

First-Trimester Emergencies: A Practical Approach To Abdominal Pain And Vaginal Bleeding In Early Pregnancy

November 2003
Volume 5, Number 11

Author

Robert Dart, MD

Chief, Emergency Services, Quincy Medical Center, Quincy, MA; Associate Professor, Boston University; Vice-Chair, Department of Emergency Medicine, Boston University School of Medicine, Boston, MA.

Peer Reviewers

Michael Blaivas, MD, RDMS

Associate Professor; Chief, Section of Emergency Ultrasound; Director, Emergency Ultrasound Fellowship; Department of Emergency Medicine, Medical College of Georgia, Augusta, GA.

Jay Kaplan, MD, FACEP

Clinical Assistant Professor in Emergency Medicine, Mount Sinai School of Medicine, New York, NY; Director of Service Excellence, California Emergency Physicians Medical Group, Oakland, CA; Medical Director, Studer Group, Gulf Breeze, FL.

CME Objectives

Upon completing this article, you should be able to:

1. identify readily available tests that can help risk-stratify women at risk for ectopic pregnancy;
2. list management strategies for treating women with nonviable intrauterine pregnancies;
3. describe one reasonable approach to managing the woman with an early pregnancy who is hemodynamically unstable on arrival to the ED;
4. list ultrasound findings that are most suggestive of the diagnosis of ectopic pregnancy; and
5. discuss the clinical utility of the quantitative B-hCG test and progesterone level in evaluating women with abdominal pain, vaginal bleeding, or both during early pregnancy.

Date of original release: November 1, 2003.

Date of most recent review: October 1, 2003.

See "Physician CME Information" on back page.

The paramedic radio goes off. Paramedics report that they have a 25-year-old pregnant female with a chief complaint of abdominal pain who was seen in your ED one week ago for the same complaint. Her husband called the ambulance today after she had a "fainting spell." On arrival in the ED, she is clammy and tachycardic. She is not obviously gravid. Vital signs reveal a supine systolic blood pressure of 70 mmHg and a heart rate of 130 beats per minute. Her abdomen is diffusely tender. The paramedics have been administering normal saline through two large-bore IVs running wide open. Your first thought is the obvious one to any experienced emergency physician—she has a ruptured ectopic pregnancy. Your second thought is, "Who was the idiot who discharged her last week?" As she's wheeled into the trauma room, you notice that her face looks familiar.

ABDOMINAL pain and vaginal bleeding are common in the first trimester of pregnancy. Patients with these vague symptoms—which may be inconsequential or may herald the onset of a critical condition—frequently present to the ED and may represent more than 1% of all ED visits.¹ The true incidence of one or both of these symptoms during the first trimester is unknown, as some women probably never seek medical attention, and those who do present to a variety of medical settings, including urgent care centers, primary care or OB/GYN offices, and EDs.

While the presenting symptoms and severity of illness may be apparent upon presentation to the ED, quickly identifying those women who are ultimately at risk for death is not so clear-cut. When first-trimester pregnant patients present to the ED with abdominal pain and/or vaginal bleeding, the emergency physician is faced with two main questions: Is the pregnancy location intrauterine or ectopic? If intrauterine, is the pregnancy viable or nonviable? With a few simple tools such as quantifiable pregnancy testing and

Guest Editor

Lance Brown, MD, MPH, FACEP, Chief, Division of Pediatric Emergency Medicine; Associate Professor, Department of Emergency Medicine; Loma Linda University Medical Center and Children's Hospital, Loma Linda, CA.

New Mexico Health Sciences Center School of Medicine, Albuquerque, NM.

W. Richard Bukata, MD, Clinical Professor, Emergency Medicine, Los Angeles County/USC Medical Center, Los Angeles, CA; Medical Director, Emergency Department, San Gabriel Valley Medical Center, San Gabriel, CA.

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Department of Emergency Medicine, Morristown Memorial Hospital.

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Gregory L. Henry, MD, FACEP, CEO, Medical Practice Risk Assessment, Inc., Ann Arbor, MI; Clinical Professor, Department of Emergency Medicine, University of Michigan Medical School, Ann Arbor, MI; President, American Physicians Assurance Society, Ltd., Bridgetown, Barbados, West Indies; Past President, ACEP.

Jerome R. Hoffman, MD, FACEP, Professor of Medicine/Emergency Medicine, UCLA School of Medicine; Attending Physician, UCLA Emergency Medicine Center; Co-Director, The Doctoring Program, UCLA School of Medicine, Los Angeles, CA.

Francis P. Kohrs, MD, MSPH, Lifelong Medical Care, Berkeley, CA.

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Editorial Board

Judith C. Brillman, MD, Residency Director, Associate Professor, Department of Emergency Medicine, The University of

bedside ultrasound, the emergency physician is frequently able to make a definitive diagnosis at the initial visit. However, in a substantial minority of patients, significant diagnostic uncertainty remains at the conclusion of the ED visit, and management decisions must be made based on an assessment of risk.

This issue of *Emergency Medicine Practice* discusses the diagnostic evaluation of the first-trimester pregnant patient with abdominal pain, vaginal bleeding, or both with a specific focus on the roles of history, physical examination, human chorionic gonadotropin (β -hCG) tests, and pelvic ultrasonography. An evidence-based diagnostic strategy and a discussion of the therapeutic options available to manage patients with ectopic pregnancies and nonviable intrauterine pregnancies are highlighted. (For a discussion of managing the pregnant trauma patient, see the January 2003 issue of *Emergency Medicine Practice*, "Trauma In Pregnancy: Double Jeopardy.")

Critical Appraisal Of The Literature

Thousands of articles regarding complications of pregnancy have been published in the medical literature. For example, a September 2003 MEDLINE search using PubMed as the gateway and using the MeSH heading "Pregnancy, Ectopic," with the search limited to human studies, articles published in English, and those articles with published abstracts, yielded 8008 articles.² Obviously, with this extensive body of literature, identifying articles relevant to the practice of emergency medicine can be daunting.

There have been several interesting and potentially important papers published recently. Kohn et al performed a retrospective medical record review of 730 women who presented to an urban ED with abdominal pain, vaginal bleeding, or both and a non-zero quantitative β -hCG.³ In this cohort, 13% of the women were ultimately diagnosed with ectopic pregnancies. Although the β -hCG was not an excellent discriminator between ectopic and normal pregnancies, a β -hCG value less than 1500 mIU/mL was more than twice as likely to be seen in women with ectopic pregnancies than in those with normal pregnancies (positive likelihood ratio, 2.24).

A similar type of analysis was published in 1997 by Dart et al, who performed a retrospective medical record review including 194 women with abdominal pain, vaginal bleeding, or both, but this study evaluated a β -hCG threshold of greater than 3000 mIU/mL and included ultrasonography in the analysis.⁴ In this study, none of 74 patients with a β -hCG level greater than 3000 mIU/mL and the absence of a gestational sac identified on ultrasonography were ultimately determined to have a normal intrauterine pregnancy. In 1998, Buckley et al published a study of 486 prospectively enrolled stable first-trimester pregnant women who presented to an ED with abdominal pain, vaginal bleeding, or both. They developed a clinical prediction model for the ED diagnosis of ectopic pregnancy.⁵ Utilizing recursive partitioning, a clinical decision prediction model was developed that

was based in part on abdominal peritoneal signs, cervical motion tenderness, fetal heart tones, tissue at the cervical os, and the absence of pain other than midline menstrual-like cramping. This type of clinical decision rule awaits prospective validation in an independent sample before its clinical use can be considered.

In 1998, Valley et al published a prospective observational study of the utility of a serum progesterone level in identifying ectopic pregnancy in a convenience sample of 300 women at risk for ectopic pregnancy presenting to their ED for care.⁶ These authors concluded that a serum progesterone level could not effectively discriminate ectopic pregnancy from spontaneous abortion in these women. There are now quite a few studies that are well-designed and have fairly large numbers of subjects. Ongoing research is being driven by changes in ultrasound technology, including the ED use of color-flow Doppler studies⁷ and the increased focus on non-laparoscopic approaches to both diagnosis and treatment.⁸⁻¹⁰

Clinical Policies

The American College of Emergency Physicians (ACEP) has published three clinical policies related to the care of pregnant women in the first trimester who present to the ED with abdominal pain, vaginal bleeding, or both. The first is titled "Clinical Policy for the Initial Approach to Patients Presenting with a Chief Complaint of Vaginal Bleeding."¹¹ This practice guideline provides a general approach to the patient with vaginal bleeding but fails to provide a clear evidence-based approach to management decisions. The importance of β -hCG and Rh testing in the ED is emphasized. Sample discharge instructions and quality assurance forms are included. This clinical policy is general in its format, and therefore may be of limited value in developing specific clinical strategies in the ED. The second ACEP clinical policy is titled, "Critical Issues for the Initial Evaluation and Management of Patients Presenting with a Chief Complaint of Non-traumatic Abdominal Pain."¹² This practice guideline is also quite general and emphasizes basic principles like the importance of β -hCG testing in the ED. The third ACEP clinical policy is titled "Critical Issues in the Initial Evaluation and Management of Patients Presenting to the Emergency Department in Early Pregnancy."¹³ This policy takes an evidence-based approach and focuses on six clinical questions ranging from the role of ultrasound when the β -hCG value is less than 1000 mIU/mL to the indications for anti-D immunoglobulin (i.e., RhoGAM) in the symptomatic early pregnancy. The discussion of indications for anti-D immunoglobulin is particularly well done.

