

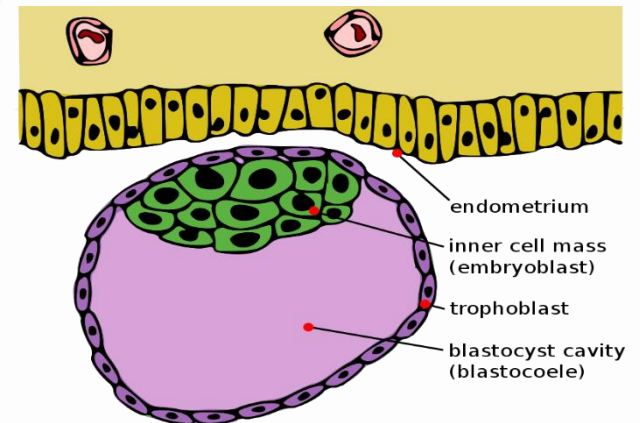
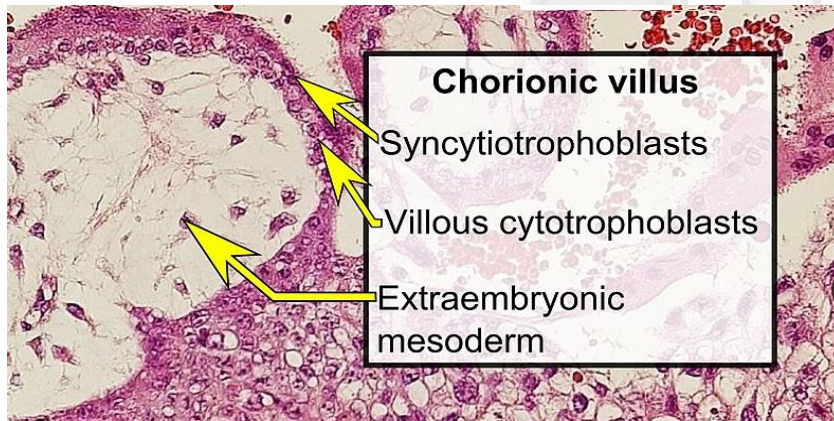
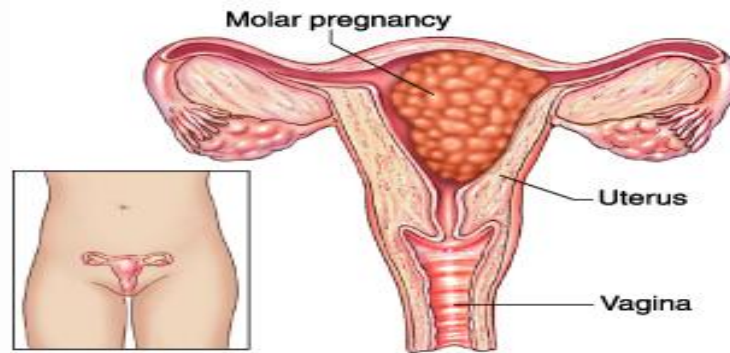


FEMALE GENITAL SYSTEM PATHOLOGY

Lec. 9

- A.P.Dr. Maather Bager Hussein
- Department of Pathology

Gestational trophoblastic disease GTD



Case scenario

A 36-year-old woman presents with vaginal bleeding at 8 weeks 3 days' gestation. She has never been pregnant before. Bright red 'spotting' commenced 7 days ago, which she thought was normal in early pregnancy.

Examination

The abdomen is soft and non tender. Speculum reveals a normal closed cervix with a small amount of fresh blood with vesicles coming from the cervical canal. Bimanually the uterus feels bulky and soft, approximately 10 weeks in size. There is no cervical excitation or adnexal tenderness.

INVESTIGATIONS

Urinary pregnancy test: positive

- The ultrasound scan shows:-
- show snowstorm appearance (uterine cavity filled with multiple sonolucent area of varying size and shape).



Figure 37.6 Ultrasonogram of a uterus showing a typical pattern of a complete hydatidiform mole. Note the characteristic vesicular ultrasonographic pattern.

This woman underwent curettage revealed a multiple vesicles as bunch of grapes as in picture



Is a spectrum of tumors and tumor-like conditions, characterized by proliferation of trophoblastic tissue.

