pleural, and sometimes, pericardial cavities.[9] Venous and arterial thrombosis are the most dreaded complications. Reports include thrombosis of the jugular, subclavian, retinal, and extremity veins and cerebral venous thrombosis. Stroke, ST-segment elevation myocardial infarction, and pulmonary embolism are also reported.[9]

ENDOMETRIOSIS AND ADENOMYOSIS

Endometriosis occurs when endometrium-like tissue outside the uterus induces a chronic inflammatory reaction. This is a common cause of pelvic pain and infertility. When endometrial tissue is in the uterine wall, it is termed adenomyosis. Both conditions cause chronic, recurrent, and cyclic pain. Dysmenorrhea and dyspareunia are often reported. US may show cystic or solid masses. Laparoscopy is the definitive method of diagnosis. Primary diagnosis is usually not made in the ED. If suspected, pain control and outpatient referral are appropriate.

FOREIGN BODY/TRAUMA

Vaginal foreign bodies (such as a retained tampon) may cause pelvic pain and vaginal discharge or bleeding. Trauma or foreign body should be considered in the differential diagnosis. Patients are not always immediately forthcoming with history due to fear or embarrassment. Complications such as abscess or perforation are rare.

OVARIAN TORSION

Ovarian torsion is a surgical emergency that requires prompt diagnosis to preserve ovarian function. Adnexal torsion is an ischemic condition almost always associated with ovarian enlargement, generally due to ovarian cysts or masses. The enlargement causes the ovary to twist, creating a fulcrum around which the oviduct revolves. Initial blockage of venous return causes congestion, leading to decreased distal arterial blood flow, which produces ischemia and necrosis of the ovary. Although the process may involve the ovary alone, torsion of both the ovary and the oviduct (adnexal torsion) is more common. Nearly 70% of torsions occur on the right side, due to the increased length of the utero-ovarian ligament on the right and the sigmoid on the left, limiting space for movement.[10]

Risk factors for torsion are pregnancy due to enlarged corpus luteum, presence of large ovarian cysts or tumors, chemical induction of ovulation (ovarian hyperstimulation syndrome), and tubal ligation. Classically, patients present with sudden-onset, severe, unilateral, lower abdominal pain that may develop after episodes of exertion. Unfortunately, atypical presentations are common, with half of patients reporting gradual onset of pain that is intermittent in nature. Nausea and vomiting is present in 70% of cases.[11]

Clinical findings classically consist of unilateral lower abdominal tenderness with guarding, unilateral adnexal tenderness on bimanual examination, and presence of a latero-uterine mass. Conversely, nearly 30% of patients have bilateral adnexal tenderness on bimanual examination, and a minority of patients may have no tenderness at all. Fifty percent of patients are initially misdiagnosed.[12]

Transvaginal US with Doppler is the primary diagnostic modality for suspected torsion. An ovary greater than 4 cm in size due to cyst, tumor, or edema is the most common ultrasonographic finding associated with torsion.[13] Conversely, given the dynamic nature of the torsion process, up to 26% of US studies reveal normal adnexa. Up to 60% of cases of torsion can be missed on arterial Doppler alone, given that arterial disruption of flow is a late clinical finding.[14] However, a positive Doppler study has a 100% positive predictive value for adnexal torsion. Recent improvements in US technology have led to assessment of venous Doppler flow, which may be the only abnormality identified in early ovarian torsion.[15] Given the dynamic nature of the torsion process, there is no one finding that conveys certainty of the absence of torsion. Thus, clinical suspicion based on history and physical exam remains important in involving gynecologic consultation if US is negative, but clinical concern remains high.[16]

Acknowledgment: We wish to gratefully acknowledge the support and assistance of our colleagues in the Department of Emergency Medicine at Indiana University who made this chapter possible.

REFERENCES

The complete reference list is available online at www.TintinalliEM.com.

CHAPTER 98

Ectopic Pregnancy and Emergencies in the First 20 Weeks of Pregnancy

Heather A. Heaton

GENERAL APPROACH TO WOMEN OF CHILDBEARING AGE

The differential diagnosis for women of childbearing potential who present with abdominal or pelvic symptoms or abnormal vaginal bleeding is broad (**Table 98-1**). The major clinical goals are, first, diagnosis of pregnancy, and then if pregnant, differentiating ectopic pregnancy from threatened abortion. Consider ectopic pregnancy in women of childbearing age who report abdominal or pelvic pain or discomfort, vaginal spotting or a cycle of amenorrhea, or unexplained signs or symptoms of hypovolemia. There are rare case reports of ectopic pregnancy in patients with ovaries but without a uterus. No combination of signs or symptoms is sufficient to exclude ectopic pregnancy. **If pregnancy is detected, ectopic pregnancy remains in the differential diagnosis until it can be either confirmed or excluded with conviction.**

PREGNANCY TESTING

The diagnosis of pregnancy is central to the diagnosis of ectopic pregnancy. Pregnancy tests currently in use rely on the detection of the β subunit of human chorionic gonadotropin (β-hCG) in the urine or serum. hCG is a hormone produced by the trophoblast. Intact hCG consists of the α and β subunits. Tests based on detection of the intact molecule or the α subunit can cross-react on immunologic assays with hormones found in the nonpregnant individual and are thus less specific than tests for the β-hCG subunit.

hCG preparations are currently standardized in relation to the Third International Reference Preparation. Other standard preparations are not equivalent. A preparation often referred to in earlier literature is the Second International Standard. The Third International Reference Preparation is

TABLE 98-1 Differential Diagnosis of Ectopic Pregnancy

All Patients	Pregnant Patients
Appendicitis	Normal (intrauterine pregnancy)
Inflammatory bowel disease	Threatened abortion
Ovarian pathology	Inevitable abortion
Cyst	Molar pregnancy
Torsion	Heterotopic pregnancy*
Pelvic inflammatory disease	Implantation bleeding
Endometriosis	Corpus luteum cyst
Sexual assault/trauma	
Urinary tract infection	
Ureteral colic	

*Heterotopic pregnancy = combined intrauterine pregnancy and ectopic pregnancy.

TABLE 98-2 Estimated β-Human Chorionic Gonadotropin (β-hCG) Levels After Conception[4]

Postconception Week	β-hCG Levels (mIU/mL)
<1 week	5–50
1–2 weeks	50–500
2–3 weeks	100–5000
3–4 weeks	500–10,000
4–5 weeks	1000–50,000
5–6 weeks	10,000–100,000
6–8 weeks	15,000–200,000
8–12 weeks	10,000–100,000

roughly equal to 1.7 times the Second International Standard. To avoid confusion when interpreting the literature, pay attention to the standard used. In this chapter, hCG and β-hCG concentrations refer to the Third International Reference Preparation unless otherwise noted.

Very early in either an intrauterine pregnancy (IUP) or an ectopic pregnancy, detectable amounts of β-hCG are released into the serum and filtered into the urine. The concentration of β-hCG is fairly closely correlated in the urine and serum, with urinary concentration also depending on urine specific gravity. Qualitative urine and serum tests for pregnancy usually use the enzyme-linked immunosorbent assay methodology. In the laboratory setting, enzyme-linked immunosorbent assay tests can detect β-hCG at concentrations <1 mIU/mL.

Qualitative tests in clinical use are typically reported as "positive" when the β-hCG concentration is ≥20 mIU/mL in urine and ≥10 mIU/mL in serum. A positive qualitative test therefore implies that β-hCG is present in at least this concentration. At this level of detection, the false-negative rate for detection of pregnancy will not be >1% for urine and 0.5% for serum. In clinical use, the performance of urine qualitative testing is 95% to 100% sensitive and specific compared with serum tests.

