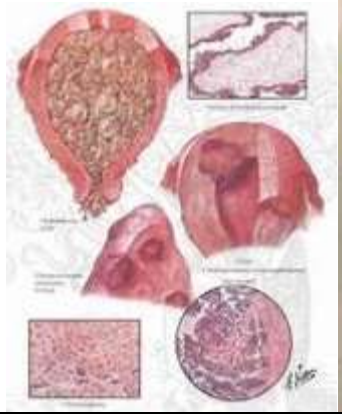
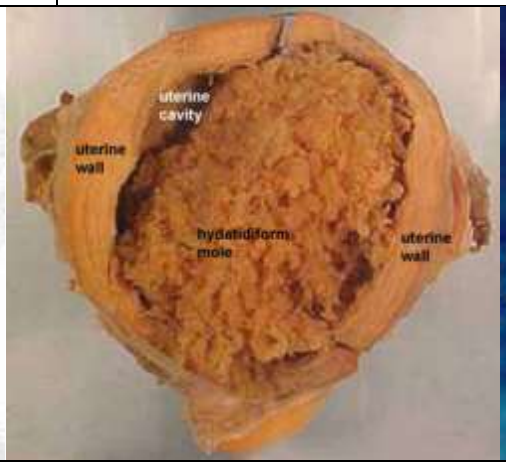
XXI. Diseases of the Female Genital System

Hydatidiform Mole (vesicular mole)

A mass of cysts:	• Moderately large	
	Cysts:	• Numerous • Small (or moderate in size) • Few are large • Appear as **grape-like vesicles** (dilated chorionic villi) • Thin-walled • Pale greyish in colour • Semi-translucent



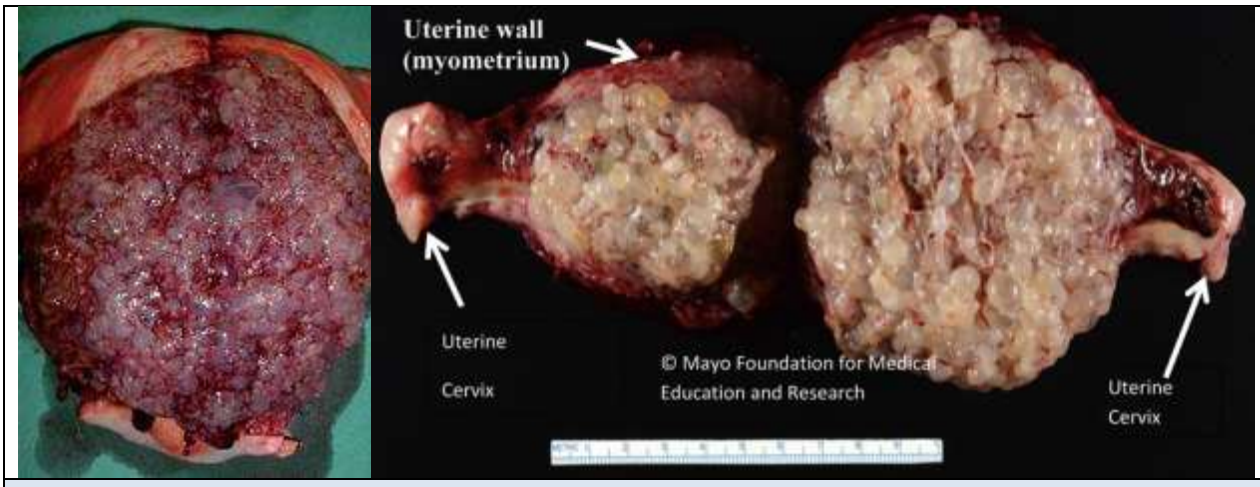


N.B.:

- These cysts are simply the trophoblastic tissue in which the chorionic villi have undergone degeneration (hydropic) and proliferation → a benign growth + over secretion of fluid.
- The mole may be regarded as a simple growth which converts the placenta into a mass of grapelike bodies resembling hydatid cysts (hence the term).
- The pregnancy test is positive.

