



Lecture 5: Disorders of Pregnancy and Placenta

wiseGEEK

▣ Important

▣ Notes

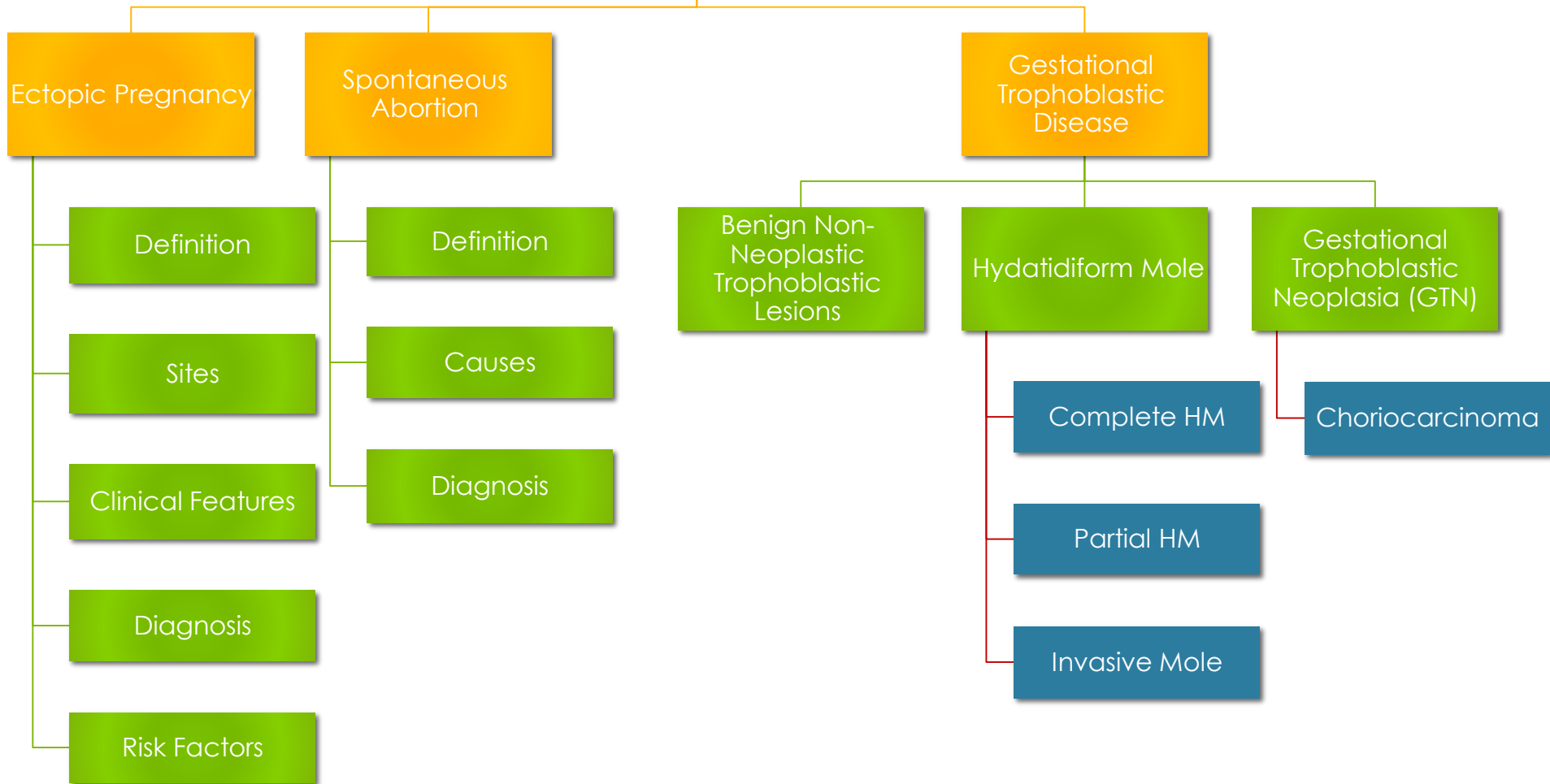
▣ Explanation

Objectives

The student should know :

- ✓ The pathology and predisposing factors of ectopic pregnancy and spontaneous abortion.
- ✓ The clinical presentation and pathology of hydatidiform mole and choriocarcinoma.