Urine tests can be performed rapidly at the bedside, and kits from some manufacturers may be used for either urine or serum. **Dilute urine may cause a false-negative urine pregnancy test**, particularly early in pregnancy when β-hCG levels are low (<50 mIU/mL). Additionally, when hCG levels are present in large amounts (generally with concentrations of 1,000,000 mIU/mL), a **"hook effect phenomenon"** can occur, giving false-negative results. This is thought to be related to excess hCG saturating both the fixed, solid-phase antibody and the labeled, soluble antibody of the assay, causing an absence of signal. The resultant false-negative test can be mitigated by diluting the sample.[1] Point-of-care hCG whole-blood assay shows promising results, with 95.8% sensitivity (negative predictive value, 97.9%) when compared with standard urine testing.[2]

When a bedside urine test is negative and ectopic pregnancy is still being considered, perform a quantitative serum test. **The sensitivity of quantitative serum testing for the diagnosis of pregnancy is virtually 100% when an assay capable of detecting ≥5 mIU/mL of β-hCG is used.**[3] Estimated β-hCG levels after conception are listed in **Table 98-2**.

ECTOPIC PREGNANCY

INTRODUCTION AND EPIDEMIOLOGY

Ectopic pregnancy occurs when a conceptus implants outside of the uterine cavity and is a leading cause of maternal death in the first trimester of pregnancy.[5]

The current incidence of ectopic pregnancy is difficult to determine but is probably increasing. Reasons include the increased incidence of sexually transmitted tubal infections, unsuccessful tubal sterilizations, assisted reproductive techniques, previous pelvic surgery, and more sensitive and earlier diagnostic techniques. Major risk factors are shown in **Table 98-3**, but a significant number of ectopic pregnancies occur in women in whom no risk factors are identified.[6,7]

TABLE 98-3 Major Risk Factors for Ectopic Pregnancy

Pelvic inflammatory disease, history of sexually transmitted infections
History of tubal surgery or tubal sterilization
Conception with intrauterine device in place
Maternal age 35–44 (age-related change in tubal function)
Assisted reproduction techniques (cause unknown, as tube is bypassed in implantation)
Previous ectopic pregnancy
Cigarette smoking (may alter embryo tubal transport)
Prior pharmacologically induced abortion

PATHOPHYSIOLOGY

Fertilization of the oocyte usually occurs in the ampullary segment of the fallopian tube. In normal pregnancy, after fertilization, the zygote passes along the fallopian tube and implants into the endometrium of the uterus. An ectopic pregnancy occurs when the zygote implants in any location other than the uterus—the fallopian tube or extratubal sites (the abdominal cavity, cervix, or ovary). Death results from maternal exsanguination after tubal rupture.

The vast majority of ectopic pregnancies implant in the ampullary portion of the **fallopian tube**. The underlying cause is most often damage to the tubal mucosa from previous infection, preventing transport of the ovum to the uterus. Other causes include tubal surgery, defects in the ovum resulting in premature implantation, and elevated estradiol or progesterone levels, which inhibit tubal migration.

Tubal implantation results in the penetration of the ovum into the muscular wall of the tube, and maternal blood seeps into tubal tissue. Intermittent distention of the fallopian tube with blood can occur, with leakage of blood from the fimbriated end of the fallopian tube into the peritoneal cavity. The aborting ectopic pregnancy and associated hematoma can be completely or partially extruded out of the end of the fallopian tube or through a rupture site in the tubal wall.

Abdominal ectopic pregnancies (~1% of ectopic pregnancies) most commonly derive from early rupture or abortion of a tubal pregnancy, with subsequent reimplantation in the peritoneal cavity.

Cervical ectopic pregnancies occur in <1% of ectopic pregnancies, with predisposing factors similar to those associated with ectopic pregnancies (previous dilatation and curettage, previous cesarean delivery, in vitro fertilization, adhesions or fibrosis of the endometrium, prior instrumentation, infertility, previous ectopic pregnancy). Patients develop profuse vaginal bleeding. Bimanual exam reveals a soft, large cervix when compared to the uterus or an hourglass-shaped uterus, and diagnosis is confirmed with US.[8,9]

Cesarean scar pregnancy is rare but can cause massive maternal hemorrhage. Diagnosis is difficult and is based on US demonstrating an empty uterine sac and cervical canal and a gestational sac in the uterine isthmus.

HISTORY

Determine the timing and characteristics of the last few periods. The menstrual history is often, but not always, abnormal. The classic sign of amenorrhea from 4 to 12 weeks after the last normal period is reported in 70% of ectopic pregnancy cases. **No missed menses are reported in 15% of ectopic pregnancy cases.** Although vaginal bleeding is often scant, heavy bleeding does not exclude an ectopic pregnancy.

Ask about previous pregnancies, pregnancy problems, and miscarriages. Typical early pregnancy symptoms may occur and may not differ from symptoms of previous normal IUPs. Discuss previous medical and surgical history, and ask about substance abuse and smoking. Ask about sexual activity and contraception. Identify risk factors for ectopic pregnancy or spontaneous abortion. Determine current medications, including over-the-counter drugs.

Pregnancy in a patient with prior tubal surgery for sterilization is assumed to be an ectopic pregnancy until proven otherwise. Patients are at particularly high risk if they have undergone laparoscopic partial

salpingectomy or electrodestruction tubal ligation at a young age (age <28 years), especially 5 to 15 years after the procedure.[10]

In a woman of childbearing age, hysterectomy with oophorectomy excludes ectopic pregnancy. In the situation of hysterectomy without oophorectomy, ectopic pregnancy is exceedingly rare. A literature review identified only 27 such case reports since 1918, after both vaginal and abdominal hysterectomies. The theory is that a fistulous tract after hysterectomy enables embryo implantation in the tube or adnexae.[11]

Abdominal pain or discomfort is the most common symptom of ectopic pregnancy and is reported in 90% of ectopic pregnancies.[12] Pain is due to tubal distention or rupture. The classic pain of rupture is lateralized, sudden, sharp, and severe. Shoulder pain due to diaphragmatic irritation from a ruptured ectopic pregnancy can also occur. Any lateral or bilateral abdominal discomfort or tenderness in a woman of childbearing age requires consideration of ectopic pregnancy. **Lack of pain in a woman with vaginal spotting or bleeding does not exclude ectopic pregnancy.**

PHYSICAL EXAMINATION

Obtain vital signs and focus on the abdominal and pelvic examination. The physical examination in ectopic pregnancy is highly variable, and ectopic pregnancy is difficult to diagnose or exclude based on physical examination. In cases of ruptured ectopic pregnancy, patients may present in shock, with no findings on pelvic examination, or with peritoneal signs and an adnexal mass and tenderness. Cervical motion tenderness can be elicited on pelvic exam in some cases. Relative bradycardia may occur as a consequence of vagal stimulation. There is poor correlation between the volume of hemoperitoneum and vital signs in ruptured ectopic pregnancy.[13] In cases of rupture without hemodynamically significant bleeding, a more benign abdominal exam may be present without significant alteration of vital signs. Fever is rare. In the more common situation of an unruptured ectopic pregnancy, the vital signs are likely to be normal.

If an adnexal mass or fullness with tenderness is detected, it may be due to ectopic pregnancy or to a **corpus luteum cyst,** a 3- to 11-cm, thin-walled, unilocular cyst seen after ovulation that can cause pain and tenderness on exam as well as menstrual irregularities, mimicking an ectopic pregnancy. Cervical motion tenderness may be seen, and blood is often present in the vaginal vault; however, the pelvic exam may be completely normal. The cervix may have a blue coloration, as in a normal pregnancy. Uterine size for estimated gestational age is most often normal. Vaginal examinations in stable women presenting with first-trimester bleeding may add little to the clinical diagnosis; some providers are moving away from routine use of vaginal examinations in initial patient assessment as long as a transvaginal US is obtained.[14]

DIAGNOSIS

The definitive diagnosis of ectopic pregnancy is made by US, by direct visualization by laparoscopy, or at surgery. No single or combination of laboratory tests has a sufficient negative or positive predictive value to completely exclude ectopic pregnancy or to definitively establish the diagnosis.