The Cochrane Database also published systematic reviews of diagnostic strategies and interventions for the management of ectopic pregnancy.^{14,15} These documents provide a comprehensive review of the current literature related to ectopic pregnancy.

Epidemiology, Etiology, And Pathophysiology

Fetal demise early in gestation is a common occurrence.¹⁶⁻¹⁸ When unrecognized pregnancies are included, it has been

estimated that 43%-78% of all conceptions fail.¹⁶⁻¹⁸ In some cases, the fertilized ova do not undergo the normal cleavage process and consequently fail to implant.¹⁹ In other cases, the blastocyst implants but then aborts early in gestation, often before the pregnancy is even clinically recognized.

An ectopic pregnancy is defined as the implantation of a fertilized ovum outside the endometrial cavity of the uterus. Ectopic pregnancies occur in up to 2% of reported pregnancies, or a total of 108,000 reported cases per year in the United States.²⁰ However, the true incidence of ectopic pregnancy in the United States is currently unknown,²¹ which is most likely due to advances in the diagnosis and treatment of ectopic pregnancy in the past few decades, a substantial decrease in inpatient hospital treatment for ectopic pregnancy, and an increase in multiple outpatient visits for a single ectopic pregnancy. These changes make traditional surveillance estimates of the incidence of ectopic pregnancy difficult to interpret.²¹

Approximately 95% of ectopic pregnancies implant in the fallopian tube. Of these, 80% implant in the ampullary portion, 12% in the isthmus, 5% in the fimbriated end of the tube, and 2% at the junction of the fallopian tube and uterus. The latter site of implantation is often referred to as either an interstitial or a cornual ectopic pregnancy. Additional sites of ectopic implantation include the abdomen, the cervix, and the ovary.

Damage to the mucosa of the fallopian tube, which prevents or delays transport of the fertilized ovum to the endometrial cavity, is the most common cause of ectopic pregnancy.²² Mucosal damage is most often a result of tubal infection.²²⁻²⁵ Tubal surgery and diethylstilbestrol exposure have also been demonstrated to play a role.²² Defects in the fertilized ovum itself may increase the risk of ectopic pregnancy, due to either decreased tubal motility or premature implantation (prior to arrival in the endometrial cavity). Hormonal factors also have been associated with an increased risk of ectopic pregnancy.

Supra-physiologic levels of estradiol or progesterone inhibit tubal migration, which may account for the increased incidence of ectopic pregnancies in patients on ovulation induction agents.²⁶

Once tubal implantation has occurred, there are four possible outcomes: The ectopic pregnancy may erode through the muscularis and lamina propria of the tube, resulting in tubal rupture; the ectopic pregnancy may persist within an intact tube with or without an associated tubal hematoma; the ectopic pregnancy may abort out of the fimbriated

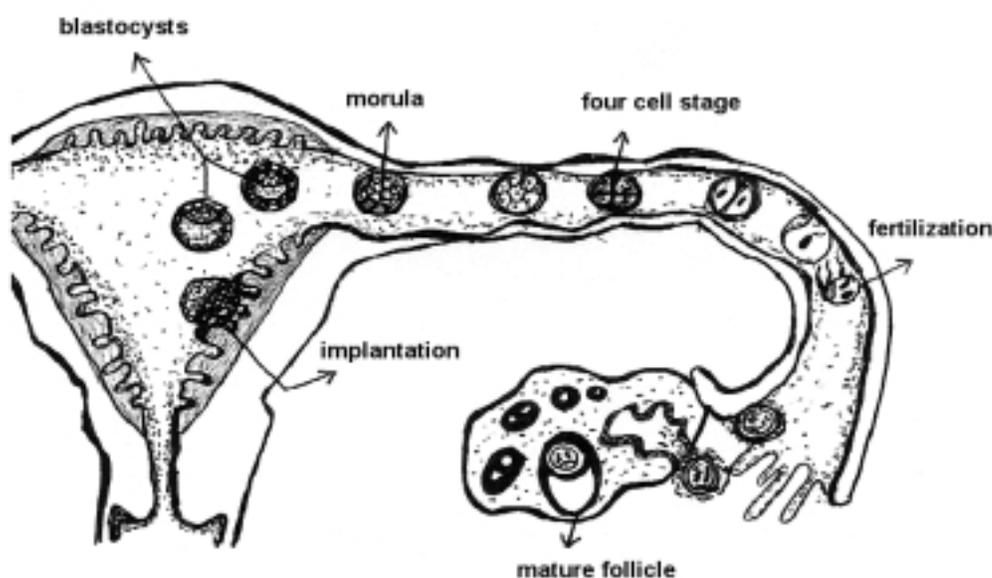
end of the fallopian tube; or the ectopic pregnancy may spontaneously involute. Intraabdominal hemorrhage may occur in the absence of tubal rupture.

A heterotopic pregnancy is the simultaneous occurrence of at least one intrauterine and at least one ectopic pregnancy. The overwhelmingly dominant risk factors for heterotopic pregnancy are ovulation induction and in vitro fertilization. The incidence of heterotopic pregnancy is very low in naturally occurring pregnancies but is relatively common when multiple simultaneous pregnancies are induced or implanted. Unfortunately, some reports of the incidence of heterotopic pregnancy combine populations of naturally occurring pregnancies with artificially induced pregnancies and thus report an incidence that is of little clinical utility.²⁷

Early Pregnancy Development

On average, ovulation occurs about two weeks after the first day of the last menstrual period. In some individuals this interval is as short as seven days, while in others it can occur as late as 21 days.²⁸ Post-ovulation, the ovum is taken up by the fallopian tube, where fertilization takes place.²⁹ (See Figure 1.) The fertilization process occurs over a 24-hour period and is completed when the male and female pronuclei fuse to form a new cell called a zygote. The zygote proceeds down the tube undergoing a number of cell divisions. While early on, the number of cells increases substantially, the volume of the cell mass remains unchanged as it is contained within the zona pellucida, a thick layer of glucoprotein that surrounds the developing zygote. At about day four after fertilization, the developing pregnancy enters into the uterus. At this point, the developing structure, now called the blastocyst, undergoes a number of morphologic changes. The zona pellucida degenerates, allowing the blastocyst to increase in size. The cells start to differentiate, forming a

Figure 1. Normal Progression Of Early Pregnancy From Egg Release To Implantation.*



*Note: Fertilization occurs in the fallopian tube.

thin outer layer of cells called the trophoblasts (which will give rise to part of the placenta) and an inner cell mass known as the embryoblast (which gives rise to the embryo). At post-fertilization day six, the blastocyst implants into the wall of the endometrial cavity. It is at this point that the initial β -hCG production begins.²⁹ Pregnancy development proceeds rapidly from this point. Approximately three weeks after fertilization—that is, two weeks from implantation (and initial β -hCG production)—a gestational sac can be visualized within the endometrial cavity using transvaginal ultrasound.^{30,31} About 1-2 weeks later, an embryo with a fetal heartbeat can be visualized.³¹

Based on the preceding discussion, important take-home points emerge. First, the interval from when a pregnancy test is first positive to when an intrauterine sac is identified on ultrasound is only two weeks. In most cases, failure to visualize a gestational sac on ultrasound is because the pregnancy is abnormal or the menstrual dates are inaccurate. Abnormal pregnancies, including ectopic pregnancies, are very likely when the β -hCG is greater than 1000 mIU/mL and a gestational sac cannot be visualized on ultrasound.³² Second, delays in tubal transport, which allow the blastocyst stage to occur in the tube rather than in the uterus, clearly increase the risk of tubal implantation.

Terminology

Threatened Abortion

In the past, clinicians used the history and physical examination to classify the status of symptomatic pregnancies. The term “threatened abortion” was used to describe patients with abdominal pain or vaginal bleeding who had no history of passing tissue, had a closed os, and had a uterus appropriately sized for dates. Early literature suggested that 30%-50% of patients classified as having a “threatened abortion” progressed to spontaneously abort.³³

The use of ultrasound has allowed for a more refined prognosis. Identification of a fetus greater than 5 mm in crown-rump length without a fetal heartbeat is consistent with fetal demise, also denoted as a “nonviable intrauterine pregnancy.”³⁴ When a fetal heartbeat is identified using ultrasound, the overall prognosis is good, with 85% of these patients advancing to a full-term pregnancy.^{35,36} Continued use of the term “threatened abortion” is appropriate in these patients. Patients in whom the diagnosis is unclear after initial ultrasound should be classified as pregnant with the location of the pregnancy unclear. These “rule out ectopic” patients will need continued follow-up until the true location of the pregnancy can be determined.

