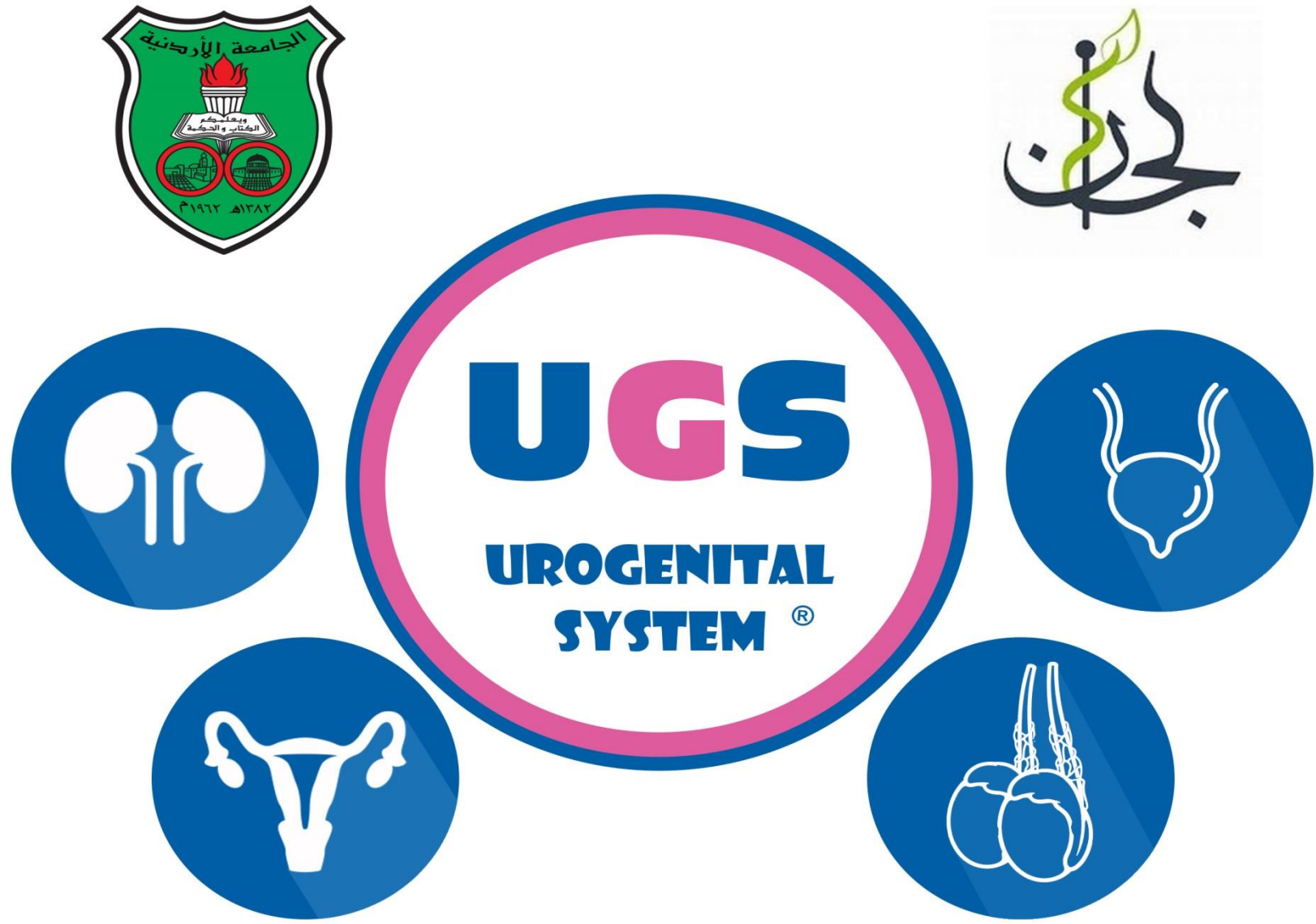


Sheets Pathology

Number: 8

Doctor: Mousa AlAbbadi

Done By: Abdullah AlZibdeh

Correction: Ammar Ramadan

Introduction

This sheet discusses the last lecture in our basic sciences years☺. In this sheet, ectopic pregnancy, gestational trophoblastic diseases and toxemia of pregnancy are discussed. Everything in the slides is included in the sheet (slides 129 to 145.)

