Approximately 15% of early pregnancies are complicated by pelvic or abdominal pain and uterine bleeding or spotting. In these situations, you must determine whether your patient has a viable intrauterine pregnancy, a pregnancy that will end in a miscarriage (spontaneous abortion), or an ectopic pregnancy.

To guide you to the correct diagnosis, a medical history and physical examination can be helpful. For example, a woman with a prior ectopic pregnancy who now has an early pregnancy complicated by pelvic pain and uterine bleeding is at high risk for an ectopic pregnancy. Physical examination also is important; if the pelvic examination reveals a dilated cervix with pregnancy tissue in the cervical os it is likely that a miscarriage is in progress. For most cases of early pregnancy complicated by pelvic pain and/or uterine bleeding, however, a pelvic sonogram and serial quantitative measurement of human chorionic gonadotropin (hCG) are needed to achieve the correct diagnosis.

Here I outline the clinical markers for transvaginal ultrasonography that indicate a viable or failed intrauterine pregnancy as well as an ectopic pregnancy. I also present data on single vs serial hCG measurement and discuss serial hCG levels that indicate viable or nonviable intrauterine or ectopic pregnancy.

Is an early gestation viable? Clinical evaluation

Transvaginal pelvic ultrasound

Transvaginal and transabdominal ultrasonography play a critical role in evaluating early pregnancy problems. In a normal pregnancy, key developmental milestones that can be observed reliably on ultrasound are:

- intrauterine gestational sac at 5 weeks
- yolk sac at 5.5 weeks
- embryonic pole and fetal heart beat at 6 to 6.5 weeks’ gestation.

A pelvic ultrasound also may provide evidence that an intrauterine pregnancy will fail and result in a miscarriage. Findings diagnostic of a failed intrauterine pregnancy include:

- crown-rump length ≥7 mm and no fetal heartbeat
- mean sac diameter ≥25 mm and no embryo
- absence of an embryo with a heart-beat more than 2 weeks after an ultrasound scan that showed a gestational sac without a yolk sac
- absence of an embryo with a heart-beat more than 11 days after a scan that showed a gestational sac with a yolk sac.

Findings suspicious for a failing intrauterine pregnancy include:

- crown-rump length <7 mm and no fetal heartbeat
- mean sac diameter of 16 to 24 mm and no embryo
- no heartbeat 7 to 13 days after an ultrasound scan that showed a gestational sac without a yolk sac
- no heartbeat 7 to 10 days after an...
ultrasound scan that showed a gestational sac with a yolk sac.

**When it’s an ectopic pregnancy.** Definitive ultrasonographic evidence of an ectopic pregnancy is identification of a fetal heartbeat outside the uterus or a gestational sac and yolk sac outside of the uterus. An adnexal mass can be identified on ultrasonography in most cases of ectopic pregnancy. In one study of 291 ectopic pregnancies, an adnexal mass was identified in 94% of cases, and a moderate to large amount of free pelvic fluid was found in 36% of cases. The adnexal masses included nonspecific (54% of all ectopic cases), a tubal ring without a yolk sac or embryo (25%), a yolk sac but no embryonic heartbeat (8%), and an embryo with cardiac activity (7%).

In clinical units with high-quality gynecologic ultrasonography available, most ectopic pregnancies will be detected on initial scan and only 10% to 15% of ectopic pregnancies will have an ultrasound finding of no intrauterine pregnancy and no evidence for an extrauterine pregnancy.

**Serial hCG measurement**

A single quantitative hCG measurement cannot reliably distinguish a viable intrauterine pregnancy from a spontaneous abortion or an ectopic pregnancy because there is a significant overlap of hCG values in these three clinical situations. However, evaluating the change between two hCG measurements, measured 48 hours apart, can help guide you toward the correct diagnosis.

Almost all (in the range of 99%) viable intrauterine pregnancies demonstrate an increase in hCG level of 53% or more over 48 hours, whereas only 21% of ectopic pregnancies demonstrate a rise of 53% or more. Most pregnancies that will end in a miscarriage demonstrate a decrease in hCG level over 48 hours. If the initial hCG value is 2,000 mIU/mL, 90% of pregnancies that will end in miscarriage will have an approximate 30% decrease in hCG over 48 hours. If the initial hCG is 1,000 mIU/mL, 95% of spontaneous abortions will have a 28% decline in 48 hours. About 10% of ectopic pregnancies also will demonstrate a 30% decrease in hCG over 48 hours.

A minor disadvantage of serial hCG measurements is that patients may become anxious and fearful as they await the result of life-altering test results.

**When a gestation is found to be nonviable**

A viable intrauterine pregnancy is highly unlikely in a woman with no ultrasound evidence of an intrauterine pregnancy or an adnexal mass and an hCG level that rises very little, plateaus, or decreases over 48 hours. In this situation, a Karman cannula aspiration of uterine contents with rush pathology analysis can help clarify the likely diagnosis and guide therapy.

