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The Practical Guide for Emergency Physicians

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While an emergency department (ED) physician is completing the chart of a young woman treated for community-acquired pneumonia, the nurse presents the clinician the results of the patient's pregnancy test. The nurse says,"It turns out she's pregnant after all. Do we need to do anything different now?" For many patients treated in the ED for common medical disorders who also happen to be pregnant, this is a challenging question. And the answer is "Yes." In many cases, the patient's pregnancy will significantly alter levels of baseline labs, the approach to diagnosis, and selection of therapeutic agents.

In 1999, the world population is projected to reach 6 billion people. According to the U.S. Census, about 8% of women from ages 14 to 44 years were pregnant during 1994, resulting in 3.9 million live births.[1] One study evaluating pregnancy rates of ED patients found that female patients presenting to this clinical environment have a pregnancy rate of around 10%.[2] As an experienced physician knows, diagnosing a patient with an "unexpected" pregnancy is hardly a rare event. Pregnant patients often present to the ED for complications relating to their pregnancy, among them vaginal bleeding, miscarriage, and early labor. But these patients also are at risk for—and suffer from—common diseases that affect non-pregnant individuals. To further complicate ED care of these patients, pregnancy may affect many aspects of a women's physiology, including changes in baseline cardiovascular and respiratory status. Accordingly, ED physicians need to be aware of the impact pregnancy will make on day-to-day diagnostic and management decisions in this patient population.

With these issues in focus, this article reviews the basic alterations of physiology associated with normal pregnancy. Most importantly, the authors present a comprehensive review of ED treatment of a variety of common medical disorders in the context of pregnancy. Disorders discussed in detail include asthma, diabetes, hypertension, pneumonia, deep venous thrombosis (DVT), pulmonary embolism (PE), urinary tract infection (UTI), pyelonephritis, and human immunodeficiency virus (HIV) infection. The authors also summarize approaches to drug therapy in pregnancy and include a discussion of drugs that are and are not safe for use in pregnancy.

— The Editor

The Pregnant Patient: Guidelines for Management of Common Life-Threatening Medical Disorders in the Emergency Department

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Physiologic Changes Associated with Pregnancy

Pregnancy affects virtually every organ system. These changes are designed to accommodate the developing fetus, and

adapt the mother's body to withstand the "growing" metabolic demands of pregnancy as it progresses. These changes also can modify the approach to pregnant women's medical care, inasmuch as baseline "normal" laboratory test levels change throughout gestation. For example, physicians should be aware that alterations occur in arterial blood gas measurements. This may affect care of the pregnant patient with asthma. For example, a woman's ability to tolerate an asthma attack in late pregnancy may be compromised as compared to her response when not pregnant. The following section will review clinically important alterations in a pregnant women's physiology and their effects on baseline laboratory tests. *(See Table 1.)*

Hematology. During pregnancy, plasma volume increases by approximately 33% (450 mL). Benefits associated with this increase include compensation for blood loss associated with delivery and minimizing the effects of gravity and maternal position on fetal circulation. This increase occurs gradually and mirrors the growth of the fetus. However, red cell mass expands at a slightly slower rate, which in turn, produces a dilutional anemia early in pregnancy that can be mistaken for a pathologic process. Survey studies suggest that the mean hemoglobin level in pregnancy is between 10.2 g/dL and 11.6 g/dL.[3] Similarly, serum proteins are also diluted, and the resulting lower colloid osmotic pressure may be responsible for dependent edema. By term, total blood volume increases by an average of 45% above pre-pregnancy levels. The clinical consequences of expanded blood volume may require dosing changes in some medications, inasmuch as an expanded intravascular space can dilute the concentration of such drugs as anticonvulsants and antihypertensive agents.

The white blood cell (WBC) count typically ranges from 5,000/mL to 12,000/mL during pregnancy. This is accompanied by a small left shift, which may confuse the clinical picture when evaluating pregnant women for signs of infection. Some authors also report decreased leukocyte function characterized by decreased chemotaxis and adherence.[4] Whether these changes induce compromised immune function in pregnancy is not conclusively established. It is established, however, that pregnancy affects the coagulation pathway. Although the clotting time of whole blood is unchanged, certain coagulation factors (VII, VIII, IX, and X) are produced at increased levels, thereby shortening prothrombin and partial prothromboplastin times. As a consequence, the risk of thromboembolism in pregnancy is 1.8 fold greater than in the non-pregnant state, and further 5.5 fold in the postpartum period.[3] Finally, the platelet count decreases slightly during pregnancy, and the blood sedimentation rate is markedly elevated from increased fibrinogen levels, which is rendered almost useless as a screening test in pregnancy.

Cardiovascular Alterations. A number of fundamental cardiovascular parameters are altered by pregnancy. These changes help accommodate anatomic alterations and metabolic demands produced by uterine growth and fetal development. In this regard, heart rate, heart size, and stroke volume are increased during pregnancy, especially in its later stages; cardiac output increases by 30-50% to 6.2 L/min.[5] The increase in cardiac work is frequently accompanied by the characteristic systolic murmur of pregnancy. Arterial blood pressure and vascular resistance also decrease during normal pregnancy; the systolic blood pressure decreases 5-10 mmHg, while diastolic pressure decreases 10-15 mmHg as compared to pre-pregnancy levels.[3] A 12% increase in heart size, combined with upward displacement of the diaphragm by an enlarging uterus, produce a larger cardiac silhouette on chest x-ray. The electrocardiogram (ECG) is also affected by a shift in the heart's position, with left-axis deviation being a common finding. Finally, ST-segment and T-wave changes have been reported in 14% of normal pregnant women.[6]

Changes in a woman's posture, especially later in pregnancy, can make a significant impact on her circulatory status. Compression of the inferior vena cava and aorta by an enlarged uterus is exacerbated when the mother is supine and can produce a 25-30% decrease in cardiac output.[7] Placing the patient in the left lateral decubitus will dramatically reduce this effect. This manipulation should be considered when caring for pregnant patients, especially those restrained by cervical spine immobi-

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Table 1. Summary of Laboratory Changes in Pregnancy

LAB TEST	NORMAL RANGE	PREGNANCY EFFECT	GESTATIONAL TIMING
Sodium	135-145 mEq/L	lower 2-4 mEq/L	By midpregnancy
Potassium	3.5-4.5 mEq/L	lower 0.2-0.3 mEq/L	By midpregnancy
Creatinine	0.6-1.1 mg/dL	lower 0.3 mg/dL	By midpregnancy
Creatinine phosphokinase	26-140 U/L	raise 2-4 fold	After labor (mb bands also)
Glucose (fasting)	65-105 mg/dL	lower 10%	Gradual fall
Fibrinogen	200-400 mg/dL	raise 600 mg/dL	By term
Urea nitrogen	12-30 mg/dL	lower 50%	First trimester
Hematocrit	36-46%	lower 4-7%	Nadir at 30-34 weeks
Hemoglobin	12-16 g/dL	lower 1.4-2.0 g/dL	Nadir at 30-34 weeks
Leukocyte count	4000-10,000/mm^3	raise 3500/mm^3	Gradual increase to term (up to 25,000/mm^3 in labor)
Platelets	150,000	400,000/mm^3	slight decrease

Adapted from: Barclay ML. Critical physiologic alterations in pregnancy. In: Pearlman MD, Tintinalli JE, eds. *Emergency Care of the Woman*. New York: McGraw Hill; 1998:303-312.

lization. Venous pressures below the diaphragm are normally increased during pregnancy, a finding that is exacerbated in the supine position. Increased venous pressure can cause dependent edema, venous stasis, varicose veins, and hemorrhoids.

Pulmonary. As pregnancy progresses and the uterus occupies a greater percentage of the abdominal cavity, the diaphragms are progressively elevated. A woman's thorax increases in circumference to compensate, and several baseline respiratory values are changed relative to the non-pregnant state. Tidal volume, alveolar, and minute ventilation are all increased in pregnancy. These changes are perceived by the mother, with 70% of normal, healthy women reporting symptoms of dyspnea in pregnancy.[5] Interestingly, respiratory rate and vital capacity are unchanged. Peak flow rates do not differ between pregnant and non-pregnant healthy women of matched build, even during the third trimester.[8] In general, the pregnant woman is in a state of partially compensated respiratory alkalosis during pregnancy. The PCO_2 is decreased by 10 mmHg to a "normal" pregnant range of about 30 mmHg.[9] Serum bicarbonate is decreased to the range of 18-22 mEq/L, and the "normal" pH in pregnancy is increased to 7.40-7.45.

Knowledge of these alterations in baseline values is important when evaluating blood gas measurements in pregnant women being treated for pneumonia, asthma, or diabetic ketoacidosis (DKA). As a rule, changes in respiratory status can help the mother perform more efficient gas exchange and compensate for additional fetal oxygen consumption. However, the increased gas exchange can lead to problems as well. Hypoxia, hypercarbia, or hypocarbia all occur more rapidly, especially with assisted ventilation. The added fetal oxygen demand and higher affinity of fetal hemoglobin for oxygen can also lead to significant maternal hypoxia, especially when the mother suffers from hypoventilation, regardless of the etiology.

Renal Effects. Pregnancy affects renal anatomy and kidney function in several ways. The expanding uterus compresses ureters in the second and third trimesters of pregnancy, putting the women at increased risk for hydronephrosis. The glomerular filtration rate (GFR) increases by 50% by the second trimester.[10] The increased GFR leads to a decreased level of "normal" creatinine. The normal serum creatinine level in pregnancy is 0.5-0.75 mg/dL. Accordingly, a serum creatinine higher than 1.0 mg/dL is considered abnormal in pregnancy. Drugs excreted primarily by the kidneys (i.e., aminoglycosides and magnesium sulfate) require special attention to dosing in pregnant patients. Impaired tubular reabsorption of glucose and increased GFR lead to glycosuria, which increases risk for urinary tract infection (UTI), including pyelonephritis.

Gastrointestinal Effects. Heartburn is frequent in pregnancy. This symptom is due, in part, to hormonally induced relaxation of the esophageal sphincter and decreased gastric tone, and from higher gastric pressures caused by uterine expansion. Moreover, depressed motility of the small bowel and increased colonic absorption of water can lead to increased complaints of constipation. Cholestasis is increased in pregnancy, and this may be due to reduced contractility of the gallbladder caused by elevated progesterone. The prevalence of symptomatic cholesterol stones is increased in pregnancy, which leads to an increased incidence of cholecystitis in pregnancy. To make matters worse, common surgical disorders such as cholecystitis or appendicitis are more difficult to diagnose in the pregnant patient. In the past, the majority (about 70%) of pregnant patients with cholecystitis were successfully managed medically,[11] in large part because pregnancy was considered a contraindication to laparoscopic treatment. However, at least one recent series suggests laparoscopic intervention is safe and effective in the pregnant patient.[12] Serum albumin decreases to 3.0 g/dL and serum alkaline phosphatase increases up to 400% compared to non-pregnant levels. These changes, along with clinical findings of spider angiomata and palmar erythema caused by increased estrogen levels, may suggest the presence of liver disease, but as a rule they are normal findings in pregnancy.

Asthma

Asthma is a chronic inflammatory disorder of the airways involving many cell types. Susceptible individuals will suffer from wheezing, dyspnea, chest tightness, and coughing.[13] The overall prevalence of asthma in the United States is nearly 5% of the population.[14] Asthma affects about one of every 100 pregnant women,[15] making it the most common respiratory disorder and potentially the most serious disease complicating pregnan-

cy.[16] The precise etiology of asthma is unknown, although genetic and environmental factors seem to be involved. *(See Table 2.)*[14] Extrinsic asthma is thought to be triggered by inhalation of an allergen, and is IgE-mediated. A person is labeled as having intrinsic asthma when no specific allergen can be identified.

