



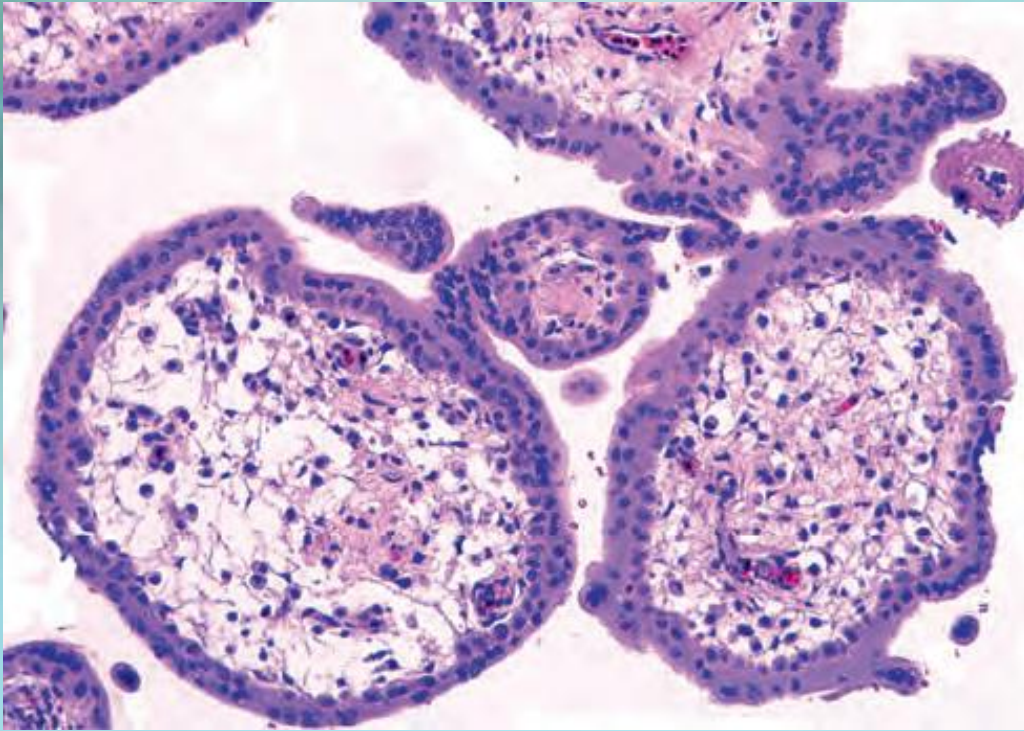
Female Genital Tract Pathology

LEC 4

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Diseases of Pregnancy

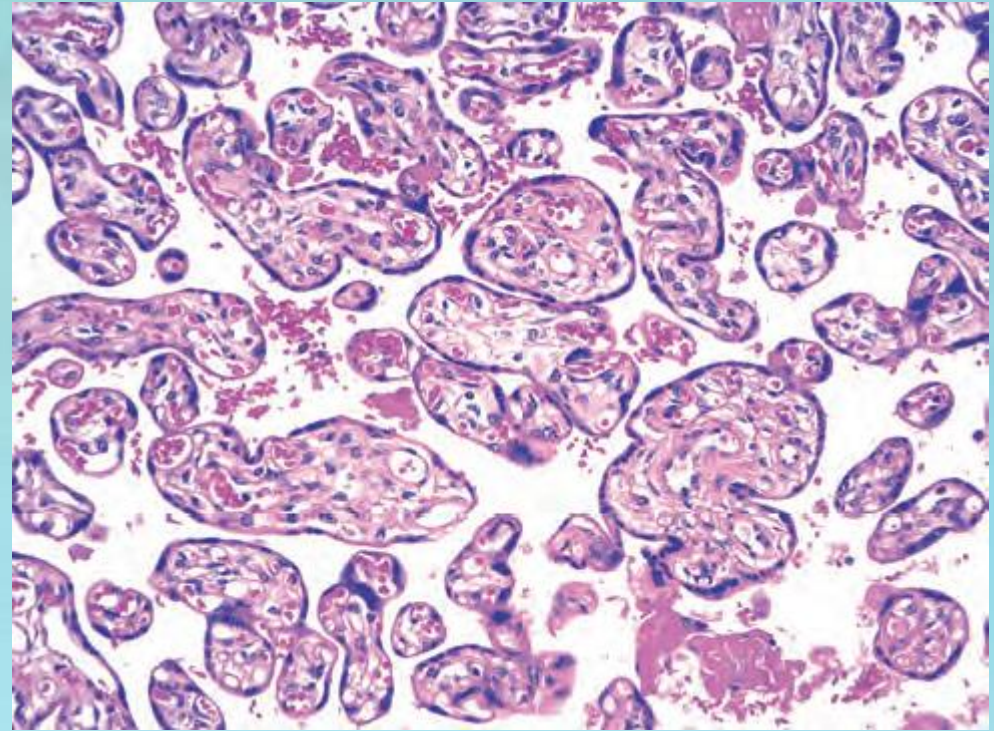
- Diseases of pregnancy and pathologic conditions of the placenta are important causes to morbidity and mortality for both mother and child. These include:
 - Spontaneous abortion
 - Ectopic pregnancy
 - Placental inflammations and infections
 - Abnormalities of Placental Implantation
 - Preeclampsia /eclampsia
 - Gestational trophoblastic diseases.



(A)

Normal placenta.

(A) **First-trimester** chorionic villi composed of delicate mesh of central stroma surrounded by two discrete layers of epithelium—the outer layer consisting of syncytiotrophoblast and the inner layer consisting of cytotrophoblast.



(B)

(B) **Third-trimester** chorionic villi composed of stroma with a dense network of dilated capillaries surrounded by markedly thinned-out syncytiotrophoblast and cytotrophoblast.

Gestational trophoblastic diseases

- **Definition:** spectrum of tumors and tumorlike conditions characterized by abnormal proliferation of placental tissue, either villous or trophoblastic
- They are divided into **three** overlapping morphologic categories:
 - 1-**Hydatiform mole (non invasive mole)**; which is of two types: Complete and Partial
 - 2- **Invasive mole**; Penetrates the uterine wall, produce hemorrhage but does not metastasize.
 - 3- **Choriocarcinoma**: highly malignant metastasize into distant organs.
- **Age incidence:** the risk greater **before 20 & after 40 yr.**
- All these disorders **elaborate human chorionic gonadotropins (hCG)**, which is detected in the blood and urine at levels considerably higher than those found during normal pregnancy, the titers progressively rising from hydatidiform mole to invasive mole to choriocarcinoma.
- This elevation in hCG important in :1-Diagnosis of these diseases 2- it can be used to monitor treatment efficacy.

❖ Hydatidiform mole (H- mole):

Voluminous mass of swollen sometimes cystically dilated chorionic villi and variable trophoblastic proliferation, appear grossly as grape like structure.

- It is of 2 subtypes: A. Complete mole B. Partial Mole

Clinically: painless vaginal bleeding 12-14 week after conception,

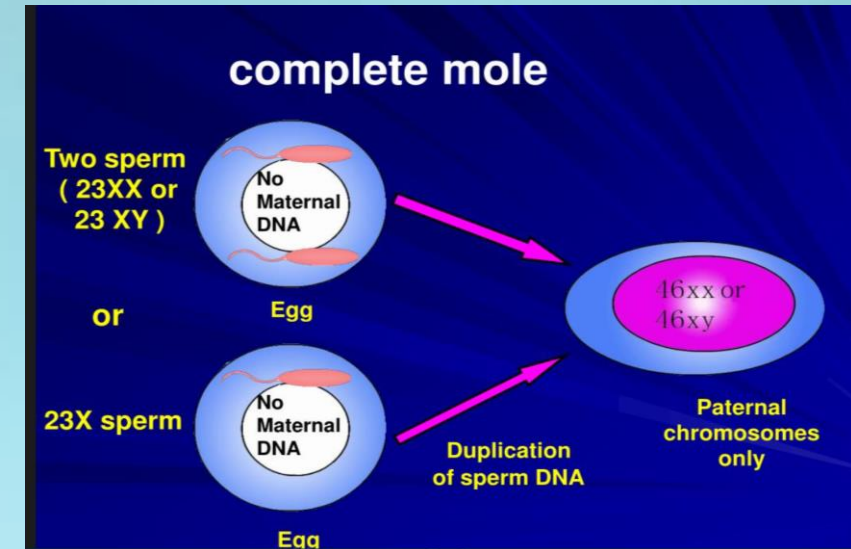
Diagnosis: In both complete and partial moles, elevation of hCG in the maternal blood & urine. and absence of fetal heart sounds are typical.

