Preeclampsia: Management and prognosis

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INTRODUCTION

Preeclampsia is a progressive, multisystem disorder characterized by new-onset hypertension and end-organ dysfunction in the last half of pregnancy (table 1). Progression from nonsevere (previously referred to as "mild") to severe (table 2) on the disease spectrum may be gradual or rapid.

A key focus of routine prenatal care is monitoring pregnancies for signs and symptoms of preeclampsia. If the diagnosis is made, the definitive treatment is delivery to prevent development of maternal or fetal complications from disease progression. Delivery leads to eventual resolution of the disease. Timing of delivery is based on a combination of factors, including disease severity, maternal and fetal condition, and gestational age.

This topic will discuss the management of pregnancies complicated by preeclampsia and maternal prognosis. Other important issues related to this disease are reviewed separately.

- (See "Preeclampsia: Pathogenesis".)
- (See "Preeclampsia: Clinical features and diagnosis".)
- (See "Early pregnancy prediction of preeclampsia".)
- (See "Preeclampsia: Prevention".)
- (See "Expectant management of preterm preeclampsia with severe features".)

PREECLAMPSIA WITH FEATURES OF SEVERE DISEASE

General approach: Delivery

- Preeclampsia with features of severe disease (formerly called severe preeclampsia) (table 2) is generally regarded as an indication for delivery in pregnancies ≥34+0 weeks of gestation [1]. Delivery minimizes the risk of serious maternal complications, such as cerebral hemorrhage, hepatic rupture, renal failure, pulmonary edema, seizure, bleeding related to thrombocytopenia, myocardial infarction, stroke, acute respiratory distress syndrome, retinal injury, or abruptio placentae, and fetal complications, such as growth restriction and fetal demise [1-4]. With the exception of fetal growth restriction, any of these life-threatening complications can occur suddenly. (See "Preeclampsia: Clinical features and diagnosis", section on 'Spectrum of disease' and "Preeclampsia: Clinical features and diagnosis", section on 'Natural history/course of disease'.)

- Pregnancies in which the fetus has not attained the gestational age at the lower limit of viability (23 to 24 weeks), pregnancies <34+0 weeks of gestation with preterm labor or prelabor rupture of membranes, and pregnancies in which the maternal and/or fetal condition is unstable are also candidates for delivery. Attempting to prolong pregnancy in these settings subjects the mother and fetus to significant risks with relatively small potential benefits; therefore, delivery is preferable.

Management of delivery is reviewed below. (See 'Intrapartum management' below.)

Expectant management of selected cases — Expectant management rather than delivery is reasonable for selected preterm pregnancies with preeclampsia with features of severe disease to reduce neonatal morbidity from immediate preterm birth, even though the mother and fetus are at risk from disease progression. Expectant management allows administration of a course of antenatal corticosteroids and may provide time for further fetal growth and maturation.

For consideration of this approach, both the mother and fetus must be stable, closely monitored in a hospital setting with an appropriate level of newborn care, and cared for by, or in consultation with, a maternal-fetal medicine specialist. We favor limiting expectant management to pregnancies ≥24 weeks and <34 weeks of gestation. Selection of appropriate candidates for this approach and management of these pregnancies are discussed separately. (See "Expectant management of preterm preeclampsia with severe features".)

Low-resource settings — In low-resource settings, delays in triage, transport, and treatment of patients with preeclampsia contribute to adverse maternal, fetal, and newborn mortality and morbidity. Three Community-Level Interventions for Preeclampsia (CLIP) trials aimed to improve adverse outcomes by addressing these delays [5-7]. The trials randomly assigned participants to usual prenatal care or a program of community-level interventions, which included community engagement regarding preeclampsia awareness, enhanced prenatal assessment, risk stratification, initiation of potentially lifesaving therapies (eg, oral antihypertensive drugs, intramuscular magnesium sulfate), and arranging safe and timely transport to a hospital when appropriate. The trials were conducted in India, Pakistan, and Mozambique and included over 60,000 pregnancies.

However, in a meta-analysis of individual patient data from these trials, the intervention group did not achieve a reduction in a predefined composite of maternal/perinatal mortality or morbidity outcomes (24.4 versus 21.9 percent, adjusted odds ratio 1.17, 95% CI 0.90-1.51) or its components [8]. The investigators hypothesized that the absence of benefit was related, in part, to lack of provision of an adequate number of well-trained community health workers to conduct at least eight prenatal care visits and lack of referral/treatment of women with only diastolic hypertension. They concluded that future community-level interventions should expand the number of community health workers, assess general (rather than condition-specific) messaging, and strengthen the health system.

PREECLAMPSIA WITHOUT FEATURES OF SEVERE DISEASE

General approach

Term pregnancies: Delivery — Experts consistently recommend delivery of women with preeclampsia at ≥37+0 weeks of gestation, even without features of severe disease (previously called "mild preeclampsia") [1,4,9].