Some patients classified as having a threatened abortion based on history and physical examination harbor an ectopic pregnancy. Stovall et al found that when history and physical examination were used as the primary mode to assess first-trimester vaginal bleeding, almost half of the ectopic pregnancies were discharged with an incorrect diagnosis.³⁷ In the group of patients

who were misclassified, about 60% were discharged with a diagnosis of “threatened abortion.”³⁷

Inevitable And Incomplete Abortions

The term “inevitable abortion” is used to describe the situation when the cervical os is open but tissue has not yet passed. The term “incomplete abortion” is used to describe the situation in which tissue has passed but the cervical os remains open, suggesting that products of conception still remain within the endometrial cavity. Previously, more patients with inevitable and incomplete abortions underwent mechanical evacuation of the uterus to decrease blood loss and minimize the risk of endometritis. Recent studies have demonstrated that ultrasound can reliably quantify the volume of remaining products of conception, and that those with a small volume of endometrial contents do well with expectant management alone.³⁸⁻⁴⁰

Complete Abortion

The term “complete abortion” has been used to describe the situation in which the patient has passed tissue and the cervical os has closed. This definition is clinically useful and is appropriate if definite products of conception are evident. Because patients frequently mistake blood clots for the products of conception, do not rely on history alone to determine whether products of conception have been passed. Inappropriate use of the term “complete abortion” to describe patients with vaginal bleeding and an empty endometrial cavity on ultrasound examination should be avoided, as these findings can be present with both an early but viable intrauterine pregnancy and an ectopic pregnancy.

Missed Abortion

The term “missed abortion” refers to the prolonged retention of products of conception in the uterus.³³ Occasionally after prolonged retention, serious complications such as coagulation defects may occur.⁴¹ These complications are more common when the gestation has reached the second trimester before fetal death occurs. With the widespread availability of ultrasonography, the complications associated with missed abortions are increasingly uncommon, as fetal death is being diagnosed closer to the time of the fetal demise. In fact, it has been suggested that the term “missed abortion” be abandoned, as the volume of fetal contents by ultrasound has been found to be a better predictor of the need for uterine evacuation than the length of the estimated time interval between fetal death and uterine evacuation.⁴²

Differential Diagnosis

The differential diagnosis of abdominal pain or bleeding in a first-trimester pregnancy includes conditions that are directly related to the pregnancy and those that simply coincide with the pregnancy. (See Table 1 on page 5.)

In patients undergoing ovulation induction, the

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Table 1. Differential Diagnosis Of Common Causes Of Abdominal Pain, Vaginal Bleeding, Or Both In Early Pregnancy.

Corpus luteal cyst

<u>Key historical features</u> Lateralized pelvic pain	<u>Key physical examination findings</u> Unilateral adnexal tenderness, possible palpable mass	<u>Helpful diagnostic tests*</u> Ultrasound revealing a measurable cyst, free fluid in the abdomen if the cyst has ruptured
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Urinary tract infection—Cystitis

<u>Key historical features</u> Midline pelvic pain, dysuria, urinary urgency, urinary frequency, urinary hesitancy, hematuria	<u>Key physical examination findings</u> Midline pelvic tenderness or a normal physical examination, absence of fever	<u>Helpful diagnostic tests*</u> Urinalysis revealing positive leukocyte esterase, positive nitrates, and white blood cells
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Urinary tract infection—Pyelonephritis

<u>Key historical features</u> Relatively gradual-onset unilateral flank pain, dysuria, urinary urgency, urinary frequency, urinary hesitancy, hematuria	<u>Key physical examination findings</u> Costovertebral angle tenderness, fever	<u>Helpful diagnostic tests*</u> Urinalysis revealing positive leukocyte esterase, positive nitrates, and white blood cells
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Appendicitis

<u>Key historical features</u> Localized, relatively gradual-onset right lower quadrant pain, anorexia, nausea and vomiting	<u>Key physical examination findings</u> Localized right lower quadrant tenderness, low-grade fever	<u>Helpful diagnostic tests*</u> Ultrasound revealing an enlarged, noncompressible appendix
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Ovarian torsion

<u>Key historical features</u> Localized abrupt-onset unilateral lower abdominal or pelvic pain	<u>Key physical examination findings</u> Unilateral adnexal mass and tenderness, may have abdominal tenderness mimicking appendicitis if the torsion is on the right side	<u>Helpful diagnostic tests*</u> Ultrasound revealing the absence of Doppler flow to the affected ovary
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Ureteral (kidney) stone

<u>Key historical features</u> Abrupt-onset unilateral flank or lateral abdominal pain, nausea and vomiting, hematuria	<u>Key physical examination findings</u> Restless, uncomfortable patient, may have poorly defined abdominal or flank tenderness	<u>Helpful diagnostic tests*</u> Urinalysis revealing red blood cells; ultrasound revealing unilateral hydronephrosis
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Ectopic pregnancy

<u>Key historical features</u> Abdominal pain, vaginal bleeding, or both	<u>Key physical examination findings</u> Unilateral adnexal tenderness, possible adnexal mass, cervical motion tenderness	<u>Helpful diagnostic tests*</u> Ultrasound revealing absence of intrauterine pregnancy, tubal mass with heartbeat, free fluid in the abdomen if ruptured
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Nonviable intrauterine pregnancy

<u>Key historical features</u> Abdominal pain, vaginal bleeding, or both	<u>Key physical examination findings</u> Uterine tenderness, cervical os may be open	<u>Helpful diagnostic tests*</u> Ultrasound revealing intrauterine mass without a heartbeat
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*in addition to the quantitative β -hCG

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ovarian hyperstimulation syndrome (OHSS) may occur.⁴³ OHSS is characterized by cystic enlargement of the ovaries and a fluid shift from the intravascular to the third space secondary to increased capillary permeability. In severe cases, gross enlargement of the ovaries may cause abdominal pain, distension, ascites, and dyspnea.⁴³ In addition, patients with OHSS are at increased risk for developing ovarian torsion.⁴³ The incidence of severe OHSS ranges from 1%-10% of patients undergoing ovarian hyperstimulation.⁴⁴

Conditions that are incidental to the pregnancy include those that would also be considered in the non-pregnant patient, such as appendicitis, urinary tract infections, and ureteral (kidney) stones. The differentiation of these conditions from those directly associated with the pregnancy is often quite challenging. Fortunately, ultrasound examinations are safe in pregnancy and can be very helpful in sorting out these diagnoses. Incorporating the results of an ultrasound examination and microscopic urinalysis results into the overall diagnostic strategy is often valuable. (See Table 1 on page 5.)

In patients with severe abdominal pain but with a viable intrauterine pregnancy by ultrasound, alternative diagnoses must be considered. The specifics of the further evaluation must be guided by sound clinical judgment, but a few caveats are worth mentioning. In patients undergoing infertility treatment, a heterotopic pregnancy must be high on the differential diagnosis. Identification of a concomitant adnexal mass by ultrasound with or without copious free fluid in the abdomen supports the diagnosis of an ectopic pregnancy co-existing with the intrauterine pregnancy.

Ovarian torsion is likely when there is an abrupt onset of severe, lateralized pain. Ovarian torsion is often accompanied by nausea and vomiting. The presence of an enlarged ovary along with evidence of markedly decreased or absent unilateral Doppler flow is typically considered diagnostic for ovarian torsion. However, color flow may be falsely reassuring in a minority of cases. Thus, the decision of whether or not to perform laparoscopy ultimately must be made based on the overall clinical picture.

The major acute life threat to the pregnant patient is shock secondary to hemorrhage. In the patient with significant hemorrhage secondary to a spontaneous

abortion, the source of bleeding is usually self-evident, given the heavy vaginal flow. In the patient with significant hemorrhage secondary to a ruptured ectopic pregnancy or a hemorrhagic ovarian cyst, the degree and source of blood loss is often less evident by history and physical examination. However, an emergently performed ultrasound examination may demonstrate an abnormal volume of free fluid in the cul de sac or abdomen. In EDs where the physicians have difficulty obtaining an emergent ultrasound examination performed by either an emergency physician or an ultrasound technician, emergent gynecology consultation is warranted.

Prehospital Care

The prehospital management of these patients is straightforward. Hemodynamically stable patients require little more than transport to an appropriate receiving facility. Unstable patients should be treated according to standard local protocols for hemorrhagic shock. This often involves large-bore intravenous lines and rapid crystalloid administration. Rapid transport for definitive care is a key component to the successful prehospital management of these critically ill patients.