Follow up after curetting the uterus is done by ultrasound examination and the serial measurement of hCG hormone monitored for 6 months to 1 year to ensure that hCG levels decrease to nonpregnant levels.

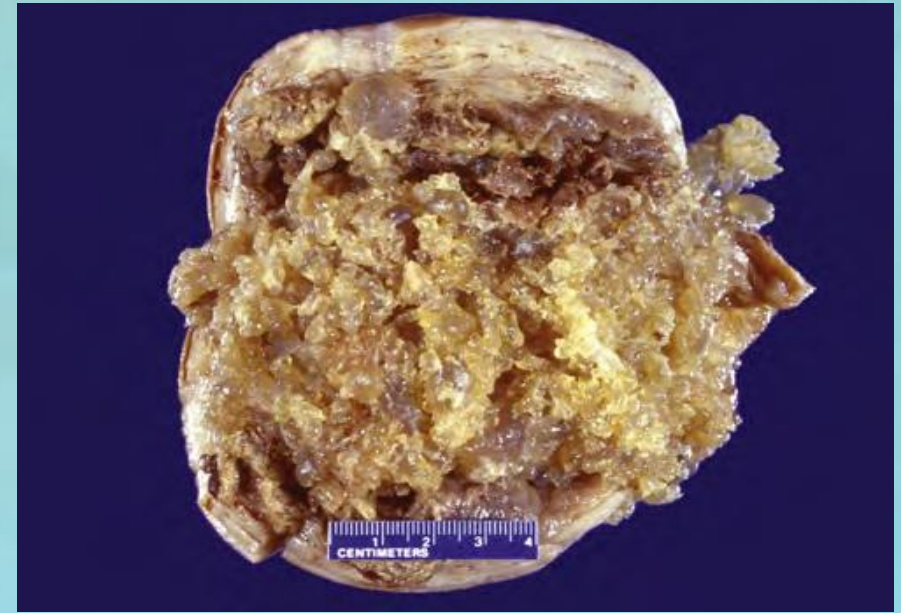
Continuous elevation of hCG may be indicative of persistent or invasive mole.