Serum β-hCG Differences in the dynamics of β-hCG production in normal and pathologic pregnancy are useful in the diagnosis of ectopic pregnancy. Early in normal pregnancy, β-hCG levels rise rapidly until 9 to 10 weeks of pregnancy and then plateau. Expected postconception ranges of β-hCG are listed in Table 98-2. β-hCG levels decline in nonviable pregnancies and in successfully treated ectopic pregnancy. Absolute levels of β-hCG tend to be lower in pathologic pregnancies than in IUPs, but there is much overlap. Due to the variability in absolute levels and the overlap between normal and pathologic pregnancies, **no single β-hCG level can reliably distinguish between a normal and a pathologic pregnancy**. *Doubling time* refers to the time needed for β-hCG concentration in the serum to double. Absolute levels of β-hCG are lower and doubling times longer in ectopic pregnancy and other abnormal pregnancies. This and many other observations have led to the widely used rule of thumb stating that the serum concentration of β-hCG approximately doubles every 2 days early in a normal pregnancy and that longer doubling times indicate pathologic pregnancy. Varying degrees of sensitivity (36% to 75%) and specificity (63% to 93%) are obtained using different criteria for evaluating the rate of increase of β-hCG levels for the diagnosis of ectopic pregnancy. The minimum hCG rise in normal pregnancy may be as low as 53% in 48 hours,[15] and the median rise in β-hCG level was 53% in 1 day and 124% in 2 days. Conversely, in spontaneous abortion, hCG is expected to fall by 21% to 35% in 2 days.[16] Thus, hCG levels that fail to increase by 53% or more in 2 days are suggestive but not diagnostic of ectopic pregnancy or an abnormal IUP. However, **an increase of >53% does not rule out ectopic pregnancy**.

In stable patients, serial measurements of β-hCG are used to either heighten or lower the suspicion for ectopic pregnancy, but are not diagnostic. Repeat serum β-hCG measurement made at least 2 days after the initial presentation is useful in characterizing the risk of ectopic pregnancy and the probability of a viable IUP.[17] Although rates of decline vary depending on the initial hCG value, a decrease of less than 21% at 2 days or 60% at 7 days suggests retained trophoblasts or an ectopic pregnancy; additional testing should be performed.[15] **Table 98-4** describes the American College of Emergency Physicians' clinical policy regarding women with early pregnancies.[17]

Progesterone Progesterone is a steroid hormone secreted by the ovaries, adrenal glands, and placenta during pregnancy. During the first 8 to 10 weeks of pregnancy, ovarian production of progesterone predominates, and serum levels remain relatively constant. After the tenth week of pregnancy, placental production increases and serum levels rise. Absolute levels of progesterone are lower in pathologic pregnancies and fall when a pregnancy fails. This observation has led multiple authors to propose various progesterone levels as a diagnostic aid in differentiating an early normal from a pathologic pregnancy. Most pathologic pregnancies have progesterone levels of ≤10 nanograms/mL. With progesterone ≤5 nanograms/mL, nearly 100% of pregnancies will be pathologic; there are no normal pregnancies reported with progesterone ≤2.5 nanograms/mL. Progesterone levels >25 nanograms/mL have 97% sensitivity for viable IUP. An empty uterus or nonspecific fluid collection on US associated

TABLE 98-4 ED Management of Early Pregnancy[17]

Clinical Issue	Recommendation	Level of Recommendation*
Use of transvaginal US to detect IUP, ectopic pregnancies when serum β-hCG <1000 mIU/mL	Perform or obtain a transvaginal US for symptomatic pregnant patients with β-hCG below the discriminatory threshold.	Level C
Use of β-hCG for predicting ectopic pregnancy in women with indeterminate transvaginal US	β-hCG values do not exclude the diagnosis of an ectopic pregnancy in patients with indeterminate transvaginal US.	Level B
Implications for ED management of women receiving methotrexate for confirmed or suspected ectopic pregnancy	Consider ruptured ectopic pregnancy for persistent abdominal pain or vaginal bleeding.	Level B
Anti-Rh_0 (D) immunoglobulin for ectopic pregnancy	50 micrograms of RhoGAM for all Rh-negative women with threatened loss or loss of established first-trimester pregnancy (full dose of 300 micrograms is not needed when the patient is at <12 weeks of gestation due to the small volume of red cells in the feto-placental circulation).	Level B

Abbreviations: β-hCG = β-human chorionic gonadotropin; IUP = intrauterine pregnancy.

*Level A: reflects high degree of clinical certainty; Level B: reflects moderate clinical certainty; Level C: reflects preliminary or conflicting evidence or based on consensus.

with progesterone ≤5.0 nanograms/mL is highly predictive of abnormal IUP or ectopic pregnancy.[18]

There is considerable overlap between progesterone levels in normal and pathologic pregnancy. Thus, very low values for serum progesterone should increase the clinical suspicion for ectopic pregnancy or abnormal IUP, but as with β-hCG levels, no value is diagnostic or can completely exclude or definitively diagnose ectopic pregnancy. Progesterone levels may not be routinely available on an urgent basis, and as noted, many patients have intermediate values, thus limiting the usefulness of the test. Consequently, the role of serum progesterone assays is currently unclear.

Numerous other serum markers for the diagnosis of ectopic pregnancy have been investigated. These include secretory endometrial protein, estradiol, the pregnancy-associated proteins A to D, and others, as well as routine laboratory tests such as amylase, creatine kinase, erythrocyte sedimentation rate, and others. None has been accepted as equal or superior to β-hCG measurements at this time.

US and Ectopic Pregnancy **The primary goal of US in early pregnancy is determination of a viable IUP and exclusion of ectopic pregnancy (Figure 98-1).**

US findings may also be useful in planning therapy when an ectopic pregnancy is discovered. Additionally, US provides information regarding fetal age and viability when an IUP is present.

It has previously been assumed that if an IUP exists, the diagnosis of ectopic pregnancy has been excluded. This assumption is based on the historical incidence of heterotopic pregnancy (combined IUP and ectopic pregnancy), reported to occur in 1 in 30,000 pregnancies. This is no longer a completely safe assumption, with heterotopic pregnancy now occurring in up to 1 in 3000 pregnancies in the general population. **In vitro fertilization and other efforts to enhance fertility with the use of ovulation-inducing drugs have resulted in a higher incidence of heterotopic pregnancy.** A study of 725 in vitro fertilization pregnancies found 4% to be ectopic pregnancies with 2 of 29 heterotopic gestations.[18] Heterotopic pregnancy should be considered even when US demonstrates an IUP in the assisted reproduction population. For other patients, demonstrating an IUP still provides a high degree of confidence in ruling out ectopic pregnancy. This confidence should be somewhat tempered when a patient has risk factors for ectopic pregnancy.

Advances in sonographic imaging and the use of transvaginal US scanning allow earlier detection of an IUP or an ectopic pregnancy. These advances have contributed to increasing use of real-time, bedside US in the ED performed by emergency physicians. ED US has the further advantage of allowing a potentially unstable patient to remain under continuous observation in the ED. When performed by trained individuals, bedside ED US in the first trimester of pregnancy is accurate and contributes to earlier diagnosis and treatment of ectopic pregnancy. However, US is operator-dependent, and there is limited validation in the community setting of the positive results obtained in academic teaching hospitals. Therefore, keep in mind the limitations of the procedure, equipment, and operator experience.[19]

The sequencing of transabdominal versus transvaginal US is situation- and operator-dependent. Usually, transabdominal scanning is performed first. Among other differences, transabdominal scanning is less invasive and offers a wider field of view and easier orientation to the pelvic organs. A full bladder is required for an appropriate acoustic window.

