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Emergencies in the Second and Third Trimesters of Pregnancy

Introduction

Emergency providers who practice in the United States may be unfamiliar with the diagnosis and management of emergencies occurring in the second and third trimesters of pregnancy. In part, this is due to advancements in prenatal care and the development of protocols that triage patients to obstetric units rather than emergency departments. However, patients in the second and third trimesters still may present to the emergency department, especially in rural or international settings. In addition, the incidences of some second- and third-trimester emergencies, such as placenta previa, are increasing as a result of higher rates of assisted reproductive technology. Furthermore, the maternal mortality rate in the United States is 17.4 in 100,000 live births — a number that has not seen significant improvement in recent years, despite advances in healthcare.[1] Common emergencies specific to the second and third trimesters will be reviewed in this paper, including preterm labor, causes of antepartum bleeding in late pregnancy, and the hypertensive disorders of pregnancy. It is important to emphasize that obstetrics consultation is recommended in most emergencies that occur in the second and third trimesters prior to initiating therapies.

Preterm Labor

Etiology and Pathophysiology

Preterm labor, also sometimes referred to as premature labor, is defined as regular uterine contractions with cervical change before 37 weeks of gestational age.[2,3] In the United States, approximately 12% of all live births occur before term, and preterm labor precedes approximately 50% of these preterm births. It is the leading cause of prenatal morbidity and mortality globally and accounts for 70% of neonatal deaths.[4] Preterm labor is responsible for two-thirds of preterm births, which are associated with long-term medical complications and neurodevelopmental impairments in neonates.[5] In the United States, the estimated annual cost of preterm birth is $26 billion.[6] Maternal risk factors for preterm labor include age younger than 18 years or older than 40 years, low socioeconomic status, African-American race, prior preterm delivery, multiple gestations, uterine and placental abnormalities, prior reproductive surgery, and substance abuse, including tobacco and cocaine.[7,8] (*See Table 1.*) Evidence suggests that spontaneous preterm labor is a syndrome resulting in pathologic

EXECUTIVE SUMMARY

- Suspect preterm labor in patients in the second half of pregnancy who report contractions or other abdominal or pelvic symptoms that persist for several hours.
- A vaginal fluid pH greater than 7 is consistent with premature rupture of membranes.
- The amount of vaginal bleeding does not correlate with the severity of the placental abruption, and bleeding is occult in 30% of patients.
- Speculum and digital vaginal examinations are contraindicated in patients who present in the second or third trimester with bright red and painless vaginal bleeding.
- Be alert to the possibility of hypertensive disorders of pregnancy in any pregnant patient with gestational age greater than 20 weeks who is found to have a systolic blood pressure greater than 140 mmHg or a diastolic blood pressure greater than 90 mmHg; perform a urine dipstick to check for protein.
- Treat eclamptic seizures with intravenous magnesium sulfate and eclamptic hypertension with intravenous hydralazine or labetalol.

activation of myometrial contractility, cervical dilatation, and rupture of the chorioamniotic membranes.[5] Intrauterine infection, vascular disorders, uterine overdistension, breakdown of maternal-fetal tolerance, cervical insufficiency, and endocrine disorders all have been implicated as inciting factors for preterm labor.[5,8]

Diagnosis

Accurately identifying patients in preterm labor is important to initiating interventions that can improve fetal outcomes and avoid unnecessary hospitalizations and treatments in patients who do not progress to preterm birth. Preterm labor should be considered in patients in the second half of pregnancy who report contractions or other abdominal or pelvic symptoms that persist for several hours.[8,9] Patients with preterm labor also may report an increase or change in the quality of vaginal discharge, vaginal bleeding, pelvic pressure, back pain, or leakage of amniotic fluid. Contractions may be painful or painless, depending on whether the cervix is closed or open.[8] The contraction frequency, duration, and intensity should be noted.

A sterile pelvic examination can help to determine if there is cervical effacement or dilation. A transvaginal ultrasound often is performed to determine the fetal weight, volume of amniotic fluid, location of the placenta, and cervical length.[7,8] The cervix shortens as it prepares for delivery, and preterm labor is unlikely if the cervical length measures more than 30 mm on transvaginal ultrasound.[10]

Noninvasive fetal and uterine monitoring is the criterion standard to distinguish preterm labor from false labor (i.e., Braxton-Hicks contractions). Obstetricians may perform additional diagnostics, such as measuring fetal fibronectin or performing an electrohysterogram, to diagnose preterm labor.[10,11] The differential diagnosis for preterm labor includes placental abruption, urinary tract infection, ovarian cyst or torsion, appendicitis, and intrauterine fetal demise.

