Vaginal bleeding in the early stages of pregnancy

A number of potential causes of early pregnancy vaginal bleeding must be considered when deciding what type of management is required.

Up to 25% of all women in the early stages of pregnancy will experience vaginal bleeding or spotting. Even more sobering, half of those women will go on to experience intrauterine fetal demise prior to the 20th week. To reduce morbidity and mortality, the astute practitioner should be able to effectively assess and manage a patient with vaginal bleeding in the first half of her pregnancy.

Causes

Appropriate assessment and management of the patient requires an understanding of the differential diagnoses of vaginal bleeding in early pregnancy (Table 1). Fifty percent of early pregnancy bleeds—defined as bleeding at <20 weeks’ gestation—occur in viable intrauterine pregnancies (IUP). A total of 30% to 50% of early pregnancy bleeds indicate fetal demise, 7% of which are attributable to ectopic pregnancy (EP), and fewer than 1% are caused by trophoblastic disease and/or lesions of the cervix/vagina.

While chromosomal abnormalities are the most common cause of fetal demise and subsequent...
The patient will present with vaginal bleeding and mild-to-moderate subpubic or midline lower abdominal pain that may radiate to the lower back.

spontaneous abortion, other causes include infection, reproductive tract abnormalities, toxin exposure and endocrine/autoimmune disease. Spontaneous abortions can be divided into four types: (1) complete (all products of conception [POC] have passed out of the uterus); (2) incomplete (some POC have passed through a dilated cervix); (3) inevitable (bleeding is present with a dilated cervix with or without POC); and (4) septic (an incomplete spontaneous abortion accompanied by infection).

A threatened abortion is defined as any vaginal bleeding that occurs in early pregnancy with an embryo/fetus present in the uterus, detectable cardiac activity, and a closed cervical os. In a missed abortion, the embryo/fetus is larger than 5 mm, without heart tones, and the POC are retained.

An EP is a conceptus that implants outside of the uterus. EP is the most common cause of pregnancy-associated death in early pregnancy, constituting 6% of all maternal deaths annually. It is estimated that the diagnosis of EP missed at initial presentation 12% of the time. Gestational trophoblastic disease (also known as molar pregnancy or hydatidiform mole) is a potentially malignant condition in which the placenta develops without an embryo. In an anembryonic pregnancy (also known as a blighted ovum), the gestational sac is larger than 18 mm in size but does not contain embryonic or fetal tissue. A subchorionic hemorrhage (blood between the chorion and uterine wall) may produce early pregnancy bleeding but does not necessarily result in the termination of the pregnancy.

History and presentation
Understanding the factors that put a woman at a higher risk for spontaneous abortion is important when taking the patient’s history. These factors include endocrine disorders; genetic aneuploidy (abnormal number of chromosomes); such immunologic disorders as systemic lupus erythematosus, such infections as gonorrhea, chlamydia, syphilis, and herpes; chemical exposure; radiation exposure; and uterine abnormalities. Usually, the patient will present with vaginal bleeding and mild-to-moderate subpubic or midline lower abdominal pain that may radiate to the lower back. The clinician should ask about prior confirmation of pregnancy, last known menstrual period, when the bleeding began, quantity and character of bleeding, and current medications (ovulation agents put a woman at risk for a heterotopic pregnancy, which is an IUP and an EP simultaneously).

Ask whether the patient has experienced any trauma. Are nausea, vomiting, syncope, fever or cramping associated with the bleeding? Carefully review the woman’s obstetric history, exposure to sexually transmitted infections (STIs), and potential bleeding disorders.

In EP, there is no set constellation of findings that confirm or exclude the diagnosis. In fact, clinicians cannot reliably exclude the diagnosis of EP on the basis of history and physical exam findings alone. However, a patient who describes the abdominal pain as “sharp” and denies recent passage of tissue is more likely to have an EP than the patient without these findings. A study found that the frequency of EP in women presenting with a positive human chorionic gonadotropin (hCG), moderate-to-severe abdominal pain, and no history of tissue passage was 25%. Approximately 75% of women with confirmed EP will report a history of amenorrhea. Factors that increase a woman’s risk for EP include an intrauterine device currently in place, a history of previous EP, in utero exposure to diethylstilbestrol, genital infection, prior tubal surgery, in vitro fertilization, infertility, and smoking.

