Obstetric Emergencies in the ICU

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Learning Objectives

1. Discover how maternal adaptations to pregnancy can alter the medical management of a pregnant patient who has sustained a traumatic injury.
2. Devise a treatment strategy for a woman who is experiencing a massive postpartum hemorrhage.
3. Demonstrate an understanding of the manifestations of severe preeclampsia and their treatment.
4. Distinguish between antihypertensive drugs used to treat hypertensive emergencies in the pregnant population.
5. Analyze cardiovascular agents for their safety in pregnancy and lactation.
6. Assess the differences between acute fatty liver of pregnancy and other similar disorders.
7. Evaluate the multitude of primary symptoms that can occur with an amniotic fluid embolism.

Introduction

Pregnant and postpartum women who require admission to an intensive care unit (ICU) are a rare and distinctive group, constituting less than 1% of all pregnancies and less than 1% of all ICU admissions. Their physiologic changes are unfamiliar to most ICU practitioners, and they are primarily admitted for obstetric conditions rather than unrelated medical complications. Fortunately, most of these women are postpartum, with exceptions for trauma and cardiomyopathy. Delivery of the fetus does not often correlate with the resolution of the disease states discussed in this chapter.

Scoring systems used in critical care settings to predict outcome do not consider normal adaptations to pregnancy or unusual laboratory results caused by pregnancy disorders. In addition, obstetric patients tend to recover more quickly than their counterparts. All of these factors lead to overestimations of mortality. One study has suggested that the Sequential Organ Failure Assessment score is a better system for predicting mortality in obstetric patients. Actual mortality rates are dependent on the disorder that has caused the ICU admission.

Pregnancy Adaptations

Many physiologic changes occur during pregnancy to adapt to the requirements of the fetus and the addition of a temporary organ system (the placenta). Modifications occur in almost all organ systems, with some more dramatic than others. These modifications play important roles in changes in hemodynamic monitoring and ventilation. The hormone progesterone is responsible for most of these adaptations because it is a potent smooth-muscle relaxant and respiratory stimulant. After delivery, it takes about 6 weeks for maternal physiology to return to normal.

The most dramatic physiologic changes during pregnancy are cardiovascular. Blood volume increases progressively by up to 50% in singleton pregnancies; this compensates for most blood loss at delivery. The placental vasculature receives almost 30% of the cardiac output, or almost 600 mL/minute at term. About one-sixth of the maternal blood volume is located in the uterus at any time. Blood pressure declines during the first trimester to a nadir (typically 85–110/50–70 mm Hg) in the second trimester.

Baseline Review Resources

The goal of PSAP is to provide only the most recent (past 3–5 years) information or topics. Chapters do not provide an overall review. Suggested resources for background information on this topic include:
- Hatzopoulos FK. Obstetric drug therapy. In: Koda-Kimble MA, Young LY, Kradjan WA, Guglielmo BJ, eds. Applied Therapeutics, 8th ed. Baltimore, MD: Lippincott Williams & Wilkins, 2005.

Blood pressures return almost to pre-pregnancy values in the latter part of the third trimester.

With significant maternal hypotension, the placenta acts separately from the vital organs and experiences vasoconstriction. This leads to hypoperfusion of the placenta, with resultant fetal hypoxia and acidosis if not quickly corrected. Fetal distress, observed as decreased variability of the fetal pulse rate or bradycardia on a monitor, may be the first sign of maternal status decline. The mother can lose up to 30% of her blood volume before her vital signs change.

Pregnant women normally have a respiratory alkalosis with a compensating metabolic acidosis; this increases the removal of fetal carbon dioxide and acidic metabolites. Maternal pulmonary changes include increases in tidal volume, minute ventilation, and oxygen consumption, as well as reductions in residual volume and functionary residual capacity. The diaphragm elevates during pregnancy as the uterus expands out of the pelvis. The chest wall flares to increase space in the thoracic cavity, but this still does not allow full expansion of the lungs. Therefore, pregnant women have less reserve when respiratory decompensation occurs. If maternal oxygen partial pressure falls below 47 mm Hg, the umbilical vein concentration begins to decline. Small decreases in maternal oxygenation below this point can lead to substantial changes in fetal oxygen saturation.

Supportive Care in the ICU

The vasopressor of choice in a pregnant woman is debatable. Most of the information available on the use of these agents deals with maternal hypotension associated with spinal anesthesia. Because vasoconstriction occurs in all vessels, it is important to select an agent that preserves uterine bloodflow as much as possible. Uterine vessels are maximally dilated and contain only α-receptors; this plays an important role in determining the sensitivity to sympathomimetic agents.

Ephedrine is often mentioned as a preferred agent because of its good safety record and minimal effect on placental perfusion at low doses. However, ephedrine crosses the placenta and has been reported to cause fetal tachycardia and acidosis, especially in the compromised fetus. Ephedrine is best used as a bolus agent for short-lived hypotensive occurrences. Phenylephrine may cause more uteroplacental vasoconstriction but not more fetal acidosis or adverse neonatal outcomes than ephedrine. Phenylephrine should be considered as an infusional agent when ephedrine would be an appropriate therapy but a longer duration of therapy is needed.

Dopamine has been studied in pregnant women with sepsis and is commonly used in this population, yet the overall effect on uterine bloodflow has not been elucidated. Data from animal trials suggest that dopamine increases the muscular tone of the uterus and blood vessels, raising mean arterial pressure and producing varying effects on pulse rate. Uterine bloodflow is decreased during infusions of both dopamine and dobutamine. However, dobutamine might be a better choice for an inotrope because it consistently increases pulse rate but not mean arterial pressure.

Vasopressin use for indications other than diabetes insipidus has not been studied. Intravenous and intramuscular administration of vasopressin has caused uterine contractions, so caution is warranted if this drug is used in the third trimester. Agents such as epinephrine and norepinephrine can cause considerable vasoconstriction of the maternal and placental vasculature in hypoxic women and are best avoided if possible. Short-term use of epinephrine for anaphylaxis does not appear to decrease fetal bloodflow. These agents seem to have opposite effects on the myometrium from differing effects on the α- and β-receptors located within the uterine muscle. Activation of β-receptors causes uterine relaxation, whereas α-receptor agonists cause contractions.

For years, succinylcholine has been the drug of choice for use in pregnant women in rapid sequence anesthesia induction. Lower concentrations of acetylcholinesterase are present during pregnancy, leading to the possibility of lower dosing requirements. However, in practice, standard doses are commonly used because succinylcholine is short acting and the clinical sequelae of overdosing are minimal.

The nondepolarizing agents are also good choices for inducing anesthesia and maintaining muscle relaxation during mechanical ventilation. All of these agents are ionized at physiologic pH and have low lipid solubility; therefore, little drug is expected to cross the placenta and reach the fetus. However, prolonged neuromuscular blockade can still occur with these agents when standard doses based on pregnancy weight are used. This should be considered when therapy is withdrawn; more time may be required for the patient to recover respiratory muscular function.