Pregnancy alters the course of asthma in the gravid woman in the following way: One-third of pregnant patients experience improvement, one-third remain the same, and one-third experience worsening of their symptoms.[17] There is significant risk to both the mother and child with worsening of asthma symptoms. Asthma was associated with an increased perinatal mortality two times that of controls in one recent study.[18] Moreover, another study noted an increase in complications such as hyperemesis, preeclampsia, and hemorrhage in patients with asthma, as well as an increase in neonatal mortality and premature birth.[19] Encouragingly, another study found no differences in mortality when comparing pregnant asthmatic women who were treated with steroids to those without asthma.[20] These data underscore the importance of aggressive medical management of pregnant patients who present to the ED with acute exacerbations of bronchial asthma.

Table 2. Common Asthma Triggers and How to Avoid Them

TRIGGER	AVOIDANCE
Allergy	Common allergans include dust and mold in the home. Air filtration may be helpful.
Exercise	Get plenty of exercise, but warm up before. Swimming may be preferred to other sports.
Respiratory Infections	Avoid people with colds and flu by avoiding crowded indoor areas in winter when risk of infection is high. Consider influenza and pneumococcal vaccines.
Emotional Stress	Learn to relax and breath properly during an attack. Learn coping skills and stress management techniques.
Lung Irritants	Avoid known irritants. Stay indoors when air pollution is bad. Never smoke and avoid being near smokers.
Weather	Cover mouth with a scarf on cold days.
Drugs	Avoid aspirin, NSAIDS, drugs that contain them.

Adapted from: Mawhinney H, Spector SL. Optimum management of asthma in pregnancy. *Drugs* 1986;32:178-87.

Pathophysiology. As mentioned previously, numerous physiologic and structural changes alter pulmonary function during pregnancy. Hyperemia, hypersecretion, and mucosal edema of the respiratory tract result from increases in circulating estrogen levels. The gravid uterus increases abdominal girth, elevates the diaphragm, and widens the costal angle.[21] Pregnant women experience an increase in tidal volume, a decrease in expiratory reserve volume, residual volume, and functional residual capacity, while vital capacity is unchanged.[22] Alveolar hyperventilation results in a decreased PCO_2 from 34-40 to 27-34 mmHg, which is typically seen by 12 weeks of gestation.[9] As might be expected, the frequency of asthma exacerbations peaks around the sixth month of gestation;[23] the most severe symptoms occur between the 24th and 36th weeks.[24]

Briefly, the pathophysiology of asthma includes the following: 1) contraction of airway smooth muscle resulting in increased airway resistance; 2) increased mucus secretion with small airway obstruction; 3) hyperinflation of the lungs with increased residual volume; and 3) bronchial hyperreactivity caused by histamine, prostaglandins, and leukotrienes. Mast cell degranulation appears to trigger the asthma cascade and results in the release of chemical mediators, which lead to increased airway resistance and bronchospasm. In the case of pregnancy, respiratory alkalosis cannot be maintained in the face of reduced ventilation, and acidosis develops. Because of the baseline changes in arterial blood gas values in pregnancy (decreased PCO_2 and increased pH), it is important to realize that a PCO_2 of 38- 40 mmHg and pH of 7.38-7.4 in a symptomatic pregnant patient is evidence that normally expected alveolar hyperventilation is no longer being maintained. A patient with these arterial blood gas values is at significant risk for maternal hypoxemia, subsequent fetal hypoxia, and respiratory failure.

Presentation. The pregnant patient presenting with an exacerbation of asthma may complain of dyspnea, productive or nonproductive cough, and/or a tight chest. Symptoms tend to be worse at night and may be preceded by allergic rhinitis or a viral illness. On physical exam, the patient typically has an increased respiratory rate, a rapid pulse, and elevated blood pressure. Auscultation of the chest reveals diminished breath sounds, wheezing, rhonchi, and a prolonged expiratory phase. In addition, the patient may be utilizing accessory muscles. Recalling that "all that wheezes is not asthma," the differential diagnosis should include acute bronchitis, vocal cord dysfunction, pulmonary embolism, and congestive heart failure.[14] Although rare, peripartum cardiomyopathy can produce new onset congestive failure that is accompanied by wheezing and dyspnea. These patients often have no history of previous symptoms of heart failure and the diagnosis can be missed if not considered.

Management. Leukocyte count with differential may show eosinophilia, and pulmonary function tests consistent with an obstructive pattern may be seen. A hand-held peak flow meter may be used in place of spirometry. The chest x-ray may be normal, it may demonstrate hyperinflation, or reveal complications such as pneumonia, pneumothorax, or pneumomediastinum.[14] Clearly, the possible deleterious effects to the fetus are a concern when ordering roentgenograms in the pregnant woman. However, recent data indicate that x-ray doses used in clinical radiography (30-100 millirads for a single film) are below the level at which statistically significant increases in

fetal anomalies arise (> 5 rad). Nevertheless, abdominal shielding is recommended as it reduces external scatter of radiation.[25]

Management of the pregnant asthmatic in the ED includes administration of oxygen to maintain a PaO_2 a level greater than 60 mmHg or 95% O_2 saturation. Inability to maintain PO_2 higher than 60 mmHg is an indication for intubation and for possible emergency delivery if the fetus has developed to a viable stage.[26] In all patients with significant symptoms, baseline arterial blood gases and pulse oximetry should be performed. In patients with significant symptoms and potentially viable pregnancies (gestational age > 24 weeks), fetal monitoring (ideally in the form of a continuous heart monitor) is mandatory. The presence of abnormal fetal heart patterns (heart rate > 160 bpm or < 120 bpm) require emergent obstetrical consultation. Because formal pulmonary function tests are impractical or unavailable in the ED, peak expiratory flow rates should be measured and followed for improvement. Beta-agonists such as albuterol should be administered via a nebulizer up to every 20 minutes for up to three doses. Alternatively, for patients who experience difficulty with inhaled medications, terbutaline 0.25 mg may be injected subcutaneously every 20-30 minutes as needed for a total of three doses. Epinephrine may be injected subcutaneously 0.1 mg to 0.3 mg of a 1:1,000 solution in patients who are failing initial therapy.

If the patient's peak expiratory flow rate returns to 70% of normal, she may be discharged to home. Patients with severe disease may be given a short course of oral corticosteroids (40 mg q day or 20 mg po bid for 5 days) in consultation with their obstetrician. If the peak flow is less than 70%, the patient should be hospitalized, continued on beta agonists, and methylprednisolone should be initiated at a dose of 80 mg every six hours. A peak flow rate below 25% or a PCO_2 greater than 35 mmHg is indicative of respiratory failure and warrants intensive care unit admission, and if indicated, intubation.[27] Other signs indicating the need for hospitalization include persistent tachycardia (> 120 bpm), respiratory rate higher than 30 /min, or if the patient is unable to walk unaided for short distances in the ED.

Fortunately, most pregnancies complicated by asthma are uneventful. However, poorly controlled asthma requiring inpatient admission carries an increased risk of prematurity and low birth weight.[28] Other fetal complications of uncontrolled asthma include increased risk of perinatal death, intrauterine growth retardation, pre-term birth, and low birth weight.[16] In addition, uncontrolled asthma and maternal hypoxia may result in fetal hypoxia. Conditions associated with uncontrolled asthma such as hypertension, hypocapnia, alkalosis, and dehydration may reduce uteroplacental blood flow, thereby further reducing fetal oxygenation.[29]

Management of asthma during pregnancy with the possible exception of oral steroid therapy, does not differ significantly from that of the nonpregnant population.[14] The mainstay of prophylaxis is inhaled corticosteroids. In one study, inhaled steroids resulted in a 75% reduction of asthma exacerbations compared to the control group.[30] Rescue therapy still requires a beta-agonist. Additional therapies, among them, cromolyn, nedocromil, long-active beta-2 agonists, theophylline, leukotriene antagonists, and ipratropium bromide, have been used without evidence of adverse outcomes on pregnancy.[14] Although steroids may be used in severe cases, one study found these agents may increase the risk of preeclampsia.[31] While routinely used for outpatient treatment of non-pregnant patients, use of oral steroids should not be initiated for outpatient management without discussing this treatment plan with the patient's obstetrician. ED physicians must be cautious when prescribing medications in the pregnant patient. As a rule, pregnant patients are concerned about potential, drug-related effects on their baby and look to their obstetrician for approval before taking medications. Accordingly, the ED physician should not hesitate to contact the patient's obstetrician for advice on medications. Disposition from the ED should include educating the patient about avoiding potential asthma triggers such as allergens, exercise, infection, emotional stress, lung irritants, weather changes, and certain medications.[15]

Hypertension

Hypertension is one of the most common complications of gestation, affecting almost 10% of all pregnancies in the United States.[32] Fetal complications include intrauterine growth retardation, fetal death in utero, and premature delivery. Adverse maternal outcomes, which are similar to those in the non-gravid population, include stroke, heart disease, and renal failure.[33] Worldwide, hypertensive disorders are responsible for 15-20% of maternal deaths.[33]

Although pregnancy is characterized by an increase in cardiac output and expanded blood volume,[34] the gravid woman undergoes such marked vasodilatation that the mean arterial pressure typically falls by approximately 10 mmHg.[35] As seen in Table 1, the definition of hypertension in pregnancy is a blood pressure higher than 140/90 mmHg. The American College of Obstetricians and Gynecologists (ACOG) has classified hypertensive disorders into four broad categories: preeclampsia-eclampsia; chronic hypertension; chronic hypertension with superimposed preeclampsia; and transient hypertension.[36] Table 3 lists precise definitions of each of these four types of hypertension encountered in pregnancy.

Preeclampsia. The clinical hallmark of preeclampsia includes the classic triad of hypertension, edema, and proteinuria.[32] In preeclampsia, elevated blood pressure is defined as a systolic blood pressure increase of 30 or more mmHg over average readings which were obtained before 20 weeks gestation, or an increase of 15 mmHg or greater in diastolic blood pressure compared to early or pregestation measurements. If baseline pressures are not known, a systolic blood pressure of 140 mmHg or a diastolic blood pressure of 90 mmHg is sufficient to meet the criteria for preeclampsia. This classification scheme defines proteinuria as 30 mg per dL, ("1+") on a dipstick urine, or greater than 300 mg in a 24-hour urine collection. Edema is defined as 1+ pedal edema that fails to resolve with rest; facial or hand edema; or weight gain exceeding 2 kg in a one-week period.[32]

Risk factors associated with preeclampsia include nulliparity, extremes of reproductive age, a family or personal history of preeclampsia, a previous diagnosis of hypertension, renal disease, diabetes mellitus, multiple gestations, hydatidiform mole, and hydrops fetalis.[32,37]

The etiology of preeclampsia is currently debated. One theory proposes that preeclampsia is related to defective implantation of the placenta with subsequent placental hypoperfusion.[38] The placenta releases substances that, in turn, induce the vascular endothelium to produce procoagulants, vasoconstrictors, and mitogens.[38] Pathologic changes seen in the brain, heart, and liver of patients with preeclampsia mimic the changes seen in hypovolemia, indicating that hypoperfusion rather than hypertensive vascular injury may be responsible for the clinical finding in preeclampsia.[37,39] Other theories include imbalances of prostacyclin and thrombaxane, immunologic abnormalities, increased vascular reactivity to vasoactive agents, and genetic variations of the angiotensinogen gene. To date, no one theory has been proven conclusively.[38]

Maternal complications of preeclampsia include convulsions, cerebral hemorrhage, placental abruption with disseminated intravascular coagulopathy, pulmonary edema, renal failure, liver hemorrhage, and death.[40] The HELLP Syndrome (hemolysis, elevated liver enzymes, and low platelet count) may occur with hepatic ischemia and intravascular coagulation.[41] Complications of preeclampsia are the second leading cause of maternal death in pregnancies beyond 20 weeks.[42] In the fetus, preeclampsia may cause growth retardation, hypoxemia, acidosis, prematurity, and death.[40]