When transabdominal US is not diagnostic, transvaginal scanning should be performed. A full bladder is not required. The shallower depth of field and higher frequencies made possible by the lack of interposed abdominal fat allow better visualization of early pregnancies. There are reports of negative transvaginal but positive transabdominal US in cases of ectopic pregnancy, so both studies should be performed if the study performed first is not diagnostic. However, in one study of >5000 women with early pregnancy, pregnancy location was accurately diagnosed in >90% with a single transvaginal scan.[20]

When US reveals an unequivocal IUP and no other abnormalities, ectopic pregnancy is effectively excluded unless the patient is at high risk for heterotopic pregnancy. An embryo with cardiac activity seen within the uterine cavity is referred to as a *viable IUP*. When an embryo without cardiac activity is visualized within the uterus, the diagnosis of fetal demise can be entertained, provided that the crown–rump length is at least 5 mm. Briefly, transvaginal scanning can usually visualize the early sonographic signs of pregnancy, the gestational sac, yolk sac, and fetal pole, at 4.5, 5.5, and 6.0 weeks, respectively. Visualization by transabdominal scanning can be done approximately 1 week later.

No further diagnostic testing is needed when sonographic findings confirm or are highly suggestive of ectopic pregnancy. An empty uterus with embryonic cardiac activity visualized outside the uterus is diagnostic of ectopic pregnancy. This is seen in <10% of ectopic pregnancies using transabdominal scanning, but in up to 25% of cases when the transvaginal approach is used. When a pelvic mass or free pelvic fluid is seen in conjunction with an empty uterus, ectopic pregnancy is considered highly likely (**Figure 98-2**). The combination of an echogenic adnexal mass with free fluid in the setting of an empty uterus confers a risk of ectopic pregnancy near 100%, whereas a large amount of free

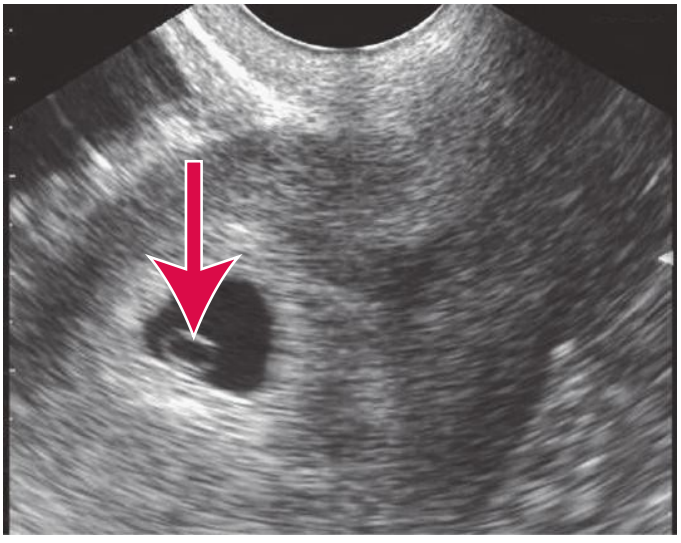

FIGURE 98-1. Yolk sac (*arrow*) within an intrauterine gestational sac. Normal early pregnancy. Transvaginal image. [Reproduced with permission from Ma OJ, Mateer JR, Reardon RF, Joing SA: *Ma & Mateer's Emergency Ultrasound,* 3rd ed. © 2014, McGraw-Hill Inc., New York.]

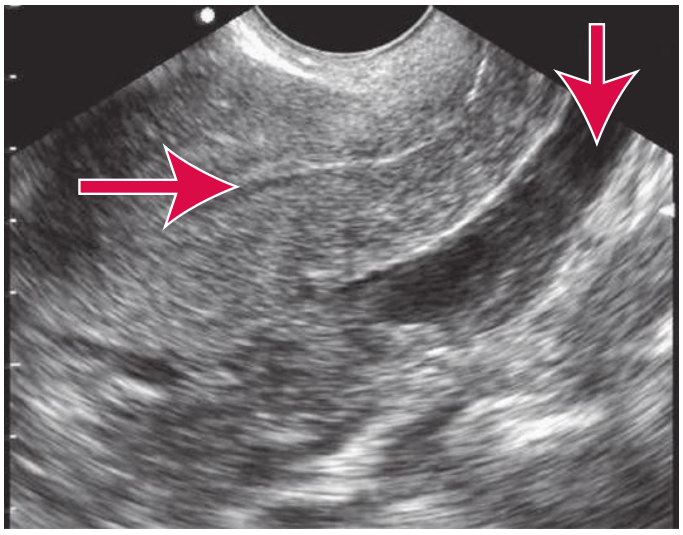

FIGURE 98-2. Ectopic pregnancy: empty uterus and free fluid in the posterior cul-de-sac. Transvaginal sagittal image. *Horizontal arrow* points to empty uterus (uterine stripe), and *vertical arrow* points to fluid in the cul-de-sac. [Reproduced with permission from Ma OJ, Mateer JR, Reardon RF, Joing SA: *Ma & Mateer's Emergency Ultrasound*, 3rd ed. © 2014, McGraw-Hill Inc., New York.]

TABLE 98-5 Ancillary US Findings Suggestive of Ectopic Pregnancy in High-Risk Patients

Ancillary Findings	Risk of Ectopic Pregnancy (%)
Any free pelvic fluid	52
Complex pelvic mass	72
Moderate/large amount of free pelvic fluid	86
Tubal ring	>95
Mass and free fluid	97
Hepatorenal free fluid	~100

Source: Reproduced with permission from Ma OJ, Mateer JR, Reardon RF, Joing SA: *Ma & Mateer's Emergency Ultrasound*, 3rd ed. New York: McGraw-Hill Inc., 2014; Table 14-2, p. 404.

fluid alone has a 86% risk (**Table 98-5**). In addition to a living extrauterine pregnancy, an extrauterine gestational sac is highly predictive of ectopic pregnancy (**Figure 98-3**). Any adnexal mass (other than a simple cyst) seen with US also has high positive predictive value for the diagnosis of ectopic pregnancy.[21,22] It has also been suggested that increased thickness of the endometrial stripe is predictive of ectopic pregnancy when no other diagnostic findings are noted on US. However, the wide overlap between endometrial stripe thickness in normal and ectopic pregnancy limits the usefulness of this observation.[23]

The Discriminatory Zone If US fails to reveal a definite IUP or fails to show findings strongly suggestive or diagnostic of an ectopic pregnancy, the test should be considered indeterminate and interpreted in light of quantitative serum β-hCG levels. The concept of the "discriminatory zone" was developed to relate β-hCG levels and US findings in a clinically useful way.[22] The discriminatory zone is the level of β-hCG at which findings of an IUP are expected on US. A β-hCG level higher than the discriminatory zone and an empty uterus on US suggest an ectopic pregnancy. An empty uterus with a β-hCG level below the discriminatory zone is indeterminate, neither confirming nor negating the diagnosis of ectopic pregnancy. The actual level of β-hCG representing the discriminatory zone is operator- and technique-dependent. With transvaginal scanning, the discriminatory zone is often considered to be 1500 mIU/mL. For transabdominal scanning, an IUP should be detectable when the β-hCG level reaches about 6000 mIU/mL. Clinicians should understand this concept and collaborate closely with imaging specialists in equivocal cases to avoid confusion. **When ectopic pregnancy is suspected, US should be performed even in patients with low β-hCG levels**, because ectopic pregnancy can occur even at very low (<500 mIU/mL) β-hCG levels.[24] Further, decision to intervene on a pregnancy should not be made solely on a single hCG level; if the patient is hemodynamically stable with a β-hCG greater than the discriminatory zone and no visible intrauterine or extrauterine pregnancy, watchful waiting is an appropriate management strategy with close follow-up and strict return precautions.[25]

