THE UNIVERSITY OF JORDAN

Trophoblastic diseases

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Trophoblastic diseases

- A group of rare diseases that involve abnormal growth of cells inside a 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". In time, these will develop into placenta that will protect and nourishes the growing fetus.
- Trophoblastic diseases consist of several types; they can be benign or malignant

Types of trophoblastic diseases

- Hydatidiform mole
- Invasive mole
- Choriocarcinoma
- Placental-site trophoblastic tumor
- Epithelioid trophoblastic tumor

Trophoblastic ??

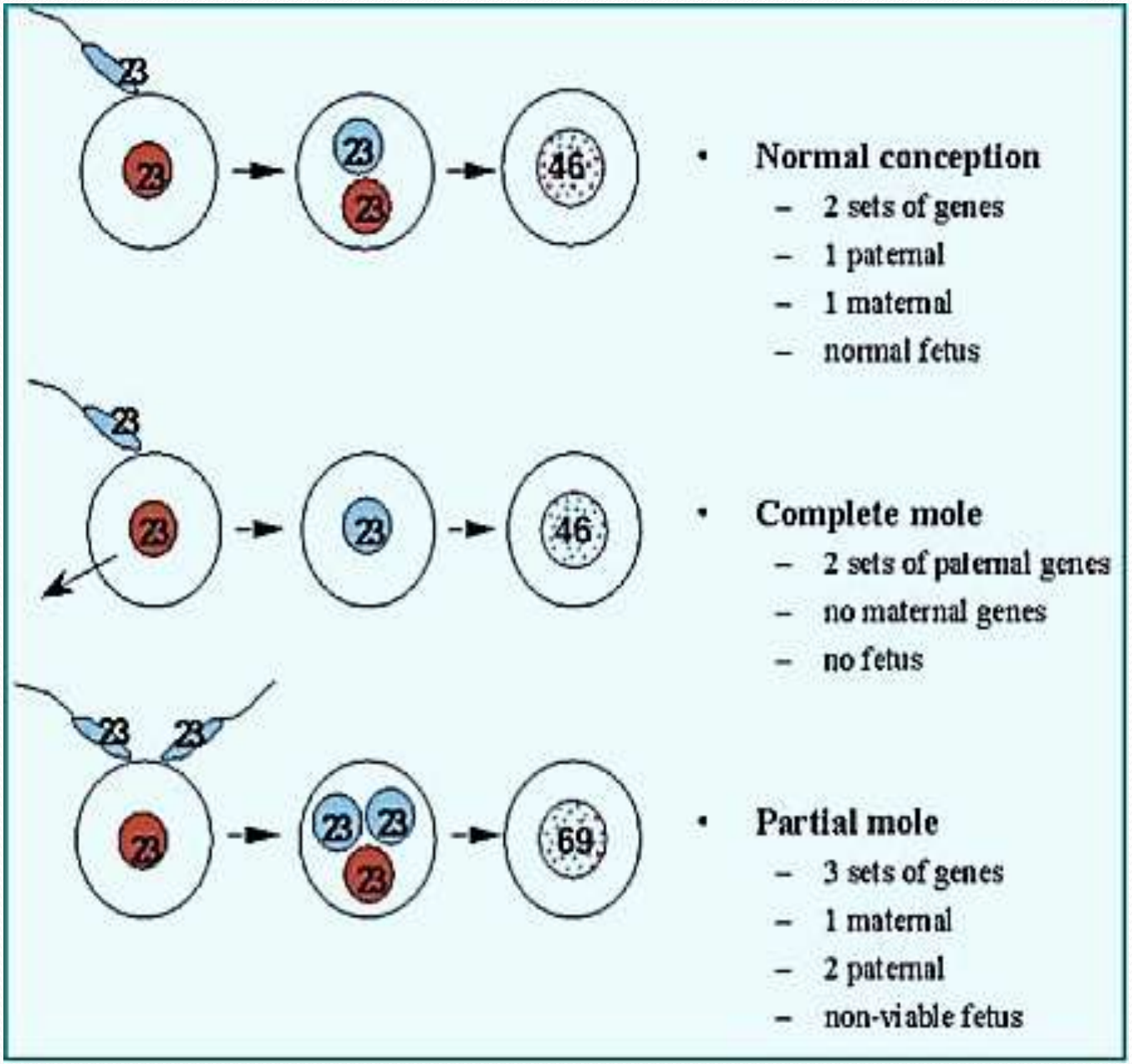
- Trophoblast: is the outer layer of cells of the blastocyst, are present four days after fertilization in humans.
- Trophoblasts provide nutrients to the embryo and develop into a large part of the placenta.
- They may be involved in different types of disorders
- Today we will be discussing 2 types of trophoblastic diseases:

1-Hydatidiform Mole (Molar pregnancy)

2- Gestational Choriocarcinoma

Hydatidiform Mole

- 2 forms of abnormal gestational processes, result from abnormal fertilization:
- 2 types:
- **complete mole:** an empty egg is fertilized by two spermatozoa (or a diploid sperm), yielding a **diploid** karyotype composed of entirely paternal genes
- **partial mole:** a normal egg is fertilized by two spermatozoa (or a diploid sperm), resulting in a **triploid** karyotype with a predominance of paternal genes

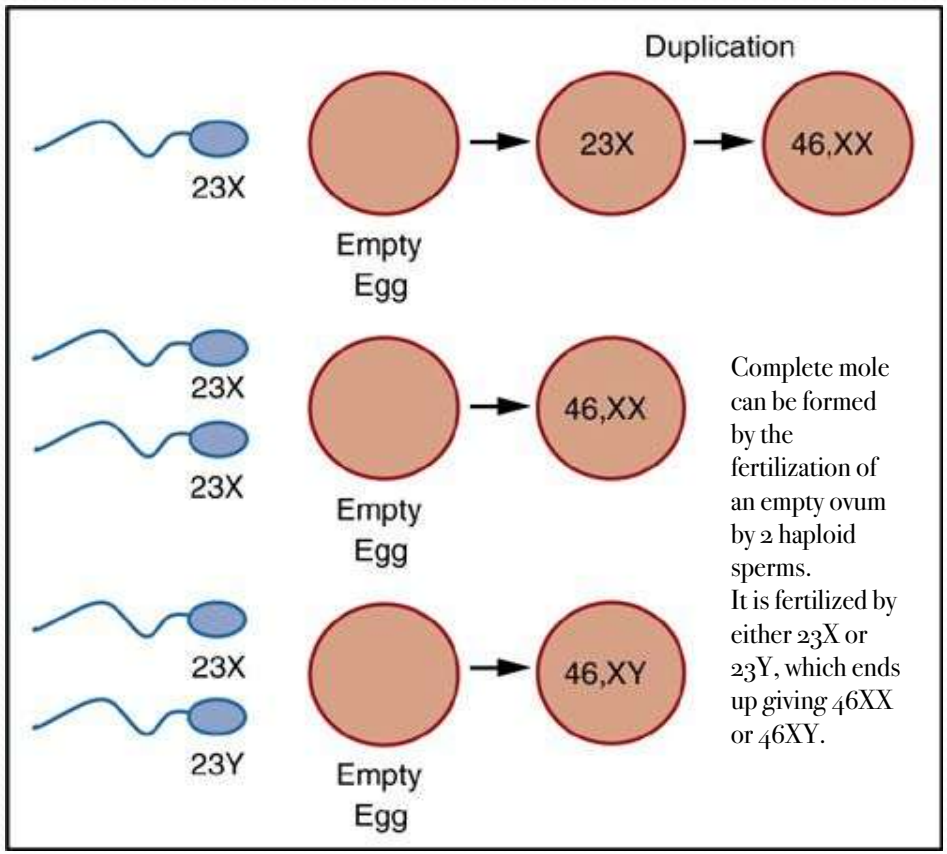


- In normal conception, a single sperm, which is haploid (contains 23 chromosomes), would fertilize a single ovum that is also haploid.
- The result is two sets of genes, one paternal, one maternal, totaling 46 chromosomes.
- This leads to the production of a normal fetus.

- In the case of a complete mole (a case of abnormal fertilization), a haploid sperm would fertilize an empty ovum, meaning this ovum is abnormal in that it has lost its maternal DNA, such that the sum of chromosomes inside the ovum before fertilization is zero.
- The haploid sperm would fertilize the empty egg and duplicate its DNA content, ending up with 46 chromosomes, all of paternal origin.
- So we have 2 sets of paternal genes, with no maternal genes.
- In this case, no fetus will develop.

- In the case of partial mole, dispermy occurs, where 2 haploid sperms would fertilize a single normal haploid ovum.
- Now, the fertilized ovum contains 3 sets of genes, 2 of which are paternal.
- The fertilized ovum ends up having 69 chromosomes, not normal.
- Even if the fetus developed early on, it will not continue to develop, it won't be viable, therefore it results in non-viable fetus.

