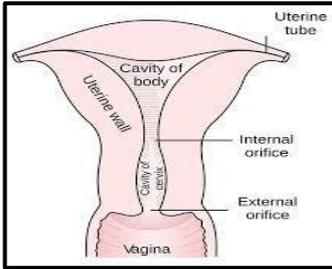
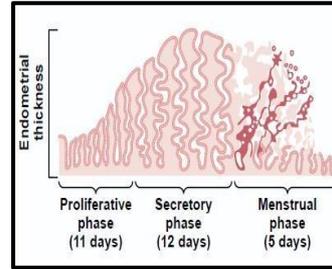
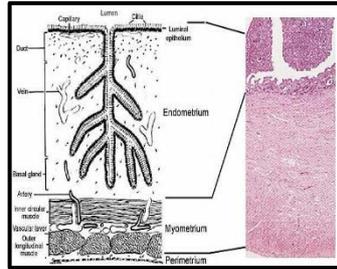


# Pathology of Uterus and GTDs

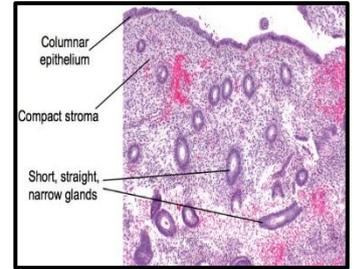
## Uterus



Structure of the uterus



Endometrium



## 1 Abnormal Uterine Bleeding (AUB)

### I Definition

- ✦ Any **increased deviation** from a normal menstrual cycle pattern.
- ✦ **The key characteristics** are regularity, frequency, heaviness of flow, and duration of flow.

### II Causes

#### ✦ 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.

### Causes of abnormal uterine bleeding in different age groups

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

2

## Endometritis

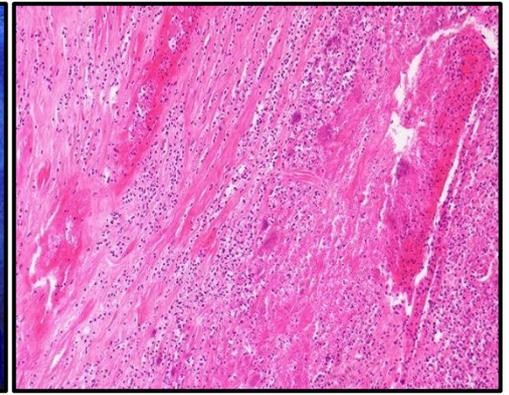
**Definition:** Inflammation of the endometrial lining of the uterus. is classified as acute or chronic.

### Acute Endometritis

<b>Incidence</b>	It is uncommon, may progress to puerperal sepsis	
<b>Puerperal sepsis</b>	<b>Definition</b>	<ul style="list-style-type: none"> <li>★ It is endometrial infection during puerperium (after labor or abortion).</li> <li>★ Caused by Strept. H., staph. Aureus, E. coli, pseudomonas</li> </ul>
	<b>Predisposing causes</b>	<ul style="list-style-type: none"> <li>★ Uterine <b>retention</b> of products of conception and blood clots provide a culture medium for bacteria.</li> <li>★ <b>Traumatic</b> lacerations during childbirth</li> </ul>
<b>N/E</b>	<ol style="list-style-type: none"> <li>1) Uterus is bulky (<b>sub-involutad</b>), soft and flabby.</li> <li>2) Uterine cavity contains septic necrotic material, remnants of placenta and pus.</li> <li>3) <b>Endometrium is</b> hyperemic, edematous with necrosis and ulceration.</li> <li>4) <b>Myometrium show:</b> <ul style="list-style-type: none"> <li>⊗ Septic inflammation which may form abscesses.</li> <li>⊗ Dilated myometrial veins containing septic thrombi.</li> </ul> </li> </ol>	
<b>M/E</b>	<ol style="list-style-type: none"> <li>1) <b>Uterine cavity contains septic material and pus.</b></li> <li>2) <b>Endometrium show:</b> <ul style="list-style-type: none"> <li>⊗ Ulceration of surface epithelium with acute suppurative inflammation.</li> </ul> </li> <li>3) <b>Myometrium show:</b> <ul style="list-style-type: none"> <li>⊗ Suppurative myometritis which may lead to myometrial abscesses.</li> <li>⊗ Myometrial veins contain septic thrombi.</li> </ul> </li> </ol>	
<b>Complications</b>	<ul style="list-style-type: none"> <li>★ <b>Direct spread</b> to pelvic structures</li> <li>★ <b>Blood spread:</b> Pyemia (septic thrombi phlebitis), Septicemia.</li> <li>★ <b>Severe toxemia</b></li> </ul>	



