

Trophoblastic Diseases





Objectives

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

Know the clinical presentation and the pathology of hydatidiform mole and choriocarcinoma.

THIS LECTURE WAS PRESENTED BY DR.MARIA ARAFAH & DR.HAMADA AL JAEDI

Osmosis video has some parts that included in the Embryology & Other Extra parts you can skip it



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Editing File

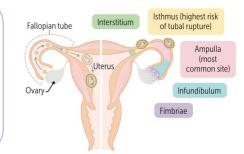
Color index : Main text (black) Female Slides (Pink) Male Slides (Blue) Important (Red) Dr's note (Green) Extra Info (Grey)





Definition

Ectopic pregnancy is defined as implantation of a fertilized ovum in any site other than the endometrium of the uterine cavity. About 1% of all pregnancies are ectopic



Site of ectopic pregnancy **Over 90% of ectopic pregnancies occur** Tubal (95% in the fallopian tubes (tubal pregnancy) Perito Ovaria Other sites of ectopic pregnancy include the ovaries, abdominal cavity and uterine cervix. **Clinical features** Many present as A woman with an abnormal an emergency ectopic tubal bleeding with tubal rupture, pregnancy may severe acute following a abdominal pain present with period of and hemorrhagic pelvic pain amenorrhea. shock. **Deep Focus Question** How does PID lead to infertility and ectopic pregnancy? PID can cause destruction of follicles in the ovary. Α. Β. PID can cause adhesions in the uterine cavity. C. PID can cause persistent inflammation impeding implantation.

D. PID can cause ovarian failure.

E. PID can cause scarring and fibrosis in the fallopian tubes, leading to occlusion. Answer: E

Ectopic pregnancy

Diagnosis

Clinical	Microscopically	Lap work
abdominal/pelvic ultrasound gestational sac within fallopian tube or other location	placental tissue or fetal parts	positive HCG levels
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Tubal ectopic pregnancy

Location

Fallopian tubes are the most common location for ectopic pregnancies

Factors

Any factor that retards passage of the ovum through the tubes predisposes to tubal ectopic pregnancy.

Causes

In about half of the cases, it is due to chronic inflammation and scarring in the oviduct.

Other places for ectopic pregnancy

Ovarian pregnancy

probably result from rare instances in which the ovum is fertilized just as the follicle ruptures.

Within the abdominal cavity

Gestation within the abdominal cavity occurs when the fertilized egg drops out of the fimbriated end of the oviduct and implants on the peritoneum.

Ectopic pregnancy

Risk factors:

Pelvic inflammatory disease/infections/salpingitis is the most common cause. The inflammation can damage ciliary activity, cause tubal obstruction, pelvic adhesions with scarring and distortion of the fallopian tubes. Women who have had pelvic infections have a five times greater risk of ectopic pregnancy (infection is usually by **Neisseriae gonorrhea & chlamydia**).

Abdominal/pelvic surgery or tubal ligation surgery (previous surgery) and Intrauterine tumors and endometriosis.

Smoking can decreased tubal motility by damaging ciliated cells or it may predisposing them to pelvic inflammatory disease (due to the impaired immunity in smokers).

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 and History of multiple sexual partners increase chance of pelvic inflammatory disease and therefore are high risk for ectopic pregnancy , Intrauterine device users are at higher risk of having an ectopic pregnancy should pregnancy occurs.

History of infertility: there is higher risk of ectopic pregnancy in the infertile population. This 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: please note that in many tubal pregnancies, no anatomic cause is evident.

Spontaneous Abortion "Miscarriage"

Definition

It's the spontaneous of a pregnancy (without medical intervention) at 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.

Diagnosis

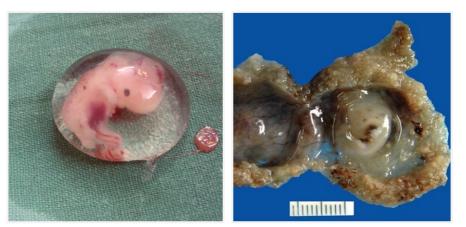
Ultrasound

They make sure that the endometrial cavity is empty and the placenta and fetal tissue has passed.

Microscopic Examination of the Conception Products Chorionic Villi.
 Fetal parts and changes in the endometrium (hypersecretory).

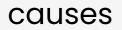
Genetic Tests

To look for any chromosomal anomalies



Pale spongy tissue =placenta

Spontaneous Abortion "Miscarriage"



The causes of miscarriages cannot always be determined
Miscarriages can occur for many reasons.

