

**American College of Radiology
ACR Appropriateness Criteria®**

Clinical Condition:

First Trimester Bleeding

Variant 1:

Positive urine or serum pregnancy test.

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
US pelvis transabdominal	9	Correlate finding with quantitative β -hCG.	O
US pelvis transvaginal	9	Correlate finding with quantitative β -hCG. M-mode for fetal heart rate.	O
US pelvis with Doppler	7	Pulsed Doppler of the embryo should be avoided.	O
MRI pelvis with or without contrast	4	See Summary of Literature Review for use of MRI and contrast in pregnancy.	O
CT pelvis with or without contrast	1	See Summary of Literature Review for use of CT and contrast in pregnancy.	☢ ☢ ☢
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

FIRST TRIMESTER BLEEDING

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Summary of Literature Review

Ultrasonography (US) has evolved as the primary imaging modality in the evaluation of patients presenting with bleeding in the first trimester of pregnancy. Magnetic resonance imaging (MRI) and computed tomography (CT) play a minor role in problem solving when the US findings are indeterminate or for treatment planning. By correlating US studies with serum human chorionic gonadotropin (β -hCG) levels, the various etiologies of first trimester vaginal bleeding can usually be differentiated. This includes differentiating an intrauterine from an ectopic pregnancy and a live from a failed pregnancy. The following is an overview of US and associated β -hCG findings that have been shown to be diagnostically useful.

Intrauterine Fluid Collection

The first visible US evidence of an intrauterine pregnancy is the gestational sac (chorionic sac). Using current high-frequency transducers, sacs as small as 2-3 mm (mean sac diameter) may be visualized, corresponding to 4.5-5 weeks of gestation [1]. Before any structures are visualized within the gestational sac, two signs may be used to distinguish an intrauterine gestational sac from a fluid collection within the endometrial cavity, known as a "pseudogestational" sac. The double decidual sign consists of two concentric echogenic rings, each with associated fluid. The inner fluid collection is the gestational sac surrounded by the echogenic decidual capsularis. This "ring" bulges into the endometrial cavity which contains some fluid that outlines the second echogenic "ring" of the decidua vera [2]. The double decidual sign is nearly 100% specific, but only 64 %

sensitive [3]. The intradecidual sign consists of an intrauterine fluid collection with a discreet echogenic rim eccentrically positioned in the endometrium and separate from the distinct echogenic line that represents the collapsed endometrial cavity [4,5]. This sign, which can be visualized as early as 4.5 weeks, has been less well validated, though a recent study cites a sensitivity and specificity of 60%-68% and 97%-100%, respectively [6].

The generally accepted discriminatory level of β -hCG for the gestational sac (level at which a gestational sac should definitely be identified) is 1000-2000 mIU/ML [7,8]. However, because of human variation as well as the technical limitation of studies, this level should not be taken as an absolute. Furthermore, despite the presence of either the intradecidual or double decidual signs, and particularly in a patient at high risk for ectopic pregnancy, US follow-up may be warranted to confirm definitive (intrasac) findings of an intrauterine pregnancy. The interval for follow-up should be based on established parameters of the normal growth rate of the gestational sac and corresponding quantitative levels of β -hCG.

Definitive Intrauterine Gestation

Since the normal gestational sac grows at a rate of 1 mm/day mean sac diameter, it is typically only a matter of waiting a few days to visualize the yolk sac, which is the first definitive sign of an intrauterine pregnancy. The yolk sac should usually be visualized in a gestational sac between 5 to 13 mm using an endovaginal probe at 9-5 MHz [9]. The yolk sac should be visualized in any gestational sac >8 mm [10], and with a discriminatory level of β -hCG of 5,000 mIU/ML. The yolk sac is a discreet, round, thin-walled structure, which is usually eccentrically located within the gestational sac and grows slowly during the first trimester.

The embryo will initially appear as a thickened, linear echogenic structure between the yolk sac and the gestational sac, possibly seen at 8 mm sac size, but definitely by 16 mm [10], with a discriminatory β -hCG level of 10,000 mIU/ML. Absence of cardiac activity may be normal in embryos \leq 5 mm [11]. Embryonic demise may be diagnosed with an embryo >5 mm without cardiac activity. The normal range of heart rate from 6.2-7 weeks is 100-120 beats per minute, and after 7 weeks the mean heart rate is 137-144 [12,13]. M-mode should be used to document cardiac activity and measure the rate.