Sequels:

1. ***Early in pregnancy:***
   (a) Persistence of the mole.
   (b) Disappearance of placenta and foetus.
2. ***Late in pregnancy :***
   (a) Presence of mole and atrophy of foetus.
   (b) Abortion.
   (c) Haemorrhage.
   (d) Transformation to Chorioncarcinoma.

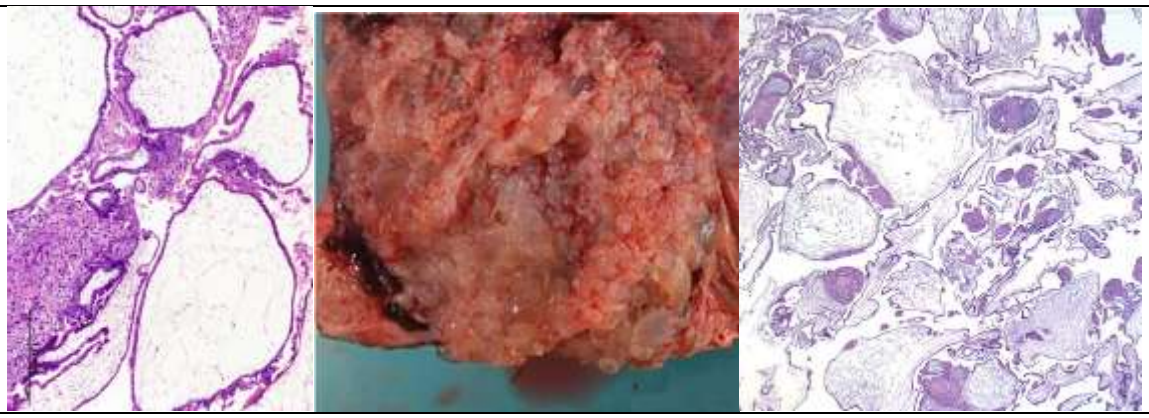


Chorio-carcinoma (on top of mole)

Uterus:	• Is enlarged • Shows a tumour	

	The tumour:	• Is large in size
		• Fills the cavity of the uterus
		• Shows large blood clots (dark red)
		• Some evidence of recent haemorrhage
		• Areas of necrosis
		  ○ Is composed of:
		  ▪ Cysts
		  ▪ A solid mass

	Cysts:	• Appear as a mole, hydatid-like in form • Markedly invading the wall • Infiltration of myometrium (malignancy)
	The mass:	• Is attached to the wall of uterus and invading it (malignancy) Variable in consistence • Friable (in many parts)
	Ovaries:	• Are attached to the wall of the enlarged uterus • Are rather enlarged



N.B.:

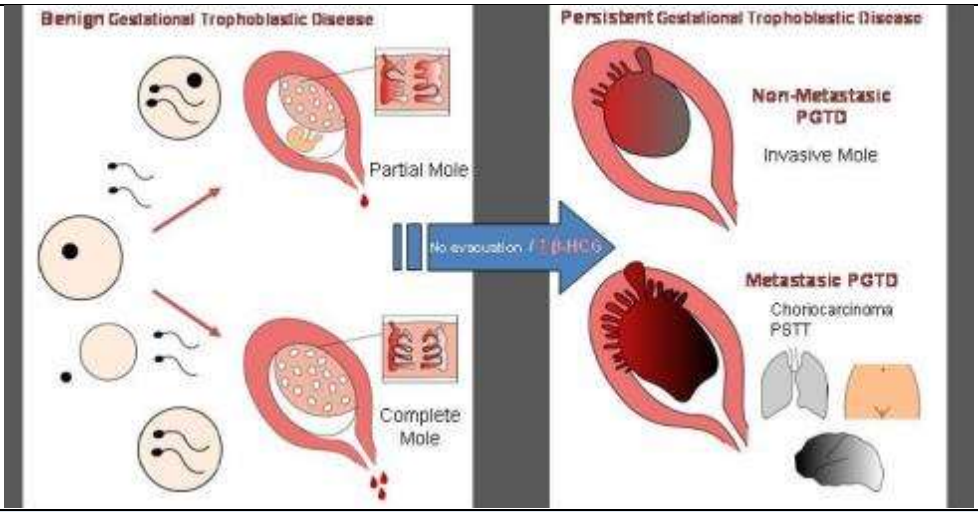
- In chorio-carcinoma, the pregnancy test is positive; and, quantitative tests are useful.
- The ovary and the testis are very rare sites for this tumour (in a teratomatous tissue).
- It is a malignant tumour **of the foetal tissue** which commences at the placental site, usually in the fundus, and projects into the cavity of the uterus, and then it invades its muscular wall as well as the vagina.
- It may follow abortion (arising from a retained placenta) or may follow a full-term pregnancy: and, in about 30% of cases, the tumour may be preceded by a hydatidiform mole (as in the present case).