Emergency Department Evaluation

Triage And Initial Management

Unstable Patients

In a manner similar to other critically ill patients, quickly move hemodynamically unstable women in early pregnancy to a major resuscitation area, start two large-bore intravenous lines, and begin resuscitation with boluses of isotonic saline. (See "Clinical Pathway: Management Of The Hemodynamically Unstable Patient In Early Pregnancy" on page 10.) Rapid assessment of anemia and confirmation of the pregnancy are high priorities. If available, bedside hemoglobin testing and a rapid urine qualitative pregnancy test can add clarity to what can become a hectic situation involving a critically ill, presumably pregnant young woman. As the intravenous lines are being placed, a complete blood count, type and crossmatch blood bank specimen including Rh testing, and a rapid quantitative pregnancy test should be ordered. The need for blood products will be determined by the degree of hemodynamic instability and the response to fluid resuscitation. Emergent ultrasound examination and gynecology consultation

Key Points In Managing First-Trimester Emergencies

1. Except in rare circumstances, the history and physical examination alone should not be used to exclude ectopic pregnancy.
2. Ultrasound is the best initial test to evaluate the severely symptomatic pregnant patient.
3. The combination of ultrasound findings and the quantitative β -hCG is useful in stratifying patients with regard to their risk for ectopic pregnancy.
4. Given other indications, the quantitative β -hCG value is the best predictor of success with methotrexate treatment.
5. In patients with nonviable intrauterine pregnancies, the volume of endometrial contents at ultrasound is the best predictor of the need for surgical evacuation. ▲

should be anticipated.

Stable Patients

Patients with mild pain or bleeding and stable vital signs can typically wait in the waiting room if an exam room is not immediately available. Frequent reassessment by the triage nurse is important to recognize patients whose clinical condition worsens while waiting.

History

History Of Present Illness

Patients with a complaint of abdominal pain should be queried about the location, character, onset, and severity of the pain. Pain originating from the uterus is typically midline and crampy. Pain originating from the adnexa is typically unilateral and sharp. If hemorrhage into the pelvis from an adnexal process has occurred, the pain often becomes bilateral. Pain originating from the bladder is midline in location and is often associated with dysuria.

Patients with an ectopic pregnancy more often rate the intensity of their pain as moderate to severe compared to those with an intrauterine pregnancy.⁴⁵ Approximately 10% of patients with an ectopic pregnancy, however, are pain-free at the initial ED presentation.¹ For those patients with vaginal bleeding, the volume of blood loss may be a clue to diagnosis. A rough way to characterize the volume of blood loss is the number of sanitary pads the patient needs to change over a 24-hour period. Patients who use more than five pads in a 24-hour period have a higher rate of nonviable pregnancy compared to those who use fewer.⁴⁵ In addition, the report of passing tissue increases the rate of nonviable pregnancy, although the passing of clots is often confused with the passing of tissue.^{45,46}

Review Of Systems

Syncope or near-syncope suggests hypovolemia. Hypovolemia may arise from water loss or blood loss. Water loss typically occurs in the setting of decreased oral

intake from the nausea of early pregnancy with or without vomiting. When nausea and vomiting are associated with the onset of abdominal pain, diagnoses such as appendicitis, ovarian torsion, or ureteral colic should be considered. Blood loss may be from vaginal bleeding or intraabdominal hemorrhage. Fever suggests an infectious process, such as a urinary tract infection or appendicitis, but may also be seen when endometritis complicates a spontaneous or therapeutic abortion. The patient should be asked about the date of her last normal menstrual period, the date and results of any home pregnancy tests, and the outcome of any doctor visits during her current pregnancy.

Past Medical History

Ask the patient about her past medical history, with a particular focus on the outcome of prior pregnancies, past gynecologic surgeries, intrauterine device (IUD) use, prior ectopic pregnancies, infertility treatments, and a history of pelvic inflammatory disease or sexually transmitted diseases. The presence of any of these features in the past medical history increases the likelihood of ectopic pregnancy.²³ Of all of the risk factors for ectopic pregnancy, a past history of tubal ligation presents the greatest risk.⁴⁵ A prior spontaneous abortion places a patient at increased risk for a recurrent spontaneous abortion.

As a note of caution, clinicians need to be aware that other than the confirmed performance of a hysterectomy, no current form of birth control (including a reported history of abstinence or tubal sterilization) completely excludes the possibility of pregnancy. Approximately 10% of ectopic pregnancies occur in patients who had previously undergone a tubal sterilization procedure.⁴⁵

Medications

Ask the patient about current medications, method of birth control, as well as the use of ovulation induction

Cost-Effective Strategies For Managing Emergencies In the First Trimester

1. In women presenting with pelvic pain with or without vaginal bleeding, determining whether or not the patient is pregnant is one of the key branch points in dictating the course of the diagnostic evaluation. Performing a urine pregnancy test at triage can be helpful in streamlining the evaluation while avoiding unnecessary testing such as quantitative β -hCG, progesterone, and Rh determinations in those women who are not pregnant.
2. Patients known to be pregnant will often have had Rh typing performed during an earlier visit. If the blood type is available in the medical record or from the hospital blood bank, look it up instead of routinely ordering Rh typing on every patient.
3. Perform the ultrasound yourself.
4. Choose the most cost-effective strategy based on the clinical situation. With regard to ectopic pregnancy management, the β -hCG appears to be an effective decision node for this. Mol et al reported that when the β -hCG was less than 3000 mIU/mL, methotrexate was more cost-effective than surgical treatment, but when the β -hCG was above 3000 mIU/mL, surgical treatment was more cost-effective.¹⁰⁰ ▲

agents. Along with OHSS and ovarian torsion, patients on ovulation induction agents are at increased risk for ectopic pregnancy, including heterotopic pregnancy.^{26,47}

Physical Examination

Vital Signs

Since these patients seldom have problems with their airways or breathing, the key to starting the evaluation usually rests with the vital signs and the assessment of circulation. Significant tachycardia with or without hypotension suggests hypovolemia. However, bradycardia has been known to occur with intraabdominal hemorrhage even though the patient is in hemorrhagic shock.⁴⁸ This seemingly paradoxical response is thought to be a vagal phenomenon. The presence of fever suggests an infectious process.

Abdominal Examination

Lateral or bilateral abdominal tenderness more frequently occurs with an ectopic pregnancy than with an intrauterine pregnancy.⁴⁵ Evidence of peritoneal irritation on examination increases the likelihood of ectopic pregnancy but is a nonspecific finding that may also be seen with other conditions, such as the rupture of a hemorrhagic ovarian cyst or appendicitis.^{5,45} The location of the tenderness may be helpful. Although not entirely convincing due to very small numbers, one study of eight patients with right lower quadrant abdominal pain reported that no cases were diagnosed as appendicitis when the tenderness was localized to within 2 cm of the medial aspect of the right inguinal ligament.⁴⁹

Pelvic Examination

Although it would seem intuitive that one should find an adnexal mass in cases of tubal ectopic pregnancies, this is not always the case. In fact, an adnexal mass is found in a minority of patients with ectopic pregnancy.⁴⁵ Surprisingly, even when an adnexal mass is present on physical examination, the ectopic pregnancy is determined to be located on the *contralateral* side in up to one-third of cases at laparoscopy.⁴⁵

The presence of an open internal cervical os is suggestive of the diagnosis of nonviable intrauterine pregnancy. However, in one prospective study, only 72% of patients with an open cervical os at pelvic examination had a final diagnosis of nonviable pregnancy.⁴⁵ One possible explanation for this finding is that clinicians might have mistaken an open external os (a common finding in multiparous patients) with an open internal os. Another possible explanation is that the pelvic examination is occurring at a time when the os transiently opens to allow passage of blood clots in a patient with vaginal bleeding but an otherwise viable or ectopic pregnancy.

The one physical finding that confirms the diagnosis of a nonviable intrauterine pregnancy is identification of definitive products of conception that are either brought to the ED by the patient or are identified in the vaginal canal or cervical os during the pelvic examination.⁵ An enlarged

uterus on physical examination decreases the likelihood of ectopic pregnancy but does not exclude the diagnosis. Secondary hormonal influences may increase the size of the uterus even though the patient has an ectopic pregnancy. Alternatively, the patient may have unrelated and unrecognized uterine enlargement from fibroids.⁴⁵

Diagnostic Studies

β -hCG

The β -hCG test is one of the most important and accurate laboratory tests available to emergency physicians. It is exceedingly rare for a pregnancy, whether normal or abnormal, to be present when β -hCG is absent from the serum.^{50,51} Historically, only serum β -hCG assays were used to exclude ectopic pregnancy, but current urine qualitative tests have excellent sensitivity and yield results within minutes at the bedside.⁵² Given the potentially grave consequences of a false-negative pregnancy test, however, it has been recommended that a quantitative serum β -hCG be performed if the urine test is negative and the clinical suspicion for pregnancy is high.⁵³

There are a few general principles about quantitative serum β -hCG tests that are useful for emergency physicians to know. First, at the same gestational age, nonviable intrauterine pregnancies and ectopic pregnancies tend to have lower quantitative β -hCG values than viable intrauterine pregnancies.^{1,54-56} In fact, symptomatic patients with β -hCG levels less than 1000 mIU/mL are four times more likely to have an ectopic pregnancy than those with higher β -hCG values.^{1,54} Second, the direction and rate of change of the β -hCG at follow-up is useful in the evaluation of suspected ectopic pregnancies.^{5,39-42} A patient with an early, viable intrauterine pregnancy will have serum quantitative β -hCG values that double about every 48 hours.⁵⁷ Approximately 85% of normal intrauterine pregnancies will have a rise in the serum β -hCG of greater than 66% of the initial value at 48 hours, whereas only 15% of ectopic pregnancies will have as great a rise.⁵⁷⁻⁶¹ In fact, up to one-half of ectopic pregnancies will have falling β -hCG values at 48-hour follow-up.^{62,63}

Progesterone

Progesterone is produced by the corpus luteum during the first eight weeks of pregnancy. Progesterone levels rise at the time of ovulation and are affected much less by changes in gestational age compared to β -hCG values. Numerous studies have demonstrated that both nonviable intrauterine pregnancies and ectopic pregnancies have significantly lower progesterone values compared to viable intrauterine pregnancies.^{46,64-68} A progesterone value greater than 25 ng/mL is strongly associated with the diagnosis of a viable intrauterine pregnancy.^{64,65,68} A progesterone value less than 5.0 ng/mL accurately excludes the diagnosis of a viable intrauterine pregnancy, although it does not distinguish an ectopic pregnancy from a nonviable intrauterine pregnancy.⁶⁵⁻⁶⁷ Although not currently available in every ED, this test may play an increasingly important role in the future, necessitating more widespread availability.