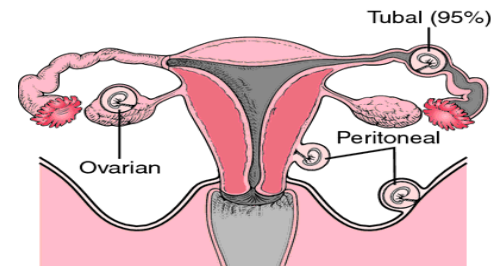
Disorders of Pregnancy and Placenta



Ectopic Pregnancy

Definition :

- Implantation of a fertilized ovum in any site other than the endometrium of the uterine cavity. About 1% of all pregnancies are ectopic. .



Sites :

- Over 90% of ectopic pregnancies occur in the **fallopian tubes** (tubal pregnancy).
- Other sites of ectopic pregnancy include the ovaries, abdominal cavity and uterine cervix.

Clinical features :

- A woman with an ectopic tubal pregnancy may present with pelvic pain or period of amenorrhoea followed by abnormal bleeding.
- The majority will present as an emergency with tubal rupture and hemorrhagic shock.

Diagnosis :

- **Abdominal/pelvic ultrasound:** shows mass (gestational sac) within fallopian tube, plus positive hCG levels
- **Microscopic:** placental tissue or fetal parts (**confirmation**)

Ectopic Pregnancy

Risk factors :

Any factor that retards passage of the ovum through the oviducts predisposes to ectopic pregnancy. In about half of the cases, it is due to chronic inflammation and scarring in the oviduct. The risk factors are as follows:

- **Pelvic inflammatory disease** is one of the most common cause. may cause tubal obstruction, pelvic adhesions with scarring and distortion of the fallopian tubes.
- Abdominal/pelvic surgery or tubal ligation surgery.
- Intrauterine tumors and endometriosis.
- Smoking may contribute to decreased tubal motility.
- Congenital anomaly of the tubes.
- In-utero diethylstilbestrol (DES) exposure increases the risk of ectopic pregnancy due to abnormal tubal morphology.
- History of previous ectopic pregnancy
- History of multiple sexual partners (may lead to pelvic inflammatory disease)
- Intrauterine device users
- History of infertility (may be due to the underlying infertility related issues or fertility drugs and treatments)
- In vitro fertilization has been associated with an increased risk of ectopic pregnancy including cervical pregnancies
- **NOTE: In the other 50% of tubal pregnancies, no anatomic cause is evident.**
- **Ovarian pregnancies** probably result from rare instances in which the ovum is fertilized just as the follicle ruptures.
- **Gestation within the abdominal cavity** occurs when the fertilized egg drops out of the fimbriated end of the oviduct and implants on the peritoneum.

Spontaneous Abortion

Definition :

- It is the spontaneous end of a pregnancy at a stage where the embryo or fetus is incapable of surviving
- Miscarriages that occur before the sixth week of gestation are called **early pregnancy loss or chemical pregnancy**.
- Miscarriages that occur after the sixth week of gestation are called **clinical spontaneous abortion**.
- Most miscarriages occur during the first **13 weeks of pregnancy** (mostly within the first trimester)

Causes :

The cause of a miscarriage cannot always be determined, The causes are as follows:

1. Chromosomal abnormalities : most common cause

more common with aging, and women over age 35 have a higher rate of miscarriage than younger women.

2. Hormonal problems :

- Cushing's Syndrome
- Thyroid disease
- Polycystic ovary syndrome (PCOS).
- Diabetes
- It is suggested that inadequate function of the corpus luteum in the ovary leads to progesterone deficiency which may lead to miscarriage.

3. Infections :

Listeria monocytogenes, Toxoplasma gondii, parvovirus B19, rubella, herpes simplex, cytomegalovirus and lymphocytic choriomeningitis virus etc

Spontaneous Abortion

4. **Maternal health problems can predispose to miscarriages e.g.** systemic lupus erythematosus and antiphospholipid antibody syndrome
5. **Lifestyle :** smoking, drug use, malnutrition, excessive caffeine and exposure to radiation or toxic substances
6. **Maternal age :** SABs increase after age 35 due to ovum abnormalities
7. **Maternal trauma**
8. **Abnormal structural anatomy of the uterus :**
 - Septate or bicornate uterus affect placental attachment and growth.
 - Uncommonly uterine fibroids can interfere with the embryo implantation and blood supply, thereby causing miscarriage
9. **Others :** surgical procedures in the uterus during pregnancy.

