Pathology

Uterine Corpus and Gestational Trophoblastic Diseases.

Learning Outcomes

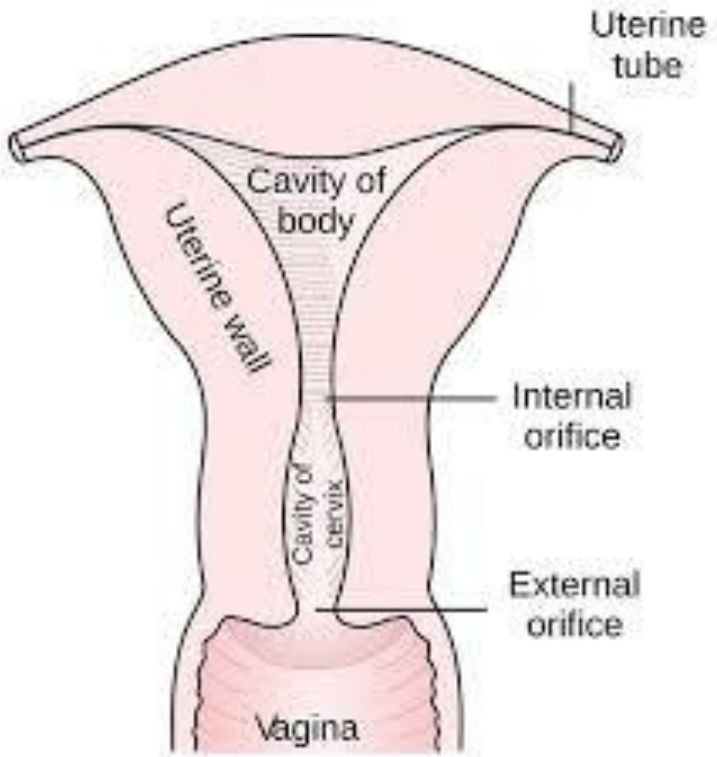
By the end of the lecture, you will be able to:

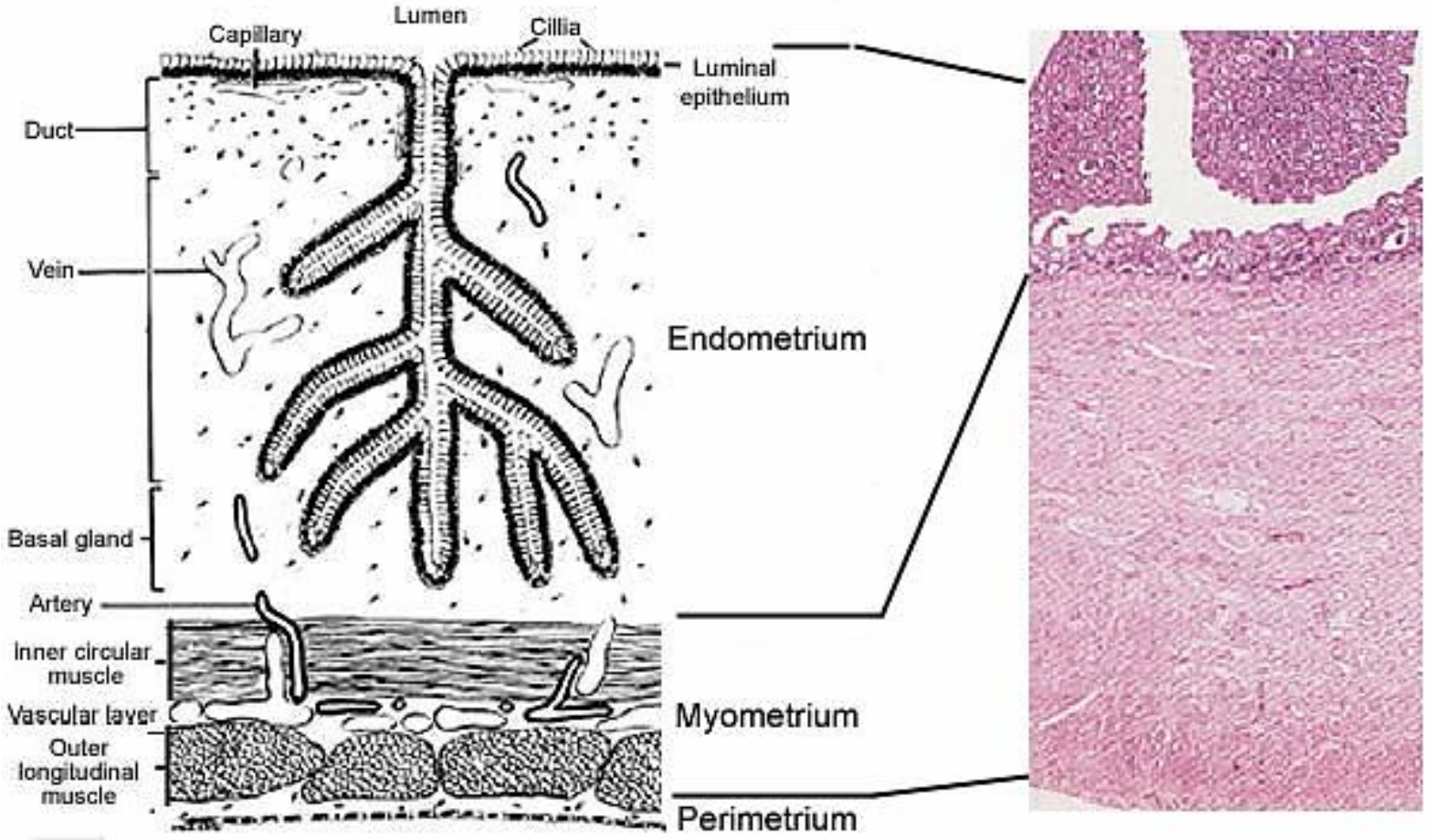
1. Identify non neoplastic lesions involving the uterine corpus and their underlying mechanisms.
2. Be aware of tumours originating in the body of uterus
3. Know a simplified idea about the different entities of GTD and their clinical significance.

Agenda

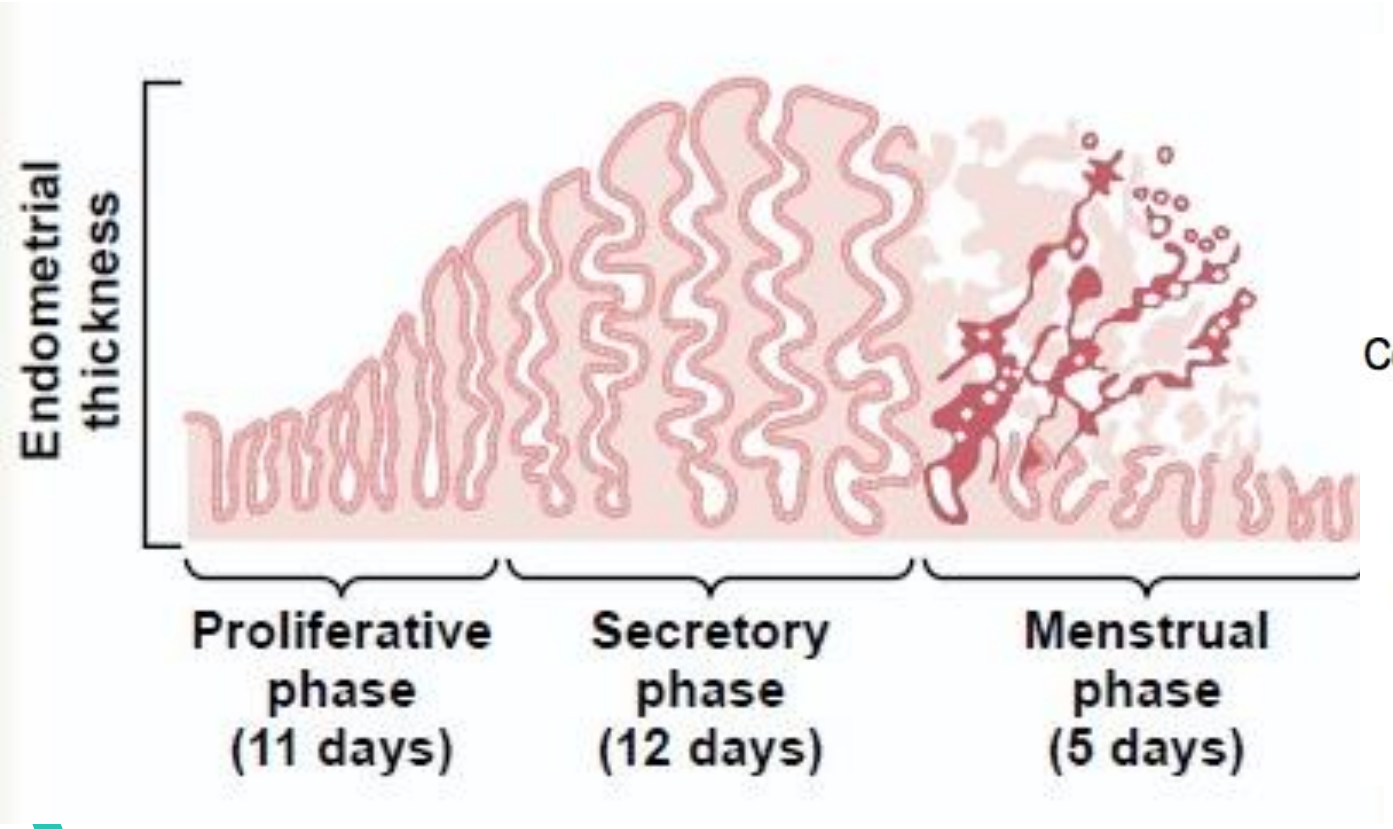
- Abnormal uterine bleeding
- Endometritis
- Endometriosis
- Endometrial polyp
- Endometrial hyperplasia
- Tumours of uterine body
- Gestational trophoblastic diseases

