplex virus may produce significant acute or chronic cervicitis.

- May be associated with upper genital tract disease, complications during pregnancy, and sexual transmission.

### Acute cervicitis:

The cervix is congested, swollen and shows profuse purulent discharge. The inflammation may resolve or more often passes to a chronic stage.



Acute cervicitis

# Cervix

## Cervicitis

**Chronic cervicitis:** Common

**N/E:**

The cervix is red, swollen ± ulcers, polyps or cysts. External os is wide, irregular with muco-purulent discharge.

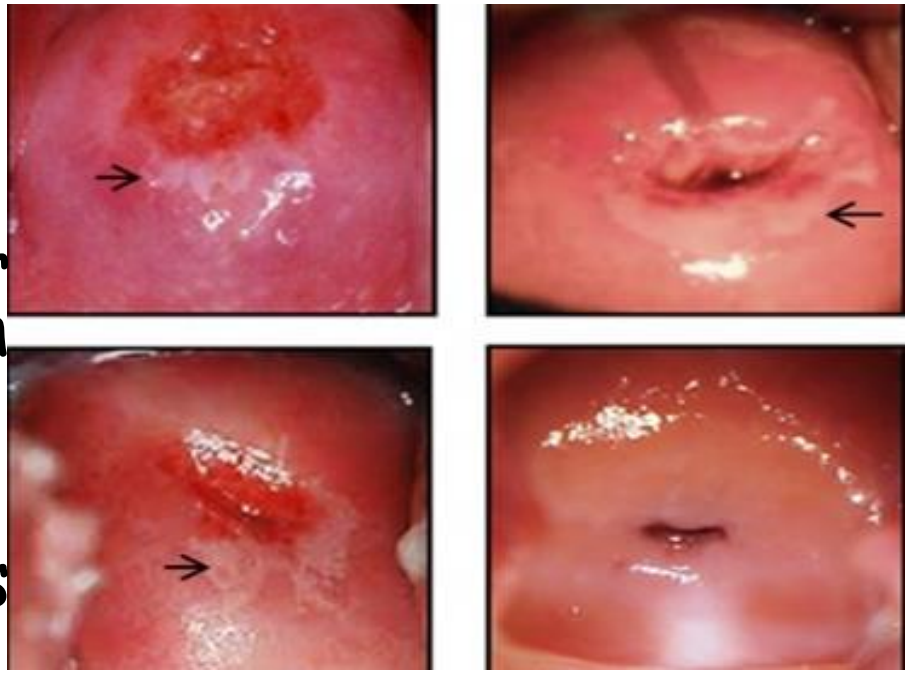
**M/E:**

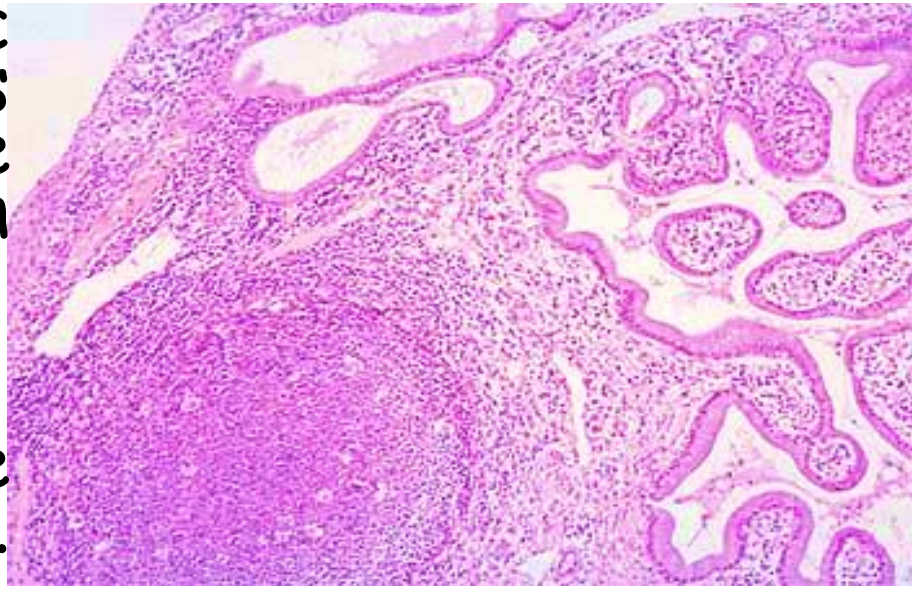
**Endocervix:**

- Lining epithelium shows squamous metaplasia ± dysplasia.
- Subepithelial tissue shows chronic inflammatory cells + endarteritis obliterans + fibrosis and some neutrophils. Some glands are cystically dilated (Nabothian cysts).
- Inflammatory polyp

**Ectocervix:**

Extension of endocervical mucosa to replace ectocervical epithelium around external os. Squamous metaplasia occurs later.

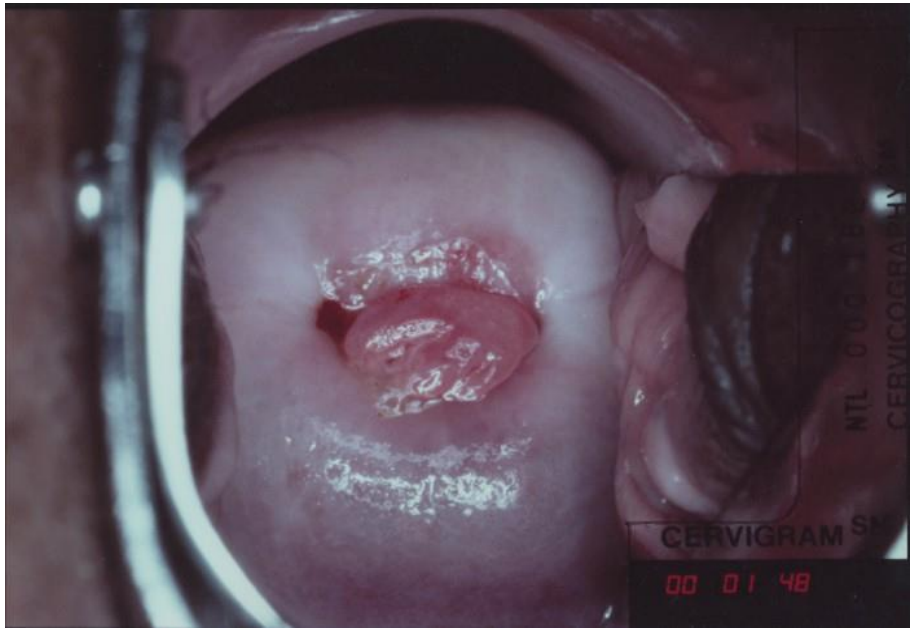




Chronic cervicitis

# Cervix

## Endocervical Polyps



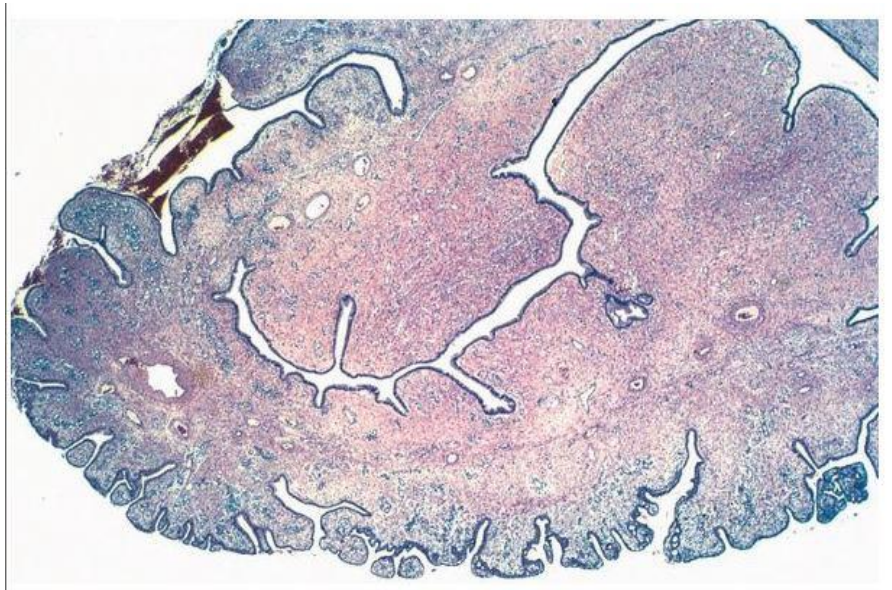

*Benign exophytic growths
*Usually arise from the endecervix.
*Cause irregular vaginal bleeding.

NE:

Polyps are soft, almost mucoid.

ME:

composed of central vascular and edematous connective tissue core containing proliferated dilated cervical glands and chronic inflammatory cells. It is covered by columnar epithelium with areas of squamous metaplasia.



# Cervix

## Carcinoma of the cervix

### Predisposing factors:

- Persistent infection with oncogenic HPVs (16 & 18). HPVs infect immature basal cells of the squamous epithelium. Integration of HPV DNA interferes with the p53 & RB genes.
- Smoking reduces local cervical immunity.
- Early age at first intercourse.
- Multiple sexual partners.
- Presence of other sexually transmitted diseases like HIV and genital herpes (Herpes simplex type II).
- Having a partner with a sexually transmitted disease.
- Long term Oral contraceptive pills use and multiple pregnancies
- Immunosuppression.