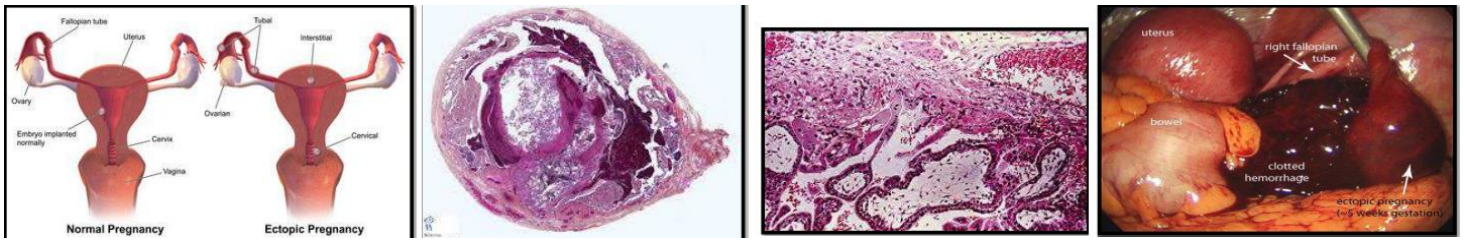
Ectopic Pregnancy

Ectopic pregnancy is fertilization of ova outside uterus. As many as 1% of pregnancies are ectopic. In more than 90% of these cases, implantation occurs in the oviducts (tubal pregnancy).

Causes include conditions that result with slow ova movement, such as: salpingitis, uterine tumors and endometriosis. 50% of tubal pregnancies, no anatomic cause is evident. Tubal ectopic can cause hemosalpinx, enlargement, and may rupture (acute abdomen and sometimes fatal bleeding). So, ectopic pregnancy should be discovered and treated early.

Presentation*; clinical scenario*

A woman presents with threatened abortion with vaginal bleeding. A curettage and ultrasound investigations have been obtained. Ultrasound does not show fetal heart. Pathologists study the curettage and cannot spot **fetal tissue or chorionic villi** (these are the basic evidence for intrauterine pregnancy). This means that pregnancy is ectopic.



Treatment

- Salpingotomy with evacuation: with conservation of fallopian tubes; especially in young women who plan to get pregnant again.
- Salpingectomy: for large lesions.

Remember: right lower abdominal pain can be caused by ovarian cysts, ectopic pregnancy, appendicitis or other causes.

Gestational Trophoblastic Diseases

Abnormal proliferation of fetal trophoblasts include molar and nonmolar diseases. Molar diseases are partial, complete or invasive hydatidiform mole. Nonmolar diseases include choriocarcinoma, which is an aggressive tumor. Choriocarcinoma can be gestational or nongestational (occurs in males and females).

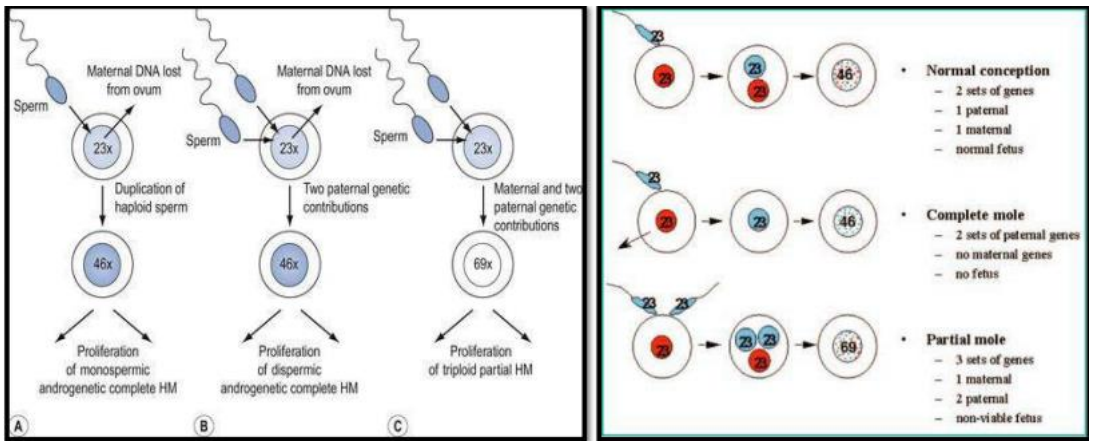
All these diseases have high levels of hCG in serum and urine. hCG levels are highest in choriocarcinoma, and are less elevated in partial molar disease. Levels of hCG are important for diagnosis and monitoring of therapy. For example, evacuation of complete mole is accompanied with a decrease in hCG levels. After 3 months (or sometimes a year), the woman is allowed to get pregnant again.

