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First Trimester Pregnancy Emergencies: Recognition and Management

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Abstract

Timely management of patients presenting to the ED while in their first trimester of pregnancy can improve outcomes for both the patient and the fetus. Common obstetric problems encountered include vaginal bleeding and miscarriage, ectopic pregnancy and pregnancy of undetermined location, and nausea and vomiting of pregnancy, including hyperemesis gravidarum. Optimal diagnostic approaches and management strategies are covered, including which antiemetics are safe to give in pregnancy. Common nonobstetric problems include asymptomatic bacteriuria, urinary tract infections including pyelonephritis, and acute appendicitis. This article also reviews the various imaging modalities available for pregnant patients and reviews the risks of ionizing radiation as well as various contrast media.

Case Presentations

Your first patient of the shift is a 23-year-old woman whom the nurse has rushed into the resuscitation bay due to hypotension and altered mental status. The patient's blood pressure is 70/40 mm Hg, with a heart rate of 70 beats/min, and she states that she has had abdominal pain and vaginal bleeding since this morning. You wonder what would be the fastest way to get this patient diagnosed and treated…

The patient in the room next door is a 19-year-old woman who presents due to light vaginal spotting for the past few hours. She says she came in because she has been trying to get pregnant for months, and finally had a positive pregnancy test yesterday. This is her first visit to a doctor since learning of her pregnancy. She is tearful, and asks, "Does this mean I am going to lose my baby?" You are not quite sure how to answer her question, and you ask yourself what tests need to be done today in the ED...

Later that shift, you evaluate a 26-year-old woman who has a confirmed intrauterine pregnancy at 11 weeks' gestation and presents for fever, dysuria, and right flank pain. An ultrasound was performed in triage that showed bilateral mild hydronephrosis. You are not sure what to make of that finding, which antibiotics would be safe for treatment, and whether she can be managed as an outpatient…

Introduction

Patients in their first trimester of pregnancy frequently present to the emergency department (ED) with both obstetric and nonobstetric complaints that range from benign to life-threatening for both mother and fetus. Managing these patients is an important skill, but a recent survey demonstrated that only 56% of emergency medicine residents felt they had adequate exposure to obstetric emergencies. On a multiple-choice test covering knowledge of obstetric emergencies, a mean of 58% of items were answered correctly.[1] This identifies an important area for further education and training, as timely diagnosis and appropriate management can improve outcomes.

Common obstetric problems in the first trimester of pregnancy include vaginal bleeding and the spectrum of miscarriage (experienced by 7%-27% of pregnant patients)[2], nausea and vomiting (85%)[3], hyperemesis gravidarum (3%), and ectopic pregnancy (2%)[4]. Common nonobstetric problems include appendicitis and urinary tract infections (UTIs). The most recent report on pregnancy-related mortality, published in 2017 and encompassing 2011-2013 data for pregnancies in the United States, showed a stable rate of 17 deaths per 100,000 pregnancies, but with significant racial-ethnic disparities.[5]

This issue of *Emergency Medicine Practice* reviews important issues that affect patients in their first trimester, management pearls and pitfalls, and a review of the literature surrounding current recommendations.

Critical Appraisal of the Literature

Medical Subject Headings (MeSH) via PubMed were searched for *pregnancy trimester, first* (14,929 articles), *hyperemesis gravidarum* (1379 articles), *ectopic pregnancy* (13,953 articles), and *abortion, spontaneous* (34,256 articles). These articles were further limited to English language only, human subjects, and then divided into reviews and clinical trials.

Guidelines from the American College of Obstetricians and Gynecologists (ACOG) were reviewed, including evidence-based Practice Bulletins on critical care in pregnancy (2016)[6], medical management of first-trimester abortion (2014)[7], tubal ectopic pregnancy (2018)[8], nausea and vomiting of pregnancy (2018)[9], and prevention of RhD alloimmunization (2017)[10]. ACOG Committee Opinions on the risk of birth defects with antibiotics for UTI (2017)[11] and guidelines for imaging in pregnancy (2017)[12] were also reviewed. The American College of Radiology Practice Parameter for imaging of pregnant women (2013)[13], a consensus-based guideline based on the review of the available evidence, was reviewed, along with the 2005 guidelines from the Infectious Diseases Society of America (IDSA) on asymptomatic bacteriuria.[14]

The Cochrane Database of Systematic Reviews has reviews on interventions for nausea and vomiting in pregnancy (2015)[15], hyperemesis gravidarum (2016)[16], antibiotic regimens for asymptomatic bacteriuria (2010)[17], UTIs (2011)[18], expectant versus surgical management of miscarriage (2012)[19], and medical treatments for incomplete miscarriage (2017)[20]. Most of these reviews include multiple randomized controlled trials, and the data are generally good for these topics. The American College of Emergency Physicians (ACEP) released a 2017 update on their Clinical Policy, "Critical Issues in the Initial Evaluation and Management of Patients Presenting to the ED in Early Pregnancy," although no new significant

updates were added since their previous 2012 recommendations.[21,22]

The relevant literature that guides ED management of first trimester emergencies is, overall, very good, and many of the recommendations in this issue of *Emergency Medicine Practice* can be made based on robust data. Some data, such as the utility of a pelvic examination when an ultrasound is performed, are underpowered to detect potential small, but true, differences in outcomes and are areas for further study.

Etiology and Pathophysiology

Miscarriage

In the literature, the terms *miscarriage*, *spontaneous abortion*, and *early pregnancy loss* are all utilized to describe loss of an intrauterine pregnancy (IUP) within the first trimester. To avoid confusion of terminology, we will use the term *miscarriage* here to refer to the loss of an IUP in the first trimester.

Miscarriage rates vary widely based on age and risk factors, but it is experienced by 7% to 27% of pregnant patients. Miscarriage risks increase with age: among women aged 20 to 30 years, the risk is 9% to 17%; a woman aged 35 years has a 20% risk; and by age 40, the risk increases to 40%.[23] Overall rates of vaginal bleeding in pregnancy approach 25% and are most common between the fifth and eighth gestational weeks.[24] Heavy bleeding, especially in conjunction with pain, is associated with a higher risk of miscarriage (odds ratio [OR], 3.0). In patients with only spotting, there does not appear to be a significant difference in rates of miscarriage (OR, 1.1, confidence interval [CI], 0.9-1.3).[2]

In a study that analyzed the cytogenetics of miscarriages from patients with recurrent miscarriage, it was found that approximately half of miscarriages were due to fetal chromosomal abnormalities.[25] There appears to be a roughly 2-fold increased risk of subsequent maternal and fetal adverse outcomes (eg, preterm birth, low birth weight, and antepartum hemorrhage) in women who have a threatened miscarriage in the first trimester of pregnancy.[26]

Ectopic Pregnancy

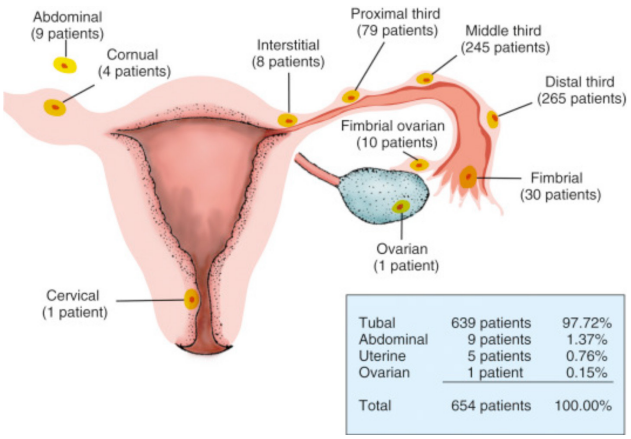
An ectopic pregnancy is implantation of a fertilized ovum outside of the endometrial cavity, occurring in up to 2% of all pregnancies. Almost all abnormal implantation sites are in the fallopian tube (98%), but they can also be in the ovary itself, the abdomen, or at the junction of the fallopian tube and uterus (termed an *interstitial ectopic pregnancy*). **(See Figure 1.)**

The greatest risk factors for an ectopic pregnancy include a history of salpingitis, a history of sexually transmitted infections, a history of pelvic inflammatory disease, and prior ectopic pregnancy. There is also a dose-response relationship between smoking and ectopic pregnancy, with heavier smokers having a higher risk (> 1 pack/day smoking having an OR of 4), thought to be due to ciliary dysmotility causing impaired transport to the uterus.[27] Although intrauterine devices (IUDs) are highly effective at preventing pregnancy, if a patient becomes pregnant while an IUD is in place, over half of these pregnancies may be ectopic.[28] Because ectopic pregnancy is relatively common, nearly half of patients will have no risk factors for the condition; the presence or absence of risk factors should therefore not alter the approach to these patients.

