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Summary file

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Pathology

Trophoblastic Diseases



439

Color index

- Important
- Doctor's note
- Extra info
- Main text



Revised & Approved



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تجعل الحزن اذا شئت سهلا

Objective

01

Understand the pathology and predisposing factor of ectopic pregnancy and spontaneous abortion

02

Know the clinical presentation and pathology of hydatidiform mole and choriocarcinoma

Overview

Lecture content

Ectopic pregnancy

Spontaneous abortion

Gestational trophoblastic disease

Benign non-neoplastic trophoblastic lesions

Exaggerated placental site

Placental site nodule

Hydatidiform mole

Complete hydatidiform mole

Partial hydatidiform mole

Invasive mole

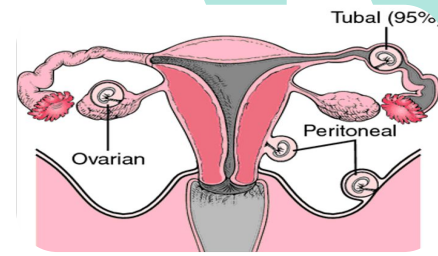
neoplasia (GTN)

Choriocarcinoma

Placental site trophoblastic tumor

Epithelioid trophoblastic tumor

Ectopic Pregnancy الحمل خارج الرحم

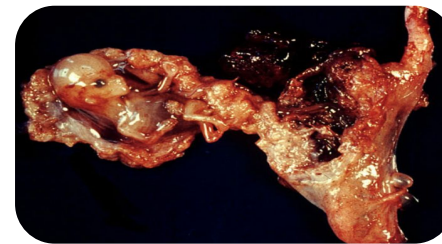


Introduction

- ❖ **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:**
 - >90% of ectopic pregnancies are in the **fallopian tubes** (the ovum does not travel to the uterus) (tubal pregnancy).
 - The rest are in the:
 - **Ovaries:** rarely when ovum is fertilized just as the follicle ruptures.
 - **Abdominal cavity:** when fertilized egg drops out of the fimbriated end of the oviduct and implants on the peritoneum.
 - **Uterine cervix.**

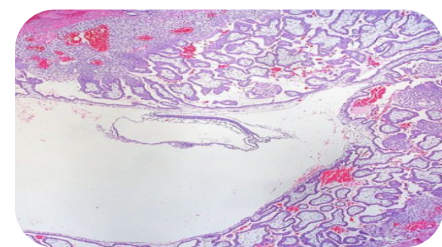
Clinical features

- ❖ **Tubal pregnancy:**
 - Pelvic pain and abnormal bleeding **following a period of amenorrhea.**
- ❖ Many present as an **emergency** with tubal rupture, severe acute abdominal pain and hemorrhagic shock, **mimic appendicitis**



Diagnosis

- ❖ **Clinically:**
 - Abdominal/pelvic ultrasound: Gestational sac within fallopian tube .
 - A positive pregnancy test (high HCG levels).
- ❖ **Microscopically:** Placental tissue or fetal parts within the tube.



Risk factors

- ❖ Any factor that retards passage through the tubes predisposes to ectopic pregnancy.

Inflammation & multiple sexual partners	Infertility	Diethylstilbestrol
<ul style="list-style-type: none"> - Pelvic inflammatory disease/infections/salpingitis (inflammation of the fallopian tube) is the most common cause. - Inflammation causes: <ol style="list-style-type: none"> 1. Damage ciliary activity (the ovum will stuck in fallopian tube). 2. Tubal obstruction. 3. Pelvic adhesions with scarring. 4. Distortion of the fallopian tubes. - Pelvic infection causes 5 times greater risk of ectopic pregnancy, (usually by N. gonorrhoea & chlamydia). - Chronic inflammation causes ½ the cases of ectopic and scarring of oviduct part of Fallopian tube . 	May be due to: <ul style="list-style-type: none"> - Underlying infertility related issues. - Fertility drugs and treatments. - In vitro fertilization أطفال الأنابيب. 	<ul style="list-style-type: none"> - Exposure in utero increases the risk due to abnormal tubal morphology and causes congenital anomaly.
	Smoking	Surgery
	<ul style="list-style-type: none"> - Decrease tubal motility by damage ciliated cell - Predispose to pelvic inflammatory disease (due to decreased immunity). 	<ul style="list-style-type: none"> - Abdominal/pelvic surgery. - Tubal ligation surgery. Cause inflammation and scarring
Congenital anomaly of tubes		Intrauterine tumors and endometriosis
Intrauterine contraceptive device (IUD)		History of previous ectopic pregnancy