N/E of puerperal sepsis



M/E of puerperal sepsis

## Chronic Endometritis

I

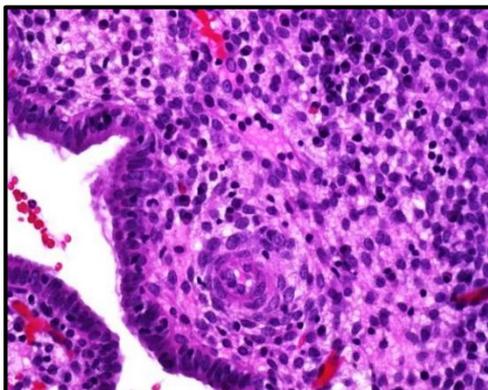
C/P &amp; M/E

- ★ **Clinical picture:** Presented with bleeding, pain, discharge and infertility.
- ★ **M/E:** plasma cells

III

Causes

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



ME of Chronic endometritis



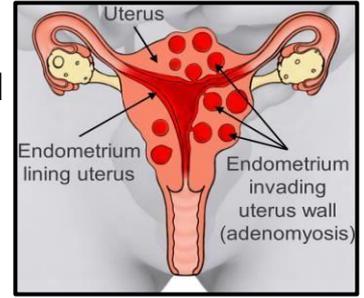
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Endometriosis

I

Definition

- ★ 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.



II

Classification

	External Endometriosis	Internal Endometriosis
Definition	<ul style="list-style-type: none"> <li>★ <b>Presence</b> of endometrial tissue (glands and intervening stroma) outside the uterus.</li> <li>★ <b>Frequently</b> is <u>multifocal</u> and often involves <u>pelvic structures</u> (ovaries, Douglas pouch, uterine ligaments, tubes, and rectovaginal septum)</li> </ul>	<p>Presence of endometrial tissue (glands and stroma) in the <u>myometrium</u> of uterine wall.</p>
Site	<p>Outside the myometrium (e.g. Abdomen)</p>	<p>Myometrium of body of uterus called <b>Adenomyosis</b></p>
Pathogenesis	<ul style="list-style-type: none"> <li>★ <b>The regurgitation theory:</b> during menstruation, viable endometrial fragments pass via fallopian tube to implant on the peritoneum</li> <li>★ <b>Metaplasia of serosal cells</b> leads to peritoneal lesions.</li> <li>★ <b>Vascular and lymphatic dissemination theory</b></li> </ul>	<p><b>Abnormal growth</b> activity of the endometrium, the basal zone of endometrium <b>dips</b> into the adjacent myometrium.</p>
N/E	<ul style="list-style-type: none"> <li>★ <b>Hemorrhagic lesions</b> (as the endometrial tissue undergoes cyclic menstrual bleeding). <b>It excites</b> excessive fibrous tissue around them</li> <li>★ <b>Ovarian endometriosis (chocolate cysts):</b> cyst with dark red brown altered blood content.</li> <li>★ <b>Fibrous adhesion</b> with surroundings.</li> </ul>	<ul style="list-style-type: none"> <li>★ The uterus is <b>symmetrically enlarged</b></li> <li>★ The uterine wall is <b>thickened</b></li> <li>★ The lesions form dark <b>red foci</b></li> </ul>
M/E	<ul style="list-style-type: none"> <li>★ Lesion consists of endometrial glands and stroma with hemosiderin.</li> <li>★ Fibrosis and hemosiderin laden macrophage.</li> </ul>	<p>Nests of <u>endometrial glands and stroma</u> in myometrium <b>between muscle bundles</b></p>