The benefits of this approach are best supported by a multicenter trial (HYPITAT) that randomly assigned 756 women with mild preeclampsia or gestational hypertension at 36+0 to 41+0 weeks of gestation to induction of labor within 24 hours of randomization or expectant management with maternal/fetal monitoring [10]. Intervention had favorable effects on maternal outcome, without incurring an increase in cesarean delivery or neonatal morbidity. Specifically:

- Induction resulted in a 30 percent reduction in a composite of serious maternal outcomes (31 versus 44 percent, relative risk [RR] 0.71, 95% CI 0.59-0.86), which was primarily driven by a reduction in patients who developed severe hypertension. The composite included maternal mortality, maternal morbidity (eclampsia, HELLP syndrome [hemolysis, elevated liver enzymes, low platelets], pulmonary edema, thromboembolic disease, placental abruption), progression to severe hypertension or proteinuria, and major postpartum hemorrhage.
- Induction resulted in a lower rate of cesarean delivery (14 versus 19 percent).

- Induction did not result in statistical differences between groups in any neonatal outcome measure, even though the induced group delivered, on average, 1.2 weeks earlier than the control group. The possibility of small differences in newborn outcomes could not be definitively excluded because of the small number of adverse outcomes.

Follow-up analyses have shown that an unfavorable cervix is not a reason to avoid induction [11,12]. In a secondary analysis of data from this trial and DIGITAT (pregnancies complicated by fetal growth restriction), induction of labor at term in women with a median Bishop score of 3 (range 1 to 6) was not associated with a higher risk of cesarean delivery than expectant management, and approximately 85 percent of women in both groups achieved a vaginal delivery [12]. Prostaglandins or a balloon catheter were used for cervical ripening.

In addition, an economic analysis of the HYPITAT trial conducted in the Netherlands concluded induction was 11 percent less costly overall than expectant management with monitoring [13].

Management of delivery is reviewed below. (See 'Intrapartum management' below.)

Preterm pregnancies: Expectant management — At preterm gestational ages, the risks for serious sequelae from disease progression needs to be balanced with the newborn risks resulting from preterm birth. When mother and fetus are stable and have no findings of serious end-organ dysfunction, an expectant approach with close monitoring for evidence of progression to the severe end of the disease spectrum is reasonable to achieve further fetal growth and maturity. However, at any gestational age, evidence of severe hypertension, serious maternal end-organ dysfunction (table 2), or nonreassuring tests of fetal well-being are generally an indication for prompt delivery.

Before 34 weeks — Before 34+0 weeks, guidelines from major medical organizations generally recommend expectant management of preeclampsia without features of severe disease, based on expert opinion, given the high risk of neonatal complications from preterm birth [1,4,9]. We concur with this approach.

34+0 to 36+6 weeks — There is less consensus about the optimum management of preeclampsia without features of severe disease and stable maternal and fetal condition at 34+0 to 36+6 weeks. Although there are serious maternal risks with expectant management, we believe expectant management until 37+0 weeks is reasonable in fully informed patients because the absolute maternal risk of a serious adverse outcome is low, and there are modest neonatal benefits from delivery at 37+0 weeks rather than earlier. After a discussion of the risks and benefits of planned late preterm delivery (34+0 to 36+6 weeks) versus planned early term delivery at or shortly after 37+0 weeks, the timing of delivery should ultimately be a shared decision.

The PHOENIX trial provided quantitative data for patient counseling [14]. This multicenter randomized trial compared planned early delivery within 48 hours with expectant management (usual care) in 901 singleton or dichorionic diamniotic twin preeclamptic pregnancies at 34+0 to 36+6 weeks of gestation. In contrast to previous trials, such as HYPITAT, PHOENIX excluded hypertensive women who did not have preeclampsia. Compared with expectant management, planned early delivery:

- Reduced adverse maternal composite outcome (maternal morbidity or systolic blood pressure ≥160 mmHg: 289/448 [65 percent] versus 338/451 [75 percent]; adjusted RR 0.86, 95% CI 0.79-0.94). Severe systolic hypertension accounted for at least 60 percent of the composite outcome in both groups.

- Increased adverse perinatal composite outcome (perinatal death or neonatal intensive care unit [NICU] admission: 196/471 [42 percent] versus 159/475 [34 percent], RR 1.26, 95% CI 1.08-1.47). However, there were no perinatal deaths. Thus, this difference derived from a greater number of infants in the planned early delivery group admitted to the NICU, most of whom were admitted because of preterm gestational age alone; respiratory morbidity was not increased compared with expectant management.