In addition to the classic triad of hypertension, edema, and proteinuria, the preeclamptic patient may present with a multitude of constitutional signs and symptoms. She may have visual changes, tinnitus, headache, tachycardia, nausea, vomiting, hematemesis, and oliguria.[41] On physical exam, the blood pressure should be noted and compared to pregestational or early gestation measurements. The blood pressure should also be measured in the sitting position after five minutes of rest.[43] In addition to maternal vital signs, the fetus should be monitored for signs of distress. Other findings on physical exam may include hyperreflexia, diplopia, hepatomegaly, and edema.[41]

Multiple laboratory findings are associated with preeclampsia, although there is no single test that serves as a reliable early indicator. Uric acid levels are typically elevated (greater than or equal to 5 mg per dL). A complete blood count (CBC) may be useful for detecting thrombocytopenia. The hematocrit increases with preeclampsia, but may actually decline if hemolysis develops. A peripheral smear may demonstrate schistocytes. Other supporting labs include an elevated lactate dehydrogenase level, an elevated transaminase level, a rising serum creatinine, hypoalbuminemia, and prolonged prothrombin and activated partial thromboplastin time.[44]

When possible and appropriate, definitive and curative therapy for preeclampsia is delivery of the fetus.[37] Consequently, any ED patient in whom preeclampsia is considered a possible diagnosis will require urgent obstetrical consultation. Specific indications for delivery include imminent eclampsia, multiorgan dysfunction, fetal distress, or gestational age beyond 34 weeks.[45] Some researchers have described protocols for expectant management of the preeclamptic patient at less than 34 weeks of gestation.[40]

Other therapies that should be initiated in the ED include blood pressure control and careful monitoring of fluid status. Parenteral hydralazine has traditionally been used in pregnancy and is considered safe and effective for management of preeclampsia.[46] A 5 mg bolus of hydralazine is initiated followed by 5-10 mg every 20-30 minutes to achieve a goal systolic pressure of 130-150 mmHg and a diastolic pressure of 90-100 mmHg.[32, 47] If hydralazine is ineffective, a second agent may be required. Labetalol or nitroprusside may be used. Angiotensin-converting enzyme (ACE) inhibitors should not be used in pregnancy because serious fetal side effects (i.e., renal damage) are possible. Fluid intake should be limited to 100 cc per hour. If pulmonary edema or oliguria develops, a pulmonary artery catheter may be placed to monitor hemodynamic status.[32]

Although a comprehensive discussion outlining management of eclampsia is beyond the scope of this review, seizure prophylaxis is an integral part of preeclampsia management.[48] Magnesium sulfate is the drug of choice, a loading regimen consisting of a 6 gram bolus given over 30 minutes, followed by 2 grams per hour continuous infusion is recommended.[40] The serum target range for magnesium is a level of 4-7 mEq/L (from a baseline of around 2 mEq/L).

Exceeding this target range will put the woman at serious risk for magnesium toxicity so levels should be monitored closely. Clinical findings of toxicity include loss of deep tendon reflexes (around 10 mEq/L) and, ultimately, respiratory depression and cardiac arrest (> 13 mEq/L). Because the magnesium ion functions as a weak calcium channel blocker, the treatment for magnesium "overdose" is 1 gram of calcium gluconate IV over 2 minutes. Because delivery of the fetus is frequently the definitive treatment for the preeclamptic woman, consultation with an obstetrician is critical and should be initiated early in the patient's care.

Table 3. Classification of Hypertension During Pregnancy

Chronic Hypertension: Hypertension (BP > 140/90 mmHg) that is present and observable before pregnancy or that is diagnosed before the 20th week of gestation. Hypertension diagnosed for the first time during pregnancy and persisting beyond the 42nd day postpartum.

Preeclampsia-eclampsia: Increased blood pressure accompanied by proteinuria, edema, or both of which usually occur after 20 weeks gestation (or earlier with trophoblastic diseases such as hydatidiform mole or hydrops).

PREECLAMPSIA SUPERIMPOSED

On Chronic Hypertension: Chronic hypertension (defined above) with increase in blood pressure (30 mmHg systolic, 15 mmHg diastolic, or 20 mmHg mean arterial pressure) together with the appearance of proteinuria or generalized edema.

Transient Hypertension: The development of elevated blood pressure during pregnancy or in the first 24 hours postpartum without other signs of preeclampsia or preexisting hypertension (a retrospective diagnosis).

Adapted from: National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol* 1990:163(5 Pt 1):1691-1712.

Chronic Hypertension. Chronic hypertension in pregnancy may be diagnosed if the patient has a history of hypertension before pregnancy, has persistently elevated blood pressures greater than or equal to 140/90 mmHg before 20 weeks gestation, or persistent hypertension beyond 42 days postpartum.[37] Chronic hypertension complicates approximately 2-5% of all pregnancies.[31] The cardiovascular changes of pregnancy have been described earlier. Peripheral vasodilatation may lead to a drop in blood pressure during pregnancy, thus masking hypertension in a patient previously diagnosed with this condition. Between 15% and 20% of chronic hypertensives will develop superimposed preeclampsia, which is diagnosed by quantitative urine protein measurement, assessing for edema, and monitoring previously mentioned labs. Patients with chronic hypertension carry a three-fold increased risk for placental abruption and subsequent maternal hemorrhage.[49] In patients with superimposed renal insufficiency, there is a higher incidence of preeclampsia, preterm delivery, and fetal growth retardation.[50] Fetal complications include fetal growth restriction, as well as higher mortality rates, primarily due to the increased incidence of superimposed preeclampsia.[33, 51]

Chronic hypertension usually is detected from routine vital signs, although the patient with severe hypertension may present with signs and symptoms attributable to end organ damage. The differential diagnosis includes preeclampsia, superimposed preeclampsia, and secondary hypertension. The most common forms of secondary hypertension are the result of renal disease, renovascular disease, hyperaldosteronism, Cushing's syndrome, and pheochromocytoma.[33]

When evaluating a pregnant patient with chronic hypertension, several physical findings and laboratory tests may direct the course of therapy. The physical exam should include appropriate blood pressure measurements as previously described, a fundoscopic examination, chest auscultation, and a survey for renal artery bruits. Coarctation of the aorta is a rare but potentially serious problem that needs to be considered in this patient population.[52] Laboratory tests should include a metabolic panel to assess renal function and glucose. Persistently elevated serum glucose with fluctuating blood pressure warrants an assay for urine vanillylmandelic acid and metanephrines to rule out pheochromocytoma. Urinalysis should be performed to assess for proteinuria. A 24-hour urine collection may be necessary to measure creatinine clearance. A chest x-ray and electrocardiogram may be necessary if heart failure is suspected.[52]

When deciding whether to treat elevated blood pressure, the emergency physician must evaluate and weigh the maternal risks vs. fetal risks of drug exposure. Consultation with the patient's obstetrician is advised to assist in making this decision. Current guidelines recommend treatment if the diastolic blood pressure exceeds or equals 100 mmHg. If renal disease or other end organ damage is present, then treatment should be initiated if the diastolic pressure is 90 mmHg.[32] The most widely used antihypertensive drugs for pregnant patients are methyldopa and hydralazine. Once the maximum dose of methyldopa (4 grams per day) and hydralazine (400 mg per day) have been reached, a third agent may be added. Labetalol, atenolol, and nifedipine are recommended options.[52] Propranolol, thiazide diuretics, and angiotensin converting enzyme inhibitors should not be used due to potential adverse maternal and fetal side-effect profiles.[53]

Pneumonia

Pneumonia is the most common non-obstetric infectious cause of death during pregnancy and the puerperium.[54] In the pre-antibiotic era, maternal mortality due to pneumonia was as high as 32%,[55] but use of antibiotics has reduced this rate to as low as 3.5%.[56] However, immunocompromised states associated with HIV, the increased incidence of drug use, and postponed childbearing may be contributing to the recent increase in the number of cases of pneumonia complicating pregnancy.[57]

While the frequency of pneumonia in the pregnant patient is similar to that in the nongravid population, multiple respiratory, physiological, and mechanical changes, along with alterations in cellular immunity, make the gravid woman more susceptible to pulmonary insults.[57] As discussed previously, the gravid uterus elevates the diaphragm and widens the costal angle. An increase in the transverse diameter of the chest makes clearing respiratory secretions more difficult and further aggravates airway obstruction from pulmonary infections.[58] Diminished functional residual capacity associated with pregnancy is accompanied by a 20% increase in oxygen consumption that makes brief periods of hypoxia difficult to tolerate.[59] Immunologically, there is a diminished lymphocyte proliferation response, decreased natural killer cell activity, and decreased numbers of helper T-cells.[60] While these changes in immunity do not necessarily place the pregnant woman at greater risk for infection, they may make viral and fungal pneumonias more virulent.[61]

Pathophysiology. Pathogens causing pneumonia in pregnant women are similar to those encountered in the general population. Two-thirds are bacterial in nature, with *Streptococcus pneumoniae* being the most common organism.[61] Patients typically present with complaints of fever, chills, pleuritic chest pain, cough productive of purulent or blood-tinged sputum, and dyspnea.[57] On physical exam, the patient may have dullness to percussion, tactile fremitus, and egophany.[61] Adjunctive tests include a complete blood count with differential, a chest x-ray, sputum gram stain with culture, and blood cultures.[57] The second most common bacterial pathogen is *Haemophilus influenza*. This gram-negative bacillus is more likely to occur in patients with chronic illness, smokers, and in patients with influenza infection.

Klebsiella pneumoniae may develop in immunocompromised patients and cause abscess formation. *Staphylococcus aureus* is a potential pathogen when the patient is recovering from influenza.[61.] Atypical organisms, such as *Mycoplasma, Legionella,* and *Chlamydia* cause pneumonias which have a gradual onset with antecedent myalgias, headaches, and low grade fevers. The cough is more non-productive, but sputum produced may be more mucoid than purulent. Chest x-ray demonstrates interstitial patchy infiltrates rather than lobar consolidation. Adjunctive tests include complete blood count, serum cold agglutinins, and titers for suspected pathogens.[57]

The most common viral pneumonia is influenza, typically type A.[61] The patient may complain of malaise, headache, fever, chills, cough, and other upper respiratory symptoms.[61] The

physical examination may not elicit typical findings of pneumonia. Adjunctive tests include a chest x-ray, which may show a unilateral patchy infiltrate.[61] Of potential concern is the development of bacterial superinfection with *Staphylococcus aureus, Haemophilus influenzae, pneumococcus,* or gram-negative organisms.[61] In addition to influenza, *varicella* is a potential etiologic agent in pneumonia in the gravid patient. In fact, pneumonia more often complicates *varicella* infection in pregnant patients as compared to the general population.[62] It occurs most frequently during the third trimester and develops approximately five days after the appearance of the typical rash of varicella. In addition to the skin lesions, the patient may present with oral lesions, dyspnea, cough, pleurisy, and malaise. The chest x-ray may demonstrate patchy infiltrates.[61]

Other potential pathogens include *Pneumocystis carinii, Mycobacterium, Cryptococcus, Coccidioides immitis,* and *Blastomycoses*. *Pneumocystis carinii* pneumonia (PCP) is the principal cause of pregnancy-associated AIDS death in the United States.[61] Patients with PCP may present with fever, tachypnea, dyspnea, and nonproductive cough. Adjunctive tests include an arterial blood gas which shows a decrease in PO_2 and respiratory alkalosis, and a chest x-ray which demonstrates bilateral alveolar disease. Sputum silver stains are diagnostic.[61] While uncommon, varicella pneumonia carries grave risk for both mother and child, with a maternal mortality reported to be as high as 35%.[3] The key to the diagnosis is appearance of pneumonia symptoms 2-5 days after the onset of varicella fever and rash. Because of the high potential for mortality, any pregnant woman with varicella pneumonia requires hospitalization and treatment with acyclovir.[57]

Management. Pregnant patients presenting to the ED with respiratory complaints should have a thorough history, including immunization history and documentation of previous immunity to *varicella*. The social history should address habits such as smoking, alcohol abuse, drug abuse, high-risk sexual behaviors, occupational history, and travel history.[57] The medical history should address chronic medical conditions, including heart disease, asthma, bronchitis/pneumonia, anemia, and immunocompromising conditions such as HIV, hemoglobinopathies, renal disease, and advanced age. The practitioner should also ascertain whether the patient is undergoing chemotherapy or taking other immunosuppressive agents.[57]

The differential diagnosis of upper respiratory complaints in the gravid female includes dyspnea of pregnancy, pneumonia, bronchitis, asthma, pulmonary embolism, pneumothorax, pulmonary edema, congestive heart failure, and hyperventilation. Management of the patient includes antimicrobials as indicated, as well as supportive care and careful monitoring of maternal and fetal health. Obstetrical consultation is advised for each of these steps. Pre-term labor has been reported in women with pneumonia. While disagreement continues to persist regarding the need for hospitalization, some authors would recommend inpatient admission for all pregnant women with a radiographically confirmed pneumonia.[63.] Given the fact that leading researchers recommend parenteral antibiotics, hospitalization becomes a logical choice for patient care.[57] Other factors to guide one's decision to admit include severity of illness and comorbid factors. Certainly, no pregnant women with pneumonia should be sent home without consulting her obstetrician.