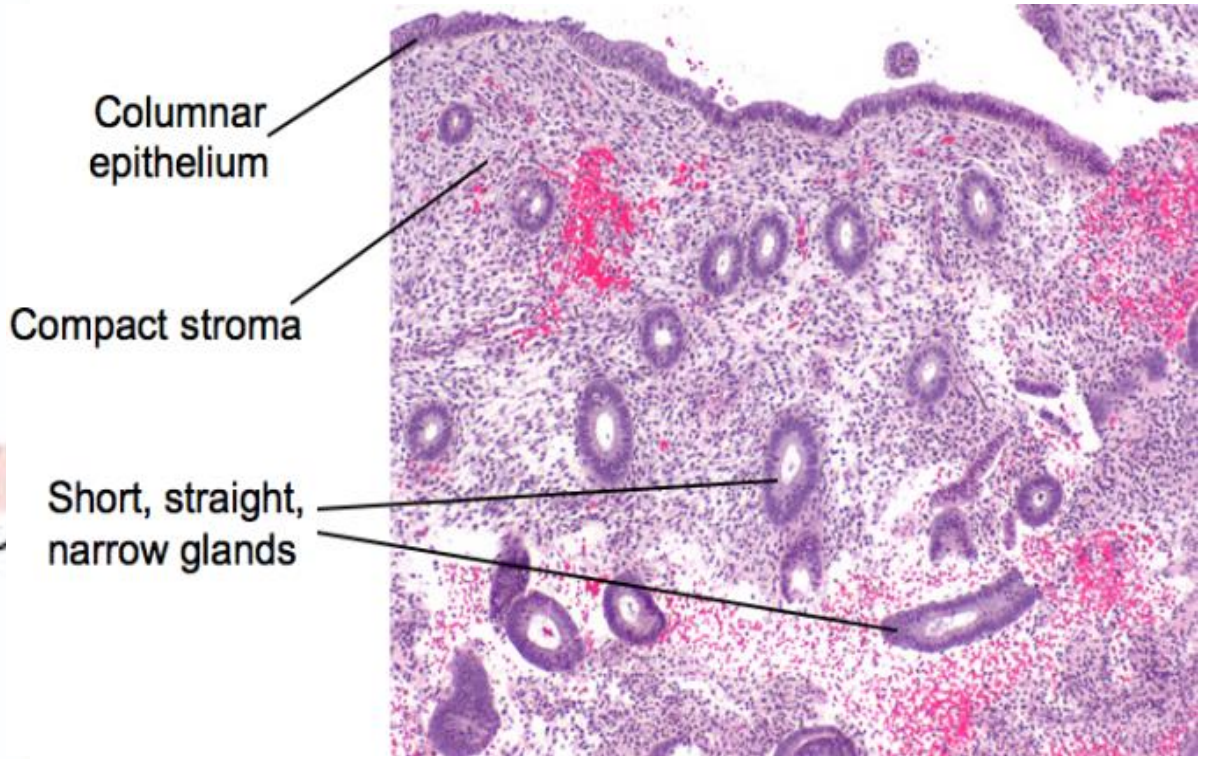
Stucture of uterus





Endometrium





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.

Abnormal Uterine Bleeding (AUB)

Age Group	Causes
Prepuberty	Precocious puberty (hypothalamic, pituitary, or ovarian origin)
Adolescence	Anovulatory cycle, coagulation disorders
Reproductive age	Complications of pregnancy (abortion, trophoblastic disease, ectopic pregnancy)
	Organic lesions (leiomyoma, adenomyosis, polyps, endometrial hyperplasia, carcinoma)
	Anovulatory cycle
	Ovulatory dysfunctional bleeding (e.g., inadequate luteal phase)
Perimenopausal	Anovulatory cycle
	Irregular shedding
	Organic lesions (carcinoma, hyperplasia, polyps)
Postmenopausal	Organic lesions (carcinoma, hyperplasia, polyps)
	Endometrial atrophy

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

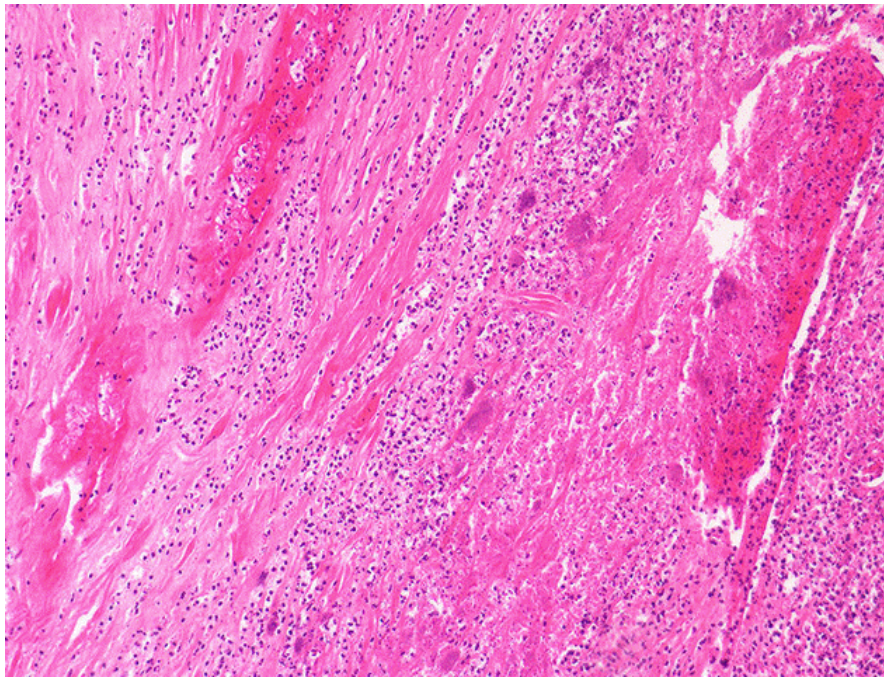
Puerperal sepsis:

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

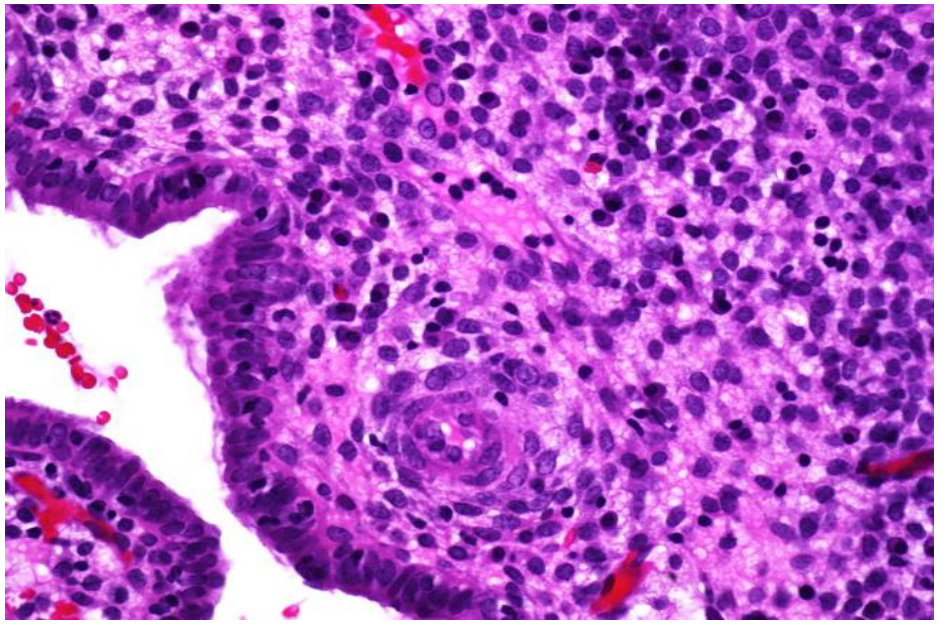
Chronic Endometritis:

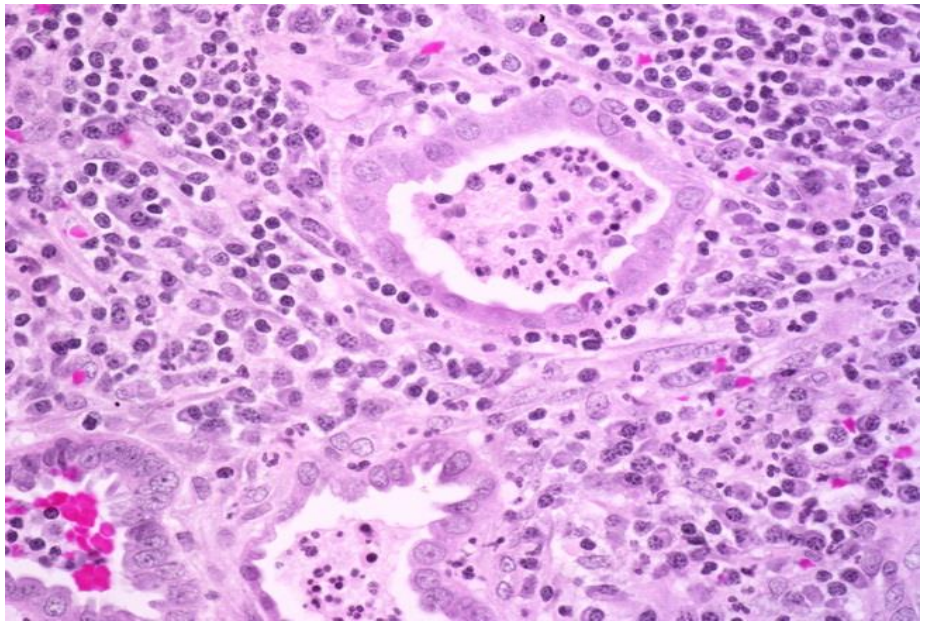
Presented with bleeding, pain, discharge and infertility.

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).



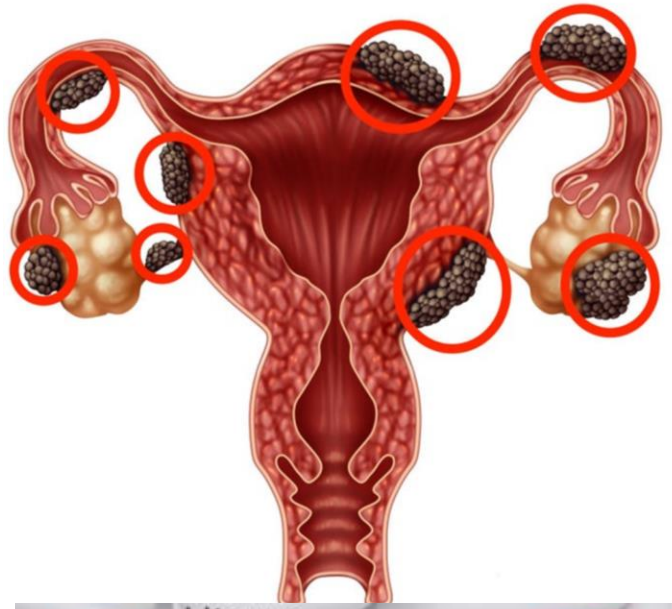


Endometriosis

- 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.