4

## Endometrial polyp

I

## Definition

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

II

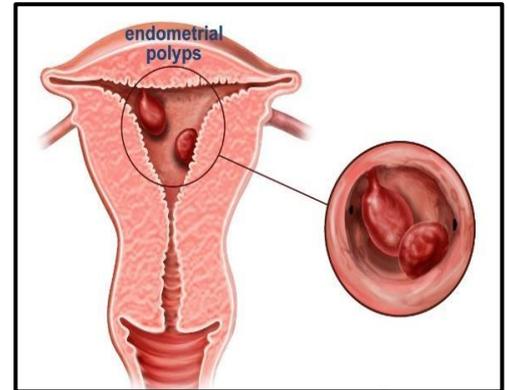
## Effect

It may cause abnormal **bleeding**.

III

## Types

- ★ **Functional endometrium**
- ★ **Hyperplastic endometrium**, in association with endometrial hyperplasia
- ★ Endometrial polyps in association with the **administration of tamoxifen**, an antiestrogen therapy of breast cancer



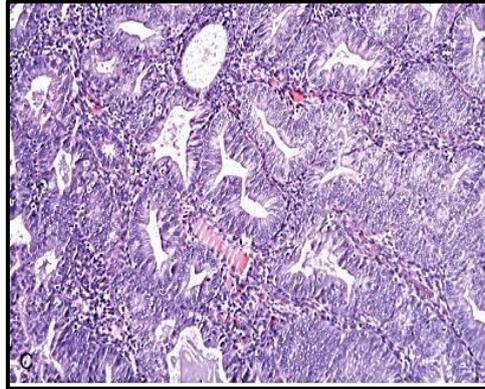
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## Endometrial Hyperplasia

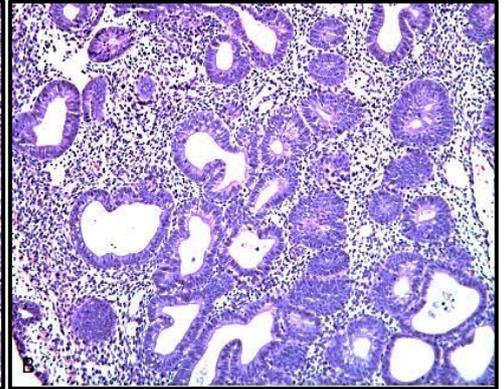
<b>Definition</b>	Increased proliferation of the endometrial glands relative to the stroma, resulting in an <b>increased gland-to-stroma ratio</b> when compared with normal proliferative endometrium.
<b>Effect</b>	Abnormal uterine bleeding
<b>Causes</b>	<p><b><u>prolonged unopposed estrogen stimulation:</u></b></p> <ul style="list-style-type: none"> <li>⊗ Repeated anovulatory menstrual cycles,</li> <li>⊗ Obesity.</li> <li>⊗ Estrogen secreting tumors</li> <li>⊗ Polycystic ovarian disease</li> </ul>
<b>N/E</b>	Endometrial hyperplasia appears as <b>increased endometrial thickness</b>
<b>ME</b>	<ul style="list-style-type: none"> <li>★ <b><u>Characterized by:</u></b> <ul style="list-style-type: none"> <li>⊗ Glandular proliferation and crowding</li> <li>⊗ Increased gland to stromal ratio</li> </ul> </li> <li>★ <b><u>Categories of Endometrial Hyperplasia:</u></b> <ul style="list-style-type: none"> <li>⊗ <b>Hyperplasia without atypia:</b> Carries a low risk (between 1% and 3%) for progression to endometrial carcinoma.</li> <li>⊗ <b>Hyperplasia with atypia (also called endometrial intraepithelial neoplasia, EIN):</b> Associated with a much higher risk (20%–50%).</li> </ul> </li> </ul>