Lower beta-human chorionic gonadotropin (beta-hCG) levels are present in ectopic pregnancies compared to patients with an IUP because the syncytiotrophoblast cells grow less readily compared to an appropriate uterine implantation. Women with pain or bleeding and a serum beta-hCG level < 1500 mIU/mL are at a 2-fold higher risk of eventually being diagnosed with an ectopic pregnancy.[29] Rupture of an ectopic pregnancy can occur at very low beta-hCG levels. Of mortality related to ectopic pregnancy, the clear majority are due to rupture, causing fatal hemorrhagic shock (94% of all ectopic pregnancy-related deaths in United States populations).[5]

A heterotopic pregnancy is the coexistence of an IUP and an ectopic pregnancy and is estimated to occur in between 1 in 4000 and 1 in 30,000 patients. This risk is substantially greater (nearly 1 in 100) in patients undergoing assisted reproductive technology.[30]

Figure 1. Sites of Ectopic Pregnancy Implantation



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Nausea and Vomiting of Pregnancy (and Hyperemesis Gravidarum)

Though the majority of pregnant women will have nausea and vomiting of pregnancy (NVP), a small subset of patients (3%) will have hyperemesis gravidarum. Hyperemesis gravidarum is the most severe form of NVP. Although there is no universal definition of hyperemesis gravidarum, it is often defined as a loss of 5% of prepregnancy body weight as well as persistent nausea, vomiting, and ketosis. Although common, NVP is a diagnosis of exclusion; other etiologies for the nausea and vomiting must be ruled out first.

NVP appears protective for pregnancy loss, with nausea being protective (hazard ratio [HR] 0.44); nausea and vomiting being even more protective (HR, 0.20).[31] Nonetheless, NVP has a significant impact on a pregnant woman's quality of life; one study showed that a quarter of women with severe NVP had considered pregnancy termination, and three-quarters of those women stated they would not want to get pregnant again due to these symptoms.[32]

Asymptomatic Bacteriuria and Urinary Tract Infections

During pregnancy, there are many changes in the urinary tract from both an anatomical and physiological standpoint. Hydroureteronephrosis can occur by the seventh week of gestation and is thought to be due to both hormonal changes and mechanical compression from the uterus. Urinary stasis can occur due to displacement of the bladder by the uterus.

As with all patients, pregnant patients can develop asymptomatic bacteriuria, which is defined as bacteriuria without any symptoms or signs suggestive of a UTI (eg, abdominal pain, dysuria, urgency, frequency, etc). However, due to urinary stasis, asymptomatic bacteriuria in pregnancy is a risk factor for developing pyelonephritis. A multicenter prospective cohort study screened 248 pregnant women for asymptomatic bacteriuria and then randomized that subgroup to treatment with nitrofurantoin or placebo. In the placebo arm, 2.4% of patients developed pyelonephritis compared with 0.6% of nitrofurantoin-treated women, with no differences in the rate of preterm birth.[33]

Acute Appendicitis in Pregnancy

Acute appendicitis is the most common surgical problem in pregnancy; however, based on epidemiologic data, pregnant women are less likely to have appendicitis then age-matched, nonpregnant women.[34] Despite traditional dogma, right lower quadrant pain is the most common location of pain in appendicitis in pregnancies of all gestational ages.[35] Peritonitis is more common in pregnant women with appendicitis (OR, 1.3; 95% CI, 1.2-1.4) compared with nonpregnant patients, with an increase in rates of sepsis, septic shock, bowel obstruction, and prolonged length of stay, among other adverse outcomes.[36]

Differential Diagnosis

The differential diagnosis for abdominal pain or vaginal bleeding in the first trimester of pregnancy is broad and includes both pregnancy-related conditions as well as the typical conditions that cause these same symptoms in nonpregnant women. Pregnancy-related conditions such as the spectrum of miscarriage (threatened, complete, missed, inevitable, incomplete, and septic) and ectopic pregnancy must be considered. Exclusion of vaginal or cervical lacerations in the appropriate clinical context (eg, genitourinary trauma) should be considered. Ovarian torsion can occur in pregnancy, especially during the first trimester, due to the corpus luteum, which maintains the pregnancy. Patients undergoing ovarian stimulation as part of assisted reproductive technology are at greatly increased risk for ovarian torsion due to increased ovarian size.[37] For abdominal pain or vaginal bleeding unrelated to pregnancy, the differential diagnosis is the same as for nonpregnant women. **See Table 1** for a list of common causes of abdominal pain in the first trimester of pregnancy.

Table 1. Differential Diagnosis for Abdominal Pain in Pregnancy

Diagnosis	Comments
Gynecologic Causes	
Miscarriage	Evaluate with ultrasound and physical examination to confirm
Septic abortion	Presents with fever, uterine tenderness
Ectopic pregnancy	Must be evaluated for in any patient with pregnancy of unknown location
Corpus luteum cyst	Presents with focal lateral pain, no fever; evaluate with ultrasound to differentiate from ovarian torsion
Ovarian torsion	Presents with severe lateral pain
Pelvic inflammatory disease	Rare in pregnancy
Nongynecologic Causes	
Appendicitis	Presents with right lower quadrant pain, fever
Cholecystitis	Presents with right upper quadrant pain
Hepatitis	Evaluate with liver function testing
Pyelonephritis	Presents with flank pain, fever; evaluate with urinalysis and culture

Adapted from *Rosen's Emergency Medicine: Concepts and Clinical Practice*. 9th edition. Ron Walls, Robert Hockberger, Marianne Gausche-Hill. Page 2249. Copyright 2018, with permission from Elsevier.

Prehospital Care

Standard prehospital protocols should be followed. If known, a brief obstetric history including number of weeks' gestation (or last menstrual period if unknown), whether an IUP has been confirmed previously for this pregnancy, prior history of ectopic pregnancy, and volume of vaginal bleeding, if present, are all helpful. For unstable patients, early contact with the base station assists in mobilization of appropriate obstetric resources. Prehospital discussion with the base station regarding which facility to transport the patient to is helpful to ensure that the best decision is made with regard to transport time and availability of obstetric resources.

Emergency Department Evaluation

History

If there is vaginal bleeding or spotting, ask about the amount (eg, number of pads, more/less than typical menses, etc). This will help assess for significance of blood loss and prognosticate the likelihood of miscarriage in first trimester vaginal bleeding.

If there is abnormal vaginal discharge, note whether passage of tissue occurred (as may occur in a complete miscarriage) and the characteristics of discharge (as may occur with vulvovaginal candidiasis or a sexually transmitted infection).

Ask about the patient's prior obstetrical history, describing (1) gravida, (2) parity ("para"), and (3) abortus. *Gravida* refers to the number of times the woman has been pregnant, regardless of pregnancy outcome, regardless of the number of fetuses per pregnancy, and inclusive of the current pregnancy. (For example, a woman who is having her first pregnancy and has twins is a G1.) *Parity* describes the number of pregnancies reaching a viable gestational age, and *abortus* describes the total number of induced abortions or miscarriages.

When noting parity and abortus, the 4-digit "term-preterm-abortus-living" (TPAL) method is most descriptive and is widely used. The "T" notes the number of term births (> 37 weeks' gestation); the "P" notes the number of premature births; the "A" notes the number of miscarriages or abortions; and the "L" notes the number of living children. For example, a woman who is currently pregnant but had 2 previous pregnancies that were both premature but still alive now would be described as "G3P0202."

The pregnancy history should include a history of prior ectopic pregnancies, as this is a risk factor for recurrent ectopic pregnancy. Nonetheless, no historical features can exclude or confirm an ectopic pregnancy with high reliability. Positive predictors for ectopic pregnancy include pain that is lateral (not midline, given the usual location for ectopic pregnancy implantation), severe pain, and sharp pain.[38] The use of assisted reproductive technologies should raise suspicion for a heterotopic pregnancy. Prior sexual history can be helpful to screen for risk of sexually transmitted infections, which increase the risk for ectopic pregnancy.

Pregnancy is a risk factor for abuse, and the safety of the patient's home situation should be assessed if there is any concern.

Physical Examination

Because pregnant patients can have nonobstetric etiologies for their presentation, a focused physical examination should include what would be done for a nonpregnant patient.