Once an intrauterine gestation is definitely established by US, various US findings may be seen in patients with first trimester bleeding that predict or are associated with a poor outcome. These include: bradycardia [14,15], slow growth rate of the embryo, abnormally small [16] or abnormally large [17] gestational sac compared to embryo, enlarged amniotic cavity [18], empty amniotic cavity [19], abnormal size or shape of the yolk sac [20], and low position or irregular shape of the gestational sac. Though follow-up US can be performed in these situations, clinical follow-up is often adequate.

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Subchorionic hemorrhage, a common finding during the first trimester, is associated with a poor outcome when it is moderate to large in comparison to the size of the gestational sac [21].

Ectopic Pregnancy

Whenever an intrauterine pregnancy is not identified, scanning must proceed to evaluate extrauterine locations for the pregnancy [22,23]. This involves identification of the ovaries and corpus luteum and a careful search for any nonovarian “mass” since most ectopic pregnancies are located in the fallopian tubes. In at least 80% of cases, the ectopic pregnancy is located ipsilateral to the corpus luteum and must be distinguished from it. The corpus luteum is characterized by a circumferential rim of low-resistance color Doppler flow supplied by a prominent ovarian artery branch. The gray scale appearance of the corpus luteum may vary from solid and hypoechoic to heterogeneous or anechoic. Pressure with the endovaginal transducer on the ovary can help to confirm the intraovarian location of the corpus luteum, distinguishing it from any extraovarian mass.

While visualization of an extrauterine gestational sac with an embryo is 100% specific for an ectopic pregnancy, this situation is relatively uncommon. More likely, though slightly less specific, is an extrauterine tubal ring which may be empty or contain a yolk sac and/or a nonviable embryo. Frequently, the ectopic pregnancy will appear as a complex, extraovarian, extrauterine “mass” representing a hematosalpinx. In most cases, the echogenicity of the tubal ring is greater than the echogenicity of the normal ovary. In comparison, the echogenicity of the corpus luteum is either equal to or less than the ovarian echogenicity [24,25]. Because the vascularity of ectopic pregnancies is variable, color and pulsed Doppler imaging are not necessarily useful. If the resistive index of the arterial flow is very low or very high, it is more typical of an ectopic pregnancy than a corpus luteum [26]. However, the vascularity in many ectopic pregnancies is typical low-resistance trophoblastic flow with waveforms similar to corpus luteal flow. In addition, some ectopics are avascular. While color Doppler imaging may be helpful in identifying a small ectopic pregnancy, gray-scale identification of an extraovarian sac or “mass” is the most important feature.

Assessment of the nature and amount of any free fluid is essential in the evaluation for an ectopic pregnancy. In this setting, echogenic material within the free fluid is assumed to be free blood. The presence of free or clotted blood, even without identification of an extraovarian mass, is significant presumptive evidence of an ectopic pregnancy [27-29]. The infrequent mimic of this situation occurs when there is rupture of a hemorrhagic cyst with an early, nonvisualized intrauterine pregnancy. If blood is identified in the pelvis, transabdominal US should be extended into the flanks and dependent locations in the right upper (Morison’s pouch) and left upper quadrants. Larger amounts of blood correlate with ruptured ectopic pregnancy but in one-third of cases with significant free fluid, the fallopian tubes are intact [30]. Clotted blood in

the pelvis can be very mass-like and, when it surrounds an ectopic pregnancy, may simulate a uterus. The clotted blood can blur the margins of the uterus and ovaries, making their identification more difficult. In such instances, color Doppler may be helpful to show that all of this solid-appearing material is avascular [31-34].

In a small percentage of cases, probably less than 4%, the ectopic pregnancy may be in an unusual location. Intrauterine ectopic locations include interstitial (cornual), cervical, and within a Cesarean section scar, and they account for the majority of unusual ectopic pregnancies. Extrauterine ectopic locations, including the ovary and abdominal cavity, are extremely rare. Heterotopic pregnancies (an intrauterine and an extrauterine pregnancy) are also extremely rare. Thus, in the routine population, identification of a normally positioned intrauterine pregnancy essentially rules out the possibility of a coexisting ectopic pregnancy. Patients who have conceived through assisted reproduction have a higher incidence of heterotopic pregnancies.

While US is usually sufficient for the diagnosis of unusually located ectopic pregnancies, there are increasing reports of using MRI to aid in these diagnoses. An interstitial pregnancy is characterized on MRI by the presence of a junctional zone between the uterine cavity and the interstitial pregnancy which is partially surrounded by myometrium [35]. The typical MRI appearance of a cervical ectopic pregnancy consists of a lobulated, solid mass with heterogeneous signal intensity containing enhancing papillary projections due to fetoplacental remnants [36]. MRI may also help in cases of unusual implantation sites in women with uterine anomalies.

