



PATHOLOGY

- SHEET NO. 11
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Trophoblastic disease

It means a group of rare diseases that involve abnormal growth of cells inside woman's uterus. They develop from trophoblasts (the cells that would normally form the placenta during pregnancy).

During early embryo development, trophoblasts form tiny projections called "chorionic villi". With time, these villi form the placenta which protects and nourishes the growing fetus.

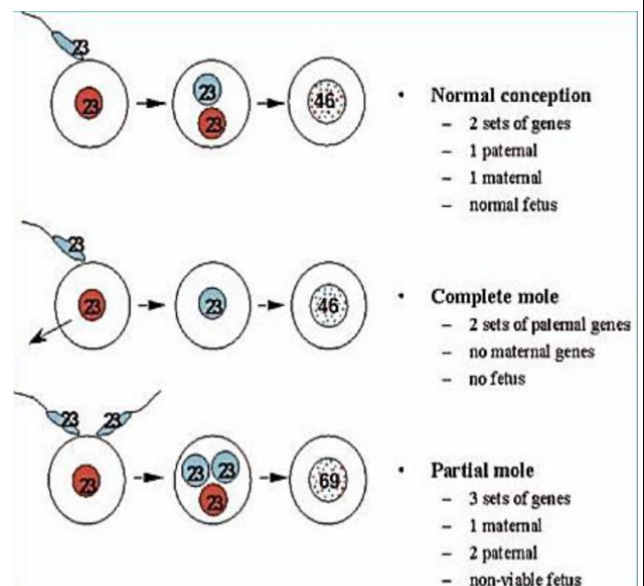
They consist of several types (can be malignant or benign):

- 1) Hydatidiform mole
- 2) Invasive mole
- 3) Choriocarcinoma
- 4) Placental-site trophoblastic tumor
- 5) Epithelioid trophoblastic tumor

Hydatidiform Mole

It is a form of abnormal gestational processes that result from abnormal fertilization.

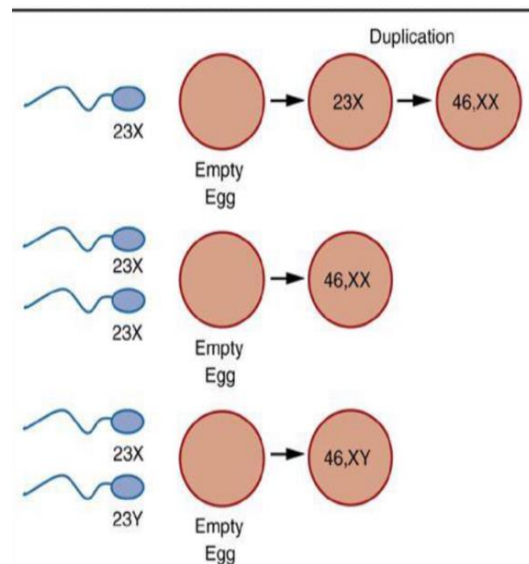
- ❖ In the normal fertilization, a single sperm which is haploid (23 chromosomes) fertilizes a haploid single ovum. After fertilization, there will be one paternal and one maternal set of genes (total of 46 chromosomes) in the fertilized ovum.
- ❖ Other cases like complete mole and partial mole represent abnormal fertilization.
- ❖ There are 2 types of hydratidiform mole:
 - A. **complete mole:** an empty egg (does not contain any maternal DNA / sum of chromosomes inside the ovum before fertilization is 0) is fertilized by two spermatozoa (or a diploid sperm). Then, duplication of the DNA in fertilized ovum takes place yielding a diploid karyotype composed of entirely paternal genes. As a consequence, no fetus develops.



Now, from a genetic point of view, the following possible karyotypes are seen in cases of complete mole:

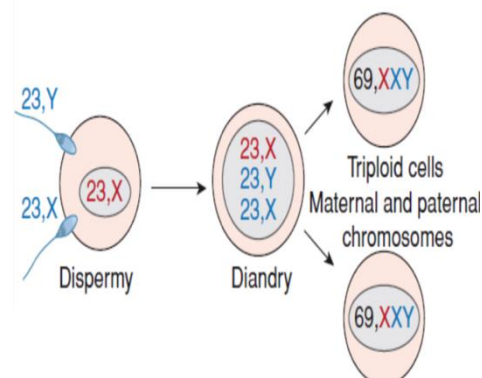
- The empty egg is fertilized by one sperm and this DNA would undergo duplication to give us the end result of (46 chromosomes)
- empty egg would be fertilized by 2 sperms each is haploid and is either 23X or 23Y

In both cases, we will end-up with chorionic epithelial cells that are diploid (46,XX or, uncommonly, 46,XY).