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Chromosomal Abnormalities	 Half of the 1st trimester miscarriages have abnormal chromosomes. Chromosomal abnormalities also become more common with age, and women over the age of 35 have a higher rate of miscarriage than younger women. A pregnancy with a genetic problem has a 95% probability of ending in a miscarriage. Chromosomal abnormalities of the fetus are the most common cause of early miscarriages.
Hormonal Problem	 Cushing's Syndrome Thyroid diseases Polycystic ovary syndrome Diabetes: good control of blood sugar during pregnancy is important. If the diabetes is not well controlled, there is an increase risk of miscarriages and also of the baby having birth defects. Inadequate function of the corpus luteum in the ovary (which produces the progesterone necessary for maintenance of the very early stages of pregnancy) leads to progesterone deficiency which may lead to a miscarriage.
Abnormal Structural Anatomy	Abnormal structural anatomy of the uterus can also cause miscarriages e.g. septate or bicornate uterus affect placental attachment and growth. Therefore, an embryo implanting on the septum would be at increased risk of a miscarriage. Uncommonly uterine fibroids can interfere with the implantation and blood supply, thereby causing a miscarriage.
Maternal Health Problems	can predispose to miscarriages e.g.: systemic lupus erythematosus and antiphospholipid antibody syndrome
Infections	 Listeria Monocytogenes & Toxoplasma Gondii Parvovirus B19, Rubella, Herpes Simplex, Cytomegalovirus and lymphocytic choriomeningitis virus etc are associated with an increased risk of pregnancy loss
Others	surgical procedures in the uterus during pregnancy e.g. amniocentesis and chorionic villus sampling.
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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 gestational trophoblastic diseases:

Benign non-neoplastic trophoblastic lesions	Hydatidiform mole	Gestational trophoblastic neoplasia (GTN)
 Diagnosed as Incidental finding on an endometrial curettage or hysterectomy specimen. 1. Exaggerated placental site. 2. Placental site nodule. 	 Result from abnormalities in fertilization. Benign, but may develop to choriocarcinoma. Complete hydatidiform mole. risk factor to progress into malignant choriocarcinoma more than Partial hydatidiform mole. Partial hydatidiform mole. Invasive mole / chorioadenoma destruens 	 Tumors that have the potential for local invasion & metastases. 1.Choriocarcinoma 2. Placental site Trophoblastic tumor. 3. Epithelioid trophoblastic tumor.

Hydatidiform mole

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.

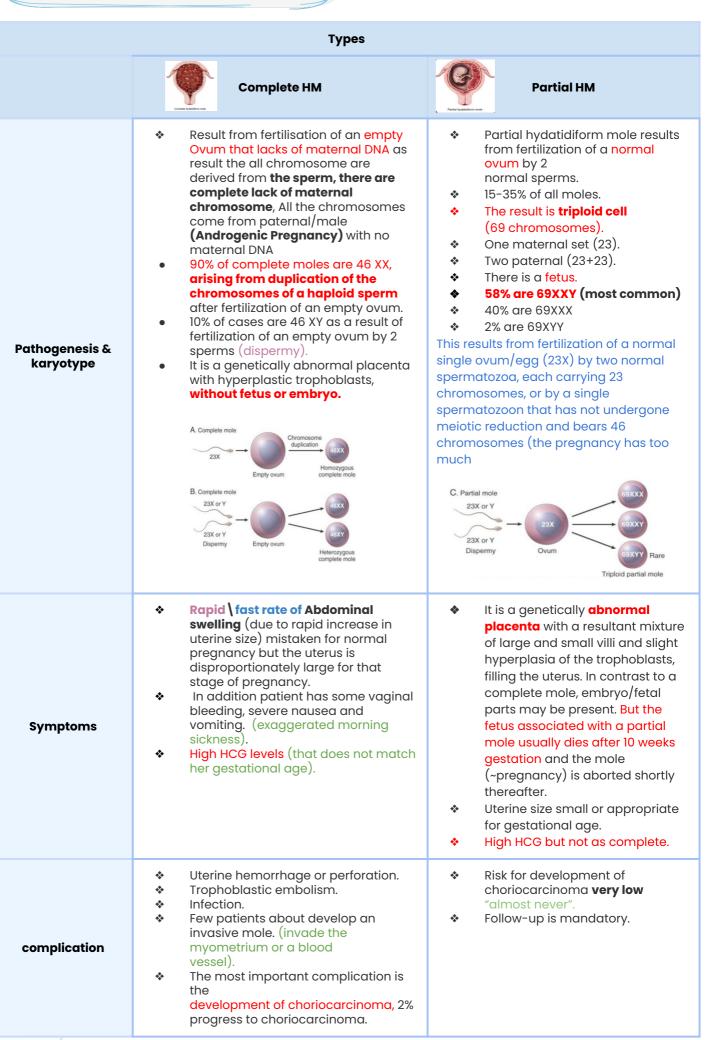
It is caused by Abnormal gametogenesis and fertilization.