Complete mole

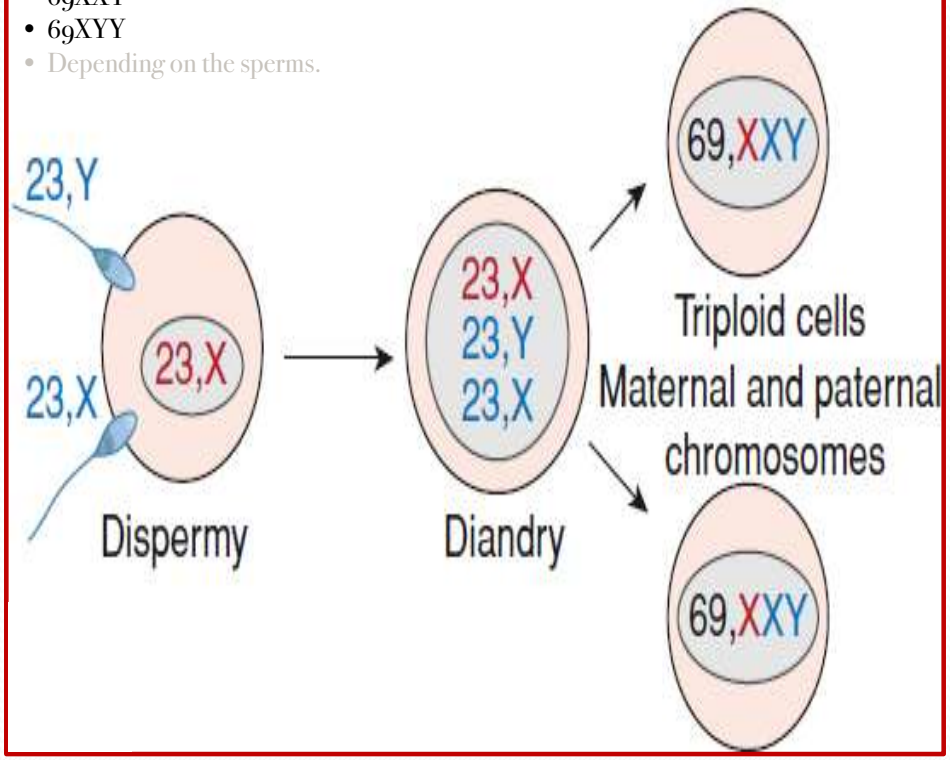


Complete mole can be formed by the fertilization of an empty ovum by 2 haploid sperms.
It is fertilized by either 23X or 23Y, which ends up giving 46XX or 46XY.

Partial mole

In this case, the possible karyotypes include:

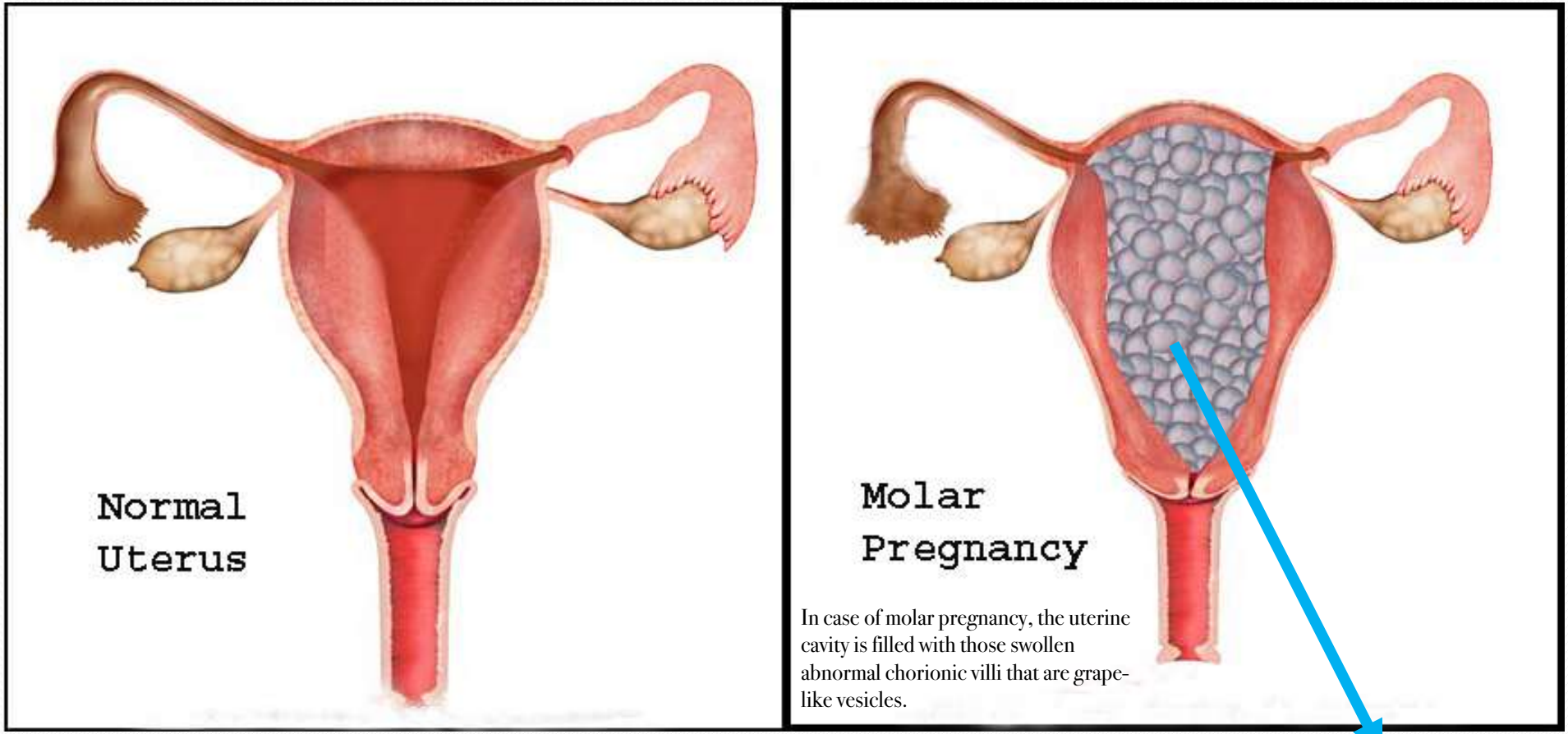
- 69XXX
- 69XXY
- 69XYY
- Depending on the sperms.



- ***complete*** **hydatidiform mole→** does not permit embryogenesis = never contains fetal parts, and the chorionic epithelial cells are diploid (46,XX or, uncommonly, 46,XY).

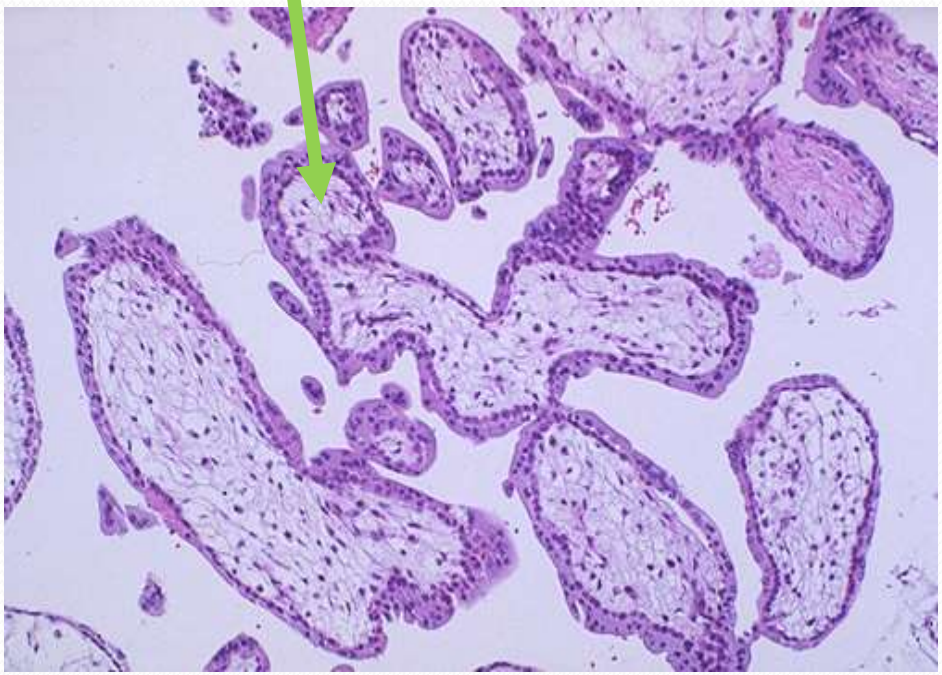
- ***partial*** **hydatidiform mole →** compatible with early embryo formation and may contain fetal parts, has some normal chorionic villi, and is almost always triploid (e.g., 69,XXY).