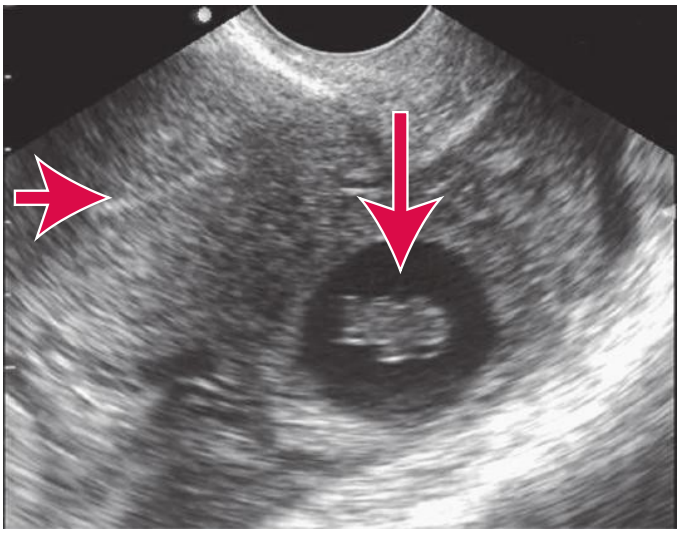

FIGURE 98-3. US of ectopic pregnancy. A living embryo in the adnexa and empty uterus is seen in this ectopic pregnancy (endometrial echo is visible in the left upper portion of the image). Embryonic cardiac activity was present on real-time imaging. Transvaginal image. *Horizontal arrow* points to empty uterus (uterine stripe), and *vertical arrow* points to ectopic pregnancy in the adnexa. [Reproduced with permission from Ma OJ, Mateer JR, Reardon RF, Joing SA: *Ma & Mateer's Emergency Ultrasound*, 3rd ed. © 2014, McGraw-Hill Inc., New York.]

Other Diagnostic Modalities **MRI** has high sensitivity and specificity for the diagnosis of ectopic pregnancy, but cost, availability, and the time to perform the study make the use of MRI of only theoretical interest at the present time.

Culdocentesis has been supplanted by tests for β-hCG in combination with US, but it may have use when US is unavailable. A positive test facilitates an appropriate, rapid surgical intervention. Possible results include a dry aspiration, which has no diagnostic value. If clear, nonbloody peritoneal fluid is aspirated, the tap is considered negative. Aspiration of nonclotting blood constitutes a positive tap and is considered indicative of an ectopic pregnancy. However, there is no consensus regarding the criteria for a positive test. Various authors have proposed volumes between 0.3 and 10 mL, with hematocrit from 3% to 15%. The pathophysiologic basis for culdocentesis is that a ruptured ectopic pregnancy will bleed into the pelvic peritoneal cavity. Some 85% to 90% of patients with a ruptured ectopic pregnancy will have a positive culdocentesis. Surprisingly, up to 70% of patients with an unruptured ectopic pregnancy will also have a positive result. A basic limitation of the technique is that it is less sensitive in the diagnosis of unruptured than ruptured ectopic pregnancy. Another cause of false-negative results is that, in cases of rapid bleeding, intraperitoneal blood may clot due to the lack of sufficient dwell time to produce defibrination. False-positive results occur because of technical errors (entering a vein or other vascular structure with the needle) or a ruptured corpus luteum cyst. Aspiration of purulent material may indicate another diagnosis, such as pelvic inflammatory disease.

Laparoscopy may be both diagnostic and therapeutic. Laparoscopy is primarily useful in patients with suspected ectopic pregnancy and a nondiagnostic US. It may provide an earlier diagnosis and a possible route for definitive treatment when compared with serial β-hCG measurements and US. As with other invasive techniques, results vary with the skill of the operator and the quality of the available equipment.

Dilatation and curettage may provide a definitive diagnosis of IUP, thus excluding ectopic pregnancy except in cases of heterotopic pregnancy. Dilatation and curettage diagnoses an IUP when chorionic villi are obtained from the uterine cavity. The procedure terminates an IUP and is applicable only when termination of pregnancy is desired or when a nonviable pregnancy has been documented.

TREATMENT

The treatment of ectopic pregnancy can be divided into surgical and medical approaches. If laparoscopy is needed for diagnosis, a surgical approach is most appropriate. For unruptured ectopic pregnancy, the most frequently used surgical approach is laparoscopic salpingostomy; the most frequently used medical approach is systemic methotrexate treatment. There is no difference in success rates between methotrexate, salpingotomy, and salpingectomy in appropriately selected women with unruptured ectopic pregnancies.[26,27] Laparotomy is the treatment of choice in hemodynamically unstable patients. Laparoscopy is preferred in a hemodynamically stable patient.

Methotrexate **Methotrexate** is the only drug currently recommended as a medical alternative to surgical treatment of ectopic pregnancy and is ideally used in patients with hemodynamic stability, minimal abdominal pain, the ability to follow up reliably, and normal baseline liver and renal function tests. Contraindications to methotrexate use are listed in

TABLE 98-6 Contraindications to Methotrexate Administration[28]

Absolute Contraindications	Relative Contraindications
Intrauterine pregnancy	Embryonic cardiac activity detected by transvaginal US
Evidence of immunodeficiency	Human chorionic gonadotropin concentrations >5000 mIU/mL
Moderate to severe anemia, leukopenia, or thrombocytopenia	Ectopic pregnancy >4 cm in size as imaged by transvaginal US
Sensitivity to methotrexate	Refusal to accept blood transfusion
Active pulmonary disease	Inability to reliably return for follow-up
Active peptic ulcer disease	
Clinically important hepatic or renal dysfunction	
Breastfeeding	
Hemodynamic instability	

Table 98-6.[28] Methotrexate is a folic acid antagonist that inhibits dihydrofolate reductase, causing depletion of cofactors needed for DNA and RNA synthesis. Different methotrexate regimens have been used, including both systemic IM injections and direct injection into the ectopic gestational sac. IM methotrexate is the most commonly used approach, eliminating the need for laparoscopy or US guidance. The failure rate is 14.3% or higher with single-dose methotrexate when pretreatment β-hCG levels are >5000 mIU/mL, compared with 3.7% for levels <5000 mIU/mL.[29] If β-hCG levels are higher than 5000 mIU/mL, multiple doses may be appropriate.[30] The success rate of the multiple-dose regimen was statistically significantly higher than that seen with a single dose of methotrexate (92.7% vs 88.1%).[31]

The most common side effects associated with methotrexate include abdominal pain after treatment (up to 75% of patients) followed by flatulence and then stomatitis. Lower abdominal pain lasting up to 12 hours is common 3 to 7 days after methotrexate treatment and is thought to be secondary to methotrexate-induced tubal abortion or tubal distention due to hematoma formation ("separation pain").[32] The pain is usually self-limited and may respond to nonsteroidal anti-inflammatory drugs.