Ultrasound

In conjunction with the β -hCG, ultrasound is the most useful test for evaluating women with abdominal pain, vaginal bleeding, or both during early pregnancy. At times, the results of the ultrasound are unequivocal. Often, a definitive intrauterine pregnancy is identified. A fetus or yolk sac clearly identified within the endometrial cavity is diagnostic of an intrauterine pregnancy. The identification of a fetal heartbeat within the uterus is reassuring, as most of these pregnancies will progress to delivery. Alternatively, absence of a fetal heartbeat when the embryo is greater than 5 mm in length is strong evidence that the pregnancy is nonviable.³⁴ At other times, the ultrasound is definitive for or highly suggestive of ectopic pregnancy. Indirect evidence of an ectopic pregnancy includes an adnexal mass separate from the ovary or pelvic fluid with an abnormally large volume or echoic shadows. An ectopic pregnancy is definitively diagnosed when a yolk sac or fetus is identified outside the uterus.

Unfortunately, there are times when the ultrasound does not yield definitive results. The term “indeterminate ultrasound” encompasses a range of endometrial findings. A simple five-group subclassification system has been developed for evaluating these indeterminate ultrasound findings.⁶⁹ (See Table 2.) The subclasses are defined as follows:

- *Empty uterus*: an empty endometrial cavity with or without a thickened endometrium
- *Normal sac*: anechoic intrauterine fluid collection less than 10 mm in mean sac diameter with a regular echogenic border
- *Abnormal gestational sac*: anechoic intrauterine fluid collection either greater than 10 mm in mean sac diameter or with a grossly irregular border
- *Nonspecific fluid*: anechoic intrauterine fluid collection less than 10 mm in mean sac diameter without

Table 2. Subclasses Of Indeterminate Ultrasound Findings And The Incidence Of Ectopic Pregnancy.

Indeterminate ultrasound finding*	Incidence of ectopic pregnancy
Empty uterus	14%
Nonspecific fluid	5%
Echogenic material	4%
Abnormal gestational sac	0%
Normal gestational sac	0%

* See text for the definition of terms

Source: Dart RG, Burke G, Dart L. Subclassification of indeterminate pelvic ultrasonography: prospective evaluation of the risk of ectopic pregnancy. *Ann Emerg Med* 2002 Apr;39(4):382-388.

an echogenic border

- *Echogenic material*: echogenic material within the endometrial cavity without a defined sac or multiple discrete anechoic collections of varying sizes divided by echogenic septations

This subclassification system has been shown to be helpful in determining the risk of ectopic pregnancy when the ultrasound is indeterminate.⁶⁹ If an empty uterus is identified on ultrasound examination, the risk of an ectopic pregnancy is five times greater than if any of the other subclasses are identified.⁶⁹

One concerning finding on ultrasound is a complex adnexal mass with solid and fluid components present. It has been estimated that these complex masses represent ectopic pregnancies about 70% of the time in general and 90% of the time if abnormal fluid is present in the pelvis.^{70,71} In a minority of cases, these complex masses may be hemorrhagic corpus luteal cysts. The corpus luteum is formed after the expulsion of the egg from a dominant ovarian follicle. Compared to simple ovarian cysts, the corpus luteum has a thickened wall. At the time of ovulation, hemorrhage into the corpus luteum commonly occurs. This can cause the corpus luteum to enlarge and hemorrhage within the cyst, which can give it a complex appearance on ultrasound examination. Consequently, a hemorrhagic corpus luteal cyst may simulate the appearance of an ectopic pregnancy. Nevertheless, given the relative frequencies, a complex adnexal mass should be considered an ectopic pregnancy until proven otherwise.

The volume and character of free pelvic fluid is associated with the risk for ectopic pregnancy. Pelvic fluid is categorized by volume (typically, none, small, moderate, or large) and whether or not the fluid contains internal echoes. Anechoic fluid contains no internal echoes and will appear black on ultrasound examination. Anechoic fluid is typically either serous fluid or blood. A small amount of anechoic fluid in the pelvis is a normal finding. The volume of fluid is directly related to the likelihood that the fluid is secondary to pelvic hemorrhage. Approximately 20% of patients with a moderate volume of anechoic fluid in the cul-de-sac will ultimately be diagnosed with an ectopic pregnancy even without an adnexal mass identified on ultrasound examination.⁷² Pelvic fluid with echogenic shadows (appearing predominantly black with white specks on ultrasound examination) is typically due to the presence of pus or clotted blood. Increasing volumes of fluid raise the risk that the fluid is secondary to pelvic hemorrhage. Identification of any volume of complex fluid increases the likelihood of ectopic pregnancy.^{70,73} When the volume of fluid is large or the fluid is complex, the rate of ectopic pregnancy increases to 70%.⁷²

Risk Stratification

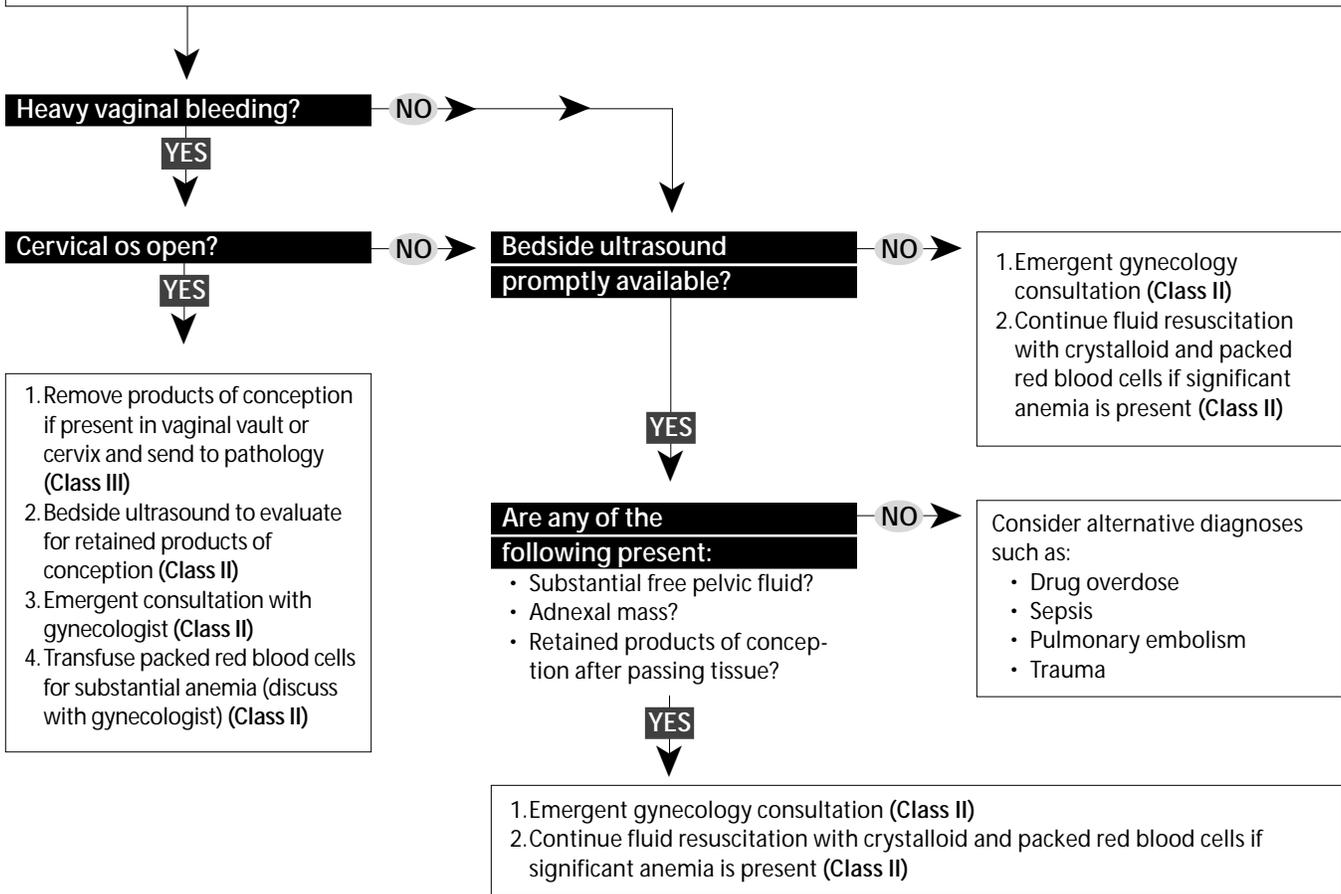
Combining the history, physical examination, laboratory values, and ultrasound findings, the emergency physi-