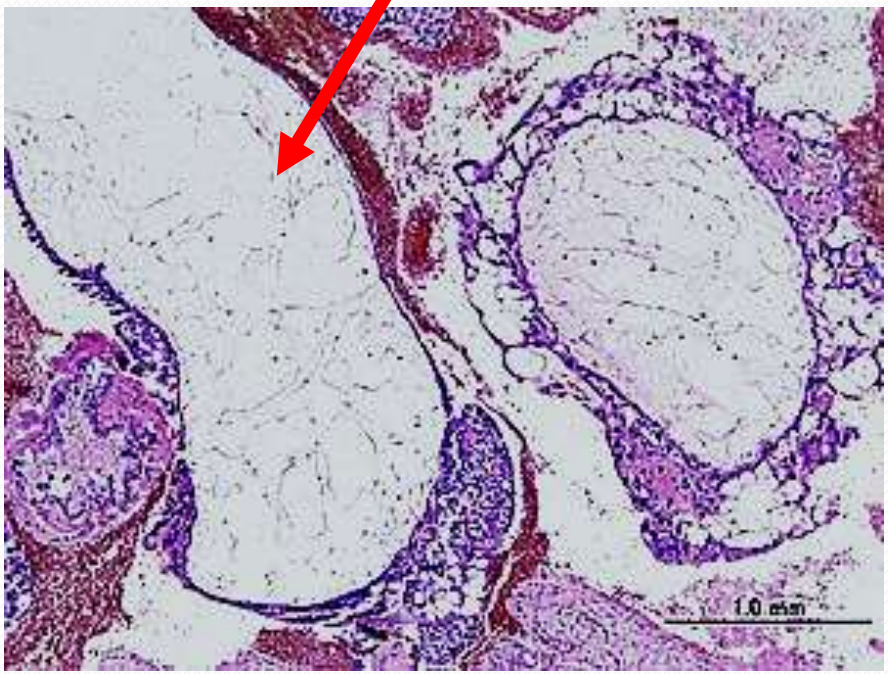
Normal uterus vs mole pregnancy



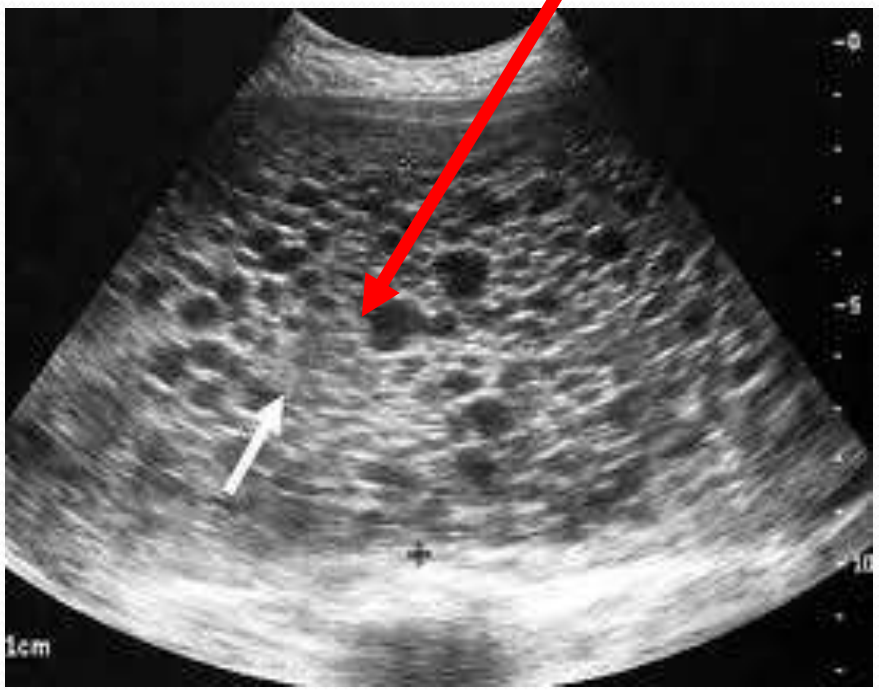
Normal Pregnancy versus Mole – histology

Notice the difference in size between the normal chorionic villi and those of the molar pregnancy that are markedly swollen and are grape-like vesicles.