The main types of GTD are:

- **A. The pre-malignant conditions:**
 - **Complete hydatidiform mole**
 - **Partial hydatidiform mole.**
- **B. Malignant gestational trophoblastic neoplasias (Gestational trophoblastic tumour (GTT))(malignant disorders):**
 - **invasive mole**
 - **choriocarcinoma**
 - **placental site trophoblastic tumour. very rare**

Overall, GTD is a rare disease. The incidence of GTD varies greatly between different parts of the world. The reported incidence of hydatidiform mole is 1 to 1000 – 2000 pregnancies. The incidence of the malignant forms of GTD is much lower, only about 10% of the incidence of hydatidiform mole

Hydatidiform mole

The name Hydatiform stems from the Greek word hydatis, meaning droplet of water



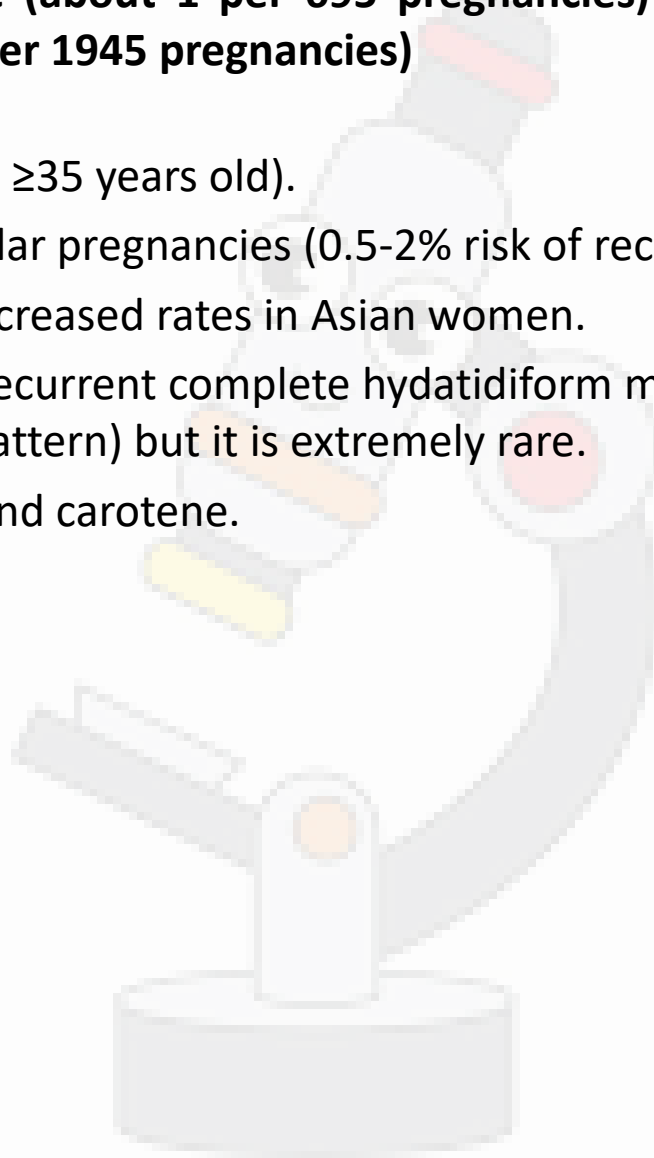
- It is a Benign tumor of trophoblast and the **commonest form of GTD**.
- Are characterized by cystic swelling of chorionic villi, accompanied by variable trophoblastic proliferation;
- Risk of a mole is highest at either extreme of the reproductive years (<20y & >35y);
- Are classified as **complete and partial** , based by histologic, cytogenetic content
- Rarely, a molar pregnancy may develop as a twin to a normal embryo.
- These can be precursors of choriocarcinoma

• Epidemiology:

Incidence of partial mole (about 1 per 695 pregnancies) is **3 times higher than complete mole** (about 1 per 1945 pregnancies)

• Risk factors:-

- Maternal age (≤ 20 and ≥ 35 years old).
- Previous history of molar pregnancies (0.5-2% risk of recurrence)
- Ethnic variation and increased rates in Asian women.
- Familial syndrome of recurrent complete hydatidiform mole (inherited in autosomal recessive pattern) but it is extremely rare.
- Deficiency in protein and carotene.



Pathophysiology (cytogenetics)

Complete H. MOLE

Arise from an **ovum with absent or inactivated nucleus** that has been fertilized by a **haploid sperm**, which then duplicates its own chromosomes.

- Karyotype: **diploid 46XX (90% cases); 46XY(10%)** , Are genetically **entirely paternal in origin**.