Few data exist on the long-term use of sedatives in pregnant women. Opioids, benzodiazepines, and barbiturates are relatively safe in pregnancy, even though they easily cross the placenta. Infusions of these agents in an intensive care setting are justifiable even if the woman delivers while still receiving them. The newborn may experience withdrawal effects if any of these therapies have been used for more than a few hours before delivery. These agents also

cross into breast milk and may cause considerable sedation in newborns, especially those born prematurely. Fentanyl may be a better choice of opioid because oral absorption is low, but high-dose infusions could still cause respiratory depression in the newborn.

Both propofol and dexmedetomidine cross the placenta and into breast milk in animals, but only case reports exist regarding their use in humans. Propofol enters breast milk in small amounts only, likely because of high protein binding. The data on propofol in pregnant patients include reports on its use with cesarean section and other surgical procedures. Propofol infusions during prolonged neurosurgery in two pregnant women were changed to other agents when acidosis developed at hours 10 and 11. This nonanion gap metabolic acidosis was not consistent with propofol infusion syndrome. Data from cesarean sections indicate that propofol has no fetal or neonatal effects. In another surgical procedure using both dexmedetomidine and propofol, no acidosis was reported. Dexmedetomidine use allowed lower amounts of propofol and alfentanil to maintain anesthesia. An infusion of dexmedetomidine in labor and a subsequent cesarean section showed no adverse effects on the newborn.

Trauma in Pregnancy

Trauma affects about 6% to 7% of all pregnancies and is the leading cause of nonobstetric maternal demise. The risk of injury increases by trimester, with at least 50% of mothers or fetuses wounded when trauma occurs in the third trimester. Most trauma occurs secondary to automobile collisions; domestic violence and falls are the second and third most common causes, respectively. Pregnancy may be a risk factor for assault, often with intent to harm the fetus. Intimate partner violence may start or escalate during pregnancy.

Blunt trauma, such as that experienced by rapid deceleration or by being punched, can lead to placental separation from the uterine wall (placental abruption) or, rarely, uterine rupture. Fetal demise can result from either of these indirect complications. Other important maternal injuries include splenic and hepatic injuries or a pelvic fracture with subsequent retroperitoneal bleeding. Moreover, maternal pelvic fractures can lead to injuries to the fetus (e.g., skull fractures, intracranial bleeding) and can cause shock or death in the mother.

Evaluation of these injuries requires radiography. Exposure from chest and abdominal radiographs would total about 0.1–1 rads (0.001–0.01 Gy). The computed tomography scan is higher at about 2.8 rads (0.028 Gy). Exposure of up to 5000 millirads (0.5 Gy) is not associated with teratogenic effects on the fetus. Radiation exposure in utero, though, may place the child at higher risk of malignancies later in life.

Penetrating trauma can cause direct fetal injury, especially when inflicted in the lower abdomen during the third trimester. Gunshot wounds are more common than stab wounds, but both cause fewer fatalities in pregnant women than in the general population.

Fetomaternal hemorrhage is a concern in rhesus-negative women. Normally, the maternal system runs in parallel with the fetal circulation and no mixing of blood occurs. A Kleihauer-Betke test can determine how much, if any, fetal blood entered the maternal circulation by measuring the fetal hemoglobin concentration. If exposure occurs, intramuscular rhesus immune globulin should be administered within 72 hours to prevent the production of maternal antibodies to the rhesus antigen (isoimmunization).

Cardiopulmonary Resuscitation

Cardiac arrest is rare, occurring in about 1 in 30,000 pregnancies; however, many pregnancy-related conditions and complications can be predisposing factors. Pregnancy-related physiologic changes can also affect the ability to successfully provide cardiopulmonary resuscitation (CPR).

Intubation should occur early in resuscitative efforts. Pregnant women are at higher risk of aspiration because of delayed gastric emptying. They are also at risk of difficult ventilation and failed intubation because of edema of the upper airway. Maintenance of good oxygenation is imperative because of the increased risk of hypoxia in the mother and fetus. After 20 weeks, the uterus has enough mass to compress the inferior vena cava when the mother is supine. In turn, venous return is reduced, compromising stroke volume and placental perfusion.

During CPR, the pregnant woman should be kept in a left lateral position using a wedge, or the uterus should be displaced manually. When performed on a 27° angle, chest compressions provide only 80% of the maximal force achieved with the supine position. Nonetheless, CPR should continue even if a cesarean section is performed. Maternal injuries that could occur during resuscitation include lacerations of the liver or spleen and uterine rupture.

Algorithms for the resuscitation of pregnant patients vary only slightly from those of their nonpregnant counterparts. Normal doses of drugs should be used, and defibrillation is not contraindicated. The use of sodium bicarbonate is controversial. Rapid reversal of maternal acidosis could normalize the mother's carbon dioxide partial pressure ($Paco_2$) but increase the fetal $Paco_2$, worsening the fetal acidosis. The fetus can tolerate respiratory acidosis only for a short time; some experts find it preferable to restore the maternal circulation and correct the hypoxia than to use sodium bicarbonate.

Obstetric Hemorrhage

Most obstetric hemorrhages occur after the fetus is delivered. Postpartum hemorrhages complicate up to 5% of deliveries. Drug therapy with oxytocin immediately after

delivery is the standard of care, with additional oxytocin given if bleeding continues.

Carboprost, methylergonovine, and misoprostol are considered second- and third-line therapies. Methylergonovine, an ergot alkaloid metabolized by cytochrome P450 3A4, primarily acts on uterine smooth muscle. It can cause severe hypertension and myocardial ischemia when given intravenously. It is standard of care to continue with oral therapy for at least 24–48 hours after the initial intramuscular dose.

The prostaglandins carboprost (15-methyl prostaglandin F2α) and misoprostol (prostaglandin E_1 analog) are more commonly used in hypertensive women. Carboprost can cause significant contraction of smooth muscles. This is evidenced by the incidence of diarrhea associated with carboprost (about 60%), which often requires loperamide therapy. Misoprostol is inexpensive and has been studied for rectal, oral, and sublingual administration. The vaginal route is not often recommended because bleeding may dilute or eliminate the effect of the dose (typically 800 mcg or 1000 mcg). Because more information is available on the other agents, misoprostol is often used as a third-line agent.

If several of these agents fail, uterine tamponade strategies followed by surgical interventions should be performed. These include artery ligation or embolization; uterine compression sutures; or, as a last resort, hysterectomy. Of course, blood products should be infused as needed before and during surgical treatments. Recombinant activated factor VII (rf VIIa) has a potential role, often before surgical modalities are undertaken but after failure of other drug management.

Recombinant activated factor VII is not approved for use in obstetric patients; however, data exist on its use within a European registry and as case reports from many parts of the world, including the United States. Like other off-label uses, there is no recommended standard dose of rf VIIa for treating obstetric hemorrhage. This agent should be used after standard methods of controlling postpartum hemorrhage have failed.