Management

If preterm labor is suspected, an obstetrician should be consulted. Patients with preterm labor at greater than 34 weeks of gestational age typically are admitted for anticipated delivery, although less than 10% of patients diagnosed with preterm labor give birth within seven days, and approximately 30% of preterm labor spontaneously resolves.[12] The goals of management in patients with preterm labor are to identify the inciting causes of preterm labor, especially those that are life-threatening to the patient or fetus (e.g., sepsis), and to prolong gestation as long as possible unless there is a contraindication to doing so (e.g., maternal instability). Medical management fails in approximately 25% of patients with preterm labor.[13]

Tocolytics. Tocolytic medications, including magnesium sulfate and beta-agonists, prolong gestation in preterm labor by inhibiting uterine activity. They are effective for up to 48 hours and should be initiated only after consultation with an obstetrician. Magnesium sulfate acts as a tocolytic by antagonizing intracellular calcium and allowing uterine relaxation. Side effects include neurologic and respiratory depression, hypotension, and arrhythmias. Therefore, cardiac monitoring and assessment of maternal reflexes are recommended.[7] Toxicity associated with magnesium sulfate can be reversed by administering calcium-containing medications, such as 1 gram of calcium gluconate given intravenously.[14]

Beta-agonists, such as terbutaline, activate enzymes that bind calcium, thereby inducing smooth muscle relaxation.[7] Beta-agonists can cause maternal hypotension, arrhythmias, tachycardia-related myocardial ischemia, and pulmonary edema. Beta-agonists also cross the placenta and can cause fetal tachycardia and subsequent intraventricular hemorrhage. No study has demonstrated improved neonatal outcomes when tocolytics are used alone.[7]

Absolute contraindications to tocolysis include gestational age greater than 34 weeks, active vaginal bleeding, fetal distress, chorioamnionitis, preeclampsia/eclampsia, disseminated intravascular coagulopathy (DIC), and maternal instability.

Corticosteroids. Corticosteroids (e.g., betamethasone, dexamethasone) accelerate fetal lung maturity and have been shown to decrease the incidence of neonatal respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis in patients with preterm labor.[15] A single course of corticosteroids is recommended for pregnant women between 24 weeks and 34 weeks of gestational age who are at risk

Table 1. Risk Factors for Preterm Labor

- Maternal age < 18 years or > 40 years
- Low socioeconomic status
- Prior preterm delivery
- Prior reproductive surgery or spontaneous abortion
- Multiple gestations
- Uterine abnormalities
- Placenta previa or abruption
- Genitourinary infections (e.g., chorioamnionitis)
- Cocaine or tobacco use
- African-American race

Table 2. Medications to Treat Preterm Labor[2]

Medication	Dose	Adverse Effects
Tocolytics		
Magnesium sulfate	Load 4 g to 6 g intravenous over 30 minutes, then 2 g/hour to 4 g/hour	Neurologic depression (e.g., hyporeflexia), tetany, respiratory depression, hypotension, dysrhythmias, cardiac arrest
Terbutaline (beta-agonist)	2.5 mg to 5 mg oral every two to four hours *or* 0.25 mg to 0.5 mg subcutaneous every two to four hours	Maternal: hypotension, arrhythmia, myocardial ischemia, pulmonary edema Fetal: tachycardia-related intraventricular hemorrhage
Corticosteroids		
Betamethasone	12 mg intramuscular every 24 hours for two doses	If used with tocolytics, maternal pulmonary edema can occur. In patients with preterm premature rupture of membranes, may increase rates of perinatal and maternal infections.
Dexamethasone	6 mg intramuscular every 12 hours for four doses	Same as betamethasone

of delivery within seven days, including women with preterm premature rupture of membranes (PPROM) and multiple gestations.[2] (*See Tables 2 and 3.*)

Preterm Premature Rupture of Membranes

Etiology and Pathophysiology

Premature rupture of membranes (PROM) is defined as the rupture of the fetal membranes at least one hour before the onset of labor at any gestational age.[9] "Premature" refers to the membrane rupture before labor and not prematurity due to gestational age. Preterm premature rupture of membranes (PPROM) is PROM that occurs before 37 weeks' gestational age and is the inciting event in roughly one-third of all preterm deliveries. Most patients with PPROM spontaneously begin labor within days, although a small proportion can remain undelivered for weeks or months.[9] An estimated 10% of pregnant women are affected by PROM and 3% are affected by PPROM.[16]

Risk factors for PROM and PPROM include genitourinary infections, low socioeconomic status, tobacco use, connective tissue disease, and a history of PPROM and prematurity.[17] (*See Table 4.*) Patients with PROM or PPROM are at increased risk of developing intrauterine infections, such as chorioamnionitis, which can further lead to fetal infections, including pneumonia and meningitis.[18] Up to 20% of cases of PPROM lead to neonatal sepsis.[19] Non-infectious complications of PPROM include umbilical cord prolapse, fetal distress, and placental abruption.[7]

Diagnosis

Patients with PROM commonly experience a gush of vaginal fluid, followed by a persistent leakage, which may be mistaken for urinary incontinence or increased physiologic vaginal secretions. A sterile speculum examination often is performed to collect fluid and to identify umbilical cord or fetal prolapse. Digital examination of the cervix should be avoided in case membranes are intact and to avoid introducing infection.[7,20]

Amniotic fluid may be distinguished from vaginal secretion by identifying "ferning" on a slide or using nitrazine paper, which measures the pH of vaginal fluid. The normal pH of vaginal secretions is 3.8-4.5 and the pH of amniotic fluid is 7.1-7.3. Therefore, a pH of the vaginal fluid above 7 is consistent with PROM. A false-positive test for PROM may occur in the presence of blood, semen, alkaline antiseptics, certain lubricants, trichomonas, or bacterial vaginosis. A false-negative test for PROM may occur with prolonged membrane rupture and minimal residual fluid. Ultrasound typically is performed in cases of suspected PPROM to assess the volume of amniotic fluid and to determine fetal age, weight, and presentation.[7]