A. The Complete H. mole is characterized by:

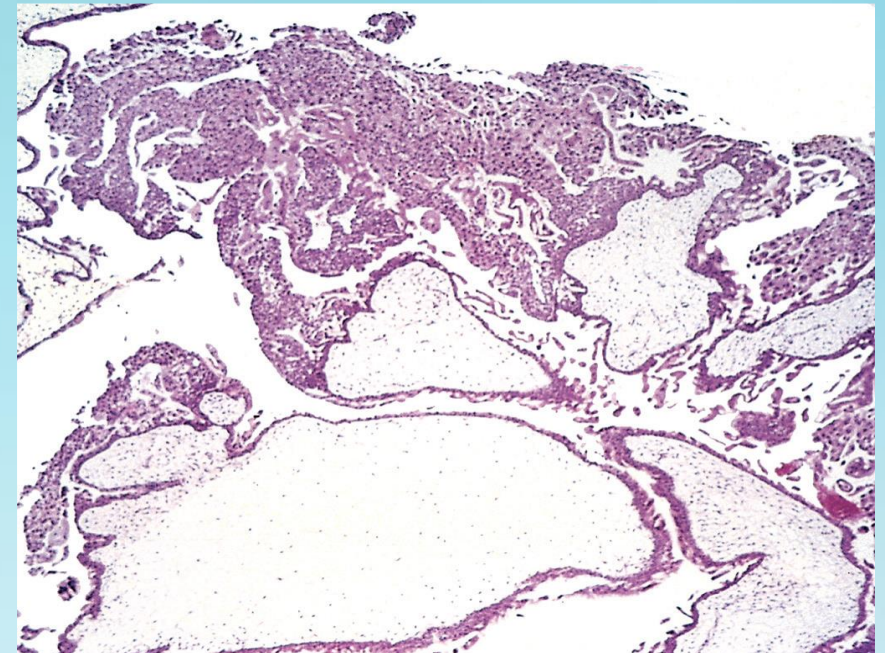
- Results from fertilization of an empty egg (that has lost its female chromosome), and as a result the genetic material is completely paternally derived. (In 90% of cases : **duplication of the genetic material of one sperm**, 10% result from the fertilization of an empty egg by two sperm).
- **karyotype**: The chorionic epithelial cells are **diploid**
- All chorionic villi are abnormal (hydropic changes---cystic dilated).
- Patients have 10 % risk of invasive mole and 2-3 % risk of subsequent choriocarcinoma.



- **Gross:** uterine cavity filled with **delicate friable masses** of thin wall translucent cystic grapelike structures **without fetal parts**.

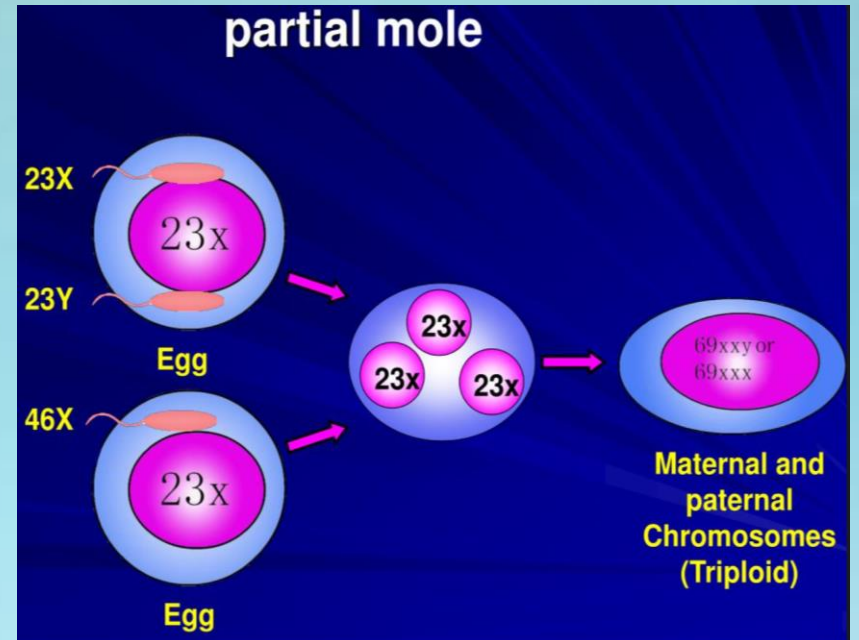


- **Mic.:** almost **all villi are enlarged** and hydropic with a loose, myxomatous, edematous stroma and **circumferential** abnormal proliferation of both cytotrophoblasts and syncytiotrophoblasts.