Continued on page 12

Clinical Pathway: Management Of The Hemodynamically Unstable Woman In Early Pregnancy

General management

- Place patient on monitored bed; address airway and breathing problems (Class II)
- High-flow oxygen by facemask (Class III)
- Prompt vascular access with large-bore peripheral venous catheters (Class II)
- Confirmatory bedside qualitative urine pregnancy test if any doubt exists about pregnancy (Class I)
- Check bedside glucose if mental status is not normal, treat hypoglycemia (Class I)
- Check bedside hemoglobin if available, identify anemia (Class II)
- Fluid resuscitate with normal saline 1L rapid bolus (Class I)
- Frequently reassess vital signs (Class II)
- Send complete blood count, blood bank specimen for type and cross and Rh testing (Class II)



CAUTION! Women undergoing fertility treatments may have multiple pregnancies, including heterotopic pregnancies (at least one intrauterine and at least one ectopic pregnancy). Visualization of an intrauterine pregnancy in these women **does not** rule out ectopic pregnancy to the same degree that it does in other women.
Rh-negative women should be given Rh immune globulin (e.g., RhoGAM) if they have vaginal bleeding.

The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

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Ten Pitfalls To Avoid

1. "She clearly didn't have an ectopic pregnancy because she wasn't having any pain."

Overreliance on the history and physical examination is one of the great mistakes when evaluating women for suspected ectopic pregnancy. Although it seems intuitive that all patients with an ectopic pregnancy should complain of pain, approximately 10% of patients with a final diagnosis of ectopic pregnancy have no pain at their initial presentation.⁴⁵

2. "What do you mean she had an ectopic? The radiologist said the ultrasound looked normal!"

The description of an empty uterus, no adnexal mass, and no free fluid on ultrasound as being "normal appearing" may be misleading. Both very early pregnancy and ectopic pregnancy can give these findings.

3. "What do you mean she now has an intrauterine pregnancy? Last week she had a complex mass on ultrasound and her β -hCG was only 800 mIU/mL. We started her on methotrexate!"

Although identification of a complex adnexal mass suggests the presence of an ectopic pregnancy, this finding is not conclusive. It is imperative that the possibility of a viable intrauterine pregnancy be excluded prior to the initiation of methotrexate treatment.

4. "The β -hCG is rising appropriately; it couldn't be an ectopic pregnancy."

Approximately 15% of ectopic pregnancies will have a "normal" rise in their β -hCG value at the first follow-up blood draw. In fact, in the setting of an empty uterus on ultrasound, a "normal" β -hCG rise increases the likelihood of an ectopic pregnancy being present.

5. "I ruled out an ectopic pregnancy, and she wasn't bleeding much last week. What do you mean she's back with profound anemia and hypotension? Her gynecologist should have been able to take care of her."

Many times it is difficult for patients to get in to see doctors in their offices. Assisting patients in arranging follow-up with a specific doctor at a specific location at a given time can help.

6. "I knew she was bleeding a lot, but what was I supposed to do? I couldn't take her to the operating room myself!"

Although most emergency physicians do not perform uterine evacuation procedures, some simple techniques can help stabilize a patient while awaiting the arrival of the gynecologist. One simple maneuver is to remove

products of conception that are within the cervical os. The removal of this material will often make the uterus contract and may slow the bleeding.

7. "I didn't see any reason to check a quantitative β -hCG. She said that she had just had a therapeutic abortion a couple days prior to the visit."

It can be very challenging to evaluate a patient who has recently undergone a D&E and presents to the ED with abdominal pain, vaginal bleeding, or both. If records from the facility where the procedure was performed are available, these can be very helpful. The "big miss" happens when the D&E occurred in the setting of an undiagnosed ectopic pregnancy. Tubal rupture can then occur at a later date. Comparison of a β -hCG post-procedure with the pre-procedure β -hCG can be helpful, particularly if the β -hCG is *rising*! If unable to obtain prior β -hCG results for comparison, the emergency physician should perform a standard diagnostic evaluation to rule out an ectopic pregnancy.

8. "The ultrasound just showed some retained products of conception, and she wasn't bleeding too heavily in the ED. I prescribed methergine and ibuprofen and told her to check with her gynecologist in a couple of weeks."

Unfortunately, radiology reports often state that retained products of conception are present when echogenic material is visualized within the endometrial cavity. Although this is true in most cases, this ultrasound finding is also consistent with the presence of clotted blood following the passage of the products of conception and ectopic pregnancy.

9. "I know her ultrasound showed a mass, but her quantitative β -hCG was low and she really wanted this pregnancy."

Adnexal masses should be presumed to be ectopic pregnancies until proven otherwise. One helpful test might be a serum progesterone level. Close gynecologic follow-up is critical in these cases.

10. "She was undergoing fertility treatment and had severe pain and tenderness. I really thought she had an ectopic pregnancy, but her ultrasound showed an intrauterine pregnancy, so I sent her home."

This patient had both! Although heterotopic pregnancies are rare in unassisted pregnancies, the rate of heterotopic pregnancy is markedly increased in those women undergoing fertility treatments. Consultation with the patient's gynecologist is key to cases like this. ▲

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cian can develop a rough estimate of the risk of ectopic pregnancy for a woman with abdominal pain, vaginal bleeding, or both during early pregnancy. (See Table 3.)

Treatment

The ED treatment is based on the presumptive diagnosis and the acuity of the patient. The range of treatments spans from reassurance to emergent resuscitation and prompt operative management.

There are three broad categories of patients who require treatment: ectopic pregnancies, nonviable intrauterine pregnancies, and others that are classified simply as “threatened abortions.” Based on the presumptive diagnosis, the emergency physician can develop a relatively safe and rational management plan for women with abdominal pain, vaginal bleeding, or both during early pregnancy.

Ectopic Pregnancy

There are two approaches to managing a confirmed ectopic pregnancy: a surgical approach and a pharmacological approach.

Surgical Approach

The two main surgical options for treatment of ectopic pregnancy are salpingectomy (excision of the affected tube) and tubal preserving surgery. Tubal preserving surgery is intuitively appealing because it would seem that the likelihood of future fertility would be enhanced by the preservation of a fallopian tube. There are two main drawbacks, however, to tubal preserving surgery. First, it is possible for some residual trophoblastic tissue to remain in the tube, resulting in persistence of the ectopic gestation. This occurs in approximately 5% of patients treated with tubal preserving surgery.⁷⁴ Because of this potential complication, these patients require postoperative β -hCG testing until their quantitative β -hCG values return to below detectable levels. Patients with evidence of a persistent ectopic pregnancy based on

rising or unchanged β -hCG values can, in most cases, be managed with methotrexate treatment (see below).⁷⁵ In one study, the rate of persistent ectopic pregnancy was significantly lower in those who were treated with a single dose of methotrexate after tubal preserving surgery than controls.⁷⁶ The second problem with tubal preserving surgery is that the tube that was the site of the initial ectopic pregnancy may have been abnormal and therefore would remain a site for potential ectopic pregnancy implantation.

Salpingectomy is most appropriate when the affected tube is ruptured or severely diseased, future fertility is not desired, or the contralateral tube is normal. When the contralateral tube is normal, performing a salpingectomy on the involved tube gives similar fertility rates compared to those found if tubal conserving surgery was performed.⁷⁷

Pharmacological Approach

Methotrexate is the primary chemotherapeutic agent used to treat ectopic pregnancy. It is a structural analog of folic acid and inhibits the formation of nucleotides that are necessary for DNA and RNA synthesis. Rapidly dividing cells, such as pregnancies, are particularly susceptible to the inhibitory effects of methotrexate. Methotrexate is most appropriate for women who are hemodynamically stable, would prefer to avoid surgery, are reliable, are available for weekly follow-up visits, have a β -hCG of 3000 mIU/mL or less, and have ultrasound examinations that reveal no fluid outside of the pelvis and a mass less than 4.0 cm maximal diameter (< 3.5 cm if a fetal heartbeat is present on ultrasound). Contraindications to primary methotrexate therapy include neutropenia, thrombocytopenia, liver dysfunction, and kidney disorders with serum creatinine greater than 1.5 mg/dL. Although a number of predictors of the success of primary methotrexate therapy have been studied,⁷⁸⁻⁸² the best predictor of success is a low β -hCG.⁸⁰ Methotrexate has been reported to be 98% successful with β -hCG levels less than 1000 mIU/mL, 92% successful with β -hCG values of 1000-4999 mIU/mL, and 76% successful with β -hCG values of 5000 mIU/mL or

Table 3. Likelihood Of Ectopic Pregnancy In Women With Abdominal Pain, Vaginal Bleeding, Or Both In Early Pregnancy.