It is reasonable to perform a pelvic examination as part of the standard examination for patients presenting with first trimester vaginal bleeding with a known IUP, but the utility of this is not certain. A 2017 randomized controlled trial attempted to determine whether a pelvic examination was necessary in the presence of a visualized IUP on ultrasound.[39] There were no differences in outcomes found between subjects randomized to pelvic examination or no pelvic examination; however, the study was able to enroll only 202 of a planned 720 patients, so it may have been underpowered to detect a smaller true difference. As expected, patients randomized to a pelvic examination reported feeling more uncomfortable.[39]

A pelvic examination should always be performed if the emergency clinician suspects that it would change management, such as identifying the source of bleeding or investigating for a cervical or vaginal laceration, a sexually transmitted infection, or pelvic inflammatory disease. In a suspected miscarriage, visualization of the cervical os can assist in diagnosis of an incomplete miscarriage (if products of conception are visualized in the cervix) or an inevitable miscarriage (if the patient has an IUP but an open cervical os).

Unstable patients in the first trimester of pregnancy should be assumed to have a ruptured ectopic pregnancy until proven otherwise. Patients with a ruptured ectopic pregnancy will commonly have abdominal tenderness and can have peritoneal signs. In the presence of intra-abdominal blood, patients can have paradoxical bradycardia due to vagal stimulation from irritation of the peritoneum. A bedside ultrasound can help elucidate whether the patient has free intraperitoneal fluid (suggestive of a ruptured ectopic pregnancy) or if she has an IUP (which, in the absence of risk factors for a heterotopic pregnancy, would essentially exclude the diagnosis of a coexisting ectopic pregnancy).

Similar to the history, no physical examination features can reliably rule in or rule out ectopic pregnancy. However, there is some positive

predictive value for peritoneal signs and adnexal tenderness and some negative predictive value for a uterine size that was estimated to be compatible with > 8 weeks' gestation.[38]

Diagnostic Studies

Urine Pregnancy Testing

A urine pregnancy test should be obtained in all women of reproductive age who present to the ED with abdominal pain or vaginal bleeding. Standard urine pregnancy tests will become positive at hCG levels of 20 to 50 mIU/mL, usually 6 to 8 days after fertilization, and generally by the time the patient has recognized that she has missed her period. With the lower detection limits of the newer tests, dilute urine is unlikely to cause a false-negative result unless the dilution is extreme. One study found that when women had a 5-fold dilution of their urine osmolality (by having them drink 1 L of water), 100% sensitivity persisted with tests that had a detection threshold of 20 mIU/mL.[40] Despite the test being very sensitive at low beta-hCG levels, there is a theoretical "hook" effect where, if the hCG is too high, the urine test will read as negative. For newer tests, this effect does not occur below an hCG level of 500,000 mIU/mL. False-positive tests are rare, but can be due to recent loss of a pregnancy (even if undetected by the patient), exogenous hCG usage, or a malignancy that secretes hCG.

Diagnostic Studies in Miscarriage and Ectopic Pregnancy

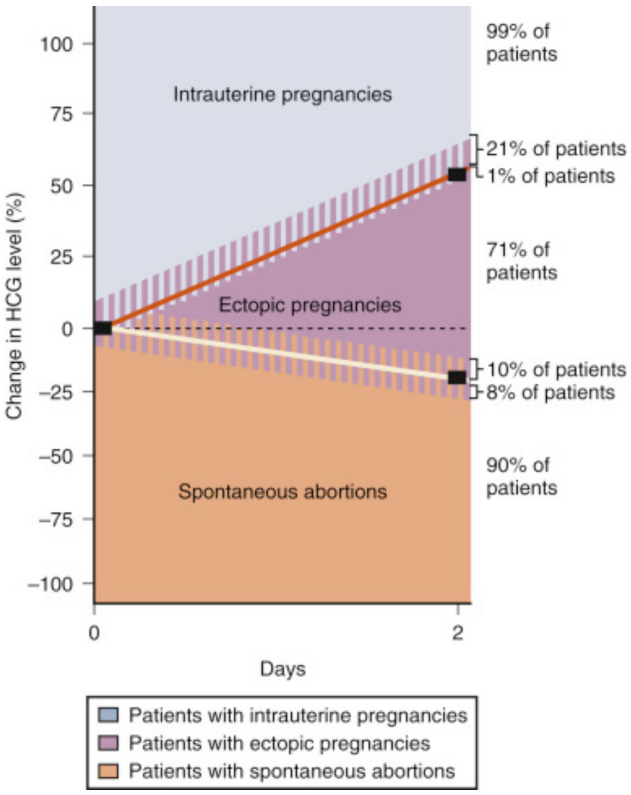
Diagnosis of an IUP is made when a gestational sac with a yolk sac or embryo is visualized in the uterus on ultrasound. Because the risk of heterotopic pregnancy in the general population is estimated to be 1 in 4000 to 1 in 30,000, confirming an IUP essentially rules out an ectopic pregnancy; however, if the patient is using assisted reproductive technology, a heterotopic pregnancy should be considered, since the risk is as high as 1 in 100 patients.[30]

The workup and management of a patient with a pregnancy of unknown location is different for stable and unstable patients. Stable patients should receive a quantitative beta-hCG test and a transvaginal ultrasound. The concept of a *discriminatory zone* of beta-hCG describes when an IUP is expected to be visualized on ultrasound. The discriminatory zone is generally thought to be 1500 mIU/mL for transvaginal studies. A 2013 retrospective study found that the beta-hCG threshold values for visualization of a gestational sac, yolk sac, and fetal pole were 390 mIU/mL, 1094 mIU/mL, and 1394 mIU/mL, respectively. However, the values where the structures would be seen 99% of the time were much higher at each value (3510 mIU/mL, 17,716 mIU/mL, and 47,685 mIU/mL, respectively). It is unclear at this time what the appropriate discriminatory zone should be.[41] ACOG currently recommends that if a discriminatory zone is used, to set this value conservatively high, recommending at least 3500 mIU/mL for a transvaginal ultrasound.

Similarly, the lack of an IUP with a beta-hCG level above the discriminatory zone does not diagnose an ectopic pregnancy but rather highly suggests a nonviable pregnancy (which could be a nonviable IUP or an ectopic pregnancy).

If an IUP is not visualized on ultrasound, serial beta-hCG testing can be helpful; in general, the beta-hCG will double within 48 hours for a viable IUP but typically should rise at least 53%.[42] **(See Figure 2.)** This generalization does not take into account that the rise of beta-hCG is curvilinear, meaning that there is a faster normal rate of rise when initial beta-hCG values are low and a slower normal rate of rise when the initial beta-hCG is higher. In addition, a study that evaluated the rate of change of beta-hCG in patients who had an ectopic pregnancy showed that approximately one-third of patients who were eventually diagnosed with an ectopic pregnancy had a rise of at

Figure 2. Changes in hCG Levels Over 48 Hours in Patients With Intrauterine Pregnancies, Ectopic Pregnancies, and Spontaneous Abortion / Miscarriage



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least 53% at the 48-hour recheck, and 20% of patients had a decline consistent with the rate of decline seen with miscarriage.[43] Therefore, trends cannot be relied on to exclude the diagnosis of an ectopic pregnancy.

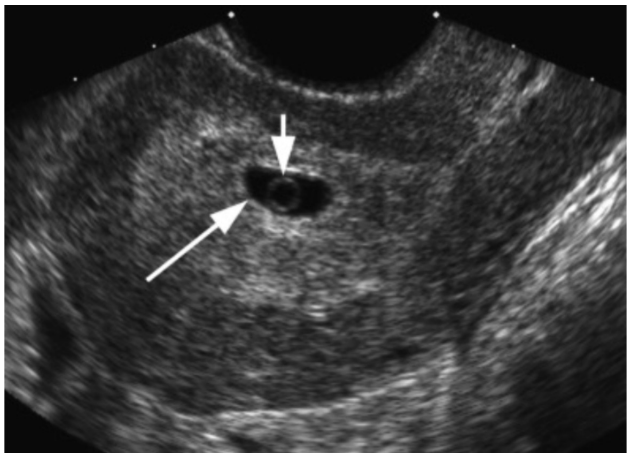
Imaging Studies

Patients with a known IUP and vaginal bleeding should receive an ultrasound (either formal or bedside) in addition to a pelvic examination to evaluate for miscarriage. **See Table 2** for physical examination and ultrasound findings associated with miscarriage.