B. Partial H. mole is characterized by:

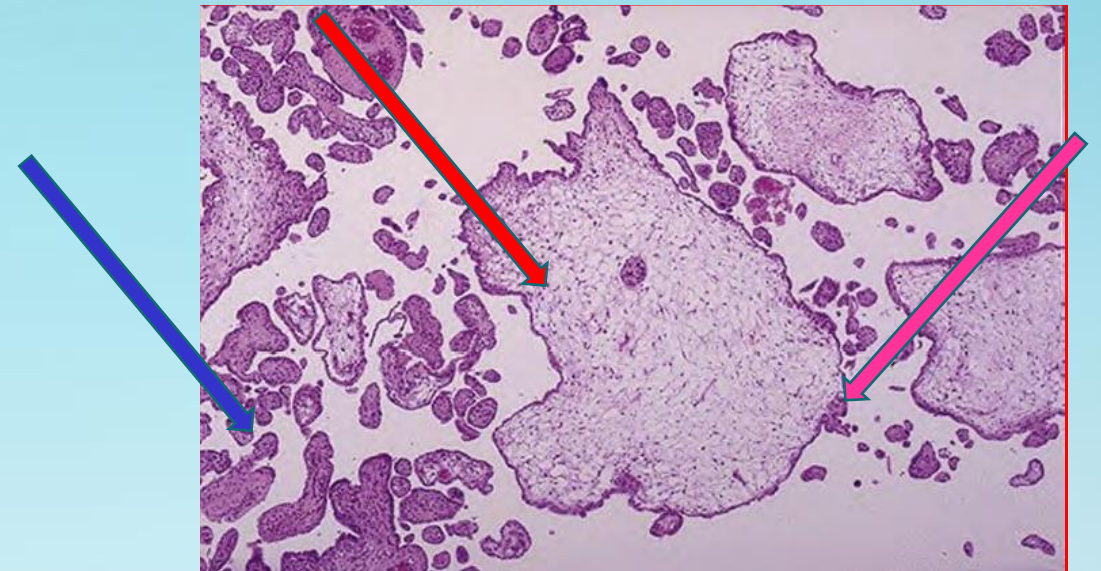
- Result from fertilization of normal egg with two sperm. the karyotype is triploid (e.g., 69,XXY)
- The villous edema involve only some villi & trophoblastic proliferation is focal & slight.
- In partial mole, there are parts of fetus (in complete mole no fetal parts).
- Partial moles have an increased risk of invasive molar disease but are rarely associated with choriocarcinoma.



- **Gross:** hydropic change involving **only** some villi. Fetal tissue may be present.
- **Mic.:** only some of the villi is enlarged and edematous, and the **trophoblastic proliferation is focal and slight.**



In partial moles, some villi appear normal whereas others are swollen and grapelike. There is minimal trophoblastic proliferation.



| Feature | Complete mole | Partial mole |
|------------------------------------|---|---|
| -Karyotype | Diploid (46 XX or 46 XY), two sperms fertilize an empty egg. All genetic material is paternal | -Triploid (e.g 69 XXY). Two sperms fertilize an egg with normal chromosomes |
| Fetal parts | -absent | Usually present with abnormalities |
| Villous edema | -All villi | -Some villi |
| Trophoblastic proliferation | - Diffuse & circumferential | -Focal and slight |
| Serum hCG | - Elevated | - less elevated |
| -Tissue hCG | -++++ | - + |
| Risk of subsequent choriocarcinoma | - 2% | rare |