Spontaneous Abortion

Introduction

- ❖ **Definition:** It is the spontaneous end of a pregnancy (**without medical intervention**) at a stage where the embryo or fetus is incapable of surviving.
- ❖ **Miscarriages that occur:**
 - **Before** the 6th week are called **early pregnancy loss or chemical pregnancy** (before fetal heartbeats).
 - **After** the 6th week of gestation are called **clinical spontaneous abortion** (after heartbeats).
- ❖ About 10-25% of all pregnancies end in miscarriage.
- ❖ Most miscarriages occur during the **first trimester** (13 weeks) of pregnancy.

Causes

- ❖ The cause of a miscarriage cannot always be determined.
- ❖ The causes are as follows:



Chromosomal abnormalities

- ½ of the 1st trimester miscarriages have abnormal chromosomes (**most common cause**).
- **Age:** women over age 35 have a higher rate of miscarriage
- A pregnancy with a genetic problem has a 95% probability of ending in miscarriage.

Hormonal abnormalities

- Cushing's Syndrome.
- Thyroid , **adrenal gland** disease
- Polycystic ovary syndrome (PCOS)
- Poorly controlled DM increases the risk of birth defects.
- **Inadequate function of the corpus luteum:** progesterone produced will not be enough for maintenance.

Infections

- Listeria monocytogenes.
- Toxoplasma gondii
- Parvovirus B19.
- Rubella.
- Herpes simplex.
- Cytomegalovirus.
- Lymphocytic choriomeningitis virus.

Maternal health problems

- **Systemic Lupus Erythematosus (SLE)**
- **Antiphospholipid antibody syndrome.** (which leads to **thrombosis** → affecting blood supplying pregnancy).
- maternal trauma

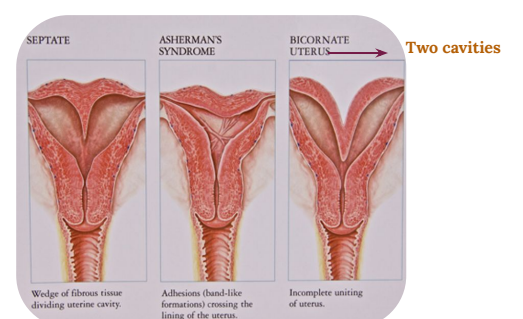
Lifestyle & trauma

- Smoking.
- Drug use.
- Malnutrition.
- Radiation exposure.
- Toxic substances.
- Trauma to the mother.

Abnormal structural anatomy

- Septate or bicornuate¹ uterus affect placental attachment and growth → an embryo implanting on the septum will be at risk of miscarriage.
- Uterine fibroids can interfere with the embryo implantation and blood supply, thereby causing miscarriage. (rare)

- ❖ **Others:** surgical procedures in the uterus during pregnancy e.g. amniocentesis and chorionic villus sampling.