Management

In cases of suspected PPROM, obstetrics should be consulted, and patients commonly are admitted. Urgent delivery is indicated if cord prolapse or fetal bradycardia (typically caused by cord compression from decreased amniotic fluid volume) is identified. The presence of chorioamnionitis also often is an indication to deliver. The

Table 3. Contraindications to Tocolytic Medications[8]

Maternal Contraindications	Fetal Contraindications
• Severe preeclampsia • Hemorrhage • Significant cardiac disease	• Gestational age ≥ 34 weeks • Lethal fetal anomalies • Intrauterine fetal demise • Chorioamnionitis • Fetal compromise requiring delivery

Table 4. Risk Factors for PROM and PPROM

- Genitourinary infections
- Low socioeconomic status
- History of PPROM and prematurity
- Tobacco use
- Connective tissue disease

PROM = premature rupture of membranes; PPROM = preterm premature rupture of membranes

use of tocolytics and corticosteroids in PPROM is controversial because of the associated increased risk of maternal and neonatal infections.[21] The administration of broad-spectrum, prophylactic antibiotics decreases overall rates of neonatal sepsis and prolongs pregnancy; however, it is associated with an increased proportion of gram-negative and ampicillin-resistant organisms causing sepsis.[22] The optimal antibiotic regimen is unclear, and multiple regimens have demonstrated benefit.[16]

Chorioamnionitis

Etiology and Pathophysiology

Chorioamnionitis, defined as an acute inflammation of the membranes and chorion of the placenta, most commonly results from an ascending polymicrobial infection from the cervix or vagina in the setting of membrane rupture.[23] Mycoplasmas are the most commonly identified pathogens.[24] Rarely, chorioamnionitis is caused by hematogenous spread.[25] The inflammatory response to the infection is postulated to lead to prostaglandin release, cervix ripening, membrane injury, and labor.[23] In addition to causing fetal sepsis, chorioamnionitis also has been linked to the development of cerebral palsy and other neurologic disorders in neonates.[23] Chorioamnionitis complicates 40% to 70% of preterm births and 5% of term births.[7,23,26] Risk factors include young maternal age, multiple vaginal examinations, and preexisting genital tract infections. (*See Table 5.*)

Diagnosis

Patients with chorioamnionitis may present with fever (present in 95% to 100% of cases), uterine tenderness, or purulent vaginal discharge.[23] Fetal monitoring may reveal tachycardia and decreased beat-to-beat variability. Laboratory findings, such as leukocytosis or increased proportions of bands, may raise clinical suspicion for chorioamnionitis. In addition to blood cultures, cervical cultures for *Escherichia coli* and gonorrhea and vaginal cultures for chlamydia, mycoplasma, and group B *Streptococcus* typically are obtained in patients suspected of having chorioamnionitis. Obstetricians also may obtain amniotic fluid cultures via amniocentesis to confirm the diagnosis. Other conditions in the differential diagnosis of chorioamnionitis include epidural anesthesia-associated fever, urinary tract infection, appendicitis, and placental abruption.

Management

Prompt administration of broad-spectrum antibiotics reduces maternal and neonatal complications of chorioamnionitis.[27] A typical antibiotic regimen is intravenous ampicillin given every six hours and intravenous gentamicin given every eight to 24 hours.[27] In patients with an allergy to penicillin, vancomycin is an alternative option.[28] Maternal complications of chorioamnionitis include sepsis, endometritis, pelvic abscess, postpartum hemorrhage, and the need to deliver via cesarean section.[29] Neonatal complications include pneumonia, sepsis, preterm birth, placental abruption, cerebral palsy, intraventricular hemorrhage, and death.[30]

Antepartum Hemorrhage

Normal physiologic changes that occur in late pregnancy may make it difficult to assess the hemodynamic status of patients who present with bleeding. For example, heart rate normally increases by 10-20 beats per minute in the third trimester, blood pressure is expected to nadir in the second trimester but increase in the third trimester, and total blood volume, plasma volume, and red blood cell mass increase throughout pregnancy.[31] However, the general principles of managing hemorrhagic shock in late pregnancy are similar to other patients: Judicious crystalloid volume resuscitation and early administration of blood products are recommended.