Women with documented villi on pathology likely are experiencing a miscarriage and can have their hCG level followed to resolution. Women with no documented villi and no decrease in hCG after the Karman...
Experts agree: Do not use methotrexate after a single hCG measurement

Many experts have counseled against the use of a single hCG measurement in the discriminatory zone of 1,500 to 2,000 mIU/mL to trigger methotrexate treatment. Here is a sampling of their advice:

“An hCG level of 2,000 mIU/mL, without ultrasound findings of intrauterine pregnancy, while suggestive of abnormal pregnancy, is not diagnostic. Per the results of recent studies, it is reasonable to closely follow up rather than treat many of these early, stable cases of ectopic pregnancy.”

—Mehta et al.1

“Our data demonstrate that using a single value of serum hCG in a pregnancy of unknown location (PUL) population is of limited value.... A significant proportion of failing PULs and early intrauterine pregnancies in a PUL population have high serum hCG levels at presentation.”

—Condus et al.2

“The hCG discriminatory level should not be used to determine the management of a hemodynamically stable patient with suspected ectopic pregnancy, if sonography demonstrates no findings of intrauterine or ectopic pregnancy.”

—Doubilet et al.3

“There is almost no reason to give methotrexate on first encounter with a patient. If a patient is symptomatic with severe pain or signs of rupture, a surgical approach is indicated and methotrexate is contraindicated.”

—Barnhart et al.4

[When using the discriminatory zone]... “there is a chance of harming a viable intrauterine pregnancy, especially if the hCG level is 2000 to 3000 mIU/mL.... There is limited risk in taking a few extra days to make a definitive diagnosis in a woman with a pregnancy of unknown location who has no signs or symptoms of rupture and no ultrasonographic evidence of ectopic pregnancy.”

—Doubilet et al.3

“Viable intrauterine pregnancy is possible in patients with pregnancy of unknown location and hCG levels above the generally accept discriminatory zone, strict adherence to which can potentially disrupt a normal pregnancy. We support the need for judicious use of the hCG discriminatory level in hemodynamically stable patients with pregnancy of unknown location, and the decision to intervene should not be based solely on a single hCG level.”

—Ko and Cheung.5

Cannula aspiration can be presumed to have an ectopic pregnancy. If stable, these women may be candidates for treatment with methotrexate.8,9

Stop using the discriminatory zone and a single hCG measurement to trigger clinical intervention

As noted above, a single hCG measurement is of very little value in determining whether an early pregnancy is a viable or nonviable intrauterine pregnancy or is ectopic. Many experts have reported that if a single hCG measurement shows a value of more than 1,500 mIU/mL and a pelvic ultrasound shows no intrauterine pregnancy, an ectopic or nonviable intrauterine pregnancy is likely. Some experts have used the presence of an hCG value of more than 1,500 mIU/mL plus an ultrasound scan without evidence of an intrauterine pregnancy to clinically diagnose the absence of a viable intrauterine pregnancy and administer methotrexate to treat a presumptive ectopic pregnancy. Many experts believe, however, that this approach will necessarily result in the treatment of viable intrauterine pregnancies with methotrexate.5,10

Based on one analysis, for 100 women with an initial hCG value between 2,000 and 3,000 mIU/mL and no intrauterine pregnancy or adnexal mass seen on ultrasound, follow-up will reveal that 65.5% had a failed intrauterine pregnancy, 33% had an ectopic pregnancy, and 1.5% had a viable intrauterine pregnancy.3,10,11 If all of these 100 women had been treated with methotrexate for a presumed ectopic pregnancy, approximately two women with a viable intrauterine pregnancy would have been exposed to methotrexate.5

References


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This exposure would likely result in either a pregnancy loss or, if the pregnancy continues, an increased risk of fetal anomalies.

If the patient is obese, has fibroids, or has adenomyosis, she has an increased risk of an ultrasound failing to detect an early intrauterine pregnancy when the hCG value ranges from 1,500 to 3,000 mIU/mL. If the discriminatory zone is raised to 4,000 mIU/mL, the likelihood of mistakenly diagnosing a viable intrauterine pregnancy as a failed or ectopic pregnancy is much less (but not zero).

There is almost no clinical situation in which methotrextate should be given to a patient suspected of having an ectopic pregnancy on the first visit, unless ultrasound demonstrates an adnexal mass indicative of ectopic pregnancy. If the patient has severe pain or bleeding, or has signs consistent with a ruptured ectopic pregnancy, surgical intervention likely is warranted. If the patient is clinically stable, a safe option is to repeat the hCG measurement in 48 hours, with an ultrasound if indicated.

The discriminatory zone is an interesting and elegant idea. But in practice it is fraught with serious dangers, the greatest of which is methotrextate administration to a patient with a viable intrauterine gestation. My advice is that gynecologists should stop relying on a discriminatory zone of 1,500 to 2,000 mIU/mL to trigger clinical intervention. €

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