

# Vaginal Bleeding

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## PERSPECTIVE

### Epidemiology

Abnormal uterine bleeding occurs in women of all ages and is the most common reason that women seek gynecologic care.<sup>1</sup> Abnormal vaginal bleeding in nonpregnant women is rarely life-threatening, but may herald serious underlying pathology, such as cancer. Bleeding as a complication of pregnancy poses significant risk of morbidity and mortality to the fetus and mother.

### Pathophysiology

#### Nonpregnant Patients

The mean time between menstrual periods is 28 days ( $\pm 7$  days), with menstruation generally lasting for 5 days. It is considered abnormal to bleed for more than 7 days. On average, 35 mL of blood is lost per menstruation; a loss of more than 80 mL is abnormal.<sup>2</sup>

There has been an important change in the accepted nomenclature used to describe abnormal bleeding in nonpregnant women. Since 2011, the American Congress of Obstetricians and Gynecologists (ACOG) has recommended the PALM-COEIN classification system, which uses the all-inclusive term *abnormal uterine bleeding* (AUB) and divides the causes of AUB into structural and nonstructural causes. Structural causes include **polyps**, **adenomyosis**, **leiomyomas**, and **malignancy (PALM)**. Nonstructural causes include **coagulopathy**, **ovulatory dysfunction**, **endometrial**, **iatrogenic**, and **not yet classified causes (COEIN)**.<sup>3,4</sup> The use of the term *dysfunctional uterine bleeding* is no longer recommended.

Approximately 50% of cases of excessive menstruation fall under the nonstructural PALM-COEIN category of ovulatory dysfunction, which includes anovulatory bleeding. If a woman does not ovulate, there is no corpus luteum to produce progesterone, which results in estrogen being unopposed. Unopposed estrogen causes the endometrium to proliferate to the point at which it becomes unstable and begins to break down, causing irregular and unpredictable bleeding to occur. Heavy bleeding can also occur in the setting of regular ovulation (ovulatory bleeding).

Benign structural causes such as leiomyomas (fibroids) were classically thought to cause heavy bleeding by increasing endometrial surface area and disrupting the endometrial vascular supply and the ability of the uterus to contract to stop bleeding. Recent evidence has shown that aberrantly regulated growth factors may also play a role in fibroid-related bleeding.<sup>5</sup> Cervical polyps, which commonly occur in multiparous women in their 40s and 50s, are friable and prone to bleeding.<sup>6</sup>

#### Pregnant Patients

Pregnant women may experience bleeding throughout their pregnancy. In early pregnancy, ectopic pregnancy causes hemorrhage into the fallopian tube by disrupting of the blood supply to the

ectopic gestational sac. Also, the size of the growing gestational sac can rupture through the tubal wall.

After the 20th week of pregnancy, vaginal bleeding can be caused by placenta previa, in which the placenta completely or partially covers the internal cervical os. As the lower part of the uterus becomes thinner during the third trimester in preparation for labor, bleeding can occur. Placental abruption causes bleeding when the placenta tears away from the uterine wall. This can occur spontaneously or secondary to abdominal trauma, with transmission of forces to the uterus. It is important to note that a large amount of concealed blood can be retained between the detached placenta and uterus, and the extent of the hemorrhage may not be fully appreciated until delivery.<sup>7</sup> The most significant risk factor for abruption is a history of abruption in prior pregnancies (10-fold increased risk). An increased incidence is also seen in pregnancies complicated by hypertensive disorders, including preeclampsia, eclampsia, the HELLP (**hemolysis, elevated liver enzymes, and low platelets**) syndrome, and abnormal implantation of the placenta (eg, placenta previa, accreta, increta, percreta). Smoking and cocaine use also increase the risk for abruption.

In the immediate postpartum period (first 24 hours), bleeding is usually the result of uterine atony if the uterus fails to contract. Atony is more likely to occur with conditions that overdistend the uterus, such as a large for gestational age fetus, polyhydramnios, and multiparity. Prior history of postpartum hemorrhage, prolonged labor, induced labor, augmentation of labor with oxytocin, and instrumentation delivery also increase the risk of postpartum hemorrhage.<sup>7,8</sup> After 24 hours postpartum, retained products of conception (POCs) is the most common cause of bleeding.