# Cervix

## Carcinoma of the cervix

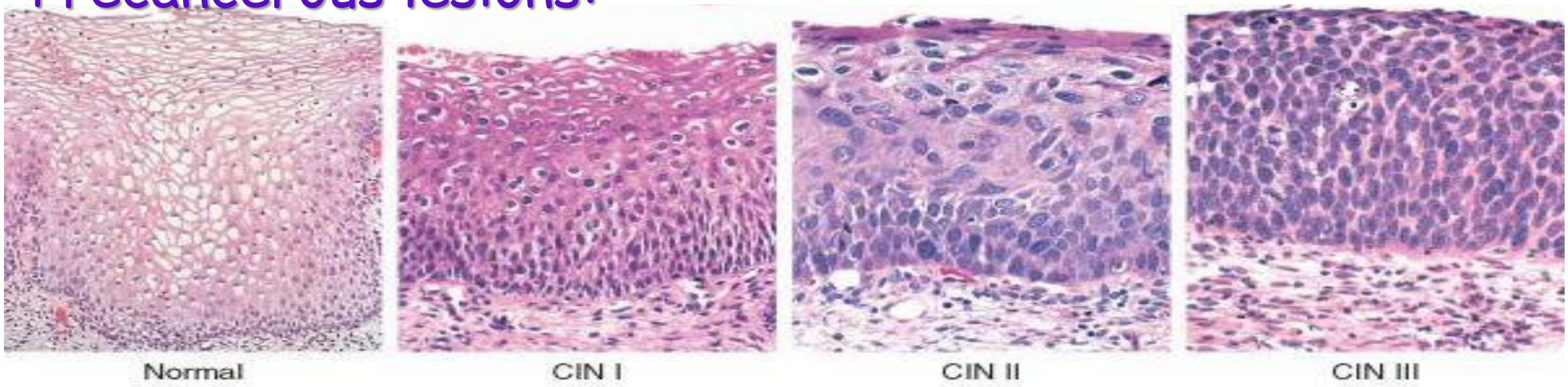
### Precancerous lesions:

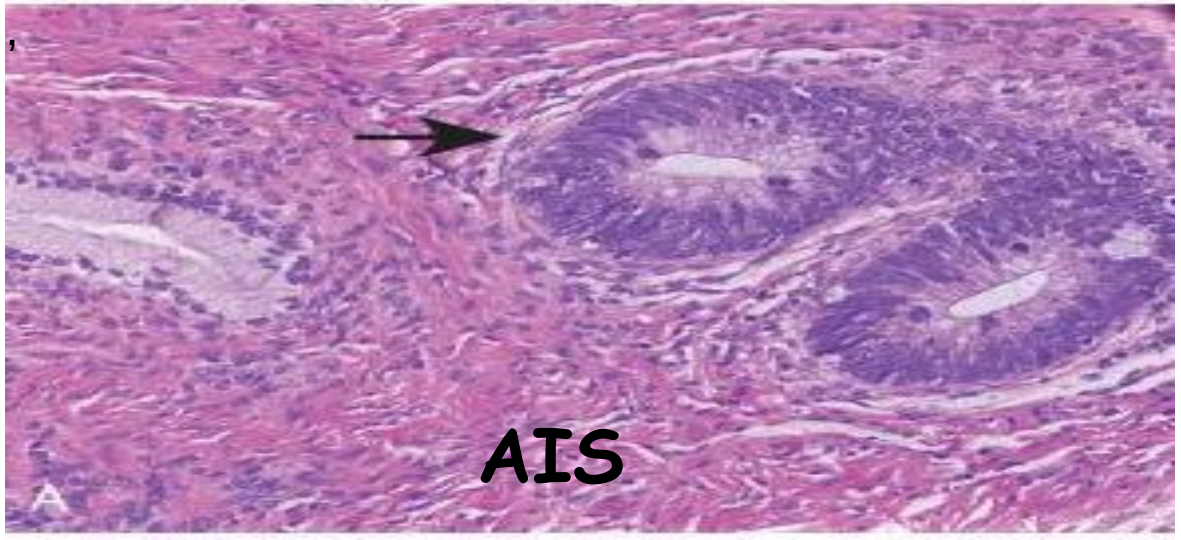
- Cervical Intraepithelial Neoplasia (CIN) is the precancerous lesion of cervical squamous cell carcinoma. It is classified as:
  CIN1 → minimal dysplasia in lower 1/3 → low risk to develop carcinoma, called low grade squamous intraepithelial lesion (LSIL)
  CIN2 → moderate dysplasia in lower 2/3
  CIN3 →the most severe where the atypical cells involve the whole thickness of the epithelium.
  Both 2 ,3 risk to develop carcinoma, called high grade squamous intraepithelial lesion (HSIL)
- Adenocarcinoma insitu (AIS): is the precancerous lesion for invasive adenocarcinoma.

# Cervix

## Carcinoma of the cervix

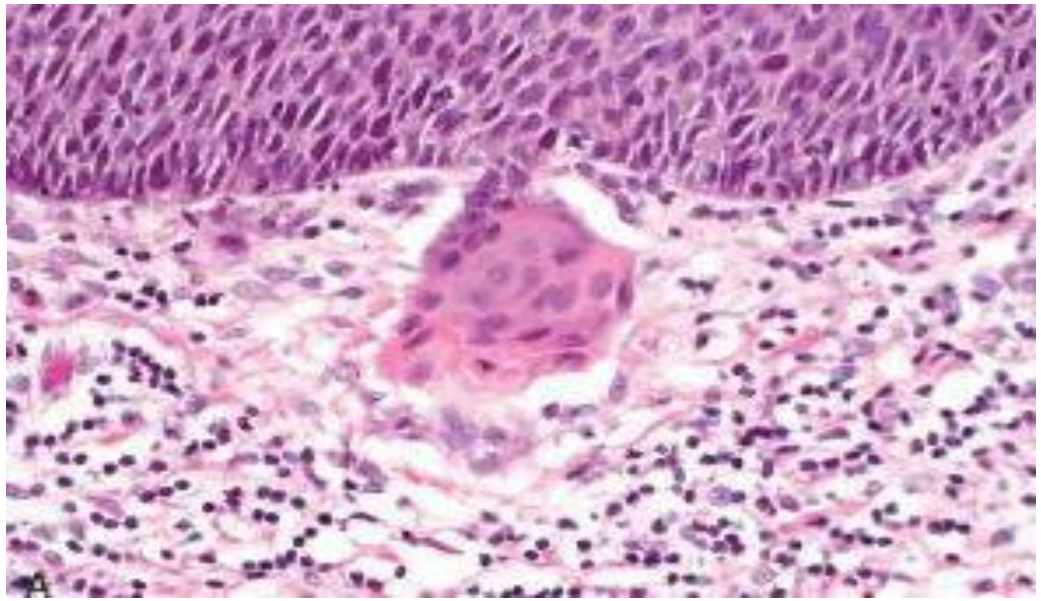
### Precancerous lesions:



# Invasive carcinoma

- One of the commonest cancer in females.
- The age peak of incidence is 45 years.



**Microinvasive SCC**

# Cervix

## Carcinoma of the cervix

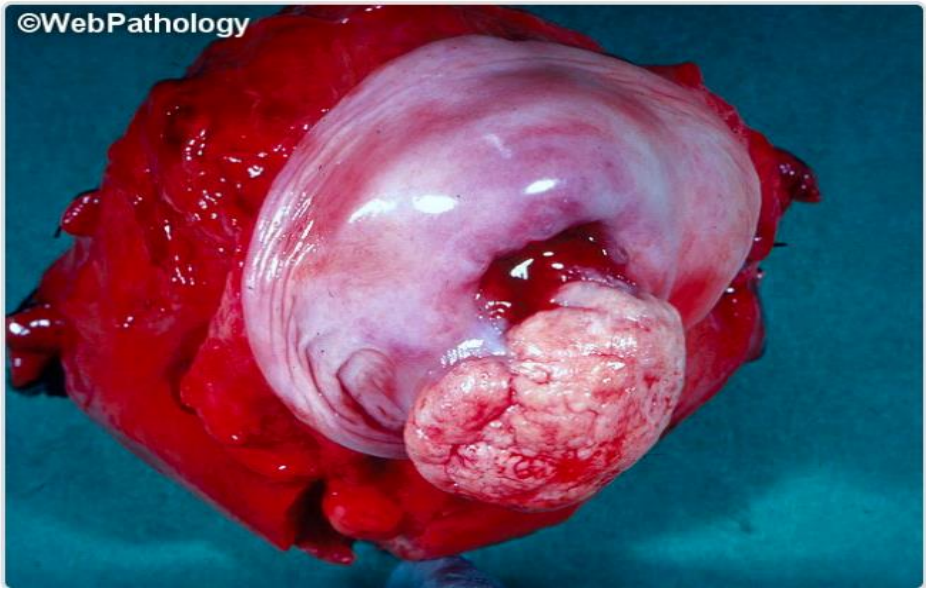
### Gross:

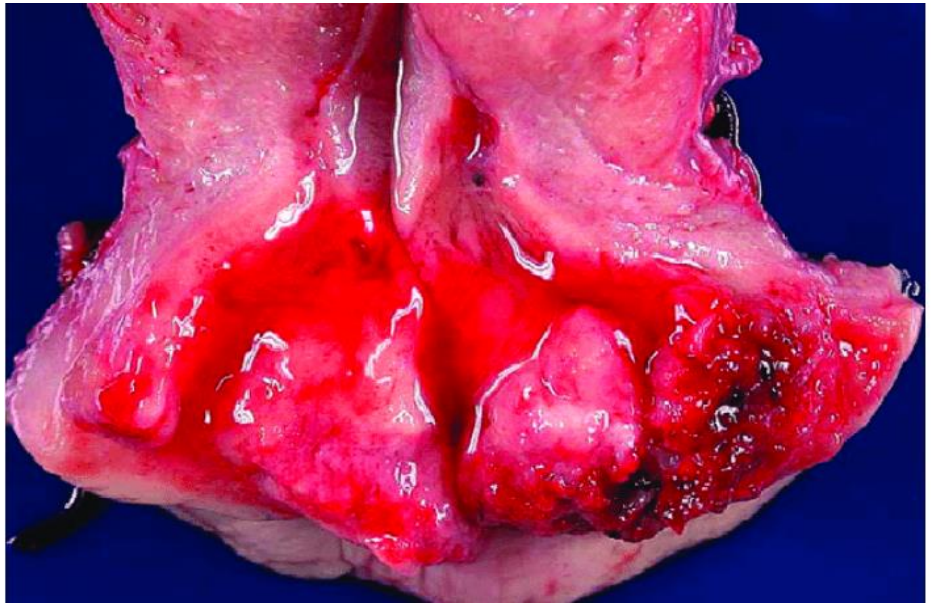
Site:

- Squamous columnar junction.
- Endocervix with sq. metaplasia

Shape:

- Carcinoma in situ: a focal thickening & induration of cervix.
- Invasive carcinorna.
  - -Fungating (exophytic)
  - -Infiltrating (endophytic) → induration & deformity of the cervix.
  - -Ulcerating (malignant ulcer)



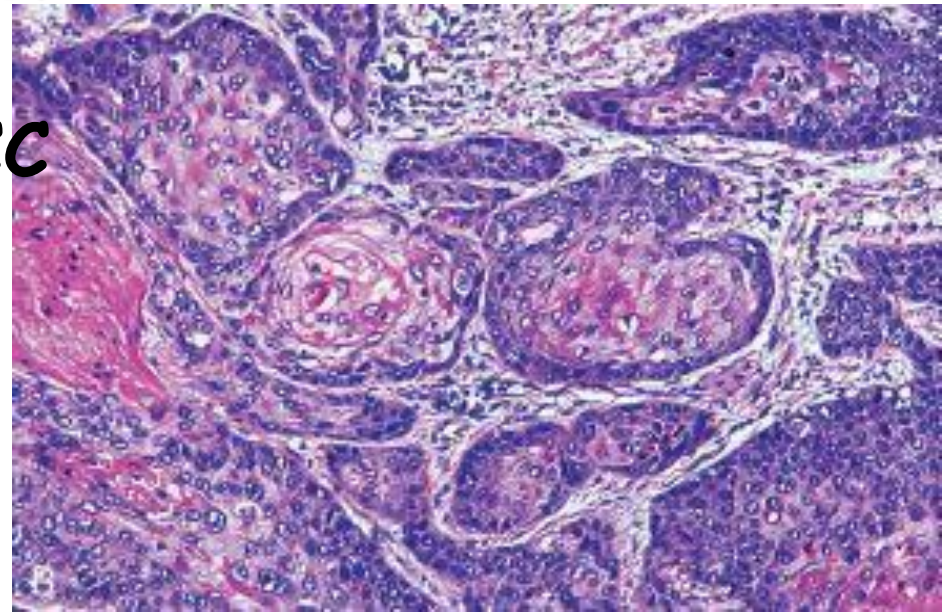
# Cervix

## Carcinoma of the cervix

### Microscopically:

- **Squamous cell carcinomas** either keratinizing or nonkeratinizing. The most common (80% of cases)
- **Adenocarcinomas** (15% of cases).are characterized by formation of glandular structures.
- **Other types** (5%)include adenosquamous carcinoma and neuroendocrine carcinoma.

SCC



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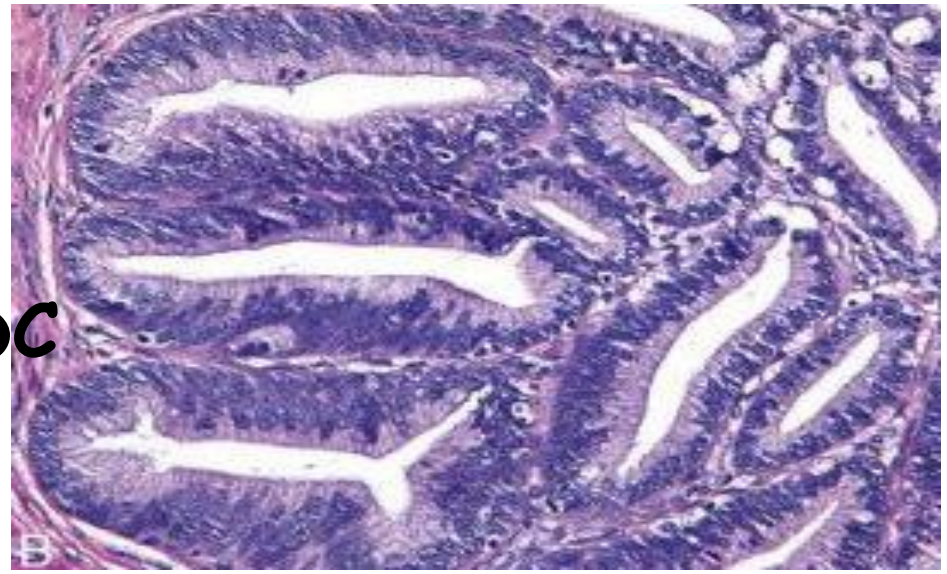


# Cervix

## Carcinoma of the cervix

### Spread:

- Local to the peritoneum , bladder and rectum.
- Lymphatic to local and distant lymph nodes metastasis
- Hematogenous metastasis to liver lung and bone.

### Prognosis:

- Because of screening programs, most of patients are discovered in early stages.
- Patients with stage IV cancer of poor prognosis die as a consequence of local extension of the tumor.

# Cervix
## Carcinoma of the cervix

### Prevention:

- Vaccination against HPV introduced to girls at school age hopefully may reduce the cervical cancer risk.
- Screening programs

  -Aim: to detect precancerous lesions or abnormal cells early.

  -Method : PAP smear and HPV testing.

# Pathology

## The breast

# Clinical presentation of breast disease

1-Lump (mass)

2-Pain

3-Discharge

4-Inflammatory changes

5-Gynecomastia (in male breast)

# DD of breast lump

1. Traumatic: hematoma and traumatic fat necrosis.
2. Inflammatory: breast abscess, mammary ductectasia and granulomatous as T.B.
3. Fibrocystic disease of the breast.
4. Neoplastic mass: Fibroadenoma, duct papilloma, phylloides tumor and breast cancer

# Non neoplastic breast lesions

# Mastitis

Definition: Inflammation of the breast could be infective or non infective

➢**Infective mastitis and breast abscess**

**Predisposing factors**:

It occurs during lactation especially in primipara due to:

1- Ignorance of nipple hygiene.

2- Nipple abrasion .

3- Retained milk.

**Cause**: Bacteria usually staphylococcus aureus.

**Pathology**: Acute inflammatory changes which can progress to form single or multiple abscesses. It may be acute or chronic.

➢**Non Infective Mastitis**

1- Traumatic fat necrosis.

2- Periductal plasma cell mastitis (Mammary ductectasia)

# Mammary duct ectasia
# (Periductal plasma cell mastitis)

-Inflammatory disease usually affects multipara 40 and 60 years of age.

## Pathogenesis:

- Inspissation of milk in the main excretory ducts.
- Dilatation of proximal ducts and rupture.
- Escape of milk leading to marked periductal chronic inflammation rich in plasma cells.

## N/E:

l- Lesion feels as a bag of worms in one or more segments of the breast.
2- C/S: dilated ducts containing cheesy material
3- Later, forms a firm periareolar mass with nipple retraction, nipple discharge

## M/E:

1- Dilatation of ducts, destruction of their lining epithelium and may rupture.
2- Ducts are filled with granular debris, lipid laden foamy macrophages.
3- Periductal tissue is infiltrated by chronic inflammatory cells rich in plasma cells, occasional granulomas and fibrosis

# Fibrocystic Diseases of The Breast
# (Cystic Mammary Hyperplasia)

**Incidence**:

- The most common breast disease.
- It affects over half the women during reproductive period
- It is not premalignant

**Aetiology:**

- Hyperestrogenemia.

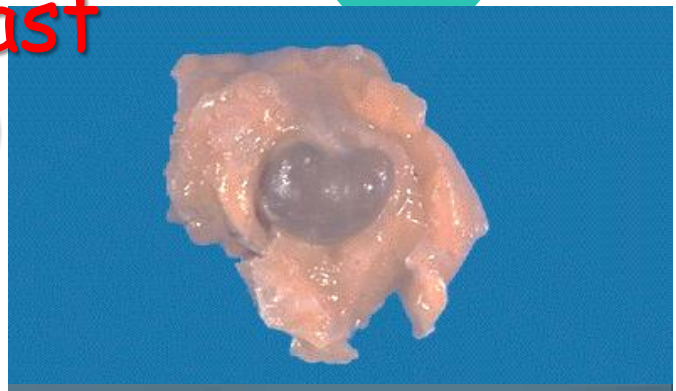
**Pathogenesis:**

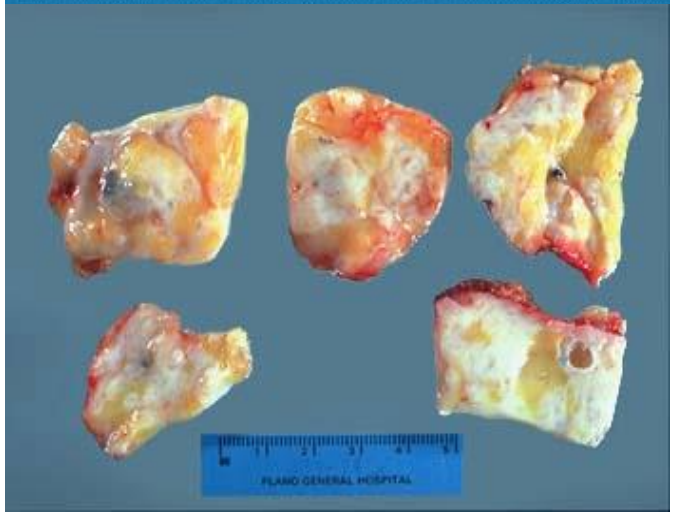
- Derangement of cyclic breast changes that occur normally during menstrual cycle.