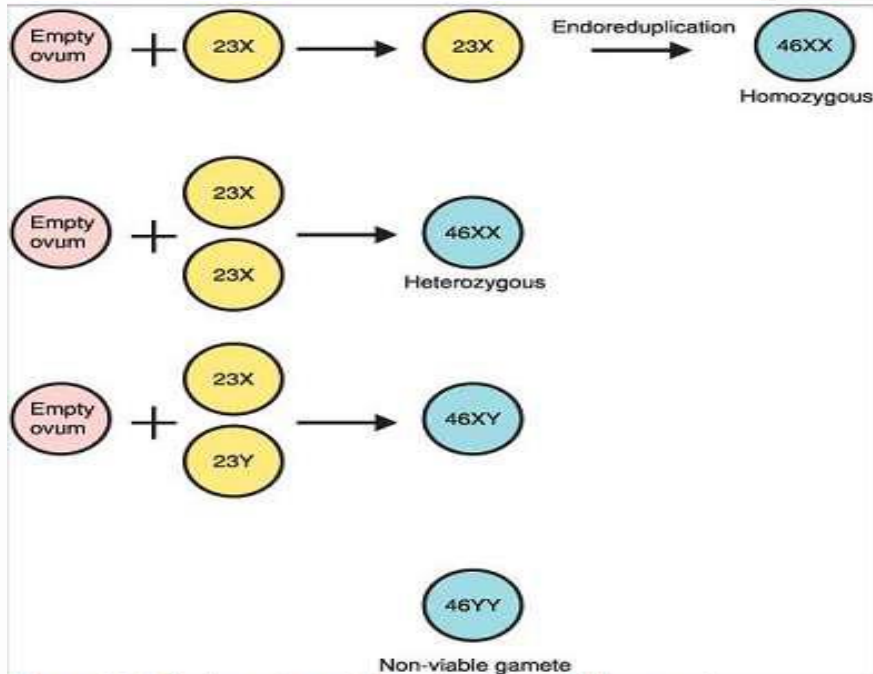


Figure 37.2 The karyotype of complete hydatidiform mole.

Partial H. Mole

Are genetically **biparental** , Usually with a **triploid karyotype** and arise due to **two sperm fertilize an ovum** so it has 2 set of chromosome from paternal origin and one from maternal origin (triploid) **69XXX, 69XXY, 69XYY**.

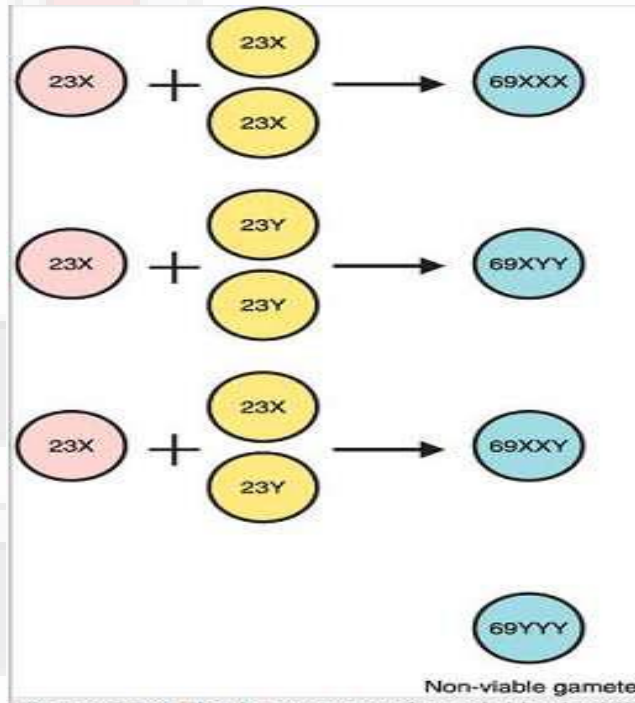


Figure 37.4 The karyotype of partial hydatidiform mole.

Diagnosis

Typical clinical feature in H mole:

- **Amenorrhea .**
- **Painless Vaginal bleeding**
- Symptoms of pregnancy is in **exaggerated form.**
- **Spontaneous expulsion of vesicles** from vagina around 16 weeks.(if undiagnosed before).
- **Uterus is often large for date and feel very soft and doughy in consistency.**
- **Ovarian enlargement occurs in 1/3 of cases and difficult to palpated until uterus evacuated**
- **Or Discovered accidentally** by ultrasound at booking (about 9-10 weeks).

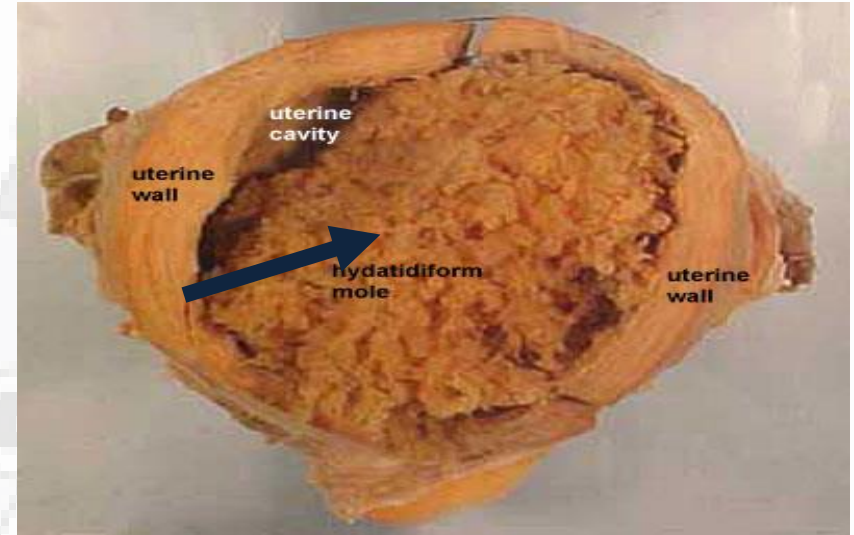
β -human chorionic gonadotrophin (β -hCG) :- It is high but does not give useful distinction between mole and normal pregnancy.