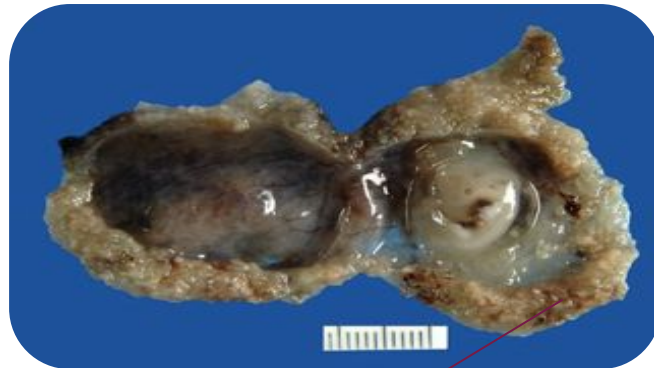


1. In addition to Asherman's syndrome where the uterus is filled with fibrous adhesions.

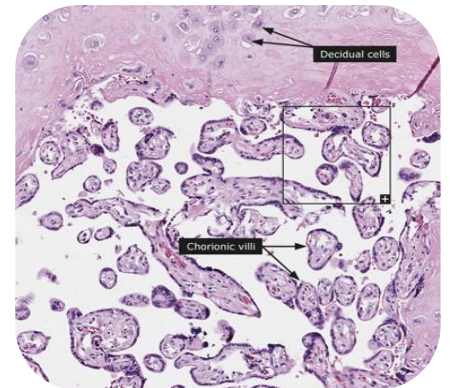
Spontaneous Abortion

Diagnosis

- ❖ A miscarriage can be confirmed:
 - By ultrasound study.
 - They make sure that the endometrial cavity is empty and the placenta and fetal tissue has passed.
 - By the examination of the passed tissue microscopically for the products of conception. The products of conception include:
 - **Chorionic villi.**
 - Trophoblasts.
 - Fetal parts and changes in the endometrium (hypersecretory).
- ❖ Genetic tests may also be performed to look for chromosomal anomalies.



Pale spongy tissue = placenta



Gestational trophoblastic disease

Introduction (Males slides)

- ❖ **GTD**: a group of related disorders in which there is abnormal proliferation of placental trophoblasts.
- ❖ Abnormal fertilization causes the growth of a placenta without fetal tissue.
- ❖ The maternal age >40 years has a 5 times more risk of trophoblastic disease.
- ❖ Most women who have had gestational trophoblastic disease can have normal pregnancies later.
- ❖ Most GTD produces the beta subunit of human chorionic gonadotropin (HCG).
- ❖ Even though **HCG is high** in both GTD and normal pregnancy, it is only persistent after the 14th week in GTD.

Types of GTD

Benign non-neoplastic trophoblastic lesions	★ Hydatidiform mole ¹	Gestational trophoblastic neoplasia (GTN)
<ul style="list-style-type: none"> ❖ Incidental finding on an endometrial curettage or hysterectomy specimen. 	<ul style="list-style-type: none"> ❖ Result from abnormalities in fertilization. ❖ Benign, but may develop to choriocarcinoma 	<ul style="list-style-type: none"> ❖ Tumors that have the potential for local invasion & metastases.
<ul style="list-style-type: none"> - Exaggerated placental site. - Placental site nodule. 	<ul style="list-style-type: none"> - Complete hydatidiform mole risk factor to progress into malignant choriocarcinoma more than Partial hydatidiform mole - Partial hydatidiform mole. - Invasive mole /chorioadenoma destruens 	<ul style="list-style-type: none"> - Choriocarcinoma - Placental site trophoblastic tumor - Epithelioid trophoblastic tumor

Hydatidiform mole

Introduction

- ❖ **Definition**: It is an **abnormal placenta** due to excess of paternal genes.
- ❖ The **most common form of GTD**; occurs in 1/1,000-2,000 pregnancies.
- ❖ It is caused by **Abnormal gametogenesis and fertilization**.


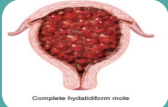

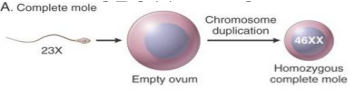
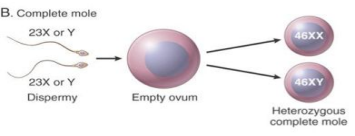
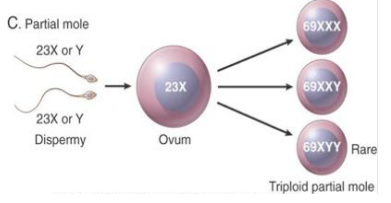
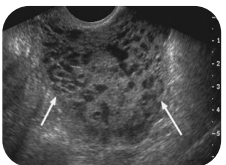
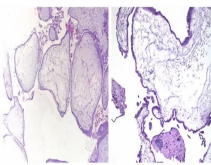