Hydatidiform Mole

In this disease, gestation is noticed to be "too large for dates" (the lady is 6 weeks pregnant, but in ultrasound it appears as 10 weeks pregnancy). Large for gestational age (LGA) is an indication of high prenatal growth rate. In this section, we discuss pathogenesis of the disease, complete mole and partial mole.

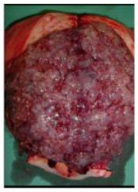
Pathogenesis of Mole

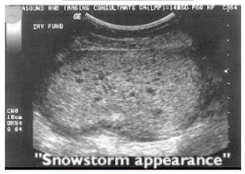
In a complete mole, the entire genetic content is supplied by two spermatozoa (or a diploid sperm), yielding diploid cells containing only paternal chromosomes, and the maternal DNA is lost. Whereas in a partial mole, a normal egg is fertilized by two spermatozoa (or a diploid sperm), resulting in a triploid karyotype with a preponderance of paternal genes.

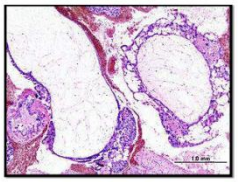


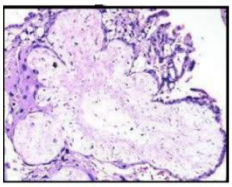
Complete Mole

- Large mass of abnormally swollen cystically dilated villi (grape-like); concentric and surrounded by trophoblastic proliferations
- Normal or atypical chorionic epithelium
- No fetal tissue
- Diploid (46XX or 46XY) two spermatozoa; so if histological features failed in diagnosis, karyotyping can help
- 1/2000 pregnancies (> in Asia)
- “Large for date”
- Antepartum care increased early detection (U/S exam)
- Before 20 and after 40 years of age; but can occur in 30's
- Gives a snowstorm appearance on ultrasound; with no fetal parts present
- Outcomes: after complete evacuation, 90% of cases get back to normal, and the patient can get pregnant again (hCG levels fall). 10% progress to invasive mole after curetting, and 2-3% develop into gestational choriocarcinoma. In these cases, hCG levels persist and rise.









Note: notce that the histology of normal chorionic villi shows that that the villi are avascular, not swollen and surrounded by two layers.

00:00 – 10:00

Partial Mole

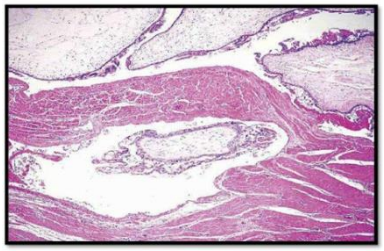
- Less swollen and less proliferation or incomplete proliferation
- Can have fetal tissue
- Triploid (i.e. 69XXY); one egg fertilized by 2 spermatozoa; can be thought of as chromosomal abnormality
- Risk of cancer or progression to invasive mole is very low or not present; if a partial mole patient later develops choriocarcinome, then the case has been misdiagnosed, and the patient had complete mole instead

TABLE 19.5 Features of Complete and Partial Hydatidiform 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
Serum hCG	Elevated	Less elevated
Tissue hCG	++++	+
Risk of subsequent choriocarcinoma	2%	Rare

hCG, Human chorionic gonadotropin.

Invasive Mole



It is a complete mole invading uterine myometrium and sometimes causing rupture (life-threatening hemorrhage). This hard-to-diagnose case can present as follows:

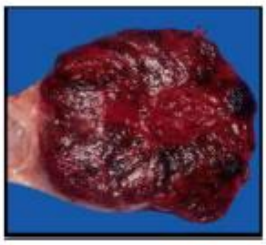
By radiologic examination, or through examining a curette (obtained by the common procedure DNC) from a complete mole, it is noted that this case is unusual in that the tissue is stuck (deep mole).

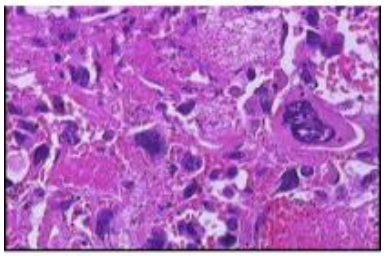
If no invasion of the myometrium is found, then the diagnosis should not be invasive mole. Histologically, you can find atypia, dilated cisterns, with proliferations and invasion of the myometrium. Although no metastasis can occur, it may cause distant emboli.

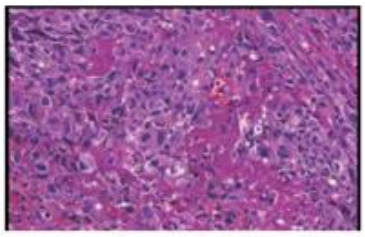
Treatment is done by surgery and chemotherapy, in addition to preventing pregnancy for two years, for those who do not want to undergo Hysterectomy. hCG levels are used for follow-up.