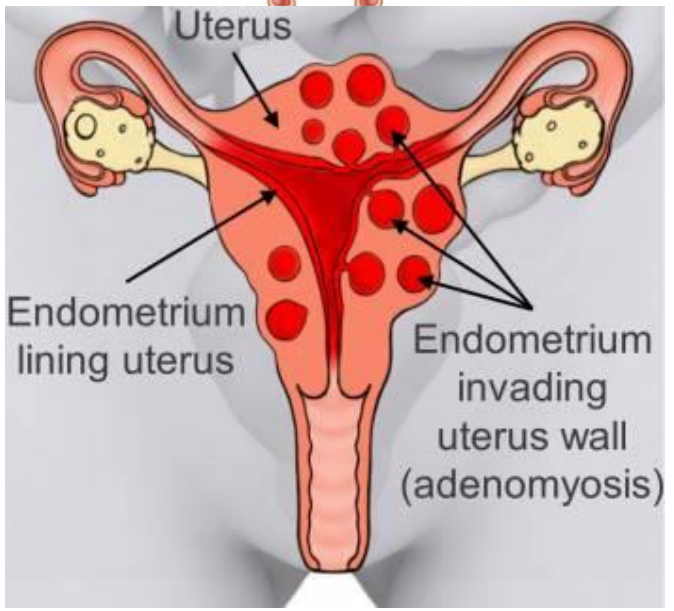
External Endometriosis

- 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)



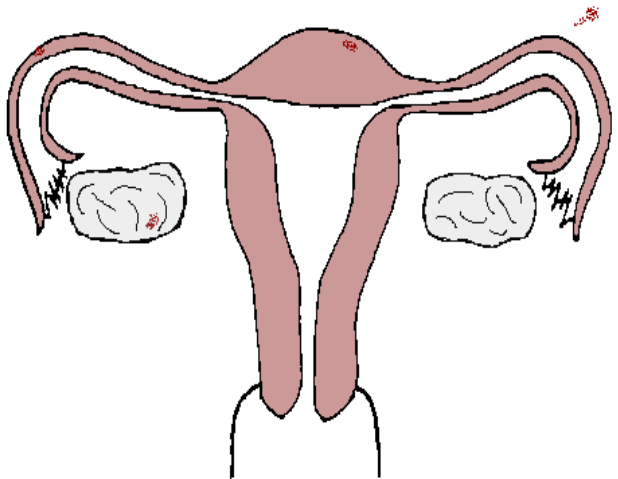
Internal Endometriosis (adenomyosis)

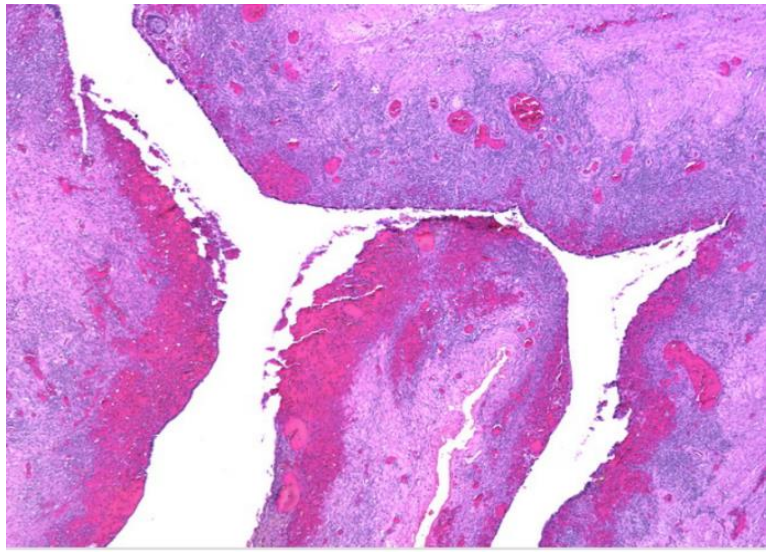
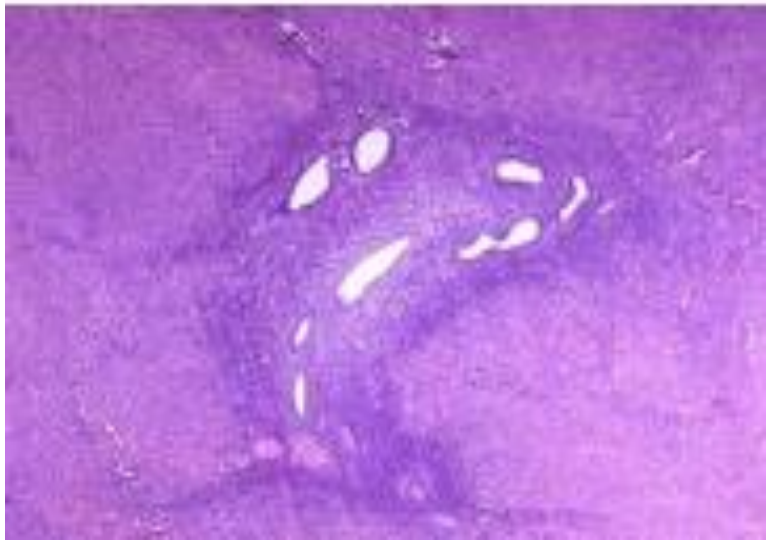
- Presence of endometrial tissue (glands and stroma) in the myometrium of uterine wall.



	External Endometrisis	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 2. Metaplasia of serosal cells leads to peritoneal lesions. 3. Vascular and lymphatic dissemination theory.	**Abnormal growth activity of the endometrium**, the basal zone of endometrium dips into the adjacent myometrium.

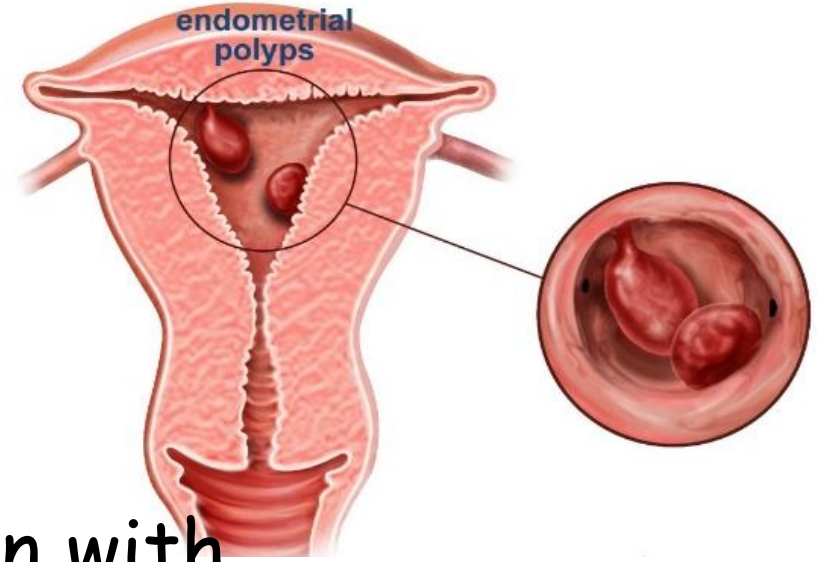
	External Endometrisis	Internal Endometrisis
N/E	Hemorrhagic lesions (as the endometrial tissue undergoes cyclic menstrual bleeding). It excites excessive fibrous tissue around them •Ovarian endometriosis (chocolate cysts): cyst with dark red brown altered blood content. • Fibrous adhesion with surroundings.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



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

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

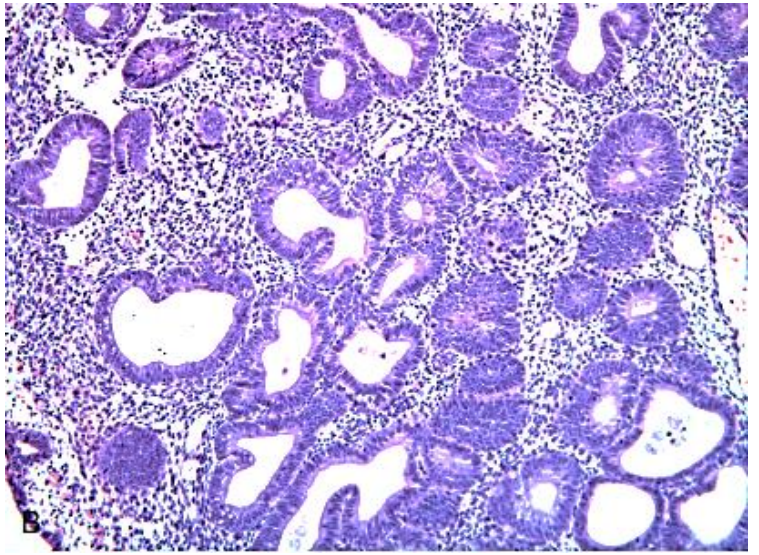
ME:

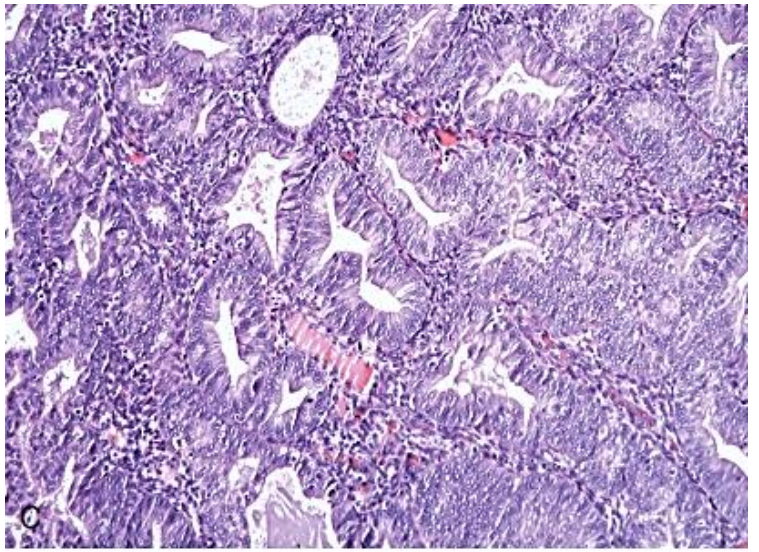
-Charcterized by glandular proliferation and crowding

-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%).