NE of Endometrial Hyperplasia



Hyperplasia with atypia

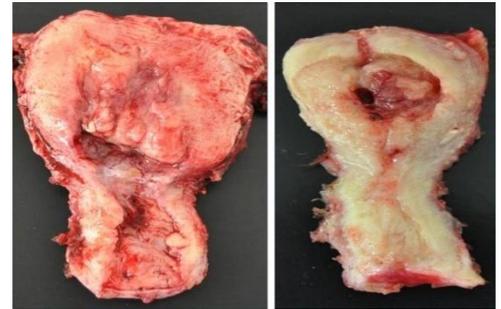


Hyperplasia without atypia

6

## Endometrial tumors

- ★ Endometrial Carcinoma
- ★ Carcinosarcoma (Malignant Mixed Mullarian Tumor)
- ★ Endometrial Stromal Tumors:
  - ⊗ **Benign:** Stomal nodule
  - ⊗ **Malignant:** Endometrial Stromal Sarcoma (ESS)



## Endometrial Carcinoma

## I Incidence &amp; Types

- ★ **Endometrial carcinoma (EC)** is the **most common cancer** of the female genital tract
- ★ Endometrial carcinoma has two broad categories:
  - ⊗ **type I:** Endometrioid 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

## II N/E

- ★ It may be polypoid or infiltrative.
- ★ **Type II tends** to be bulkier and more diffuse.



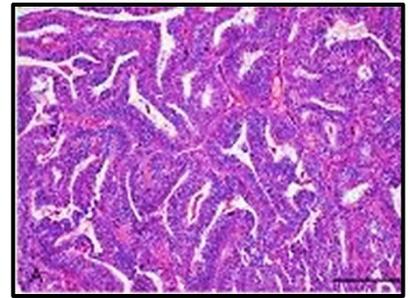


III

M/E

★ **Type I:**

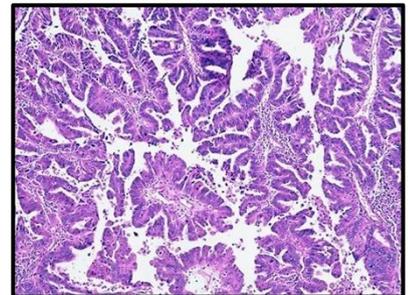
- ⊗ Resembling endometrial glands.
- ⊗ According to the degree of glandular differentiation, endometrioid carcinoma is graded into GI, GII and GIII.



Type I

★ **Type II:** Usually of serous histology (simulating tubal epithelial lining)

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 endometrial hyperplasia Endometrioid intraepithelial neoplasia (EIN)	Endometrial intraepithelial carcinoma (EIC)
Molecular genetics	<i>PTEN</i>	<i>p53</i>
Behavior	Indolent Spreads via lymphatics	Aggressive Intraperitoneal and lymphatic spread



Type II

7

Tumors of Myometrium

★ **Benign:** Leiomyoma

★ **Malignant:** Leiomyosarcoma

Leiomyoma

I

Origin

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**.

II

Incidence & Etiology

★ **Incidence:** Leiomyomas are the **most common benign tumor in females**, affecting 30% to 50% of women of reproductive age.

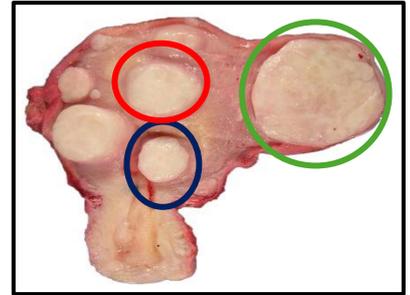
★ **Etiology:** Associated with prolonged hyperestrogenism.



