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Pathology GUS

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Trophoblastic diseases

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Trophoblasts : the cells that differentiate from the fertilized ovum and later on will form a large part of the placenta , and they are responsible for providing nutrients to the developing embryo in the earliest stages of the embryonal development which is the same role of the placenta which will nourish , support and protect the developing fetus

الحمل العنقودي

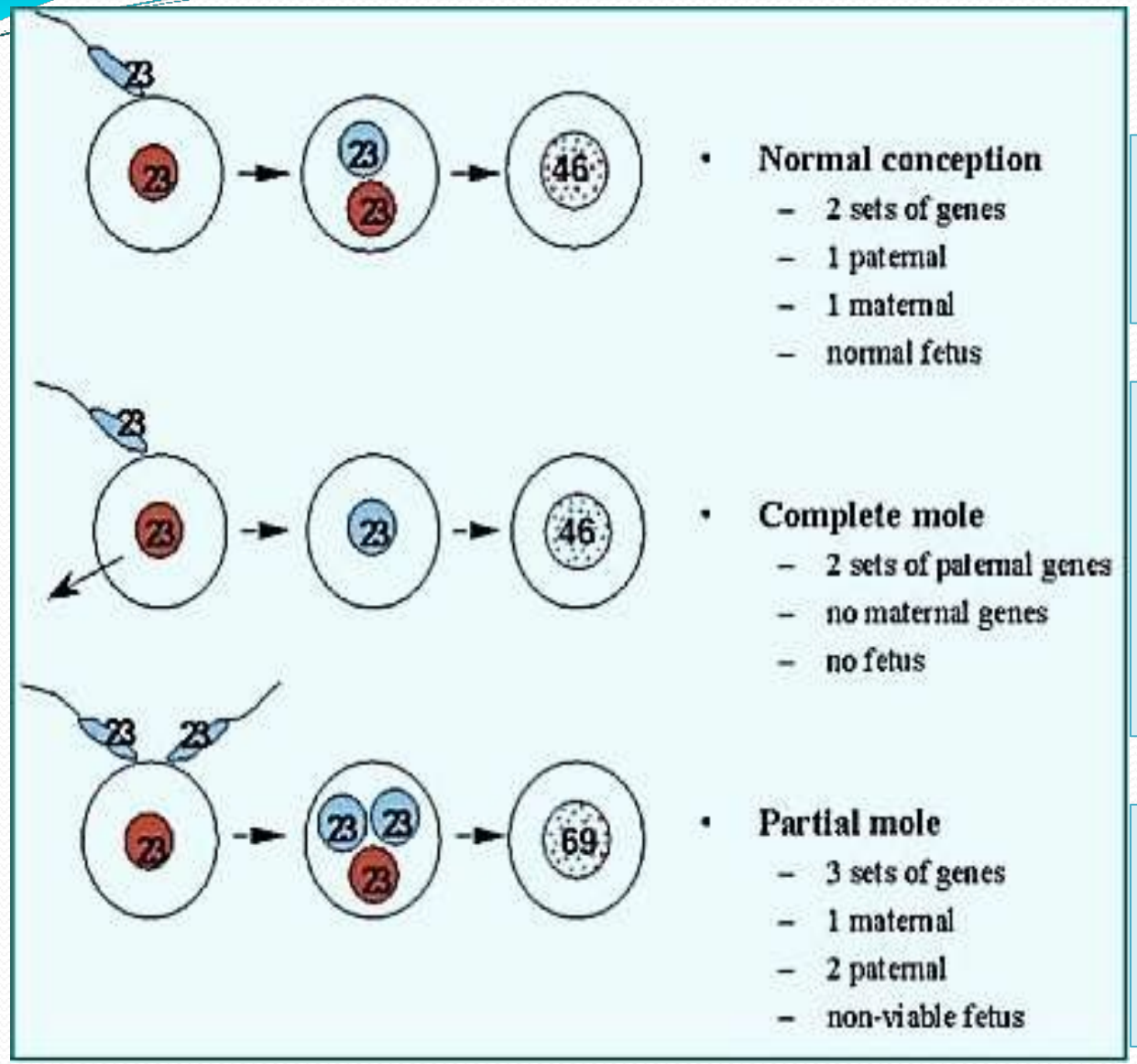
Hydatidiform Mole

= molar pregnancy

The main problem is in the fertilization