## DIAGNOSTIC APPROACH

### Differential Considerations

In nonpregnant women, the differential diagnosis is extensive (Box 31.1), and it is helpful to categorize the differential diagnosis by the age of the patient. In prepubescent girls, causes of vaginal bleeding include vaginitis, foreign bodies, sexual abuse, tumors, and trauma. In adolescent girls, the most common cause of abnormal vaginal bleeding is persistent anovulation due to immaturity of the hypothalamic-pituitary-ovarian axis.<sup>9</sup> Underlying bleeding disorders and coagulopathies, such as von Willebrand disease, may also first present in adolescence. Sexually transmitted infections may also cause abnormal bleeding in this age group. For women in their reproductive years, structural lesions such as polyps and fibroids frequently cause abnormal bleeding. Black women are more likely to have fibroids, and they experience disproportionately more morbidity from heavy bleeding.<sup>5</sup> Endocrine causes, such as polycystic ovarian syndrome, should be considered in women with signs of androgen excess—obesity, acne, hirsutism. In perimenopausal woman, anovulatory cycles become common as ovarian function declines. Endometrial atrophy is the most common cause of abnormal bleeding in postmenopausal women; however, cancer should be considered until proven otherwise.

## BOX 31.1

## Differential Diagnosis of Abnormal Uterine Bleeding In Nonpregnant Females

## STRUCTURAL CAUSES

- Polyps
- Fibroids
- Malignancy
- Hyperplasia
- Endometriosis

## NONSTRUCTURAL CAUSES

- Coagulopathies
  - von Willebrand disease
  - Factor XI deficiency
  - Thrombocytopenia
  - Idiopathic thrombocytopenic purpura
- Endocrine
  - Polycystic ovarian syndrome
  - Hypothyroidism
  - Hyperprolactinemia
  - Adrenal hyperplasia
  - Cushing's disease
- Weight loss, extreme exercise
- Stress
- Obesity
- Trauma
  - Sexual abuse
- Infections
  - Sexually transmitted infection
  - Tuboovarian abscess
  - Vaginitis
- Systemic disease
  - Liver disease
  - Kidney disease
- Foreign bodies
- Medications
  - Antiepileptics
  - Antipsychotics
  - Anticoagulants
  - Hormonal medications
  - Steroids
- Intrauterine device

**NOTE:** Divide patients with vaginal bleeding into groups based on age when formulating a differential diagnosis.

From Borhart J: Emergency department management of vaginal bleeding in the non-pregnant patient. *Emerg Med Pract* 15:1–20, 2013.

Regardless of age, review a patient's medication list for drugs that are known to cause abnormal bleeding (eg, antiplatelet agents, anticoagulants), antiepileptic agents (especially valproic acid), and typical and atypical antipsychotics and steroids can cause abnormal uterine bleeding.

For pregnant women with vaginal bleeding, the differential diagnosis can be refined based on whether the bleeding occurs in early or late pregnancy or postpartum. For patients with vaginal bleeding in early pregnancy (before the 20th week of gestation and prior to fetal viability), the differential diagnosis includes miscarriage, ectopic pregnancy, implantation bleeding, molar pregnancy, and ruptured corpus luteum cyst. Bleeding in early pregnancy is common, affecting up to 20% of pregnancies. Miscarriage, defined as the spontaneous termination of pregnancy before the 20th week of gestation is also common; approximately 50% of women with early bleeding will miscarry. Miscarriages are described as threatened, missed, inevitable, incomplete, or complete depending on the status of the internal cervical os and if any POCs have

been passed. The most concerning diagnosis in patients with bleeding in early pregnancy is ectopic pregnancy, a pregnancy implanted outside the uterus. Ectopic pregnancy is the leading cause of first-trimester maternal death<sup>10</sup> and is common among patients presenting with pain or bleeding in the first trimester of pregnancy. Risk factors for ectopic pregnancy include pelvic inflammatory disease, previous ectopic pregnancy, prior tubal surgery, use of an intrauterine device, and endometriosis. An important subgroup of patients are women undergoing assisted reproduction or in vitro fertilization (IVF). These patients are at increased risk for heterotopic pregnancies, which is a simultaneous intrauterine pregnancy (IUP) and ectopic pregnancy.<sup>11</sup> Heterotopic pregnancies are rare in the general population.