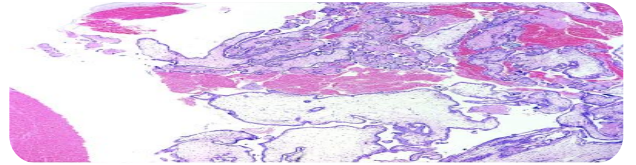
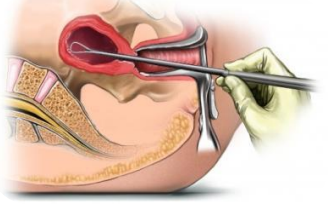
Risk Factors

- ❖ **Maternal age**: 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.

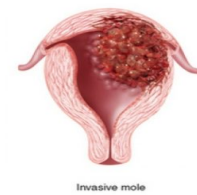
Histological feature

cystic **swelling of chorionic villi** with variable **trophoblastic proliferation** result from **abnormal fertilization**

Types of Hydatidiform Mole

	 Complete HM 	 Partial HM
Pathogenesis & Karyotype	<ul style="list-style-type: none"> - Result from fertilisation of an empty Ovum that lacks of maternal DNA as result the all chromosome are derived from the sperm cell, there are complete lack of maternal chromosome, All the chromosomes come from paternal/ male. (Androgenic Pregnancy) - The full set of chromosomes arise from duplicated chromosomes of a haploid sperm. - The result usually <u>diploid 46XX</u> - Duplication: 90% of are 46 XX, after fertilization, the one sperm duplicates its DNA. - Dispermy: while, 10%, 46 XY, two sperms that fertilized the egg. - It is a genetically abnormal placenta with hyperplastic trophoblasts without fetus.  	<ul style="list-style-type: none"> - Partial hydatidiform mole results from fertilization of a normal ovum by 2 normal sperms. - 15-35% of all moles. - The result is triploid cell (69 chromosomes). - One maternal set (23). - Two paternal (23+23). - Abnormal placenta: uneven villi, with hyperplasia of trophoblast. - There is a fetus. - 58% are 69XXY (most common) - 40% are 69XXX - 2% are 69XYY 
Symptoms	<ul style="list-style-type: none"> - Abdominal swelling (due to rapid increase in uterine size) mistaken for normal pregnancy , with <u>absent of embryo</u> . - However, the rapid increase is disproportionate to the stage of pregnancy. - Vaginal bleeding, nausea, vomiting (exaggerated morning sickness). - High HCG levels that does not match her gestational age. 	<ul style="list-style-type: none"> - embryo/ fetal parts may be present , but The fetus usually dies after 10 weeks' gestation and the mole (pregnancy) is aborted shortly thereafter. - Uterine size small or appropriate for gestational age. - High HCG but not as complete.
Morphology	<ul style="list-style-type: none"> - Microscopical feature : (Large , edematous , hydropic , swollen) villi with prominent (markedly proliferation) trophoblastic cell - Gross feature : Cluster of grapes - Radiological description: Pelvic Ultrasound: snowstorm appearance, indicating abnormal placenta, absent of embryo and amniotic fluid .    	<ul style="list-style-type: none"> - Abnormal placenta: uneven (large and small) villi also normal villi may be present , with slight hyperplasia of trophoblast (mild proliferation) less than complete HM . - Gross: mixture of large chorionic villi and normal appearing smaller villi. 
Treatment	<ul style="list-style-type: none"> - Evacuation (removal of these villi) of uterus by curettage and sometimes chemotherapy. - With appropriate therapy cure rate is very high. 	<ul style="list-style-type: none"> - Evacuation of uterus by chemotherapy. 
Complications	<ul style="list-style-type: none"> - Uterine hemorrhage or perforation. - Trophoblastic embolism. - Infection. - Few patients about 25% develop an invasive mole (invade the myometrium or a blood vessel). - The most important complication is the development of choriocarcinoma , 2% progress to choriocarcinoma 	<ul style="list-style-type: none"> - Risk for development of choriocarcinoma very low "almost never". - Follow-up is mandatory.