Diagnosis :

- A miscarriage can be confirmed via **ultrasound** and by the examination of the passed tissue **microscopically** for the products of conception including chorionic **villi, trophoblasts, and fetal parts.**
- Genetic tests may also be performed to look for chromosomal anomalies.



Gestational Trophoblastic Disease (GTD)

- Gestational trophoblastic disease comprises a heterogeneous group of related lesions arising from **abnormal proliferation** of placental trophoblasts.
- Most GTD **produces the beta subunit** of human chorionic gonadotropin (HCG).
- Serum HCG is also elevated in normal and ectopic pregnancy but it is **markedly increased** in GTD. In addition the serum HCG levels in GTD **continue to rise** even after 14th weeks in contrast to normal pregnancy in which the HCG levels **drop** after 14 weeks gestation.
- Most women who have had gestational trophoblastic disease can have **normal pregnancies later**.
- The maternal age **above 40 years** has a **5 fold increased risk** of trophoblastic disease compared to the mothers below 35 years.

Types of GTD

Benign Non-Neoplastic Trophoblastic Lesions	Hydatidiform Mole (HM)	Gestational Trophoblastic Neoplasia (GTN)
Diagnosed as an incidental finding on an endometrial curettage or hysterectomy specimen.	<ul style="list-style-type: none"> • Result from abnormalities in fertilization. • Essentially benign, but carry an increased risk of developing malignant choriocarcinoma. 	<ul style="list-style-type: none"> • A group of tumors. • Have potential for local invasion and metastases. • In contrast to other more common malignancies, GTN is curable in majority (85-100%) of cases.
They are: <ul style="list-style-type: none"> - Exaggerated placental site. - Placental site nodule. 	They are: <ul style="list-style-type: none"> - Complete hydatidiform mole. - Partial hydatidiform mole. - Invasive mole/chorioadenoma destruens. 	They are: <ul style="list-style-type: none"> - Choriocarcinoma. - Placental site trophoblastic tumor. - Epithelioid trophoblastic tumor.

Hydatidiform Mole :

Definition

- It is an **abnormal fertilization** resulting in an **abnormal placenta** due to **excess of paternal (from father) genes**. It is caused by abnormal **gametogenesis** and **fertilization**.
- The most common form of gestational trophoblastic disease; occurs in 1/1,000-2,000 pregnancies.
- Results in the formation of **enlarged** and **edematous placental villi**, which **fill the lumen of the uterus**.
- Passage of tissue fragments, which appear as small grapelike masses, is common. The serum **hCG concentration is markedly elevated**, and are rapidly **increasing**.

Risk factors

- Maternal age: girls **younger than 15** years of age and women **over 40** are at higher risk.
- Ethnic background: incidence higher in **Asian women**.
- Women with a **prior hydatidiform** mole have a **20-fold** greater risk of a subsequent molar pregnancy than the general population.

There are 2 types of hydatidiform mole (HM) :

1- Complete HM

2- Partial HM

1- Complete Hydatidiform Mole :

- Complete mole results from **fertilization of an empty ovum** that lacks **maternal DNA**. Most commonly, a **haploid (23X)** set of paternal chromosomes **duplicates to 46XX**. The characteristic feature is **complete lack of maternal chromosomes**.
- Chromosomal analysis shows 46XX karyotype and all the chromosomes come from the **male/paternal side**. (i.e. it is an **androgenetic pregnancy with no maternal DNA**.)
- Uterus is distended and filled with swollen/large villi with prominent trophoblastic cell proliferation. **No embryo, or fetal tissue** is present. Grossly it looks like a **bunch of grapes**.
- It is a genetically abnormal placenta with **hyperplastic trophoblasts**, **without fetus or embryo**.