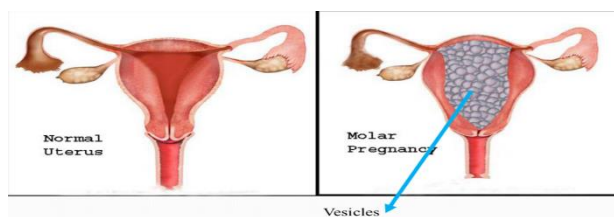
complete hydatidiform mole does not permit embryogenesis = never contains fetal parts

- B. Partial mole:** a normal egg (23 chromosomes) is fertilized by 2 spermatozoa (or a diploid sperm), resulting in a triploid karyotype with a predominance of paternal genes (2 of which are paternal and 1 is maternal, so even if the fetus had developed early on, it will not continue to develop, it will be non viable) has some normal chorionic villi, and is almost always triploid (e.g., 69 XXX, 69 XXY and 69 XYY)

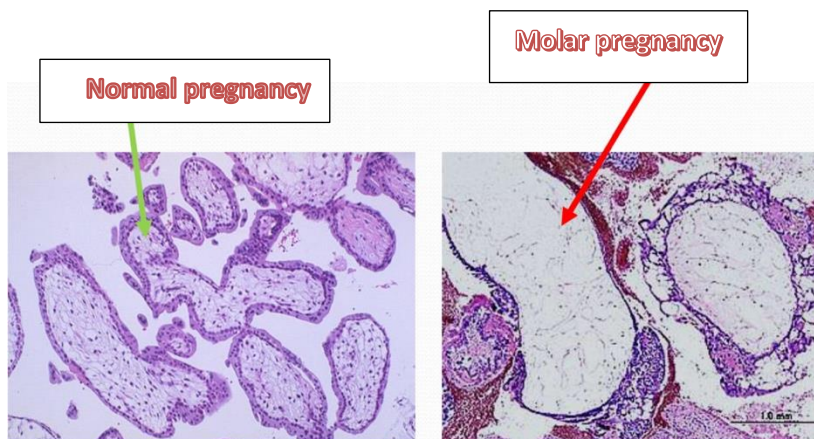


partial hydatidiform mole is compatible with early embryo formation and may contain fetal parts

This picture is to show the difference between uterus in normal vs molar pregnancy, in case of molar pregnancy the uterine cavity is filled with those swollen abnormal chorionic villi that will look like grape-like structures or vesicles.

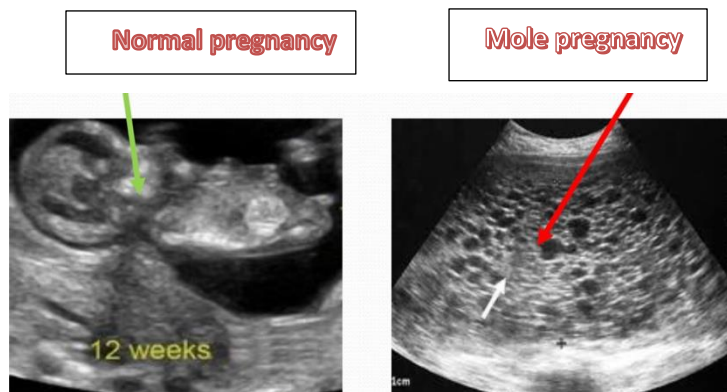


- Under the microscope, the major difference is the size of chorionic villi. As you can see in molar pregnancy, the chorionic villi are markedly swollen and look like grape vesicles.