Normal Pregnancy versus Mole – Ultrasound

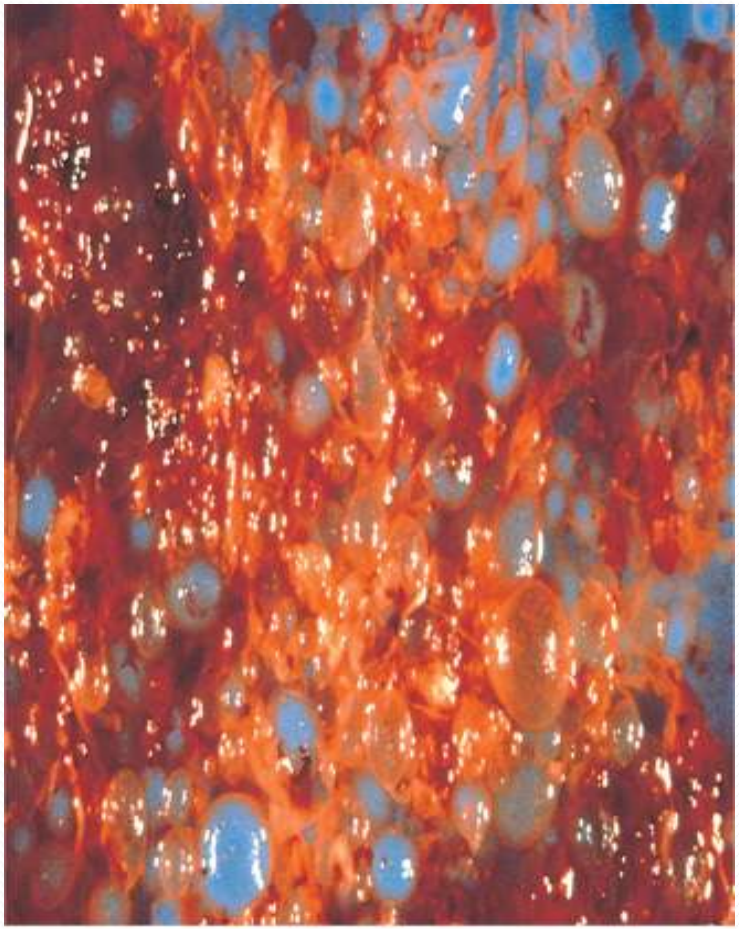


Vesicles

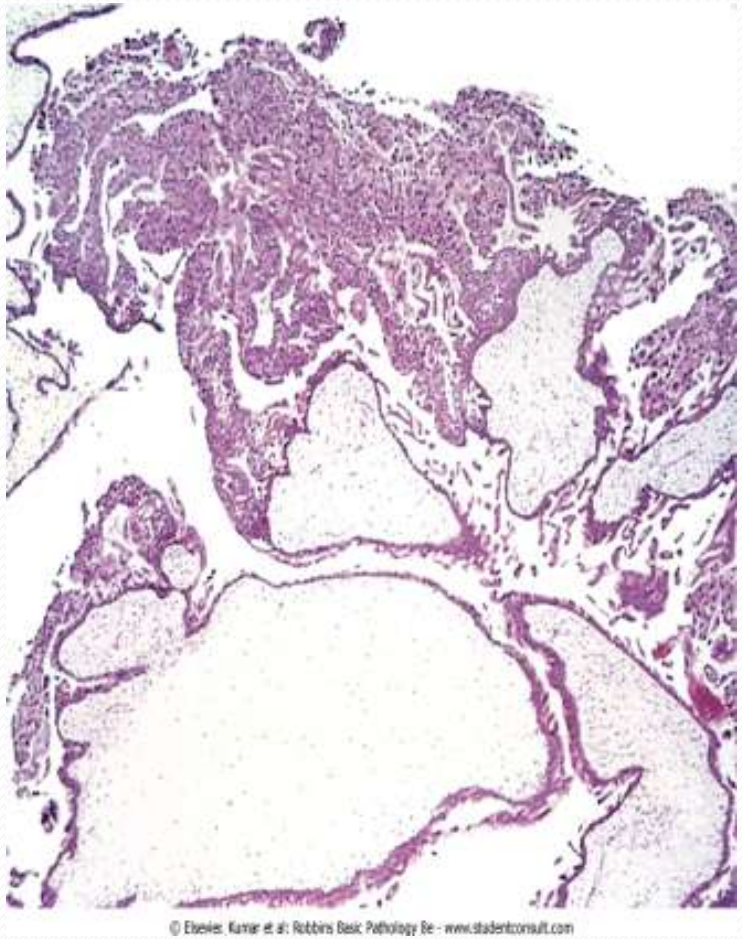
"Snow storm"