Vaginal bleeding after the 20th week of pregnancy is less common, occurring in approximately 4% of pregnancies. Bleeding complications in late pregnancy generally occur in the third trimester and include placenta previa, placental abruption, and uterine rupture.

## Pivotal Findings

## Symptoms

Begin by eliciting the timing and duration of bleeding. Volume of blood loss is difficult to quantify because historical features, such as the frequency of changing a sanitary pad or tampon, have not been shown to predict blood loss consistently. Normal menstrual blood does not clot; therefore, the presence of clots indicates heavy bleeding. A report of dizziness, syncope, or weakness could also indicate significant blood loss. Associated symptoms such as abdominal pain, fever, vaginal discharge or odor, and postcoital bleeding could indicate a possible sexually transmitted infection or pelvic inflammatory disease. Postcoital bleeding can also indicate a cervical lesion, and occurs more commonly in pregnancy due to increased cervical blood flow. A history of trauma should be noted. Vaginal injuries can be sustained in a number of ways and range in severity from minor contusions to deep lacerations. The most common mechanism of genital injury in adult women is coitus.<sup>12</sup> In pregnancy, blunt trauma, such as falls, motor vehicle accidents, and interpersonal violence, is associated with a significantly increased risk of maternal and fetal morbidity and mortality.

## Signs

For any patient presenting with vaginal bleeding, begin by determining the patient's hemodynamic status and performing a complete abdominal and pelvic examination. The pelvic examination may reveal the source of bleeding because masses, polyps, ulcers, foreign bodies, and evidence of trauma or inflammation may be visualized. After the 20th week of pregnancy, a pelvic examination should be deferred until after an ultrasound has been performed to exclude placenta previa as the cause of bleeding. In pregnant patients of sufficient gestational age, the fetal heart rate and fundal height should also be assessed. Fetal heart rate can be measured using the M mode on bedside ultrasound as opposed to Doppler because this is thought to transmit less acoustic energy to the fetus. Fetal cardiac activity may be measured as early as 6 weeks. Uterine size can be estimated by palpating the fundus. The uterus is palpable at the level of the umbilicus at 20 weeks. The fetal age is more than 24 weeks (ie, viable) if the uterus can be felt at least four fingerbreadths above the umbilicus. This method may be less reliable in multiple pregnancies or other conditions that might affect the distention of the uterus or abdomen, such as large fibroids, polyhydramnios, oligohydramnios, intrauterine growth restriction, and obesity.<sup>13</sup> Bedside ultrasound can also be used to estimate fetal age.

## Ancillary Testing

Pregnancy status is an essential data point in the evaluation of any woman of reproductive age presenting with vaginal bleeding. Other critical laboratory tests in hemodynamically unstable patients include complete blood count, type and crossmatching of blood, coagulation studies and, if pregnant, a quantitative  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) level determination.

Bedside ultrasound has become increasingly used in the emergency department (ED) evaluation of pregnant women with vaginal bleeding to determine whether an IUP is present. A yolk sac is the first sonographic evidence of a definite IUP and can be visualized using transvaginal ultrasound, beginning around the 5th week of pregnancy. *Pregnancy of unknown location* (PUL) is the term used to categorize pregnancy in a woman with a positive pregnancy test when no pregnancy can be visualized using transvaginal ultrasound.<sup>11</sup> In this case, the quantitative  $\beta$ -hCG level has traditionally been used to determine if the level is in the discriminatory zone. The discriminatory zone is the level of  $\beta$ -hCG in which an IUP, if present, should be seen consistently. For transvaginal ultrasound, the discriminatory zone is generally accepted as from 1000 to 2000 IU/mL. However, the value of the discriminatory zone has recently been called into question because it is not as reliable at excluding a viable pregnancy as previously thought.<sup>14</sup> Multiple studies have reported that a normal intrauterine pregnancy not visualized on ultrasound is possible if  $\beta$ -hCG levels are above the discriminatory zone.<sup>15,16</sup> Therefore, caution should be used when interpreting a single  $\beta$ -hCG measurement because a normal gestation could potentially be disrupted. It is appropriate to repeat transvaginal ultrasound and  $\beta$ -hCG

measurements in hemodynamically stable patients instead of initiating medical or surgical intervention for possible ectopic pregnancy based on the discriminatory zone alone. There is no  $\beta$ -hCG level at which an ectopic pregnancy could be completely ruled out.