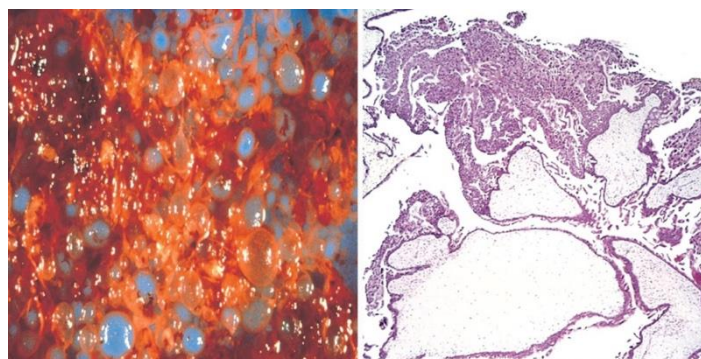


- This picture compares between normal pregnancy and molar pregnancy at the calculated gestational age of 12 weeks using ultrasound examination.

- In the normal one & as you can see, we have a good view of the developing fetus. We can see the head, some details of the face, a developing trunk and the buds of the upper limbs and lower limbs.
- While in the molar pregnancy at 12 weeks of the calculated gestational age, the only thing that will be evident by ultrasound is those vesicles and this morphology using the ultrasound is described by clinicians as snow storm ☁



- ❖ **Morphology:** cystically dilated chorionic villi (grape-like structures) that are covered by varying amounts of mildly to highly atypical chorionic epithelium



- ❖ The **incidence** of molar pregnancy is not common, it ranges from 1 to 1.5 per 2000 pregnancies; higher incidence in Asian countries.
- ❖ Regarding the maternal age, moles are more commonly detected before maternal age 20 years and after age 40 years.
- ❖ Early monitoring of pregnancies by ultrasound -> early diagnosis of hydatidiform mole nowadays mainly during the first trimester of pregnancy.

❖ **Signs and symptoms** are less dramatic in partial mole compared to complete moles and they include:

- I. Vaginal bleeding during the 1st trimester of pregnancy (m/c), so when the patient has a positive HCG test thinking normally that she is pregnant, and during the calculated first trimester, she experiences multiple attacks of vaginal bleeding.
- II. Elevations of hCG in the maternal blood
- III. Hyperemesis (severe nausea and vomiting)
- IV. absence of fetal parts by ultrasound
- V. Passage of vaginal tissues described as grape like vesicles
- VI. Pre-eclampsia تنسم الحمل
- VII. Uterus size looks larger than expected for normal pregnancy and this is usually correct in cases of complete mole.

This table is a brief comparison between complete mole and partial mole:

Feature	Complete Mole	Partial Mole
Karyotype	46,XX (46,XY)	Triploid (69,XXY)
Villous edema	All villi	Some villi
Trophoblast proliferation	Diffuse; circumferential	Focal; slight
Atypia	Often present	Absent
Serum hCG	Elevated	<u>Less elevated</u>
hCG in tissue	++++	+
Behavior	2% choriocarcinoma	Rare choriocarcinoma

- HCG stands for human chorionic gonadotropin, and its elevation either in serum or tissue are seen in both types of molar gestations, but they are more pronounced in cases of complete mole.

The general behavior or prognosis of these diseases are also slightly different. Actually, it is slightly worse for a complete mole, because there is a 2% risk of developing a malignancy (known as choriocarcinoma) in those trophoblasts, while the behavior in partial mole is somewhat better and rarely develops into choriocarcinoma.

Treatment

1. stabilize patient's condition; if a patient experiences massive hemorrhage that is compromising her vital signs, then she needs to be stabilized and given blood units, & If the patient is experiencing preeclampsia because of her molar pregnancy, then her blood pressure needs to be stabilized.
2. Surgical evacuation of the uterine contents should be undertaken.
3. Close monitoring of serum HCG (because HCG is tumor marker for those trophoblastic diseases) and if its levels are persistently high, then further investigations must be done to rule out invasive mole or malignancy.

Prognosis

complete moles:

- 80% to 90% would be cured by surgical management alone and the patient would experience no recurrence.
- less than 10% would progress into invasive mole (invades myometrium).
- 2% to 3% would develop to more serious type of trophoblastic disease, which is choriocarcinoma.

Partial mole : better prognosis and rarely gives rise to choriocarcinomas.