III

N/E

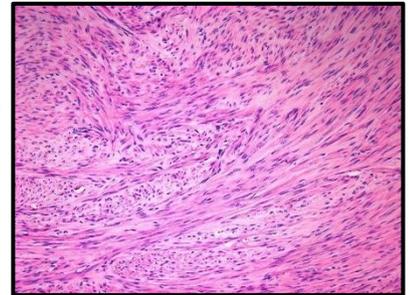
- ★ **Site:** Commonly arises in the body of uterus and cervix.
- ★ **Submucous** (project in the uterine cavity under the endometrium)
- ★ **Intramural** (within the wall of the uterus)
- ★ **Subserous** (projects to outside under the peritoneum)
- ★ **Shape:** Rounded masses,
- ★ **Capsule:** surrounded by pseudo-capsule of compressed uterine muscle and interstitial tissue.
- ★ **Cut surface:** whorly appearance
- ★ **Consistency:** firm



IV

M/E

- ★ **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.



V

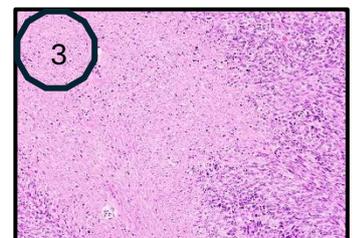
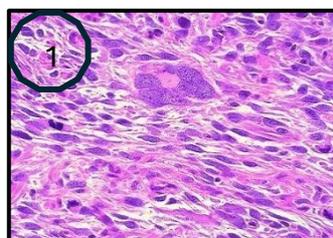
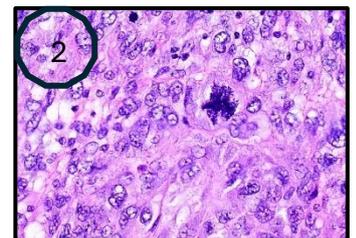
Complications

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

### Leiomyosarcoma

- ★ **On microscopic examination; three criteria to exclude malignancy:**

- 1) Atypia
- 2) Increased mitotic figures
- 3) Coagulative necrosis.





## Gestational Trophoblastic Diseases (GTDs)

I

### Definition

#### ★ Group of diseases characterized by:

- ⊗ Proliferation of **pregnancy-associated trophoblastic (placenta) tissue**
- ⊗ Has a malignant potential.

II

### Classification

#### ★ Molar GTD (Villous): Characterized by formation of chorionic villi

##### ⊗ **Hydatiform mole:**

- Complete
- Partial

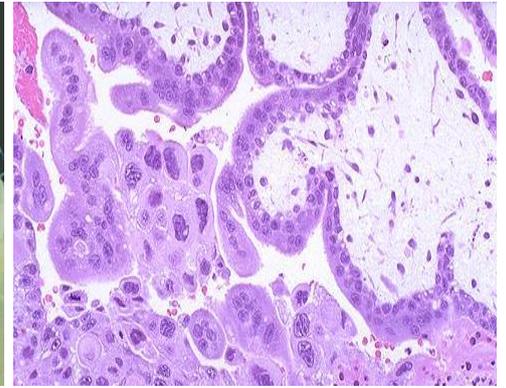
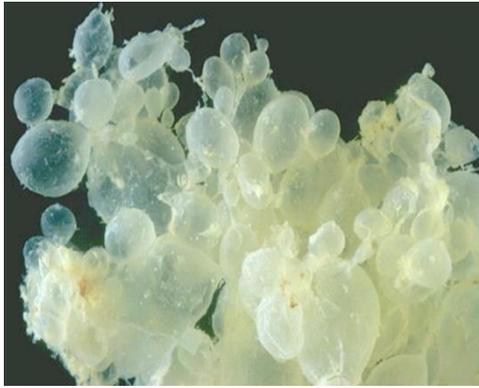
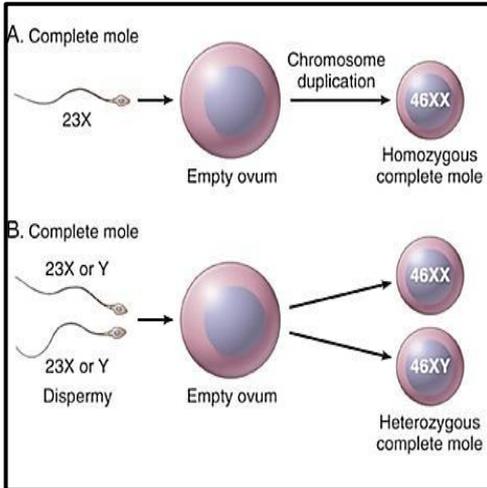
##### ⊗ **Invasive mole**