As in early pregnancy, RhD-negative women with vaginal bleeding in the third trimester are at risk of alloimmunization when carrying an RhD-positive fetus, which can lead to significant fetal morbidity in future pregnancies.[32] Therefore, anti-D immune globulin is administered prophylactically to RhD-negative women at 28 weeks' gestational age and within three days of delivery.[33] Additional anti-D immune globulin is not needed during episodes of bleeding in late pregnancy unless it has not been given previously.[33,34]

If there is a question of whether a dose of anti-D immune globulin is sufficient to prevent alloimmunization (e.g., cases of maternal trauma or severe vaginal bleeding), an obstetrician may perform the Kleihauer-Betke test, which involves dissolving adult and fetal hemoglobin in acid, to quantify the extent of fetal-to-maternal transplacental hemorrhage.[35] As a general rule, any patient in the third trimester who presents with greater than 500 mL of vaginal bleeding should be presumed to have placental abruption and should

Table 5. Risk Factors for Chorioamnionitis

- Young maternal age
- Low socioeconomic status
- Multiple vaginal examinations
- Extended duration of labor or rupture of membranes
- Genital tract infections (e.g., bacterial vaginosis)
- Nulliparity
- African-American race
- Tobacco use
- Colonization with group B *Streptococcus*
- Epidural anesthesia

Table 6. Risk Factors for Placental Abruption

- Maternal hypertension
- Advanced maternal age
- Multiparity
- Tobacco, cocaine, or alcohol use
- Premature rupture of membranes and preterm premature rupture of membranes
- History of placental abruption
- In vitro fertilization
- Diabetes
- Thrombophilia
- Preeclampsia
- Polyhydramnios
- Chorioamnioititis
- Blunt external trauma

be taken emergently to the operating room.[36]

Placental Abruption

Etiology and Pathophysiology

Placental abruption occurs when there is either partial or complete detachment of the placenta from the uterus after 20 weeks of gestation but before delivery.[37,38] The highest reported incidence of abruption is at 24-26 weeks' gestational age, after which the incidence decreases until delivery.[38] Placental abruption occurs in 0.4% to 1% of pregnancies in the United States.[39,40] It results in decreased oxygen exchange and nutrient supply for the fetus, which can lead to low birth weight and prematurity.[39] The main risk factor for placental abruption is maternal hypertension.[39] Additional risk factors are listed in Table 6. Patients with a history of placental abruption have an increased risk of placental abruption in future pregnancies. Placental abruption is the second most common injury in pregnant women who sustain trauma, after blunt solid organ injury, which is most often due to motor vehicle accidents, falls, or domestic violence.[41,42]

Diagnosis

Patients with placental abruption classically present with vaginal bleeding, lower abdominal pain, and contractions.[43] The amount of bleeding does not correlate with the severity of the placental abruption, and bleeding is occult in 30% of patients.[7] The majority of cases of placental abruption occur before the onset of labor.[43] If placental abruption is suspected, an obstetrician should be consulted for fetal and uterine monitoring.[44] Although ultrasound is the recommended first-line imaging in patients with suspected placental abruption, it has low sensitivity (24%) because of the similar echogenicity of abruption-related hematoma and normal placenta, the inconspicuous appearance of small hematomas, and the escape of blood from the vagina at the time of the ultrasound.[38,45] However, ultrasound findings of placental abruption are highly specific (92% to 94%).[38] In the context of maternal trauma, external fetal heart rate monitoring is the standard of care to assess fetal wellbeing.[46] Computed tomography may be performed and has a reported sensitivity of 100% in detecting placental abruption.[47]

Management

Given that maternal hemorrhage and fetal distress can develop suddenly, blood products should be prepared if placental abruption is suspected. In stable patients with a gestational age less than 36 weeks, expectant management may be appropriate. Unstable patients may require emergent cesarean delivery. In patients who sustain trauma and are found to have abnormal fetal heart rate tracings (e.g., fetal bradycardia or prolonged/late decelerations), a trial of resuscitative methods is recommended, such as oxygen administration, intravenous fluid administration, or changing maternal positioning.[47] If the abnormal tracings continue, delivery is recommended.

Maternal complications of placental abruption include sepsis, amniotic fluid embolism, venous thromboembolism, acute kidney injury, DIC, hemorrhage, the need for hysterectomy, and death.[7,48-52] Fetal complications of placental abruption include intrauterine growth restriction, preterm delivery (up to 60% of cases of abruption), and intrauterine fetal demise.[43,53] Placental abruption is associated with an estimated 10% perinatal mortality rate and it is responsible for 35% of all fetal mortality.[54,55] Approximately half of perinatal deaths associated with abruption are attributed to preterm birth.[56] Long-term complications of in utero exposure to hypoxia related to abruption include increased risk of cerebral palsy, chronic lung disease, and epilepsy in neonates.[40] (*See Table 7.*)

Placenta Previa

Etiology and Pathophysiology

Placenta previa occurs when the placenta implants in the lower segment of the uterus and partially or completely

Table 7. Grades of Placental Abruption

Grade 1 (40% of patients): asymptomatic or small amount of vaginal bleeding. May see mild uterine irritability without changes in fetal heart rate.
Grade 2 (45% of patients): moderate vaginal bleeding, uterine tenderness, and prolonged contractions. May develop maternal tachycardia/shock and fetal distress.
Grade 3 (15% of patients): severe vaginal bleeding with maternal shock and fetal demise. High risk of developing disseminated intravascular coagulopathy.