Invasive Mole (not tumour)



Introduction

- ❖ It is **NOT** a tumor, it is an aggressive behavior of a disease .
- ❖ Invasive mole is when the villi of a hydatidiform mole **especially complete CM** extends/infiltrates into the **myometrium** of the uterus.
- ❖ Enter into the veins of the myometrium, and a times spread via the vascular channels to distant sites, mostly the **lungs** (if not treated, she will have respiratory symptoms) (not fatal).
- ❖ It occurs in about 15% of complete moles and rarely in partial mole.
- ❖ Can cause hemorrhage and uterine perforation.

Choriocarcinoma malignant



Introduction

- ❖ **Definition:** Malignant tumor of placental tissue, composed of a proliferation of malignant cytotrophoblast and syncytiotrophoblast, **without villi formation, presence of hemorrhage and necrosis** .
- ❖ It is an **aggressive** malignant neoplasm.
- ❖ Choriocarcinomas are **aneuploidic** (abnormal number of chromosomes, ٢٣ مضاعفات ٢٣).

Predisposition

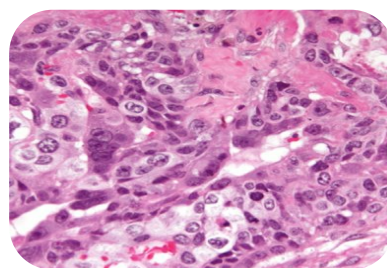
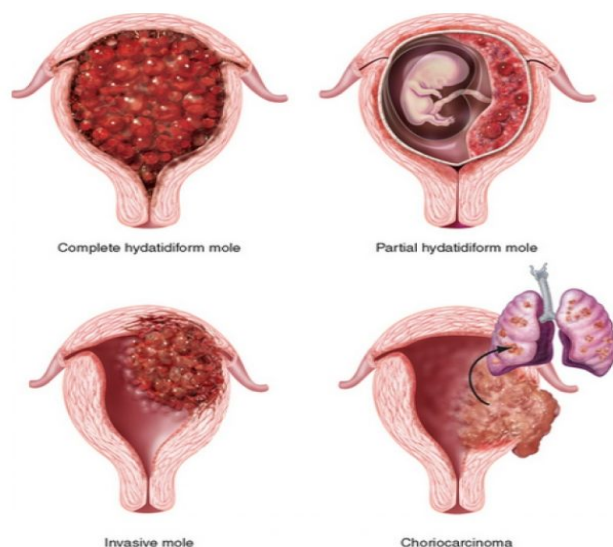
- ❖ 50% are **preceded by complete hydatidiform mole**.
- ❖ Can preceded by partial mole (rare), abortion, ectopic pregnancy and occasionally a normal term pregnancy.
- ❖ It can also arise as a spontaneous germ cell tumor. (poorer response to chemotherapy)

Clinical feature

- Very high levels of serum HCG. (used as a marker and stain for diagnosis)

Prognosis

- ❖ **Metastasis:** via blood to the lungs and other organs.
- ❖ Responds to chemotherapy **but the prognosis is poor** .



Solid sheaths of trophoblasts No fetal cells





Summary

Ectopic pregnancy

Introduction	-Implantation of a fertilized ovum in any site other than the endometrium of the uterine cavity - Sites: fallopian tubes, ovaries, abdominal cavity, uterine cervix
Clinical features	Pelvic pain, abnormal bleeding, amenorrhea, severe acute abdominal pain, hemorrhagic shock
Diagnosis	Clinically: Ultrasound & High HCG levels Microscopically: Placental tissue or fetal parts within the tube
Risk factors	Inflammation, multiple sexual partners, smoking, surgery, IUD, infertility .