Higher likelihood of ectopic pregnancy

- β -hCG < 1000 mIU/mL
- Progesterone < 5 ng/mL
- Empty uterus on ultrasound
- Adnexal mass on physical examination or ultrasound
- Moderate to large amount of free pelvic fluid on ultrasound
- Fertility treatments
- Falling β -hCG on repeat testing, but < 50% at 48 hours
- History of pelvic inflammatory disease or other pelvic infection
- History of tubal ligation
- History of prior ectopic pregnancy
- History of intrauterine device (IUD) use
- Localized, sharp pain with cervical motion tenderness
- Peritoneal signs

Lower likelihood of ectopic pregnancy

- β -hCG > 3000 mIU/mL
- Progesterone > 25 ng/mL
- Intrauterine fetus on ultrasound
- Uterine size appropriate for dates (especially if > 8 week size)
- Small amount of anechoic pelvic fluid on ultrasound
- No fertility treatments
- Rising β -hCG on repeat testing, > 66% at 48 hours
- Midline, crampy pain

greater.⁸⁰ Patients who are given methotrexate must be told to avoid vitamins containing folic acid (because it counteracts the action of the methotrexate), avoid alcohol, and refrain from intercourse until the β -hCG returns to normal.

The primary advantage to selecting methotrexate as the treatment modality is the avoidance of surgical risk. However, the administration of methotrexate is not a risk-free option. Nieuwkerk et al reported that most patients would prefer methotrexate over salpingectomy if it were part of a completely nonsurgical management strategy.⁸³ However, in a follow-up study that measured overall health-related quality of life, methotrexate-treated patients reported a higher negative impact on health-related quality-of-life measures than those patients who underwent laparoscopic salpingectomy.⁸⁴ The patients in the methotrexate group reported more limitations in physical functioning, had worse health perceptions, more pain, more physical symptoms, and a worse overall quality of life.⁸⁴ Finally, with methotrexate treatment, delayed tubal rupture occurs in 3%-20% of cases depending on the study population.^{10,79,81}

Methotrexate has a variety of side-effects, including an increase in abdominal pain, which occurs in about 30%-60% of patients who are successfully treated.^{78,85} This is problematic for the emergency physician, because it can be very difficult to distinguish abdominal pain due to methotrexate from pain due to tubal rupture. The presentations may be clinically indistinguishable from each other.⁷⁸ Patients who report abdominal pain following methotrexate treatment for an ectopic pregnancy require an ultrasound examination, a hematocrit, and a gynecologic consultation. If the amount of pelvic fluid on the ultrasound has not significantly increased from that measured before methotrexate treatment was begun and the hematocrit has not significantly fallen, continued methotrexate treatment is a reasonable strategy.⁷⁸ Other side-effects of methotrexate treatment include nausea, vomiting, and diarrhea, which occur in 5%-20% of cases.⁸⁵

Nonviable Intrauterine Pregnancy

A variety of treatment modalities are available for the management of patients with failed intrauterine pregnancies. Emergent surgical evacuation (dilatation and evacuation [D&E]) of the uterus is mandatory in cases of circulatory compromise, persistent heavy vaginal bleeding, a clinically significant fall in the hematocrit, or signs of infection. Other patients may be treated with surgical evacuation, but they also may be appropriate candidates for pharmacological or even expectant management. Factors to consider include the clinical presentation, the gestational age of the pregnancy based on the ultrasound examination, and the patient's preference once the risks, benefits, and alternatives have been explained.

Surgical Approach

Dilatation and curettage (D&C) using a sharp curette was the preferred method of uterine evacuation until the middle of the 20th century, when the D&E with vacuum

evacuation was developed. With vacuum evacuation, a suction cannula is attached to plastic tubing, which is then connected to a vacuum pump. It is thought that the D&E is safer and easier to perform than the sharp D&C. Although both techniques carry the risk of uterine perforation, endometrial infection, and hemorrhage, patients managed with D&E have been shown to have significantly lower intra-operative blood loss, a lower complication rate, less need for analgesia, a shorter operative time, and significantly higher follow-up hemoglobin levels than patients treated with D&C.^{86,87}

Another option for surgical evacuation is manual vacuum aspiration. Manual vacuum aspiration is performed using a 50 cc vacuum-locked syringe attached to a suction cannula. This procedure is appropriate for pregnancies of seven weeks or less in gestational age by ultrasound. Since the typical volume of endometrial material at this gestational age is limited, a smaller-sized cannula is used. The use of the smaller-sized cannula allows a manual vacuum aspiration to be performed with little or no cervical dilation.⁸⁸

Pharmacological Approach

Medical management of the failed intrauterine pregnancy has developed as an offshoot of research on the use of medications, primarily prostaglandin analogs, to induce therapeutic abortions. Prostaglandin analogs work by speeding cervical dilation and initiating uterine contractions, leading to the expulsion of the products of conception. Of the prostaglandin analogs, misoprostol has become the drug of choice because it does not require refrigeration and is less expensive than other comparative prostaglandin agents.⁸⁹ Although the success rate with misoprostol to induce a therapeutic abortion has been reported to be only about 50%, success approaches 90%-95% when the pregnancy is nonviable.^{90,91} The onset of action is reasonably fast, averaging about six hours, and 83% of women treated with misoprostol spontaneously expel products of conception within 12 hours.⁹²⁻⁹⁴ Recent studies have demonstrated that medical management with misoprostol resulted in significantly fewer short-term and long-term complications than surgical evacuation.⁹²⁻⁹⁴

To maximize the likelihood of success, appropriate patient selection is critical. To be eligible for treatment with misoprostol, nonviability and a gestational age of eight weeks or less should be confirmed by ultrasound. Contraindications include maternal anemia, Crohn's disease, and previous adverse reactions to prostaglandins. After the products of conception have been expelled, a follow-up ultrasound is needed to see if there are retained products of conception. Complications associated with misoprostol treatment include vaginal bleeding and crampy pain. For this reason it is reasonable to discharge the patient with a short supply of a narcotic analgesic. Some women experience gastrointestinal discomfort, especially if the misoprostol is given orally rather than intravaginally. It is difficult to accurately time when expulsion of the products of conception will occur;

thus, some women will inconveniently experience this process outside of their home or the hospital. Despite these problems, most women managed with misoprostol find their experience to be acceptable.⁹⁵

Expectant Management

In the past few decades, early pregnancy failure was thought to require surgical intervention. However, recent studies have shown that some women do well with observation alone. In a trial comparing expectant management of nonviable intrauterine pregnancies with surgical management, approximately 80% of those randomly allocated to expectant management had no ultrasonographic evidence of retained products of conception three days after enrollment in the study.⁹⁶ In this study, those patients managed expectantly had a lower overall complication rate than those treated with surgical evacuation (3% vs. 11%).⁹⁶ Expectant management is most successful in very early pregnancy, when the gestational sac is small.^{39,97}

There are a number of drawbacks to expectant management. Women managed expectantly typically experience greater vaginal bleeding than those managed surgically.⁹⁶ In a study by Jurkovic et al, 16% of expectantly managed women failed expectant management and required surgical evacuation.⁹⁷ An additional 1.2% experienced hemorrhages sufficient to require a blood transfusion.⁹⁷ Thus, the expectant approach can be inconvenient and costly because of the need for frequent follow-up visits and repeated ultrasound examinations to ensure that the abortion has progressed to completion. In this study by Jurkovic et al, 58% of the women in the expectant management group requested surgery within 48 days of the original diagnosis.⁹⁷

Threatened Abortion

The management of the patient with a threatened abortion is usually straightforward. The patient should follow up with her obstetrician in one week. Although not evidence-based, it is generally recommended that the patient should refrain from douching or intercourse in order to avoid introducing an ascending infection through an open cervical os.

Special Circumstances

Rh-Negative Patients

Rh isoimmunization may occur in ectopic pregnancy or threatened abortion even without fetal loss. It is typically recommended that the Rh status of all symptomatic pregnant patients be checked regardless of the presumed gestational period and that anti-D immunoglobulin be administered to all Rh-negative patients with vaginal bleeding or threatened abortions.⁹⁸ The ACEP Clinical Policies Committee provided a comprehensive review of the topic of Rh seroconversion in first-trimester pregnancy.¹³ This ACEP committee recommended the administration of anti-D immunoglobulin among women in the first trimester with threatened abortion, complete

abortion, ectopic pregnancy, or minor trauma.

Fertility Treatments

Women undergoing fertility treatments often have multiple pregnancies (i.e., twins, triplets, or more). These women are at much higher risk for heterotopic pregnancy (at least one intrauterine pregnancy and at least one ectopic pregnancy) than women who have become pregnant without fertility treatments. Close consultation with the patient's gynecologist is recommended.

Cutting Edge And Controversies

There are still many questions to be answered regarding the best diagnostic and management approach to women with abdominal pain, vaginal bleeding, or both during early pregnancy.