Abdominal pain after methotrexate treatment represents a clinical dilemma. It is difficult to differentiate expected pain from therapeutic tubal abortion and hematoma formation with fallopian tube distension (separation pain) from pain associated with rupturing persistent ectopic pregnancy.[32] Suggested evaluation of patients presenting with abdominal pain in this time frame after methotrexate administration includes a CBC and abdominopelvic US to rule out tubal rupture and hemoperitoneum and consideration of other causes of abdominal pain.[3] Such patients may need admission to the hospital for observation. Hemodynamic instability and/or falling hematocrit require consideration for surgical intervention. Many centers will proceed to surgical intervention in patients with moderate to severe pain, free fluid in the cul-de-sac, or rebound tenderness, although conservative treatment has proven successful in stable patients after methotrexate therapy.[32] Prognostic factors associated with a higher failure rate for methotrexate treatment include larger tubal diameter, higher initial β-hCG levels, severe abdominal pain, and fetal cardiac activity.[33]

Methotrexate administration in properly selected patients with ectopic pregnancy may be initiated in the ED, clinic, or obstetrician/gynecologist's office. Treatment initiated in the ED should be in close conjunction with an obstetrician/gynecologist or other physician capable of providing follow-up care. Keep pelvic examinations after methotrexate treatment to a minimum to decrease the risk of tubal rupture. Patient instruction on discharge should include the following points:[34]

- Treatment failure occurs in up to 36% of cases.
- Elective or emergency surgical treatment may be necessary if medical therapy fails or tubal rupture occurs (~5% of cases).
- Vaginal bleeding, abdominal pain, weakness, dizziness, or syncope after treatment should be evaluated immediately as possible signs of tubal rupture.[16]
- Patients should refrain from sexual intercourse for 14 to 21 days after treatment (until β-hCG levels are undetectable), because it may increase the risk of tubal rupture.

Rh Seroconversion and Indications for Anti-D Immunoglobulin

Rh_0 (D) antigen can be detected as early as 5.5 weeks and certainly by 6 weeks of gestation. Alloimmunization can occur with as little as 0.1 mL of fetal blood admixing with the mother's. Alloimmunization can occur from ectopic pregnancy. Circulating blood volume of the fetus is <5 mL in the first trimester. **Both the American College of Emergency Physicians and the American College of Obstetricians and Gynecologists recommend treatment with 50 micrograms of RhoGAM for Rh-negative women with ectopic pregnancy when diagnosed prior to 12 weeks of gestation due to the small volume of red cells in the fetoplacental circulation, although administration of a full dose of 300 micrograms is acceptable as well.**

DISPOSITION AND FOLLOW-UP

When a patient with signs or symptoms suggestive of ectopic pregnancy is found to be pregnant, determine if the pregnancy is intrauterine (**Figure 98-4**). The nature and timing of additional diagnostic measures depend on the clinical condition of the patient. Unstable patients with suspected ectopic pregnancy should receive resuscitation, urgent consultation, and operative intervention. Surgery may be both diagnostic and therapeutic if an ectopic pregnancy is found or may reveal another cause for the patient's condition. When bedside ED US is available, it may be valuable even in unstable patients, as it should not interfere with resuscitation, consultation, and rapid transfer to the operating room.

Ideally, all pregnant patients with suspected ectopic pregnancy should receive immediate US. However, issues of availability during off hours may make this impractical. Stable patients who are judged to be at low risk for ectopic pregnancy can be considered for discharge and outpatient follow-up. Such patients should have a quantitative β-hCG level obtained to facilitate subsequent management. Culdocentesis remains an option where US is unavailable, but currently is used rarely due to its limitations and the unfamiliarity of many emergency physicians with the technique.

Stable patients with β-hCG levels above the discriminatory zone and an empty uterus on US, with or without other US findings of an ectopic pregnancy, are presumed to have an ectopic pregnancy. These patients should receive consultation in the ED.

Management options for stable patients with a β-hCG level below the discriminatory zone and indeterminate US include consultation in the ED or discharge for follow-up in 2 days for reexamination and repeat β-hCG levels. Culdocentesis, dilatation and curettage, and laparoscopy are also options in this circumstance; however, the decision is normally left to the obstetrician's discretion. Figure 98-4 illustrates a suggested diagnostic approach.

OTHER CAUSES OF BLEEDING IN THE FIRST 20 WEEKS OF PREGNANCY

Common causes of bleeding during early pregnancy are listed in **Table 98-7**.

SPONTANEOUS ABORTION

The World Health Organization defines spontaneous abortion as loss of pregnancy before 20 weeks or loss of a fetus weighing <500 grams. Estimates of pregnancies that abort spontaneously range from 20% to 40%. Approximately 75% of spontaneous abortions occur before 8 weeks of gestation (**Table 98-8**).

The most common cause of fetal loss is chromosomal abnormalities. Other associations include advanced maternal age, prior poor obstetric history, concurrent medical disorders, previous abortion, infection (including syphilis and human immunodeficiency virus), and some anatomic abnormalities of the upper genital tract. Exposure to some agents, such as certain anesthetic agents, certain heavy metals, and tobacco, may also contribute to the incidence of abortion.

Bleeding with or without abdominal pain is the most common presenting complaint.