Because CT is contraindicated in the first trimester of pregnancy, it is also not a primary imaging modality for ectopic pregnancy. The few existing case reports of CT with ectopic pregnancy were done for other reasons or in patients not known to be pregnant. On contrast-enhanced CT, the ectopic pregnancy may demonstrate a brightly enhancing rim, similar to a corpus luteum. [37,38]. When a patient is clinically unstable, a delay in any type of imaging may be unwarranted.

Pregnancy of Unknown Location

A first trimester patient with bleeding and no identifiable intrauterine or extrauterine pregnancy may have had a spontaneous abortion. Clinical findings will often support this diagnosis based on cramping pain and passage of identifiable tissue. If a prior pelvic US had demonstrated an intrauterine pregnancy, the empty uterus on a follow-up scan is definitive proof of a miscarriage. US may provide further information about the possibility of retained products of conception. The presence of focal thickening or material within the endometrial canal with adjacent low-resistance arterial flow in an endometrial or subendometrial location is highly suggestive of retained products of conception.

Not infrequently a first trimester sonogram in a pregnant patient with bleeding may be “normal” without any

intrauterine or extrauterine pregnancy or any abnormal free fluid. In this situation, the differential diagnosis includes the “triple rule out” of an early intrauterine pregnancy <4.5 weeks, an early nonvisualized ectopic pregnancy or a spontaneous abortion. These patients may also be considered to have a “pregnancy of unknown location” (PUL). In this situation, the American Society of Reproductive Medicine [39] advocates uterine curettage to rule out an ectopic pregnancy when the β -hCG is >2,400 mIU/ML. However, this approach will result in the loss of some early intrauterine pregnancies. Thus, if the patient is clinically stable, many authors recommend observation. A quantitative β -hCG should be obtained and then followed. In a normal intrauterine pregnancy, the level should approximately double every 48 hours. If the initial level was low, when it reaches the discriminatory zone a repeat pelvic sonogram may be obtained to confirm an intrauterine pregnancy. If the level drops appropriately, resolution of a nonvisualized PUL is assumed. If the level fails to decline and plateaus, an ectopic pregnancy is more likely. In such situations, follow-up US may be obtained and/or medical therapy for a presumptive ectopic pregnancy.

Miscellaneous Diagnoses

When the US does not show an intrauterine gestational sac or pseudosac, but rather a moderate or even significant amount of mixed cystic and solid material within the uterus, one should consider the possibility of a first trimester molar pregnancy, the most common form of gestational trophoblastic disease. Unlike the classic US findings in the second trimester of a distended endometrial cavity filled with innumerable small cystic spaces, in the first trimester the appearance is variable. The US appearance may include a small, echogenic endometrial mass without cystic spaces as well as mixed echogenic and cystic material [40]. The US findings overlap those of a failed intrauterine pregnancy with hydropic degeneration and retained products of conception. Thus, the differential diagnosis should include these possibilities. The β -hCG is often, but not always, inappropriately elevated. Complete molar pregnancies are usually intrinsically avascular, and thus color Doppler imaging does not typically aid in the diagnosis. Molar pregnancies may be associated with theca lutein cysts in the ovaries in 20%-50% of cases, but this is less common in the first trimester. In complete molar pregnancies hydropic degeneration occurs with absence of vessels in the villi. Thus, complete moles are relatively avascular, and color Doppler imaging does not typically aid in the diagnosis. With invasive moles, color and pulsed Doppler imaging is very helpful to estimate the degree of invasion [41].

Usually the combination of US and clinical factors is sufficient for diagnosing gestational trophoblastic disease. However, in confusing cases, pelvic MRI may be helpful to differentiate it from incomplete abortion and ectopic pregnancy, as well as to help in the diagnosis of persistent gestational trophoblastic disease, which requires

chemotherapy [42]. CT can also be helpful to detect extrauterine spread of gestational trophoblastic disease.

US can also depict some unusual causes of first trimester bleeding. These include vascular abnormalities such as pseudoaneurysm and arteriovenous malformation. The latter entity may overlap with the findings of retained products of conception. Color Doppler imaging is crucial in these diagnoses. Treatment typically includes transcatheter embolization [43].