Means of spread:

1. Early and mainly by the blood to the Lungs and other organs.
2. Outer and lower parts of uterus.
3. Vaginal wall.

Secondaries in the lung:

- Are haemorrhagic.
- Occasionally may retrogress provided early removal of the primary tumour or/and chemotherapy with folic acid antagonists.



Chorio-carcinoma

Uterus:	• Is enlarged • Shows a tumour	
	The tumour:	• At the placental site of the uterus
	Inner wall:	• Broad-based • Infiltrating myometrium (malignancy)
	Cut surface:	• Deep red • Haemorrhagic • With brown markings (blood clots) • Opaque yellow patches (necrosis)
	Peripherally:	• An irregular zone of pale infiltrating tissue (in parts)
	Consistence:	• Friable in most parts

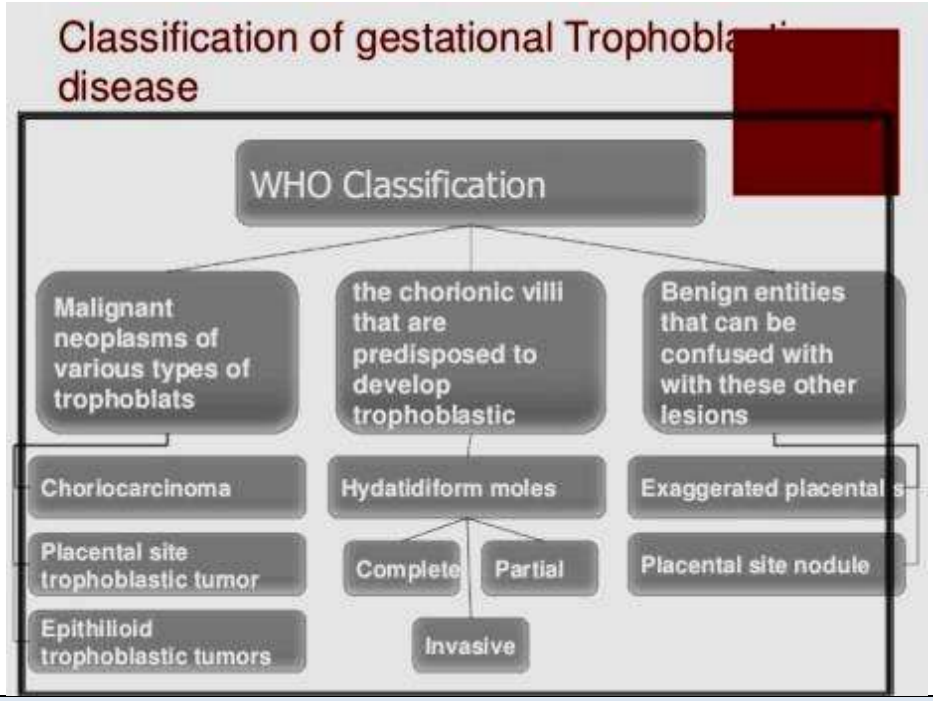
N.B.I:

- Histologically, it proved to be chorio-carcinoma.
- This case has followed abortion and resulted in a metastasis as malignant tumour without villous disturbance.