#### ★ Non- Molar GTD (Non- villous):

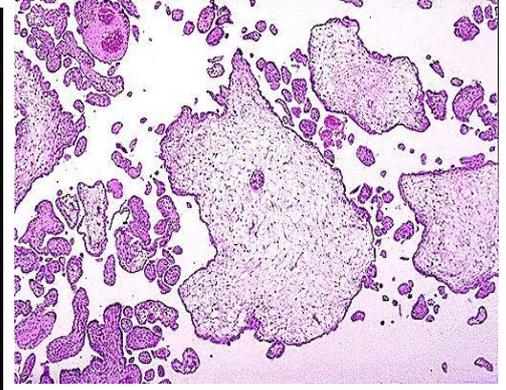
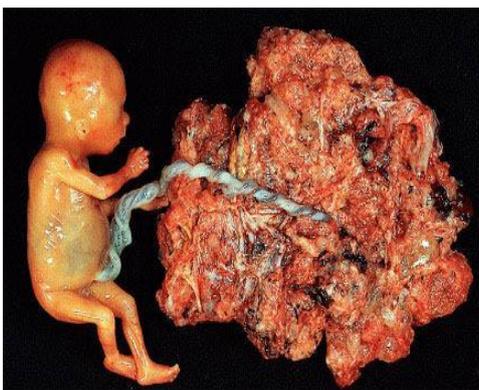
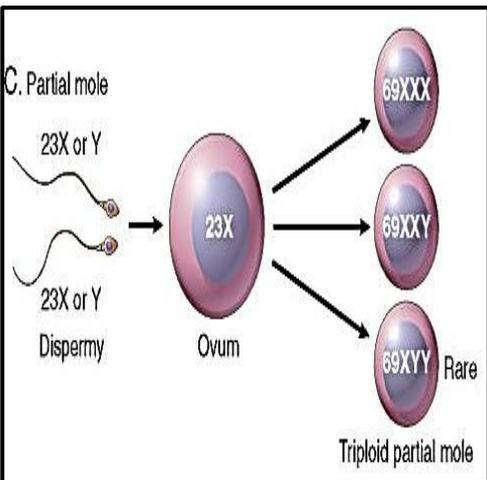
- ⊗ No villi
- ⊗ Choriocarcinoma

## 1 Hydatiform mole (vesicular mole)

<b>Incidence</b>	During reproductive period, (20-40 years) related to pregnancy.	
<b>Types</b>	<b>Complete</b>	<b>Partial</b>
<b>Description</b>	<ul style="list-style-type: none"> <li>⊛ One or two sperm fertilize an <b>empty ovum</b> (without DNA).</li> <li>⊛ All <b>chromosomes are paternal</b> (Diploid with 46 XX, 46 XY)</li> </ul>	<ul style="list-style-type: none"> <li>⊛ Fertilization of an ovum by <b>one diploid</b>, or <b>two haploid</b> sperm,</li> <li>⊛ Triploid (69 XXX, 69 XXY or 69 XYY)</li> </ul>
<b>N/E</b>	<ul style="list-style-type: none"> <li>⊛ It is filled with a mass that resembles a <b>punch of grape</b>. It is formed of clusters of vesicles</li> <li>⊛ <b>No trace of embryo</b>, amniotic sac or umbilical cord</li> </ul>	<ul style="list-style-type: none"> <li>⊛ Normal placenta with few chorionic villi is swollen</li> <li>⊛ <b>Abnormal fetus</b> is seen</li> </ul>
<b>M/E</b>	Oedema of some chorionic villi	Normal chorionic villi with few abnormal swollen chorionic villi
<b>Prognosis</b>	<ul style="list-style-type: none"> <li>⊛ May complicate to invasive mole</li> <li>⊛ 5% pass into choriocarcinoma</li> </ul>	Very rare to pass into choriocarcinoma