- **U/ S**
- a. show snowstorm appearance (uterine cavity filled with multiple sonolucent area of varying size and shape).
- b. absence of fetus (complete) .



Figure 37.6 Ultrasonogram of a uterus showing a typical pattern of a complete hydatidiform mole. Note the characteristic vesicular ultrasonographic pattern.

Gross



As multiple vesicles as bunch of grapes in complete mole



Complete H. Moles exhibit characteristic chorionic swelling and trophoblastic hyperplasia.

Partial H. Moles

- 1- Chorionic villi of varying size with focal swelling, cavitation and trophoblastic hyperplasia.**
- 2- fetal tissue (blood)**

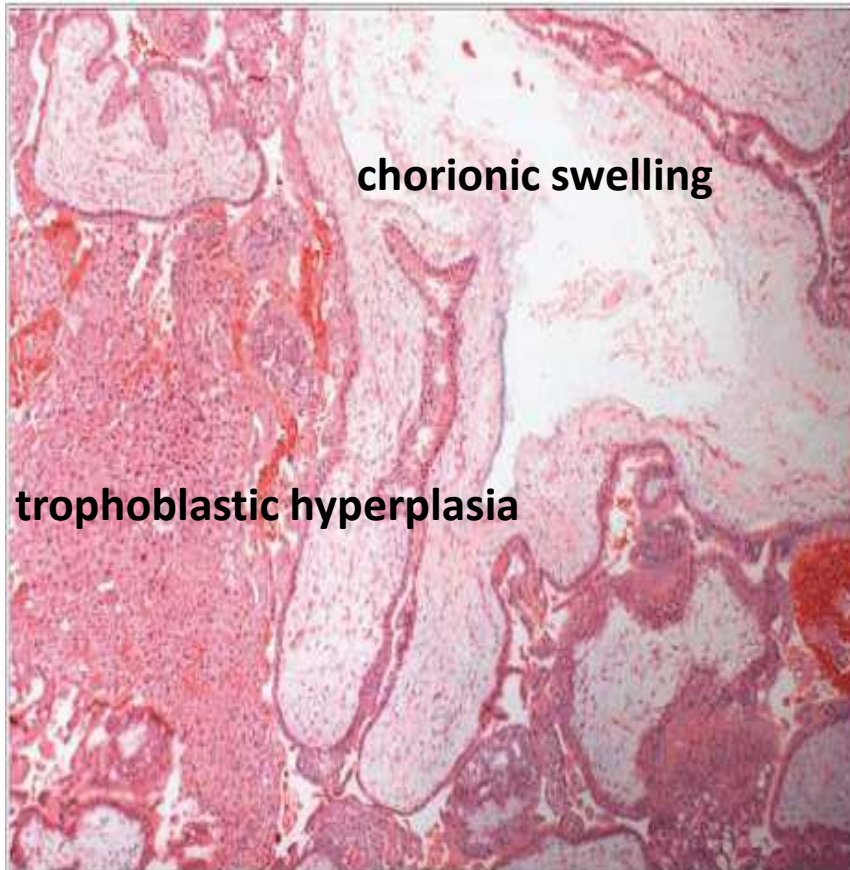


Figure 37.1 Photomicrograph of complete mole demonstrating enlarged villous with central cavitation and surrounding trophoblastic hyperplasia.