N.B.2:

Rare tumours of placenta:

- ***Chorioangioma*** (a haemangioma in the form of a small vascular nodule which may be associated with hydramnios and prematurity).
- ***Syncytial endometritis*** (a benign tumour-like condition that may follow a hydatidiform mole with a more tendency of the syncytial cells to pass deep into the intermuscular septa of the myometrium).
- ***Chorioadenoma destruens*** (an invasive hydatidiform mole which penetrates the uterine wall, is locally-destructive and invasive to the surrounding structures but is non-metastasizing).



Gestational trophoblastic disease

Types

GTD is the common name for five closely related tumours (one benign tumour, and four malignant tumours):

- **The benign tumour**
  - Hydatidiform mole
    - Here, first a fertilized egg implants into the uterus, but some cells around the fetus (the chorionic villi) do not develop properly.
    - The pregnancy is not viable, and the normal pregnancy process turns into a benign tumour.
    - There are two subtypes of hydatidiform mole: complete hydatidiform mole, and partial hydatidiform mole.
- **The four malignant tumours**
  - Invasive mole
  - Choriocarcinoma

- Placental site trophoblastic tumour
- Epithelioid trophoblastic tumour
    - All five closely related tumours develop in the placenta.
    - All five tumours arise from trophoblastic cells.
    - The trophoblast is the membrane that forms the wall of the blastocyst in the early development of the fetus.
    - In a normal pregnancy, trophoblastic cells aid the implantation of the fertilized egg into the uterine wall.
    - But in GTD, they develop into tumour cells.

Modified WHO Prognostic Scoring System[34]

	0	1	2	4
Age	<40	≥40	–	–
Antecedent pregnancy	mole	abortion	term	–
Interval months from index pregnancy	<4	4–6	7–12	>12
Pretreatment serum hCG (IU/L)	$<10^3$	10^3–10^4	10^4–10^5	$>10^5$
Largest tumor size (including uterus)	<3	3–4 cm	≥5 cm	–
Site of metastases	lung	spleen, kidney	gastrointestinal	liver, brain
Number of metastases	–	1–4	5–8	>8
Previous failed chemotherapy	–	–	single drug	≥2 drugs

What Is Gestational Trophoblastic Disease?

- Tumors can grow anywhere in the body and happen when cells in the body begin to grow out of control.
- Some tumors might have cancer cells within them, and some might not.
- Cells in nearly any part of the body can become cancer, and can spread to other areas of the body.
- Gestational trophoblastic disease (GTD) is a group of rare tumors that involve abnormal growth of cells inside a woman's uterus.
- GTD does not develop from cells of the uterus like cervical cancer or endometrial (uterine lining) cancer do.
- ***Instead, these tumors start in the cells that would normally develop into the placenta during pregnancy. (The term gestational refers to pregnancy.)***
- GTD begins in the layer of cells called the **trophoblast** that normally surrounds an embryo. ***(Tropho- means nutrition, and -blast means bud or early developmental cell.)***
- Early in normal development, the cells of the trophoblast form tiny, finger-like projections known as villi.
- The villi grow into the lining of the uterus.
- In time, the trophoblast layer develops into the placenta, the organ that protects and nourishes the growing fetus.
- You might hear GTDs called gestational trophoblastic disease, gestational trophoblastic tumors, or gestational trophoblastic neoplasia. (Neoplasia simply means new growth.)
- Most GTDs are benign (not cancer) and they don't invade deeply into body tissues or spread to other parts of the body.
- But some are malignant (cancerous).
- ***All forms of GTD can be treated.***
- ***And in most cases the treatment produces a complete cure.***

Types of gestational trophoblastic disease

The main types of gestational trophoblastic diseases are:

- **Hydatidiform mole (complete or partial)**
- **Invasive mole**
- **Choriocarcinoma**
- **Placental-site trophoblastic tumor**
- **Epithelioid trophoblastic tumor**

Hydatidiform mole

- The most common form of gestational trophoblastic disease (GTD) is a hydatidiform mole, also known as a **molar pregnancy**.
- It is made up of villi that have become swollen with fluid.
- The swollen villi grow in clusters that look like bunches of grapes.
- This is called a molar pregnancy, but it is not possible for a normal baby to form.
- Still in rare cases (less than 1 in 100), a normal fetus can develop alongside the molar pregnancy.
- Hydatidiform moles are not cancerous, but they can develop into cancerous GTDs.