The overall number of serious adverse events was similar in both groups. Neither group had a stillbirth or neonatal death. Both groups included four patients with abruption. Although PHOENIX is the largest randomized trial to address this issue,

the number of adverse events was still relatively small, and thus, the trial was underpowered to find statistical differences in individual outcomes of clinical importance in shared decision making. For example, expectant management had statistically significant favorable perinatal effects at 34 and 35 weeks of gestation, which were attenuated by including pregnancies at 36 weeks.

In the expectantly managed group, the median additional prolongation of pregnancy was five days (three days after adjustment of confounders), more than one-half of the women in this group had an indicated delivery before 37 weeks, and 74 percent progressed to preeclampsia with severe features (versus 64 percent in the planned delivery group). The only maternal death occurred in the expectantly managed group in a woman with underlying medical comorbidities who died unexpectedly five days postpartum; her death was not thought to be related to expectant management.

Components of expectant management

Inpatient versus outpatient care — Close maternal monitoring upon diagnosis of preeclampsia is important to establish disease severity and the rate of progression. Hospitalization is useful for making these assessments and facilitates immediate intervention in the event of rapid deterioration. After the initial in-hospital diagnostic evaluation, outpatient care is a cost-effective option for women found to be stable over a period of several days and with no severe features of preeclampsia [15-19]. Patients offered outpatient monitoring should be well-informed and understand the importance of calling for symptoms/signs of worsening disease, able to comply with modified activity at home, live close to a hospital, have someone at home at all times to call in the event of an unexpected adverse event, able to have blood pressure measured twice daily, and willing to come in for antenatal visits twice a week for fetal monitoring and blood tests. Readmission is indicated for progression of disease.

Outpatient care can be provided in the patient's home or, where available, at an antenatal day care unit, which is a common approach in the United Kingdom [20]. If signs or symptoms of disease progression are noted, hospitalization for more intensive monitoring and possible delivery is indicated.

There are limited data on outcome of outpatient management of women with preeclampsia. An observational study and a randomized trial reported good outcomes, but these studies had too few subjects to detect small but clinically significant differences in outcome between inpatient and outpatient management [16,17]. A systematic review of three trials with a total of 504 women with various complications of pregnancy observed no major differences in clinical outcomes for mothers or infants for care in an antenatal day unit versus hospital admission [20]. The American College of Obstetricians and Gynecologists considers ambulatory management at home an option for women with preeclampsia without severe features as long as the patient is well informed and serial, frequent maternal and fetal monitoring are performed, including blood pressure, ultrasonography, and laboratory studies (platelet count, serum creatinine, liver enzymes), as described below [1].

Patient education — All women with preeclampsia should be aware of the signs and symptoms at the severe end of the disease spectrum (table 2) and should monitor fetal movements daily. If a woman develops a severe or persistent headache (ie, does not respond to one dose of acetaminophen), visual changes, new shortness of breath, or right upper quadrant or epigastric pain, she should notify her health care provider immediately. Women who self-monitor blood pressure should be instructed about the correct procedure. (See "Treatment of hypertension in pregnant and postpartum women", section on 'Technique for accurate measurement of blood pressure'.)

As with any pregnancy, decreased fetal movement, vaginal bleeding, abdominal pain, rupture of membranes, or regular uterine contractions should be reported immediately, as well.

Activity — For outpatients, strict bedrest is unnecessary as there is no evidence that bedrest improves pregnancy outcome or delays progression of the disease [21]. Furthermore, strict bedrest in hospitalized pregnant women has been associated with an increased risk of venous thromboembolism [22].

Restricted activity (eg, no heavy lifting, resting for a total of eight hours during the day with the feet elevated) is often recommended since blood pressure is lower in rested patients. Resting in the left lateral decubitus position can augment uteroplacental flow, which may benefit pregnancies in which this is a concern. In all pregnant women, avoiding the supine sleep position can have favorable fetal effects and appears prudent [23].

Laboratory follow-up — The minimum laboratory evaluation should include platelet count, serum creatinine, and liver chemistries. These tests should be repeated at least twice weekly in women with preeclampsia without severe features to assess for disease progression, and more often if clinical signs and symptoms suggest worsening disease.

Although other laboratory abnormalities may occur (see "Preeclampsia: Clinical features and diagnosis", section on 'Potential laboratory findings'), the value of monitoring additional laboratory tests is unclear. A rising hematocrit can be useful to look for hemoconcentration, which suggests contraction of intravascular volume and progression to more severe disease, while a falling hematocrit may be a sign of hemolysis, although an elevated serum indirect bilirubin and/or LDH concentration is a better marker for hemolysis. Hemolysis can be confirmed by observation of schistocytes and helmet cells on a blood smear (picture 1A-B). (See "HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets)".)