Table 8. Risk Factors for Placenta Previa

- Advanced maternal age
- Chronic maternal hypertension
- Tobacco and cocaine use
- Multiparity
- Previous placenta previa
- Previous elective abortion or cesarean delivery

covers the internal cervical os.[57] It accounts for 20% of third-trimester bleeding.[58] Many cases spontaneously resolve as the placenta migrates higher into the uterus during the pregnancy.[59] Placenta previa occurs in an estimated 1 in 200 pregnancies at term.[60] Risk factors for placenta previa are reviewed in Table 8.[60] The incidence of placenta previa is increasing as a result of rising rates of cesarean delivery, increased use of assisted reproductive technology, and more women delivering at advanced ages.[61]

Diagnosis

Patients with placenta previa classically present with bright red and painless vaginal bleeding. Contractions occur in 20% of patients.[7] Speculum and digital pelvic examinations generally are contraindicated or performed only after preparing the operating room, because of concerns of further tearing the placenta and causing hemorrhage.[59] However, transvaginal ultrasound is safe in cases of suspected placenta previa and preferred over transabdominal ultrasound, which may be falsely negative in patients who are obese or have posteriorly located placentas.[61]

Management

Management of placenta previa is similar to placental abruption and includes obstetrics consultation, fetal and uterine monitoring, and administration of blood products as needed.[61] Patients diagnosed with placenta previa often receive antenatal corticosteroids to prevent adverse neonatal outcomes associated with prematurity.[61] Patients should be admitted to a facility with transfusion capabilities and access to critical care. In patients with a gestational age greater than 37 weeks and uterine activity or persistent bleeding, cesarean delivery is the standard of care.[7] In preterm, stable patients with bleeding that resolves, expectant management may be appropriate.

Maternal complications of placenta previa include hemorrhage, DIC, and the need for emergent hysterectomy.[62] Fetal complications of placenta previa include preterm delivery, intrauterine growth restriction, respiratory distress syndrome, anemia, and fetal and neonatal death.[63,64]

Additional Causes of Antepartum Hemorrhage

Vasa Previa

Vasa previa occurs when one of the fetal vessels crosses the internal cervical os before inserting onto the placenta, thereby becoming trapped between the fetus and cervix. If the vessel passes through the os prior to the fetus during delivery, its rupture can lead to fetal exsanguination. Vasa previa is rare (< 2% of pregnancies), more common in multiple gestations, and associated with 50% fetal mortality rate.[7] Vasa previa may be detected incidentally on routine second-trimester ultrasound. It also should be suspected in pregnant patients who present with acute vaginal bleeding and abrupt fetal distress (e.g., fetal tachycardia followed by fetal bradycardia on monitoring), which typically requires an emergent cesarean delivery.

Placenta Accreta

Placenta accreta is a spectrum disorder that refers to a placenta that abnormally adheres to or invades into the uterine wall. In patients with placenta accreta, failure of the placenta to detach during delivery can lead to maternal hemorrhage, with an estimated maternal mortality of up to 7%.[61] Placenta accreta occurs in one in 2,000 pregnancies.[61] Risk factors for placenta accreta include a history of prior placenta accreta, cesarean delivery, or other uterine instrumentation.

Ultrasound is highly accurate at diagnosing placenta accreta. Patients should have a planned delivery at 35-36 weeks' gestational age in a specialist center with access to adult and neonatal critical care.[61] The preferred delivery method often is cesarean delivery with hysterectomy with the placenta left in place.[61]

Circumvallate Placenta

A circumvallate placenta develops when the edge of the placenta rolls under itself, creating a membranous shelf that can separate from the uterus and cause bleeding. A circumvallate placenta should be suspected in a patient with painless vaginal bleeding but no evidence of placenta previa on ultrasound. Similar to placenta previa, a circumvallate placenta can cause maternal hemorrhage and fetal distress necessitating emergent cesarean delivery.

Hypertensive Disorders in Pregnancy

Approximately 5% of all pregnancies are complicated by hypertension.[65,66] In the United States, nearly 20% of maternal deaths result from complications of pregnancy-related hypertension.[67] Chronic hypertension, defined

Table 9. Risk Factors for Gestational Hypertension

- Nulliparity
- Multiple gestations
- High altitude
- Age younger than 20 years
- Preexisting obesity, hyperlipidemia, or diabetes
- African-American race
- Family history of gestational hypertension

as a systolic blood pressure greater than 140 mmHg or diastolic blood pressure greater than 90 mmHg on two or more occasions, may precede and continue into pregnancy and predisposes patients to preterm delivery and abruption.[68] In addition, pregnancy itself may induce hypertensive disorders, including gestational hypertension, preeclampsia, and eclampsia. Patients with chronic hypertension have an increased risk of developing preeclampsia and eclampsia.[69] Maternal and neonatal outcomes also are worsened in the presence of chronic hypertension when compared to de novo pregnancy-induced hypertensive disease.[70]

Gestational (Transient) Hypertension

Gestational hypertension, also referred to as transient or pregnancy-induced hypertension, is defined as a systolic blood pressure greater than 140 mmHg or diastolic blood pressure greater than 90 mmHg, without proteinuria or edema, that develops after 20 weeks' gestational age and resolves within 12 weeks after delivery.[71,72] Risk factors for gestational hypertension include nulliparity, multiple gestations, age younger than 20 years, high altitude, obesity, hyperlipidemia, preexisting diabetes, African-American race, and family history of gestational hypertension.[73-75] (*See Table 9.*) Patients with gestational hypertension generally are asymptomatic, although rare maternal complications include hepatocellular necrosis, acute kidney injury, microangiopathic hemolysis, and thrombocytopenia.[76]