There are 2 types of hydatidiform moles: complete and partial.

A complete hydatidiform mole

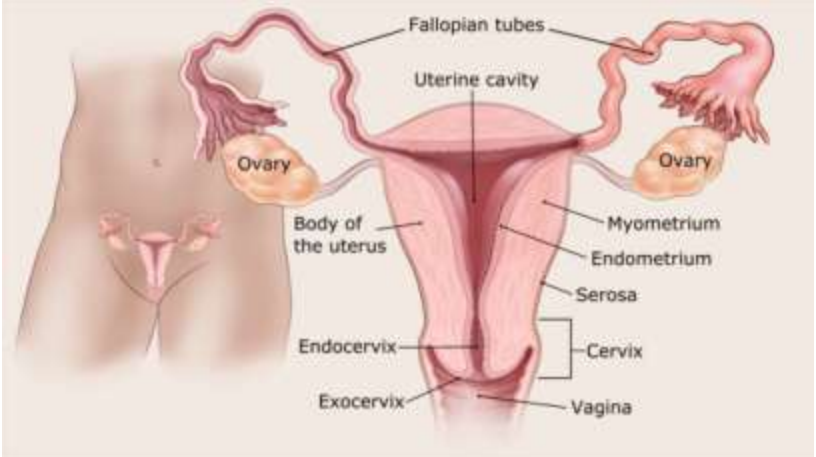
- Most often develops when 1 or 2 sperm cells fertilize an egg cell that contains no nucleus or DNA (an "empty" egg cell).
- All the genetic material comes from the father's sperm cell.
- Therefore, there is no fetal tissue.
- Surgery can totally remove most complete moles, but as many as 1 in 5 women will have some persistent molar tissue.
- Most often this is an invasive mole, but in rare cases it is a choriocarcinoma, a malignant (cancerous) form of GTD.
- In either case it will require further treatment.

A partial hydatidiform mole

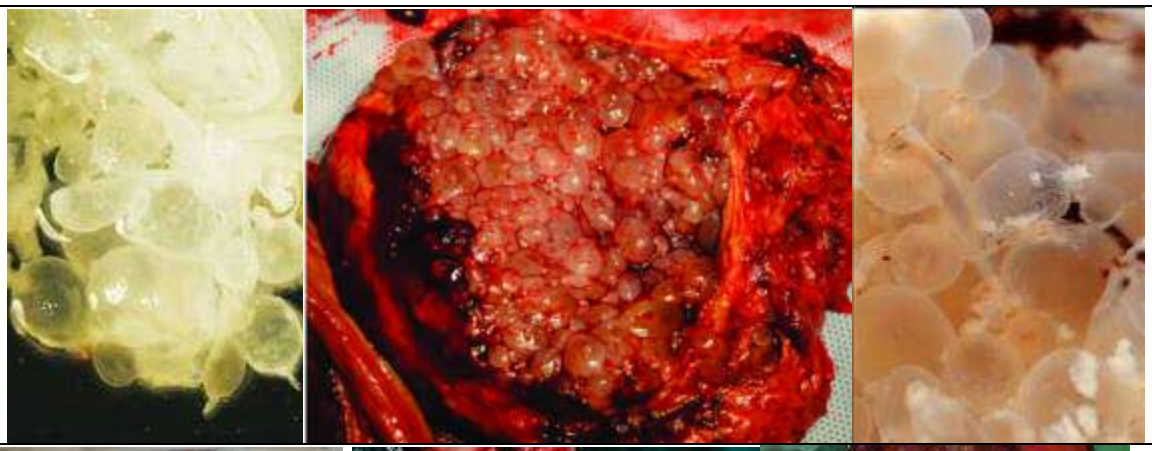
- Develops when 2 sperm fertilize a normal egg. (3N)
- These tumors contain some fetal tissue, but this is often mixed in with the trophoblastic tissue.
- It is important to know that a viable (able to live) fetus is not being formed.
- Partial moles usually are completely removed by surgery.
- Only a small number of women with partial moles need further treatment after initial surgery.
- Partial moles rarely develop into malignant GTD.