It 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 grape-like masses, is common. Serum HCG concentration is markedly elevated, and they rapidly increase.

Risk factor	 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
• • • •	males Slides
Histological feature	 cystic swelling of chorionic villi with variable trophoblastic proliferation
	sperm 23 \rightarrow 23 \rightarrow 46 ova result
	Normal fertilization: a single sperm of 23 chromosomes fertilizes a normal egg of 23 chromosomes

Hydatidiform mole



Hydatidiform mole

Hyddidiloitittiloie				
	Types			
	Complete HM	Partial HM		
Histopathology	The uterus is distended and filled with swollen/large villi with prominent trophoblastic cells proliferation. No embryo, or fetal tissue is present.	Abnormal placenta: uneven (large and small). Normal villi may be present, with slight hyperplasia of trophoblast (mild proliferation) less than complete HM.		
Gross	 it looks like a bunch of grapes Ultrasound: will show a "cluster of grapes" appearance or a " snowstorm" appearance, signifying an abnormal placenta. 	Gross: mixture of large chorionic villi and normal appearing smaller villi.		
Treatment	Evacuation (removal of these villi) of uterus by curettage and sometimes chemotherapy. • With appropriate therapy cure rate is very high.	Evacuation of uterus by curettage or chemotherapy.		
Karyotype	Usually diploid 46 XX.	Usually triploidy 69 XXY. (Most common)		
Villi	All villi are hydropic; no normal villi seen.	Normal villi may be present.		
Fetal tissue	Not present.	Usually present.		
Trophoblast	Marked proliferation.	Mild proliferation.		
Serum HCG	Markedly elevated.	Less elevated.		
Invasive mole	Occurs in 15% of CMs.	Very rare.		
Behavior	2% progress to choriocarcinoma.	Very rarely progress to choriocarcinoma.		

invasive mole

- 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.

The mole sometime enter into the veins of the myometrium, and a times spread via the vascular channels to distant sites, mostly **the lungs** (note: death from such spread is unusual). (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



As an ovum being fertilised with 2 Sperms may seem odd , what is more odd is that a **twin could have different fathers from different sperms is a condition called : heteropaternal superfecundation** "Heteropaternal" signifies different fathers and "superfecundation" means the fertilization of two ova during the same menstrual cycle by separate mating actions. In other words, it is a phenomenon where a second egg is released, and two acts of sexual intercourse can lead to the fertilization of these eggs by two different sources of sperm. The short story is they're just fraternal twins with an extra twist.

The key ingredient is hyperovulation At the beginning of a cycle, the ovaries build up structures called follicles. Typically, at around day 8 of the cycle, all but one of these follicles degenerate. The last one standing develops the ovum (egg), and will then rupture near day 14, ejecting the egg – that's called ovulation. This process is regulated by hormones, particularly follicle-stimulating hormone (FSH). High FSH levels are thought to be responsible for multiple ovulation, causing more than one follicle to become dominant, or multiple instances of follicle development to occur in the same period. This means the two eggs can get ejected by the same ovary, or one egg can get ejected from each.That's how you get fraternal twins – two eggs, two sperm, two babies. Note that identical twins arise from one egg splitting into two after fertilization.

	Choriocarcinoma
Overview	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)
Prepositions	 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: early via blood to the lungs and other organs. Responds to chemotherapy but the prognosis is poor.

Deep Focus Question

What pattern is seen on an ultrasound scan of a patient with a hydatidiform mole?

- A. Pseudosac
- B. Heterogeneous uterus
- C. Non-homogenous echoic pattern
- D. Snowstorm pattern
- E. Double decidual sac.

Answer: D



Which of the following is associated with a complete hydatidiform mole?