Bacterial pneumonia, as well as viral pneumonia complicated by bacterial superinfection, should be treated with correct spectrum antibiotics. A second- or third-generation cephalosporin, combined with erythromycin or intravenous azithromycin, will cover most anticipated pathogens as well as atypical organisms. Gram-negative and anaerobic coverage using an aminoglycoside or clindamycin, respectively, may be added as clinically indicated.[57] Penicillins, cephalosporins, erythromycin, azithromycin, and clindamycin have no known harmful effects on the fetus. However, gentamicin poses a risk of ototoxicity and nephrotoxicity to both the mother and the fetus.[64] A beta-lactam with a beta-lactamase inhibitor, third-generation cephalosporin, or an anti-pseudomonal antimicrobial may be added for nosocomial pneumonias.[64]

Published reports have described use of amantadine and ribavirin for treatment of influenza pneumonia, with successful outcomes and no evidence of teratogeny.[65] Pregnant patients with PCP should be treated with trimethoprim-sulfamethoxazole, a category "C" drug. (See section on drugs in pregnancy on page 69).

Because trimethoprim is a folic acid antagonist, folate supplementation should be given. Sulfamethoxazole has the potential to cause kernicterus if given near the time of delivery.[61]

Supportive measures include supplemental oxygen, chest physiotherapy, and beta agonist breathing treatments if reactive airway disease is also present. The head of the bed should be elevated, and positional changes should be encouraged. Adequate control of fever is also recommended. Beyond 24 weeks gestation, the fetus should be continuously monitored. Maternal fluid status and electrolytes should be followed closely, and intubation should be performed as clinically indicated. Delivery should occur for obstetric purposes only.[57]

Maternal outcomes have improved dramatically since the aggressive use of antibiotics. Complications in the gravid female are similar to those of the general population, including respiratory distress necessitating intubation, empyema, and pneumothorax. Comorbid illness and underlying risk factors may dictate severity of disease and subsequent complications.[61] Similarly, poor fetal outcomes are associated with comorbid medical illness in the mother. Premature labor and fetal death have been documented as complications of maternal pneumonia with a frequency ranging from 4% to 44%.[61] These data do not account for the unknown effects of specific microorganisms, medications, fever, and hypoxia.

Deep Venous Thrombosis

Venous thromboembolism (VTE) is another leading cause of maternal morbidity and mortality in pregnancy, accounting for 14% of all maternal deaths from 1980-1985.[66] VTE is five times more likely to occur during pregnancy when compared to a nonpregnant woman of similar age,[67] with some authors suggesting VTE occurs in 1 in 1000 to 1 in 2000 pregnancies.[67] Evidence suggests that VTE is more likely to occur postpartum than in the antepartum period, and that the risk is higher in patients who have undergone cesarean section vs. vaginal delivery.[68] Other risk factors for VTE include history of VTE, instrumentation during delivery, bedrest, obesity, advanced maternal age, multiparity, and blood abnormalities. These include presence of

Table 4. Guidelines for Anticoagulation in Pregnancy

PREGNANT:

1. Baseline lab values: CBC, PT, PTT.
2. Heparin loading dose: 80 U/kg (or 5000 U) IV bolus.
3. Continuous heparin infusion of 1300 U/hr for DVT and 1500 U/hr for PE.
4. Check PTT every 6 hours and adjust infusion to maintain PTT between 1.5 and 2.5 times the patient's baseline.
5. Rebolus with 5000 U heparin if PTT is not prolonged and increase rate of infusion.
6. Repeat PTT every 6 hours for first 24 hours, then check daily unless outside of therapeutic range.
7. Check platelets every day or every other day for first 10 days of heparin to monitor for heparin-induced thrombocytopenia.

POSTPARTUM:

Heparin therapy as above including:

1. Begin warfarin (Coumadin) therapy on the first day of heparin treatment at 5 mg to 10 mg daily.
2. Check the PT daily and adjust dose to maintain INR between 2.0 and 3.0.
3. Stop heparin after INR of 2.0 to 3.0 is reached for 4 to 7 consecutive days.
4. Continue oral anticoagulation for 3 months to maintain INR of 2.0 to 3.0.

Adapted from: Rutherford SE, Phelan JP. Deep venous thrombosis and pulmonary embolism in pregnancy. *Obstet Gynecol Clin North Am* 1991;18:345-370.

antiphospholipid antibody, activated protein C resistance, antithrombin III deficiency, myeloproliferative disorders, paroxysmal nocturnal hemoglobinemia, deficiency of protein C or protein S, homocystinemia, hyperprothrombinemia, and dysfibrinogenemia.[69]

Pregnancy is a risk factor for venous thrombosis, as each element of Virchow's triad (stasis, endothelial damage, and hypercoaguability) is present.[67] Physiologic increases in venous distensibility and capacitance lead to increased stasis, which is exacerbated by compression of pelvic vessels. Endothelial damage occurs during delivery, as the placenta separates, or during surgery. Hypercoaguability in pregnancy is caused by an increased concentration of coagulation factors, especially factors II, VII, X, and fibrin. *(See Table 4.)* Concomitantly, there is a decrease in protein S, a coagulation inhibitor. This is accompanied by inhibition of the fibrinolytic system, which is greatest during the third trimester.[67]

Pregnant patients who present to the ED with suspected DVT may complain of leg discomfort and ankle swelling, which are also encountered as part of pregnancy. Accordingly, one should inquire about risk factors. On physical exam, the affected lower extremity may be tender and swollen with a 2 cm increased circumference relative to the unaffected limb.[70] DVT usually begins in the deep proximal veins and has a predilection for the left leg during pregnancy.[71] Homan's sign is present in less than one-third of patients with DVT.[67] Other signs suggestive of DVT include a palpable cord, change in limb color, or cool extremities.[70]

Diagnosis. The differential diagnosis for DVT includes a number of musculoskeletal disorders, as well as superficial thrombophlebitis, impaired venous or lymphatic flow, and Baker's cyst. [67] Because pregnant patients are at increased risk for DVT and because this diagnosis is virtually impossible to confirm from a history and physical alone, any pregnant patient with complaints suggestive of a DVT should have an imaging study performed. Noninvasive imaging such as duplex Doppler scanning is the preferred initial test for the diagnosis of DVT. When performed by an experienced practitioner, sensitivity approaches 98% for detecting symptomatic calf or proximal DVT with a 95% specificity.[72] Iliac vessels may be difficult to visualize in the presence of a gravid uterus, so comparison with the unaffected leg is useful. Repeating the Doppler exam in 2-3 days has also proven useful for detecting thrombi not previously visualized.[70] Impedance plethysmography (IPG) has a sensitivity of 95% and specificity of 98% for detecting proximal vein thrombi.[73] IPG records changes in electrical resistance caused by venous volume changes in the involved limb.[70]

Venography has been the standard against which other imaging studies are evaluated for their usefulness in detecting DVT. Nevertheless, the majority of physicians prefer duplex Doppler scanning for obvious reasons. Venography is a technically difficult, invasive exam associated with potential side effects from the contrast dye, such as pain, swelling, tenderness, and erythema;[70] these symptoms can simulate the presence of a DVT. In addition, DVT may be a complication of venography. And while duplex Doppler scanning and IPG are considered safe to maternal and fetal health, venography carries small, but potential risks associated with radiation exposure to both the mother and the fetus.[70] However, it should be stressed that the amount of radiation required for routine venography has not been associated with adverse fetal outcomes.[67]

From a practical, radiation exposure perspective, venogram of one extremity exposes the fetus to 0.3 rad; exposure to the fetus of less than 5 rad has not been associated with fetal abnormalities. Advantages of venography include the ability to detect calf and proximal iliac clots, which may be missed by Doppler study. Most experts recommend either serial Doppler study or venography in a woman with an initially negative Doppler and a high clinical suspicion of DVT.[67-70] Serial Doppler studies are typically performed 2-7 days following the initial exam. Proponents of this approach argue that this will prevent pregnant women from getting potentially unnecessary antigcoagulation; the disadvantage is that a patient with a DVT may have treatment withheld until a second study yields the diagnosis.

Pulmonary Embolism

When evaluating a pregnant patient for DVT, the diagnosis of PE should also be considered. The classic symptoms of PE include shortness of breath and pleuritic chest pain. Additional symptoms include cough and hemoptysis. On physical exam, the patient may appear tachypneic and apprehensive. Chest auscultation may reveal crackles, an increased pulmonic second heart sound, and a pleural friction rub. The differential diagnosis includes asthma, dyspnea of pregnancy, pneumonia, bronchitis, pulmonary edema, congestive heart failure, and pneumothorax.

Although a discussion of diagnostic testing for PE follows, some clinicians argue that in some situations treatment without a confirmed diagnosis of PE may be acceptable. In other words, a patient with chest pain who has newly diagnosed DVT may be assumed to have a pulmonary embolism and managed clinically without additional testing.

Usually, however, adjunctive testing will be necessary to make the diagnosis of PE, as well as to rule out other causes of dyspnea. The arterial blood gas (ABG) may reveal a diminished PO_2 of more than 85 mmHg, or widened alveolar-arterial gradient (> 20 mmHg). While up to 20% of patients with PE will have normal ABG readings (20% have a PO_2 > 80 mmHg), a much smaller percentage will have a normal A-a gradient.[74] During the third trimester, the ABG should be obtained in the sitting position, as the PO_2 may be lowered by as much as 15 mmHg when obtained from the patient in the supine position.[67] As pregnancy changes the baseline pulmonary physiology, ABG testing may be even more important in "sicker" patients to obtain data on their oxygenation and carbon dioxide retention. In contrast, ABG screening may not be necessary in healthy appearing patients in whom PE simply needs to be "ruled out"; these patients can proceed directly to VQ scan.

The most common abnormality noted on electrocardiogram is tachycardia; however, right axis shift, T-wave inversion, and the classic $S_1Q_3T_3$ pattern, though rare, may be present.[70] A shielded chest x-ray is necessary to rule out pneumonia and pulmonary edema, and can also be used to interpret ventilation-perfusion (VQ) scans if performed. Nonspecific abnormalities such as atelectasis, pleural effusion, and elevation of the hemidiaphragm may be present in up to 80% of patients.[67] Lastly, although D-dimer levels may be sensitive for diagnosis of PE in non-pregnant patients, their use in pregnant patients has not been evaluated.