Safety Issues

Magnetic Resonance Imaging

Pelvic MRI has been in use for over 20 years with no evidence of adverse effects to the fetus in both clinical and laboratory investigations [44]. Nevertheless, safety concerns regarding potential heating effects of radiofrequency pulses and acoustic injury to the fetus when exposed directly to the magnetic field (eg, with abdominopelvic or lumbar spine MRI) have not been completely dispelled [45]. While no fetal harm has been reported with ≤ 1.5 -T scanning, little experience has been reported at higher field strengths. Guidelines on practice procedures for MR imaging of pregnant patients are outlined in ACR White Paper on MR Safety [46]. Gadolinium contrast agents administered to a pregnant woman crosses the placenta and enters the fetal circulations, filtered via the fetal kidneys and excreted into the amniotic fluid where they may remain for an indeterminate time. In animals, fetal gadolinium exposure to repeated and higher doses than that used clinically has been reported to result in increased rates of intrauterine growth restriction and birth defects [47]. To date, no such adverse effects to the human fetus have been reported. Nevertheless, gadolinium contrast agents should be administered only after an in-depth risk-benefit analysis argues for an overwhelming benefit to the mother and child that outweighs the potential risks to the fetus from exposure to free gadolinium ions. Guidelines on practice procedures for gadolinium administration in pregnant patients are outlined in [ACR Manual on Contrast Media](#) [48].

Computed Tomography

Despite its diagnostic utility, pelvic CT, which delivers ionizing radiation, should be selectively used in evaluating children and women in their reproductive years. It should be noted that, to date, no direct evidence has been reported to demonstrate that exposure to a diagnostic CT scan causes cancer or birth defects. Nevertheless, a pelvic CT in a pregnant patient is estimated to deliver up to 2.5 rad (0.025 Gy) thereby increasing fetal radiation dose to approximately 10-fold above background [49,50]. While this dose is still well below the estimated threshold risk for fetal malformations (5 rad or 0.05 Gy) [51], a small but not completely negligible increase in cancer risk to both the mother and child is theoretically possible. Linear extrapolation from cancer rates observed in atomic bomb survivors many of whom experienced higher radiation doses suggests that a pelvic CT could increase the risk for developing cancer by 0.3% or 1/300 in a fetus in utero, 0.25%, or 1/400 in a

10 year-old girl, and 0.1%, or 1/1000 in a 30 year-old woman [51,52]. This risk is thought to be additive with repeat scans. Iodinated contrast agent administered to a pregnant woman crosses the placenta, resulting in possible fetal thyroid depression by exposure to free iodine [53]. While such an effect has never been directly demonstrated, infants of mothers who received iodinated contrast during pregnancy should be tested for hypothyroidism, already a standard neonatal screening procedure in the United States. No evidence suggesting that iodinated contrast is teratogenic or carcinogenic has been reported. Guidelines on practice procedures for iodinated administration in pregnant patients are outlined in [ACR Manual on Contrast Media](#) [48].

Ultrasound

US is generally considered safe during pregnancy. As in any imaging procedure, the ALARA (as low as reasonably achievable) principle should be followed. Cardiac activity may be documented in real time, or M-mode imaging. Because of higher energy levels, pulsed and color Doppler of the embryo should be avoided if possible. Pulsed and color Doppler may be extremely useful for other first trimester issues, including retained products of conception and adnexal masses [54].

Summary

- Transabdominal or transvaginal US may be used for patients with first trimester bleeding.
- Higher frequency transvaginal imaging will be more sensitive for earlier pregnancies.
- Transabdominal imaging is particularly useful to assess the amount of free fluid and for abnormalities beyond the field of view of a high-frequency vaginal probe.
- The results of imaging should be correlated with the quantitative β -hCG level.
- M-mode imaging should be used to document embryonic viability.
- Pulsed Doppler should not be used on an embryo.
- Color and pulsed Doppler US imaging can be extremely useful for abnormalities or findings unrelated to a live embryo, including uterine and adnexal vascular abnormalities, ovarian torsion, retained products of conception, and adnexal masses.
- MRI of the pelvis may be used if US is insufficient for unusual ectopic pregnancies, gestational trophoblastic disease, or vascular abnormalities.
- CT may be useful in pregnant patients with trauma, for staging of malignancy, or if MRI is not possible.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective

dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☼	<0.1 mSv	<0.03 mSv
☼ ☼	0.1-1 mSv	0.03-0.3 mSv
☼ ☼ ☼	1-10 mSv	0.3-3 mSv
☼ ☼ ☼ ☼	10-30 mSv	3-10 mSv
☼ ☼ ☼ ☼ ☼	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as NS (not specified).

Supporting Document(s)

- [ACR Appropriateness Criteria® Overview](#)
- [Procedure Information](#)
- [Evidence Table](#)

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.