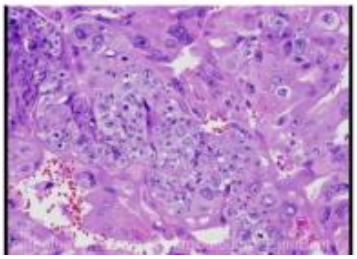
10:00 – 20:00

Choriocarcinoma









Choriocarcinoma, a very aggressive malignant tumor, arises either from gestational chorionic epithelium or, less frequently, from totipotential cells within the gonads (as a germ cell tumor; in males and females). In the United States, they occur in about 1 per 30,000 pregnancies but are much more common in Asian and African countries. For gestational choriocarcinoma, 50% arise from complete mole, 25% after abortions and 25% after normal pregnancies. Remember that 10% of complete mole cases progress to invasive mole, whilst 2-3% progress to choriocarcinoma. This means that complete mole cases should be monitored well.

Patients present with bloody vaginal discharge with rising serum β- HCG levels. When hCG levels rise with no pregnancy, look for choriocarcinoma. In histological sections, anaplastic tumor cells are found with no chorionic villi. If you find chorionic villi, then it is not a choriocarcinoma.

The lesions are usually hemorrhagic, with high cellularity and many anaplastic cells. Sometimes the lesion presents with apoptosis and necrosis that is so extensive that little viable tumor remains. Indeed, the primary lesion may “self-destruct,” and only the metastases tell the story. Diagnosis in this case depends on morphology, immune stains and hCG levels.

A raise in hCG levels with no chorionic villi found is choriocarcinoma until proven otherwise. If no lesion is found, treatment should be initiated. However, physicians usually find metastasized lesions in lungs, vagina, brain, liver, or kidneys (central areas).

Clinical Features of Choriocarcinoma

Gestational choriocarcinoma is 100% sensitive to chemotherapy (cure rate is very high), even after metastasis. However; non gestational choriocarcinoma (testicular and ovarian) *do not* respond well to chemotherapy. This may be because paternal antigens make gestational choriocarcinoma sensitive to chemotherapy, because maternal immunity fights against foreign paternal antigens.

Placental Site Trophoblastic Tumor (exaggerated trophoblastic reaction)

This hard-to-diagnose tumor arises from intermediate trophoblastic cells. Cells have diploid XX karyotype. This can be useful in diagnosis. This tumor arises few months after pregnancy. Serum β-HCG can be normal or slightly elevated. Human placental lactogen can be a better marker for this tumor.

Prognosis is favorable if confined to uterus. This tumor can be viewed as an in-situ malignancy; hysterectomy can solve the problem. This tumor is not sensitive to chemotherapy, like choriocarcinoma. Accordingly, advanced stages may be hard to treat.

Patients can present with post-partum vaginal bleeding and amenorrhea. Curette shows villi, atypia and trophoblastic proliferation, sometimes invading the myometrium.

Preeclampsia/Eclampsia (Toxemia of Pregnancy/TOP)

Because of the proper antenatal care systems, preeclampsia is caught early nowadays, and eclampsia cases are extremely rare. By long-existing precedent, preeclampsia and eclampsia are still sometimes referred to as *toxemia of*

pregnancy. No blood-borne toxin has ever been identified, and this historically sanctified term is a misnomer.

Preeclampsia

The development of hypertension, accompanied by proteinuria and edema in the third trimester of pregnancy, is referred to as *preeclampsia.* (Because edema can normally occur in pregnancy (with gravid uterus), we can say that hypertension and proteinurea are the two major signs of preeclampsia.)

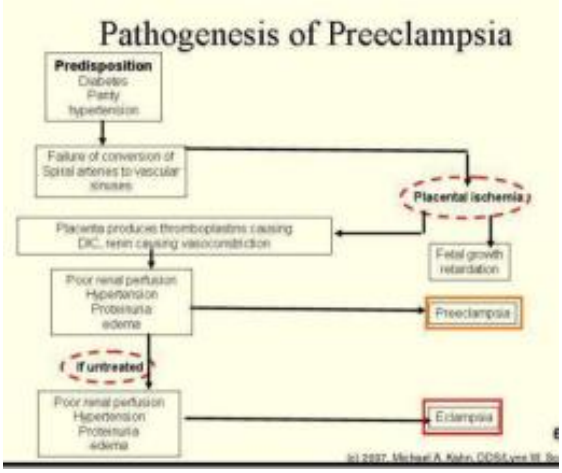
This syndrome occurs in 5% to 10% of pregnancies, **particularly with first pregnancies** in women older than age 35 years. Such patients *should* be admitted and monitored cautiously.