And now you can answer,

A 40-year-old female presents with a long history of dysmenorrhea. A hysterectomy was performed. Histologic examination of the uterus reveals areas of extensive adenomyosis. Which of the following describes this patient's uterine pathology?

(A) Atypical endometrial hyperplasia.

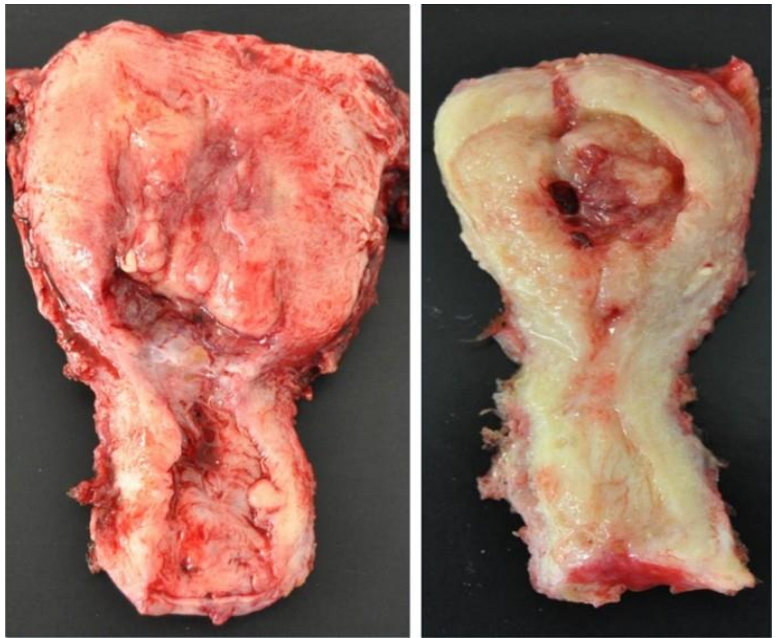
(B) Displacement of endometrial glands and stroma.

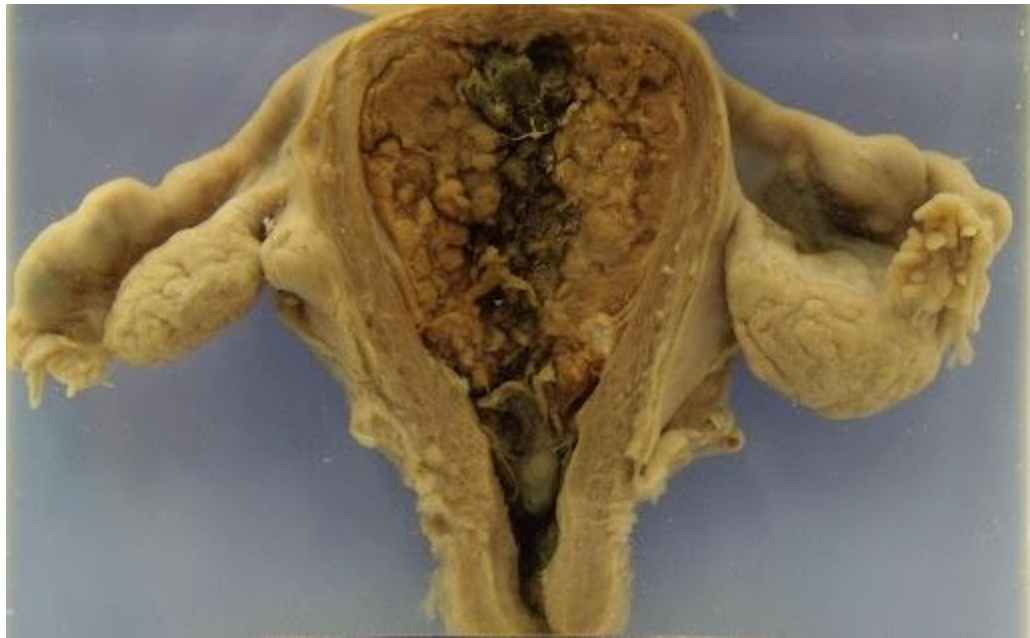
(C) Proliferation of uterine smooth muscles.

(D) Benign tumor of uterine glandular epithelium.

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).

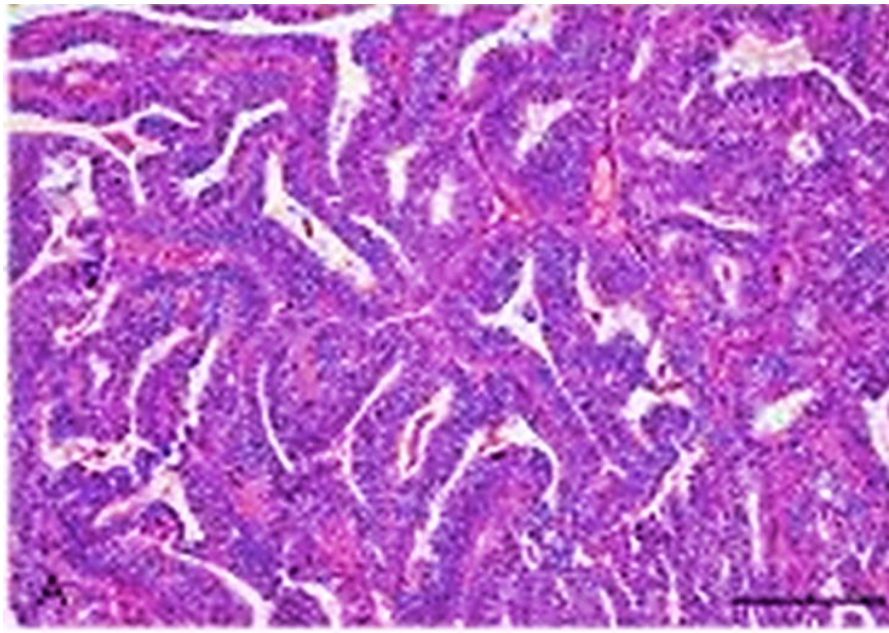
Precursor (precancerous, preneoplastic) lesions:

- 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.

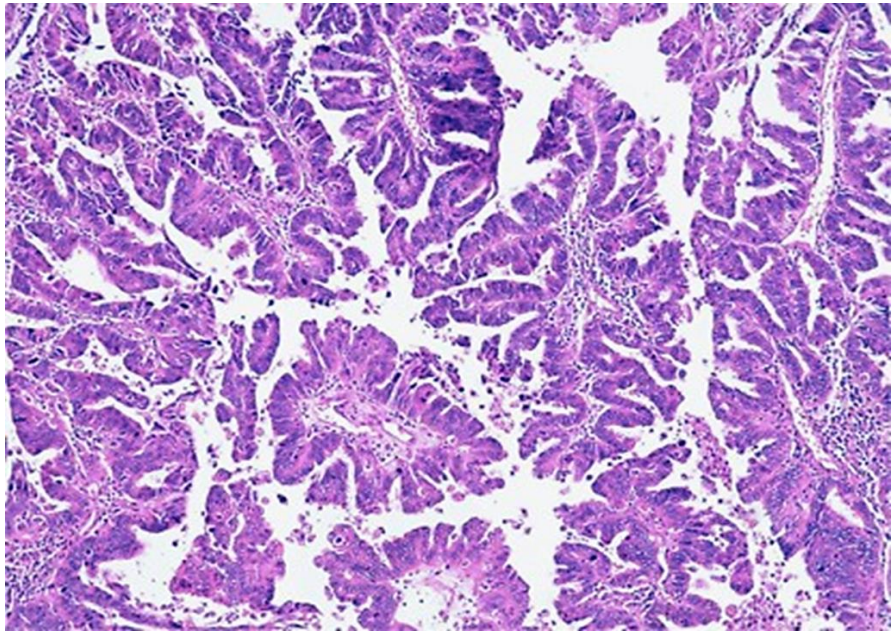


ME:

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).

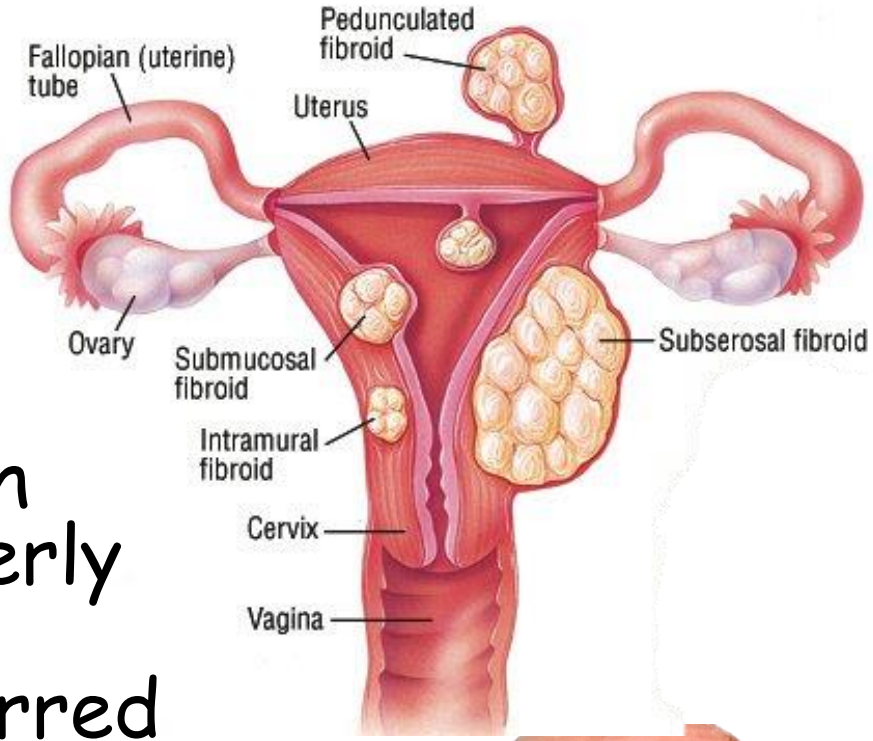


Endometrial Carcinoma

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

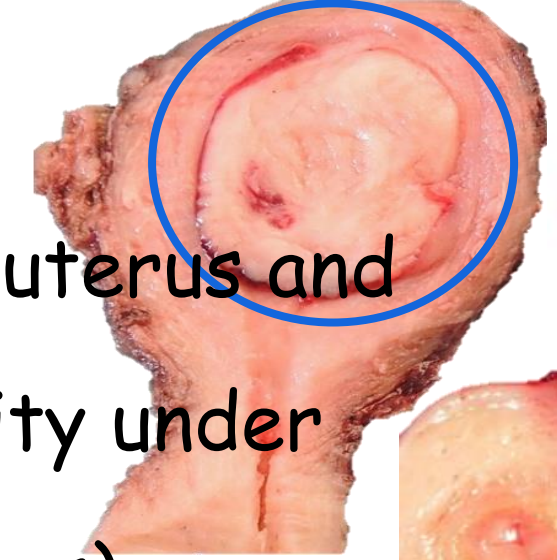
NE:

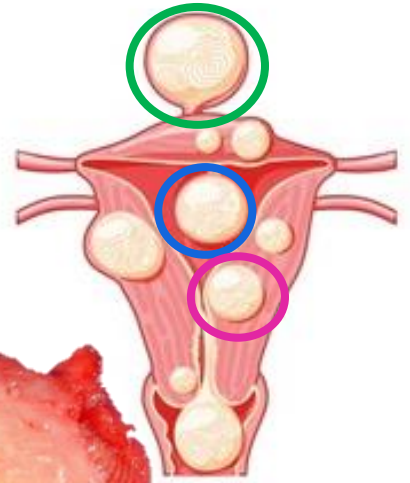
- Site: Commonly arises in the body of uterus and cervix.

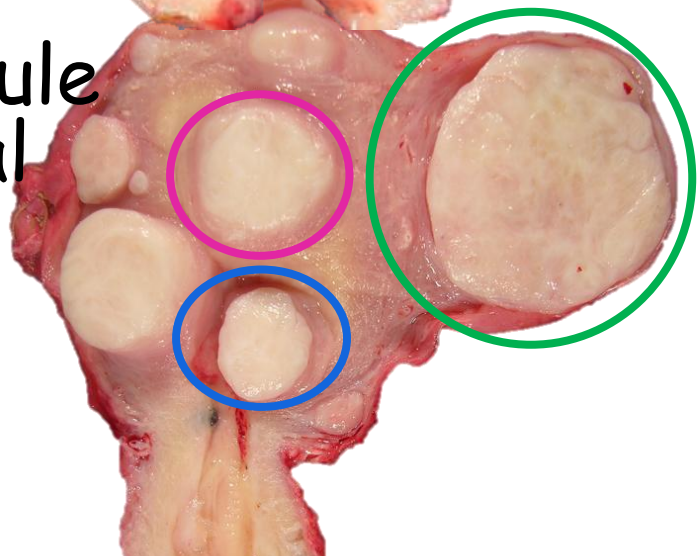
Submucous (project in the uterine cavity under the endometrium

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

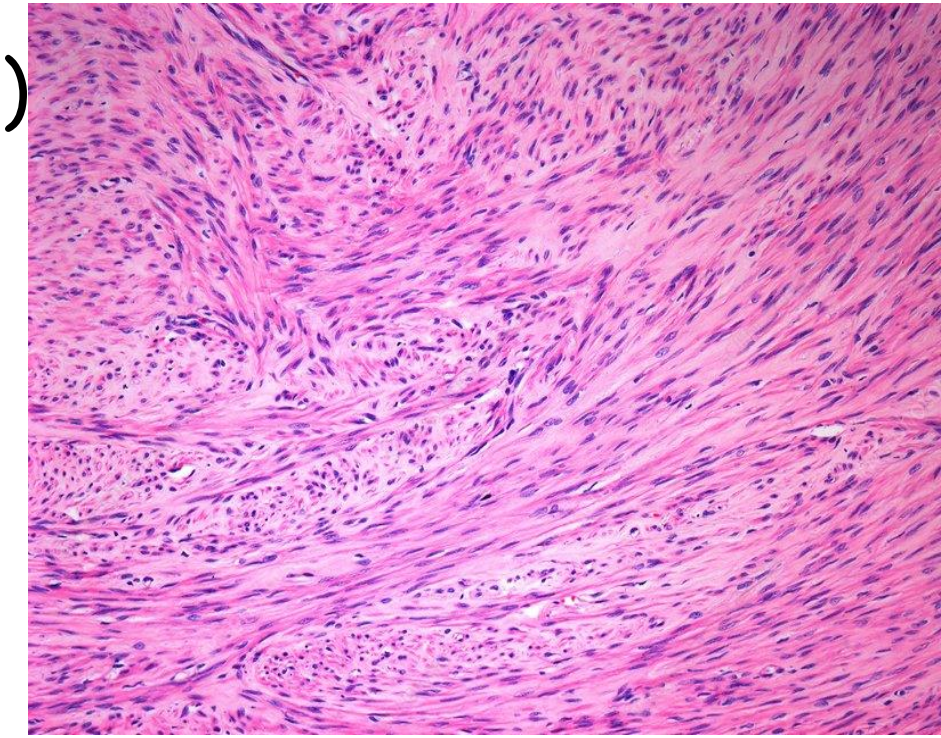
Leiomyoma

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.



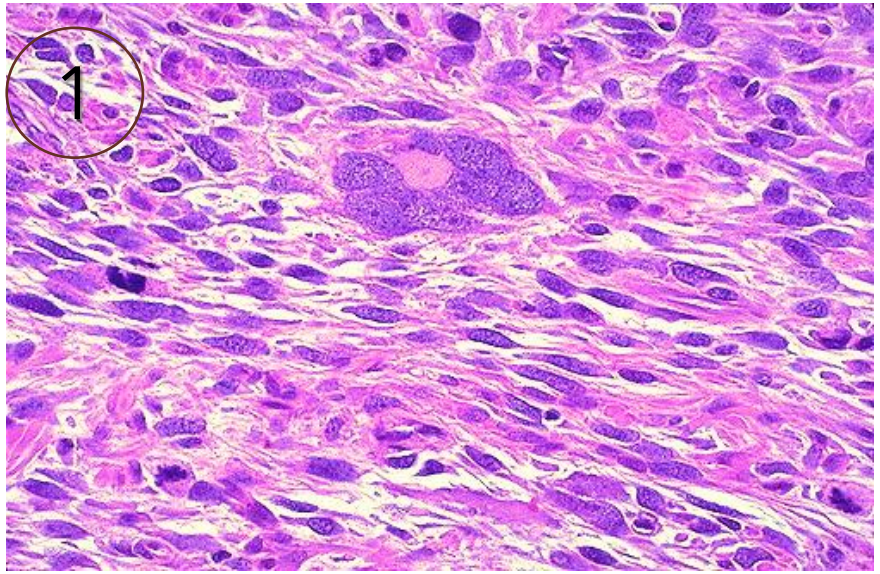
Complications:

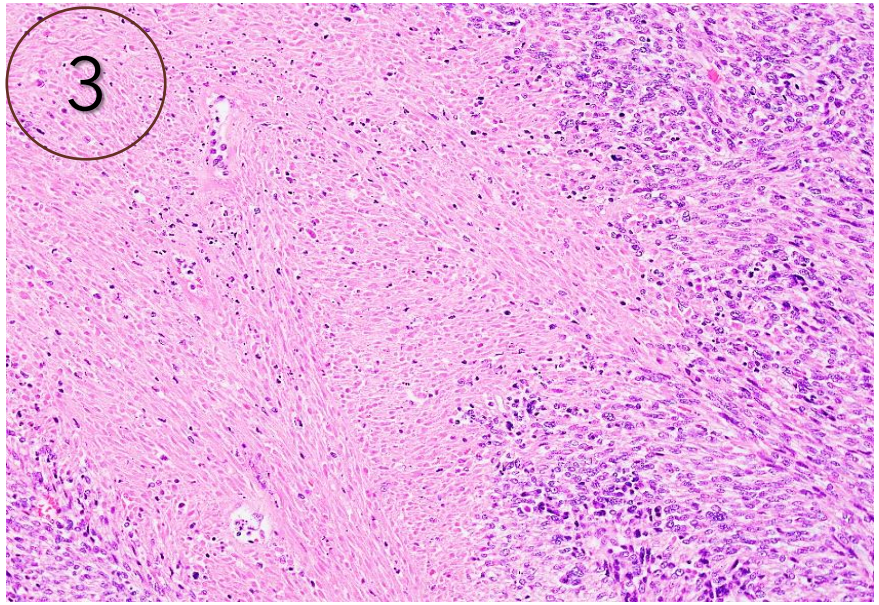
1- Abnormal uterine bleeding.
2- Infertility due to prevention of implantation of fertilized ovum.
3- Risk of abortion.
4- Interfere with child birth.
5- Iron deficiency anemia
6- Malignant transformation to Leiomyosarcoma (rare, 1%).