The most important screening test for PE in the pregnant patient is the VQ scan. A high probability scan is sufficient to warrant treatment.[69] A normal or near normal scan excludes the diagnosis of PE. Unfortunately, most patients with a PE have a VQ scan interpreted as low or intermediate probability for PE. These patients must then undergo the more invasive pulmonary angiography. Patients should be reassured that the amount of radiation exposure from the combined chest x-ray, VQ scan, and angiography is less than the amount of exposure associated with adverse fetal outcomes.[67] Disadvantages of VQ scan include the time required for the test (2-3 hours) and the potential difficulty of obtaining the test in a timely manner during the middle of the night. Chest CT scan is another alternative to the VQ scan, but specific data in pregnant patients are lacking compared to non-pregnant populations.

The issue of additional radiation exposure from chest CT is also of concern. Advantages however, include the fact that CT is usually easier to obtain than a VQ scan and takes much less time to perform. Newer technology of helical CT, and CT angiography are even more accurate that standard CT scan but still may miss more distal (smaller) emboli. The accuracy of CT angiography also depends on the quality of the bolus contrast injection. More information about the use of CT scanning for the diagnosis of PE can be found in a recent review.[75] Radiation exposure can be of concern to expectant mothers undergoing testing in the ED, and one can reassure the patient that VQ scans are considered safe in pregnancy.[76] Exposure to less than 5 rad per year is considered safe in humans, and a chest CT will expose the patient to between 2 and 5 rad. For reference, an abdominal film will expose the patient to between 0.9 rad and 2.2 rad, depending on the size of the patient. New generation CT scans have very focused beams with minimal scatter, and shielding of the abdomen during the study will protect the fetus from nearly all radiation exposure.

Management. A pregnant patient with suspected pulmonary embolism or a clinically evident DVT warrants hospitalization, anticoagulation, and supportive care in consultation with the patient's obstetrician.[67] Supplemental oxygen should be provided to reverse hypoxia and maintain a PO_2 of more than 60 mmHg. Intubation criteria are similar to those given for asthma, with intubation indicated for inability to maintain adequate fetal oxygenation (i.e., PO_2 of < 60 mmHg) or for uncontrolled rising maternal PCO_2. Patients with hypercapnia and obtundation may require intubation with mechanical ventilation. Fluid resuscitation and pressors such as dopamine may be required to maintain adequate blood pressure (systolic pressure > 80 mmHg), with the realization that uterine blood flow may be compromised. Narcotic analgesics should not be withheld.[67]

Only pregnant patients with life-threatening manifestations of PE (i.e., a large PE with hypoxia and hypotension) should be treated with a fibrinolytic agent such as tissue plasminogen activator.[68, 77] There are currently no data on the risk of placental abruption or potential injury to the fetus. These agents are contraindicated post partum secondary to bleeding complications. Other contraindications include recent surgery, bleeding disorders, and marked hypertension.[69] Emergency thoracotomy and embolectomy may be beneficial as a last-ditch effort for critically ill patients, but this procedure is beyond the purview of most ED physicians. It should be stressed, however, that when a pregnant patient near term (> 34-36 weeks) does arrest, emergency C-section offers the only chance of survival for the fetus and greatly increases the effectiveness of CPR in the mother.

Anticoagulation for DVT and/or PE should be initiated with heparin, generally adhering to the same recommendations as for nonpregnant patients. Heparin is relatively safe during pregnancy as it does not cross the placenta. Some studies have been done evaluating heparin in pregnancy that support its safety.[68,70] An initial bolus of 80 units/kg is followed by a continuous infusion of 18 units/kg of heparin per hour intravenously. The activated partial thromboplastin time (aPTT) is measured every six hours for the first two days of therapy, and adjustments in heparin infusion are made to keep the aPTT between 1.5 and 2.5 times the patient's baseline.

After 5-7 days of intravenous heparin, therapy throughout the remainder of pregnancy consists of 2-3 subcutaneous injections of heparin daily, with dosing being adjusted based on the aPTT. Subcutaneous heparin should be discontinued with the onset of regular uterine contractions. Protamine sulfate may be administered if the aPTT is greater than 2.7 times the control. Thrombocytopenia is a well-known side effect of heparin administration, and therefore a baseline platelet count is necessary. Platelet counts should be monitored daily or every other day during the first 10 days of therapy.[79] Up to one-third of women on long-term heparin therapy suffer from reduction in bone density.[68]

Low molecular weight heparin (LMWH) has proven to be effective in preventing and treating DVT, and has been used in at least one small study of six women; no complications were reported and effective DVT prevention was confirmed in these patients.[80] A more extensive study is required to establish safety of LMWH use in pregnant patients. However, in support of LMWH use, data indicate that it does not cross the placenta; LMWH has less heparin-induced thrombocytopenia, and in the case of enoxaparin, can be given as a once-daily injection. Oral warfarin therapy may be initiated safely in the postpartum period, but not during pregnancy.[67] Warfarin is a known teratogen, causing nasal hypoplasia, stippled epiphyses, and central nervous system abnormalities. In addition, because warfarin crosses the placenta, the fetus is at increased risk of neonatal hemorrhage during delivery.[68] A final option for treatment is a Greenfield filter. Use of this filter has been reported in pregnant patients to prevent PE.[81] Newer, removable filters are being tested currently in non-pregnant patients and may provide treatment alternatives in the future.[82]

Urinary Tract Infection

Pathophysiology. The three most common forms of urinary tract infections in pregnant women can be characterized as asymptomatic bacteriuria, cystitis, and pyelonephritis. While most urinary tract infections in pregnancy are asymptomatic, it should be stressed that maternal and fetal complications can occur in the absence of symptoms. Furthermore, normal physiologic changes of pregnancy increase the maternal risk for development of pyelonephritis and its associated complications. As early as the seventh week of gestation, dilation of the renal pelvis and ureters occurs, resulting in hydroureter, which progresses until term.[83] The right collecting system is affected more than the left because of to the drop of the right ureter into the pelvic cavity.[84]

Throughout gestation, the kidneys increase in length by one centimeter, and the bladder changes position, becoming an abdominal rather than a pelvic organ.[85] Elevated progesterone levels facilitate smooth muscle relaxation, resulting in bladder expansion and diminished ureteral peristalsis.[86] There are also data to suggest that the physiologic and anatomic effects of estrogens in pregnancy may increase the virulence of E. coli.[87] Diminished renal concentrating ability may decrease the natural antibacterial properties of urine.[83] Other risk factors for urinary tract infections in pregnancy include a history of recurrent urinary tract infections, an anatomic abnormality in the urinary tract, neurogenic bladder, diabetes mellitus, lower socioeconomic status, multiparity, sexual intercourse, and sickle cell trait.[88]

Organisms causing urinary tract infection are derived from normal perineal flora and affect both pregnant and nonpregnant patients. Most organisms grown in culture are coliforms, with *E. coli* being the most common, followed by *Klebsiella* and *Enterobacter* species, as well as *Proteus mirabilis*.[89] Occasional gram-positive organisms have been isolated.[88] Recent data demonstrate uropathogenic strains of *E. coli* which predominate in pregnant women.[90]

Asymptomatic Bacteriuria. Asymptomatic bacteriuria is defined as persistent bacterial colonization of the urinary tract without urinary tract symptomatology.[86] The prevalence of asymptomatic bacteriuria is 5-10%, which is the same for pregnant and nonpregnant women.[91] The gravid woman with bacteriuria, however, is at increased risk for developing pyelonephritis. This complication occurs in up to 20-30% of untreated gravid women.[86] In addition, asymptomatic bacteriuria has been associated with preterm delivery and low birth weight.[86] Diagnosis is typically confirmed by detection of greater than 100,000 colony-forming units of a single organism per milliliter of urine on culture, although some authors also recommend treatment with lower colony counts (20,000-50,000).[92] Gram staining is reported to be the best, most rapid screening test available with a 90% sensitivity and 88% specificity rate, but it can be technician dependent.[93] In many obstetric offices, urine cultures are typically the diagnostic test of choice, inasmuch as a routine urinalysis is inadequate to diagnose infection of the urinary tract during pregnancy.[94] Newer, rapid-culture techniques have been advocated, but none have become widely accepted as good screening tests.[86] In the ED, it is recommended that physicians use a catheterized specimen to help guide treatment. Cultures can be sent, but only they are of practical value if follow-up on culture results is obtained. Many EDs have personnel dedicated to this task, but another option is to communicate with the patient's obstetrician that tests have been sent to assure follow-up. Treatment of asymptomatic bacteriuria is essentially the same as that for cystitis.

Cystitis. Cystitis presents as dysuria, hematuria, urinary frequency, urgency, and suprapubic discomfort; a positive urine culture with absence of pyelonephritis symptoms is characteristic.[86] Cystitis complicates 0.3-1.3% of pregnancies.[95] Because many of the symptoms of cystitis can be encountered in pregnancy without the presence of infection, the urine culture remains the gold standard for diagnosis.[86] As mentioned above, ED physicians should rely on a urinalysis by catheterization in combination with clinical symptoms to diagnose cystitis in these patients. Pathogens isolated in cystitis are similar to those recovered in asymptomatic bacteriuria.[95] However, a patient with symptoms of cystitis and a "sterile" urine culture should be evaluated and/or treated for *Chlamydia trachomatis* infection. A single dose of 1 gram of azithromycin has been shown to be effective for uncomplicated *Chlamydia* infection in pregnancy.

Much effort has been focused on evaluating single dose therapy vs. three-day and 7- to 10-day courses of antibiotics for asymptomatic bacteriuria and cystitis. Approximately 70-80% of patients have elimination of bacteriuria after 7-10 days of antibiotics. The efficacy rates are similar for three-day courses of antimicrobials[88] or single-dose treatment. Although single dose therapy has showed promising results, some authors recommend further study to evaluate this treatment duration.[86,96] Regardless of length of therapy, appropriate follow up to document eradication of bacteriuria is essential.[88]

Historically, ampicillin and amoxicillin have been used because they have proven safe in pregnancy and achieve high urinary concentrations. However, ampicillin resistance to *Escherichia coli* has approached 30% in the United States.[97] Cephalexin 250 mg to 500 mg four times daily for 3-7 days has been advocated. Cephalexin costs around $0.60 per 250 mg, but resistance to *Enterococcus* can be up to 90%.[98] Cephalosporins along with penicillin have a well-documented risk of anaphylax-

is. Nitrofurantoin 100 mg four times daily has extensive use during pregnancy but poses a risk of hemolytic anemia in patients with glucose-6-phospate dehydrogenase deficiency. In addition, nitrofurantoin costs around $1.50 per 100 mg and resistance of up to 20% by organisms causing cystitis has been reported.[99] Sulfisoxazole 500 mg, four times daily is another option but should be avoided near term secondary to risks of hyperbilirubinemia. Trimethoprim is relatively contraindicated in the first trimester due to its antifolate properties.[86,88] Trimethoprim/sulfisoxazole costs roughly $0.40 per tablet and resistance has been reported to be in the 30% range.[99] As bacterial resistance can vary by geographic region, becoming educated about resistance rates reported in one's area of practice is advised.