**Prognosis:**

- Epitheliosis increase incidence of breast cancer which is more evident with atypical hyperplasia

# Fibrocystic Diseases of The Breast (Cystic Mammary Hyperplasia)



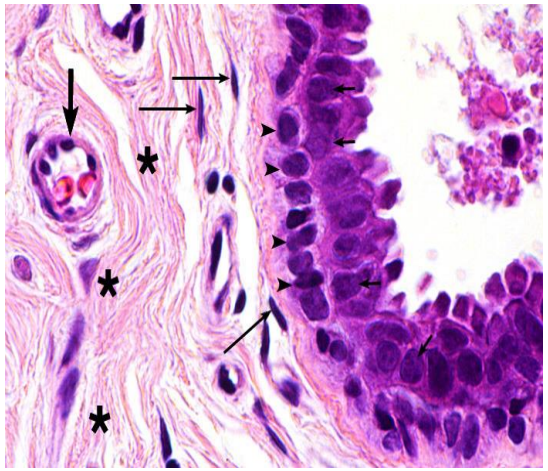


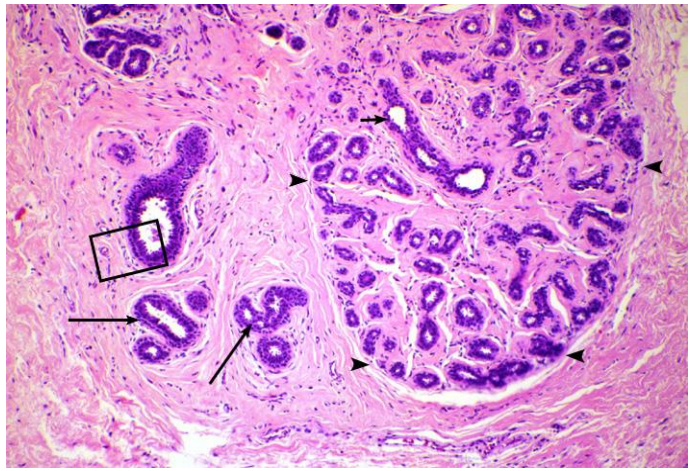
**N/E:**

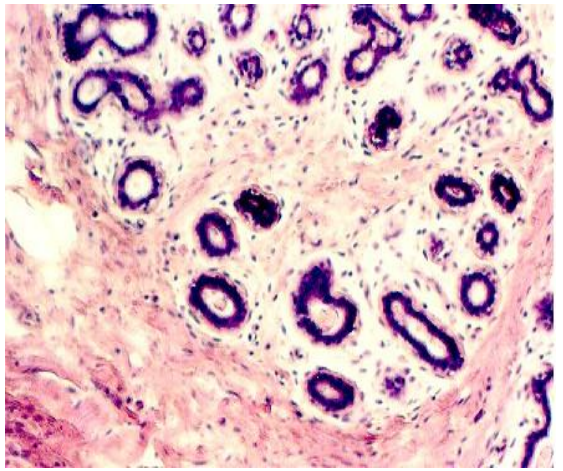
- Unilateral or bilateral.
- Single or multiple.
- Not-encapsulated, ill defined, firm rubbery in consistency.
- Mobile
- C/S : Grey white in colour.
- Show variable sized cyst containing serous or hemorrhagic fluid.

**M/E:**

- Fibrosis.
- Adenosis.
- Epitheliosis.
- Cystic formation.







# Neoplastic breast lesions

# A- Benign Tumors

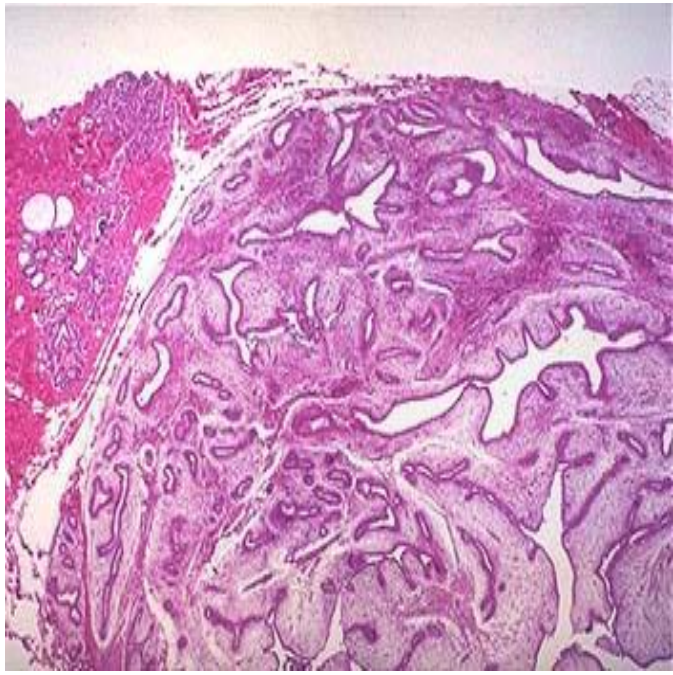
## I- Fibroadenoma

- Commonest benign tumor of female breast.
- Mixed (fibrous and epithelial).
- Peak incidence is in 3rd decade.
- Caused by estrogen stimulation

N/E:

- Usually single, well circumscribed, round or oval.
- Encapsulated, well-defined.
- Firm, freely mobile.
- C/S: greyish white

M/E:



- Mixed tumor formed of epithelial lined ducts separated by fibrous stroma.
- Surrounded by true capsule.
- It may be: 1. Pericanalicular.
  2. Intracanalicular
  3. Mixed

Prognosis: Does not recur after excision
Malignancy is rare.

## II-Phyllodes tumor(phyllodes is Greek for "leaf like")

- Less common than fibroadenomas
- A fibroepithelial tumor of unpredictable behavior.
- Detected in older females.

N/E: Large, rounded, circumscribed mass .

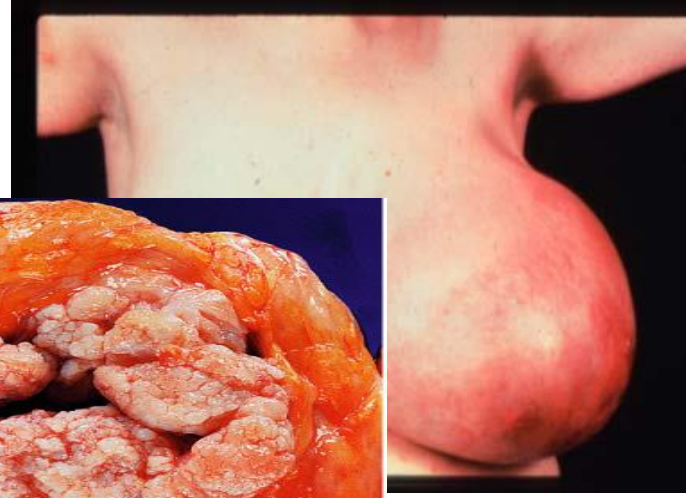
- Consistency: firm
- C/S: greyish white with slits and cysts.

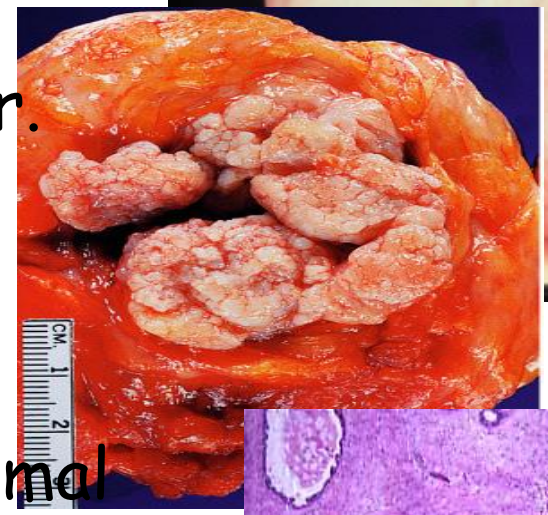
M/E: Fibroepithelial tumor with abundant the stromal element and cellular element forms leaf like projections.

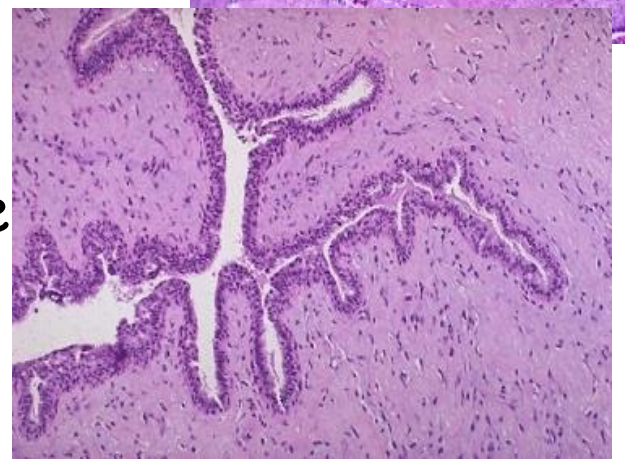
Changes suggesting malignancy are:

1.stromal hypercellularity 2.anaplasia
3.high mitotic activity. 4.rapid increase in size
5. infiltrative margins

Prognosis: Most phyllodes tumors are benign but few are malignant with hematogenous spread.







# III- Duct papilloma

- Intra-ductal growths.
- Frequently causes nipple bleeding/discharge or small sub-areolar mass.
- Usually occur in 4th or 5th decade.

N/E:

- Site: usually within a large duct (principal lactiferous duct or sinus) near the nipple.
- Shape: Delicate branching papillary growth .
- Size: small usually less than 1cm.
- Consistency: friable.

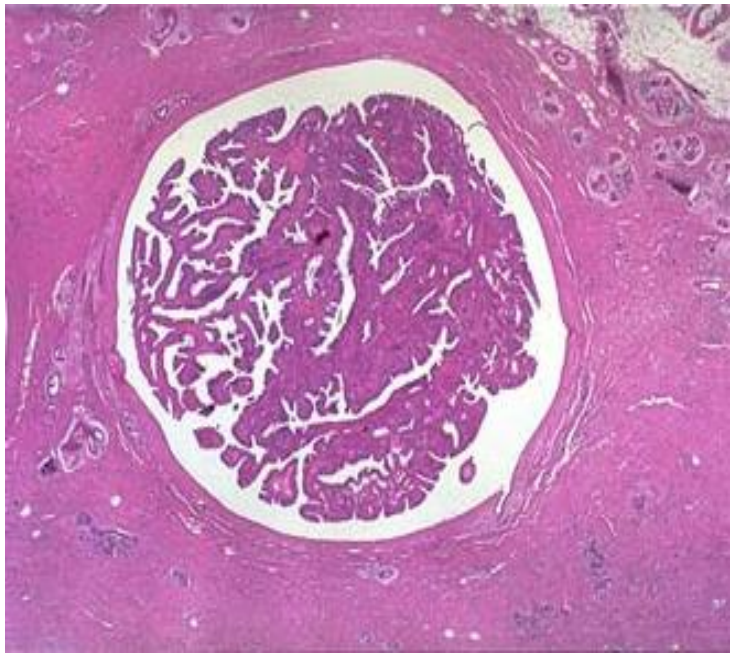
M/E:

- Branching papillae within the dilated duct formed of
- fibrovascular core covered by two layers of cells, luminal cuboidal or columnar and outer myoepithelial.