Some clinicians have used rf VIIa for secondary prophylaxis, administering the drug together with other successful interventions. Its high cost does not justify its use for prophylaxis, and it should be reserved for treatment only. In published reports, doses of rf VIIa are typically 60–90 mcg/kg, although the total dose in milligrams is occasionally reported instead. Good response is reported in more than 80% of women. Second doses have been used when the first is unsuccessful at reassessment between 30 minutes to several hours later. Failure of the agent has been noted in women with severe metabolic abnormalities, acidemia, hypothermia, an inadequate quantity of coagulation factors and platelet count, or with insufficient dosing. Few adverse reactions have been reported with immediate postpartum use. Reports of deep venous thrombosis and pulmonary embolism are uncommon in this population despite pregnancy being a hypercoagulable state.

Antepartum hemorrhage is most often related to placenta previa, placental abruption, and uterine rupture. Postpartum issues that could cause massive blood loss include uterine atony, placental abnormalities, retained placenta, genital tract trauma, coagulation defects, and other less common issues. Preventive techniques, such as uterine massage, should occur after every delivery. However, a woman may continue to ooze blood after delivery, or a hematoma could form in an occult area. Maternal vital signs and symptoms are critical in evaluating blood loss. Most women can tolerate a blood loss of 1500 mL without symptoms of hemorrhagic shock.

Before delivery, uterotonics cannot be used to help control bleeding, leaving few available options if major bleeding occurs. Persistent vaginal bleeding in a pregnant woman led to the administration of rf VIIa in one case report; this stopped the bleeding from a partial placental abruption within hours. The authors opted for a dose of 20 mcg/kg based on a higher dose obtained from the manufacturer for women with factor VII deficiency (30 mcg/kg). A lower dose was selected to reduce the risk of thromboembolic complications in the mother. Because of its high molecular weight, rf VIIa does not cross the placenta; no neonatal adverse effects were noted.

In addition to peripartum hemorrhage, obstetric reasons for the development of disseminated intravascular coagulation (DIC) include amniotic fluid embolism (AFE), severe hypertensive complications, retention of a fetus (greater than 20 weeks) for more than 4 weeks after demise, and sepsis. Sepsis can occur from the development of chorioamnionitis or other maternal infections. Severe blood loss can also lead to the development of Sheehan syndrome (necrosis of the anterior pituitary caused by hypotension). The pituitary enlarges during pregnancy and becomes more susceptible to adverse effects of hypotension.

SEVERE PREECLAMPSIA AND ITS COMPLICATIONS

Severe Preeclampsia

Preeclampsia occurs in about 6% to 8% of pregnancies. It may also be superimposed on chronic hypertension or worsening hypertension and proteinuria in women with underlying renal disease. The development of the classic triad—hypertension, proteinuria, and edema—after 20 weeks gestation defines this diagnosis, although most experts now agree that edema should no longer be included in the condition. Rapid weight gain is sometimes substituted for edema.

Mild forms of preeclampsia typically occur in the last weeks of pregnancy; however, severe preeclampsia can occur at any time. Early onset of severe preeclampsia can be associated with some types of thrombophilia. A postpartum evaluation of coagulation defects is warranted in this population when laboratory measures have returned

to their normal prepregnancy values. Severe preeclampsia typically shows some form of end-organ dysfunction.

Diagnostic criteria include the presence of preeclampsia and at least one of the following: severe headaches; two blood pressure readings greater than 160/110 mm Hg at least 6 hours apart; proteinuria greater than 5 g in 24 hours or 3+ protein on urinalysis; fetal growth restriction; oliguria or renal failure; right upper quadrant/epigastric pain; laboratory values indicating hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome; DIC; or eclampsia. More severe complications (e.g., intracerebral venous thrombosis, cardiopulmonary failure, acute respiratory distress syndrome, sepsis, shock) occur less commonly but could lead to ICU admission. The only cure for preeclampsia is delivery of the fetus and the placenta.

The most important treatment goals for severe preeclampsia are the prevention of eclampsia and lowering maternal blood pressure below the severe range of 160/110 mm Hg. Magnesium sulfate is the drug of choice to prevent eclampsia; its mechanism of action is unknown, but magnesium does suppress neurotransmitter release by replacing calcium at nerve endings. A continuous infusion of magnesium sulfate to maintain serum concentrations at 5–8 mg/dL is very effective. This is achieved by administering a bolus of 6 g over 20 minutes followed by an infusion of 2 g/hour. If intravenous access is not obtained, 5 g of magnesium can be administered in each hip, followed by 5 g every 4 hours. Women experiencing renal dysfunction should have their infusion rate reduced or, for anuria, the loading dose may suffice to maintain therapeutic magnesium concentrations. Magnesium has a relatively narrow therapeutic range; loss of deep tendon reflexes is often the first sign of concentrations exceeding 8 mg/dL. Toxic reactions begin above a concentration of 12 mg/dL; these include muscular paralysis and respiratory difficulties at concentrations of 15–17 mg/dL, and cardiac arrest with concentrations greater than 20 mg/dL.

Women with preeclampsia often have a depleted intravascular volume, despite being total body fluid overloaded even though they usually receive low amounts of intravenous fluids while in labor and delivery. Treatment with diuretics to mobilize fluid is not appropriate unless pulmonary edema occurs. Fetal bloodflow can be compromised, especially in a patient with severe hypertension. If a woman's blood pressure exceeds the severe range on more than two readings at least 20–30 minutes apart, treatment should be initiated.

Extreme elevations in blood pressure in this population can lead to a cerebrovascular accident (CVA), loss of cerebral autoregulation, and placental abruption. However, a very rapid decline in blood pressure will compromise the uteroplacental bloodflow, causing fetal distress. A slow decrease to a blood pressure in the mild hypertension range is more appropriate. Blood pressure should not be decreased by more than 25% over minutes to hours. Several doses repeated at 15- to 20-minute intervals as needed may

be required to achieve this goal. Hypertensive encephalopathy or a systolic blood pressure greater than 250 mm Hg should be treated immediately, with an eventual goal of a 15% to 25% reduction in the mean arterial pressure. Small decreases should occur during the first hour to lower the diastolic blood pressure to less than 110 mm Hg.

Few drugs have been well studied during pregnancy for severe hypertension. Intravenous hydralazine and labetalol are first-line agents. Nifedipine can be used if the patient is able to take oral drugs. Clonidine has not been studied recently, but older resources agree that is an effective drug in pregnancy; it is a safe alternative oral therapy for women who are either resistant to other agents or cannot swallow larger pills.

Pregnant women are more sensitive to centrally acting agents, so initiation of therapy with hydralazine should be at doses lower than commonly used (5 mg). A meta-analysis suggested that hydralazine and labetalol were equally effective, but hydralazine causes more maternal hypotension and tachycardia, and infants had lower neonatal wellness assessment (Apgar) scores at 1 minute of life. Compared with hydralazine, labetalol has the benefit of not causing rebound tachycardia and has a faster onset of action. Progressively higher amounts of labetalol should be used when repeated doses are needed, to the maximum of a 300-mg cumulative intravenous dose.