- A. Some villi that are edematous
- B. 2 sperm and 1 egg
- C. Fetal parts
- D. Triploid chromosome
- E. High risk for choriocarcinoma Answer: E



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Keywords



Ectopic Pregnancy	 Most common site is fallopian tube tubal rupture, severe acute abdominal pain and hemorrhagic shock Placental tissue or fetal parts within the fallopian tube Positive pregnancy test (High HCG Levels). Risk factors : salpingitis , Tubal obstruction , Pelvic adhesions with scarring , N. gonorrhea & chlamydia 		
Spontaneous Abortion	 Most miscarriages occur during the first trimester (13 weeks) of pregnancy Causes : ½ of the 1st trimester miscarriages have abnormal chromosomes, Systemic Lupus Erythematosus (SLE), Antiphospholipid antibody syndrome. Microscopic Examination of Conception : Chorionic Villi, Trophoblasts, Fetal parts and changes in the endometrium (hypersecretory). 		
	Benign non-neoplastic lesions	 Incidental finding Exaggerated placental site. Placental site nodule. 	
Gestational trophoblastic disease		 Complete Hydatidiform Mole : fertilisation of an empty Ovum & lacks of maternal DNA as result the all paternal Duplication : 46 XX, arising from duplication of the chromosomes of a haploid sperm (most common) Dispermy : 46 XY as a result of fertilization of an empty ovum by 2 sperms uterus is disproportionately large for that stage of pregnancy. High HCG levels (that does not match her gestational age). development of choriocarcinoma, Gross feature: Cluster of grapes Pelvic Ultrasound: snowstorm appearance, villi. absence of embryo and amniotic fluid. Marked proliferation of Trophoblasts All villi are hydropic; no normal villi seen. 	
	Hydatidiform mole	 Partial Hydatidiform Mole : Partial hydatidiform mole results from fertilization of a normal ovum by 2 normal sperms. result is triploid cell (69 chromosomes) : One maternal set (23), Two paternal (23+23). 69XXY (most common) genetically abnormal placenta embryo/fetal parts may be present fetus usually dies after 10 weeks gestation Normal villi may be present. Mild proliferation of Trophoblasts 	
		 Invasive mole: extends into the myometrium of the uterus. spread via the vascular channels to distant sites, mostly the lungs 	
	Choriocarcinom a	 Malignant tumor of placental tissue, composed of a proliferation of malignant cytotrophoblast and syncytiotrophoblast No villi formation, preceded by complete hydatidiform mole. Very high levels of serum HCG. 	

YOU	Question 2
Question 1 Which of the following considered a Hydatidifo mole Gestational Trophob Disease?	is orm is brown is b
chorioadenoma des	diagnosis?
Choriocarcinoma	Partial HM
Placental site trophok tumor	olastic chorioadenoma destruens
Epithelioid trophobla tumor	Complete HM
Question 3 In contrast to a complete Partial Mole has which o	of the 🔰 👘 most common karyotype for
following? Higher chance to progre choriocarcinoma	ess to 47 XXY.
No Fetal tissue prese	ent 45 XO.
Mild proliferation of Trophoblast	69 XXY.
All Villi are hydropic an normal villi are see	

YOU VŚ MCQs

Question 5

What is the most common cause of spontaneous abortion during the first trimester?

Chromosomal abnormalities

Drugs

Polycystic ovarian syndrome

Pelvic inflammatory disease

Question 6

Which one of the following is the most important risk factor for ectopic pregnancy?

Ovarian neoplasm

Multiparty

Endometriosis

Chronic salpingitis

Question 7

Which of the following is complete mole?

High HCG, no fetus, 46XX

High HCG, with fetus, 46XX

High HCG, no fetus, 64XXY

High HCG, with fetus, 64XXY

Question 8

39-year-old woman presents for ante-natal care. Clinical examination showed that the uterus is larger than expected and ruptured. In addition, her serum Beta HCG was higher than expected. Ultrasound examination showed no fetus. Histologic examination of the uterine contents showed proliferating synctio-and cytotrophoblasts. Which one of the following is the most likely diagnosis?

Partial HM

Dysgerminoma

Embryonal carcinoma

Choriocarcinoma

5- A / 6-D / 7- A / 8-D



Cases



1.A 22-year-old woman presents to the emergency room with a 2-hour history of acute abdominal pain and vaginal bleeding. Her vital signs are normal. Physical examination reveals blood oozing from the vaginal opening. Laparotomy shows an enlarged right fallopian tube with hemorrhage and rupture. What is the most likely cause of hemorrhage in this patient?

A.Choriocarcinoma

B.Ectopic pregnancy C.Infarcted tubal polyp

D.Intramural leiomyoma

2.A 17-year-old woman presents to her gynecologist with a 5-day history of vaginal bleeding. A home pregnancy test had been positive 1 week previously. This morning, the patient passed tissue with the appearance of small grapes. An ultrasound shows a dilated endometrial cavity but no evidence of a fetus. Endometrial evacuation of the uterus by suction curettage reveals grapelike clusters, with individual units measuring up to 5 mm in diameter (shown in the image). Cytogenetic examination



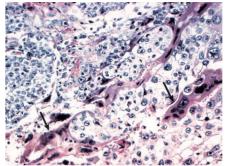
of this tissue will most likely demonstrate which of the following genetic patterns?