Choriocarcinoma

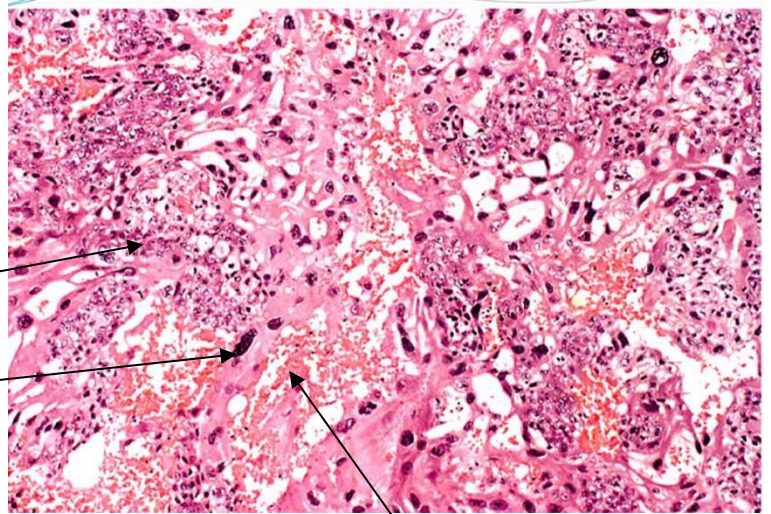
- Very aggressive malignant tumor that arises from gestational chorionic epithelium or from gonads. (we will discuss the gestational type)
- rare (1 in 30,000 preg); more common in Asian and African countries.
- Risk greater before age 20 and after age 40.
- Risk factors include complete hydatidiform and abnormal gestations like abortions. So, 50% arise in complete hydatidiform moles; 25% arise after abortion, and most of the rest (20 -25%) arise in normal pregnancy.

Clinically: bloody, brownish discharge and very high titer of hCG in blood and urine. if we have a look at choriocarcinoma tumor in the uterus, we will see that it consists of very hemorrhagic & necrotic masses.

As you can see in the picture, in choriocarcinoma, we have large numbers of 2 shapes of cells:

chorionic villi are not formed; tumor is composed of anaplastic cytotrophoblast and syncytiotrophoblast.

1. **Cytotrophoblasts:** smaller sized cells with a single nucleus and they are wrapped by clusters
2. **Syncytiotrophoblasts:** large numbers of large sized cells that contain multiple nuclei



between these masses of tumor cells, we have large amounts of **blood (bleeding)**, so as we said these tumors are known for being very hemorrhagic and necrotic.

Prognosis:

- Aggressive disease
- widespread dissemination via blood
- The favored sites of metastasis are the lungs (50%), vagina, brain, liver, and kidneys.
- Lymphatic invasion is uncommon
- Despite its extreme aggressiveness, it has a good response to chemotherapy, that is why the survival rates have been rising.

Past Papers

1-ONE is true about hydatidiform mole:

- a. Serum hCG is higher in partial moles than in complete moles
- b. Complete moles have a lower risk for development of choriocarcinoma
- c. Partial mole's most classic karyotype is 46, XX
- d. Complete mole has a diploid karyotype that is entirely paternal
- e. Partial mole never contains fetal parts

2-All of the following are associated with complete moles and not partial moles except:

- a. Diploid (46, XX)
- b. Diploid (46, XY)
- c. Fetal parts are never found
- d. Triploid (69, XXY)

3-Which of the following statements is true?

- a. Cervical carcinoma is the most frequent cancer in women
- b. Choriocarcinoma is chemosensitive so it can be treated with chemotherapy
- c. Non-invasive intraepithelial neoplasia is treated with surgery
- d. Mild dysplasia is confined to the epithelium and equivalent to carcinoma in situ

4-ONE is a correct description of the trophoblastic condition that carries the karyotype (69, XXY):

- a. A neoplasm composed of syncytiotrophoblasts and cytotrophoblasts
- b. All genetic makeup of cells is coming from paternal origin
- c. An abnormal gestation containing both maternal and paternal DNA
- d. A type of tumor with large epithelioid trophoblastic cells
- e. A type of gestation that arises from implantation within fallopian tubes

Answers: 1. D 2. D 3. B 4. C