Preeclampsia and HELLP

Preeclampsia is defined as a systolic blood pressure greater than 140 mmHg or diastolic blood pressure greater than 90 mmHg with pathologic edema or proteinuria (1+ on a urine dipstick or > 300 mg in 24 hours).[77] Recently, the definition of preeclampsia has been expanded to include other signs of end-organ damage (e.g., liver failure, renal failure, hematologic dysfunction), with or without proteinuria.[78] In comparison to the edema seen in normal pregnancy, which usually is dependent, the edema associated with preeclampsia often is generalized, involving the hands and face, and persists throughout the day.

Patients with preeclampsia may present with headache, visual disturbances, or epigastric or right upper quadrant pain. In patients with underlying chronic hypertension, superimposed preeclampsia should be suspected if there is new or worsening proteinuria, worsening of previously well-controlled hypertension, or elevated liver enzymes.

Hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome occurs in 5% to 10% of patients with preeclampsia and is characterized by microangiopathic hemolytic anemia and thrombocytopenia (< 100,000 platelets/mm^3), which can lead to decreased placental perfusion and increased fetal and maternal morbidity and mortality.[77-79]

Eclampsia

Eclampsia is defined by the occurrence of seizures or coma in a patient with preeclampsia, without another underlying cause.[79] A pregnant patient who presents with a seizure should be evaluated for other causes of pregnancy-related seizure (e.g., subarachnoid hemorrhage, cerebral venous thrombosis). Approximately one in 3,250 pregnancies in the United States are affected by eclampsia.[65] Eclampsia is associated with a maternal mortality rate of up to 14% and a fetal mortality rate of approximately 1%.[80,81] Up to one-third of eclampsia-induced seizures occur after delivery and have been reported as late as 28 days postpartum.[82]

Etiology and Pathophysiology

The underlying etiology of pregnancy-induced hypertension remains unclear. Proposed mechanisms include pregnancy-related changes in prostacyclin hormones, increased vascular reactivity to vasoactive agents, abnormal placental implantation, and variations in the angiotensin gene.[7,70] In preeclampsia, changes related to hypertension can lead to vasospasm, ischemia, and thrombosis of the placenta, which ultimately can cause placental abruption, fetal death secondary to hypoxia, prematurity, and damage to maternal organs.[71]

Diagnosis

Clinicians should be alerted to the possibility of hypertensive disorders of pregnancy in any pregnant patient with gestational age greater than 20 weeks who is found to have a systolic blood pressure greater than 140 mmHg or a diastolic blood pressure greater than 90 mmHg. Patients also may present with nonspecific symptoms, including headache, abdominal pain, or edema. A urine dipstick should be performed in all hypertensive pregnant patients and, if protein is detected, the diagnosis of preeclampsia is presumed until proven otherwise. Additional laboratory studies often are performed to assess for anemia, thrombocytopenia, and kidney or liver dysfunction. If HELLP syndrome is suspected, a lactic acid dehydrogenase level may help to identify hemolysis. A point-of-care glucose test should be performed immediately in any pregnant patient who presents with seizures. Computed tomography of the head in patients with eclampsia commonly reveals patchy hemorrhage, small cortical infarcts, and cerebral edema.[83]

Treatment

Pregnant patients who are incidentally found to have gestational hypertension should be referred for outpatient monitoring of blood pressure, urine protein, and maternal weight gain. Oral labetalol 100 mg taken twice daily is recommended for non-severe hypertension in pregnant patients who

do not have reactive airway disease or bradycardia.[84,85] The American College of Obstetricians and Gynecologists recommends starting oral aspirin 81 mg daily in women at risk of developing preeclampsia, starting at 16 weeks' gestational age and continued until delivery.[86] Hydralazine, nifedipine, and methyldopa are other oral antihypertensives that are considered safe in pregnancy.[84,85]

Patients with gestational hypertension or preeclampsia may require admission if blood pressure persists above 140/99 mmHg or if laboratory studies reveal end-organ dysfunction (e.g., hepatic, renal, or hematologic abnormalities).[79] Delivery is the only definitive treatment for gestational hypertension, preeclampsia, and eclampsia.[87] In patients with preeclampsia without significant end-organ dysfunction, bed rest has not been shown to reduce blood pressure.[88]

In patients who develop seizures, magnesium sulfate has been shown to be a more effective treatment than phenytoin, diazepam, or nimodipine.[79,89-91] The exact mechanism of action of magnesium in preventing and treating eclamptic seizures is unknown. Typically, a loading dose of 6 grams of magnesium is administered intravenously, followed by a continuous intravenous rate of 2 grams per hour.[92] Patients should be monitored for hyporeflexia and respiratory depression when given magnesium. If these develop, 1 gram of calcium gluconate can be administered intravenously to reverse the effects. The goal is to decrease blood pressure to less than 160/105 mmHg without dropping the diastolic pressure below 90 mmHg (to maintain placental perfusion), which is achieved commonly with administration of magnesium sulfate alone. Intravenous hydralazine and labetalol may be given in cases of severe hypertension.[66,70] Diuretics and hyperosmotic agents should be avoided to prevent volume loss and subsequent decreases in placental perfusion. (*See Table 10.*)