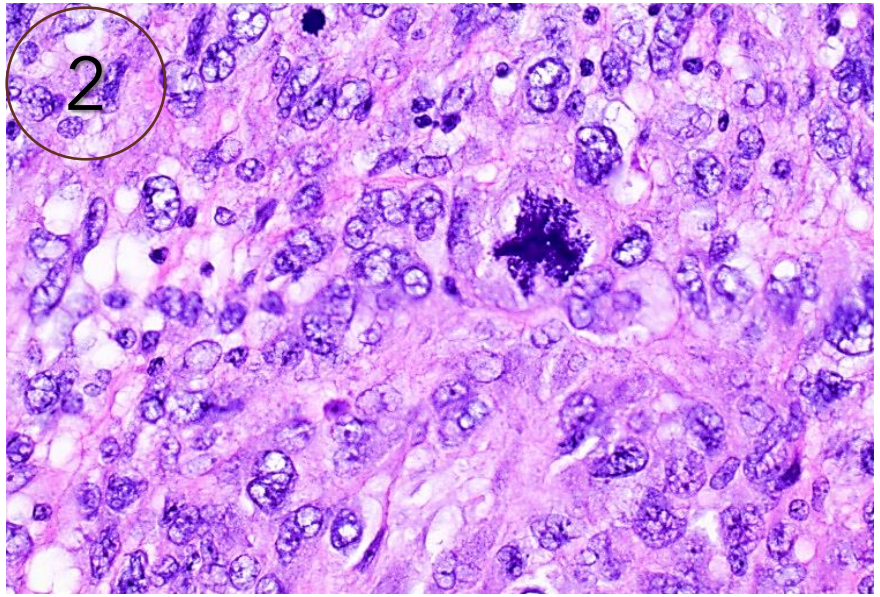
Leiomyosarcoma

On microscopic examination:

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







Gestational Trophoblastic Diseases (GTDs)

Definition:

Group of diseases characterized by:

- proliferation of pregnancy-associated trophoblastic tissue
- Has a malignant potential.

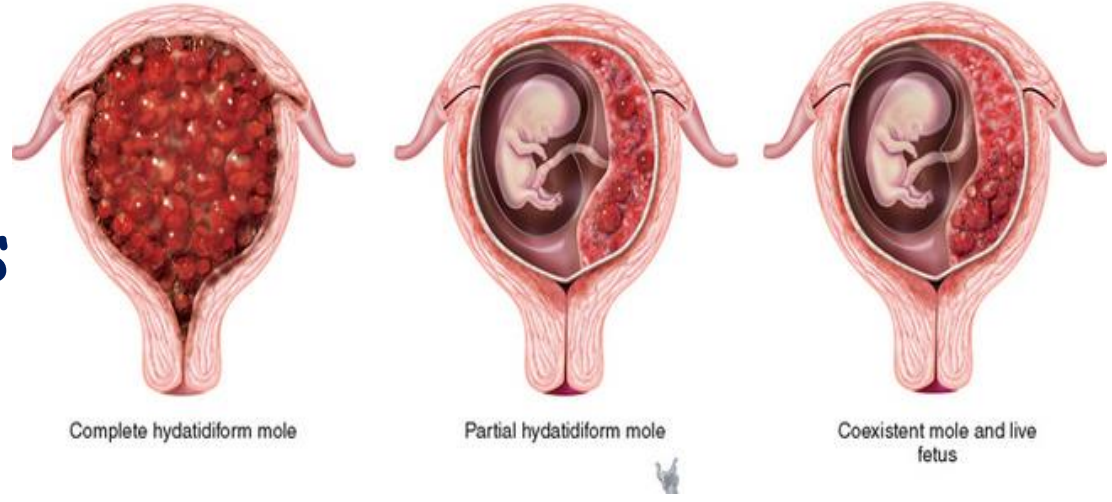
Classification:

1.Molar GTD (Villous):Characterized by formation of chorionic villi

- Hydatiform mole:
  - Complete
  - Partial
- Invasive mole

2.Non- Molar GTD (Non- villous No villi

- Choriocarcinoma



Hydatiform mole

Called vesicular mole

Incidence:

During reproductive period, (20-40 years)related to pregnancy.

Types:

Complete mole

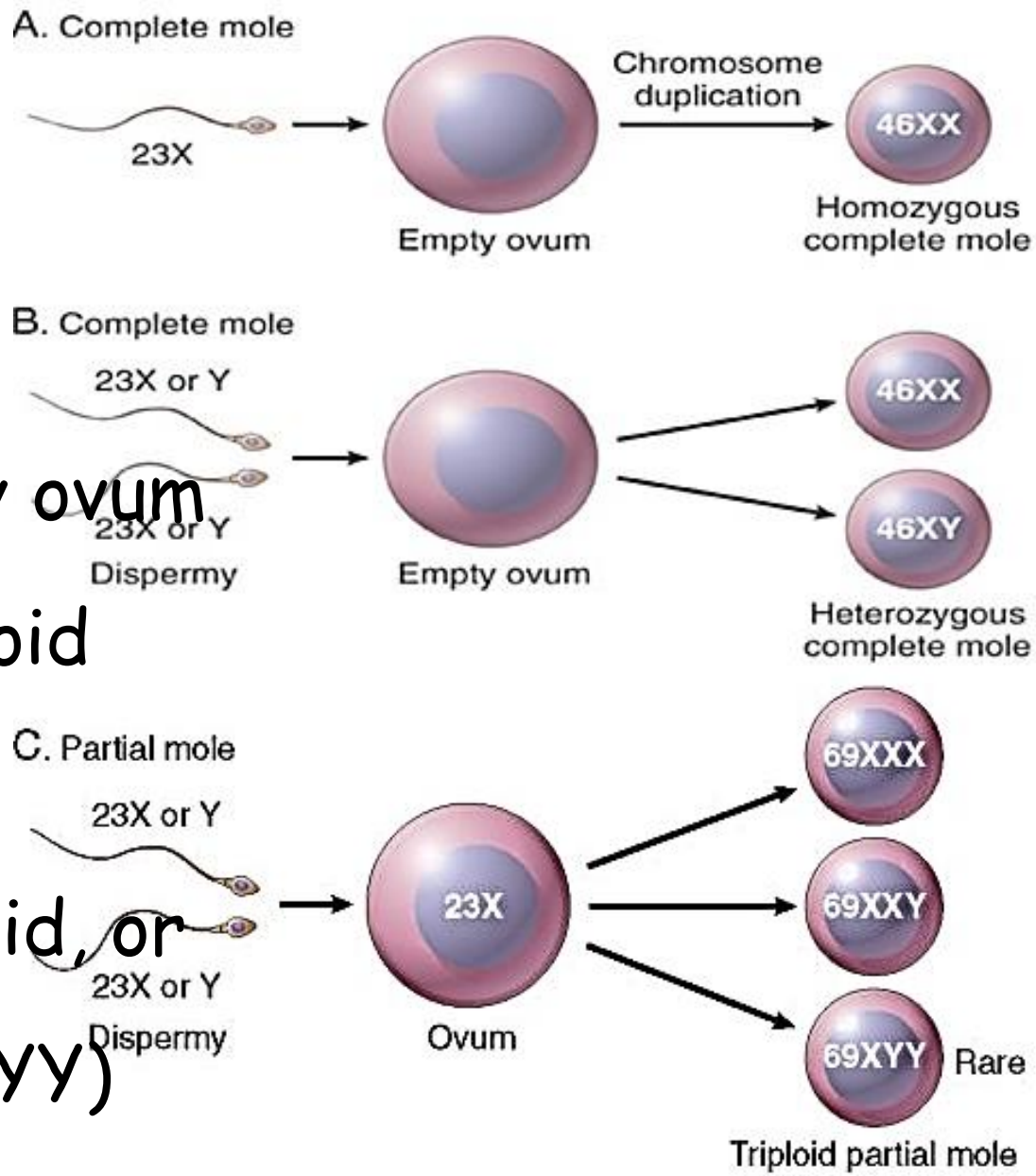
One or two sperm fertilize an empty ovum (without DNA).

-All chromosomes are paternal (Diploid with 46 XX, 46 XY)

Partial mole

Fertilization of an ovum by one diploid, or two haploid sperm,

-Triploid (69 XXX, 69 XXY or 69 XYY)



Complete Hydatiform mole

N/E:

-It is filled with a mass that resembles a punch of grape. It is formed of clusters of vesicles

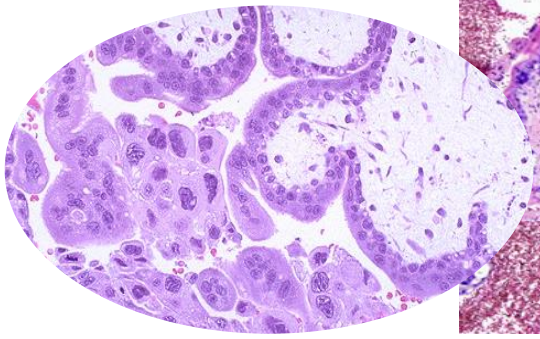
-No trace of embryo, amniotic sac or umbilical cord

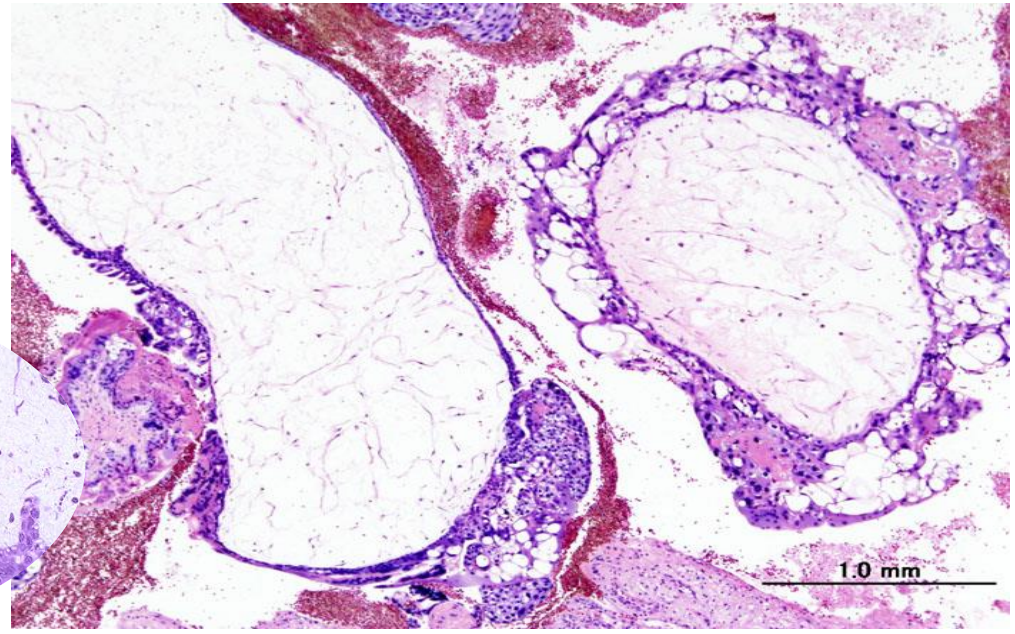
M/E:

- Odema of some chorionic villi

Prognosis:

- May complicate to invasive mole
- 5% pass into choriocarcinoma





Partial Hydatiform mole

N/E:

-Normal placenta with few chorionic villi are swollen

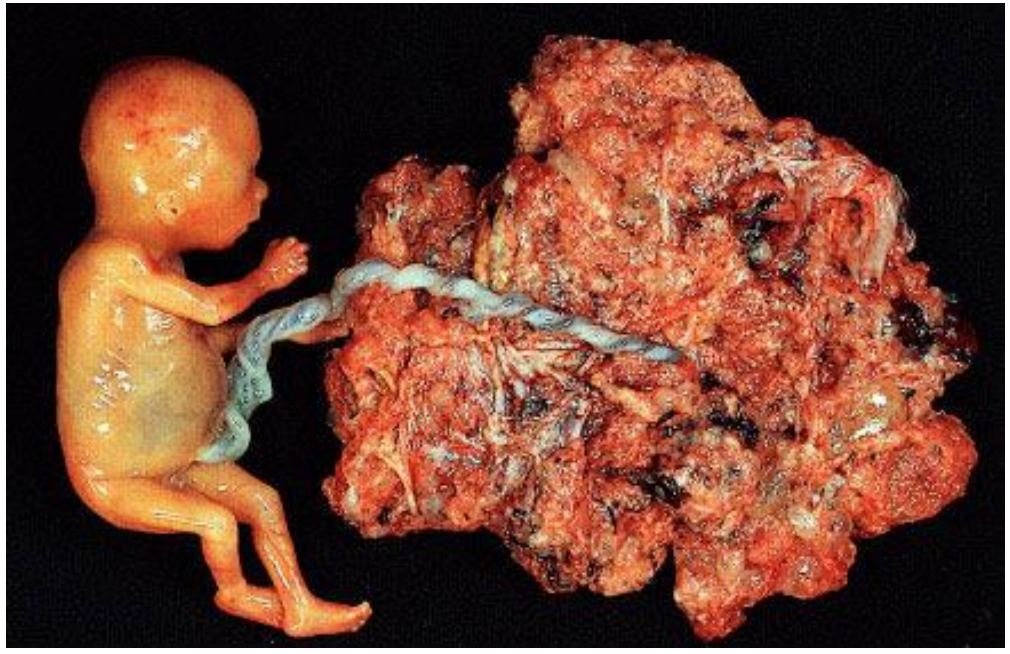
-Abnormal fetus is seen.

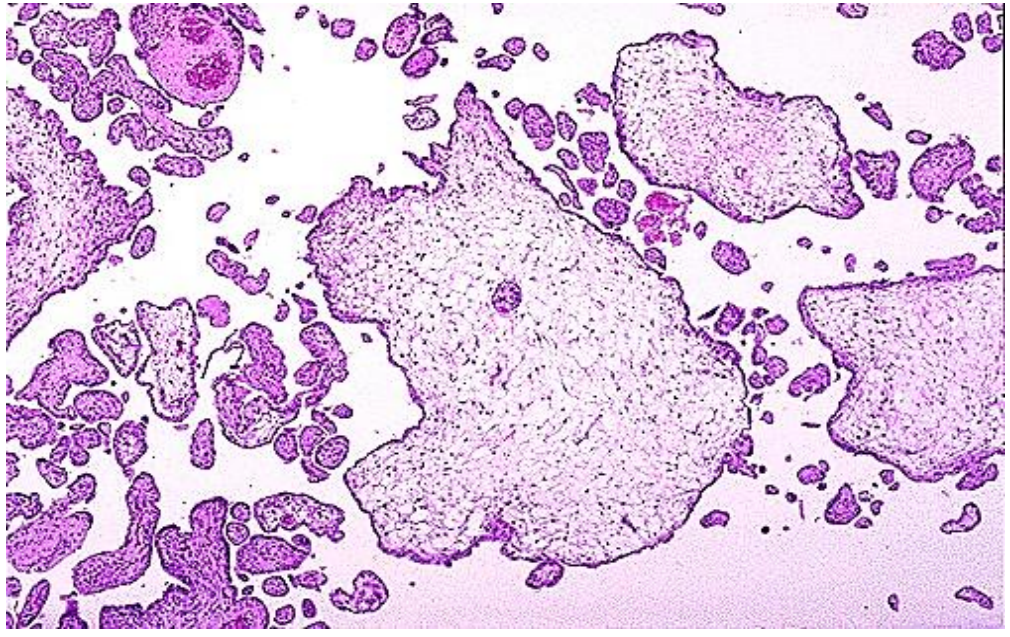
M/E:

- Normal chorionic villi with few abnormal swollen chorionic villi

Prognosis:

Very rare to pass into choriocarcinoma





Invasive mole

It complicates complete mole.

N/E:

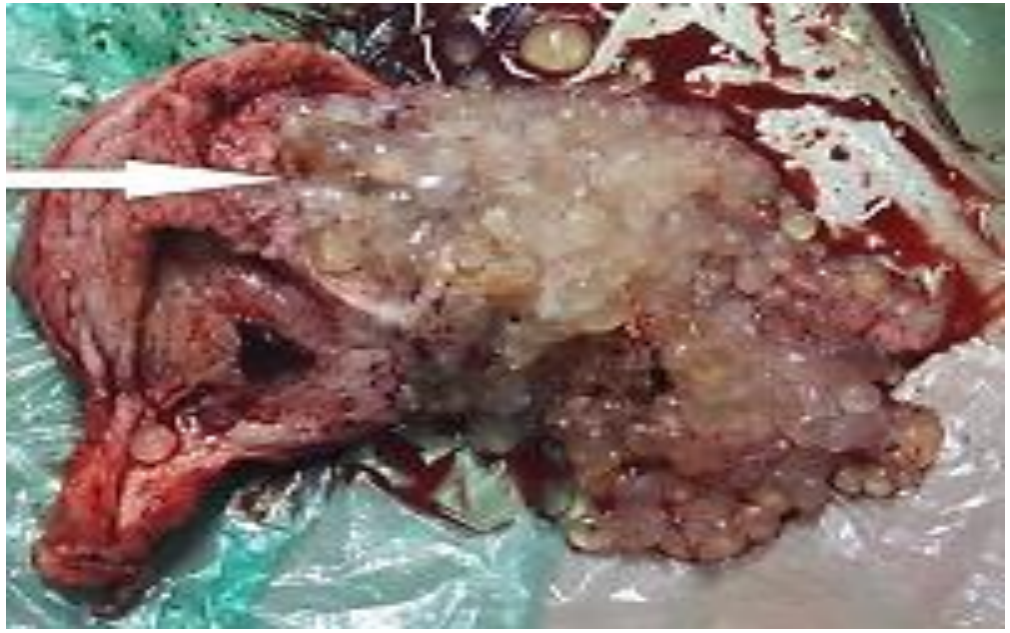
- Clusters of vesicles attached deeply to the myometruim.

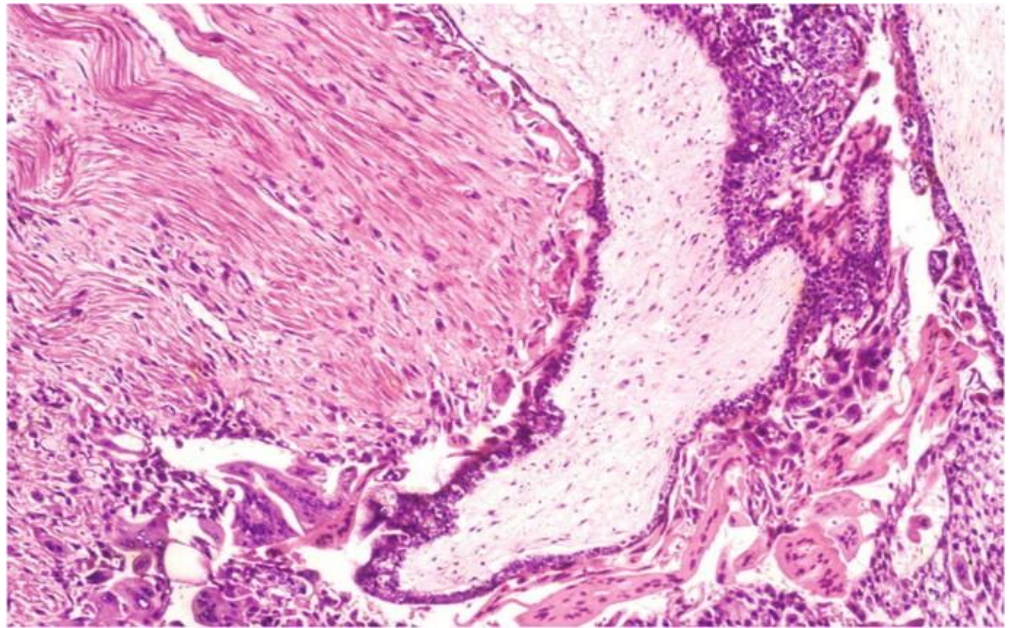
M/E:

Villi become invasive to myometrium and blood vessels

Prognosis:

Spread to distant sites





Choriocarcinoma

Gestational choriocarcinoma is a malignant neoplasm of trophoblastic cells

Incidence:

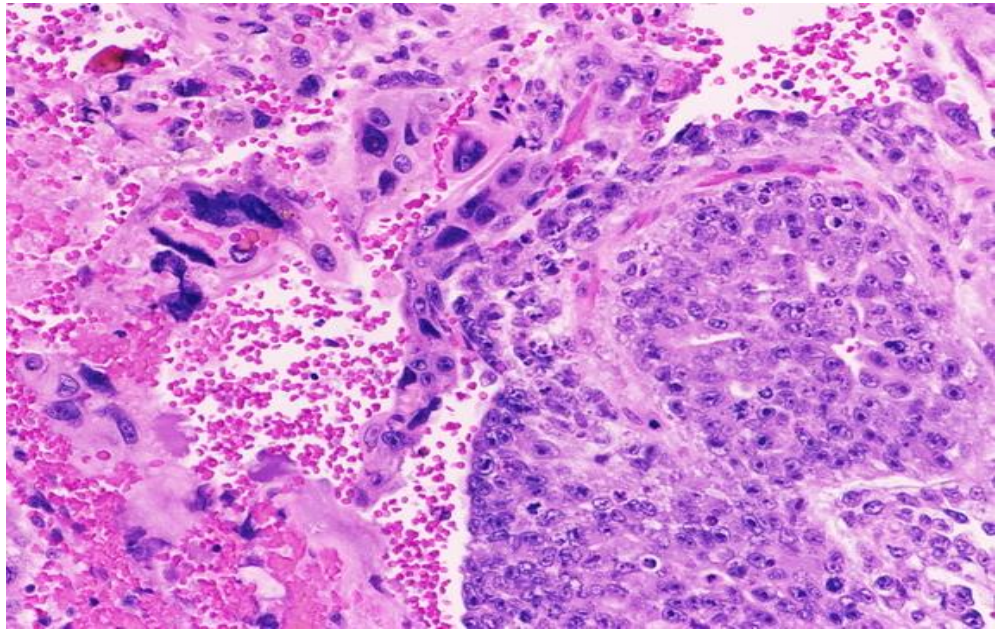
50% arise in hydatidiform moles,
25% in previous abortions,
≈ 25% in normal pregnancies

N/E:

Uterus contains a soft, friable, fleshy mass invading the uterine wall. very hemorrhagic, and necrotic

ME:

Large sheets of malignant cytotrophoblasts and syncytiotrophoblasts with little or no stroma and wide areas of necrosis and hemorrhage.