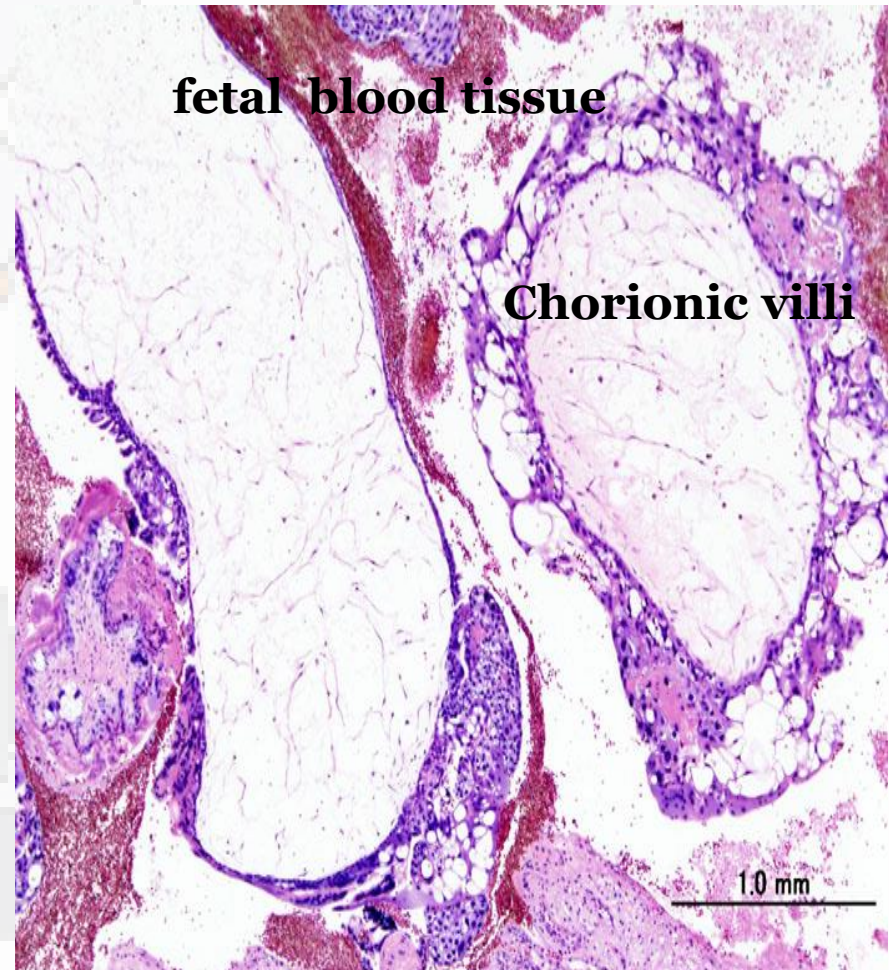


TABLE 22-3 Features of Complete Versus Partial Hydatidiform Mole

Feature	Complete Mole	Partial Mole
Karyotype	46,XX (46,XY)	Triploid
Villous edema	All villi	Some villi
Trophoblast proliferation	Diffuse, circumferential	Focal; slight
Atypia	Often present	Absent
Serum hCG	Elevated	Less elevated
hCG in tissue	++++	+
Behavior	2% choriocarcinoma	Rare choriocarcinoma

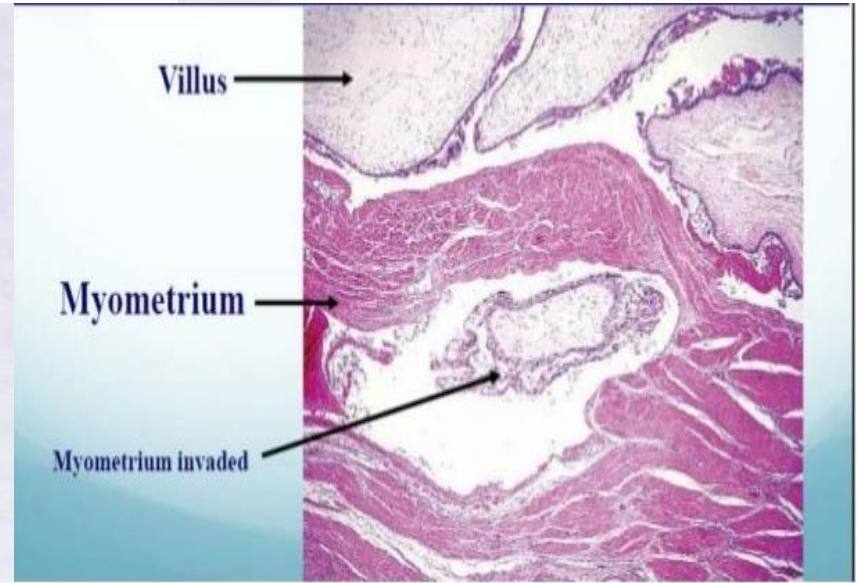
hCG, Human chorionic gonadotropin.

Invasive Mole:-

An invasive mole penetrates and may even perforate the uterine wall, this due to its associated with aggressive proliferating cytotrophoblasts and syncytiotrophoblasts;

The villi in invasive mole can embolize to distant sites.

Invasive moles are associated with **persistently elevated HCG**. The tumor responds well to chemotherapy but can result in uterine rupture.



Choriocarcinoma

50% arise in hydatid form moles, 25% in previous abortions, 22% in normal pregnancies, and the rest in ectopic pregnancies.