Prognosis:

1-Involution leading to atrophy and hyalinization.

2- Rarely it changes to duct papillary carcinoma.



# Breast Carcinoma

20% of all cancers in women

## Risk factors

1- **Age**: risk increases with increasing age, especially after menopause except in familial cases. Very rare before age 25

2- **Genetic and familial predisposition**: Positive family history . Familial cases are characterized by increase incidence in: - 1 st degree relatives. - Younger age (premenopausal). - Bilateral breast cancer . - - Genetic mutations, BRCA1 and BRCA2

**3- Reproductive life**:

-More in nullipara.

-More with late age of birth of first child .

-More with long reproductive period of life with early menarche.

4-Prolonged exposure to exogenous **estrogen** postmenopausally.

5- **Ionizing radiation** to the chest only women in whom irradiation occurred before age of 30 during breast development are affected.

6- **Other risk factors**: a- Obesity due synthesis of estrogen in adipose tissue.
b- A diet rich in fat. c- Alcohol consumption. d- Cigarette smoking.

7- **Precancerous lesions**:

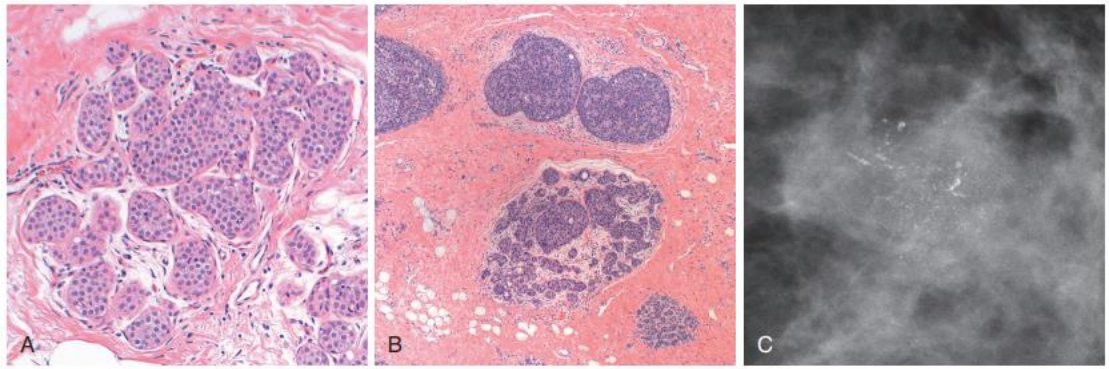
a- Proliferative fibrocystic change especially with atypical hyperplasia.

b - Carcinoma in situ: - In situ duct carcinoma - In situ lobular carcinoma.

c - Carcinoma of other breast. d- Benign tumors as duct papilloma

# Breast Carcinoma

## Classification of breast carcinoma

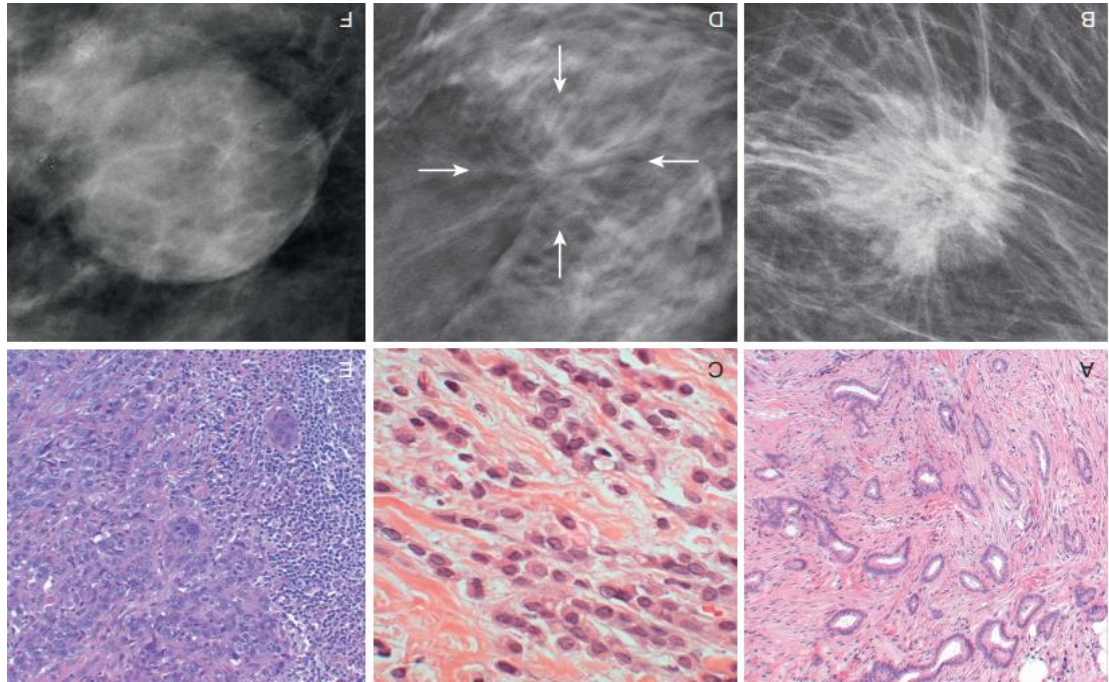



**A. Noninvasive**

1. Ductal carcinoma in situ
2. Lobular carcinoma in situ

**B. Invasive**

1. Invasive ductal carcinoma (includes all carcinomas that are not of a special type)—70% to 80%
2. Invasive lobular carcinoma
3. Carcinoma with medullary features
4. Mucinous carcinoma (colloid carcinoma)
5. Tubular carcinoma
6. Other types



# Breast Carcinoma

## A- Non invasive (in situ) carcinoma

### Ductal carcinoma insitu (DCIS)

- It is a preinvasive neoplasm which has not yet broken through basement membrane of the ducts.

N/E:

1-small hard masses

2- Bloody or serous nipple discharge

C/S: shows dilated ducts filled with papillary structures (papillary intraduct carcinoma) or necrotic tissue (comedocarcinoma).

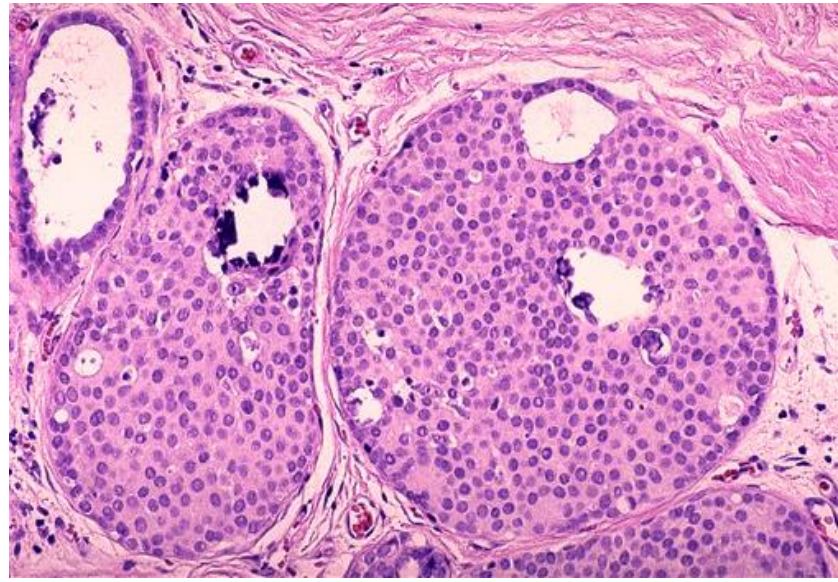
M/E:

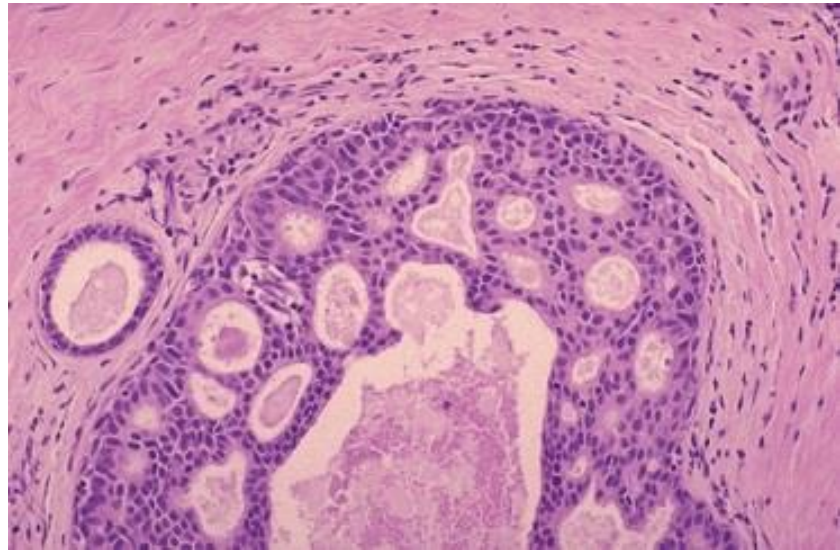
The ducts are dilated and distended by malignant cells without invasion of the basement membrane. The malignant cells are arranged within the ducts in the following patterns:

**papillary** , **cribriform** or **solid** that may have central necrosis called **Comedo type**. Calcification of central necrosis may occur

Prognosis:

Good with complete excision





# Breast Carcinoma

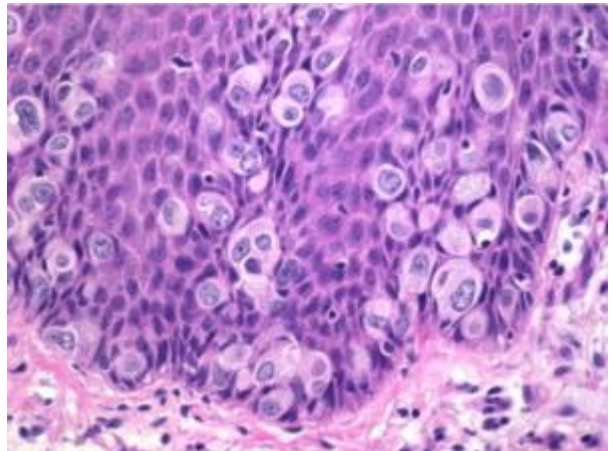
## A- Non invasive (in situ) carcinoma

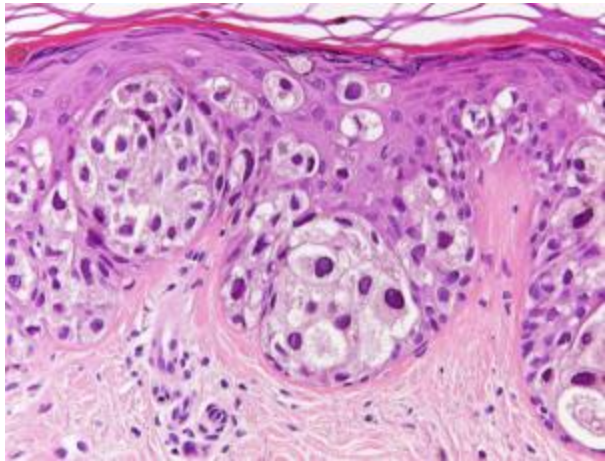
### Paget's disease:

- It is intraduct carcinoma extends to the epidermis covering the nipple and areola which shows eczema (the skin appears red, swollen, granular, fissured, eroded, ulcerating and oozing)

M/E:

The epidermis is thickened and show round, large pale vacuolated cells called Paget's cells.





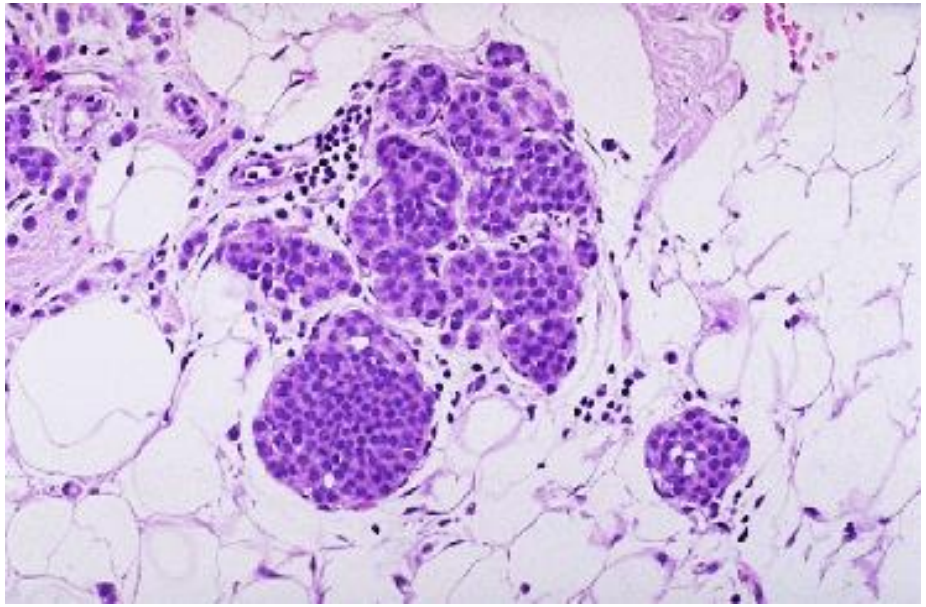
Prognosis:

Good with complete excision

# Breast Carcinoma

## A- Non invasive (in situ) carcinoma

### Lobular carcinoma insitu (LCIS):



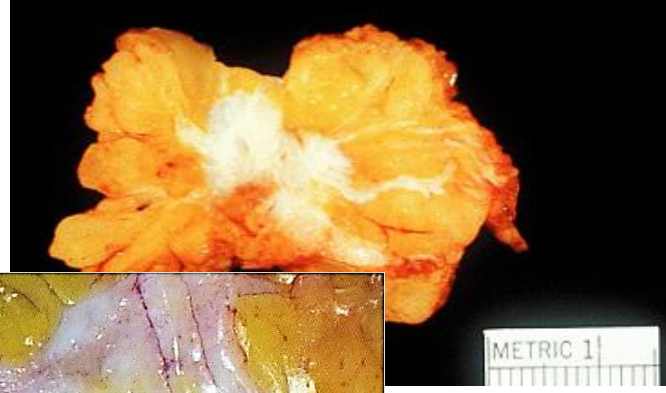
N/E: hard breast mass.

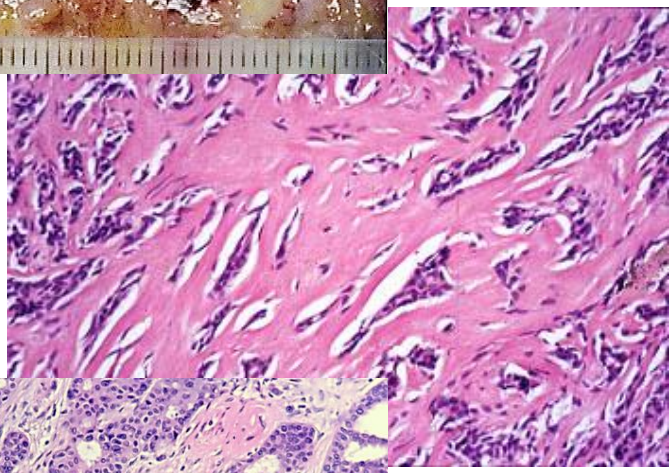
M/E: in one or more breast lobules all terminal ductules and acini are distented with malignant cells which are non-cohesive monomorphic with bland round nuclei

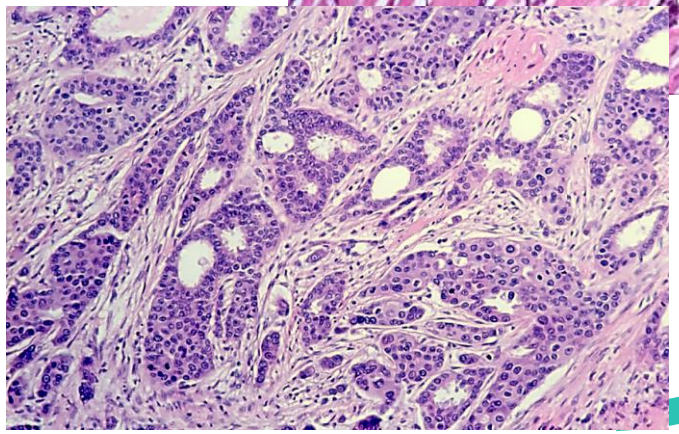
Prognosis: LCIS is both a marker of an increased risk of carcinoma in both breasts and a direct precursor of some cancers

# Breast Carcinoma

## B- Invasive Carcinoma





**N/E:**

- Ill-defined mass greyish white .
-Stony hard in consistency. -Fixed.
-C/S: retracted hard with gritty sensation, with hemorrhage, necrosis.
- Skin changes (late with locally advanced tumors): the skin covering the breast shows **dimpling**, **retraction of the nipple**, **ulceration**, **cancer en cuirasse** or **peau d'orange**

In addition, some microscopic types have other NE features

**Microscopic Types:**

**1. Invasive ductal carcinoma (NST)**

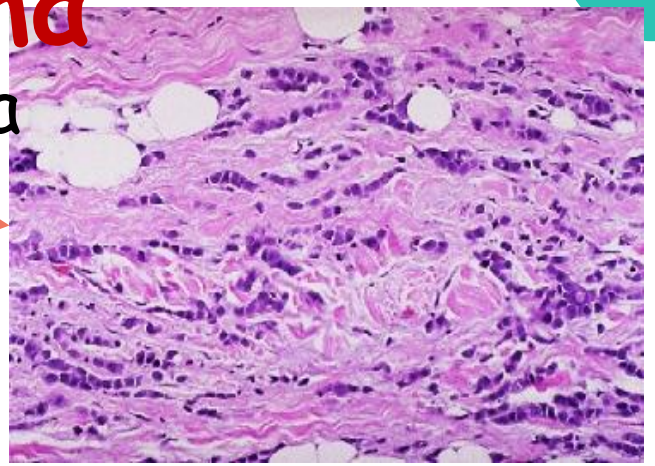
The commonest type (65%-80% of all mammary carcinoma).