In contrast, unstable patients should receive immediate bedside ultrasound if there is a provider who is credentialed in obtaining and interpreting the images. A focused assessment with sonography in trauma (FAST) examination can identify free intraperitoneal fluid, and a bedside transabdominal or transvaginal ultrasound can assess whether an IUP is present. **(See Figure 3.)** Emergency physicians are highly accurate in determining an IUP. A 2010 meta-analysis showed a negative predictive value for ectopic pregnancy of 99.96% when an emergency physician identified an IUP on bedside ultrasound.[44]

If transabdominal ultrasound is nondiagnostic, the emergency clinician should consider performing a transvaginal ultrasound. This should be done only by clinicians who are credentialed and comfortable with performing the procedure. A definitive ectopic pregnancy is diagnosed when there is extrauterine identification of a yolk sac or embryo. **(See Figure 4.)**

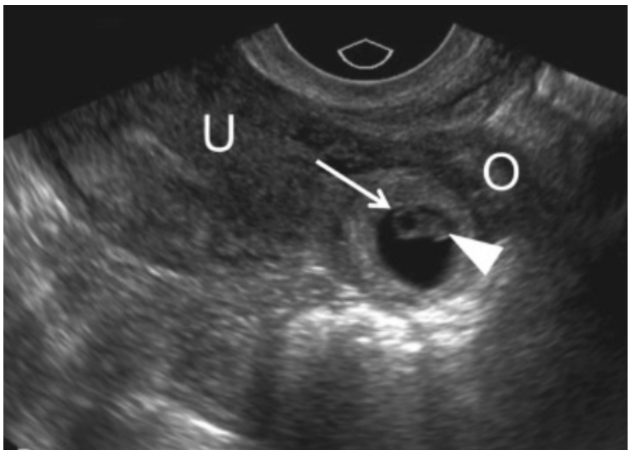
Figure 3. Definitive Intrauterine Pregnancy on Ultrasound



There is a gestational sac (long arrow) containing a yolk sac (short arrow) without an embryo seen.

Reprinted from *Callen's Ultrasonography in Obstetrics and Gynecology.* 6th Edition. Mary E. Norton, Leslie M Scoutt, Vickie A. Feldstein, eds. Chapter 4, Ultrasound of the Early First Trimester. Peter M. Doubilet, Carol B. Benson. Pages 82-97. Copyright 2017, with permission from Elsevier.

Figure 4. Definitive Ectopic Pregnancy on Ultrasound



There is a yolk sac (arrow) and embryo (arrowhead) outside of the uterus (U) and next to the ovary (O).

Reprinted from *Callen's Ultrasonography in Obstetrics and Gynecology.* 6th Edition. Mary E. Norton, Leslie M Scoutt, Vickie A. Feldstein, eds. Chapter 33, Ectopic Pregnancy. Oksana H. Baltarowich, Leslie M. Scoutt. Pages 966-1000. Copyright 2017, with permission from Elsevier.

Table 2. Types of Miscarriage and Associated Physical Examination and Ultrasound Findings

Type of Miscarriage/ Abortion	Cervical Os	IUP on Ultrasound?	Description
Threatened	Closed	Yes	Vaginal bleeding with a viable IUP
Complete	Closed	No (but previously with IUP)	Passage of all products of conception
Missed	Closed	Crown-rump length of ≥ 7 mm without cardiac motion; other criteria exist as well[23]	A nonviable uterine gestation
Inevitable	Open	Yes	An IUP without passage of products of conception, but an open cervical os
Incomplete	Open	Partially expelled	An IUP with passage of some products of conception
Septic	Any	Any	Intrauterine infection, usually characterized by uterine tenderness, fever, and/or discharge, in the setting of a miscarriage or therapeutic abortion

Abbreviation: IUP, intrauterine pregnancy.

If no definite IUP is identified on bedside ultrasound, utilize a urine or blood point-of-care beta-hCG device to ascertain whether the patient is pregnant. See the "Controversies and Cutting Edge" section (page 13) for data on using whole blood samples on a urine point-of-care beta-hCG device.

Rh Status

If a patient is considered to be a candidate for Rh(D)-immune globulin (see the "Treatment" section for considerations), obtain the Rh status and evaluate whether the patient is Rh-positive or Rh-negative and whether the patient is sensitized to anti-D antibodies.

Diagnostic Studies in Nausea and Vomiting of Pregnancy

Diagnosis of NVP as well as hyperemesis gravidarum is focused first on excluding other pathology that could cause similar symptoms. There are no mandated routine studies, but in severe cases, a chemistry panel is helpful to assess for electrolyte derangements. A urinalysis can evaluate for a UTI (or asymptomatic bacteriuria) as well as assess for ketonuria.

Diagnostic Studies in Asymptomatic Bacteriuria and Urinary Tract Infections

A positive urinalysis should prompt the emergency clinician to treat for asymptomatic bacteriuria and UTI empirically, but a negative test may miss true bacteriuria. A culture should always be sent if there is suspicion for a UTI because (1) a negative urinalysis lacks sufficient negative predictive value for bacteriuria, and (2) it may guide further antibiotic therapy by elucidating antimicrobial sensitivity. A 2016 systematic review found no reliable evidence supporting routine screening for asymptomatic bacteriuria; therefore, send urine (urinalysis and culture) only if there is suspicion for an infection.[45]

Diagnostic Studies in Acute Appendicitis in Pregnancy

Ultrasound is still considered by many to be the first-line imaging modality to evaluate for acute appendicitis in pregnancy. However, a retrospective study of 140 pregnant women found the visualization rates of the appendix to be as low as 7%, with a sensitivity reported as 18%, compared to magnetic resonance imaging (MRI), which had 100% sensitivity. [46] Both modalities are highly specific for the diagnosis (ranging from 97%-99%), so a positive test for appendicitis with either imaging modality can be relied on as accurate.

A 2016 meta-analysis showed that the sensitivity and specificity of MRI for acute appendicitis in pregnant patients were 94% and 97%, respectively.[47] This suggests that a noncontrast MRI, if feasible to obtain, should be the first imaging test ordered in a pregnant patient with suspected appendicitis. The MRI for ruling out appendicitis should always be ordered without intravenous (IV) contrast.

Exposure to MRI in the first trimester of pregnancy was not associated with any fetal risk or even later risk to the child (evaluated to age 4 years), as noted in a retrospective cohort study that included over 1.4 million pregnancies. In that study, gadolinium-enhanced MRI was associated with increased rates of stillbirth, neonatal death, and multiple rheumatologic and inflammatory skin conditions.[48] Therefore, although MRI itself is safe in pregnancy, gadolinium contrast should, in general, be avoided unless absolutely necessary for diagnosis as there is demonstrable risk to the fetus.

If ultrasound is inconclusive and MRI is not available, computed tomographic (CT) imaging is highly sensitive and specific for the diagnosis of appendicitis. Although it uses ionizing radiation (see the "Special Circumstances" section, page 13), a single study for appendicitis would not exceed the threshold dose for fetal harm. In addition, delay in diagnosis of appendicitis can worsen both maternal and fetal outcome. For example, a 2014 study found that pregnant patients with appendicitis who developed peritonitis had a 4-fold higher rate of preterm birth.[49]

Treatment

Prevention of Rh Alloimmunization

There are no well-designed studies demonstrating any benefit to anti-D immune globulin administration to Rh(D) negative patients who have first trimester vaginal bleeding.[50] In 2017, ACOG stated that "...whether to administer anti-D immune globulin to a patient with threatened pregnancy loss and a live embryo or fetus at or before 12 weeks of gestation is controversial, and no evidence-based recommendation can be made." It is reasonable to withhold administration in early first trimester, especially in cases of minimal bleeding. Discussion with your hospital obstetrics department is suggested before making any departmental policy changes. For heavy bleeding or in pregnancies closer to 12 weeks' gestational age, administration of anti-D immune globulin can be considered.

Only women who are Rh(D) negative and unsensitized should be considered to receive Rh(D)-immune globulin within 72 hours in an intramuscular dose of 50 mcg. If the 50-mcg dose is unavailable, the more commonly available 300-mcg dose can be used. For significant abdominal trauma, there is an expert opinion to administer Rh(D)-immune globulin to eligible patients, but this is not based on high-quality evidence; it is reasonable to administer based on your clinical judgment.

Miscarriage

Patients with a threatened miscarriage—especially if fetal cardiac activity is detected on ultrasound—can be counseled that they are likely to go on to have a normal pregnancy, although close follow-up is important, given the increased risk for subsequent adverse maternal and fetal outcomes.[26] In one prospective study, only 3.4% of patients with threatened miscarriage who demonstrated fetal cardiac activity went on to have miscarriages, although other studies showed significantly higher rates (especially in cases of heavy bleeding, where the miscarriage rate was as high as 11%-18%).[2] The data supporting bed rest are sparse, and there is no definite benefit demonstrated.