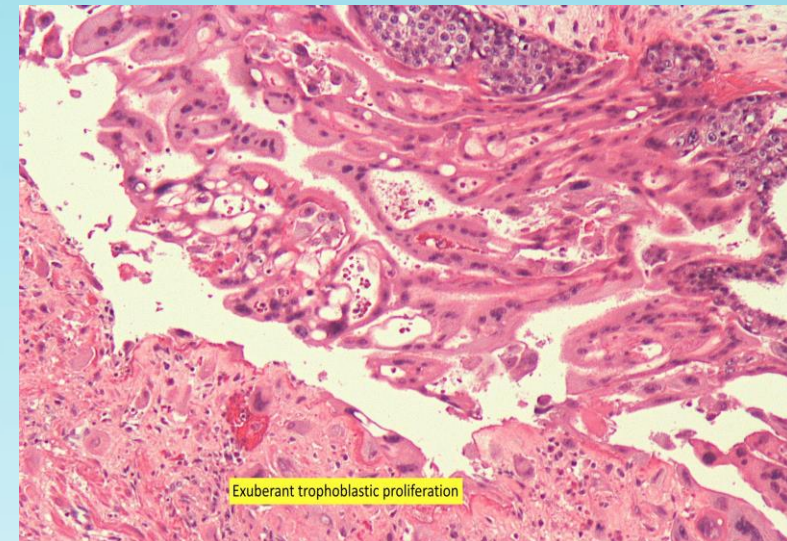
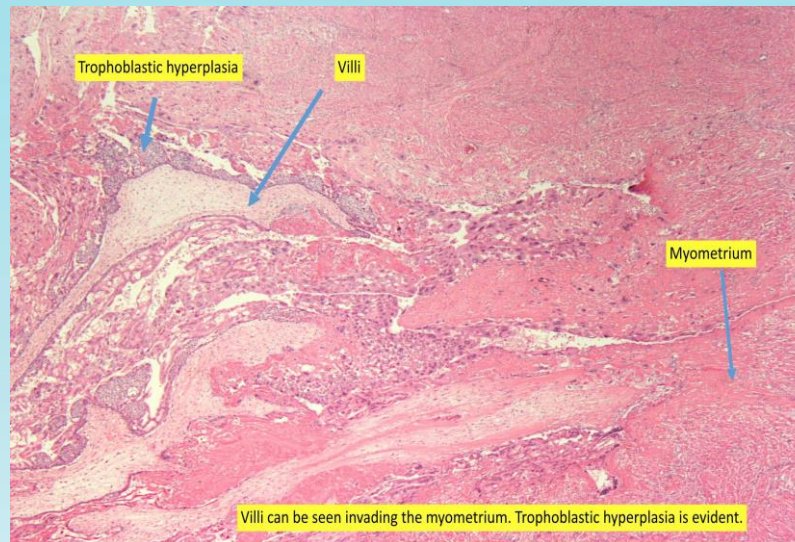
❖ Invasive mole

- Invasive moles are **complete moles that are locally invasive but lack the metastatic** potential of choriocarcinoma.
- An invasive mole **retains hydropic villi, which penetrate the uterine wall deeply, possibly causing rupture and sometimes life-threatening hemorrhage.**
- **Clinically** vaginal bleeding and irregular uterine enlargement, **persistently elevated serum HCG.**
- **Treatment:** Because invasive mole is difficult to remove completely by curettage, therefore if serum β -hCG remains elevated, further treatment is required. Fortunately, in most cases cure is possible with chemotherapy.

- **Gross:**

Erosive and hemorrhagic lesion caused by hydropic villi, which penetrate uterine wall deeply