- In normal pregnancy, can see the fetus normally with its structures.
- While in molar pregnancy, the only thing evident are vesicles, this morphology is described as "snow storm."

Morphology: cystically dilated chorionic villi (grapelike structures); villi are covered by varying amounts of mildly to highly atypical chorionic epithelium



Vesicles



- Gross is cystically dilated chorionic villi forming grape-like structures
- Under the microscope, a vesicle shows the dilated swollen chorionic villus covered by large amounts of atypical chorionic villi.

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	Less elevated
hCG in tissue	++++	+
Behavior	2% choriocarcinoma Slightly worse prognosis in the case of a complete mole.	Rare choriocarcinoma

Seen in both types of molar gestations but more pronounced in cases of complete mole.

- **incidence** → 1 to 1.5 per 2000 pregnancies; higher incidence in **Asian** countries.
- Moles are most common **before <u>maternal</u>** age 20 years and **after** age 40 years
- Early monitoring of pregnancies by ultrasound → early diagnosis of hydatidiform mole. During the first trimester of pregnancy.
- Clinically: Elevations of hCG in the maternal blood and absence of fetal parts by ultrasound

Signs and symptoms

- Vaginal bleeding during 1st trimester of pregnancy (m/c)
- Elevations of hCG in the maternal blood
- Hyperemesis (severe nausea & vomiting)
- absence of fetal parts by ultrasound
- Passage of vaginal tissue described as grape-like vesicles
- Pre-eclampsia
- Uterus size looks larger than expected for a normal pragnancy
- **Less dramatic in partial mole compared to complete mole**

Most common presentation, with positive hCG test in urine or blood, so she thinks that she's pregnant.

Dilated abnormal chorionic villi.

This is usually in complete mole.

Treatment

- Stabilize patient condition
- Surgical evacuation of uterine contents
- Close monitoring of serum hCG levels → if persistently high → further evaluation to role out invasive mole or malignancy

hCG level is considered a tumor marker for those trophoblastic diseases.

- If patient is experiencing massive hemorrhage that is compromising the vital signs, the patient first needs to be stabilized, given transfusions.
- Also, if patients is experiencing preeclampsia, her hypertension needs to be stabilized.
- Then we move to step 2:

- **Prognosis:**
- **complete moles:**

- 80% to 90% → no recurrence Cured by surgical management alone.
- 10% → invasive mole (invades myometrium)
- 2% to 3% → choriocarcinoma.

- **Partial moles:**
- better prognosis and rarely give rise to choriocarcinomas.

Gestational Choriocarcinoma

- very aggressive malignant tumor arises from gestational chorionic epithelium or from gonads.
- rare (1 in 30,000 preg); more common in Asian and African countries.
- Risk greater before age 20 and after age 40.
- 50% arise in complete hyaditidiform moles; 25% arise after an abortion, and a few in normal pregnancy (25%)