In the event of an incomplete miscarriage, if there are visible products of conception, they should be removed at bedside with ring forceps. Consider sending the products of conception to pathology for analysis, especially if the patient has had recurrent miscarriages.

If a patient is found to have a nonviable pregnancy (such as a missed miscarriage or a stable patient with an incomplete miscarriage), consultation with an obstetrician is advised. Options for the stable patient include expectant management, medical management, or surgical management. A 2012 Cochrane review failed to find clear superiority in stable patients for any choice among the options of expectant, medical, and surgical management.[19]

Expectant management has varied success, depending on patient characteristics (eg, a patient with an incomplete miscarriage with an already-open os is more likely to complete without intervention than a patient with a missed miscarriage), but generally, 50% to 80% of patients will have a complete miscarriage within 7 to 10 days.

Medical management with 800 mcg of intravaginal misoprostol is an option. One randomized trial found high rates of success with medical management (91% effective in 7 days vs 100% for surgical intervention) and recommended this in low-resource settings, but no control group for expectant management was used as a comparison arm.[51]

A randomized trial of medical and surgical management found high effectiveness rates and high satisfaction rates in both arms.[52] Another trial found more unplanned admissions and unplanned surgical management in patients who had initially attempted either medical or expectant management (up to 40%).[53] A 2017 Cochrane review demonstrated both medical management and expectant management were acceptable alternatives to routine surgical evacuation.[20] In stable patients, surgical management is effective and results in lower rates of incomplete miscarriage, bleeding, and need for transfusion.

Surgical management is mandatory for patients who have significant hemorrhage or hemodynamic instability.

If a patient is Rh-negative and unsensitized, administration of 50 mcg of Rh(D)-immune globulin should be considered.

Managing Communication Around Pregnancy Loss

A qualitative study by telephone survey of 10 women who had a miscarriage diagnosed in the ED showed that many women felt that there was a lack of information provided to them and there was overall poor communication from emergency clinicians about their miscarriage.[54] In 2018, the National Perinatal Association published guidelines on how to provide better support to patients with actual or potential pregnancy loss.[55] Expert consensus recommended giving ED personnel the education and training to enable them to:

1. Assess the meaning of the pregnancy loss to the woman and her family, and direct care accordingly.
2. Give the news to the patient in a culturally competent, compassionate, supportive, and honest manner.
3. Inform the family that grief takes different forms and time frames for each culture and each individual within a culture, and give them permission to grieve in their own way.
4. Learn to feel comfortable with showing products of a miscarriage or fetal loss to the woman and her family should she ask for this.
5. Provide support with decision-making about procedures, family involvement, memory-making, and saying goodbye.
6. Provide names and contact information for local grief counselors or pregnancy-loss support groups and community caregivers dedicated to pregnancy-loss support.[55]

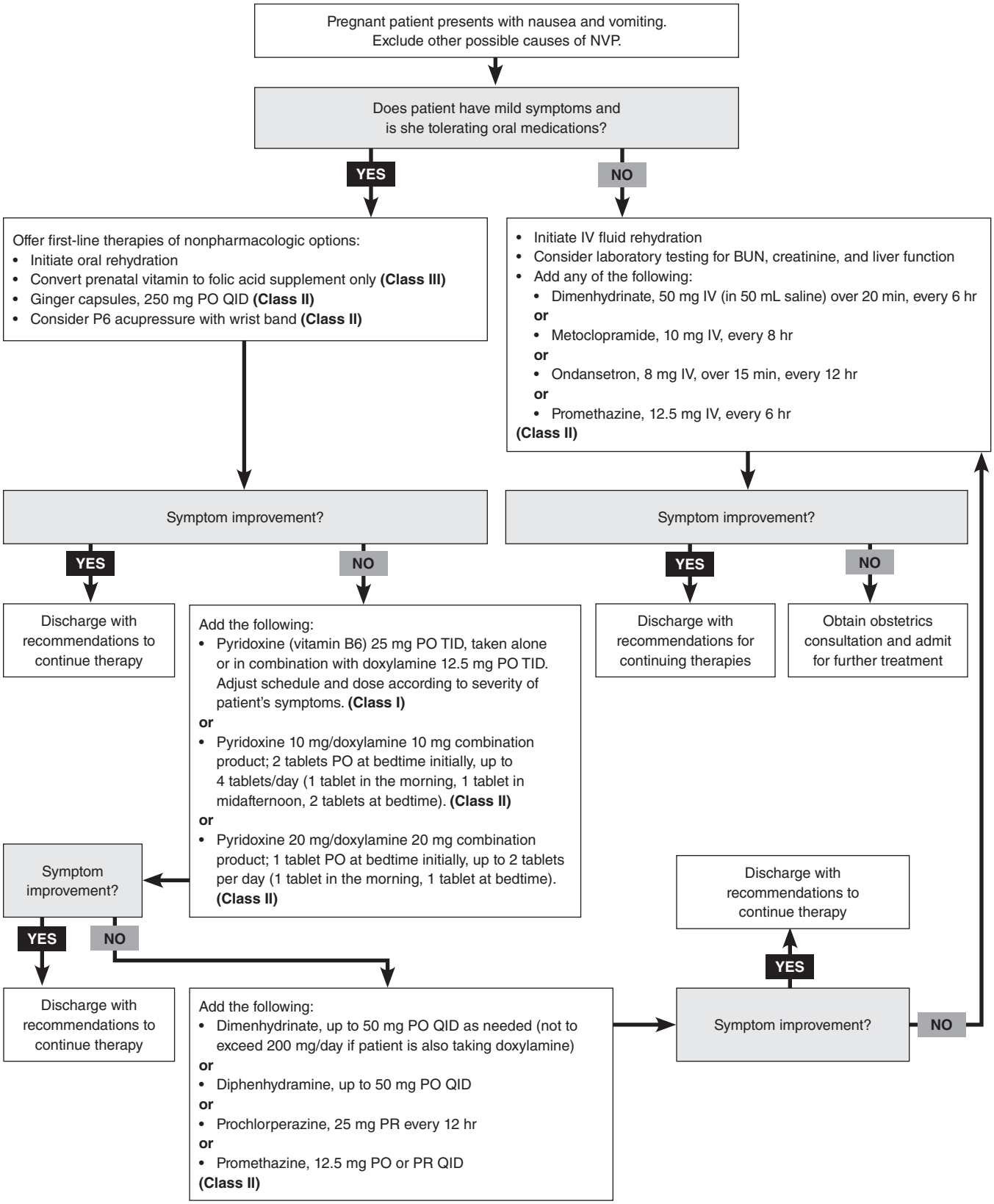
The full guidelines are available at:
www.nationalperinatal.org/resources/Documents/Position Papers/Pregnancy Loss ER_2017.pdf

Pregnancy of Unknown Location and Ectopic Pregnancy

Unstable patients with suspected or proven ectopic or heterotopic pregnancy should be immediately resuscitated and prompt consultation with an obstetrician for surgical intervention should be obtained.

Pregnant patients who are stable and have no IUP on ultrasound have a *pregnancy of unknown location* and should be discharged with instructions to follow up in 48 hours for repeat beta-hCG testing and ultrasound. Typically, *stability* would be defined as normal vital signs, no ultrasonographic evidence of a ruptured ectopic pregnancy, and a patient who is reliable for follow-up should they worsen before the next recheck. Stable patients with a beta-hCG above the discriminatory zone (see page 6) are likely to have a nonviable IUP or an ectopic pregnancy,

Clinical Pathway for Emergency Department Management of Nausea and Vomiting of Pregnancy



Abbreviations: BUN, blood urea nitrogen; IV, intravenous; NVP, nausea and vomiting of pregnancy; PO, by mouth; PR, per rectum; QID, 4 times per day; TID, 3 times per day.

For Class of Evidence definitions, see page 11.

but they can similarly follow up closely with an obstetrician. Beta-hCG trends are useful, but because they do not always follow the expected course in all cases, 48-hour repeat examinations should continue until a definite diagnosis is established (eg, a definite IUP, a definite ectopic pregnancy, or an undetectable beta-hCG that confirms a completed miscarriage) or the patient becomes unstable.

Hemodynamically stable patients with a confirmed nonruptured tubal ectopic pregnancy have a broader spectrum of management options. Management should always be in consultation with an obstetrician, but it generally includes either medical management with intramuscular methotrexate (either single- or multiple-dose regimens) or surgical management with salpingostomy or salpingectomy.