Complete and partial : regarding the no. Of chromosomes

- 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

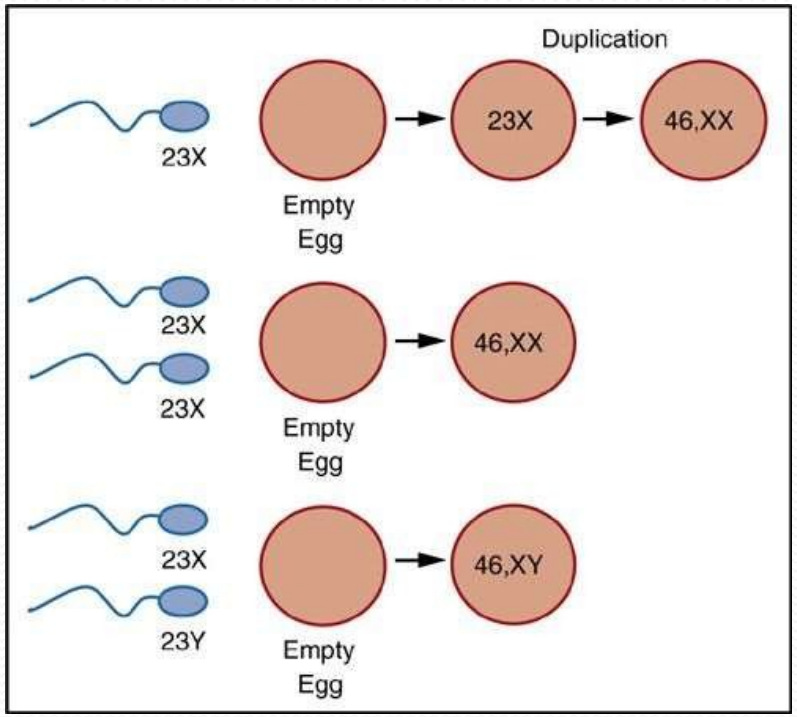


The normal conditions : an oocyte is fertilized by one sperm .both of them has a haploid no. of chromosomes

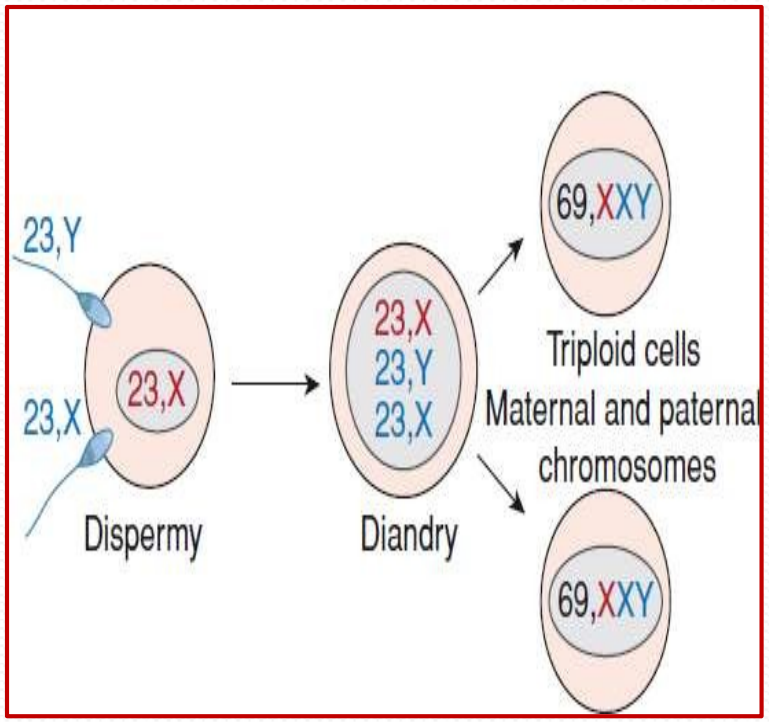
The oocyte is empty, a haploid sperm fertilizes the oocyte then duplication of the chromatin occurs or 2 sperms fertilize the oocyte . and the result is 46 paternal chromosomes, all of the DNA content is from the father and consequently there is no fetus

A normal haploid oocyte is fertilized by two sperms , so we have 3 sets of chromosomes (69) , 2 of them are paternal and one is maternal and the result is non-viable fetus