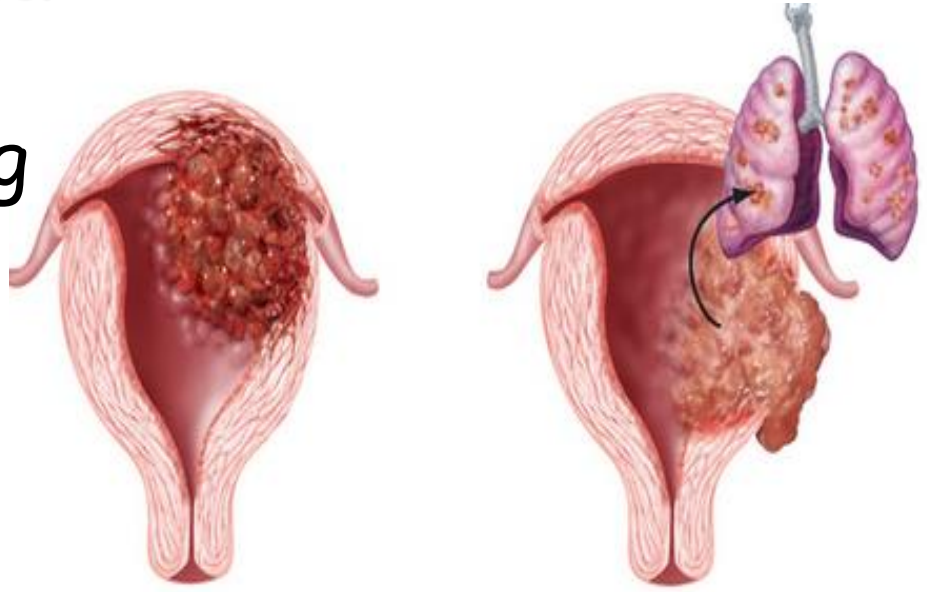


Choriocarcinoma

Spread:

-Direct spread: Into uterine wall leading to perforation →peritoneal Metastases and peritoneal hemorrhage.

-Blood spread: The main method of distant spread, occurs early → Lung, liver, brain, bone, vulva and kidney are involved.



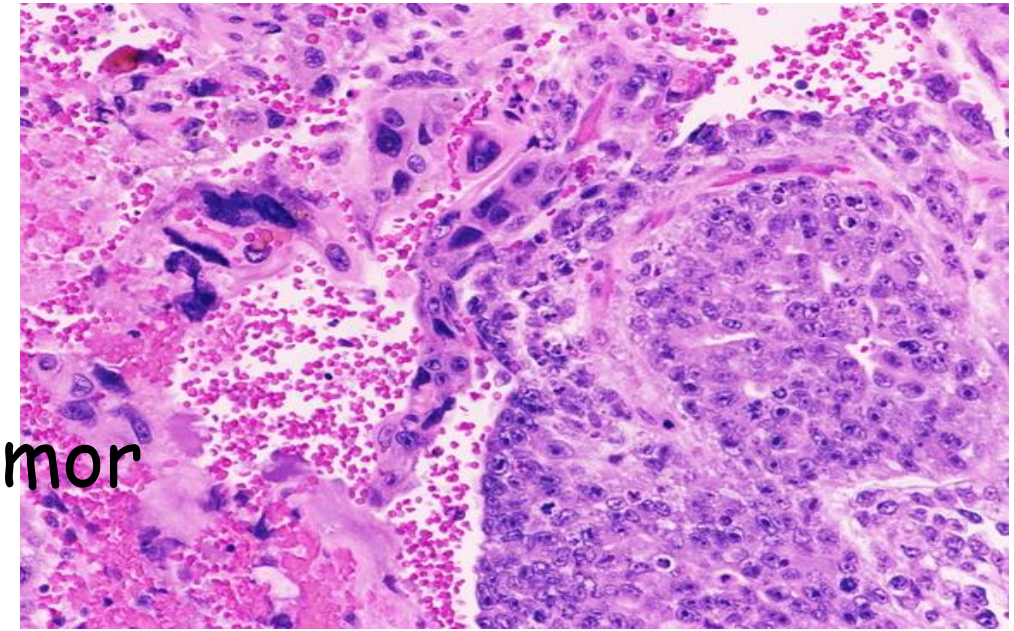
Effects:

Abnormal uterine bleeding, marked ↑↑HCG hormone in blood and urine

Prognosis:

1- Chemotherapy produce high percent cure rate.

2- Spontaneous disappearance of tumor may occur due to immune reaction.



Now....you can answer this

A 20 years old female presents with vaginal bleeding. A pregnancy test was positive. Evacuation of uterine content revealed grape like vesicles measuring 1-5 mm in diameter. The most likely diagnosis is:

(A) Choriocarcinoma.
(B) Abortion.
(C) Hydatiform Mole.
(D) Endometrial hyperplasia.

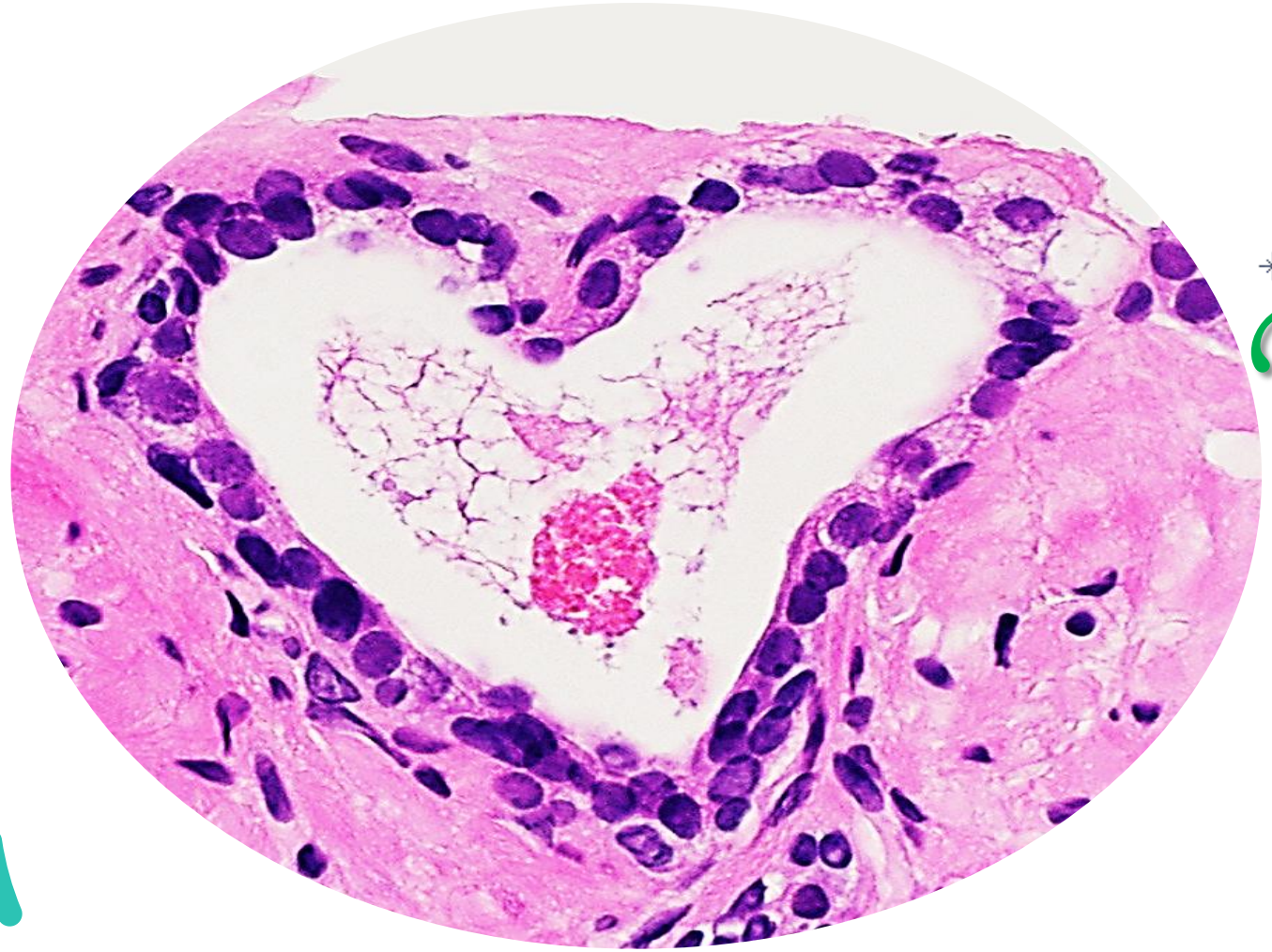
Discussion & Feedback

References & recommended readings

1. Robbins & Cotran Pathologic Basis of Disease, (Robbins Pathology), 2018 ISBN: 978-0-323-35317-5, Edition: 10th
2. Webpath:

   https://webpath.med.utah.edu/webpath.html

   https://www.pathologyatlas.ro/index.php



Thank you