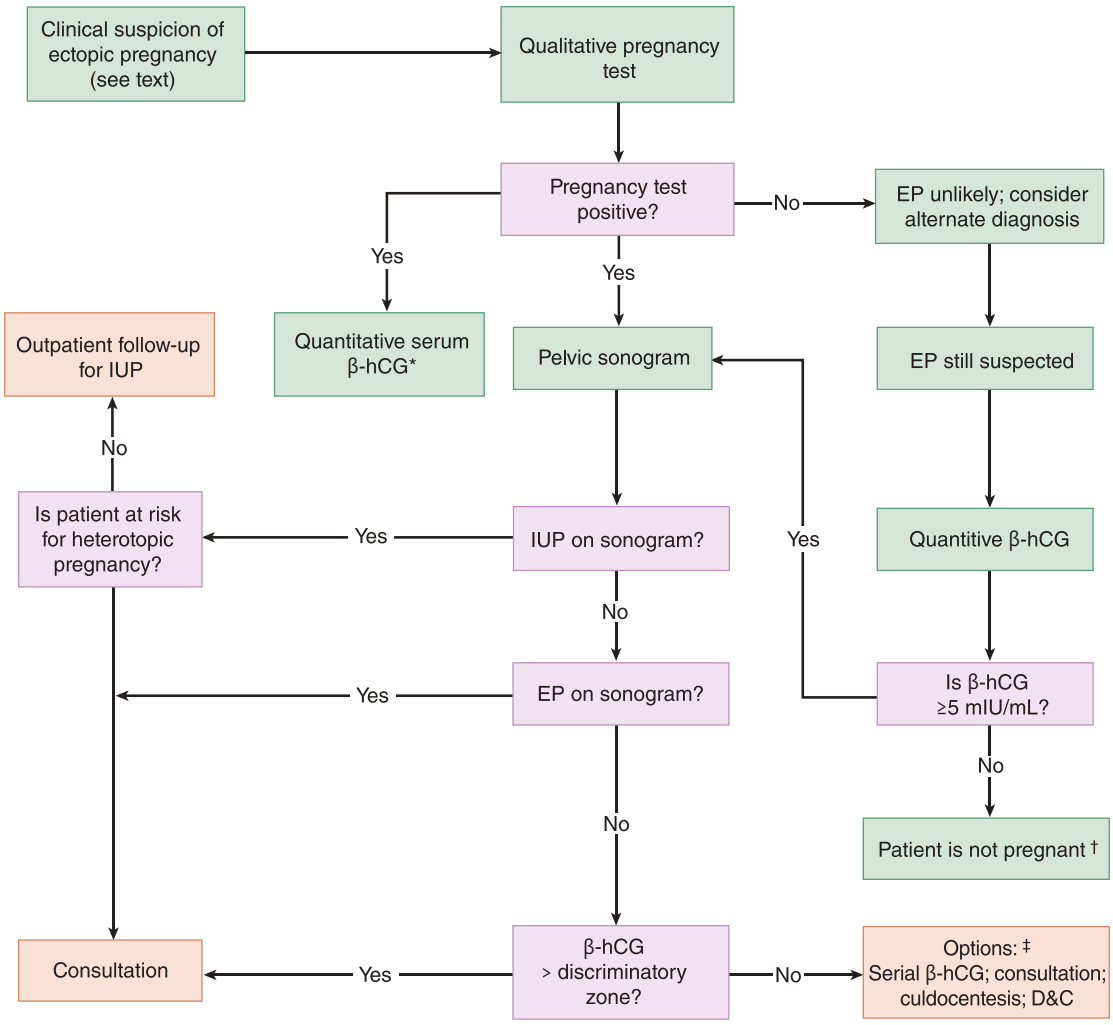

FIGURE 98-4. Diagnostic algorithm for suspected ectopic pregnancy. *Quantitative measurement of β subunit of human chorionic gonadotropin (β-hCG) before US may facilitate rapid patient disposition by saving time. †There have been extremely rare reports of pregnancy with β-hCG <5 mIU/mL. ‡Serial outpatient β-hCG measurements are recommended only for stable patients judged to be at low risk for ruptured ectopic pregnancy. D&C = dilatation and curettage; EP = ectopic pregnancy; IUP = intrauterine pregnancy.

TABLE 98-7 Common Causes of Vaginal Bleeding During the First Trimester of Pregnancy

Abortion
Ectopic pregnancy
Gestational trophoblastic disease
Implantation bleeding (physiologic)

TABLE 98-8 Spontaneous Abortion Terminology

Terminology	Definition
Threatened abortion	Pregnancy-related bloody vaginal discharge or frank bleeding during the first half of pregnancy without cervical dilatation
Inevitable abortion	Vaginal bleeding and dilatation of the cervix
Incomplete abortion	Passage of only parts of the products of conception
	More likely to occur between 6 and 14 weeks of pregnancy
Complete abortion	Passage of all fetal tissue, including trophoblast and all products of conception, before 20 weeks of conception
Missed abortion	Fetal death at <20 weeks without passage of any fetal tissue for 4 weeks after fetal death
Septic abortion	Evidence of infection during any stage of abortion

DIAGNOSIS

In addition to the standard medical history, determine the amount of bleeding as pads used per hour to anticipate blood loss, last menstrual period, and past obstetric history. A pelvic examination is needed to define the type of abortion and to determine the amount and site of bleeding, whether the cervix has dilated, and whether any tissue has been passed.

The diagnosis of pregnancy is central to the diagnosis of abortion. Obtain a quantitative serum β-hCG level, CBC to evaluate for blood loss, blood type, Rh factor and antibody screen, and urinalysis (urinary tract infection has been associated with increased fetal wastage). US can help rule out ectopic pregnancy, aid as a prognostic tool for fetal viability, and diagnose retained products of conception. US studies combined with determinations of β-hCG levels can be both diagnostic and prognostic. Although a β-hCG of 1500 IU/mL is a somewhat arbitrary value when evaluating pregnancy, it is still useful when comparing with US findings. Although institution-dependent, an IUP should be visible on transvaginal US at this concentration. **Table 98-9** describes expected US findings at certain gestational ages and β-hCG values.[35]

TREATMENT

Patients with threatened abortion can be discharged safely if follow-up is ensured. Although a low level of activity and even bed rest are

TABLE 98.9 Comparison of Gestational Age, β-hCG, and US Findings

Gestational Age	β-hCG (mIU/mL)	Transvaginal US Findings	Transabdominal US Findings
4–5 weeks	<1000	Intradecidual sac	N/A
5 weeks	>2000	Yolk sac (± embryo)	Gestational sac
6 weeks	10,000–20,000	Embryo with cardiac activity	Yolk sac (± embryo)
7 weeks	>20,000	Embryonic torso/head	Embryo with cardiac activity

Source: Reproduced with permission from Ma OJ, Mateer JR, Reardon RF, Joing SA: *Ma & Mateer's Emergency Ultrasound*, 3rd ed. New York: McGraw-Hill Inc., 2014; Table 14-1, p. 400.

sometimes advised, there is no proven effectiveness of this practice. Generally speaking, a miscarriage cannot be avoided. Patients should avoid intercourse and tampons to minimize risk of infection.

Patients with a diagnosis of incomplete abortion should have the uterus evacuated. The decision to proceed with medical treatment, such as PO misoprostol, 600 micrograms, or surgical treatment, such as dilatation and curettage, should be made in consultation with the patient and an obstetrician.[36]

Patients with a complete abortion, as shown by US and complete passage of products of conception, can be discharged safely, with follow-up ensured. If there is any doubt, obtain obstetrics consultation for possible dilatation and curettage.

Patients with a nonviable fetus can be either admitted or discharged to be followed up within 1 week, depending on the comfort level of the patient and physician with this decision. Patients should return immediately if there is heavy bleeding (more than one pad per hour for 6 hours), pain, or fever.

Pregnant women with vaginal bleeding who are Rh-negative should be treated with Rh_0 (D) immunoglobulin (RhoGAM). RhoGAM should be administered before discharge, if possible, but it also can be administered within 72 hours by the primary care physician or obstetrician when the woman presents several days or weeks after vaginal bleeding has begun.

SEPTIC ABORTION

A septic abortion is a spontaneous or other abortion complicated by a pelvic infection. Presenting complaints include fever, abdominal pain, vaginal discharge, vaginal bleeding, and history of recent pregnancy. The most common causes are retained products of conception due to incomplete spontaneous or therapeutic abortion and introduction of either normal or pathologic vaginal bacteria by instrumentation.

Perform a history and physical examination, including a pelvic examination. Obtain a quantitative serum β-hCG level, CBC to evaluate for anemia due to blood loss, blood type, Rh factor and antibody screen, urinalysis, and blood cultures. An US will help identify retained products of conception in the uterus, adnexal masses, and free fluid in the cul-de-sac. Treatment consists of fluid resuscitation, broad-spectrum IV antibiotics, and early obstetric consultation for evacuation of the uterus. Antibiotics, such as ampicillin/sulbactam, 3 grams IV, or clindamycin, 600 milligrams, plus gentamicin, 1 to 2 milligrams/kg IV, should cover both normal vaginal flora and those causing sexually transmitted disease.

GESTATIONAL TROPHOBLASTIC DISEASE

Gestational trophoblastic disease consists of a broad spectrum of conditions ranging from an uncomplicated partial hydatidiform molar pregnancy to stage IV choriocarcinoma with cerebral metastases.[37] It is a neoplasm that arises in the trophoblastic cells of the placenta. It complicates 1 in 1700 pregnancies in North America and is more common in Asian women. The noninvasive form of the disease is the hydatidiform mole, which is either complete or partial. Complete moles are more common, and in this form, there is no actual fetus, whereas in the partial mole, a deformed, nonviable fetus is present. Both moles and invasive forms are composed of trophoblasts that produce β-hCG. Patients with a history of hydatidiform molar pregnancy are at increased risk of future molar pregnancies, with a risk of 1% in subsequent gestations after one molar pregnancy and a risk as high as 23% after two molar gestations.