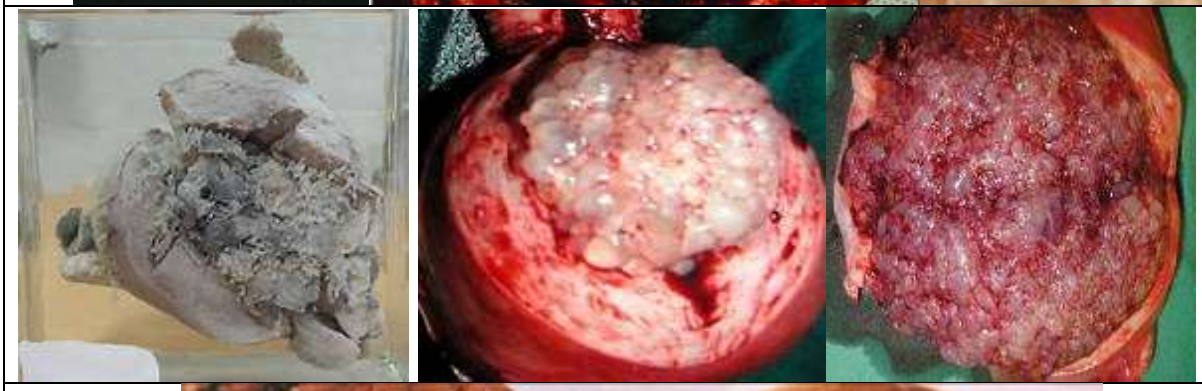
Persistent gestational trophoblastic disease is GTD

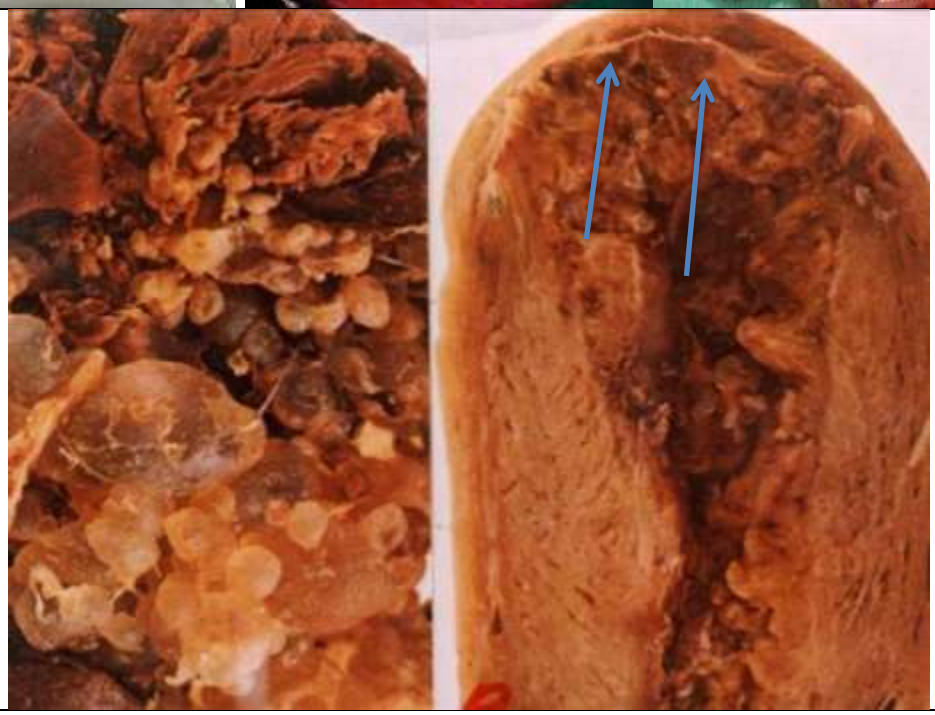
- That is not cured by initial surgery.
- Persistent GTD occurs when the hydatidiform mole has grown from the surface layer of the uterus into the muscle layer below (the myometrium).
- The surgery used to treat a hydatidiform mole (called suction dilation and curettage, or D&C) scrapes the inside of the uterus.
- This removes only the inner layer of the uterus (the endometrium) and cannot remove tumor that has grown into the muscular layer.