Other β-blockers such as esmolol can be associated with fetal bradycardia and should be avoided. Nifedipine (10 mg or 20 mg) has been given every 30 minutes to a maximum of 50 mg in 1 hour with good success. However, there are potentially significant interactions between calcium channel blockers and magnesium (e.g., severe hypotension, neuromuscular blockade). Less often, sodium nitroprusside can be used when other agents fail. Titration should occur slowly, allowing a gradual decrease in blood pressure without overshooting the target range. The duration of sodium nitroprusside should be limited, primarily using this agent intrapartum. Cyanide toxicity can occur in the neonate, and some experts have suggested that exposure be less than a few hours.

Nicardipine has also been studied for rapid blood pressure control. In a study evaluating its use after other antihypertensive drugs failed, nicardipine was successful in achieving the target blood pressure in all cases. Maternal tachycardia was observed in 5 of 27 women, and no hypotension was observed in women also receiving magnesium sulfate.

Women may require antihypertensive drugs after delivery, either acutely or chronically, and their blood pressure should be monitored often to assess the need for continuing therapy. Although methyldopa is effective and commonly used in pregnant women for hypertension, the increased sensitivity to centrally acting agents wanes postpartum, making the drug no longer an optimal choice.

Appropriate agents are determined by the breastfeeding status of the mother and the drugs that were efficacious

before the pregnancy. Furosemide can hasten the recovery from preeclampsia by assisting fluid mobilization when given after the onset of postpartum diuresis, improving blood pressure readings more quickly than placebo. However, data are limited on this use, and diuretics can inhibit breast milk production. Compounds that easily cross into breast milk usually have higher lipid solubility, lower protein binding, a low molecular weight (less than 400 daltons), and are not ionized (Table 1-1). The milk-to-plasma ratio can help determine which drugs appear in lower quantities in breast milk. These agents are often safer, although important information is still unknown about many of the antihypertensive drug classes.

HELLP Syndrome

The HELLP syndrome, first described and named in 1982, complicates up to 20% of pregnancies with severe preeclampsia The diagnosis of HELLP syndrome can be difficult, especially when a woman meets some but not all of the criteria. Hemolysis should be determined by indicators for microangiopathic hemolytic anemia; however, serum lactate dehydrogenase and bilirubin concentrations are often obtained with no peripheral blood smear. Elevated lactate dehydrogenase concentrations can indicate hemolysis, although they are more likely to be abnormal when the liver has experienced ischemia. Typically, alanine aminotransferase and aspartate aminotransferase values greater than twice the upper limit of normal (more than 70 units/L) are also needed to make the diagnosis of HELLP syndrome.

Platelet counts for diagnosis vary in the literature, but the most common value used is less than 100,000/mm^3. Many women present with vague symptoms such as malaise, right upper quadrant pain, nausea, and vomiting. They often have severe hypertension and/or proteinuria (more than 5 g every 24 hours). Some patients will present with signs related to thrombocytopenia. The development of HELLP syndrome can occur postpartum, which may increase the risk of pulmonary edema and severe renal dysfunction.

Other morbidities associated with HELLP syndrome include DIC, hepatic damage, placental abruption, sepsis, adult respiratory distress syndrome, and CVA, in addition to a higher risk of maternal death. When HELLP syndrome presents earlier in pregnancy, it is of more concern because the maternal and fetal outcomes are worse than when the syndrome develops later. Neonatal outcomes are related primarily to gestational age at delivery and ensuing issues of prematurity.

Some women with HELLP syndrome can be expectantly managed, but progressive worsening and rapid decline in status are usually observed. Most women have some resolution in the first 48 hours after delivery without intervention. Postpartum HELLP syndrome occurs primarily in the first 2 days, but it has been described as late as 7 days after childbirth. Women who develop HELLP syndrome during pregnancy are at an increased risk of preeclampsia and its complications with all future pregnancies. Preeclampsia occurs in about 20% of successive pregnancies, whereas HELLP syndrome develops again in 2% to 19% of patients.

Researchers have used dexamethasone to transiently improve laboratory values (e.g., platelet count to avoid a transfusion) and maternal and neonatal outcomes. The doses of dexamethasone used (e.g., 10 mg intravenously every 12 hours for four doses) are above those for fetal lung maturation and are sometimes divided evenly before and after delivery. The studies of dexamethasone for HELLP syndrome have all been small, but improvements in liver function tests, urine output, platelet count, and mean arterial pressure have been observed. The objectives of treatment are appropriate management of hypertension and prevention of eclampsia. Platelet transfusions may be necessary in women with values less than 20,000/mm^3 or in whom bleeding or oozing continue after surgery.

Eclampsia

Eclampsia is an uncommon event that manifests as tonic-clonic seizures indistinguishable from other generalized convulsions such as epilepsy. Persistent headaches, blurred vision, photophobia, right upper quadrant pain, and an altered mental status often precede an eclamptic seizure. Hypertension, proteinuria, and facial edema are often seen in these women, but these signs are absent in about 20% of patients.

Other etiologies for seizures should be considered, especially in patients with focal neurologic deficits or in the absence of preceding preeclampsia. Diagnoses to consider include CVAs, brain tumors, infection, thrombotic thrombocytopenic purpura, metabolic disorders, hypertensive encephalopathy, illicit drug use, postdural puncture syndrome, epilepsy, and posterior reversible encephalopathy syndrome. Severe preeclampsia and eclampsia are common causes of posterior reversible encephalopathy syndrome, which usually presents similarly to eclampsia but is more often associated with recurrent seizures and visual disturbances.

Eclampsia complicates 1% to 2% of preeclamptic pregnancies; however, the recurrence rates of preeclampsia and eclampsia are about 25% and 2%, respectively. Eclampsia may develop during pregnancy, in labor, or in the first 2 days postpartum, but it can occur as much as 4 weeks later. It most commonly occurs after 32 weeks gestation, antepartum or intrapartum.