The clinician should suspect an anembryonic pregnancy if the woman reports that her pregnancy symptoms have regressed. A transvaginal ultrasound (TVUS) should be performed to confirm the presence of the fetal heartbeat. Trophoblastic disease will present with hyperemesis, irregular and/or heavy bleeding, and vaginal pain in the first half of the pregnancy.

Physical examination
The physical examination of a woman with early pregnancy bleeding will be focused on the abdominal/pelvic area. If the woman presents with fever in the presence of adnexal/peritoneal symptoms and such signs as rebound tenderness, rigidity and/or guarding, consider a diagnosis of septic abortion. Hypotension, absent or diminished bowel sounds, abdominal distension, and shoulder pain on the ipsilateral side could signify a ruptured EP. The pelvic and abdominal examination will often yield inconclusive findings, making ultrasound and quantitative hCG the diagnostic tests of choice. The physical exam is particularly important if there is no access to ultrasound or hCG or if the results of either are inconclusive. Physical findings that indicate a viable IUP include minimal cervical and abdominal tenderness, benign adnexa, a closed os, and absence of POC. Because these findings may also be present in a nonviable...
Identification of an embryo/fetus with cardiac activity located outside of the uterus is conclusive evidence of an ectopic pregnancy.

pregnancy, the diagnosis of a normal pregnancy should be made primarily through ultrasonography.2 The size and position of the uterus should be assessed for size-date discrepancy.1,3 Molar pregnancies will present with a uterus larger than gestational dates would suggest; in women with an excluded IUP, a uterus size smaller than what would be expected at 8 weeks’ gestation may point to EP.2,8 The bimanual exam may reveal masses and cervical motion tenderness, leading the clinician to consider EP, but these findings are not definitive.1,8 The classic EP triad of pain, vaginal bleeding, and adnexal mass is nonspecific and is interestingly more often associated with a diagnosis of miscarriage. Literature states that the pelvic-exam findings in diagnosing an EP are unreliable in isolation.2

The speculum exam may identify such nonobstetric causes of bleeding as polyps, STI, cancer, or trauma.1 Any tissue in the os indicates a dilated cervix. If the os is dilated, inevitable, incomplete, and/or septic spontaneous abortions are in the differential. If the os is closed, threatened, complete, embryonic demise, and/or septic abortion are included.6 The speculum exam also allows the practitioner to quantify the amount of blood present and remove any POC. Many women who eventually miscarry have inconclusive physical exam findings. For example, a dilated os is found in only 24% of women who go on to miscarry, and the finding of POC on speculum exam is only present in 13% of women who go on to miscarry.2 To summarize, the findings needed to diagnose embryonic demise, and/or septic spontaneous abortions are included.6 The speculum exam also allows the practitioner to quantify the amount of blood present and remove any POC. Many women who eventually miscarry have inconclusive physical exam findings. For example, a dilated os is found in only 24% of women who go on to miscarry, and the finding of POC on speculum exam is only present in 13% of women who go on to miscarry.2 To summarize, the findings needed to diagnose

Diagnostic workup
The diagnostic workup of a women presenting with early pregnancy bleeding includes a complete blood count, WBC count with differential to rule out infection, urinalysis to rule out urinary tract infection, gonorrhea/chlamydia swab, R-h-type, qualitative β-hCG, transvaginal ultrasound, quantitative β-hCG, and serum progesterone levels.1,3,9 Currently, the TVUS and the quantitative β-hCG are considered first-line for diagnosis in early pregnancy bleeding.2 Data show that 91% of EPs are diagnosed with TVUS,10 which is preferred over transabdominal ultrasound because of increased sensitivity.1