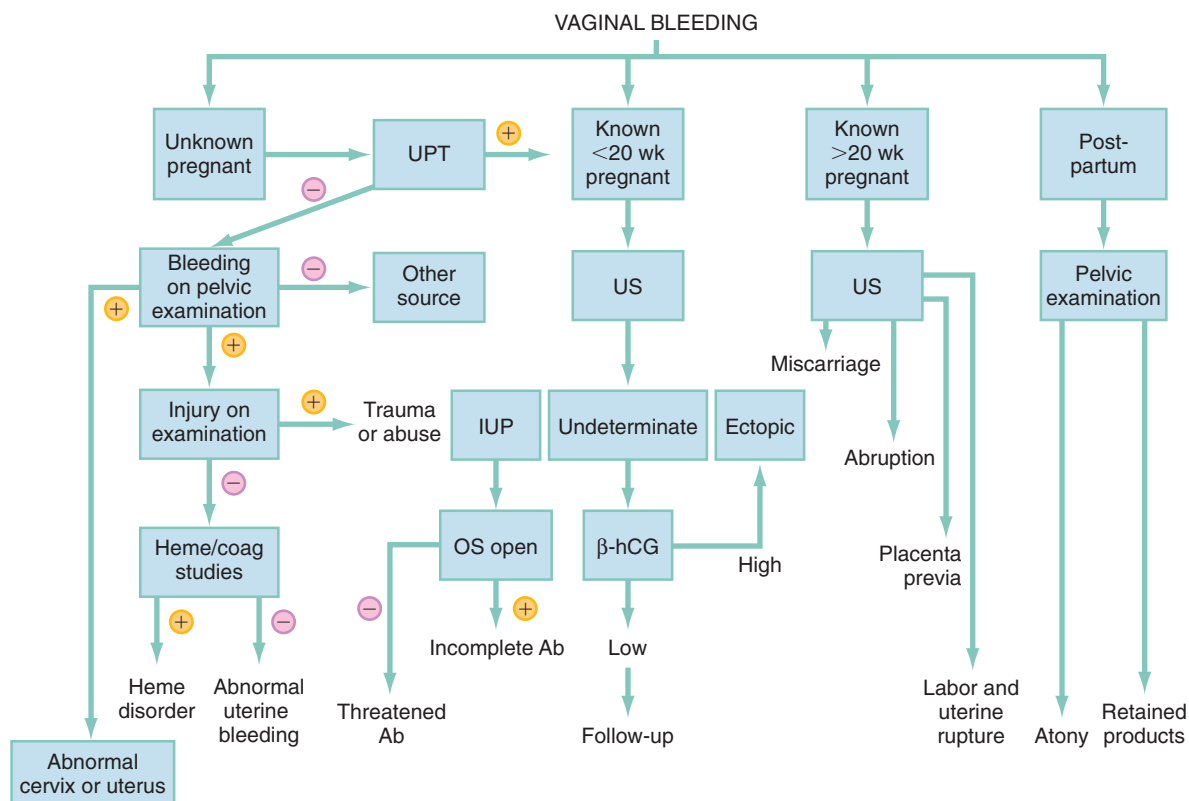
Additional testing for the stable, nonpregnant ED patient, such as thyroid and other hormonal studies, is usually performed on an outpatient basis. This also includes a complete pelvic ultrasound because the results will rarely change ED management.

## DIAGNOSTIC ALGORITHM

The single most important determination to make when evaluating a woman with vaginal bleeding is to determine if she is pregnant or nonpregnant (Fig. 31.1). If the patient is not known to be pregnant or immediately postpartum, a urine pregnancy test should be performed. Next, determine the age of the pregnancy in weeks. The most critical diagnoses to make in patients less than 20 weeks pregnant are ectopic and heterotopic pregnancies. Bedside ultrasound is useful to establish if an IUP is present. If the ultrasound is indeterminate, a quantitative  $\beta$ -hCG determination can help risk-stratify the patient further. Usually, the diagnosis will be threatened miscarriage.

For patients of more than 20 weeks gestation, the crucial diagnoses to make are placenta previa, placental abruption, uterine rupture, and arteriovenous malformation. Ultrasound should be performed before a pelvic examination in these patients.