Most common follow a term pregnancy or miscarriage

Rapidly growing both myometrium and blood vessels

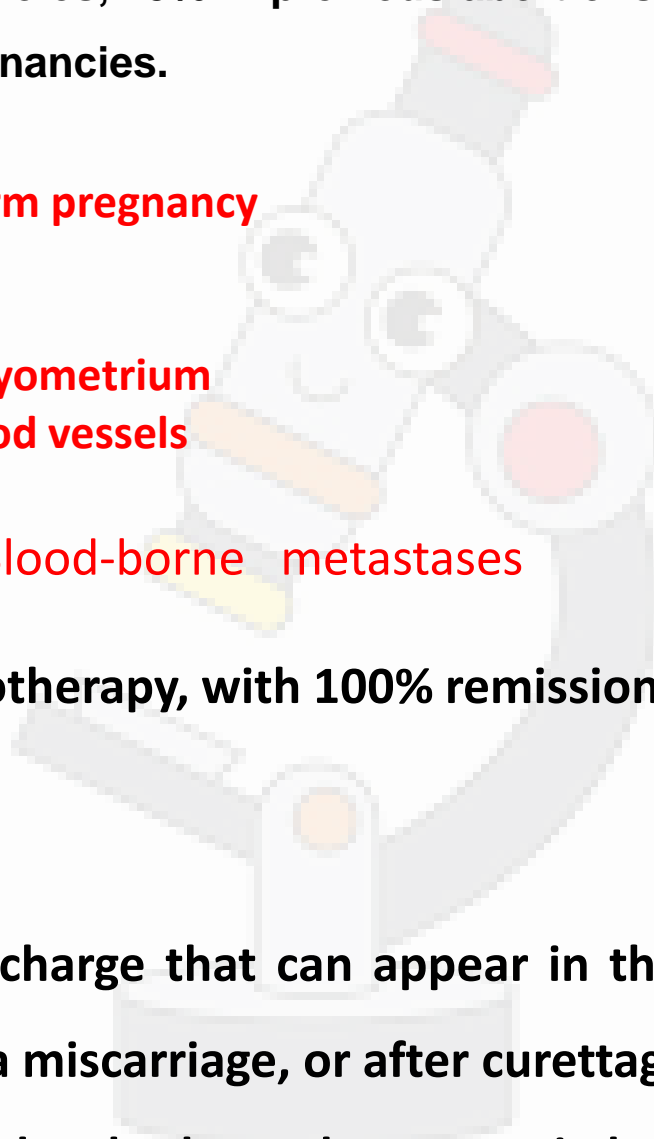
Commonly, widespread Blood-borne metastases

Highly sensitive to chemotherapy, with 100% remission and rates.

Clinical Features :-

Vaginal bleeding and discharge that can appear in the course of an apparently normal pregnancy, after a miscarriage, or after curettage;

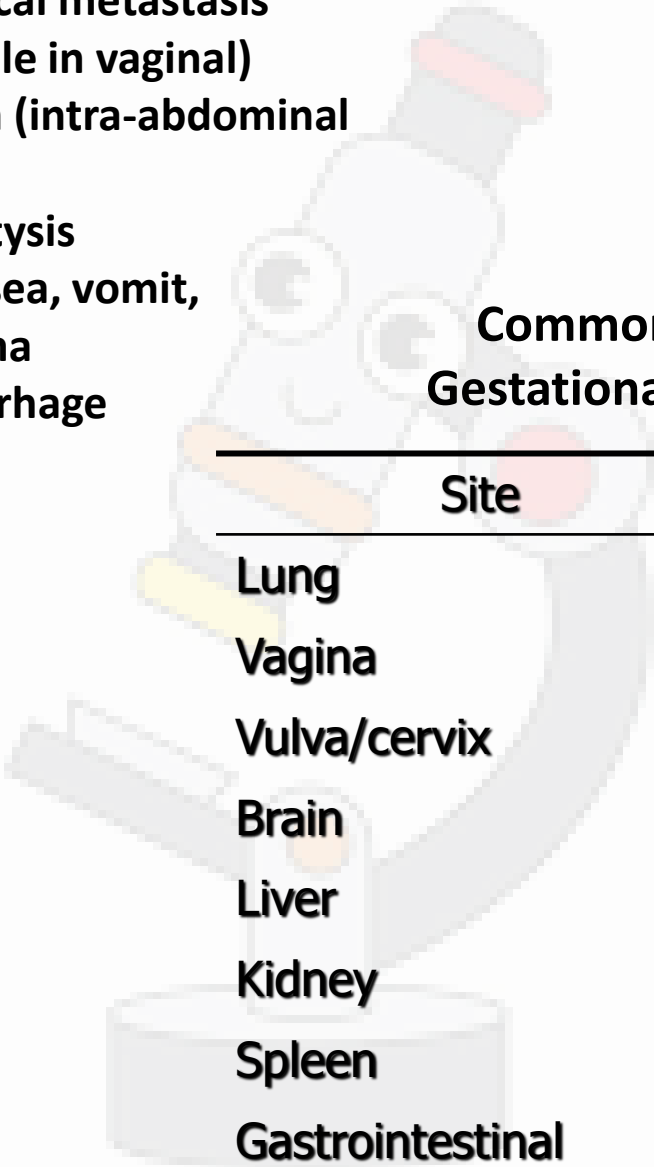
hCG titers are elevated to levels above those seen in hydatid form mole.