Confirmation of a viable IUP is achieved by visualization of the yolk sac by TVUS five to six weeks after the start of the last menstrual period, or when β-hCG levels are between 1,500–2,000 mIU/mL.1,3 This range is referred to as the discriminatory zone. If β-hCG levels are too low, serial β-hCG levels may be taken every 48 hours (doubling time) until the discriminatory zone is reached. At that point, the TVUS would prove effective in assessing for IUP.3 Findings of a normally progressing IUP include a normal gestational sac consisting of a central blastocyst surrounded by a double ring of echogenic chorionic villi and decidua. Visualization of this structure and absence of a pseudogestational sac rules out an EP. Cardiac activity is noted when the crown–rump length is >5 mm (around 10 to 11 weeks’ gestation).1 The presence of a detectable heart beat decreases the risk of pregnancy loss by 10%,2 and the absence of the above findings allows the clinician to identify failure of the pregnancy.1

All women presenting with signs and symptoms suggestive of EP should have an ultrasound, regardless of specific findings in the history and physical examination, as the specificity of the TVUS in detecting IUP is around 98% with greater than 90% sensitivity.8,11 When an IUP is verified, the EP is ruled out, but care must be taken not to miss a heterotopic pregnancy.11 An adnexal mass or free fluid in the pelvis is an EP until proven otherwise. Identification of an embryo/fetus with cardiac activity located outside of the uterus is conclusive evidence of an EP. If an intrauterine embryo/fetus without cardiac activity is identified and there is tissue and/or cervical os dilation, fetal demise has most likely taken place. Pathologic examination of tissue from the cervical os in a suspected inevitable spontaneous abortion should show chorionic villi. Lack of fetal heartbeat by 10 to 11 weeks’ gestation in the absence fetal tissue within the gestational sac signifies an anembryonic pregnancy. Gestational trophoblastic disease presents with classic “snowstorm” appearance of material within the uterine space. Subchorionic hemorrhage may be present in a normally progressing pregnancy, but once hemorrhage is identified, verification of heartbeat is necessary.1

A serum progesterone level >25 ng/mL suggests a viable IUP.5 High serum progesterone levels will rule out an EP, but its predictive value depends on the serum β-hCG levels.8 Serum progesterone levels are less helpful when β-hCG levels are <2,000 IU/L and within the first four weeks of gestation. A β-hCG level >2,000 IU/L and a serum progesterone level >22 ng/mL together confer greater than 30% specificity for ruling out an EP. The best role for serum progesterone is in identifying women at low risk for EP when paired with β-hCG levels.4
Ectopic pregnancy is an emergent diagnosis that must be rapidly ruled out in all women presenting with abdominal pain and early pregnancy bleeding.

Increasing \( \beta \)-hCG serum levels are the first definitive marker of pregnancy, and levels begin to increase approximately eight days after conception.\(^1\) A \( \beta \)-hCG level <5 mIU/mL is negative for pregnancy, and a level >25 mIU/mL is positive.\(^2\) \( \beta \)-hCG levels should predictably increase 80% to 100% every 48 hours until the eighth or 10th week of a healthy pregnancy, at which time it peaks, usually around 100,000 U/mL.\(^1,6\) If levels are too low, a failing IUP or an EP should be suspected, and if levels are too high, the possibility of gestational trophoblastic disease should be investigated. An increase <53% deems the pregnancy nonviable.\(^1\)

**Management**

The management of early pregnancy bleeding includes expectant (watchful waiting), medical, and surgical approaches.\(^1\) No interventional methods have been proven to prevent SA.\(^3\) There is evidence to support the administration of RhoGam (50 µg of anti-D immune globulin) to Rh-negative patients at <12 weeks’ gestation presenting with any bleeding.\(^3\) The hemodynamically unstable patient presenting to the emergency department should be given IV fluids and oxygen and admitted to the hospital.\(^6\)

EP is an emergent diagnosis that must be rapidly ruled out in all women presenting with abdominal pain and early pregnancy bleeding.\(^11\) Early detection of EP allows for conservative, nonsurgical treatment and conservation of the fallopian tubes.\(^2\) Expectant management is recommended in patients diagnosed with an EP and declining \( \beta \)-hCG values <1,000 mIU/mL.\(^1\) Medical management with methotrexate (Abitrexate, Folex, Mexate) is the best option for a stable patient with an unruptured EP measuring <3.5 cm, no detectable heart beat on ultrasound, and a \( \beta \)-hCG <15,000 mIU/mL. A patient with an unruptured EP and \( \beta \)-hCG levels >15,000 mIU/mL requires immediate hospitalization, stabilization and surgical intervention.\(^1,5\) The management of a ruptured EP entails hospitalization, stabilization, and open surgery.\(^1\)