**M/E:**

Groups, cords, tubules and sheets of malignant cells separated by desmoplastic stroma. The tumour cells are rounded or polygonal with uniform or pleomorphic nuclei. Mitotic figures range from absent to multiple

# Breast Carcinoma

## B- Invasive Carcinoma

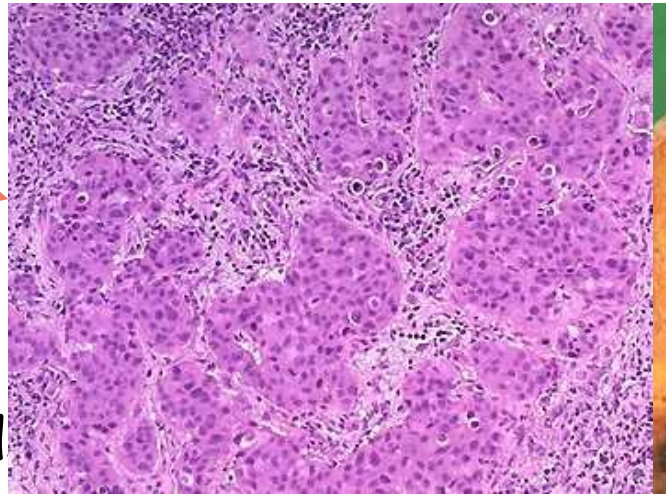


**2. Invasive lobular carcinoma**

**N/E**: Usually multicentric and bilateral

**M/E**: Strands of malignant cells of Indian file pattern separated by fibrous tissue stroma. The cells are small, uniform with little pleomorphism

**Prognosis**: worse than invasive duct carcinoma



**3. Carcinoma with medullary features**

**ME**:. They consist of sheets of large anaplastic cells associated with pronounced lymphocytic infiltrate.

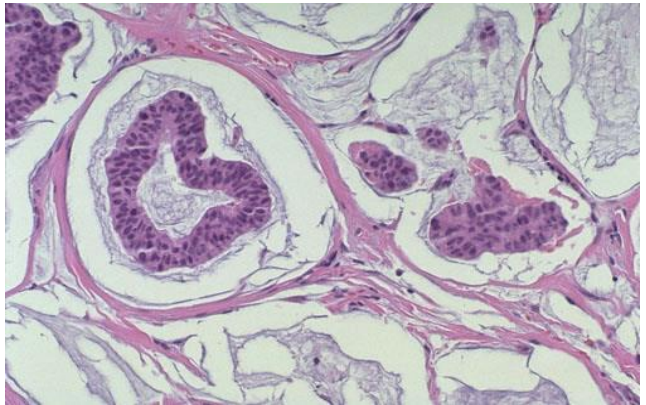
**Prognosis**: good prognosis

**4. Mucinous carcinoma (colloid carcinoma)**

**N/E**: Circumscribed soft gelatinous mass.

**M/E**: Lakes of mucin with scattered small island of malignant cells

**Prognosis**: is good .



**5. Tubular carcinoma**

**ME**: The tumor cells are arranged in well formed tubules and have low-grade nuclei.

**Prognosis**: is good

# Breast Carcinoma

## B- Invasive Carcinoma

### Spread

**Direct spread**

- Deep fascia, pect. Ms, pleura.& chest wall.
- Overlying skin causing cancer en cuirasse (thick, hard skin fixed to underlying structures) .

**Lymphatic spread:**

- Common and early, It occurs by 2 ways:

1.Lymphatic Embolization

It Leads to metastasis in :

a)L.N., axillary, int. mammary, medias. &supraclav.

b)Opposite breast.

c)liver and peritoneum

2.Lymphatic permeation (skin lymphatic)

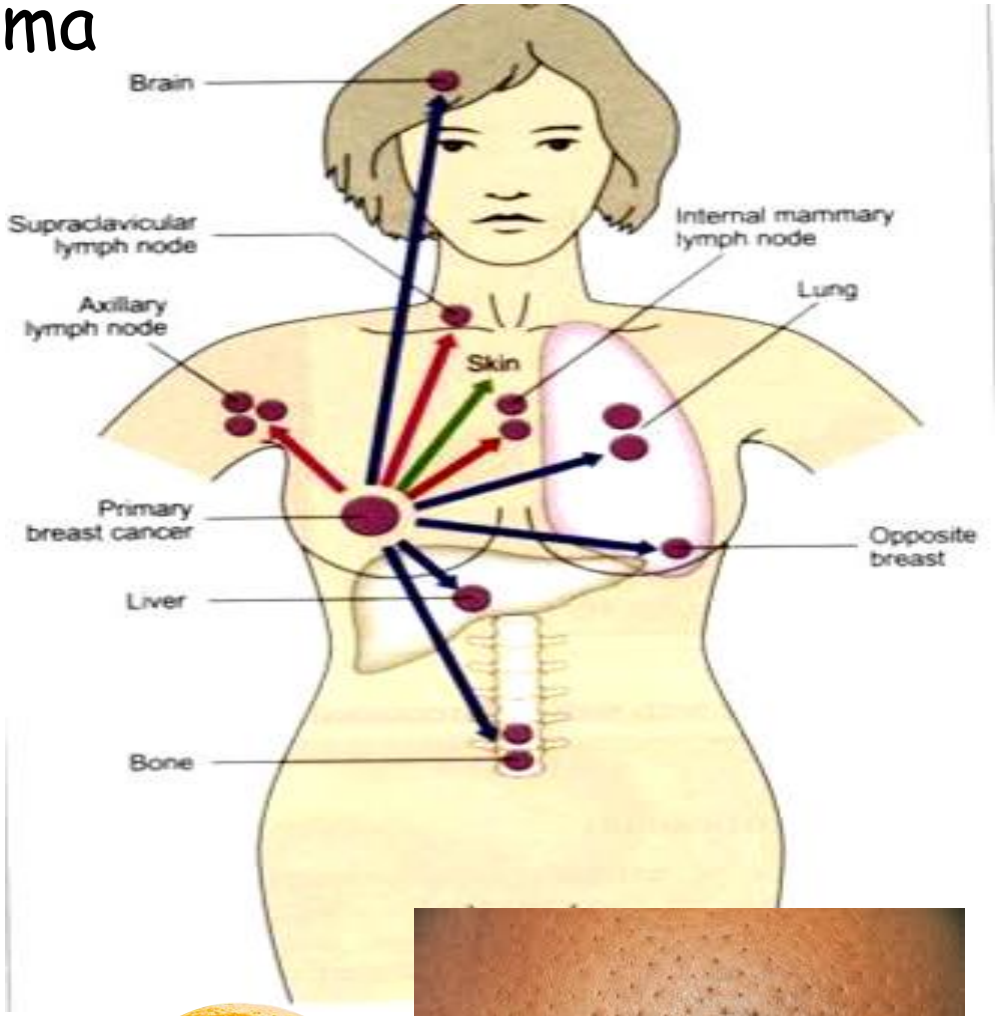
It Leads to:

a) small malignant nodules under the skin.

b) Peau d'orange due to lymphatic edema of he skin except at site of hair follicle

**Blood spread**

- Occurs early or late.
- Metastasis to lung, liver, bone, brain & adrenal gland




# Breast Carcinoma

## B- Invasive Carcinoma

## Staging

### TNM System

- **T**: Primary tumor size
  - T0 (in situ) to T4 (very large)
- **N**: Lymph node involvement:
  - N0 (no nodal involvement) to N3 (multiple involved lymph nodes)
- **M**: Distant metastases,
  - M0 (no distant metastases) to M and M2 (multiple metastases)

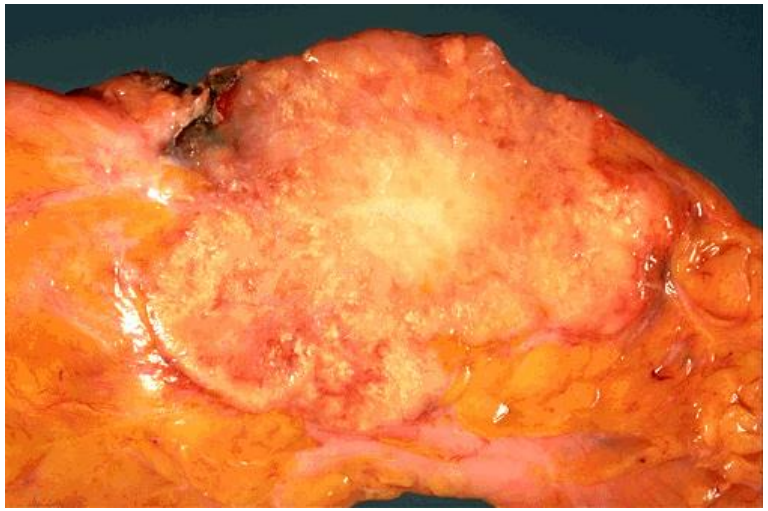
| | | | |
|---|---|---|---|
| Stage I | T1 | N0 | M0 |
| Stage II | T1 | N1 | M0 |
| | T2 | N0 | M0 |
| Stage III | T1 | N2 | M0 |
| | T2 | N2 | M0 |
| | T3 | Any | M0 |
| Stage IV | Any | Any | M1 |

| Stag | Definition | 5-year Surv (%) | 7-year Surv (%) |
|---|---|---|---|
| I | Tumor 2 cm or less without spread | 96 | 92 |
| II | Tumor 2-5cm with regional lymph node involvement but without distant metastases, OR > 5 cm in diameter without spread | 81 | 71 |
| III | Any size with skin/chest wall fixation, & axillary or internal mammary nodal involvement, without distant metastases | 52 | 39 |
| IV | Tumor of any size with or without regional spread but with evidence of distant metastases | 18 | 11 |

# Breast Carcinoma

## B- Invasive Carcinoma

## Diagnosis



**Diagnosis**

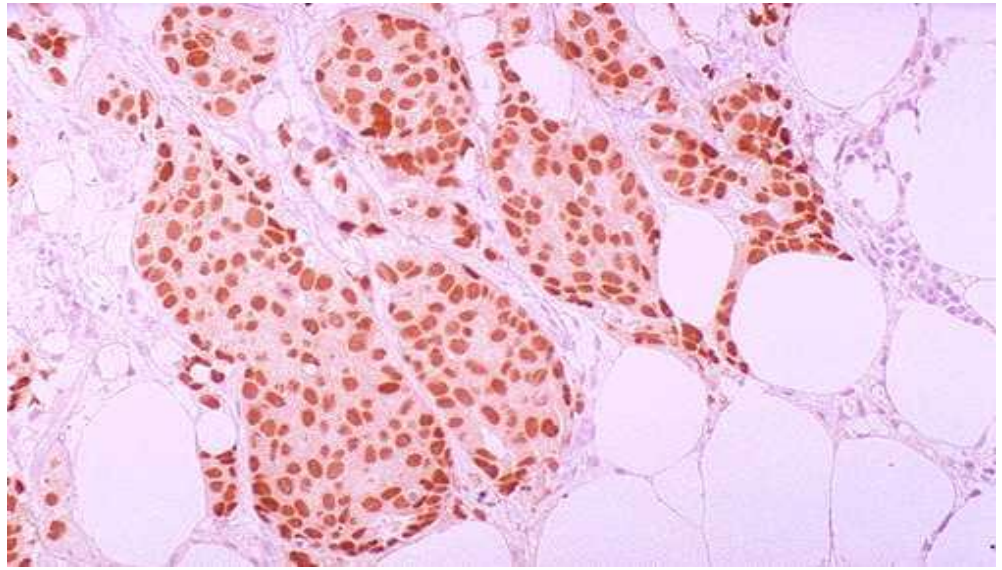
-Mammorgraphy
-Ultrasound
-Biopsy
-Immunohistochemistry
-Molecular techniques Gene mutation detection