Symptoms include vaginal bleeding in the first or second trimester (75% to 95% of cases) and hyperemesis (26%). Gestational trophoblastic disease, or molar pregnancies that persist into the second trimester, are associated with pre-eclampsia. **When pregnancy-induced hypertension is seen before 24 weeks of gestation, consider the possibility of a molar pregnancy.** The uterus is excessive in size for gestational age and shows a placenta with many lucent areas interspersed with brighter areas on US study. Because not all molar pregnancies are found on US, all tissue extracted from the uterus on suction curettage or during pelvic examination should be sent for histologic examination. If trophoblastic disease is suspected because of abnormally high β-hCG levels, a uterine size either larger or smaller than expected, and US findings suggestive of the diagnosis, obtain obstetric consultation. Treatment is by suction curettage in the hospital setting because of risk of hemorrhage. β-hCG levels that fail to decrease after evaluation are evidence of persistent or invasive disease necessitating chemotherapy. Metastasis to lung, liver, and brain may occur, but the prognosis for most patients is very good. Trophoblastic embolization, although extremely rare, may occur, with resulting rapid onset of respiratory distress resembling amniotic fluid embolus.

IMPLANTATION BLEEDING

Implantation bleeding can occur as the embryo implants into the vascular uterine decidual tissue. Bleeding can be scant or like menstrual bleeding and usually occurs at 5 or 6 weeks after the last period. Pelvic examination is normal. Implantation bleeding is diagnosed only after excluding ectopic pregnancy.

NAUSEA AND VOMITING OF PREGNANCY AND HYPEREMESIS GRAVIDARUM

EPIDEMIOLOGY

Nausea and vomiting of pregnancy generally are seen in the first 12 weeks. The etiology is unknown. Severe nausea and vomiting of pregnancy is known as hyperemesis gravidarum and is defined as intractable vomiting with weight loss, volume depletion, and laboratory values showing hypokalemia or ketonemia. It occurs in up to 2% of all pregnancies. Patients with gestational trophoblastic disease also may present with intractable vomiting for unknown reasons.

CLINICAL FEATURES

Findings on physical examination in nausea and vomiting of pregnancy are usually normal except for signs of volume depletion. Laboratory tests to consider include CBC, serum electrolytes, BUN, creatinine, and urinalysis. The finding of ketonuria is important because it is an early sign of starvation. However, there is no evidence that ketosis per se is harmful to the fetus. Serial measurements of urinary ketones can be used to determine success of therapy.

The presence of abdominal pain in nausea and vomiting of pregnancy or hyperemesis gravidarum is highly unusual and should suggest another diagnosis. Ruptured ectopic pregnancies occasionally present with nausea and vomiting, as well as diarrhea and abdominal pain. Gallbladder dilatation and biliary sludge increase in pregnancy, predisposing to stone formation. Cholelithiasis and cholecystitis are more common in pregnant women than in women of comparable age and health status who are not pregnant. Differential diagnosis of vomiting or vomiting with abdominal pain should include cholecystitis, cholelithiasis, gastroenteritis, pancreatitis, appendicitis, hepatitis,

TABLE 98-10 Antiemetics

Antiemetic	Brand Name	U.S. Food and Drug Administration Category	PO	PR	IV
Promethazine	Phenergan	C	12.5–25 milligrams every 4 h	12.5–25 milligrams every 4 h	IV administration is generally recommended against; 12.5–25 milligrams IM every 4 h
Prochlorperazine	Compazine	—	10 milligrams every 6–8 h	25 milligrams every 12 h	10 milligrams over 2 min Maximum of 40 milligrams every 24 h
Chlorpromazine	Thorazine	C	10–25 milligrams every 4–6 h	100 milligrams every 6–8 h	25 milligrams in 500 mL NS at 250 mL/h
Ondansetron	Zofran	B	4–8 milligrams every 8 h	—	8 milligrams IV over 5 min
Metoclopramide	Reglan	B	10 milligrams orally every 6–8 h	—	10 milligrams over 1–2 min every 6–8 h
Maintenance Therapy for Nausea and Vomiting					
Doxylamine with pyridoxine	Diclegis/ Diclectin	A	2 tablets every evening	—	—
Vitamin B_6	—	—	25 milligrams every 8 h	—	—
Ginger	—	—	500–1000 milligrams daily	—	—
Diphenhydramine	Benadryl	B	25–50 milligrams every 6 h	—	—

Abbreviation: NS = normal saline.

Source: Adapted with permission from Pearlman M, Tintinalli JE (eds): *Emergency Care of the Woman*. New York: McGraw-Hill, 1998.

peptic ulcer, pyelonephritis, ectopic pregnancy, fatty liver of pregnancy, and the syndrome of *h*emolysis, *e*levated *l*iver enzymes, and *l*ow *p*latelets (HELLP syndrome).

TREATMENT

Treatment consists of IV fluids containing 5% glucose in either lactated Ringer's solution or normal saline to replete volume and reverse ketonuria. A number of antiemetic drugs can be used (**Table 98-10**) for patients who remain nauseated or continue to vomit. Initially, the patient should be given nothing by mouth. Oral fluids should be started after the nausea and vomiting are controlled but before discharge.

DISPOSITION AND FOLLOW-UP

The patient may be discharged after reversal of ketonuria, correction of electrolyte imbalance, and a successful trial of oral fluids. Discharge with antiemetic medication is usually necessary. There is no clear drug of choice.

Phenothiazines can cause drowsiness or dystonic reactions in some patients. Ondansetron (Zofran®), 8 milligrams IV or 4 milligrams PO three times daily, can cause headache, constipation, diarrhea, or lightheadedness. It does not cause dystonia. Its chief disadvantage is cost. It is apparently no more effective than promethazine.[15] Doxylamine and pyridoxine (Bendectin®), a mainstay of therapy in the past, was discontinued due to fears of teratogenicity, but with new information, it does not represent an increase in fetal risk and has been reintroduced on the North America market as Diclegis/Diclectin (also put in trademark sign after Diclegis/Diclectin).[16,38]

Admission guidelines include uncertain diagnosis, intractable vomiting, persistent ketone or electrolyte abnormalities after volume repletion, and weight loss of >10% of prepregnancy weight.

REFERENCES

The complete reference list is available online at www.TintinalliEM.com.

CHAPTER 99

Comorbid Disorders in Pregnancy

Lori J. Whelan

INTRODUCTION

This chapter reviews the most common comorbid conditions encountered in pregnant women in the ED environment: diabetes and hypoglycemia; thyroid disorders; hypertensive disorders; cardiac arrhythmias; thromboembolism; asthma; renal disease; urinary tract infections; sickle cell disease; headache; seizures; substance abuse; and intimate partner violence. Drug risk during pregnancy, lactation, and fetal effects of radiation are summarized based on currently available data. Resuscitation is covered in chapter 25, "Resuscitation in Pregnancy."

DIABETES IN PREGNANCY

Maternal diabetes affects >8% of the 4 million live births annually in the United States.[1] Three fourths of pregnant patients with diabetes have either gestational diabetes or type 2 diabetes diagnosed through prenatal screening. Of the remaining 25%, 1% have preexisting type 1 diabetes, and the remaining are type 2 diabetics. Pregnant diabetic women are at increased risk for spontaneous abortion, particularly patients with poor glycemic control early in pregnancy, preexisting vascular disease, and pre-eclampsia. Pregnant diabetics are also at increased risk for several pregnancy complications, including pregnancy-induced hypertension, preterm labor, spontaneous abortion, pyelonephritis, and diabetic ketoacidosis (DKA). The goal of treatment during pregnancy is to prevent spontaneous abortions, hyperglycemia-induced congenital abnormalities and ketoacidosis, and hypoglycemia.

Oral hypoglycemic agents, such as metformin and glyburide, are occasionally used in select patients with gestational diabetes.[2] A significant portion of gestational diabetics can be managed with diet alone if they can maintain glycemic goals with frequent glucose monitoring.

The American College of Obstetricians and Gynecologists recommends the following goals for maintaining euglycemia in pregnant diabetic patients: a fasting blood glucose concentration of ≤95 milligrams/dL and a 2-hour postprandial glucose concentration