- Most cases of persistent GTD are invasive moles, but in rare cases they are choriocarcinoma or placental site trophoblastic tumors.







Invasive mole

- An invasive mole (formerly known as chorioadenoma destruens) is a hydatidiform mole that ***has grown into the muscle layer of the uterus***.
- Invasive moles can develop from either complete or partial moles, but complete moles

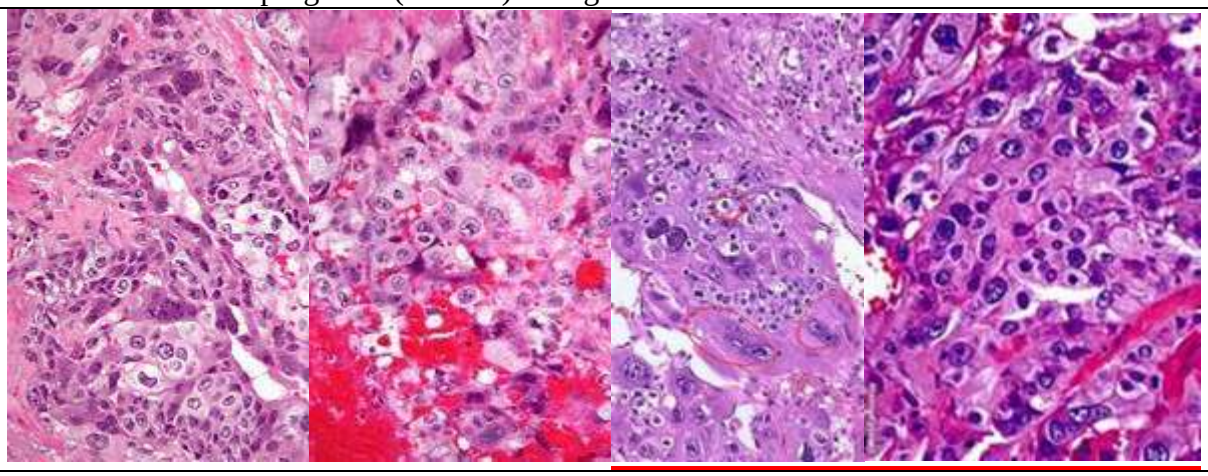
become invasive much more often than do partial moles.

- Invasive moles develop in less than 1 out of 5 women who have had a complete mole removed.
- ***The risk of developing an invasive mole in these women increases if:***
  1. There is a long time (more than 4 months) between their last menstrual period and treatment.
  2. The uterus has become very large.
  3. The woman is older than 40 years.
  4. The woman has had gestational trophoblastic disease in the past.
- Because these moles have grown into the uterine muscle layer, they aren't completely removed during a D&C.
- Invasive moles can sometimes go away on their own, but most often more treatment is needed.
  - A tumor or mole that grows completely through the wall of the uterus might result in bleeding into the abdominal or pelvic cavity.
  - This bleeding can be life threatening.
  - Sometimes after removing a complete hydatidiform mole, the tumor spreads (metastasizes) to other parts of the body, most often the lungs.
  - This occurs about 4% of the time (or 1 in 25 cases).