Two theories have been suggested for the pathophysiology of eclampsia, but neither has been proved. The first theory states that cerebral bloodflow is altered when significant hypertension causes failure of autoregulation, precipitating cerebral vasodilation, hyperperfusion, and the development of extracellular edema. The other theory involves severe hypertension leading to cerebral overregulation of the arteries, resulting in brain underperfusion, confined ischemia or infarcts, and intracellular edema. However, it appears from radiologic imaging studies that vasogenic edema is more

Table 1-1. Antihypertensive Drugs in Breastfeeding

Drug	PB	LS	Enters Milk	M/P Ratio[a]	Comments
Benazepril	H	H	Yes	0.01	There are sufficient data with captopril and enalapril to allow them to be classified as compatible by AAP; other agents likely pass into breast milk; no human reports are available to make recommendations about their use
Captopril	L	U	Yes	0.12	
Enalapril	M	U	Yes	0.43	
Fosinopril	H	U	Yes	U	
Lisinopril	L	U	P	U	
Quinapril	H	H	Yes	0.12	
Ramipril	M	U	Yes	U	
Candesartan	H	U	P	U	The low molecular weight of these agents suggests excretion into breast milk, but no human reports are available; use cannot be recommended at this time
Irbesartan	H	U	P	U	
Losartan	H	U	P	U	
Valsartan	H	U	P	U	
Acebutolol	L	L	Yes	7.1–12.2	Lower protein-bound agents cross into breast milk most easily; highly lipid soluble agents transfer to a lesser degree due to higher protein binding; high drug amounts in milk can lead to β-blockade in the newborn
Atenolol	L	L	Yes	1.5–6.8	
Metoprolol	L	M	Yes	3–3.7	
Nadolol	L	L	Yes	4.6	
Propranolol	H	H	Yes	0.33–1.65	
Carvedilol	H	U	P	U	Labetalol is compatible, no human reports with carvedilol; watch for α/β-blockade
Labetalol	M	L	Yes	0.8–2.6	
Amlodipine	H	U	P	U	Case reports are available for nifedipine, verapamil, and diltiazem, which AAP considers compatible; remaining agents have no human data but are likely to cross into milk; safety of these agents is unknown
Diltiazem	M	U	Yes	1	
Felodipine	H	U	P	U	
Isradipine	H	U	P	U	
Nicardipine	H	U	Yes	0.25	
Nifedipine	H	U	Yes	1	
Verapamil	H	U	Yes	0.6–0.94	
Bumetanide	H	U	P	U	Loop diuretics can decrease milk production; hydrochlorothiazide is considered compatible by AAP
Furosemide	H	U	Yes	U	
Hydrochlorothiazide	M	U	Yes	0.25	

[a]M/P ratio = milk-to-plasma ratio.
AAP = American Academy of Pediatrics; PB = protein binding: L less than 30%, M 30% to 90%, H greater than 90%; LS = lipid solubility: L = low; M = moderate; H = high; U = unknown; P = probable - no human case reports but would be expected to enter breast milk.
Information from: Hale TW. Medications and Mothers' Milk, 13th ed. Amarillo, TX: Hale Publishing, 2008; and Briggs GG, Freeman RK, Yaffe SJ, eds. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk. Philadelphia, PA: Lippincott Williams & Wilkins, 2008.

common in women with eclampsia. Hypertensive encephalopathy is a likely source of pathogenesis.

Appropriate seizure management (e.g., padding side rails) should be provided together with supplemental oxygen. Various therapies have been compared with magnesium sulfate to prevent eclampsia (e.g., phenytoin; diazepam; a lytic cocktail of pethidine, chlorpromazine, and promethazine), but all had higher rates of recurrent seizures and maternal deaths.

About 10% of women will have a second seizure after the initiation of a magnesium sulfate infusion. In response, an additional 2 g of magnesium sulfate can be given concurrently with the magnesium sulfate infusion. If seizures are not controlled by repeat magnesium bolus, then diazepam, lorazepam, or the agent most commonly used for

status epilepticus at a particular hospital can be administered. In addition, hypertension should be addressed with agents discussed in the preeclampsia section. Once the patient is stabilized and the maternal and fetal effects of the seizure have subsided, delivery must occur. Magnesium sulfate should be continued for at least 24 hours after the last seizure.

Maternal complications are high after the development of eclampsia. It is the main cause of ischemic CVAs and intracerebral hemorrhages during pregnancy. Placental abruption, DIC, and acute renal failure occur in up to 10% of women, and aspiration pneumonia and cardiopulmonary arrest occur in as many as 5%. Temporary neurologic abnormalities may occur after the initial insult, including cortical blindness, focal motor deficits, and coma. These are

likely caused by a transient cerebral insult such as hypoxia, ischemia, or edema. Rarely, these manifestations become permanent. Fetal deaths are primarily related to gestational age, but they can also be caused by placental abruption or asphyxia in utero.

Peripartum Cardiomyopathy

By definition, peripartum cardiomyopathy (PPCM) presents between the last month of pregnancy and the end of the fifth month postpartum. The diagnosis requires a history of no cardiac dysfunction or identifiable cause of the heart failure and new left ventricular systolic dysfunction (ejection fraction less than 45% and/or M-mode fractional shortening less than 30% with greater than a 2.7-cm/m^2 end diastolic dimension).

Some women will develop cardiac dysfunction earlier in their pregnancy; however, this may represent preexisting heart disease that is exposed when the pregnancy makes greater hemodynamic demands. The occurrence rate appears to be 1 in 3000–4000 live births, with higher rates in the Southern United States, in Africa and Haiti, and in women who receive β-agonist tocolytic therapy. Risk factors can include advanced maternal age (30 years or older), multiparity, African American heritage, multiple gestations, obesity, and gestational or chronic hypertension. However, insufficient data exist to develop guidelines for screening high-risk populations.

The presentation of PPCM is similar to idiopathic dilated cardiomyopathy and can be classified as such. Etiologies proposed as possible causes include viral myocarditis, autoimmune disease, and maladaptation to the hemodynamic stresses of pregnancy. However, the onset of symptoms is typically later than 32 weeks, when blood volume approaches the maximal amount achieved during the pregnancy.

Initial symptoms in the last month of pregnancy and early postpartum may be confused with normal complaints such as fatigue, dyspnea, and edema. Most women present with significant heart failure, with a nocturnal cough and dyspnea, new heart murmurs, chest pain, jugular vein distention, and considerable pulmonary crackles. Patients with PPCM also have a much higher rate of thromboembolism overall, with rare events reported in the literature such as coronary emboli and thrombotic cerebral infarction.

Significant maternal morbidity and mortality approaches 20%, with many in this group requiring cardiac transplantation for survival. Prognosis is dependent on the normalization of left ventricular function. About 50% of women with PPCM will recover to their baseline cardiac function or have more than a 50% improvement within 6 months after presentation, signifying a good prognosis; however, there is a significantly higher mortality rate in women who do not recover within this time. Women who present with a low ejection fraction (less than 25%) are less likely to have good long-term outcomes, even if they recover cardiac function.

Treatment of PPCM should parallel treatment strategies for congestive heart failure. Because angiotensin-converting enzyme inhibitors are contraindicated in pregnancy, hydralazine and nitrates should be used instead. Pregnant patients requiring acute treatment can receive dopamine, dobutamine, nitroglycerin, or milrinone. With the exception of nitroglycerin, experience with these agents in pregnancy is extremely limited. However, in the last month of pregnancy, the fetus should not experience teratogenic effects. In fact, bloodflow to the uterus and fetus will be improved by the use of these agents. Once stabilized, the woman should be initiated on an oral regimen of hydralazine and isosorbide dinitrate or agents appropriate for the patient's lactating status (see Table 1-1).