Symptoms :

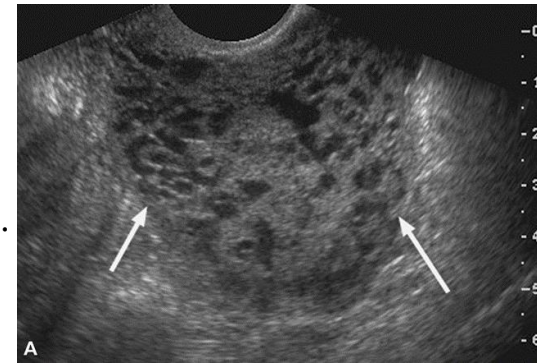
- **Fast rate of abdominal swelling** (due to **rapid increase in uterine size**) mistaken for normal pregnancy but the **uterus is disproportionately large** for that stage of pregnancy.
- In addition patient has some **vaginal bleeding**, severe **nausea** and **vomiting**. There is **elevated HCG levels**.

Ultrasound : Will show a “**cluster of grapes**” appearance or a “**snowstorm**” appearance, signifying an abnormal placenta.

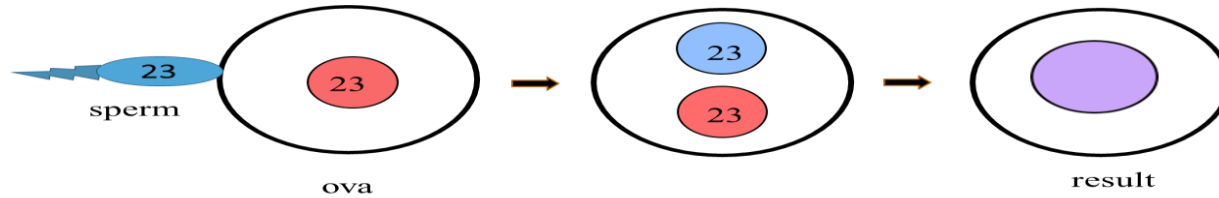
Treatment : Evacuation of uterus by **curettage** and **sometimes chemotherapy**. With appropriate therapy cure rate is very high.

Complications :