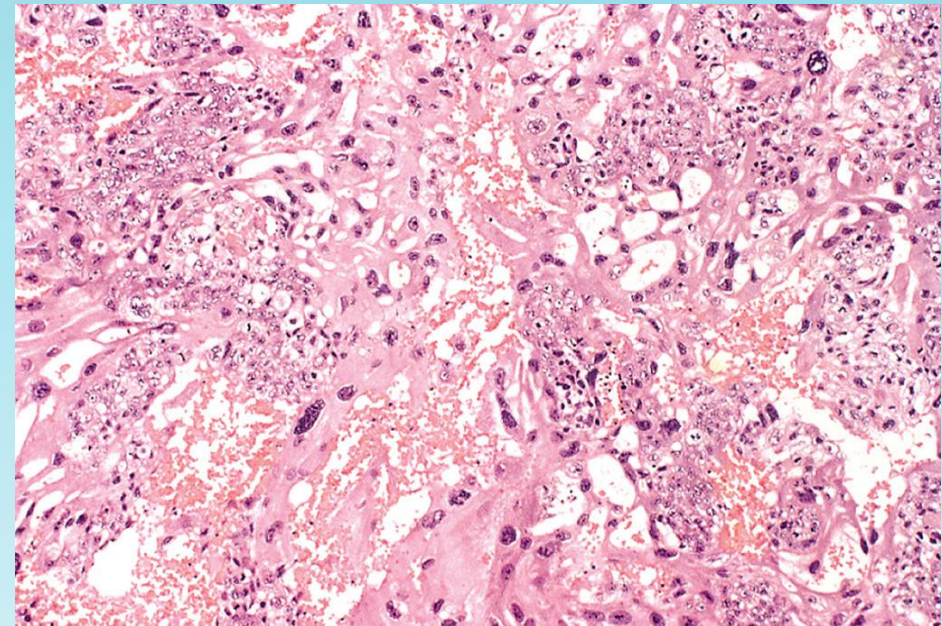
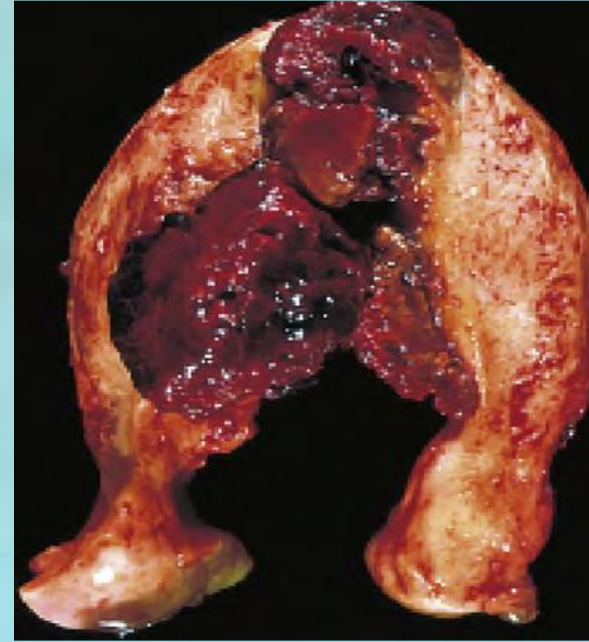
- **Mic.:** There is invasion of the myometrium by hydropic chorionic villi, accompanied by proliferation of both cytotrophoblasts and syncytiotrophoblasts.



❖ Choriocarcinoma:

- Very aggressive malignant tumor.
- **Origin: arise either** from gestational chorionic (trophoblastic) epithelium (gestational choriocarcinoma) **Or**, less frequently from totipotential cells (germ cells) within gonads (non gestational choriocarcinoma in ovaries or testes) (as a germ cell tumor).
- 50% follow complete mole & rarely follow partial mole, 25% after abortion while the remainder manifest following an apparently normal pregnancy.
- **Clinical presentation:**
 1. Irregular vaginal spotting of bloody brown fluid, which may appear in the course of normal pregnancy, after a miscarriage or after curettage (possibly months after).
 2. **Increase titer of β -hCG** in blood & urine (much higher than with mole).

- **Gross:** soft, fleshy, hemorrhagic, necrotic uterine masses. Sometimes the necrosis is so extensive that little viable tumor remains.
- **Mic.:** In contrast to H. mole & invasive mole, **villi are not formed** instead, the tumor is composed of anaplastic cuboidal cytotrophoblasts and multinucleate syncytiotrophoblasts



- **Disease course and prognosis:**

- By the time of diagnosis of choriocarcinoma, there is vascular spread usually has occurred to the lungs (50%), vagina (30%– 40%), brain, liver, or kidneys. Lymphatic invasion is uncommon.

- **Treatment:** depends on tumor **stage**. Usually **evacuation of uterus contents and chemotherapy**.

- Despite aggressiveness, **chemotherapy achieve 100% cure** even with tumor that spread beyond pelvis, vagina & into the lung.

- There is relatively poor response to chemotherapy in choriocarcinoma that arise in gonads (ovary & testis) due to **presence of paternal Ag on placental choriocarcinoma but not on gonadal lesion**, so maternal immune response against foreign (paternal Ag) help by acting as an adjuvant to chemotherapy.



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SUPER GIRL