Stable patients presenting with threatened, inevitable, complete, or missed abortions and minimal bleeding may only require observation and IV fluids\(^6\) and may be discharged home with an obstetrics follow-up and instructions to abstain from intercourse, observe bed rest, and return if bleeding worsens.\(^6\)

In the setting of incomplete abortion, watchful waiting is 90% effective.\(^3\) In a pregnancy of unknown location – defined as a pregnancy too early to be visualized, a positive pregnancy test, and no POC – a \( \beta \)-hCG ratio (levels measured at 0 and 48 hours later) of <0.87 reliably predicts that the pregnancy which will resolve spontaneously with no intervention.\(^10\) If history, physical exam, and diagnostic test findings point to a pregnancy loss of a previously confirmed pregnancy, expectant management should entail a repeat TVUS one week after initial presentation to confirm complete passage of tissue. \(^1,3\) An 80% drop in \( \beta \)-hCG levels one week after complete evacuation of tissue also confirms termination. However, if the IUP was never confirmed, continue to follow serial \( \beta \)-hCG levels to nonpregnant values to rule out EP. High fever, heavy bleeding, pelvic pain, and general malaise may indicate retained tissue or endometritis.\(^3\) Infection may be found more commonly with medical management,\(^13\) but expectant management is more likely to result in poorer outcome with embryonic demise and anembryonic pregnancy than in spontaneous abortion.\(^3\)

Dilation and curettage (D&C) is the treatment of choice after a SA or in embryonic demise or anembryonic pregnancy, but some evidence indicates that watchful waiting or treatment with the prostaglandin analogue misoprostol (Cytotec) may be safer, equally effective, and psychologically gender.\(^1,3\) However, the FDA has not approved misoprostol for the management of miscarriage, and clinical discretion must be used.\(^3\) Misoprostol will typically result in cramping and bleeding within two to six hours of initiation. Nonsteroidal anti-inflammatory and narcotic/acetaminophen pretreatment is helpful in managing discomfort, fever, and chills. Regardless of the treatment used, a follow-up appointment is necessary for these women.\(^3\)

Additional research has found that uterine aspiration may be more effective and a viable alternative to D&C in women with anembryonic gestation and embryonic demise. Uterine aspiration was found to be as safe as D&C, quicker to perform, more cost-effective, and amenable to use in the primary-care setting, but should only be used urgently if the woman is experiencing brisk bleeding, prolonged bleeding with a subsequent drop in hemoglobin, or is showing signs of infection.\(^3\)

If fetal cardiac activity is identified, as seen in a threatened abortion, the best management involves serial TVUS in place of \( \beta \)-hCG levels.\(^1\) Identification of a septic abortion is an urgent diagnosis, and treatment requires antibiotic administration, obstetrics/gynecology consultation, and evacuation of the uterine cavity.\(^1,6\)

Surgery and careful follow-up is the only method of management for the molar pregnancy (hydatidiform mole). A urine \( \beta \)-hCG four to six weeks after the pregnancy loss will confirm that there is no persistent disease.\(^1\)
Any method of contraception is acceptable immediately after a failed pregnancy, and there is no ideal interpregnancy interval.