1. *Who can be safely discharged home from the ED when the initial evaluation is nondiagnostic?* Although excellent progress has been made in this area with regard to incorporating historical features, physical examination findings, β -hCG testing, progesterone testing, and ultrasound findings into risk stratification strategies, there are still many times when the diagnosis is unclear at the conclusion of the ED visit. Further progress in this area would greatly benefit emergency physicians and their patients.
2. *Are there better pharmacological agents being developed to treat ectopic pregnancies?* New drugs and drug combinations are being explored and may be promising. An initial study of mifepristone in combination with methotrexate suggests that the burdensome follow-up period needed with single-drug methotrexate treatment may be shortened by this new drug combination.⁹⁹ Further work needs to be done before this combination can be recommended.
3. *What is the best treatment for nonviable intrauterine pregnancy?* This question has yet to be adequately answered. Each of the management options, including surgical evacuation, pharmacological treatment, and expectant management, is successful in some patients. Better refinement of the patient selection criteria for each of these options would be very helpful to physicians trying to select the best option for a particular patient.

Disposition

Discharge From The ED

Many patients are discharged home from the ED following an evaluation for abdominal pain, vaginal bleeding, or both during early pregnancy. Except for those women undergoing fertility treatments, unless there are other considerations, the following findings support discharge home from the ED with outpatient gynecologic follow-up:

- A viable intrauterine pregnancy by ultrasound
- A nonviable intrauterine pregnancy with minimal

bleeding and a small volume of intrauterine retained products of conception on ultrasound

- An intrauterine gestational sac (normal or abnormal) by ultrasound
- A progesterone level greater than 25 ng/mL
- Crampy, midline, mild pain with an inconclusive ultrasound evaluation
- Hemodynamic stability with minimal or no anemia
- An appropriate rise in β -hCG when a prior β -hCG is available for comparison

Sample discharge instructions have been developed by the American College of Emergency Physicians.¹¹ Key points to emphasize verbally and in written discharge instructions include sensible precautions (e.g., take it easy, do not take medicines without talking to your doctor first, do not put anything into your vagina), the importance of timely follow-up, and circumstances under which the patient should return to the ED sooner (e.g., increased bleeding, passage of tissue or clots, increased pain, nausea/vomiting, weakness or dizziness, or fever).

Gynecologic Consultation From The ED Or Admit

Other patients will require urgent or emergent gynecologic evaluation and treatment. The following findings support prompt gynecologic consultation:

- A history of fertility treatments
- Heavy or persistent vaginal bleeding with anemia
- Ultrasonographic findings diagnostic or suggestive of ectopic pregnancy
- Moderate or large volumes of free fluid in the pelvis on ultrasound examination
- Hemodynamic instability

When the disposition is not clear, initial phone consultation with the patient's gynecologist can help develop an appropriate, coordinated outpatient or inpatient management plan.

Summary

Using simple, readily available tests, the emergency physician can identify the etiology of hemorrhagic shock, intrauterine pregnancies, and risk-stratify women with regard to their likelihood of harboring an ectopic pregnancy. The tools exist to develop reasonably evidence-based, rational, cost-effective strategies for women who present to the ED with abdominal pain, vaginal bleeding, or both during early pregnancy. ▲

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, will be included in bold type following the reference, where available. In addition, the most informative references cited in the paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.

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Physician CME Questions

65. Ectopic pregnancy:

- is defined as the implantation of a fertilized ovum outside the endometrial cavity of the uterus.
- may be more common than is reported because of advances in the diagnosis and treatment of ectopic pregnancy in the past few decades, a substantial decrease in inpatient hospital treatment for ectopic pregnancy, and an increase in multiple outpatient visits for a single ectopic pregnancy.
- usually occurs in the fallopian tube.
- is usually due to mucosal damage, which is usually due to tubal infection.
- all of the above.

66. Heterotopic pregnancy:

- is the simultaneous occurrence of at least one intrauterine and at least one ectopic pregnancy.
- are quite common in naturally occurring pregnancies.
- are relatively rare with ovulation induction and in vitro fertilization as compared to naturally occurring pregnancies.
- can be ruled out by visualization of an intrauterine pregnancy.

67. β -hCG production begins:

- about six days after fertilization.
- about two weeks after fertilization
- about three weeks after fertilization.
- about five weeks after fertilization.

68. Abnormal pregnancies, including ectopic pregnancies, are very likely when the β -hCG is greater than 1000 mIU/mL and a gestational sac cannot be visualized on ultrasound.

- True
- False

69. If a first-trimester pregnant patient presents with abdominal pain or vaginal bleeding but also has no history of passing tissue, a closed os, and a uterus appropriately sized for dates:

- threatened abortion is the most likely diagnosis, and there is a 50% chance she will spontaneously abort.
- inevitable abortion is the most likely diagnosis, and the patient should follow up with her OB/GYN.
- an ultrasound should be performed; if the fetus is > 5 mm without a fetal heartbeat, a nonviable intrauterine pregnancy is likely, but if there is a fetal heartbeat, there is an 85% chance the patient will advance to full term.
- missed abortion is the most likely diagnosis.

70. Because patients frequently mistake blood clots for the products of conception, the passage of true products of conception should not be made by history alone.

- True
- False

71. All of the following are true regarding ovarian torsion except:

- It is likely when there is an abrupt onset of severe, lateralized pain.
- Patients undergoing ovarian hyperstimulation are at less risk for ovarian torsion.
- It is often accompanied by nausea and vomiting.
- The presence of an enlarged ovary along with evidence of markedly decreased or absent unilateral Doppler flow is typically considered diagnostic for ovarian torsion (although color flow may be falsely reassuring in a minority of cases).

72. Which of the following features of a patient's past medical history presents the greatest risk for ectopic pregnancy in a patient in early pregnancy?

- Intrauterine device use
- Prior ectopic pregnancies
- Tubal ligation
- Infertility treatments
- A history of pelvic inflammatory disease

73. Which of the following is/are true regarding abdominal pain in the first trimester?
- Pain originating from the uterus is typically midline and crampy.
 - Pain originating from the adnexa is typically unilateral and sharp.
 - If hemorrhage into the pelvis from an adnexal process has occurred, the pain often becomes bilateral.
 - Pain originating from the bladder is midline in location and often associated with dysuria.
 - All of the above.
74. Which of the following ultrasound results is associated with the greatest risk for ectopic pregnancy?
- Empty uterus
 - Normal sac
 - Abnormal gestational sac
 - Nonspecific fluid
 - Echogenic material
75. All of the following are true regarding the use of methotrexate for confirmed ectopic pregnancy *except*:
- It has been associated with a higher negative impact on health-related quality-of-life measures than laparoscopic salpingostomy in one follow-up study.
 - Delayed tubal rupture almost never occurs with methotrexate.
 - An increase in abdominal pain occurs in 30%-60% of patients who are successfully treated with methotrexate.
 - Nausea, vomiting, and diarrhea occur in 5%-20% of patients treated with methotrexate.
76. Expectant management of nonviable intrauterine pregnancies:
- is not recommended based on the currently available evidence.
 - is least successful in very early pregnancy.
 - is typically associated with less vaginal bleeding than surgical management.
 - can be inconvenient and costly because of the need for frequent follow-up visits and repeated ultrasound examinations to ensure that the abortion has progressed to completion.
77. When a serum β -hCG fails to rise by 66% at 48-hour follow-up, or falls during that interval, which of the following is most likely?
- A viable intrauterine pregnancy
 - A non-viable intrauterine pregnancy
 - An ectopic pregnancy
 - A heterotopic pregnancy

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- 78. Which of the following definitively rules out the possibility of pregnancy?**
- Confirmed prior hysterectomy
 - Reported abstinence
 - Tubal sterilization
 - Any of the above
- 79. About how many patients with an ectopic pregnancy are pain-free at the initial ED presentation?**
- Virtually none
 - About 10%
 - About 50%
 - About 85%
- 80. An adnexal mass is almost always present in cases of tubal ectopic pregnancies.**
- True
 - False

Class Of Evidence Definitions

Each action in the clinical pathways section of *Emergency Medicine Practice* receives an alpha-numerical 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
- Non-randomized or retrospective studies: historic, cohort, or case-control studies
- Less robust RCTs
- 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

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA* 1992;268(16):2289-2295.

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Date of Original Release: This issue of *Emergency Medicine Practice* was published November 1, 2003. **This activity is eligible for CME credit through November 1, 2006.** The latest review of this material was October 1, 2003.

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Emergency Medicine Practice (ISSN 1524-1971) is published monthly (12 times per year) by EB Practice, LLC, 305 Windlake Court, Alpharetta, GA 30022. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. This publication is intended as a general guide and is intended to supplement, rather than substitute, professional judgment. It covers a highly technical and complex subject and should not be used for making specific medical decisions. The materials contained herein are not intended to establish policy, procedure, or standard of care. *Emergency Medicine Practice* is a trademark of EB Practice, LLC. Copyright ©2003 EB Practice, LLC. All rights reserved. No part of this publication may be reproduced in any format without written consent of EB Practice, LLC. Subscription price: \$299, U.S. funds. (Call for international shipping prices.)