## Estrogen Receptor & Prognosis

-Estrogen receptor expression is proportional to differntiation of tumor

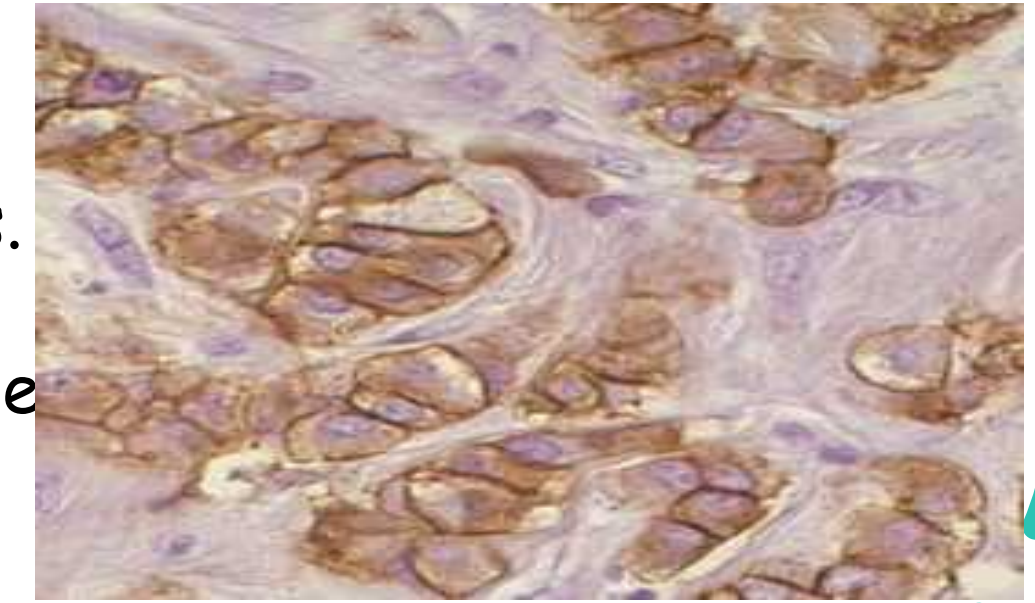
-Proportional to prognosis and response to tamoxifen (receptor antagonist) therapy.

-Demonstrated by IHC special stain.



## HER2

The HER2 proto-oncogene encodes a cell surface receptor that is overexpressed in approximately 25%-30% of breast cancers. Herceptin is the first monoclonal antibody that targets the extracelluar domain of the HER2 protein, and inhibits growth of breast cancer cells that over express this protein



# Male breast

## Gynecomastia

**Def** : enlargement of male breast.

**AE:**

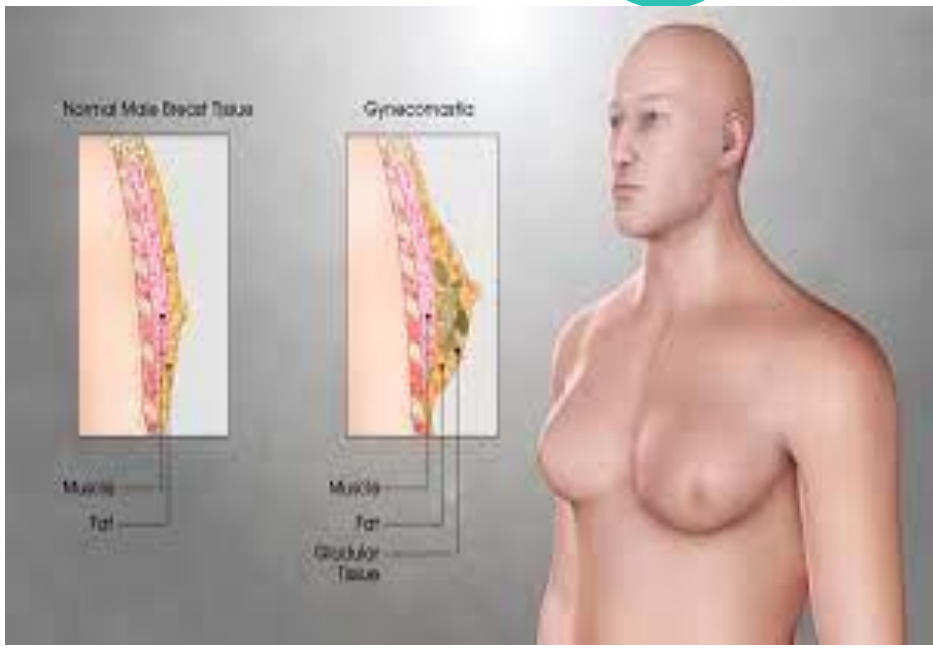
a)physiological: at puberty.

b) Increase estrogen level in

- Liver cirrhosis
- Estrogen producing tumors
- Estrogen therapy

c)Digitalis therapy.

d)Klienefilter syndrome.

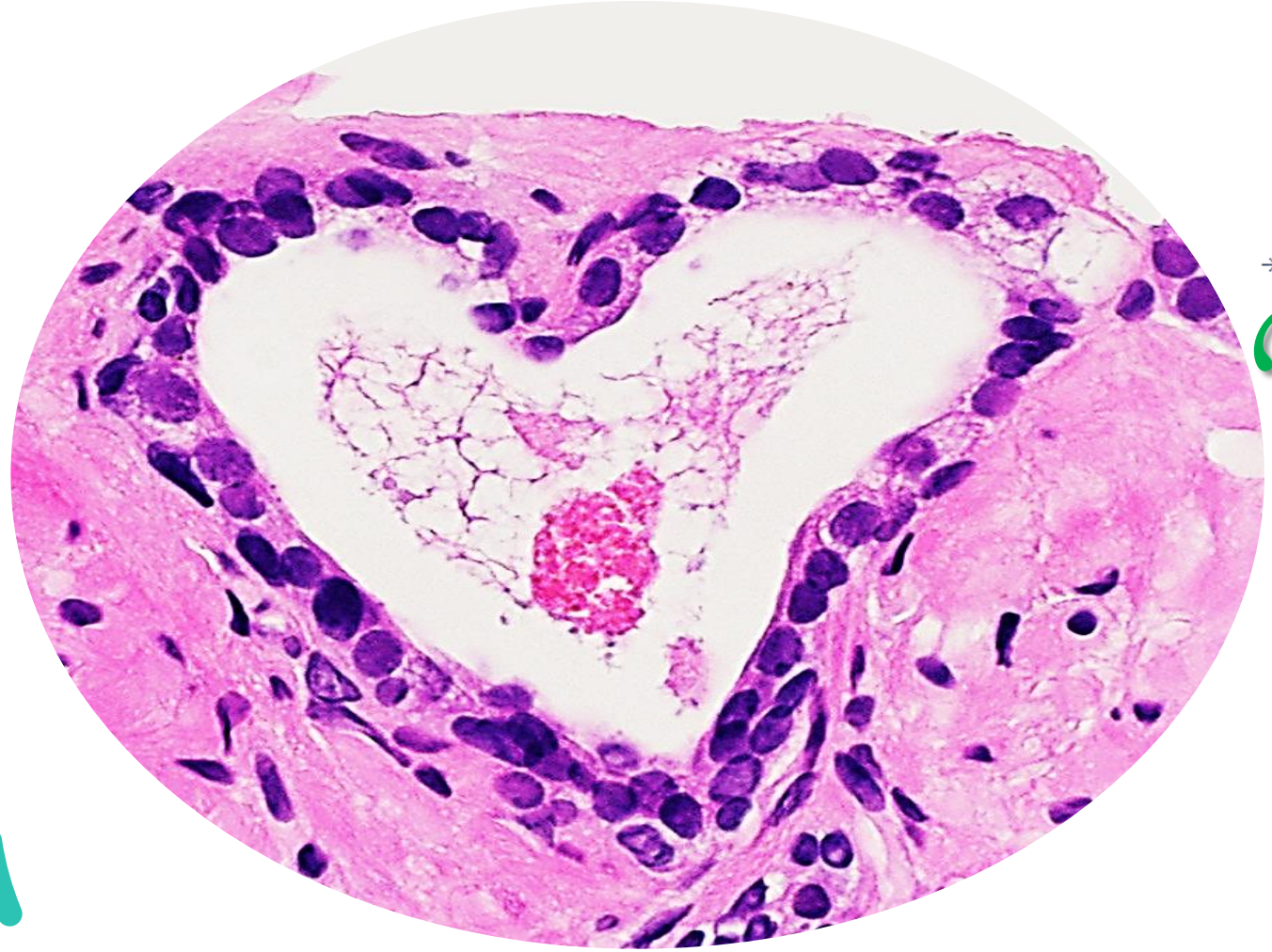



**NE:** Disc like subareolar mass
Unilateral or bilateral

**M/E:** Variable degree of epithelial hyperplasia in ducts.
Prominent stroma.

## Carcinoma of male breast

- Occurs in old age.
- Common with estrogen therapy.
- It has bad prognosis as the tumor infiltrate locally early due to small breast size



# Thank you