Ultimately, all management options for early pregnancy loss are safe, effective, and will not affect future fertility, so the specific management choice should rest with the patient.3

Follow-up
Follow-up with a woman who has experienced a failed pregnancy should include addressing issues of contraception, future fertility/pregnancy, and the emotional impact of pregnancy loss. Any method of contraception is acceptable immediately after a failed pregnancy, and there is no ideal interpregnancy interval. A woman’s menstrual cycle should resume four to six weeks after the resolution of the loss.9

Given the numerous causes of early pregnancy vaginal bleeding, the practitioner must employ sound clinical and diagnostic skills in the assessment, workup, and management of the patient. The importance of taking an appropriate history, to include asking about character, distribution, and severity of pain, cannot be overstated. A thorough physical exam, appreciating cervical-motion tenderness, a dilated cervical os, or abdominal rigidity, will aid in arriving at the correct diagnosis. The appropriate use of a TVUS and the quantitative β-hCG is also essential. Finally, the practitioner must take into consideration all clinical findings to reach a correct diagnosis and work with the patient to mutually decide on expectant, medical, or surgical management, leading to a reduction in morbidity and mortality.7

Ms. Walker is a physician assistant in the emergency department at Gwinnett Medical Center’s campuses in Duluth, Ga., and Lawrenceville, Ga. Ms. Dexter is associate professor and clinical director of the physician assistant department at Georgia Regents University in Augusta, Ga., where Dr. Dadig is associate professor and chair.

References

### TABLE 1. Differential diagnosis of early pregnancy vaginal bleeding

<table>
<thead>
<tr>
<th>Differential diagnosis</th>
<th>Definition</th>
<th>Additional history</th>
<th>Physical examination</th>
<th>Diagnostic tests</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous abortion (subtypes below)</td>
<td>Pregnancy loss at &lt;20 weeks’ gestation</td>
<td>Endocrine disorders, genetic aneuploidy, immunologic disorders, infection, chemical/radiation exposure, uterine abnormalities</td>
<td>Transvaginal ultrasound (TVUS): embryonic/fetal tissue without heart tones</td>
<td>hCG ratio &lt;0.87 reliably predicts that the pregnancy will resolve spontaneously without intervention</td>
<td></td>
</tr>
</tbody>
</table>
| Complete spontaneous abortion | All products of conception (POC) evacuated from uterus | Endocrine disorders, genetic aneuploidy, immunologic disorders, infection, chemical/radiation exposure, uterine abnormalities | Closed os | Expectant: observation, IV fluids; discharge home with obstetric (OB) follow-up and instructions to include no intercourse, bed rest, and return if bleeding worsens; repeat TVUS one week after initial presentation  
Medical: misoprostol (Cytotec) with follow-up appointment  
Surgical: dilation and curettage (D&C) |
| Incomplete spontaneous abortion | Some POC passed through dilated cervix | Endocrine disorders, genetic aneuploidy, immunologic disorders, infection, chemical/radiation exposure, uterine abnormalities | Open os with or without POC | Expectant (90% effective): observation, IV fluids, discharge home with OB follow-up and instructions to include no intercourse, bed rest, and return if bleeding worsens; repeat TVUS one week after initial presentation  
Medical: misoprostol with follow-up appointment  
Surgical: D&C |
| Inevitable spontaneous abortion | Bleeding and a dilated cervix with or without POC | Endocrine disorders, genetic aneuploidy, immunologic disorders, infection, chemical/radiation exposure, uterine abnormalities | Open os with or without POC | Pathologic examination of POC: choriocarcinoma villi observed  
Expectant: observation, IV fluids, discharge home with OB follow-up and instructions to include no intercourse, bed rest, and return if bleeding worsens; repeat TVUS one week after initial presentation  
Medical: misoprostol with follow-up appointment  
Surgical: D&C |
| Septic spontaneous abortion | Incomplete spontaneous abortion plus infection | Peritoneal symptoms, fever | Peritoneal/ adnexal signs, fever with or without dilated cervix and POC | Urgent antibiotic administration, uterine evacuation, and OB/GYN consult |
| Threatened abortion | Confirmed IUP, bleeding, cardiac activity, and closed os at <20 weeks’ gestation | | Closed os | TVUS; confirmed heart tones  
Expectant: observation, IV fluids, discharge home with OB follow-up and instructions to include no intercourse, bed rest, and return if bleeding worsens; serial TVUS in place of serial hCG levels |
### Early Pregnancy Bleeding