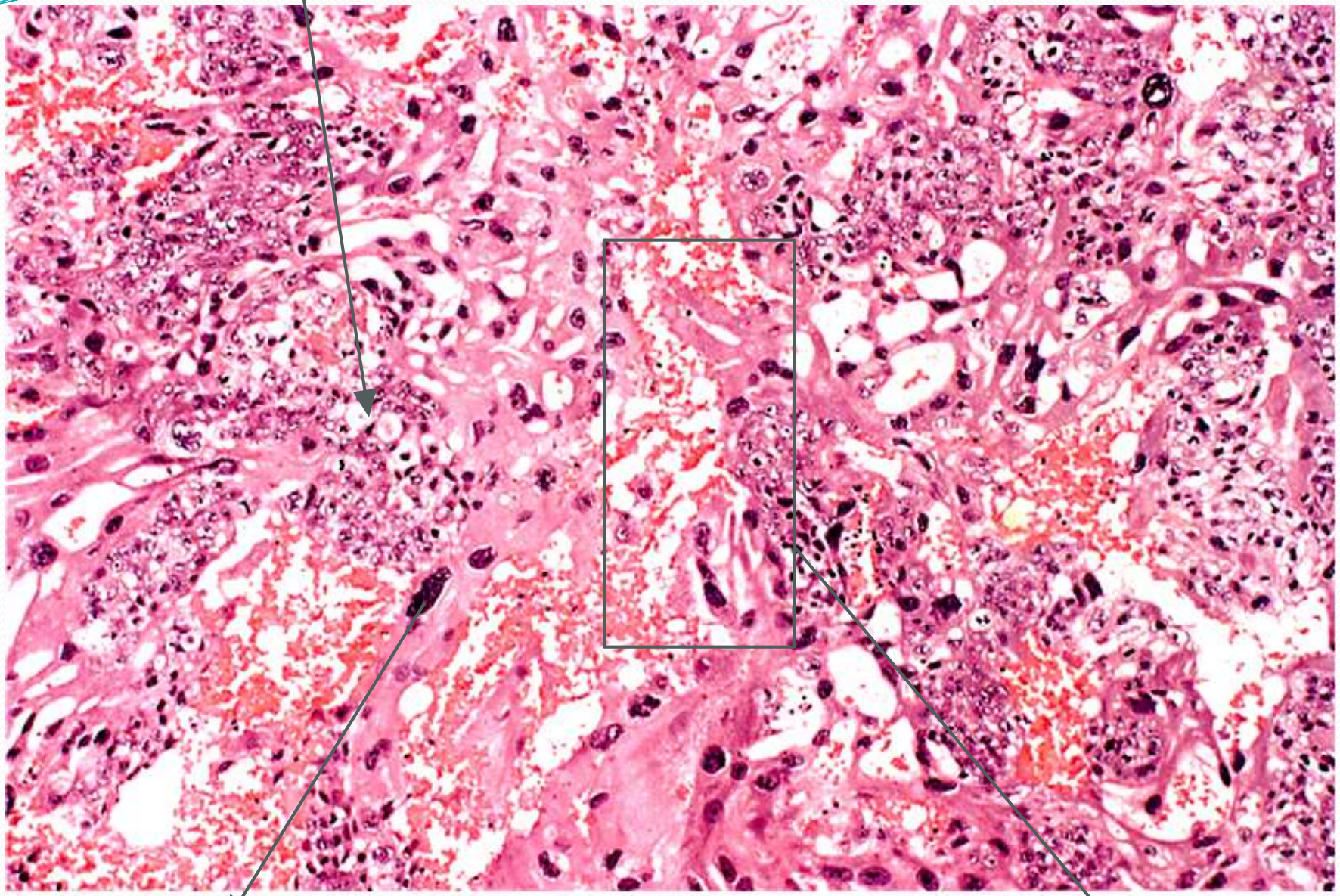
Complete hyaditidiform moles and abnormal gestations like abortions are risk factors.

- Clinically: **bloody, brownish discharge** and **very high titer of hCG** in blood and urine.
- very hemorrhagic, necrotic masses within the myometrium
- chorionic villi are not formed; tumor is composed of anaplastic cytotrophoblast and syncytiotrophoblast.

Choriocarcinoma

Cytotrophoblast: Smaller sized cells that has a single nucleus and those cells are wrapped by clusters (of syncytiotrophoblasts).

Choriocarcinoma is a tumor in which the pluripotential neoplastic germ cells differentiate into cells resembling placental **trophoblasts.** The primary tumors often are small and nonpalpable, even in patients with extensive metastatic disease. The tumor is composed of sheets of small cuboidal **cytotrophoblast like cells** that are irregularly intermingled with or capped by large, eosinophilic **syncytiotrophoblast like cells** containing multiple dark, pleomorphic nuclei (Fig. 18.8). HCG can be identified in the syncytiotrophoblastic cells by immunohistochemical staining.



Syncytiotrophoblasts: Other types of cells large in size and contain multiple nuclei.

In between these masses of tumor cells, there is large amount of bleeding (these tumors are very hemorrhagic and necrotic.)

- **Prognosis**: Gestational type choriocarcinoma.
- widespread dissemination via **blood** to lungs (50%), vagina, brain, liver, and kidneys.
- Lymphatic invasion is **uncommon**
- Despite extreme aggressiveness, good response to chemotherapy. So survival rates are rising.