For nonpregnant patients, the pelvic examination may reveal a cause of bleeding but, for most women in the emergency department, no cause will be identified. These patients will be diagnosed



**Fig. 31.1.** Diagnostic algorithm for patient with vaginal bleeding. *Ab*, Abortion;  $\beta$ -hCG,  $\beta$ -human chorionic gonadotropin; *coag*, coagulation; *DUB*, dysfunctional uterine bleeding; *IUP*, intrauterine pregnancy; *OS*, cervical os; *UPT*, urine pregnancy test; *US*, ultrasonography.

with abnormal uterine bleeding and should be referred for further gynecologic testing.

## EMPIRICAL MANAGEMENT

Patients with hemodynamic instability unresponsive to crystalloid fluid resuscitation require blood transfusion (Fig. 31.2). For women of childbearing age, use Rh-negative blood if the Rh status of the patient is unknown. In addition to hemodynamic stabilization for severe bleeding in nonpregnant women, high-dose intravenous conjugated estrogen (Premarin) is considered first-line treatment and may be administered every 4 to 6 hours for up to 24 hours (suggested dose, 25 mg). If bleeding continues, the vagina may be packed with long continuous gauze. Alternatively, a Foley catheter may be inserted transvaginally into the uterus to tamponade bleeding. Vaginal packing and catheters may be left in place for up to 24 hours.

Treatment of stable nonpregnant patients includes nonhormonal treatments such as nonsteroidal antiinflammatory drugs (NSAIDs). Despite their varying degree of platelet activity inhibition, NSAIDs decrease blood loss by reducing endometrial prostaglandin levels and promoting vasoconstriction in the uterus. Different types of NSAIDs appear to be equally effective at reducing bleeding.<sup>17</sup> Hormonal treatments such as monophasic oral contraceptive pills are also frequently used to temporize a heavy bleeding episode and are typically prescribed as a taper. Hormonal treatment is likely to be most effective for women with suspected anovulatory bleeding. Any of the monophasic pills containing less than 35 µg of ethinyl estradiol can be used; a common low-dose regimen is one pill twice daily for 5 days and then one pill daily for the remainder of the pack.<sup>18</sup> Contraindications to the use of estrogen include a history of a thromboembolic event or stroke, pregnancy, active liver disease, severe uncontrolled hypertension, and women older than 35 years who smoke. High-dose, progestin-only treatment is a frequently used alternative therapy

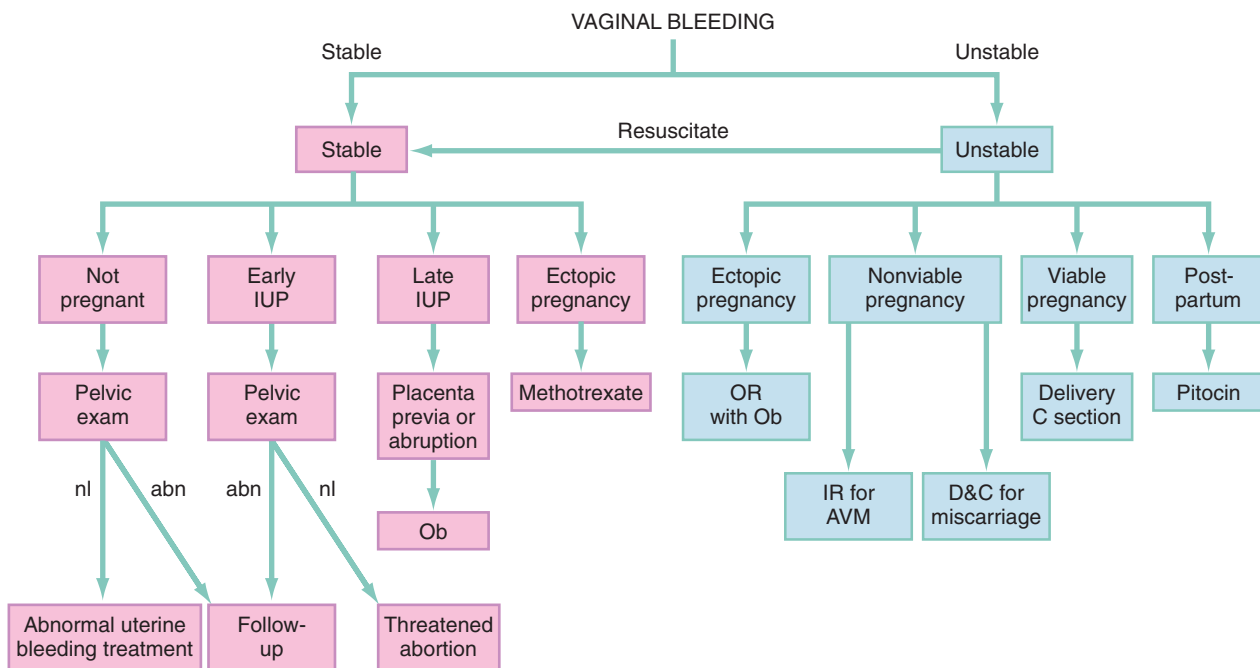
for women with contraindications to estrogen. A common regimen is medroxyprogesterone acetate (Provera) 10 mg, once daily, for 10 days<sup>19</sup> (Table 31.1).