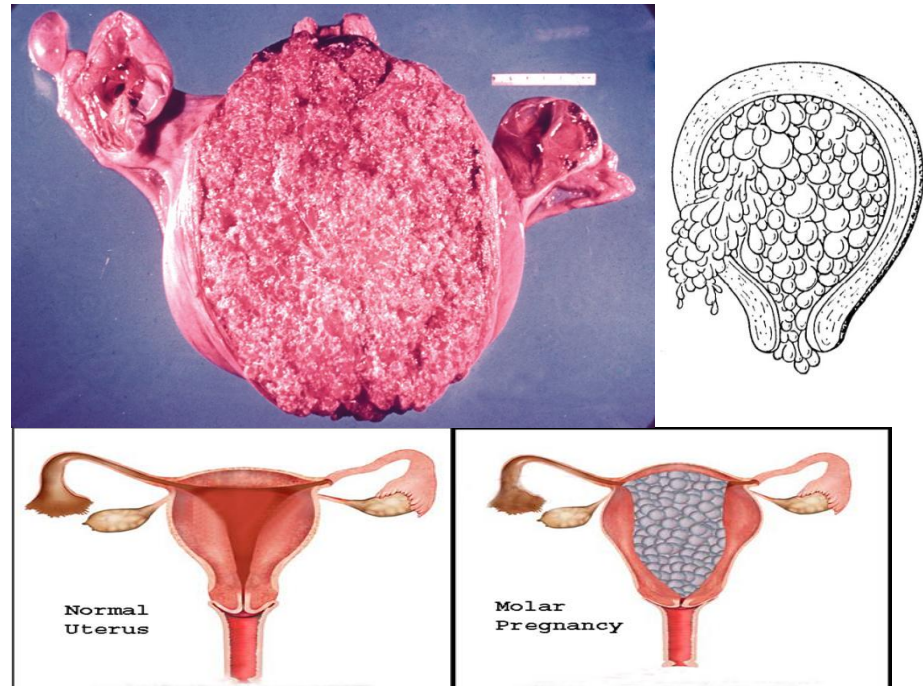
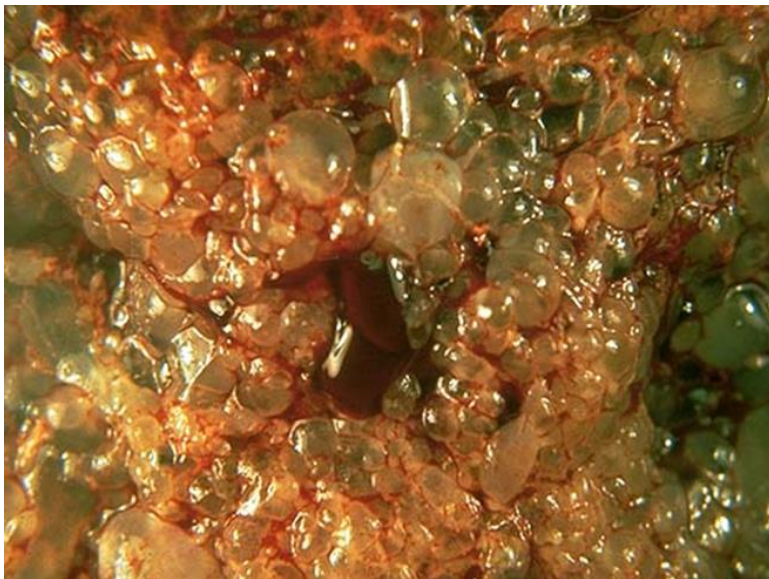
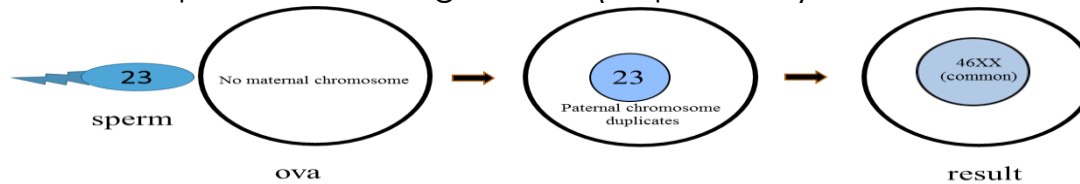
- **Uterine hemorrhage**, uterine **perforation**, trophoblastic **embolism**, and **infection**. Few patients develop an **invasive mole**.
- The **most important complication** is the development of **choriocarcinoma**, which occurs in about 2% of patients after the mole has been evacuated.



Normal fertilization: a single sperm of 23 chromosomes fertilizes a normal egg of 23 chromosomes.



Complete mole fertilization: in 90% of the cases a single sperm of 23 chromosomes fertilizes a egg that has lost its chromosomes. It then duplicates resulting in 46XX (all paternal)



2- Partial Mole (PM) :

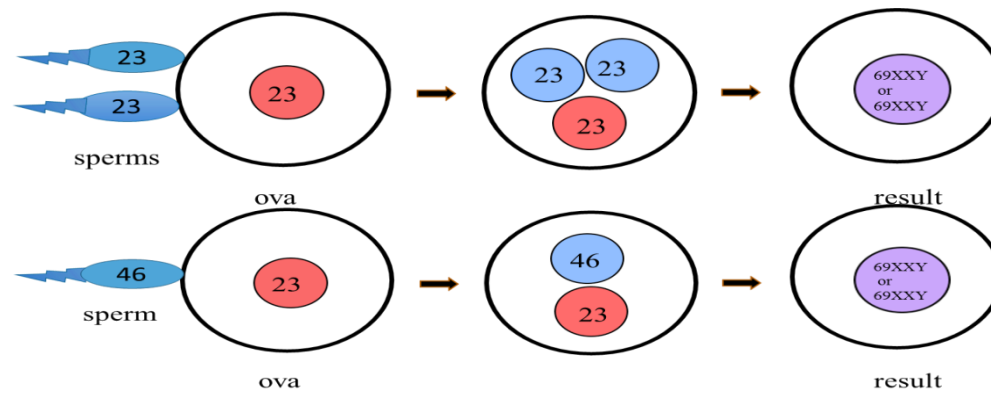
Definition: Partial hydatidiform moles have 69 chromosomes (triploidy gestation), of which **one haploid set (23,X) is maternal** and **two haploid (23,X+23X=46X) sets are paternal in origin.**