In a systematic review, single-dose methotrexate therapy in patients with initial beta-hCG values of > 5000 had an OR for failure of 5.45; therefore, values above this level are relatively contraindicated for therapy.[56] A meta-analysis also found that fetal cardiac activity was an independent risk factor for failure of methotrexate, with an OR of 9.1.[57] Lastly, candidates for methotrexate therapy should not have contraindications to the drug and should be reliable for follow-up. Absolute contraindications to methotrexate include an immunodeficiency, any cytopenia (anemia, leukopenia, thrombocytopenia), active pulmonary disease, active peptic ulcer disease, hepatic or renal dysfunction, or breastfeeding.[8] Since methotrexate may not always be successful, a patient's ability to follow up or return if they worsen is important.

There may be a small number of patients who can potentially be managed with expectant management (see "Controversies and Cutting Edge," page 13), but this is not currently common practice.

Nausea and Vomiting of Pregnancy

The 2018 ACOG Practice Bulletin on NVP has a level A recommendation for first-line pharmacologic treatment that includes pyridoxine (vitamin B6) 10 to 25 mg orally 3 or 4 times a day either alone or in combination with doxylamine, 12.5 mg orally 3 or 4 times a day.[9] For reduction of nausea, they also recommend nonpharmacologic options of P6 acupressure with wristbands, or ginger capsules, 250 mg by mouth 4 times a day.

A Cochrane review did not find benefit for acupressure.[15] A subsequent 2017 trial with women admitted to the hospital with severe NVP randomized them to acupressure using a wristband applying pressure at the P6 point or placebo wristband. There was a reduction in nausea, vomiting, ketonuria, and length of stay in the acupressure group.[58] Further studies are needed to validate this in other settings, but it may be a promising addition to standard therapy and is currently placed as a "consideration" for use by ACOG. For instructions on how to perform P6 acupressure, go to: https://exploreim.ucla.edu/self-care/acupressure-point-p6 /

A 2016 systematic review found that pyridoxine and ginger were effective for mild symptoms and pyridoxine and doxylamine were effective for moderate symptoms.[3] A 2017 trial that randomized patients with mild-to-moderate NVP found that ginger was more effective than placebo and had comparable effectiveness to pyridoxine usage.[59] A matched study found pyridoxine plus doxylamine was superior to treatment with pyridoxine alone.[60] Another randomized trial in 2016 showed that the delayed-release combination 10 mg doxylamine plus 10 mg pyridoxine was superior to placebo.[61] Therefore, for patients tolerating oral medications, pyridoxine with or without doxylamine should be used, with consideration for ginger and P6 acupressure.

If pyridoxine and doxylamine fail, a stepwise approach to drug therapies should be initiated. **(See the Clinical Pathway, page 10.)** A 2015 Cochrane review demonstrated a lack of high-quality evidence to support any specific drug over another for NVP,[15] and a 2016 review of hyperemesis gravidarum interventions found similar findings.[16] For patients with severe symptoms requiring IV therapy in the ED, metoclopramide 10 mg is a reasonable and widely

Class of Evidence Definitions

Each action in the clinical pathways section of *Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

available option that has not been associated with fetal malformations.

Ondansetron was associated with improvement in symptoms of all severities, but a 2016 systematic review concluded that there may be a small risk in the incidence of fetal cardiac abnormalities in ondansetron-exposed neonates. Therefore, it is reasonable to exhaust other options before utilizing ondansetron.[62]

Patients with severe nausea and vomiting in pregnancy will often require IV fluids. A randomized trial comparing D5NS (5% dextrose in 0.9% [normal] saline) and normal saline for hyperemesis gravidarum where patients admitted to the obstetrics/gynecology ward received 3 L of either fluid over 24 hours (125 mL/hr) found similar outcomes, except slightly decreased nausea in the D5NS group at 8 and 16 hours (but not at 1 or 24 hours).[63] Either maintenance fluid is acceptable, but if D5NS is readily available, it is reasonable to use a glucose-containing fluid. The authors of the study stated there is a theoretical risk of precipitating Wernicke encephalopathy in patients with protracted vomiting, and ACOG similarly recommends thiamine administration to patients with protracted vomiting who receive glucose.

Asymptomatic Bacteriuria and Urinary Tract Infections

Although the rates of asymptomatic bacteriuria are not necessarily higher in pregnant patients, this is a population that should have treatment if asymptomatic bacteriuria is identified, based on the 2005 IDSA guidelines.[64] Since these guidelines were published, there was a randomized trial comparing treatment of asymptomatic bacteriuria in pregnancy with either nitrofurantoin or placebo that demonstrated no association with preterm birth but an association with development of pyelonephritis. The absolute risk of development of pyelonephritis from asymptomatic bacteriuria was low, with 0.6% of nitrofurantoin-treated patients and 2.4% of untreated or placebo-treated patients developing pyelonephritis.[33] Based on a 2015 Cochrane review, shorter durations of antimicrobial therapy are likely less effective than a standard 7-day regimen.[65]

For UTIs in pregnancy, a 2011 Cochrane review concluded that there is insufficient evidence to recommend a specific drug.[18] Similarly, a 2010 Cochrane review could not definitively recommend a specific drug for treatment of asymptomatic bacteriuria in pregnancy.[17] Local antibiotic resistance patterns may guide therapy. Discussion with your local obstetricians and infectious disease specialists may be ideal to generate the best first trimester therapy, given variation in practice and antibiotic resistance.

Amoxicillin (875 mg by mouth, twice a day) or a first-generation cephalosporin such as cephalexin (500 mg by mouth, every 6 hours) are, in general, excellent first-line therapies for asymptomatic bacteriuria and cystitis in pregnancy. Nitrofurantoin is likely also very safe based on available data. A 2017 ACOG Committee Opinion analyzed the association between nitrofurantoin and sulfonamide antibiotics on birth defects and concluded that although safe in the second and third trimesters, these therapies are appropriate in the first trimester "when no other suitable alternative antibiotics are available."[11]

For pyelonephritis, most recommendations are for initial inpatient management with parenteral antibiotics such as ceftriaxone 1 g IV daily. A randomized controlled trial compared 2 days of intramuscular ceftriaxone as an outpatient and oral cephalexin to inpatient admission with IV antibiotics until afebrile for 48 hours.[66] The outpatient arm also had home health nursing and education; of the 57 patients managed in the outpatient setting, 6 were ultimately admitted for IV therapy, including 1 who developed septic shock. Currently, there is insufficient evidence to recommend outpatient management of pyelonephritis in pregnancy.

In 2015, the United States Food and Drug Administration (FDA) changed from the traditional pregnancy risk categories of A, B, C, D, and X to a new labeling system. Eventually, the pregnancy letter categories will be phased out completely and instead include an actual risk summary based on available data.[67] As more antimicrobials are released and more studies are completed on current antimicrobials in pregnancy, this will eventually provide an up-to-date, relevant reference on the literature.

Acute Appendicitis in Pregnancy

At the current time, there are no data supporting an antibiotics-only strategy in treating appendicitis in pregnancy, and all patients should be considered for surgical intervention. One small trial evaluated 20 pregnant patients with appendicitis and treated them with antibiotics alone; of these, 25% eventually had treatment failure, but there were no fetal complications.[68] A population-based matched cohort study found that, compared to nonpregnant women, pregnant women with appendicitis had more frequent complications. In the small subset of pregnant patients who were conservatively managed, there was a considerably increased risk of serious complications.[36]

Special Circumstances

Ionizing Radiation in Pregnancy

An understanding of the risks of ionizing radiation to the fetus and the performance characteristics of alternative imaging modalities is important when deciding on which radiologic examinations to obtain. Ideally, the emergency clinician should limit ionizing

radiation exposure to the fetus during pregnancy; however, if a clinician does not obtain indicated imaging for fear of radiation exposure, a missed or delayed diagnosis may result in worse fetal outcomes.

In the first trimester, there is minimal risk to the fetus from ionizing radiation outside of the abdomen and pelvis as long as standard precautions are taken. A summary of common fetal radiation doses received with various studies is shown in **Table 3.**

The American College of Radiology states that the following examinations produce such low exposure of ionizing radiation to a fetus that even assessing whether a patient is pregnant is unnecessary:[13]

- Any diagnostic examination of the head or neck;
- Extremity radiography or CT (with possible exception of the hip); and
- Chest radiography (during first and second trimesters).