Metastatic symptoms

- Profuse vaginal bleeding
- Vaginal or cervical metastasis
- (bluish nodule in vaginal)
- Abdominal pain (intra-abdominal hemorrhage)
- Cough, hemoptysis
- Headache, nausea, vomit, paralysis or coma
- Urologic hemorrhage

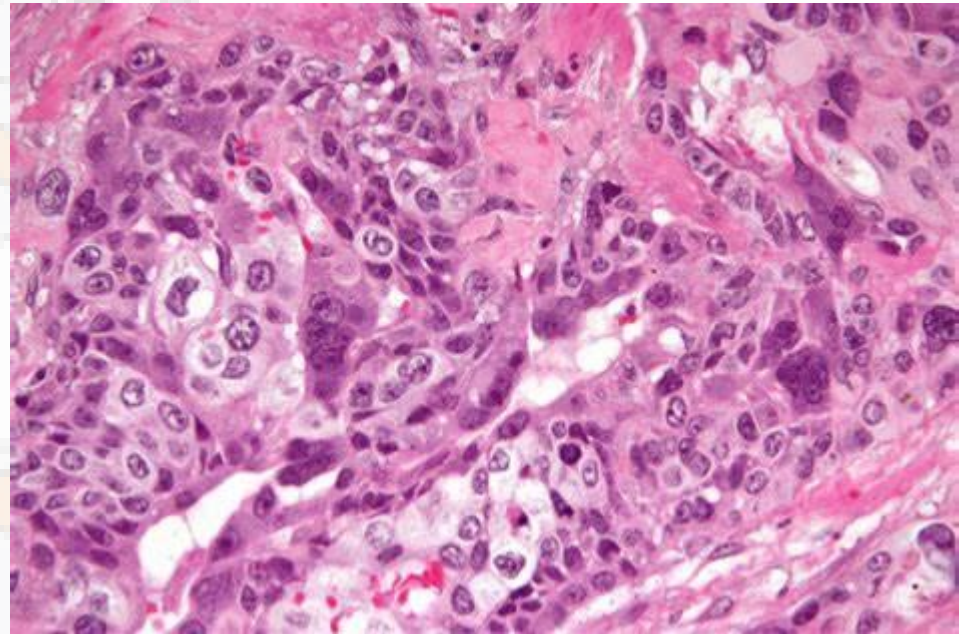
Common Sites for Metastatic Gestational Trophoblastic Tumors



Site	Per cent
Lung	60-95
Vagina	40-50
Vulva/cervix	10-15
Brain	5-15
Liver	5-15
Kidney	0-5
Spleen	0-5
Gastrointestinal	0-5

Morphology

- Grossly: Tumors are large, soft, yellow-white, fleshy masses with areas of necrosis and hemorrhage.
- **Microscopically:** Lesions consist of mixed cytotrophoblast and syncytiotrophoblast proliferations. The tumor invades the underlying endometrium, penetrates blood vessels and lymphatics, and can metastasize widely.

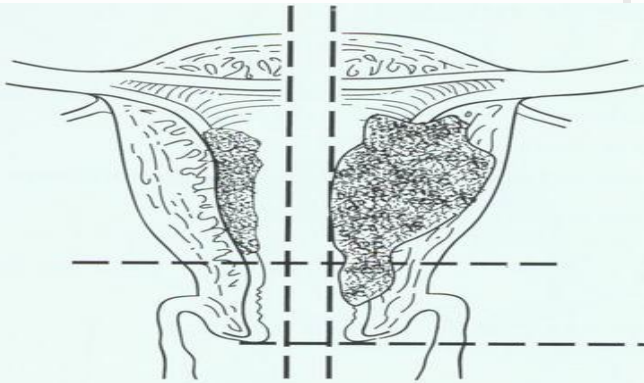


Differentiation between invasive mole and choriocarcinoma
if we see villi, it must be invasion mole
if we can't see villi, it is choriocarcinoma

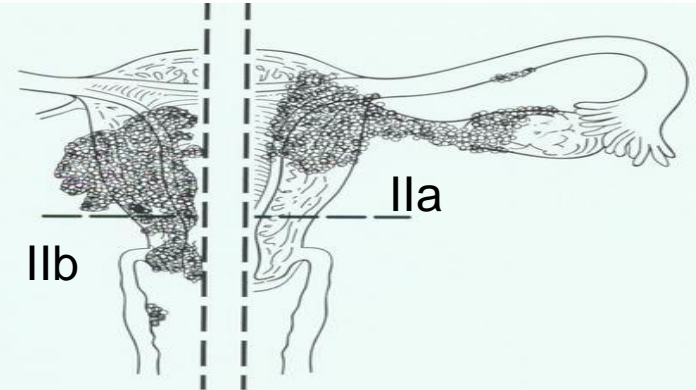
Staging

International staging of WHO may be summarized as follows:

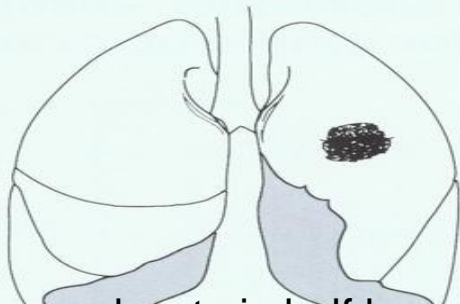
- I : lesion localized in uterus, no metastasis;
- II : lesion extends beyond uterus, but still confined to internal genitalia;
- III : pulmonary lesion
- IV : metastasis to other distant sites.



Gestational trophoblastic disease: FIGO Stage I.

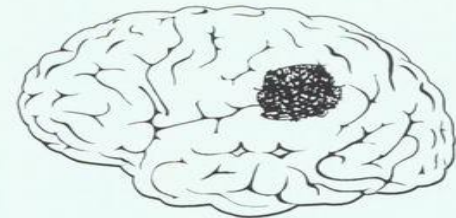


Gestational trophoblastic disease: FIGO Stage II.



IIIa < 3cm or locate in half lung
IIIb disease beyond IIIa

Gestational trophoblastic disease: FIGO Stage III (lung metastasis).

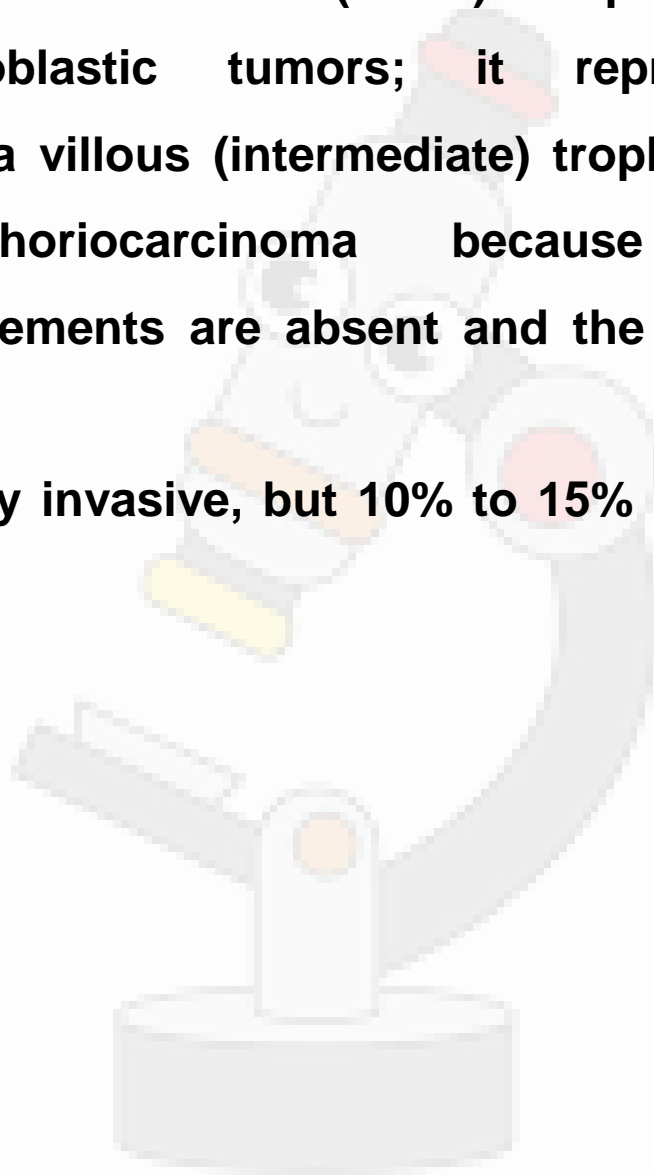


Gestational trophoblastic disease: FIGO Stage IV (brain metastasis).

Placental-Site Trophoblastic Tumor :-

Placental-site trophoblastic tumor (PSTT) comprises less than 2% of gestational trophoblastic tumors; it represents neoplastic proliferation of extra villous (intermediate) trophoblasts. The lesion differs from choriocarcinoma because syncytio- and cytotrophoblastic elements are absent and the tumors make lower levels of hCG.

Most are only locally invasive, but 10% to 15% result in metastases and death.





**THANK YOU
FOR YOUR
ATTENTION**