Other drug therapies tried with success in PPCM include immune globulin, pentoxifylline, and prolactin inhibitors. If PPCM is caused by an infection, then the use of immune modulators is logical. A faster recovery was observed in six women who received 1 g/kg/day of intravenous immune globulin for 2 days. Only one of the six patients actually had myocarditis on biopsy. The improvement on left ventricular ejection fraction was considerably more than that of the comparator women receiving conventional therapy. Another study showed no improvement in left ventricular ejection fraction with immune globulin therapy. Therapy with immune globulin is extremely expensive and, shortages can limit availability. Its use should be reserved for women in whom an infectious etiology has been diagnosed.

Inhibition of cytokines may help improve PPCM more quickly. Elevated values of tumor necrosis factor alpha (TNFα) occur in patients with left ventricular dysfunction. Pentoxifylline inhibits TNFα production, which can be helpful in idiopathic dilated cardiomyopathy. In a small nonrandomized study, women receiving pentoxifylline 400 mg three times/day for 6 months together with conventional therapy had better outcomes than those receiving only conventional therapy. Left ventricular diameter was significantly smaller, and there were fewer deaths in the pentoxifylline group.

The prolactin derivative 16 kDa appears to be involved with the development and progression of PPCM, at least in animals. Prolactin concentrations are elevated postpartum to induce breast milk production. Oxidative stress increases the production of 16 kDa, which is known to induce endothelial cell apoptosis and disrupt capillary structure. Suppressing prolactin with bromocriptine and cabergoline has produced good recoveries in the cases reported. However, bromocriptine has been associated with myocardial infarctions, CVAs, seizures, and severe hypertension. Postpartum women are at higher risk of thrombosis development, especially those with PPCM. With either of these therapies, further studies are required to confirm these results in larger, more diverse populations of women.

Acute Fatty Liver of Pregnancy

Acute fatty liver of pregnancy (AFLP) is a rare but potentially fatal condition that occurs in about 1 in 10,000–15,000 pregnancies; the maternal mortality rate can approach 18%. Lipid accumulation occurs in the liver, kidneys, pancreas, brain, and bone marrow. Ammonia produced by hepatic cells, together with the excessive fat content in the liver, causes eventual liver failure with possible focal necrosis, coagulopathy, and profound hypoglycemia. Acute fatty liver of pregnancy typically occurs late in pregnancy through the immediate postpartum period; however, cases have presented as early as 23 weeks.

The typical presentation of AFLP includes nonspecific flu-like complaints such as nausea, vomiting, fatigue, headache, and abdominal pain. Malaise is present in all patients. As the disease progresses, jaundice, fever, and/or right upper quadrant pain tend to follow. Rarely, transient diabetes insipidus occurs, causing polydipsia and polyuria. If left untreated, AFLP can progress into fulminant hepatic failure with encephalopathy or coagulopathy. Hemorrhage, sepsis, and multiorgan system failure can also occur and can be fatal. A substantial number of women will develop hypertension or preeclampsia. Fetal acid-base status may be affected by AFLP caused by maternal acidosis from serum lactate accumulation, necessitating a timely delivery.

The diagnosis of AFLP is made on the basis of laboratory and clinical findings. Hyperbilirubinemia, elevated transaminases, coagulopathy, and hypoglycemia can help distinguish AFLP from other diagnoses. Severe preeclampsia, HELLP syndrome, and acute viral hepatitis can all mimic AFLP, but liver enzymes will typically be much higher with hepatitis than with the other conditions (Table 1-2).

With the diagnosis of AFLP, laboratory values may not indicate the severity of the disease. Treatment of hypertension, hypoglycemia, and coagulation abnormalities is indicated to stabilize the mother. Renal failure is common with AFLP and may require short-term renal replacement therapy. Women can also develop pulmonary edema or acute respiratory distress syndrome. Intubation, antibiotics, and large amounts of blood products may be required to provide adequate care to the mother.

The condition can worsen during the first 2–7 days after delivery; this is usually followed by improvement in the hepatic, renal, hematologic, and pancreatic function, but permanent renal dysfunction can occur. During the next few weeks, full clinical recovery usually occurs. Rarely, liver transplantation is indicated for liver rupture with necrosis, fulminant liver failure, hepatic encephalopathy, or worsening coagulopathy.

Atypical therapies have been described in the literature. Activated protein C has been used to treat sepsis associated with AFLP; acute bleeding is a contraindication to using this agent, and numerous patients are excluded because DIC occurs in about half of all cases. The use of plasma exchange has also been described in a review of six patients at one institution. Women who were provided plasmapheresis had progressive disease with deteriorating mental status, persistent coagulopathy, renal failure, pulmonary compromise, or major fluid management issues, all of which resolved within 2 weeks after completing an average of three plasmapheresis sessions.

Amniotic Fluid Embolism

Amniotic fluid embolism, although uncommon, is a potentially devastating event. It occurs in 1 in 8000 to 1 in 80,000 pregnancies ending in a live birth and is the cause of about 10% of maternal deaths in the developed world. Outcomes vary, but death rates are as high as 61% and can occur from hours to months after the event. National registry data show only 15% of these patients survive without neurologic deficits.

The typical presentation of an AFE includes hypoxia and acute respiratory failure, fetal distress, transient hypertension followed by hypotension and shock, altered mental status or seizures, cardiovascular collapse, and DIC. Hypoxia is likely secondary to embolic changes in the pulmonary vasculature and subsequent inadequate ventilation, as well as pulmonary edema. Pulmonary hypertension and vasospasm can occur early in the presentation with right-sided heart failure. The pulmonary hypertension subsides and is replaced by acute left ventricular failure. Hypoxic effects on the brain can cause encephalopathy and resultant seizures. Seizures that occur when the mother is hypoxic likely lead to more brain injury. Fetal distress is often observed with the initial maternal symptoms.

The first priority is to deliver the fetus if the woman is still pregnant, even if she requires a perimortem cesarean section. Resuscitative and supportive care should be initiated promptly, beginning before delivery. One case report described the successful use of nitric oxide when right-sided heart failure persisted, dramatically improving all supportive care parameters, including oxygenation. The use of prostaglandin synthesis inhibitors and high-dose corticosteroids has been suggested to help treat the condition because of the inflammatory cascade initiated by fetal debris in the blood. However, these therapies are only theoretical; they have not been used clinically in humans.