A.Aneuploidy

B.Diploidy

C.Haploidy

3.A 41-year-old immigrant woman from Asia presents for prenatal care. Her uterus is significantly larger than expected, and her serum hCG level is much higher than expected for her due date. No fetus is found on ultrasound examination. The abnormal placenta is removed. One month later, this patient presents to the emergency room with abdominal pain. Exploratory laparotomy reveals rupture of the posterior uterine fundus with grape-like tissue extruding from the



D.Triploidy

defect. Two liters of blood are present in the abdominal cavity. Histologic examination of the uterine mass is shown in the image. The arrows point to syncytial cells. Which of the following is the most likely diagnosis?

carcinoma adenocarcino	A.Carcinosarcoma	B.Choriocarcinoma		D.Endometrial adenocarcinomo
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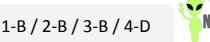
4.A 20-year-old woman presents to her gynecologist with a 3-day history of vaginal bleeding. An ultrasound shows a dilated endometrial cavity. Evacuation of the uterus by suction curettage reveals grapelike clusters and fetal parts. Cytogenetic examination of this tissue will most likely demonstrate which of the following genetic patterns?

A.Diploidy

B.Euploidy

C.Haploidy

D.Triploidy



NEED EXPLANATION ? CLICK HERE







EXTRA CASES MAY REQUIRE EXTRA INFO

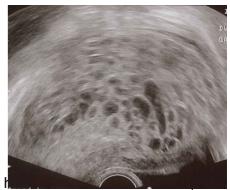
1.A 36-year-old primigravid woman comes to the office at 15 weeks gestation due to vaginal bleeding. This morning, she woke up and noticed blood in her underwear. She has also had severe morning nausea that has been worsening, resulting in multiple episodes of vomiting throughout the day for the past week. She states it has been difficult to keep down anything she eats or drinks. She denies shortness of breath, changes in vision, or chest pain. She does not use tobacco, alcohol or illicit drugs. Current temperature is 37.0° C (98.6° F), pulse is 100/min, and blood pressure is 145/85 mmHg. On physical examination, a 19-week-size uterus and bilateral adnexal masses are palpated on bimanual examination. Laboratory tests show hCG concentrations of 110,000 mIU/mL. TSH is 0.1 μ U/mL. Which of the following is the most likely diagnosis?

A.Preeclampsia

B.Complete mole

C. Ectopic pregnancy D.Partial mole

2.A 38-year-old primigravid woman comes to the office at 18 weeks gestation due to palpitations and pelvic pressure. She has been consistent with prenatal care. She is following a healthy diet and takes prenatal vitamins daily. She does not smoke or use alcohol or illicit drugs. Temperature is 37.5°C (99.5°F), pulse is 110/min,and blood pressure is 130/80 mmHg. On physical examination, the patient's skin is moist and warm. Uterus size is consistent with 22 weeks of gestation. When the patient is holding her hands stretched, a mild tremor is noted. The thyroid gland is normal to palpation and nontender. Laboratory tests show h



mIU/mL. TSH is 0.1 µU/mL. An abdominal ultrasound is obtained and shown.

B.46, XX

C.46, XO

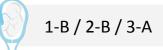
D.69, XYY

3.A 25-year-old woman comes to the clinic due to a progressive cough accompanied by mild hemoptysis. During the past 2 weeks, she has been experiencing non-productive cough, pelvic pressure, and mild vaginal bleeding. Six weeks ago, the patient had an abortion at 15 weeks gestation, and since then, her menstrual period had not yet returned. She is in good health, and she does not smoke or use alcohol or illicit drugs. She is sexually active with her male partner and currently does not use contraception. Temperature is 37.0°C (98.6°F), pulse is 100/min, and blood pressure is 135/85 mmHg. On physical examination, the uterus is soft and mildly enlarged. Vaginal examination shows minimal blood at the vaginal vault. The cervix is closed, non-erythematous. An x-ray of the chest is obtained and shows multiple, rounded nodules of variable size scattered throughout the lungs. Which of the following findings is most specific for this patient's conditions?

A.Elevated serum hCG levels

B.Positive acid-fast bacilli on sputum analysis C.Anti-glomerular basement membrane antibodies on immunofluorescence

D.Elevated d-dimer



Pathology Team