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Signs and Symptoms</th>
<th>Clinical Findings</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missed abortion</td>
<td>Embryo/fetus &gt;5 mm, no heart tones, retained POC</td>
<td>Closed os</td>
<td>TVUS: intrauterine embryonic/fetal tissue without heart tones; ( \beta )-hCG &lt;53% increase</td>
<td>Expectant: observation, IV fluids, discharge home with OB follow-up and instructions to include no intercourse, bed rest, and return if bleeding worsens, repeat TVUS one week after initial presentation. <strong>Medical:</strong> misoprostol with follow-up appointment. <strong>Surgical:</strong> D&amp;C or uterine aspiration.</td>
</tr>
<tr>
<td>Ectopic pregnancy (EP)</td>
<td>A conceptus outside the uterus</td>
<td>Severe, sharp, unilateral, or bilateral adnexal pain; no passage of POC; amenorrhea; intrauterine device in place; history of EP; in utero exposure to diethylstilbestrol; genital infection; tubal surgery; in vitro fertilization; infertility; smoking</td>
<td>Ruptured EP: hypotension, absent/diminished bowel sounds, abdominal distension, hemodynamically unstable, ipsilateral shoulder pain. Unruptured EP: uterus &lt;8 weeks' gestational size, cervical motion tenderness, adnexal mass</td>
<td>TVUS: adnexal mass, free fluid in pelvis, cardiac activity detected outside of uterus, pseudogestational sac. Progesterone: rule out EP with ( \beta )-hCG values &gt;2,000 IU/L and progesterone &gt;22 ng/mL. ( \beta )-hCG doubling rate &lt;80% to 100% every 48 hours. <strong>Ruptured EP:</strong> IV fluids, monitor, oxygen, admission, open surgery. <strong>Expectant:</strong> declining ( \beta )-hCG values &lt;1,000 mIU/mL, follow serial ( \beta )-hCG levels to nonpregnant values. <strong>Medical:</strong> methotrexate (Abiraterone, Folex, Mexate) if unruptured EP &lt;3.5 cm, stable vitals, no heartbeat, and ( \beta )-hCG &lt;15,000 mIU/mL. <strong>Surgical:</strong> immediate hospitalization and stabilization if unruptured EP with ( \beta )-hCG &gt;15,000 mIU/mL.</td>
</tr>
<tr>
<td>Gestational trophoblastic disease</td>
<td>Placental development without embryo</td>
<td>Hyperemesis, irregular and/or heavy bleeding, vaginal pain at &lt;20 weeks' gestation</td>
<td>Uterus larger than gestational dates would suggest</td>
<td>TVUS: classic snowstorm appearance within uterine cavity. Surgery and close follow-up, urine ( \beta )-hCG four to six weeks after pregnancy loss.</td>
</tr>
<tr>
<td>Anembryonic pregnancy</td>
<td>Gestational sac &gt;18 mm but no embryonic/fetal tissue</td>
<td>Regression of pregnancy symptoms</td>
<td>TVUS: lack of heart tones by 10 to 11 weeks' gestation and no tissue within gestational sac</td>
<td>Medical: misoprostol with follow-up appointment. <strong>Surgical:</strong> D&amp;C or uterine aspiration.</td>
</tr>
<tr>
<td>Subchorionic hemorrhage</td>
<td>Blood between chorion and uterine wall</td>
<td></td>
<td>TVUS: blood between chorion and uterine wall, cardiac activity confirmed.</td>
<td>Expectant management.</td>
</tr>
<tr>
<td>Benign bleed of viable IUP</td>
<td>50% of all early pregnancy bleeds</td>
<td>Minimal cervical/abdominal tenderness, benign adnexa, closed os, absence of POC, nonobstetric causes (e.g., polyps, sexually transmitted infection, vaginal trauma, cancer)</td>
<td>TVUS: yolk sac by 5 to 6 weeks' gestation, central blastocyst with chorionic villi and decidua, cardiac activity by 10 to 11 weeks' gestation with crown-rump length &gt;5 mm. Progesterone: &gt;25 ng/mL. ( \beta )-hCG: 80% to 100% increase every 48 hours until 8 to 10 weeks' gestation.</td>
<td>Expectant management.</td>
</tr>
</tbody>
</table>