Table 10. Medications to Treat Preeclampsia and Eclampsia[79,93-95]

Medication	Dose	Notes
Antiepileptics		
Magnesium sulfate	6 grams intravenous over 15-20 minutes, followed by 2 grams intravenous per hour continuous	• First-line therapy for eclamptic seizures • Monitor for respiratory and neurologic depression (hyporeflexia) and hypotension
Diazepam	40 mg intravenous bolus	• Second-line for eclamptic seizures • Monitor for sedation
Phenytoin	1,250 mg intravenous at a rate of 50 mg/minute	• Second-line for eclamptic seizures
Antihypertensives		
Hydralazine	5 mg to 10 mg intravenous every 15-20 minutes, goal diastolic pressure 90-100 mmHg	• May cause reflex tachycardia and fluid retention
Labetalol	20 mg intravenous; if ineffective, a second dose of 40 mg intravenous, then 80 mg intravenous every 10 minutes (total dose not to exceed 220 mg)	• Maternal asthma is a contraindication

Conclusion

Emergency providers are expected to diagnose and manage emergencies occurring in the second and third trimesters of pregnancy. Preterm labor is common and may progress to preterm delivery, the main cause of neonatal death worldwide. Therefore, it is important to understand the roles of tocolytics and antenatal corticosteroids in decreasing neonatal complications.

Chorioamnionitis should be considered in pregnant patients presenting with fever, since prompt administration of antibiotics has the potential to improve neonatal and maternal outcomes. Vaginal bleeding occurring in the second and third trimesters may be secondary to placental abruption, placenta previa, or other conditions that have the potential to progress rapidly to maternal hemorrhage and fetal distress. Hypertension may be detected incidentally and should always be taken seriously in pregnant patients, since 20% of maternal deaths result from complications of hypertension. Obstetrics consultation, in person or by phone, is recommended when managing emergencies in the second and third trimesters. By recognizing and understanding how to treat these and other emergencies occurring in late pregnancy, emergency providers have the opportunity to reduce neonatal and maternal morbidity and mortality.

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CME/CE Questions

1. A 24-year-old woman at 34 weeks' gestational age presents with intermittent lower abdominal pain and vaginal discharge for the past three hours. On examination, her cervix is effaced and dilated. Which of the following is *incorrect* regarding preterm labor?
   a. Preterm labor is the leading cause of prenatal mortality worldwide.
   b. Measurement of cervical length on transvaginal ultrasound may help to identify preterm labor.
   c. Noninvasive fetal and uterine monitoring is the criterion standard to diagnose preterm labor.
   d. Patients who present to the emergency department with preterm labor should be referred to outpatient obstetrics.
2. A 30-year-old woman at 35 weeks' gestational age presents with signs of preterm labor. Which of the following is true regarding the medical management of preterm labor?
   a. Beta-agonists, such as terbutaline, do not cross the placenta.
   b. Corticosteroids are recommended in all patients who present with preterm labor at a gestational age of less than 37 weeks.
   c. The presence of chorioamnionitis is a contraindication to the administration of tocolytics.
   d. Hypertension is a common side effect of magnesium sulfate.
3. Which of the following regarding chorioamnionitis is *not true*?
   a. Chorioamnionitis usually results from an ascending infection from the cervix or vagina.
   b. Chorioamnionitis is associated with an increased risk of neonatal neurologic disorders, including cerebral palsy.
   c. Fever occurs in approximately half of patients with chorioamnionitis.
   d. Broad-spectrum antibiotics have been shown to decrease maternal and neonatal complications in patients with chorioamnionitis.
4. A 24-year-old gravida 3 para 2 female at 26 weeks' gestational age presents with vaginal bleeding and lower abdominal pain for the past two hours. She admits to using cocaine throughout her pregnancy. She is tachycardic, hypotensive, and has lower abdominal tenderness. Which of the following is true regarding placental abruption?
   a. The highest incidence of placental abruption is at 24-26 weeks, after which the incidence decreases until delivery.
   b. In patients with placental abruption, the amount of vaginal bleeding usually correlates with the severity of the abruption.
   c. Transabdominal ultrasound is highly sensitive and specific for placental abruption.
   d. Placental abruption is the most common injury identified in pregnant patients who experience trauma in the second and third trimesters.
5. A 38-year-old female at 32 weeks' gestational age with a history of "low-lying placenta" presents to the emergency department with painless vaginal spotting. On examination, she is well-appearing, has normal vital signs, and has no abdominal tenderness. Which of the following is an appropriate next step in the evaluation of a patient with suspected placenta previa?
   a. Perform a bimanual pelvic examination to assess for cervical effacement and dilation.
   b. Obtain a transvaginal ultrasound to assess for placenta previa.
   c. Refer stable patients to outpatient obstetrics for repeat evaluation in two days.
   d. Avoid administration of corticosteroids, which can worsen outcomes in patients with placenta previa.
6. An 18-year-old woman at 30 weeks' gestational age presents with fatigue. On examination, she has a blood pressure of 150/90 mmHg, mild generalized edema, and pallor. Laboratory analysis is notable for: hemoglobin 8.2 g/dL, platelet count 85,0000/uL, aspartate aminostransferase 75 IU/L, and alanine transaminase 90 IU/L. What is the likely diagnosis?
   a. Preeclampsia
   b. Hemolysis, elevated liver enzymes, and low platelet count syndrome
   c. Cholestasis of pregnancy
   d. Eclampsia