A follow-up urine culture should be performed one week following therapy for asymptomatic bacteriuria or cystitis. Approximately 20-30% of pregnant patients will have another positive urine culture requiring an additional 7-10 days of therapy with a different antibiotic. A second treatment failure would require adjunctive testing for a structural abnormality.[88] Eradication of a persistent or recurrent infection may require suppressive dosing throughout the remainder of pregnancy.[88] Unlike asymptomatic bacteriuria, there are no data to suggest cystitis increases the risk of preterm delivery and low birth weight.[86]

Pyelonephritis. Acute pyelonephritis complicates 1-2% of all pregnancies. It is more common after midpregnancy and occurs unilaterally in more than 50% of cases; the right side is affected more than the left. The infectious agent usually ascends from the lower urinary tract and contains p-fimbriae adhesins in 75-90% of cases.[100] Widespread screening and treatment of asymptomatic bacteriuria has led to a dramatic decline in the incidence of pyelonephritis from 4% to approximately 1%.[95] In addition to cystitis-like symptoms, patients with pyelonephritis may present with fever, chills, flank pain, nausea, and vomiting.

On physical examination, there is often costovertebral angle tenderness. A striking aspect of fever in these patients is its labile nature, with fevers as high as 107°F, rapidly followed by hypothermia (down to 93°F).[101] These findings are thought to result from bacterial endotoxins. Adjunctive tests include urinalysis and urine culture. Presumptive diagnosis must be made, however, without the urine culture as results take 24 hours and emergent treatment is indicated. One to two bacteria per high power field in an unspun urine specimen, or 20 bacteria per high power field in a spun urine specimen correlates with 100,000 colony-forming units per milliliter on urine culture. White cell casts confirm the diagnosis but are not always present. Blood cultures are not always indicated, as isolated organisms are typically the same as in the urine culture.[86]

Nearly all pregnant patients with pyelonephritis are dehydrated because of fever and emesis; therefore, fluid resuscitation should be initiated. A subset of patients will develop sepsis syndrome with diminished cardiac output despite adequate fluid resuscitation, and vasopressors may be required. Endotoxins, which alter the alveolar-capillary permeability membrane, may lead to pulmonary edema and respiratory insufficiency in 2-8% of pregnant patients with pyelonephritis.[102] Patients with this complication are typically tachypneic, tachycardiac, and febrile. Arterial blood gas will reveal hypoxemia, and the chest x-ray will show pulmonary edema and, possibly, adult respiratory distress syndrome. Fluid overload and the use of tocolytics worsen this clinical scenario. Careful monitoring of fluid balance and supplemental oxygen should be instituted. Respiratory distress requires intubation and mechanical ventilation to prevent fetal hypoxia.[86]

Another complication of antepartum pyelonephritis is renal dysfunction. It is usually transient, occurs in 25% of cases, and resolves over several days.[86] Serum creatinine levels should be monitored and nephrotoxic antibiotics should be avoided or adjusted appropriately.[86] Pyelonephritis may be associated with preterm delivery and low birth weight, but the strength of such an association is not confirmed.[86] Most clinical symptoms resolve after the first two days of therapy. Urine cultures typically become sterile within 24 hours of initiating antibiotics. Nevertheless, 30-40% of patients suffer relapse or reinfection. Monthly urine cultures may be indicated to prevent recurrence of pyelonephritis. In addition, suppressive therapy with nitrofurantoin, 100 mg each night, may prevent recurrent disease.[92]

Traditionally, the gravid woman with pyelonephritis has been admitted to the hospital for parenteral antibiotics, supportive care, and monitoring. This practice has been called into question over the last several years, with some studies advocating outpatient treatment for selected patients.[103] A randomized, controlled trial demonstrated that outpatients receiving intramuscular ceftriaxone and inpatients receiving intravenous cefazolin had similar rates of persistent or recurrent bacteriuria and recurrent pyelonephritis.[86] Nevertheless, currently established therapy consists of intravenous antibiotics continued 1-2 days after the patient is afebrile, followed by a one- to two-week course of oral antibiotics. As with ampicillin, first-generation cephalosporins are compromised by an increasing antimicrobial resistance rate. Consequently, the addition of an aminoglycoside to ampicillin or a third-generation cephalosporin has been advocated. Many physicians question the role of aminoglycoside therapy due to concerns of maternal nephrotoxicity and fetal ototoxicity.[86] Clinical trials have demonstrated the efficacy of ceftriaxone, which is preferable due to its once-daily dosing, monotherapeutic efficacy, and safety profile.[104]

Diabetes Mellitus

Approximately 3-5% of all pregnancies are complicated by diabetes mellitus (DM). Most of these cases are attributed to gestational diabetes, while a half percent are secondary to previously diagnosed Type I and Type II diabetes mellitus.[105] Type I diabetes (insulin dependent) is usually diagnosed before the age of 30 and is characterized by a deficiency of insulin. Type II diabetics are typically older than 40 years old and overweight. Their disease process involves peripheral resistance to insulin, increased hepatic production of glucose, and a relative pancreatic insufficiency of insulin production.[106] Even though these patients typically do not require insulin, all diabetics are "brittle" during pregnancy and therefore, Type II diabetics should be converted to an insulin regimen during pregnancy. Another form of diabetes occurs secondary to various medical disorders.[107] Most obstetricians follow the White Classification of diabetes in pregnancy. This classification describes the severity of diabetes and its manifestations.[108] *(See Table 5.)*

The increased insulin resistance in pregnancy is due, in part, to secretion of human placental lactogen and placental growth hormone.[107] Patients using insulin before pregnancy may note a

Table 5. White Classification of Diabetes in Pregnancy

CLASS	DESCRIPTION
A	Abnormal glucose tolerance test, but asymptomatic or normal glucose achieved with diet control
B	Adult-onset diabetes (> age 20 yr) and short disease duration
C	Youth-onset diabetes (age 1-19 yr) or relatively long disease duration (10 to 19 years)
D	Childhood onset (< age 10 yr), very long disease duration (> 20 yr), or evidence of background retinopathy
E	Any diabetes with evidence of vascular disease in the pelvis (diagnosed by plain films)
F	Any diabetes with the presence of renal disease
R	Any diabetes with the presence of proliferative retinopathy
RF	Any diabetes with both renal disease and proliferative retinopathy
G	Any diabetes with a previous history of multiple pregnancy losses
H	Any diabetes with atherosclerotic heart disease
T	Any diabetes postrenal transplantation

Adapted from: Hare JW. Gestational diabetes and the White Classification. *Diabetes Care* 1980;3:394.

doubling of their insulin requirements during pregnancy. In addition, elevated levels of circulating estrogen, progesterone, and prolactin may diminish peripheral sensitivity to insulin during pregnancy.[109] Other complicating factors include increased body weight, increased fat deposition, higher caloric intake, and diminished physical activity, all of which decrease insulin sensitivity during a "normal" pregnancy.[107] However, in patients with Type I diabetes, hypoglycemic reactions are common during the first trimester.

In gestational diabetes, the increased demand for insulin cannot be met by endogenous production. The onset of gestational diabetes (or at least its recognition) occurs during pregnancy in patients without previous diagnosis of Type I or Type II diabetes.[110] Overall, gestational diabetes is 10 times more common than Type I and Type II diabetes combined.[107] Risk factors for gestational diabetes include history of a previous pregnancy complicated by gestational diabetes, a history of large-for-gestational-age infant, obesity, age older than 30 years, and a family history of Type II diabetes. In addition, certain ethnic groups, including Native Americans, African Americans, and Hispanic Americans, are at increased risk for developing gestational diabetes.[107] Furthermore, up to half of all patients with gestational diabetes will develop Type II diabetes later in life.[105] The American College of Obstetrics and Gynecology recommends that all pregnant women between 24 and 28 weeks gestational age be screened for diabetes.

Fetal Effects

Poor glycemic control during pregnancy is linked to fetal complications, as well as to poor maternal outcomes. Perhaps the most well known complication is fetal macrosomia. Maternal hyperglycemia leads to fetal hyperglycemia secondary to passive diffusion of nutrients across the placenta. Excessive fetal insulin production then causes increased fetal fat deposition.[111] Macrosomia increases the risk of birth asphyxia, shoulder dystocia, brachial plexus injury, fracture of the clavicles and humerus, and increases the need for forceps delivery and cesarean section. [107] Between 30% and 50% of neonates born to diabetic mothers will go on to develop neonatal hypoglycemia (serum glucose less than 40 mg/dL) secondary to elevated endogenous insulin levels and abrupt discontinuation of maternal nutrient supply.[112] Other neonatal complications include respiratory distress syndrome, neonatal hypocalcemia, and hyperbilirubinemia, all of which are linked to poor glycemic control.[107]

Congenital malformations occur at 2-4 times the expected frequency in diabetic mothers, especially in those with poor glycemic control at conception and throughout the first trimester.[113] Consequently, most of these birth defects are seen in Type I and Type II diabetics rather than in patients with gestational diabetes. The most common anomalies are ventricular and atrial septal defects, transposition of the great vessels, neural tube defects, gastrointestinal atresias, and urinary tract malformations.[107] In addition, there is an association between first trimester spontaneous abortion and diabetic pregnancies.[104] The mechanism for these complications is unclear, but may be related to hyperosmolality, ketosis, disruption of glycolysis, DNA glycosylation, oxygen free radicals, cell membrane lipid peroxidation, and inhibition of growth factors.[107]

Maternal Effect

Other medical complications of pregnancy appear to be more common in diabetics. Pre-term labor may be seen in up to 30% of diabetic pregnancies.[115] Hypertensive disorders, including preeclampsia and eclampsia also are more common in diabetes, especially in pregestational diabetics who may already have vasculopathies and renal insufficiency.[107] ED physicians are frequently the first clinicians to diagnose diabetes, and a high-risk obstetric team should be consulted when this occurs. Unfortunately, many of the birth defects described occur so early in pregnancy that complications may have already developed by the time pregnancy is diagnosed. Nevertheless, encouraging strict glycemic control can improve long-term outcomes.

Regardless of the presenting symptom, a careful history should be obtained, including last menstrual period, obstetric history, gynecologic history, medical history, medications and diet. Glucometer readings should be assessed, and the review of systems should identify any illness which may worsen glycemic control. On physical examination, vital signs must be reviewed, and the patient's mental status addressed, since fluctuations in serum glucose may alter sensorium. Fetal heart tones should be assessed, and careful documentation of the fundal height and uterine size recorded, given the propensity for macrosomia. Laboratory studies should include a serum glucose and other appropriate tests depending on the presenting complaint. If DKA is suspected, serum ketones should be drawn, and an arterial blood gas performed to evaluate acid-base status.[105]

Diabetic Ketoacidosis

As might be expected, insulin-dependent pregnant patients are at higher risk for DKA, which complicates about 2% of pregnancies in insulin-dependent patients.[116] Although maternal mortality is low, fetal mortality ranges from 50% to 90% in DKA.[117] Patients without diabetes often become ketotic during early pregnancy as a result of hyperemesis gravidarum, and hyperemesis is often a trigger for DKA. It should be stressed that the "normal" pH of pregnancy is mild alkatosis, so the patient in DKA may have a pH of near 7.40 but still be in DKA. Also, a pregnant patient is defined as hyperglycemic with a serum glucose reading of only 200 mg/dL. Thus, the criteria for diagnosis of DKA in pregnancy are much more strict than in a non-pregnant patient. In general, DKA is treated with ICU admission, insulin, fluids, and volume monitoring. However, fetal heart rate monitoring is recommended starting at gestational age of 12 weeks, and beyond 24 weeks continuous fetal and uterine monitoring are advised. Although uterine contractions are commonly seen in DKA, they ordinarily do not result in delivery if the pregnancy is not near term. Therefore, tocolytic drugs should not be used without evidence of significant cervical dilation.