20:00 – 30:00

Eclampsia

In those severely affected, seizures may occur, and the symptom complex is then termed *eclampsia.*

Etiology



What causes these syndromes is unknown, however, **imbalance between vasodilators and vasoconstrictors** and abnormal uteroplacental vascular beds are seen in patients, and these cause insufficient blood flow. This results with ischemia and infarction. (Notice the role of the renin system and thromboplastin in the pathogenesis. Renin causes vasoconstriction which leads to hypertension, proteinurea, and edema)

Note:

- Preeclampsia should be treated fast to protect the patient from progressing to eclampsia.

- Risk factors of TOP include being primigravida and having hypertension and diabetes. Patients with such risk factors require more intense antenatal care.

Consequences of TOP

- Placental infarction: infarction is estimated to assess the extent of ischemia (for example, 20% of placenta is infarcted).
- Hypertension: decrease in vasodilators (PCY & PGE2), and increase in vasoconstrictors (TBX A2) was statistically found in patients (imbalance in arachnoid acid pathway, resulting with imbalance in vasodilators and vasoconstrictors).
- Hypercoagulability: as a result of endothelial injury.
- End-organ failure: if left untreated, kidney and liver may be damaged. Such organs are vital, and damaging them would be fatal.
- 10% of severe eclampsia patients develop ***HELLP*** **syndrome.** (microangiopathic HA, elevated liver enzymes, thrombocytopenia (low platelets), DIC). DIC (Disseminated intravascular coagulation) is very difficult to treat, because it causes coagulability that cannot be treated with heparin, because platelets are consumed and the patient is at risk of bleeding.

Note: DIC can occur on top of many diseases, including sepsis.

Morphology

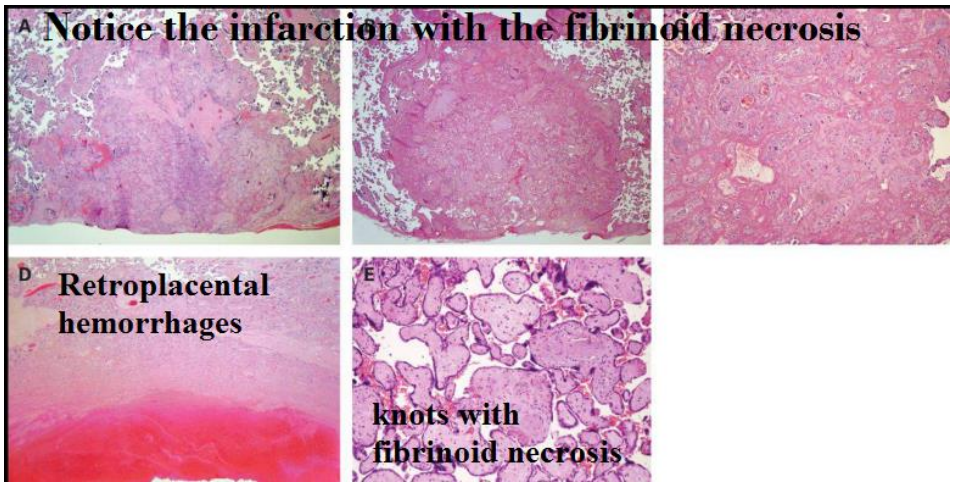
The morphologic changes of preeclampsia and eclampsia are variable and correlate to some degree with the severity of the disorder. **Placental abnormalities** include:

• **Infarcts,** which can be a feature of normal pregnancy, but are much more numerous with severe preeclampsia or eclampsia (remember that we estimate the infarction).

• **Retroplacental hemorrhages**: (abruptio placentae), here, a part of the placenta is stuck to the endometrial wall and the other part gets separated from the endometrium, and a hematoma is produced (can be during pregnancy or during delivery).

• **Premature maturation of placental villi** associated with villous edema, hypovascularity, and increased production of syncytial epithelial knots (hard to diagnose).

• **<u>Fibrinoid necrosis</u>**: very characteristic; especially in the walls of the vessels of the villi. It results from the infarction.



Treatment of TOP

Early treatment is best (before reaching eclampsia). Preeclampsia is reversible; changes are gone after delivery. This is a proof that the problem is in the placenta; once removed, the problem disappears.

Management includes NPO (nothing by mouth), antihypertensive medications, bed rest and monitoring. Patients usually continue their pregnancy, and give birth normally.

30:00 – 40:00