Spontaneous abortion

Introduction	-It is the spontaneous end of a pregnancy at a stage where the embryo or fetus is incapable of surviving. -types <ul style="list-style-type: none"> • <u>Before the 6th week</u> of gestation are called early pregnancy loss or chemical pregnancy. • <u>After the 6th week</u> of gestation are called clinical spontaneous abortion.
Causes	Chromosomal abnormalities, Hormonal problems, Infections, lifestyle, trauma, maternal health problems, abnormal structural anatomy.
Diagnosis	-Ultrasound study -Examination of the passed tissue microscopically -Genetic tests

Gestational trophoblastic disease

Introduction	Gestational trophoblastic disease is a group of related disorders in which there is abnormal proliferation of placental trophoblasts.
Types	-Benign non-neoplastic trophoblastic lesions. -Hydatidiform mole. -Gestational trophoblastic neoplasia.

Hydatidiform Mole

Introduction	Results from abnormalities in fertilization. They are essentially benign, but these patients carry an increased risk of subsequently developing choriocarcinoma
Types	-Complete HM -Partial HM -Invasive mole

Choriocarcinoma

Introduction	-Malignant tumor of placental tissue. -Aggressive and malignant.
Clinical feature	Very high levels of serum HCG.
Prognosis	-Metastases to lung and other organs. Responds to chemotherapy.



01 Which of the following is a diagnostic method for ectopic pregnancy ?			
A) high HCG levels and pelvic Ultrasound	B) high HCG levels and pelvic X-ray	C) Low HCG levels and pelvic X-ray	D) Low HCG levels and pelvic Ultrasound
02 What is the most common site of ectopic pregnancy?			
A) ovaries	B) abdominal cavity	C) peritoneal cavity	D) Fallopian tubes
03 A young female just married 6 months ago came, had a short history of couple of weeks of pelvic pain and abnormal bleeding following a period of amenorrhea. She came to the emergency due to severe acute abdominal pain which then proceeded to a hemorrhagic shock. A Microscopic sample showed Placental tissue within the Fallopian tubes. She was diagnosed with tubal Ectopic pregnancy, which of the following could be the cause of the ectopic pregnancy?			
A) ovum is fertilized just as the follicle ruptures.	B) fertilized egg drops out of the fimbriated end of the oviduct	C) chronic inflammation and scarring in the oviduct	D) chronic inflammation and scarring in the vagina
04 What is the most common cause of early miscarriages?			
A) Diabetes	B) Chromosomal abnormalities	C) Smoking	D) NSAIDS
05 Which of the following is the most common karyotype for partial Hydatidiform mole ?			
A) 46 XX	B) 47 XXY	C) 69 XXY	D) 69 XYY
06 Which of the following is considered a Hydatidiform mole Gestational Trophoblastic Disease?			
A) Choriocarcinoma	B) Placental site trophoblastic tumor	C) chorioadenoma destruens	D) Epithelioid trophoblastic tumor
07 Which of the following is a risk factor for Hydatidiform Mole?			
A) Being younger than 15 years	B) Maternal trauma	C) Diabetes	D) History of multiple sexual
08 40 years old pregnant women came to emergency complaining from vaginal bleeding, severe nausea and vomiting, uterus is disproportionately large for her stage of pregnancy. Blood sample showed Very High HCG Level, doctors requested Ultrasound which showed cluster of grapes appearance signifying an abnormal placenta. Which of the following is probably the diagnosis?			
A) partial HM	B) Complete HM	C) Choriocarcinoma	D) chorioadenoma destruens
09 Most of the choriocarcinoma are preceded by which of the following ?			
A) partial HM	B) Complete HM	C) Normal pregnancy	D) ectopic pregnancy
10 In contrast to a complete mole, Partial Mole has which of the following?			
A) All Villi are hydropic and no normal villi are seen	B) No Fetal tissue present	C) Higher chance to progress to choriocarcinoma	D) Mild proliferation of Trophoblast

MCQs Answer key	01	02	03	04	05	06	07	08	09	10
	A	D	C	B	C	C	A	B	B	D

Thank You!

We kept 438 pathology theme in the credits to remind you that this wonderful work was originally done by them

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