Conclusion

Although few women present in intensive care settings during or immediately after pregnancy, those who do have a true need for significant supportive care. Some pregnancy adaptations remain for days to weeks after delivery. During the pregnancy, the pharmacist may be able to direct physicians to therapies that pose less risk to the fetus. Pharmacists also play an important role in ensuring appropriate dosing of adjuvant agents during ICU admissions. Sometimes, the etiology is very clear, as in hemorrhage; other times,

Table 1-2. Differential Diagnosis and Complications of Acute Fatty Liver of Pregnancy

Disease State	Initial Signs and Symptoms	Later Signs and Symptoms	Laboratory Abnormalities	Maternal Complications and Comments
Acute fatty liver of pregnancy	Malaise, epigastric pain, nausea/ vomiting, jaundice	Encephalopathy, renal failure, DIC, hypoglycemia	Elevated white blood cell count; elevated ALT, AST, and bilirubin; normal LDH; low platelet count	Pancreatitis, diabetes insipidus, fulminant hepatic failure, sepsis; may also have HELLP syndrome
Severe preeclampsia	Headache, right upper quadrant pain, edema, hypertension	Hypertensive emergency, pulmonary edema	Mildly elevated ALT, proteinuria	Eclampsia, acute renal failure, hepatic capsular rupture
HELLP syndrome	Right upper quadrant pain, nausea/ vomiting, malaise, headaches, visual changes	Hematuria, petechiae, ecchymosis	Low platelet count, elevated bilirubin, elevated AST, ALT, LDH	DIC, acute renal failure, hepatic hemorrhage or failure, ARDS, sepsis, cerebrovascular accident
Viral hepatitis	Nausea, vomiting, fever, jaundice	Encephalopathy, sepsis, coagulopathy, hypoglycemia	Very elevated transaminases, elevated bilirubin, positive serology	Fulminant hepatic failure, hepatic coma, sepsis, GI bleeding
TTP	Mild fever, nausea/ vomiting, abdominal pain, petechiae	CNS effects – headache, visual changes, confusion, seizures; other organ involvement	Very low platelet count and hematocrit, very elevated LDH and bilirubin, mildly elevated ALT, AST	Diffuse subcortical microvascular disease, acute renal failure; could cause placental thrombosis
Antiphospholipid antibody syndrome	Thrombosis	Thrombotic renal disease, GI ischemia	Low hematocrit and platelet count, presence of LA, aCL, or β_2-GP-I	Multiorgan failure leading to "catastrophic antiphospholipid syndrome," development of TTP

aCL = anticardiolipin antibodies; ALT = alanine aminotransferase; ARDS = adult respiratory distress syndrome; AST = aspartate aminotransferase; β_2-GP-I = β_2-glycoprotein-I antibodies; CNS = central nervous system; DIC = disseminated intravascular coagulation; GI = gastrointestinal; HELLP = hemolysis, elevated liver enzymes, and low platelet count; LA = lupus anticoagulant; LDH = lactate dehydrogenase; TTP = thrombotic thrombocytopenic purpura.

Information from: Ko HH, Yoshida E. Acute fatty liver of pregnancy. Can J Gastroenterol 2006;20:25–30; and Sibai BM. Imitators of severe preeclampsia. Obstet Gynecol 2007;109:956–66.

the diagnosis may remain a mystery long after the patient has been discharged. Fortunately, maternal morbidity and mortality have decreased dramatically during the past several decades. Early recognition and appropriate treatment are extremely important for positive maternal and neonatal outcomes.

Annotated Bibliography

1. Gin T, Chan MTV, Chan KL, Yuen PM. Prolonged neuromuscular block after rocuronium in postpartum patients. Anesth Analg 2002;94:686–9.

   This study shows a potential overdose in postpartum patients when using total body weight to calculate a rocuronium dose. The formula for calculating lean body mass is 1.07 (total body weight) – 148 (total body weight/ height)^2, in which the total body weight is measured in kilograms and height in centimeters. The two study groups were immediate postpartum patients undergoing tubal ligation and similarly aged gynecologic laparoscopy patients. Each group received either a 0.6-mg/kg total body weight or a 0.6-mg/kg lean body mass rocuronium dose immediately before intubation. Postpartum women who received the 0.6-mg/kg dose based on total body weight had a significantly longer duration of neuromuscular block than their nonpregnant counterparts did (p<0.001). No difference existed between the groups receiving a dose based on lean body mass. However, lean body mass is not the same as lean body weight. The average total body weight in the postpartum women was 65 kg and lean body mass was 42 kg, whereas in the nonpregnant group, these weights were 51 kg and 39 kg, respectively. Using this formula, results are considerably lower than an ideal or adjusted body weight more commonly used in dosage calculations.

2. Muench MV, Canterino JC. Trauma in pregnancy. Obstet Gynecol Clin North Am 2007;34:555–83.

   This article is an overview of injuries during pregnancy; it focuses mostly on blunt or penetrating trauma but includes issues such as electric shock, burns, spinal cord injuries, and traumatic brain injury. Numerous tables describe physiologic adaptations, hemodynamic changes, and coagulation changes. The specific reasons for these alterations and how they may change therapeutic management of the patient are explained in the text. All aspects of patient assessment in the emergency department are covered, including fetal exposure to radiation and acceptable risks. The article does not include drug therapy for stabilizing the patient, nor does it discuss issues such as CPR or blood pressure support.

3. Sibai BM. Imitators of severe preeclampsia. Obstet Gynecol 2007;109:956–66.

   Written by one of the nation's experts in preeclampsia, this article should be a standard for those who see obstetric patients in a critical care setting. Distinguishing between severe preeclampsia and HELLP syndrome and other severe diseases can be extremely difficult. Acute fatty liver can resemble the elevated liver enzyme portion of HELLP, whereas thrombotic thrombocytopenia-hemolytic uremic syndrome causes more confusion with the low platelet diagnosis. Fortunately, the serum of patients with thrombotic thrombocytopenia-hemolytic uremic syndrome contains high concentrations of von Willebrand factor multimers. Antibodies against the enzyme that cleaves this factor are not found in patients with HELLP syndrome; however, the clinical usefulness of this test is difficult to establish because it is not readily available. Systemic lupus erythematosus can also lower platelet count, which could also be mistaken for HELLP syndrome. Included are tables describing laboratory values and the common signs and symptoms of each potentially confounding syndrome, which can steer the clinician toward one diagnosis or another. However, variations and superimposed conditions should be included in any discussion because there are many reports of unusual presentations of preeclampsia/HELLP syndrome.

4. Sibai BM. Diagnosis, prevention, and management of eclampsia. Obstet Gynecol 2005;105:401–10.

   Although the pathophysiology of eclampsia remains a mystery, the author sorts through the available data to present the primary theories. A long list of differential diagnoses fills a table, but it is left to the reader to know how findings would help distinguish one from another. An extensive section discusses whether eclampsia is preventable, but the actual question is whether preeclampsia can be prevented. All studies to date using various agents (e.g., aspirin, fish oil) to prevent the condition have had minimal or no effect. Magnesium therapy is recommended for every woman with preeclampsia during labor and for 12–24 hours postpartum. However, the number needed to treat to prevent one case of eclampsia ranges from 71 in women with severe preeclampsia to 139 in all pregnant patients with preeclampsia. Fortunately, eclampsia is an uncommon occurrence in developed countries, and management can be sufficiently generalized for clinicians to follow guidelines.