Complete mole



Partial mole



To remember

- ✓ Dispermy = 2 sperms
- ✓ Diandry = 2 sets of paternal DNA content
- ✓ Triploid = 3 sets of chromosomes = 3* 23 = 69
- ✓ Haploid = one set of chromosomes = 23
- ✓ Diploid = 2 sets of chromosomes = 2*23= 46

No maternal DNA = no fetus
Because the maternal DNA is crucial in the development of the fetus

You should know the Karyotype of complete & partial moles

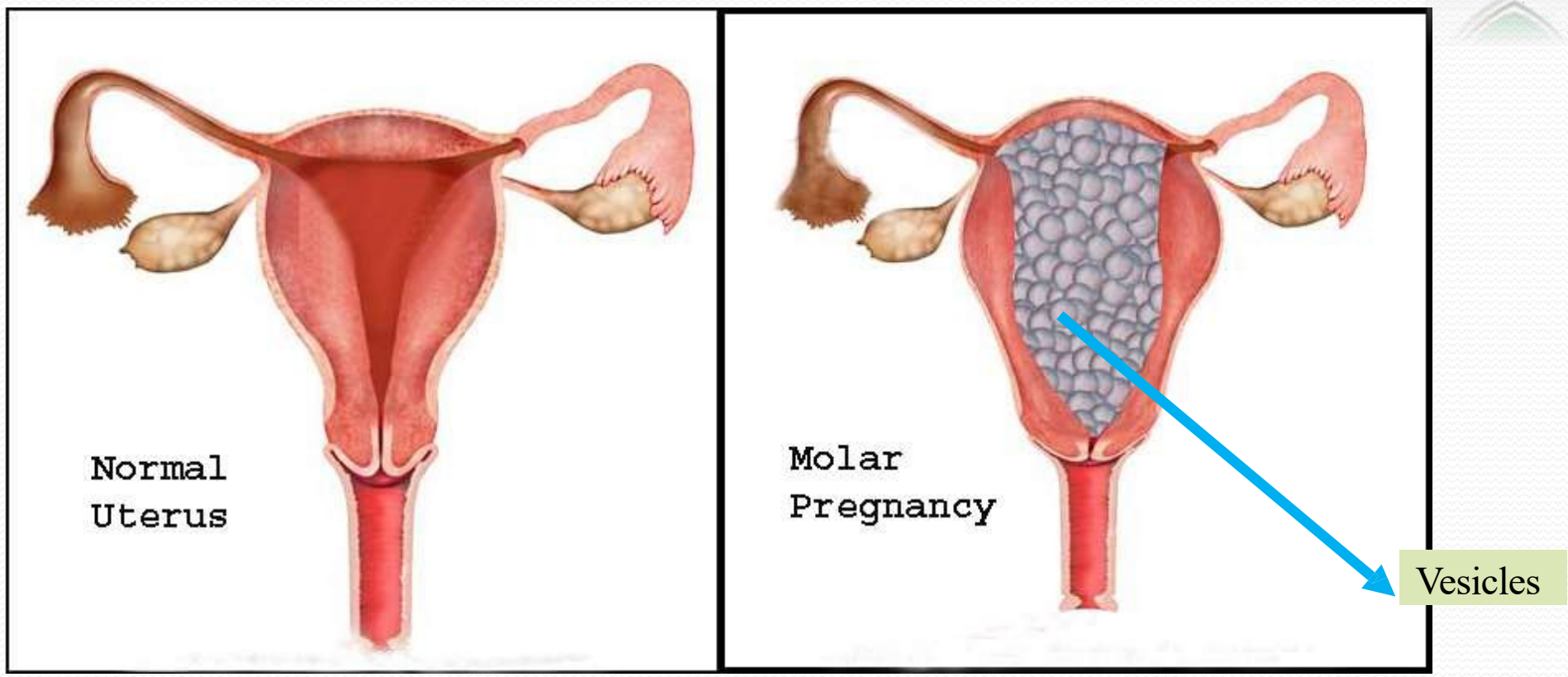
complete **hydatidiform mole→** does not permit embryogenesis = never contains fetal parts, and the chorionic epithelial cells are diploid (46,XX or, uncommonly, 46,XY).

Why there's no 46 YY ?
Because the X chromosomes is crucial for development, so it's too rare to find a case with a Karyotype of YY

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).