Disposition

The criteria for admission of pregnant patients with complications of diabetes should be emphasized. Hyperemesis gravidarum predisposes pregnant patients with diabetes to DKA and significant risk of fetal death. If a patient is unable to eat and drink adequately, the possibility of hypoglycemia should be considered. Consequently, any pregnant diabetic with hyperemesis should be admitted. As in non-diabetics, significant ketosis increases the risk of neurologic defects in the fetus. Any pregnant diabetic who cannot clear their ketosis with IV fluids in the ED should also be admitted. As many of the congenital defects seen in the children of diabetics arise from derangements in organogenesis (first trimester), diagnosis of pregnancy in a diabetic patient who is not under adequate glycemic control (abnormal serum glucose is > 200 mg/dL) should also be considered for admission. As diabetic pregnancies are, by definition, high-risk pregnancies, the ED physician should consult obstetric colleagues when caring for these patients. Many centers have a high-risk team to care for pregnant diabetics, which includes primary providers, endocrinologists, nutritionists, and social workers. Contact with consultants should be done to assure follow-up any time pregnant diabetics present to the ED and are discharged. Finally, educating diabetic patients about their disease process, including preconception counseling, is critical to improving both maternal and fetal outcomes.

Human Immunodeficiency Virus

An unfortunate reality of the HIV epidemic is infection in the pregnant woman. Nearly 25% of cases of acquired immunodeficiency syndrome (AIDS) occur in women, of which 85% are in their childbearing years.[118,119] To make matters worse, many HIV-infected women are unaware of their serostatus.[120] Vertical transmission of the virus occurs in 25-59% of deliveries if the mother is untreated.[111] This type of transmission of the HIV virus accounts for around 1800 HIV-infected babies born each year in the United States.[121] Accordingly, perinatal transmission accounts for the majority of HIV-1 infections among U.S. children.[122]

One of the relevant questions concerning vertical transmission is: How is the virus passed from mother to child? The bottom line is that although all of the risk factors are not thoroughly understood, a lower CD4 count and higher viral load in the mother increase the risk of viral transmission.

Several aspects of precipitous deliveries in HIV-positive mothers are relevant to emergency practice. For example, episiotomies and use of scalp electrodes in routine deliveries should be avoided in the ED setting unless clinically indicated, as they may play a role in transmission of the virus. Likewise, breast feeding in known HIV-positive mothers also should be avoided. Zidovudine (AZT) treatment in pregnancy has been shown to reduce rates of vertical transmission from 25% to only 8%.[123] Although relatively little data are available, use of AZT in pregnancy has not been associated with any specific congenital abnormalities. Therefore, all pregnant women seen in the ED with HIV infection not already taking AZT should be encouraged to discuss AZT use with their OB-GYN.

Often a patient will be seen in the ED, and their HIV status will be in question. There are several clinical presentations that should alert the ED physician to consider HIV infection. Recurrent sinusitis, bronchitis, or pneumonia in an otherwise young, healthy patient is one presentation. Unexplained weight loss or fever, herpes zoster, nonhealing genital ulcers, oral thrush, and chronic vaginal candidiasis are all known to be associated with HIV infection as well. Abnormal blood cell counts such as neutropenia or thrombocytopenia also raise the possibility of HIV infection. HIV screening tests should be offered to all pregnant women, although the test need not necessarily be ordered in the ED. When an HIV test is ordered in the ED, it is useful to notify the OB consultant who will be following the patient. The ED physician should also be aware that in 1993, the CDC expanded the definition of AIDS to include the following: CD4 count higher than 200/mm^3 (or < 14% total lymphocytes), pulmonary tuberculosis, recurrent bacterial pneumonia (> 1 episode in 1 year), and invasive cervical cancer. Pregnant patients presenting with any of the above scenarios should also be evaluated for HIV infection.

Table 6. Recommended Prophylactic Regimens for Pregnancy in HIV Patients

ALL PATIENTS:
• Pneumococcal vaccine (0.5 mL IM as a one time dose)
• Yearly influenza vaccine (0.5 mL IM)
• Isoniazid for patients with positive TB test, TB history, or chest x-ray evidence of previous TB (300 mg po daily for 12 months)
PATIENTS WITH CD4 COUNT < 200 MM^3:
• Trimethoprim/sulfamethoxazole for *pneumocystis carinii* pneumonia (1 single strength po daily)
PATIENTS WITH CD4 COUNT < 50 MM^3:
• Azithromycin for *Mycobacterium avium* complex (1200 mg po weekly)

Table 7. Disorders that May Present as Hyperemesis Gravidarum

CAUSES OF INCREASED VOMITING ASSOCIATED WITH PREGNANCY

- Hydatidaform mole
- Multiple gestations
- Pregnancy-induced hypertension
- Placental abruption

CAUSES OF VOMITING NOT ASSOCIATED WITH PREGNANCY

- Appendicitis
- Cholelithiasis
- Pancreatitis
- Hepatitis
- Thyrotoxicosis
- Bowel obstruction
- Peptic ulcers
- Diabetic ketoacidosis
- Increased intracranial pressure
- Pyelonephritis
- Medications

Adapted from: Hod M, Orvieto R, Kaplan B, et al. Hyperemesis gravidarum: A review. *J Reprod Med* 1994;39:605-612; Cosmas JM. Nausea and vomiting in early pregnancy. In: Pearlman MD, Tintinalli JE, (eds). *Emergency Care of the Woman.* New York: McGraw Hill; 1998:49-56.

When a pregnancy is confirmed in an HIV-positive woman in the ED, or in a patient strongly suspected of having HIV, the following maternal screening tests should be ordered: CD4 count, assay for viral load, CBC, liver function tests, tuberculin skin testing, chest x-ray, serology for toxoplasmosis and cytomegalovirus, as well as testing for other sexually transmitted diseases. Pap smears should also be done as there is an increased incidence of cervical dysplasia in HIV-positive patients. The ED physician should also be aware of the currently recommended prophylactic regimens for pregnant HIV-positive patients. *(See Table 6.)*

As mentioned above, it is recommended that all HIV-positive, pregnant patients take AZT for prophylaxis against transmission of the virus to their child. When a pregnant patient presents to the ED in labor, and is known to be HIV infected, the following additional steps are recommended. If the patient is in active labor or has had spontaneous rupture of membranes, and the patient is not enrolled in a clinical trial, the patient should be given AZT in a 2 mg/kg bolus dose followed with a 1 mg/kg/hr continuous infusion. Amniotomy, episiotomy, and scalp electrodes should not be routinely used unless clinically indicated to limit the exposure of the baby to maternal secretions. Obviously, urgent consultation with obstetric colleagues is mandatory. Lastly, infection with HIV also predisposes the mother to greater morbidity and mortality from common bacterial infections associated with childbirth and the postpartum period. Many authors recommend routine use of prophylactic antibiotics for childbirth in HIV-positive patients; as HIV treatments change frequently, the obstetric consultant should be asked for guidelines in this area.

Hyperemesis Gravidarum

While not a condition of non-pregnant women, nausea and vomiting of pregnancy and hyperemesis gravidarum affect a large number of pregnant women and generate many ED visits. Nausea and vomiting of pregnancy is characterized by the typical "morning sickness" seen early in pregnancy, but also affects some women more in the afternoon or evening than the morning. It complicates 50-90% of all pregnancies.[124] Although reoccurring daily in many cases, this type of vomiting is normally self-limited. Less commonly, intermittent vomiting will persist throughout a pregnancy.

Nausea and vomiting of pregnancy begins around the 4th to 6th week of gestation, peaks around week 8 to 12, and usually ends around the 20th week. In contrast, vomiting of hyperemesis is prolonged and intractable, and is associated with dehydration, ketonemia, electrolyte abnormalities, metabolic alkalosis, and weight loss of 5-10% of the patient's pre-pregnancy weight. Compared to nausea and vomiting of pregnancy, hyperemesis affects only 2% of pregnancies.[125] Even though not as many patients are affected, the majority of them require multiple ED visits and admissions during the course of the pregnancy. One study found a readmission rate of 27% in 140 women with diagnosis of hyperemesis.[126]

Risk factors reported for hyperemesis include multiple gestations, previous spontaneous miscarriage, and history of hyperemesis.[127] Hyperemesis also occurs more frequently in first pregnancies. Because nausea and vomiting of pregnancy are self-limiting and rarely require intervention other than rehydration, reassurance, and advice on avoiding nausea, this section will focus on a discussion of hyperemesis gravidarum.

Etiology. Many factors have been suggested and investigated as a cause of hyperemesis, but to date no clear mechanism has been elucidated. Beta-hCG levels and other hormonal factors, as well as metabolic, toxic, and psychosocial factors have all been proposed as contributing factors in many cases. Beta-hCG levels have been suggested as a cause of hyperemesis, as the incidence is higher in patients with multiple gestations and molar pregnancies. One author found 26% of patients with molar pregnancies also had hyperemesis.[128] In addition, the peak of nausea and vomiting roughly coincides with peak levels of beta-hCG in the 6th to 12th week of pregnancy. Despite these facts, comparisons of measured beta-hCG levels in patients with and without hyperemesis yield conflicting results. Some authors report a correlation,[129] while others do not.[130]

Levels of other hormones, including cortisol, estrogens, progesterone, prolactin, growth hormone, and follicle stimulating hormone, have been evaluated and do not show any abnormal levels in patients with hyperemesis.[127] Up to 66% of patients with hyperemesis will have evidence of increased thyroid function,[131] with some exhibiting transient clinical thyrotoxicosis. It appears that beta-hCG itself causes the increase in T4 in these patients,[132] although the significance of this finding is not yet clear. In addition, many women with hyperemesis also have an acquired vitamin B6 deficiency.[133] Again the significance of this fact in the cause and effect relationship of hyperemesis remains unclear. One recent article suggested a possible link between presence of *H. pylori* infection and hyperemesis; treatment of the infection resulted in resolution of symptoms.[134] Lastly, psy-

Table 8. Drugs Considered Safe in Pregnancy[151]

PAIN MEDICATIONS
Acetaminophen
Propoxyphene (Darvocet)
Codeine—can lead to addiction and newborn withdrawal if used excessively

ASTHMA MEDICATIONS
Theophylline
Terbutaline
Cromolyn Sodium
Beta-adrenergic agonists (albuterol, isoproterenol, metaproterenol)
Corticosteroids—do cross the placenta, inhaled to a much lesser degree

ANTIBIOTICS
Penicillins
Cephalosporins (except cefaclor, cephalexin and cephradine)[152]
Sulfonamides (except in 3rd trimester)
Sulfamethoxazole/trimethoprim (controversial in 1st trimester)
Nitrofurantoin (Macrodantin—will not treat bacteremia)
Antituberculosis drugs
Erythromycin (except erythromycin estolate Ilosone)
Clindamycin

ANTIVIRALS
Acyclovir
Zidovudine (AZT)

ANTIFUNGALS
Imidazoles (clotrimazole or miconazole—except in 1st trimester)

ANTICOAGULANTS
Heparin (data with low molecular weight heparin is limited)

ANTICONVULSANTS
Phenytoin, valproic acid, and carbamazepine are all associated with defined malformation syndromes but many physicians feel benefits for the mother outweigh risks to the fetus. Do not prescribe without OB or neurologist recommendation.

ANTIEMETICS*
Promethazine (Phenegran)
Proclorperazine (Compazine)
*Stress other remedies first (crackers in a.m., frequent small meals, etc.)
Ginger (shown better than placebo)
Metoclopramide (Reglan)

DECONGESTANTS*
Diphenhydramine (Benadryl)
*Nasal sprays absorbed less than po medications

ANTIHYPERTENSIVES
Methyldopa (Aldomet)
Hydralazine (Apresoline)
Atenolol (Tenormin)

GASTROINTESTINAL DRUGS
H2 blockers:
Ranitidine (Zantac)
Famotidine (Pepcid)
Sucralfate (Carafate)

ANTIDEPRESSANTS
Amitriptyline (Elavil)
Fluoxetine (Prozac)

WOUND CARE
Lidocaine

chological factors including immaturity, chemical dependency, depression, and hysteria have all been suggested as causative factors. As with other theories, the disagreement in the literature on the relationship of psychological factors and hyperemesis remains today. The most recent articles suggest they play a role, but are not causative.[135]

Diagnosis. Patients with hyperemesis will have clinical signs of dehydration. Dry mucus membranes, poor skin turgor, and orthostatic signs and symptoms are often present. Along with these findings, they often have a variety of electrolyte and laboratory abnormalities. These include elevated hematocrit, elevated blood urea nitrogen (BUN), hyponatremia, hypokalemia, ketonuria or ketonemia, and metabolic alkalosis with paradoxical aciduria. Accordingly, appropriate lab tests in patients suspected of hyperemesis include a CBC, serum electrolytes, BUN, creatinine, urinalysis, and serum ketones. Mild changes in liver enzymes and bilirubin may also be found in some patients.