All unstable pregnant and postpartum patients should be managed in close consultation with an obstetrician. Patients with viable pregnancies may require emergency cesarean section. Unstable patients with confirmed or suspected ectopic pregnancies, heterotopic pregnancies, or previable IUPs may also require operative management. Stable patients with threatened, missed, incomplete, or inevitable miscarriages may be managed expectantly or may require dilation and evacuation or curettage. Rh status should be checked and RhoGAM treatment should be initiated in the ED for patients who are Rh-negative. The management of pregnant patients is discussed in detail in Chapters 178 to 182.

## DISPOSITION

Most nonpregnant patients presenting to the ED with vaginal bleeding can be discharged home with timely gynecology follow-up. Adolescents with abnormal bleeding most likely have anovulatory cycles but should be evaluated for a possible underlying bleeding disorder. Perimenopausal and menopausal women with abnormal bleeding should have expedited follow-up because they are considered to have a malignancy until proven otherwise. If sexual abuse is suspected in prepubertal girls, a safe environment for the patient must be ensured before considering discharge. Any patient with significant or symptomatic bleeding should be admitted to the hospital.

Pregnant patients with ruptured ectopic or heterotopic pregnancies, placenta previa, placental abruption, or uterine rupture should be admitted to the hospital. Stable patients with threatened, inevitable, incomplete, or missed miscarriage can often be managed expectantly as outpatients, with close gynecology follow-up.



**Fig. 31.2.** Empirical management of the patient with vaginal bleeding. *abn*, Abnormal; *AVM*, arteriovenous malformation; *D&C*, dilation and curettage; *DUB*, dysfunctional uterine bleeding; *exam*, examination; *IR*, interventional radiology; *nl*, normal; *Ob*, obstetrician; *OR*, operating room.

TABLE 31.1

## Pharmacologic Treatment Regimens for Acute Abnormal Uterine Bleeding

DRUG	SUGGESTED DOSE <sup>a</sup>	CONTRAINDICATIONS AND CAUTIONS <sup>b</sup>
Hormonal treatments (conjugated equine estrogen)	25 mg IV every 4–6 h until bleeding stops, up to 24 h	<ul style="list-style-type: none"> <li>Contraindicated in patients with active or past thromboembolic disease, breast cancer, or liver disease</li> <li>Use with caution in patients with cardiovascular or thromboembolic risk factors</li> </ul>
Combination oral contraceptive pills	Monophasic oral contraceptive pills containing <35 µg ethinyl estradiol recommended): One pill tid PO for 7 days or One pill bid PO for 5 days, then one pill qd until pack is finished	<ul style="list-style-type: none"> <li>Contraindicated in women &gt;35 y who smoke</li> <li>Contraindicated in women who have a history of deep vein thrombosis or pulmonary embolism, breast cancer, liver disease, known thromboembolic disorders, pregnancy, ischemic heart disease, cerebrovascular disease, or uncontrolled hypertension</li> </ul>
Progestin-only oral contraceptive pills (medroxyprogesterone acetate)	20 mg tid PO for 7 days or 10 mg qd PO for 10 days	<ul style="list-style-type: none"> <li>Contraindicated in patients with active or past deep vein thrombosis or pulmonary embolism, liver disease, or breast cancer</li> </ul>
NSAIDs		<ul style="list-style-type: none"> <li>NSAIDs contraindicated in patients with advanced renal disease</li> <li>Use NSAIDs with caution in patients with history of GI ulcers or GI bleed</li> </ul>
Ibuprofen	200–400 mg tid or qid PO for 5 days	
Mefenamic acid	500 mg tid PO for 4 or 5 days or until bleeding stops	
Naproxen	500 mg PO initially, then 250 mg tid or qid for 5 days	

<sup>a</sup>Other dosages and schedules also may be effective.