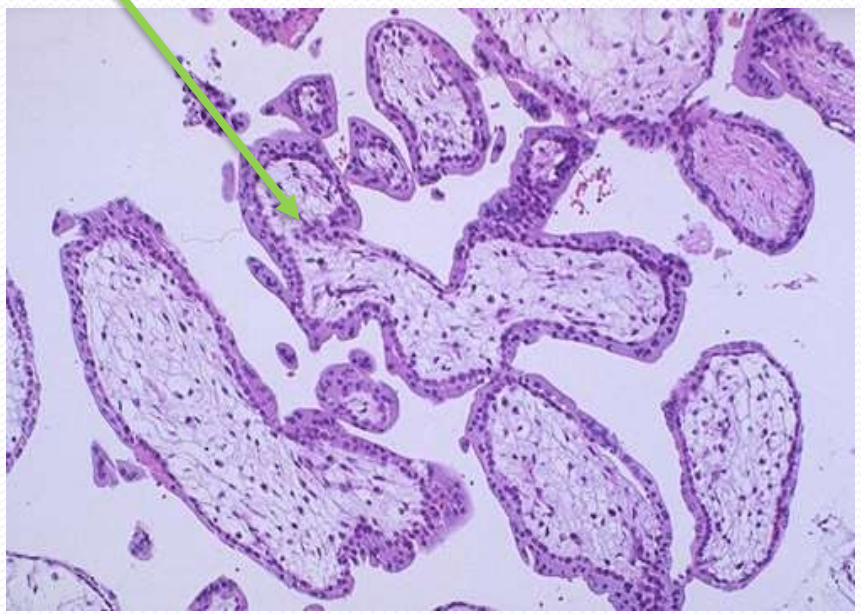
Why we study this process?
It's something that could happen at anytime or anywhere , the percentage of partial or complete mole is about 1/ 1000
And this also differs between different countries and regions , it's slightly more common in Asian countries

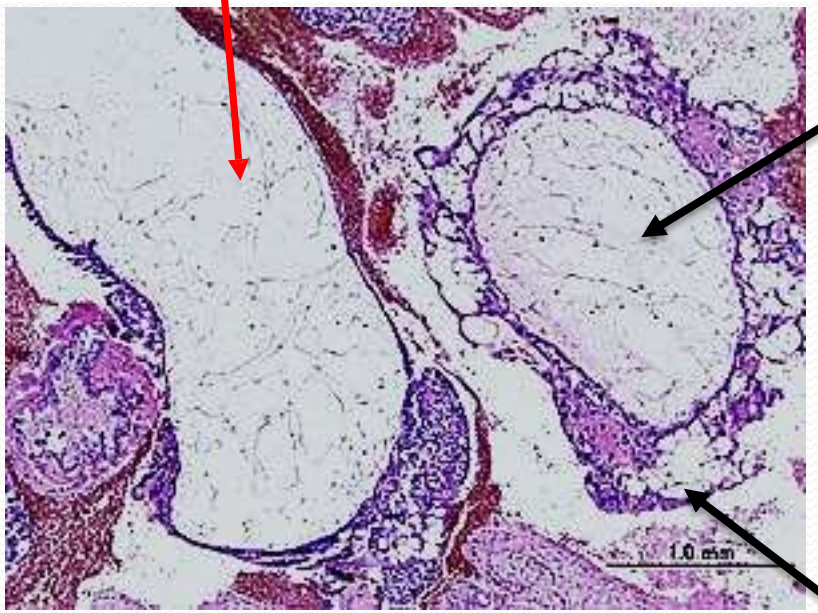
Normal uterus vs mole pregnancy



The uterus is enlarging as any normal pregnancy but instead of having a normal developing fetus we have vesicles (the dilated swollen abnormal chorionic villi) (grape like structures)