- This results from fertilization of a normal single ovum/egg (23,X) by **two normal spermatozoa, each carrying 23 chromosomes**, or by a single spermatozoon that **has not undergone meiotic reduction** and bears 46 chromosomes (**the pregnancy has too much paternal DNA**).
- It is a **genetically abnormal placenta** with a resultant mixture of **large and small villi** with slight **hyperplasia of the trophoblasts**, filling the uterus. **In contrast to a complete mole, embryo/fetal parts may be present.** The fetus associated with a partial mole usually dies after 10 weeks' gestation, and the mole is aborted shortly thereafter.
- It almost **never evolves into choriocarcinoma.**
- It makes up 15–35% of all moles
- Uterine size **usually small or appropriate** for gestational age
- Serum hCG levels are **elevated but not as high as complete mole.**
- Chromosomal analysis of partial moles shows 69XXY (i.e. 3 haploid sets also called as triploidy).

Grossly the genetically abnormal placenta has a **mixture of large chorionic villi and normal-appearing smaller villi.**

Prognosis: Risk for development of choriocarcinoma **very low.** Follow-up is mandatory.

Treatment : Evacuation of uterus by curettage and sometimes chemotherapy.



FEATURE	CM	PM
Karyotype	Usually diploid 46XX	Usually triploidy 69XXY (most common)
Villi	All villi are hydropic; no normal villi seen	Normal villi may be present
Fetal tissue	Not present	Usually present
Trophoblasts	Marked proliferation	Mild proliferation
Serum HCG	Markedly elevated	Less elevated
Behavior	2% progress to choriocarcinoma	Rare choriocarcinoma

Invasive Mole

- Invasive mole is when the villi of a hydatidiform mole **extends/infiltrates** into the **myometrium** of the uterus.
- The mole sometime tends to **enter dilated veins in the myometrium**, and a times through the **vascular channels spread to distant sites, mostly the lungs** (note: death from such spread is unusual).
- It occurs in about **15%** of **complete moles** and **rarely** in **partial mole**.
- Can cause **hemorrhage** and **uterine perforation**

Choriocarcinoma

- **Definition** : **Malignant tumor** derived from normal or abnormal placental tissue, composed of a proliferation of malignant **cytotrophoblast** and **syncytiotrophoblast**, **without villi formation**.
- It is an **aggressive** malignant neoplasm.
- It is characterized by highly **increased serum concentration of HCG**.
- Choriocarcinomas are **aneuploidic**.
- It spreads early **via blood** to the **lungs and other organs**.
- Responds **well to chemotherapy**
- About half the choriocarcinoma are preceded by **complete hydatidiform mole** . Others are preceded by **partial mole (rare)**, **abortion, ectopic pregnancy and occasionally normal term pregnancy**.



Summary

(from Robbin's basic pathology)

SUMMARY

Ectopic Pregnancy

- Ectopic pregnancy is defined as implantation of the fertilized ovum outside of the uterine corpus. Approximately 1% of pregnancies implant ectopically; the most common site is the fallopian tube.
- Chronic salpingitis with scarring is a major risk factor for tubal ectopic pregnancy.
- Rupture of an ectopic pregnancy is a medical emergency that, if left untreated, may result in exsanguination and death.

SUMMARY

Gestational Trophoblastic Disease

- Molar disease is due to an abnormal contribution of paternal chromosomes in the gestation.
- Partial moles are triploid and have two sets of paternal chromosomes. They typically are accompanied by fetal tissue. There is a low rate of persistent disease.
- Complete moles are diploid, and all chromosomes are paternal. No embryonic or fetal tissues are associated with complete mole.
- Among complete moles, 10% to 15% are associated with persistent disease that usually takes the form of an invasive mole. Only 2% of complete moles progress to choriocarcinoma.
- Gestational choriocarcinoma is a highly invasive and frequently metastatic tumor that, in contrast with ovarian choriocarcinoma, is responsive to chemotherapy and curable in most cases.
- Placental site trophoblastic tumor is an indolent and usually early-stage tumor of intermediate trophoblast that produces human placental lactogen and does not respond well to chemotherapy.

Thank You!

We hope you found this helpful and informative.

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