Choriocarcinoma

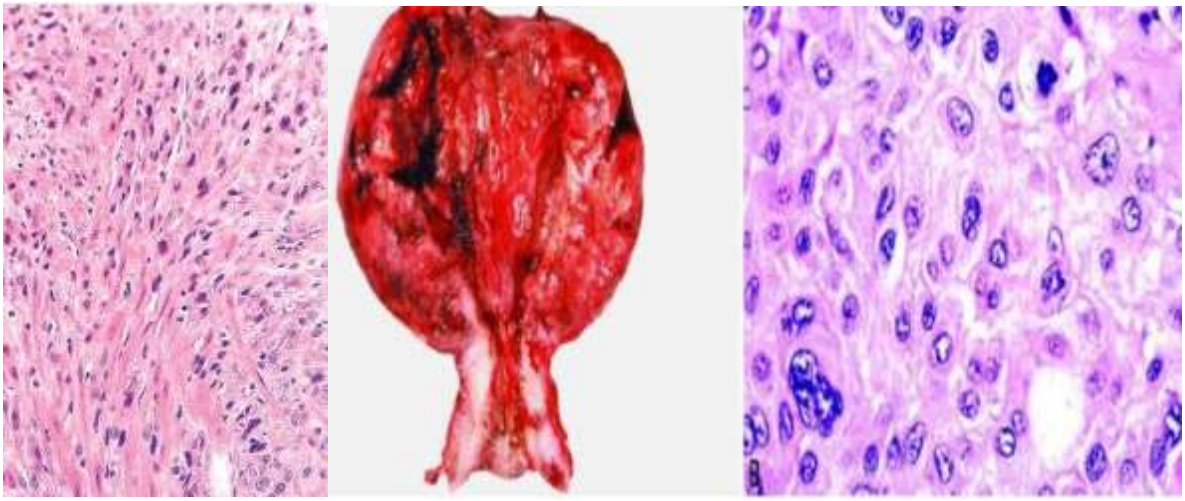
- Choriocarcinoma is a malignant form of gestational trophoblastic disease (GTD).
- It is much more likely than other types of GTD to grow quickly and spread to organs away from the uterus.
- **Half of all gestational choriocarcinomas** start off as molar pregnancies.
- **About one-quarter** develop in women who have a miscarriage (spontaneous abortion), intentional abortion, or tubal pregnancy (the fetus develops in the fallopian tube, rather than in the uterus).
- **Another quarter (25%)** develops after normal pregnancy and delivery.
- ***Rarely, choriocarcinomas that are not related to pregnancy can develop.***
- ***These can be found in areas other than the uterus, and can occur in both men and women.***
- ***They may develop in the ovaries, testicles, chest, or abdomen.***

- ***In these cases, choriocarcinoma is usually mixed with other types of cancer, forming a type of cancer called a mixed germ cell tumor.***
- Non-gestational choriocarcinoma can be less responsive to chemotherapy and may have a less favorable prognosis (outlook) than gestational choriocarcinoma.



Placental-site trophoblastic tumor

- Placental-site trophoblastic tumor (PSTT) is a very rare form of GTD that develops where the placenta attaches to the lining of the uterus.
- This tumor most often develops after a normal pregnancy or abortion, but it may also develop after a complete or partial mole is removed.
- Most PSTTs **do not spread to other sites in the body**.
- But these tumors have a tendency to grow into (invade) the muscle layer of the uterus.
- Most forms of GTD are very sensitive to chemotherapy drugs, but PSTTs are not.
- Instead, they are treated with surgery, to completely remove the disease.



Placental-site trophoblastic tumor (PSTT)

Epithelioid trophoblastic tumor

- Epithelioid trophoblastic tumor (ETT) is an extremely rare type of gestational trophoblastic disease that can be hard to diagnose.
- ETT used to be called **atypical choriocarcinoma** because the cells look like choriocarcinoma cells under the microscope, but it is now thought to be a separate disease.
- Because it can be found growing in the cervix, it can also sometimes be confused with cervical cancer.
- Like placental-site trophoblastic tumors, ETT most often occurs after a full-term pregnancy, but it can take several years after the pregnancy for the ETT to occur.
- Also, like placental-site trophoblastic tumors, ETT does not respond very well to chemotherapy drugs, so the main treatment is surgery.
- It might have already metastasized when it is diagnosed which carries a poorer prognosis (outlook).