5. Dildy GA III. Postpartum hemorrhage: new management options. Clin Obstet Gynecol 2002;45:330–44.

   This is a review article on managing postpartum hemorrhage using all the standard techniques. The medical therapy section discusses all of the available uterotonics, listing doses and contraindications for each. Oxytocin is a first-line agent because of the relative lack of adverse effects and relative ease of administration. Methylergonovine is often a second-line agent except in those with hypertension. The prostaglandins, especially carboprost, can cause bronchoconstriction. Carboprost must be refrigerated, limiting its use in developing countries. These articles are becoming rare because there have been no new data for most of these agents in years. The surgical therapies mentioned in this chapter are included for more information. This article discusses abnormal placentation (where or how the placenta forms) in great detail. Although this is a potential cause of postpartum hemorrhage, these complications are beyond the scope of the chapter.

6. Ahonen J, Jokela R, Korttila K. An open non-randomized study of recombinant activated VII in major postpartum hemorrhage. Acta Anesthesiol Scand 2007;51:929–36.

   Even though it is a nonrandomized study, the cases are well matched, and the use of rf VIIa substantially reduced the number of surgical interventions required. Twenty-six women were compared with 22 women who also experienced a massive hemorrhage but did not receive rf VIIa. The causes of hemorrhage were almost identical, although the estimated volume of blood lost was not mentioned. A larger percentage of patients in the comparison group required hysterectomies, surgery to repair torn tissue or remove the remaining parts of the placenta, or uterine artery embolization than in the treatment group. The authors make key assessments during their discussion; for example, localized consumption of clotting factors in the pelvis may appear to be DIC by laboratory values. This article does not discuss any other reports of rf VIIa use, but it does highlight the points made by several other review articles.

7. Abboud J, Murad Y, Chen-Scarabelli C, Saravolatz L, Scarabelli TM. Peripartum cardiomyopathy: a comprehensive review. Int J Cardiol 2007;118:295–303.

   Although the exact precipitator of PPCM is unknown, several theories are mentioned in this article, such as myocarditis, infection, and apoptosis. Each is discussed in detail together with evidence for and against each one. The authors discuss clinical presentation but report only electrocardiography changes that can be present and do not discuss any ways to differentiate between other types of cardiomyopathy and the cardiomyopathy that occurs with pregnancy. The basics of treatment are included, with intensive care mentioned briefly. Fetal concerns with treatment are mentioned with acute and critical therapies; no evidence to support the safe use of nitroglycerin, dopamine, dobutamine, or milrinone is presented. Heart transplant patients and their potential risks of increased rejection and mortality are discussed. Immune globulin has been used in a few women, resulting in faster cardiac function improvement.

Pregnancy outcome and overall prognoses of women complete the article.

8. Ko HH, Yoshida E. Acute fatty liver of pregnancy. Can J Gastroenterol 2006;20:25–30.

This is a review of all aspects of AFLP. Because the article is organized differently from most, etiology and other topics follow clinical presentation and diagnosis, making it a little difficult to read. Laboratory findings are discussed using the categories of mild and moderate/severe elevations or depressions instead of specific values. A comprehensive table helps distinguish between preeclampsia, HELLP syndrome, AFLP, and hepatitis using categories of disease onset (by trimester), incidence, signs and symptoms, laboratory findings, and complications. The complications section especially aids in differentiating HELLP and AFLP. The etiology portion is devoted to a possible link with fatty acid oxidation defects, but the authors do not mention that the literature contains no other theories.

9. Moore J, Baldisseri MR. Amniotic fluid embolism. Crit Care Med 2005;33:S279–S285.

This review article presents the symptoms, pathogenesis, diagnosis, management, and prognosis of an AFE. Many similarities exist between the presentation of AFE and anaphylactic or septic shock. The etiologies for hallmark symptoms are explained in detail by category. Amniotic fluid embolism is a diagnosis of exclusion, excluding possibilities such as pulmonary or air embolisms, anesthetic complications, anaphylaxis, sepsis, or eclampsia. Management steps are described, guiding the reader from oxygen initiation through vasopressor therapy. Newer treatment strategies mentioned in the article include inhaled nitric oxide and prostacyclin, cardiopulmonary bypass or extracorporeal membrane oxygenation, plasma exchange transfusions, and high-dose corticosteroids, among others. All of these possibilities have only one or two case reports each to support their use. The authors have researched the potential therapies in the treatment of this morbid and mortal syndrome well.

10. Coppage KH, Sibai DM. Treatment of hypertensive complications in pregnancy. Curr Pharm Des 2005;11:749–57.

With Sibai as coauthor, expectations are high for the quality of data presented, and the article does not disappoint. The classifications and definitions of hypertension in pregnancy are broken down into gestational, chronic, and preeclampsia. Centrally acting agents, β-blockers, calcium channel blockers, vasodilators, diuretics, and angiotensin-converting enzyme inhibitors are reviewed initially, followed by a discussion of the fetal and neonatal effects of these agents. A useful table describes blood pressure elevations with a minimum duration before treatment initiation, even though many do not wait an hour to treat a blood pressure greater than 180/105 mm Hg. Magnesium sulfate therapy is described, and a table with specific toxicities associated with increasing serum concentrations is included. Hypertensive encephalopathy is addressed well, with very specific goals described. Details of dosing on the common agents used for acute and chronic hypertension are in table

format. This article could be improved by providing more details of the intravenous agents, such as comparison studies. A section on sodium nitroprusside offers details on the antidote of sodium nitrite and sodium thiosulfate. Although incorporating this information is very unusual, it could be quite useful, especially with a drug seldom used.

11. Martin JN Jr, Thigpen BD, Moore RC, Rose CH, Cushman J, May W. Stroke and severe preeclampsia and eclampsia: a paradigm shift focusing on systolic blood pressure. Obstet Gynecol 2005;105:246–54.

This retrospective chart review discusses women who suffered a pregnancy-related CVA treated at one academic medical center. Twenty-eight women were identified who met inclusion criteria, which involved a diagnosis of severe preeclampsia or eclampsia that was associated with a CVA. Blood pressures were obtained from the first prenatal visit, immediately before the CVA, if available, and immediately after the CVA. Eighteen women had coexisting HELLP syndrome. The authors use a classification system for HELLP syndrome that is explained, but not universally used. The specific platelet count ranges and the degree of elevation of lactate dehydrogenase or AST differentiate these classes. A major drawback of the article is the lack of a comparison with women who have severe preeclampsia, eclampsia, or HELLP syndrome without a CVA and their average systolic blood pressures at the same points. Not surprisingly, women who experienced a CVA had marked elevations in blood pressure during their first prenatal visit. This is one of the largest studies in the United States to describe mortality from preeclampsia/eclampsia. The study indicates that the presence of HELLP syndrome, especially with worsening symptoms or acute onset, together with systolic hypertension, has the highest risk of cerebral hemorrhage.