Normal Pregnancy versus Mole – histology





Villus

Trophoblastic proliferation

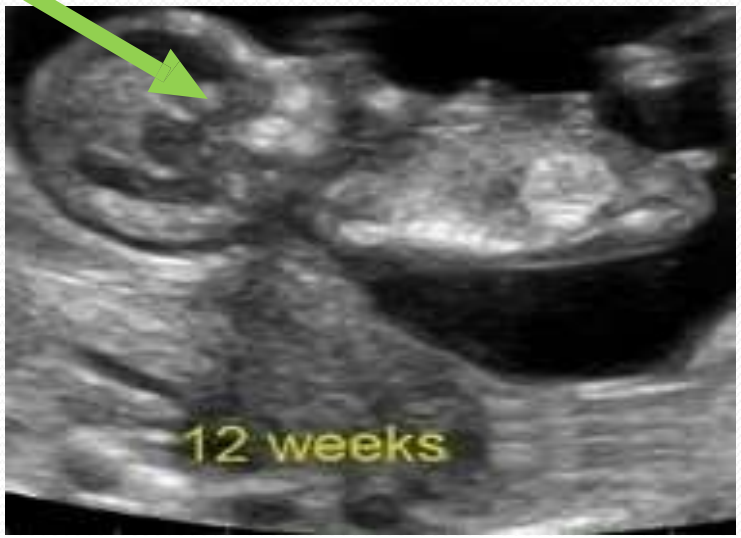
Microscopic pic of chorionic villi in a normal pregnancy versus molar pregnancy

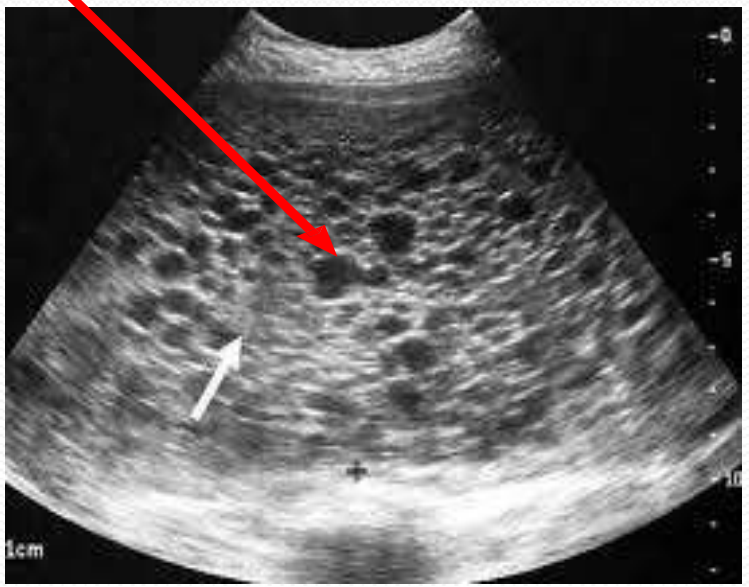
We can notice 2 main differences :

1. The size (it's bigger in molar pregnancy, looks like vesicles)
2. The trophoblastic cells proliferation around the villus in molar pregnancy which is limited in the normal pregnancy

Normal Pregnancy versus Mole – Ultrasound

How do we know that the patient has a molar pregnancy?
The patient is pregnant : she will have amenorrhea like any pregnant lady, and a positive urine or blood pregnancy test [high HCG level (human chorionic gonadotropin) which is produced by trophobalsts], but much higher elevation in molar pregnancy
Then she will go the gynecological clinic to have antenatal care , physical examination of the abdomen and ultrasound examination to the uterus is done





Vesicles
"Snow storm"

In ultrasound we can't see fetus, only what we see is vesicles variable in size described as snow storm appearance

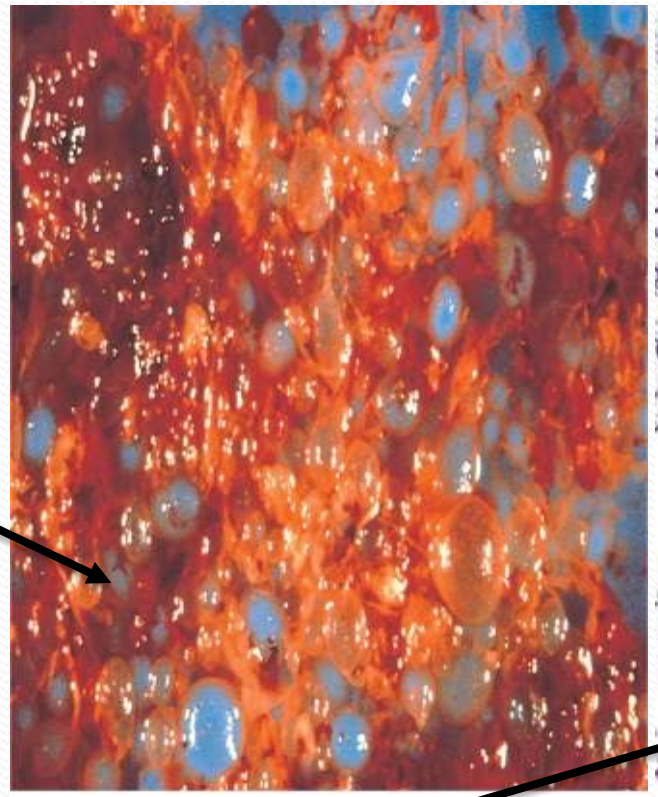
Ultrasound is one of the important diagnostic tools in molar pregnancy