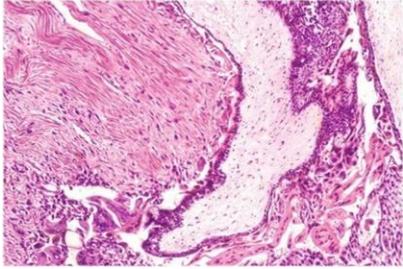
N/E and M/E of Complete Hydatiform mole



N/E and M/E of partial Hydatiform mole

2

Invasive mole

<b>Complication</b>	It complicates complete mole.	
<b>N/E</b>	Clusters of vesicles attached deeply to the myometrium.	
<b>M/E</b>	Villi become <b>invasive to myometrium</b> and blood vessels	
<b>Prognosis</b>	Spread to distant sites	



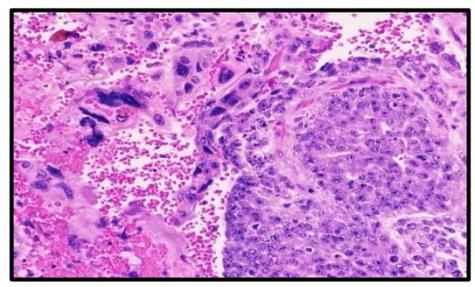
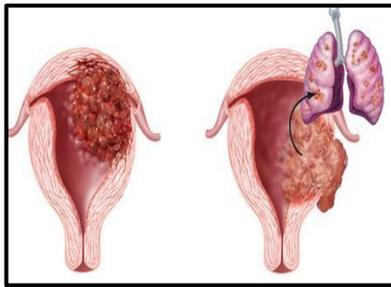
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## Gestational Choriocarcinoma

<b>Definition</b>	It is a malignant neoplasm of trophoblastic cells
<b>Incidence</b>	<ul style="list-style-type: none"> <li>✪ 50% arise in hydatidiform moles,</li> <li>✪ 25% in previous abortions,</li> <li>✪ ≈25% in normal pregnancies</li> </ul>
<b>N/E</b>	<ul style="list-style-type: none"> <li>✪ Uterus contains a soft, friable, fleshy mass invading the uterine wall.</li> <li>✪ Very hemorrhagic, and necrotic</li> </ul>
<b>M/E</b>	Large sheets of malignant cytotrophoblasts and syncytiotrophoblasts with little or no stroma and wide areas of necrosis and hemorrhage.
<b>Spread</b>	<ul style="list-style-type: none"> <li>✪ <b>Direct spread:</b> Into uterine wall leading to perforation → peritoneal Metastases and peritoneal hemorrhage.</li> <li>✪ <b>Blood spread:</b> The main method of distant spread, occurs early → Lung, liver, brain, bone, vulva and kidney are involved.</li> </ul>
<b>Effects</b>	Abnormal uterine <b>bleeding</b> , marked <b>↑↑HCG hormone</b> in blood and urine
<b>Prognosis</b>	<ul style="list-style-type: none"> <li>✪ <b>Chemotherapy</b> produces high percent cure rate.</li> <li>✪ <b>Spontaneous disappearance</b> of tumor may occur due to immune reaction.</li> </ul>



N/E of Choriocarcinoma



N/E of Choriocarcinoma

## Quiz

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.

**Answer: B**

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.

**Answer: C**