There are many disease states which, initially, can present in a similar fashion to hyperemesis, and therefore, can lead to misdiagnosis. Hence, diagnosis of hyperemesis in the ED can be considered one of exclusion. Table 7 provides a list of conditions that should be considered in the differential diagnosis of hyperemesis. Although the association with twins, molar pregnancies, and hyperemesis is well known, it is easy to overlook these as an underlying cause. The presence of a molar pregnancy carries a risk for the mother and making the diagnosis early can reduce this risk. An abnormally high beta-hCG for a particular stage of pregnancy can be a clue that one of these conditions is present, but an ultrasound will be needed to rule them out.

Many gastrointestinal disorders also can be confused with hyperemesis. As pain is not often a part of hyperemesis, any right upper or lower quadrant pain should prompt an evaluation for cholecystitis or appendicitis. Additional laboratory tests should be ordered in patients in whom pancreatitis or hepatitis is considered. As stated above, hyperemesis can produce mild elevations in liver enzymes but not the dramatic elevations as typically seen in acute hepatitis. Likewise, amylase and lipase may be slightly elevated in hyperemesis but not to the degree typically seen in acute pancreatitis. Although transient thyrotoxicosis may be seen in hyperemesis, any patient with these findings will require admission to ensure it is indeed transient. Any diabetic patient with symptoms of hyperemesis needs admission as DKA and hypoglycemia are common complications. Lastly, many medications are associated with vomiting and the patient should be asked about use of such medications, including non-prescription use.

Management. When treating ED patients with hyperemesis, the focus should be on rehydration, correcting electrolyte imbalances, and if possible, diminishing vomiting. Unless the patient has only minimal electrolyte changes, urinary ketones that can

be cleared while in the ED, can hold down po liquids, and has good OB follow-up, she will likely be admitted. General admission criteria include: weight loss of more than 10% of pre-pregnancy level, persistent vomiting when NPO, inability to correct electrolyte abnormalities, and uncertainty of the diagnosis of hyperemesis.[136]

Regardless of whether the patient is admitted or not, initial rehydration with IV fluids should be started early. At least one author suggests that rehydration and correction of electrolytes is more important and more helpful in controlling a patient's vomiting than use of medications for nausea.[127] An initial bolus of up to 40 mL/kg of 5% dextrose in either lactated Ringer's or normal saline should be started. These patients often require up to 5 liters of fluid for initial rehydration.[136] Nothing should be given by mouth until dehydration and electrolyte disturbances have been corrected. If this can be done without admission, then small amounts of clear liquids can be initiated.

Many antiemetics can be safely used in pregnancy, and these can be helpful as adjunctive therapy for intractable vomiting. *(See Table 8).* Promethazine (Phenergan), prochlorperazine (Compazine), metoclopramide (Reglan), trimethobenzamide (Tigan), diphenhydramine (Benadryl), and dimenhydrinate (Dramamine) in standard doses have all been used to treat either nausea and vomiting of pregnancy or hyperemesis without any known side effects or fetal risk.[136,137] One recent study found intravenous ondansetron was not effective in treatment of hyperemesis.[138] Several others have reported success using oral methyprednisolone, and one found it more effective than Phenergan.[139,140]

Because many patients are at risk for reoccurrence of vomiting, the following suggestions may be helpful. Patients should eat smaller, more frequent meals and avoiding strong odors, high-fat content foods, and sweet drinks. Patients can also be reassured that the presence of nausea and vomiting early in pregnancy is generally associated with improved pregnancy outcome. Lower incidence of spontaneous miscarriage and perinatal mortality is reported for women who suffer from increased nausea and vomiting early in pregnancy.[141,142] However, there are reports of a higher proportion of low birth weight infants born to women with the diagnosis of hyperemesis.[143] Another study found that intrauterine growth restriction correlated with a weight loss of more than 5% of the mother's pre-pregnancy weight.[144]

Rare and unusual complications of hyperemesis have been reported, and can require emergency intervention. These complications include Wernike's encephalopathy from thiamine deficiency, upper GI bleeding from ulcers or Mallory-

Table 9. Drugs to Avoid in Pregnancy[151]

DRUG	UNTOWARD EFFECTS
Asprin	Increases bleeding risk at delivery, decreased uterine contractility, no teratogenic effects
NSAIDS	Chronic use may lead to oligohydramnios or neonatal pulmonary hypertension, best to avoid use
Selected Cephalosporins:	
Cefaclor, Cephalexin, Cephradine	Associated with possible teratogenic effects[152]
Tetracyclines	Discolor teeth
Aminoglycosides	Ototoxicity when taken in first trimester
Quinolones	Bind to cartilage and bone, consequences are debated
Metronidazole (Flagyl)	Effects in humans at normal doses are debated
Lindane	A neurotoxin with toxicity noted primarily in overexposure
Antiseizure Drugs:	
Phenytoin, valproic acid	
Carbamazepine	All associated with defined malformation syndromes—do not prescribe without OB or neurologist recommendation
ACE inhibitors	Renal failure, oligohydramnios, limb and craniofacial deformities
Lithium	Congenital heart disease (Ebstein anomaly)
Warfarin (Coumadin)	Congenital fetal defects
Propranolol (Inderal)	Generally considered safe, may be associated with low birth weight
Terfenadine (Seldane)	Polydactyly
Phenylpropanolamine (Entex LA)	Increased risk of birth defects
Pseudoephedrine (Sudafed)	Increased risk of gastroschisis
Cimetidine (Tagamet)	Possible antiandorgenic effects in fetus
Benzodiazipines	Possible fetal syndrome similar to fetal alcohol syndrome
Oral Contraceptives	Possible cardiac defects in fetus when used in 1st trimester
Isotrentinoin (Accuatane)	Associated with multiple birth defects, spontaneous abortion
Propylthiouracil (PTU)	Induces fetal goiter
Oral hypoglycemics	Cross placenta and induce fetal hypoglycemia
Recreational Drugs:	
Tobacco	Increased prematurity, fetal growth retardation
Alcohol	Fetal alcohol syndrome
Cocaine	Increased spontaneous abortions, placental abruption, preterm labor and microcephaly

Weiss tears, retinal hemorrhage, coagulopathies from vitamin K deficiency, aspiration pneumonia, rhabdomyolysis, and renal or hepatic damage.[145-147] Similarly, some patients will require more aggressive treatment due to continued inability to tolerate po intake. Use of Dobhoff feeding tubes, total parenteral nutrition, percutaneous feeding tubes, and elective termination of the pregnancy have all been reported.[148-150]

Drugs in Pregnancy

Treating pregnant patients in the ED can be stressful if the ED physician is not aware of which drugs can and cannot be safely used in pregnant patients. Although specific drug therapies have been discussed under the appropriate disease states above, this section will provide a brief overview of drug treatment in pregnancy and concentrate on drugs that are recommended for specific conditions, as well as drugs that are known to be associated with fetal or maternal complications. Before discussing specific drugs, a review of the Food and Drug Administration categories of drug labeling for use in pregnancy is helpful.

It should be stressed that the majority of data concerning drug use in human pregnancy is anecdotal, as actual drug testing cannot be ethically performed on pregnant women. Therefore, many drugs that are considered "safe" are so because they have been used for many years without apparent effect. Pregnant patients should always be informed that, as a rule, it is best to avoid drug use in pregnancy, since long-term side effects may not be apparent for many years to come. However, they should not be deterred from using drugs that are needed to treat potentially dangerous conditions (i.e., antibiotics in cystitis), and patients should be reassured that many drugs (i.e., acetomenophen) have been used for years without any known side effects.

Category A. Controlled studies in women fail to demonstrate a risk to the fetus, and the possibility of fetal harm appears remote.

Category B. No evidence exists of risk for humans. Animal studies do not indicate a risk to the fetus, there are no controlled human studies, or animal studies do shown an adverse effect on the fetus, but well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus.

Category C. Use may cause risk to the fetus. Studies have shown the drug to have animal teratogenic or embryocidal effects, but no controlled studies in women are available. Potential benefit of use may outweigh potential harm.

Category D. Positive evidence of human fetal risk exists, but in certain situations (e.g., life-threatening situations or serious diseases for which safer drugs cannot be used or are ineffective) use of the drug may outweigh potential risks.

Category X. Studies in animals or humans have demonstrated fetal abnormalities, or evidence demonstrates fetal risk based on human experience, or both, and the risk clearly outweighs any possible benefit.

Table 9 summarizes commonly used drugs and emphasizes their recommendations for use in pregnant patients.

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Physician CME Questions

41. In the ED management of asthma in pregnant patients, which of the following is *false*?
    A. Medications including beta agonists and theophylline are considered safe for use in pregnancy.
    B. The "normal" PCO_2 in pregnancy is 30 mmHg.
    C. Pregnant women do not develop hypoxia or hypercarbia more easily than non-pregnant patients.
    D. A $PO_2 < 60$ mmHg is an indication for intubation and mechanical ventilation.

42. Discussing hypertension in pregnancy, which of the following is *false*?
    A. The classic triad of preeclampsia is hypertension, edema, and proteinuria.
    B. In general, hypertension in pregnancy is defined by BP > 140/90 mmHg.
    C. In normal pregnancy there is a drop in baseline BP of about 10 mmHg.
    D. Methyldopa and hydralazine are contraindicated in the treatment of hypertension in pregnancy.

43. When treating pneumonia in a pregnant patient, which of the following is *false*?
    A. Pneumococcal pneumonia is the most common pathogen in pregnant patients.
    B. All authors agree pregnant patients with pneumonia require admission to the hospital.
    C. The most common viral pneumonia seen in pregnant patients is varicella pneumonia.
    D. Varicella pneumonia causes high mortality for both mother and fetus.

44. Which of the following is true?
    A. DVT is more common in pregnancy, especially the postpartum period.
    B. Heparin is contraindicated in pregnancy.
    C. Warfarin (Coumadin) is safe in pregnancy.
    D. VQ scans are not safe in pregnancy.

45. Concerning UTI/pyelonephritis in pregnancy, which of the following is *false*?
    A. Because of high risk to the fetus from subsequent pyelonephritis, asymptomatic bacteriuria in pregnancy should be treated as cystitis.
    B. Trimethoprim/sulfamethoxazole is considered safe for use in the first trimester.
    C. Pyelonephritis is associated with increased preterm labor, and low fetal birth weights.
    D. The blood culture in acute pyelonephritis often identifies bacteria not found on urine cultures.

46. When treating HIV-positive pregnant patients in the ED, which of the following is *false*?
    A. AZT use in pregnancy is associated with a dramatic reduction in birth of HIV infected children.
    B. IV AZT is also given in active labor to further reduce vertical transmission of HIV.
    C. Pregnant women with HIV have an increased incidence of cervical dysplasia.
    D. Being diagnosed with bacterial pneumonia more than once in a year is not associated with HIV infection in pregnant women.

47. All of the following drugs are *not* safe in pregnancy *except*:
    A. ACE inhibitors.
    B. corticosteroids.
    C. warfarin (Coumadin).
    D. quinolones.

48. Physiological and laboratory parameters remain unchanged in pregnancy.
    A. True
    B. False

In Future Issues: Otitis Media