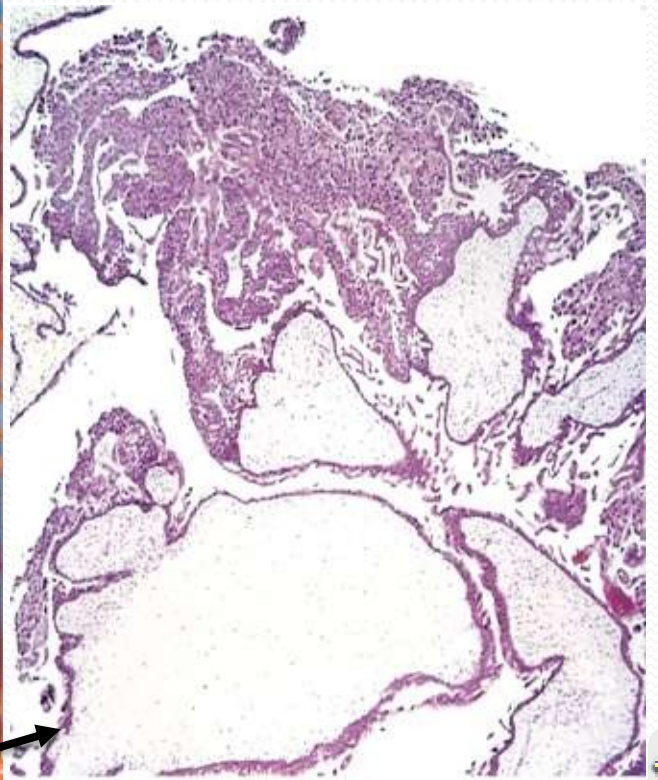
Morphology: cystically dilated chorionic villi (grapelike structures); villi are covered by varying amounts of mildly to highly atypical chorionic epithelium

The Dr will tell the patient that this is an abnormal gestational process that should be terminated by evacuation and dilatation

When she had evacuation of the uterine content we will see these vesicles which are abnormal chorionic villi

When a pathological evaluation under the microscope is done to the vesicles (for confirmation of the diagnosis and differentiation between complete and partial moles) , we see swollen chorionic villi with abnormally proliferating trophoblasts





Vesicles

Imp

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	Rare choriocarcinoma

All of these is more / worse in complete mole

Outcome

A small percentage of molar pregnancies can behave as malignant tumors , cause invasion of the myometrium , rarely can send metastasis and lead to choriocarcinoma

- **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.
- Clinically: Elevations of hCG in the maternal blood and absence of fetal parts by ultrasound

The percentage of abnormalities taking place in the development is more in the extremes of age

Prognosis:

complete moles:

- 80% to 90% → no recurrence

Continue with their lives and have another normal pregnancies

- 10% → invasive mole (invades myometrium)

Tumor that will invade the myometrium and can also send metastasis

- 2% to 3% → choriocarcinoma.

Gestational choriocarcinoma

Partial moles:

better prognosis and

rarely give rise to choriocarcinomas.

What is the difference between invasive mole and choriocarcinoma?

- Choriocarcinoma is collections of cytotrophoblasts and syncytiotrophoblasts without chorionic villi, rapidly metastasize & aggressive
- invasive mole , is the invasion of the mole into the myometrium which should be limited to the Endometrial cavity and this will lead to continuous bleeding and can send metastasis

Choriocarcinoma

- very aggressive malignant tumor arises from gestational chorionic epithelium or from gonads.