<sup>b</sup>Partial list of contraindications. The US Food and Drug Administration's labeling contains exhaustive lists of contraindications for each of these treatments. In making treatment decisions for women with abnormal uterine bleeding, emergency clinicians should consider the risks of treatment against the risk of continued bleeding on a case by case basis.

GI, gastrointestinal; IV, intravenous; NSAIDs, nonsteroidal antiinflammatory drugs; PO, by mouth.

From Borhart J: Emergency department management of vaginal bleeding in the nonpregnant patient. *Emerg Med Pract* 15:1–20, 2013.

## KEY CONCEPTS

- Pregnancy status is the single most important determination to make when evaluating a woman with vaginal bleeding.
- There are many causes of abnormal bleeding in nonpregnant patients. Most nonpregnant patients presenting to the ED with vaginal bleeding can be safely discharged home, with timely gynecology follow-up.
- The use of the term *dysfunctional uterine bleeding* is no longer recommended; instead, use the term *abnormal uterine bleeding*.
- Hormonal and nonhormonal treatments can be initiated in the ED to temporize an acute bleeding episode in a nonpregnant patient until she can follow up with her gynecologist.
- Vaginal bleeding is common in early pregnancy. Most patients will be diagnosed with threatened miscarriage, but ectopic pregnancy should always be considered at any level of serum  $\beta$ -hCG.
- Vaginal bleeding after the 20<sup>th</sup> week of pregnancy is less common and is often associated with significant morbidity and mortality for the mother and fetus. These patients should be managed in close consultation with an obstetrician.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.



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## CHAPTER 31: QUESTIONS &amp; ANSWERS

- 31.1. What is the leading obstetric cause of maternal mortality?
- Domestic violence
  - Ectopic pregnancy
  - Placental abruption
  - Postpartum hemorrhage
  - Septic abortion

**Answer: D.** Postpartum hemorrhage is the leading cause of maternal mortality. Within the first 24 hours after delivery, this is usually caused by uterine atony. After 24 hours, the cause is frequently retained products of conception.

- 31.2. A 30-year-old woman in the eighth week of her first gestation reports a 1-day history of crampy lower abdominal pain and scant vaginal bleeding. Vaginal examination reveals a minimal amount of dark blood oozing through a closed cervical os. Endovaginal ultrasonography confirms an intrauterine pregnancy of 8 weeks' gestation. The fetus has good cardiac activity. What is the most appropriate diagnosis for this patient?
- Incomplete abortion
  - Inevitable abortion
  - Missed abortion
  - Normal pregnancy
  - Threatened abortion

**Answer: E.** Bleeding during pregnancy is common but should not be considered normal. The symptoms and findings in this patient lead to a diagnosis of threatened abortion, which is described as

bleeding of intrauterine origin before the completion of 20 weeks' gestation, without dilation of the cervix, and without expulsion of products of conception. Patients with threatened abortion may or may not have uterine contractions. An incomplete abortion is the expulsion of some, but not all of the products of conception, which would be a complete abortion, before the completion of 20 weeks' gestation. An inevitable abortion is defined as bleeding of intrauterine origin before the completion of 20 weeks' gestation, with dilation of the cervical os but without expulsion of THE products of conception. Missed abortion refers to retained products of conception after demise of the embryo or fetus.

- 31.3. A 30-year-old woman who is 26 weeks pregnant describes a 1-hour history of painless vaginal bleeding after tripping and falling from a standing height. Her vital signs are normal, and physical examination of the abdomen reveals a nontender uterus with a fundal height 1 cm above the umbilicus. Of the following, which would be the most appropriate next step in evaluating this patient?
- Abdominal MRI
  - Bimanual examination
  - Sterile speculum examination
  - Ultrasound

**Answer: D.** Painless vaginal bleeding after the 20th week of pregnancy is suggestive of placenta previa. Pelvic examination (speculum or bimanual) should be deferred until ultrasound has excluded placenta previa as the cause of bleeding.