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Emergencies in the Second and Third Trimesters of Pregnancy

Risk Factors for Preterm Labor

- Maternal age < 18 years or > 40 years
- Low socioeconomic status
- Prior preterm delivery
- Prior reproductive surgery or spontaneous abortion
- Multiple gestations
- Uterine abnormalities
- Placenta previa or abruption
- Genitourinary infections (e.g., chorioamnionitis)
- Cocaine or tobacco use
- African-American race

Medications to Treat Preterm Labor

Medication	Dose	Adverse Effects
Tocolytics		
Magnesium sulfate	Load 4 g to 6 g intravenous over 30 minutes, then 2 g/hour to 4 g/hour	Neurologic depression (e.g., hyporeflexia), tetany, respiratory depression, hypotension, dysrhythmias, cardiac arrest
Terbutaline (beta-agonist)	2.5 mg to 5 mg oral every two to four hours *or* 0.25 mg to 0.5 mg subcutaneous every two to four hours	Maternal: hypotension, arrhythmia, myocardial ischemia, pulmonary edema Fetal: tachycardia-related intraventricular hemorrhage
Corticosteroids		
Betamethasone	12 mg intramuscular every 24 hours for two doses	If used with tocolytics, maternal pulmonary edema can occur. In patients with preterm premature rupture of membranes, may increase rates of perinatal and maternal infections.
Dexamethasone	6 mg intramuscular every 12 hours for four doses	Same as betamethasone

Contraindications to Tocolytic Medications

Maternal Contraindications	Fetal Contraindications
• Severe preeclampsia • Hemorrhage • Significant cardiac disease	• Gestational age ≥ 34 weeks • Lethal fetal anomalies • Intrauterine fetal demise • Chorioamnionitis • Fetal compromise requiring delivery

Risk Factors for PROM and PPROM

- Genitourinary infections
- Low socioeconomic status
- History of PPROM and prematurity
- Tobacco use
- Connective tissue disease

PROM = premature rupture of membranes; PPROM = preterm premature rupture of membranes

Risk Factors for Chorioamnionitis

- Young maternal age
- Low socioeconomic status
- Multiple vaginal examinations
- Extended duration of labor or rupture of membranes
- Genital tract infections (e.g., bacterial vaginosis)
- Nulliparity
- African-American race
- Tobacco use
- Colonization with group B *Streptococcus*
- Epidural anesthesia

Risk Factors for Placental Abruption

- Maternal hypertension
- Advanced maternal age
- Multiparity
- Tobacco, cocaine, or alcohol use
- Premature rupture of membranes and preterm premature rupture of membranes
- History of placental abruption
- In vitro fertilization
- Diabetes
- Thrombophilia
- Preeclampsia
- Polyhydramnios
- Chorioamnioitis
- Blunt external trauma

Grades of Placental Abruption

Grade 1 (40% of patients): asymptomatic or small amount of vaginal bleeding. May see mild uterine irritability without changes in fetal heart rate.

Grade 2 (45% of patients): moderate vaginal bleeding, uterine tenderness, and prolonged contractions. May develop maternal tachycardia/shock and fetal distress.

Grade 3 (15% of patients): severe vaginal bleeding with maternal shock and fetal demise. High risk of developing disseminated intravascular coagulopathy.

Risk Factors for Placenta Previa

- Advanced maternal age
- Chronic maternal hypertension
- Tobacco and cocaine use
- Multiparity
- Previous placenta previa
- Previous elective abortion or cesarean delivery

Risk Factors for Gestational Hypertension

- Nulliparity
- Multiple gestations
- High altitude
- Age younger than 20 years
- Preexisting obesity, hyperlipidemia, or diabetes
- African-American race
- Family history of gestational hypertension

Medications to Treat Preeclampsia and Eclampsia

Medication	Dose	Notes
Antiepileptics		
Magnesium sulfate	6 grams intravenous over 15-20 minutes, followed by 2 grams intravenous per hour continuous	• First-line therapy for eclamptic seizures • Monitor for respiratory and neurologic depression (hyporeflexia) and hypotension
Diazepam	40 mg intravenous bolus	• Second-line for eclamptic seizures • Monitor for sedation
Phenytoin	1,250 mg intravenous at a rate of 50 mg/minute	• Second-line for eclamptic seizures
Antihypertensives		
Hydralazine	5 mg to 10 mg intravenous every 15-20 minutes, goal diastolic pressure 90-100 mmHg	• May cause reflex tachycardia and fluid retention
Labetalol	20 mg intravenous; if ineffective, a second dose of 40 mg intravenous, then 80 mg intravenous every 10 minutes (total dose not to exceed 220 mg)	• Maternal asthma is a contraindication

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