Table 3. Fetal Radiation Doses Associated With Common Radiologic Examinations

Type of Examination	Fetal Dose* (mGy)
Very-Low-Dose Examinations (< 0.1 mGy)	
Cervical spine radiography (anteroposterior and lateral views)	< 0.001
Radiography of any extremity	< 0.001
Mammography (2 views)	0.001-0.01
Chest radiography (2 views)	0.0005-0.01
Low- to Moderate-Dose Examinations (0.1-10 mGy)	
Radiography	
Abdominal radiography	0.1-3.0
Lumbar spine radiography	1.0-10
Intravenous pyelography	5-10
Double-contrast barium enema	1.0-20
CT	
Head or neck CT	1.0-10
Chest CT or CT pulmonary angiography	0.01-0.66
Limited CT pelvimetry (single axial section through the femoral heads)	< 1
Nuclear Medicine	
Low-dose perfusion scintigraphy	0.1-0.5
Technetium-99m bone scintigraphy	4-5
Pulmonary digital subtraction angiography	0.5
Higher-Dose Examinations (10-50 mGy)	
Abdominal CT	1.3-35
Pelvic CT	10-50
F PET/CT whole-body scintigraphy	10-50

*Fetal exposure varies with gestational age, maternal body habitus, and exact acquisition parameters.

Note: Annual average background radiation = 1.1-2.5 mGy.

Abbreviations: CT, computed tomography; F, 2-[fluorine-18]fluoro-2-deoxy-D-glucose; PET, positron emission tomography.

Tremblay E, Therasse E, Thomassin-Naggara I, Trop I. Quality initiatives: guidelines for use of medical imaging during pregnancy and lactation. *RadioGraphics*. 2012;32-897-8911. Used with permission of Radiological Society of North America.

The risk of ionizing radiation varies depending on the dose and the gestational age; a single study in the ED is unlikely to exceed any threshold dose for fetal teratogenesis. There is a theoretical increase in the rate of malignancy in the children of pregnant mothers exposed to ionizing radiation, based on a pregnant manikin study where radiation markers were placed,[69] but the absolute risk is likely to be small. For studies that involve direct fetal radiation exposure (eg, abdominopelvic CT) there should be a documented discussion with the patient regarding risks and benefits.[70] If feasible, alternative imaging modalities should be considered.

Although iodinated contrast does pass through the placental barrier, it appears to present no known harm to the fetus in pregnancy (and is safe in animal studies), but only limited data are available. ACOG recommends iodinated contrast be used only if "absolutely required" for diagnosis, but this recommendation is not based on any known evidence of harm.[12] As mentioned previously, gadolinium contrast agents should be avoided unless absolutely necessary.

Controversies and Cutting Edge

Pregnancy Testing Using Whole Blood With Point-of-Care Testing Devices

Utilizing whole blood on a qualitative urine POC beta-hCG device has shown some promise in rapid determination of pregnancy status in patients who are unable to promptly provide a urine sample. Many urine POC devices are also FDA-approved for serum but not for whole blood; clinicians must know the test characteristics of the machine being used.

One study compared POC beta-hCG via urine to 2 drops of whole blood (interpreted at 10 minutes) and found similar accuracy for urine and whole blood for their assay using the Beckman Coulter ICON 25.[71] A subsequent study looked at time to pregnancy test result with blood compared to urine on a POC beta-hCG test and found that whole blood saved a mean of 21 minutes compared with urine, with excellent concordance between urine and blood testing (also using the Beckman Coulter ICON 25).[72] However, these results may not be generalizable to other settings or other brands of device; further research is required. The initial studies do demonstrate very high positive predictive value, which would suggest that a false-positive result is unlikely with this brand of device. POC whole blood beta-hCG devices that are FDA-approved do exist.

Expectant Management of Ectopic Pregnancy

Growing evidence suggests that, for a small subset of patients with ectopic pregnancy, expectant management is a potential option. A 2015 randomized

trial found that, in select patients, there were similar outcomes for intramuscular methotrexate, compared to placebo, for a tubal ectopic pregnancy.[73] Inclusion criteria were: hemodynamic stability, initial serum beta-hCG concentration < 2000 mIU/mL, declining titers of beta-hCG 48 hours prior to treatment, visible tubal pregnancy on transvaginal ultrasound, a tubal mass < 5 cm, and future fertility desired. The requirement for declining titers of beta-hCG may preclude ED generalizability. In addition, a 2017 multicenter randomized trial found that, in patients with a beta-hCG < 1500 mIU/mL, success rates of methotrexate and placebo were similar.[74]

Disposition

Patients who are hemodynamically stable and well-appearing with a pregnancy of undetermined location should be discharged with a 48-hour beta-hCG recheck and ultrasound. All hemodynamically unstable patients should be admitted.

In general, all pregnant patients with acute pyelonephritis should be admitted initially; outpatient management could be considered in consultation with an obstetrician for selected patients without comorbidities.

Patients with hyperemesis gravidarum who do not improve after initial IV rehydration and antiemetic therapy in the ED should be admitted. There are no well established parameters for admission, but patients should be well-appearing, have normalized vital signs, and be tolerating oral intake if considered for discharge.

Summary

- Obtain pregnancy testing in all reproductive-age women with abdominal complaints.
- Ectopic pregnancy must be ruled out in all pregnant women without a confirmed IUP.
- Consider a heterotopic pregnancy in women undergoing assisted reproductive technology.
- Treat NVP with pyridoxine, with or without doxylamine, as first-line therapy for patients tolerating oral medication. IV medication for NVP has less robust comparative data, but 10 mg of metoclopramide is a reasonable option because, unlike ondansetron, there does not appear to be a risk of fetal malformation.
- Either ultrasound or noncontrast MRI can be considered to be first-line imaging studies to investigate for potential acute appendicitis in pregnancy. In pregnancy, there is a high rate of nonvisualization of the appendix with ultrasound, so an indeterminate ultrasound should be followed by an MRI.
- A 2017 recommendation from ACOG neither recommends for nor against anti-D immune globulin administration to patients with first-trimester vaginal bleeding who are unsensitized and Rh-negative. Consider discussing with local obstetricians at your facility to decide on an institution-level policy.
- Although there is no evidence to support routine screening in the ED for asymptomatic bacteriuria in pregnancy, if it is discovered, it should be treated.
- Admit pregnant patients with pyelonephritis for IV antibiotics.

Case Conclusions

You immediately obtained a pregnancy test on the hypotensive 23-year-old woman because you knew that would drastically change your differential diagnosis. Her pregnancy test was positive. You performed a FAST examination, which demonstrated free intraperitoneal fluid, making your most-likely diagnosis a ruptured ectopic pregnancy. Large-bore IV access was obtained, O-negative blood was transfused, and the patient was sent to the OR for an emergent laparotomy, which demonstrated a ruptured ectopic pregnancy with 2 L of hemoperitoneum.

Your workup of the second patient's spotting demonstrated that she had a single IUP with normal fetal heart rate. She was Rh-positive and had a normal hemoglobin level. You reassured her that since she only had light spotting (which you recalled does not have a significant difference in rate of miscarriage compared to controls without bleeding) and because fetal cardiac activity was detected, that most likely she would go on to have a normal pregnancy. Because she was Rh-positive, you did not need to consider administration of anti-D immune globulin, but you remembered that the benefit in this patient would be unclear even if she were Rh-negative.

You diagnosed your third patient with pyelonephritis. Since there are not good data supporting routine outpatient management of pyelonephritis in pregnancy, you consulted her obstetrician to discuss admission. She received ceftriaxone 1 g IV, was admitted to the hospital, and recovered uneventfully. The hydronephrosis was symmetric and bilateral, which is typical during pregnancy, so no further workup for this was undertaken. She was discharged on cephalexin after sensitivities resulted.

Time- and Cost-Effective Strategies

- Usage of ED bedside ultrasound for identification of an IUP has high accuracy and shortens length of stay.
- Although further studies are needed to evaluate for accuracy in other settings and with other pregnancy test brands, whole blood may be quick and effective for ascertaining pregnancy status in unstable patients.
- Depending on availability of MRI at your institution, a noncontrast MRI may be more effective

Risk Management Pitfalls for Emergency Department Management of First-Trimester Pregnant Patients

1. **"The patient's beta-hCG was only 200 mIU/mL, so I didn't think a ruptured ectopic pregnancy would even be a possibility."**
   Ectopic pregnancy rupture can occur at very low beta-hCG levels. One study found that patients presenting to the ED with pain or bleeding and a beta-hCG < 1500 mIU/mL had a substantially increased risk for ectopic pregnancy.