Testicular or ovaries

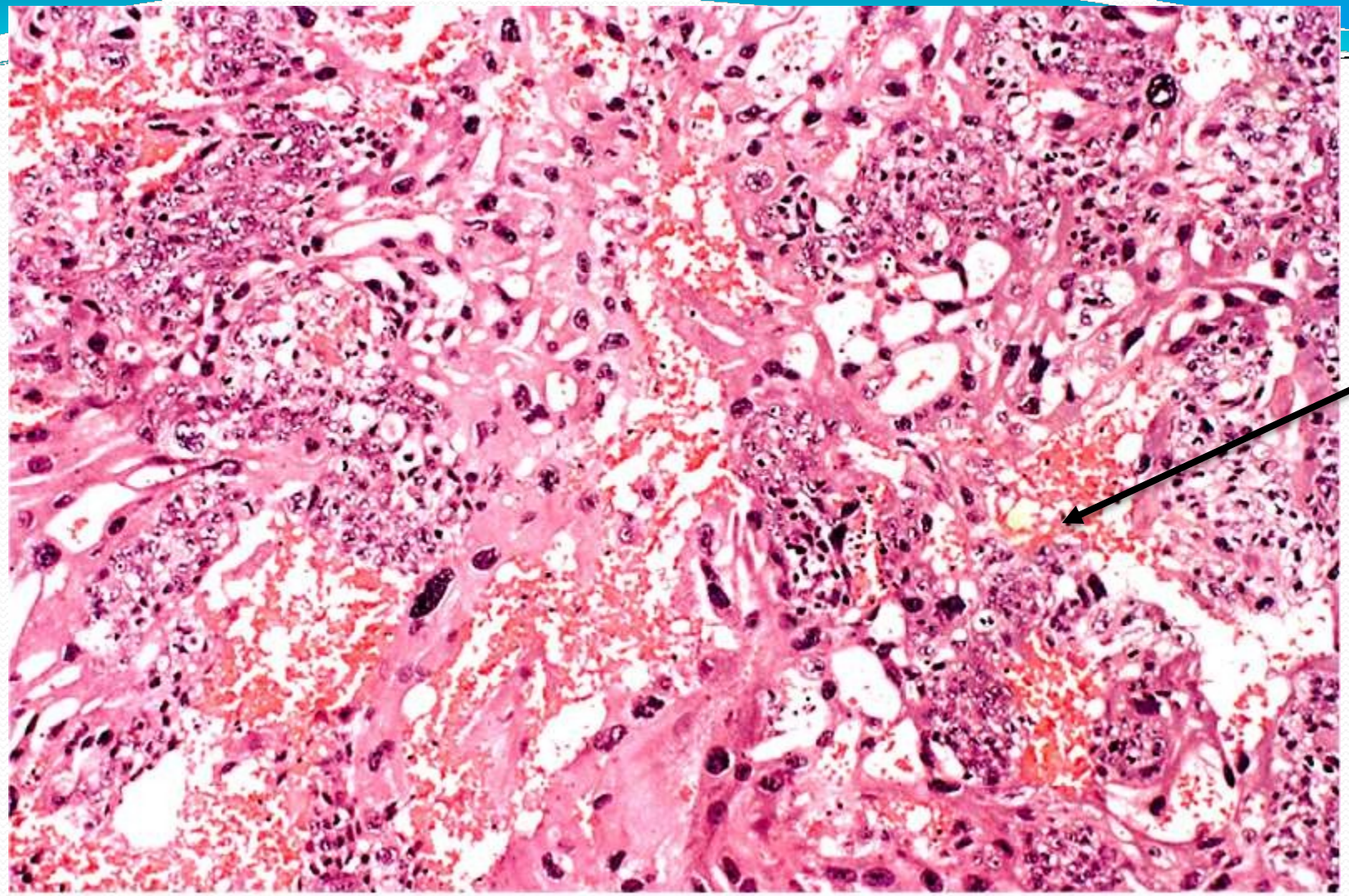
- rare (1 in 30,000 preg); more common in Asian and African countries.

For unknown reasons

- Risk greater before age 20 and after age 40.
- 50% arise in complete hyaditidiform moles; 25% arise after an abortion, and most of the rest in normal pregnancy

Pregnancy is a normal trophoblastic proliferation, sometimes this trophoblastic proliferation can turn into something abnormal or malignant

- Clinically: **bloody, vaginal 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.



Collection of cytotrophoblasts and syncytiotrophoblasts with large amounts of red blood cells (hemorrhage) in between and necrosis

- **Prognosis**:
- widespread dissemination via **blood** to lungs (50%), vagina, brain, liver, and kidneys.
- Lymphatic invasion is **uncommon**
- Despite extreme aggressiveness, good response to chemotherapy.

The prognosis and survival rate is getting better