2. **"The patient's beta-hCG went up by more than half in 48 hours; I didn't see an IUP, but thought we had ruled out an ectopic due to the rate of rise."**
   One-third of patients who were eventually diagnosed with an ectopic pregnancy had a rise of at least 53% at the 48-hour recheck. It is important to continue to evaluate serial beta-hCG levels and ultrasounds.

3. **"The patient was 11 weeks' pregnant and had pyelonephritis; she had a fever and was vomiting, but looked okay, so I sent her home with antibiotics."**
   Until further data support initial outpatient management of pyelonephritis, it is best to admit all pregnant patients with pyelonephritis for an initial course of IV antibiotics.

4. **"I figured contrast always improves images, so for my pregnant patient, I ordered the appendicitis rule-out MRI with gadolinium."**
   Noncontrasted MRI for appendicitis in pregnancy has very high sensitivity for the diagnosis. Exposure to gadolinium during pregnancy has negative effects on the fetus and should be avoided unless its use is absolutely necessary.

5. **"My patient was 10 weeks' pregnant and had nausea, so I sent her home with 60 tablets of ondansetron."**
   Although the risk of birth defects with maternal ondansetron exposure is low, there are safer alternatives for treatment of nausea and vomiting in pregnancy. Pyridoxine or pyridoxine with doxylamine should be considered first-line therapy.

6. **"I can't do a CT brain and C-spine on this trauma patient because she is 8 weeks' pregnant!"**
   Imaging outside of the abdomen and pelvis has negligible risk for fetal radiation exposure. Even a single abdominal and pelvic CT scan does not exceed safe radiation exposure levels during pregnancy, and patients should receive appropriate studies when necessary, regardless of pregnancy status.

7. **"Antibiotic-only treatment for appendicitis is a hot topic right now, so I treated my patient who was 6 weeks' pregnant with antibiotics for her appendicitis instead of referring her to a hospital with a surgeon."**
   There is insufficient evidence regarding the safety and efficacy of nonsurgical management of appendicitis in pregnancy.

8. **"Her pregnancy test was positive, and we couldn't find an IUP on ultrasound. All she had was cramping, so I told her to follow up with an obstetrician in a week."**
   Stable patients with a pregnancy of undetermined location should have 48-hour beta-hCG checks and serial ultrasounds until an IUP is definitively determined.

9. **"My patient was hypotensive and had a positive pregnancy test. I could not see an IUP, but she had free intraperitoneal fluid. I figured I would rule out other diagnoses with a CT scan, but she coded in the scanner!"**
   An unstable pregnant patient without an identified IUP with abdominal pain and/or vaginal bleeding has an ectopic pregnancy until proven otherwise. Unstable patients should proceed immediately to surgical management with an obstetrician.

10. **"They sent a urinalysis in my pregnant patient from triage; it was nitrite positive, but she came in for a stubbed toe, so I just sent her home."**
    Asymptomatic bacteriuria should be treated when discovered, as prompt treatment has been shown to decrease the rates of pyelonephritis. Although the absolute risk of progression to pyelonephritis is low (approximately 2.4%), the risk of antibiotic treatment is also low. It is not necessary to routinely screen for asymptomatic bacteriuria in the ED.

in the evaluation of appendicitis in pregnancy, given the high rate of nonvisualization of the appendix with ultrasound.
- Discuss and document the risks and benefits of ionizing radiation when obtaining CT or radiographs of pregnant patients.
- Consider offering generic prescriptions of pyridoxine and doxylamine instead of commercially combined preparations, which can be much more expensive.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study is included in bold type following the references, where available. The most informative references cited in this paper, as determined by the author, are noted by an asterisk (*) next to the number of the reference.

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CME Questions

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1. The most common nonobstetric surgical emergency in the first trimester of pregnancy is:
   a. Acute cholecystitis
   b. Acute pancreatitis
   c. Acute appendicitis
   d. Small-bowel obstruction

2. A 20-year-old woman is 10 weeks' pregnant and has severe abdominal cramping and vaginal bleeding. She is not on assisted reproductive technology and previously had an IUP confirmed at her obstetrician's office. She is tachycardic and hypotensive and has passed a large volume of blood and clots from her vagina. In addition to volume resuscitation, what would be the best next step in treating her?
   a. Pelvic examination to evaluate for incomplete miscarriage
   b. Formal transvaginal ultrasound to rule out heterotopic pregnancy
   c. Administer a single-dose of intramuscular methotrexate
   d. Administer anti-D immune globulin

3. A 37-year-old woman is on clomiphene to increase her fertility. She presents with a positive pregnancy test, abdominal pain, and hypotension to 75/30 mm Hg. A pelvic examination demonstrates exquisite right adnexal tenderness and a closed cervical os. A bedside ultrasound is positive for both an IUP as well as free intraperitoneal fluid. The next best step is:
   a. Reassurance, as she has an IUP
   b. Resuscitation and immediate obstetric consultation for heterotopic pregnancy
   c. Wait to see if a beta-hCG result is above or below the discriminatory zone
   d. Send the patient to receive a formal transvaginal ultrasound

4. **A 21-year-old woman who had an intrauterine pregnancy (IUP) is now presenting with abdominal pain and cramping. An ultrasound demonstrates an empty uterus, thin endometrial stripe, and a closed cervical os. What is the most likely diagnosis?**
   a. Complete miscarriage
   b. Incomplete miscarriage
   c. Missed miscarriage
   d. Pseudocyesis

5. **Assuming all modalities are available, the most appropriate imaging study to perform to evaluate for appendicitis in pregnancy when an ultrasound is inconclusive is:**
   a. Serial ultrasound
   b. MRI without contrast
   c. MRI with contrast
   d. CT with contrast

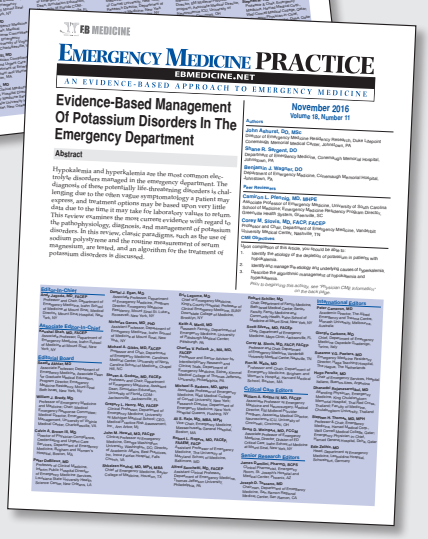
6. **Regarding anti-D immune globulin administration in the first trimester of pregnancy for a patient with vaginal bleeding, which of the following is TRUE?**
   a. Large, prospective trials demonstrate lower risk of alloimmunization with administration to patients with first trimester vaginal bleeding.
   b. Administration must be within 4 hours of the event.
   c. It should be considered for patients who are Rh-positive who have vaginal bleeding.
   d. The most recent ACOG guidelines do not recommend for or against routine administration.

7. **The management of a stable patient in her first trimester of pregnancy who has a pregnancy of undetermined location should include:**
   a. A 48-hour recheck with strict return precautions
   b. Immediate obstetrical consultation
   c. Admission for serial examinations and ultrasounds
   d. CT to evaluate for pregnancy location, as it has higher sensitivity than ultrasound

8. **A 28-year-old woman presents in her first trimester of pregnancy with mild-to-moderate nausea and vomiting. After exclusion of secondary causes, which of the following should be the first-line oral medication(s) for this patient?**
   a. Ondansetron
   b. Pyridoxine with or without doxylamine
   c. Corticosteroids
   d. Metoclopramide

9. **A woman presents in her tenth week of pregnancy with fevers, chills, vomiting, and dysuria. She is found to have acute pyelonephritis and is tachycardic to 120 beats/min. The next most appropriate step is:**
   a. Admission for IV antibiotics
   b. CT with IV contrast to evaluate for a perinephric abscess
   c. CT without contrast to evaluate for hydronephrosis
   d. Discharge with nitrofurantoin

10. **A patient is 8 weeks' pregnant and sustains injuries in a significant motor vehicle accident. Her blood pressure in the field was 80/40 mm Hg but has improved to 110/60 mm Hg with fluids given en route by EMS. She has diffuse peritonitis and a dense seatbelt sign over the lower abdomen. Her heart rate is 90 beats/min and blood pressure remains stable. An eFAST is negative except for demonstrating an IUP. Which of the following is the best imaging test?**
   a. MRI abdomen and pelvis
   b. Formal ultrasound to evaluate for free fluid
   c. CT abdomen and pelvis
   d. Plain x-rays only



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