Since several clinical studies have shown that neither the rate of increase nor the amount of proteinuria affects maternal or perinatal outcome in the setting of preeclampsia [24-27], repeated urinary protein estimations are not useful once the threshold of 300 mg/24 hours or random urine protein/creatinine ratio ≥0.3 mg/dL for the diagnosis of preeclampsia has been exceeded. At that point, serum creatinine alone can be used to monitor renal function. It is the practice of some providers, including the authors, to confirm a low positive protein creatinine ratio (0.3 to 0.6) with a 24-hour collection. (See "Evaluation of proteinuria in pregnancy and management of nephrotic syndrome" and "Expectant management of preterm preeclampsia with severe features".)

Monitoring blood pressure and treatment of hypertension — Blood pressure should be measured twice daily at home in patients being managed expectantly with preeclampsia without severe features, and at least twice weekly in the office when the patient comes in for laboratory and fetal evaluation. There was no evidence of a systematic difference between self-monitored blood pressure readings and clinic readings in a meta-analysis of individual patient data [28].

A sustained elevation of systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg for ≥15 minutes should prompt immediate hospitalization for further evaluation and management. Antihypertensive therapy should be initiated as soon as reasonably possible, ideally within 30 to 60 minutes, with the goal of preventing stroke and possibly placental abruption. (See "Treatment of hypertension in pregnant and postpartum women", section on 'Acute therapy of severe hypertension'.)

The use of antihypertensive drugs to control mild hypertension (defined as systolic blood pressure <160 mmHg and diastolic blood pressure <110 mmHg) in the setting of preeclampsia does not alter the course of the disease or diminish perinatal morbidity or mortality, and is best avoided in most patients. It does, however, reduce the occurrence of progression to severe hypertension. The indications for starting antihypertensive therapy, the choice of drug, and blood pressure goals are discussed in detail separately. (See "Treatment of hypertension in pregnant and postpartum women", section on 'Our approach'.)

Sodium restriction below the recommended daily intake and diuretics have no role in routine therapy [29-31]. Although intravascular vascular volume is reduced, a randomized trial showed that plasma volume expansion did not improve maternal or fetal outcome [32]. Diuretics are only indicated for the treatment of pulmonary edema.

Assessment of fetal growth — Early fetal growth restriction may be the first manifestation of preeclampsia and is typically a sign of severe uteroplacental insufficiency. At the time of diagnosis of preeclampsia, we perform sonography to estimate fetal weight and assess amniotic fluid volume for evaluation of fetal growth restriction and oligohydramnios. If the initial examination is normal, we repeat the ultrasound examination for fetal growth every three to four weeks.

Management of the growth restricted fetus is reviewed separately. (See "Fetal growth restriction: Evaluation and management".)

Assessment of fetal well-being — There are no data from randomized trials on which to base recommendations for the optimal type and frequency of antepartum fetal monitoring. At a minimum, we suggest daily fetal movement counts and twice weekly nonstress testing plus assessment of amniotic fluid volume, or twice weekly biophysical profiles, beginning at the time of diagnosis of preeclampsia. Fetal testing should be performed promptly if there is an abrupt change in maternal condition or decreased fetal activity. (See "Overview of antepartum fetal surveillance".)

Evaluation of umbilical artery Doppler velocimetry indices is useful if fetal growth restriction is suspected, as the results help in optimal timing of delivery. In a meta-analysis of 16 randomized trials in high-risk pregnancies (n = 10,225 infants), knowledge of umbilical artery Doppler velocimetry resulted in a 29 percent reduction in perinatal death (RR 0.71, 95% CI 0.52-0.98; 1.2 versus 1.7 percent; number needed to treat 203, 95% CI 103-4352), primarily in pregnancies complicated by preeclampsia and/or growth restriction [33]. The frequency of Doppler assessment depends on the findings; weekly assessment is reasonable when the indices are normal. The significance of abnormal umbilical artery Doppler velocimetry in the setting of a well grown fetus with normal amniotic volume is unclear. (See "Fetal growth restriction: Evaluation and management", section on 'Doppler velocimetry'.)

Antenatal corticosteroids — A course of steroids (eg, betamethasone) is administered when the clinician believes delivery within the next seven days is likely and neonatal resuscitation is planned. Although preeclampsia may accelerate fetal lung maturation, neonatal respiratory distress remains common in preterm neonates of pregnancies with preeclampsia [34,35].

Antenatal corticosteroids to promote fetal lung maturity should be administered to women <34+0 weeks of gestation since they are at increased risk of preterm delivery because of progression to severe disease. However, delivery should not be delayed solely for administration of a full course of steroids. Use of steroids at ≥34+0 weeks is more controversial and discussed separately. (See "Antenatal corticosteroid therapy for reduction of neonatal respiratory morbidity and mortality from preterm delivery", section on 'Candidates for a first ACS course by gestational age'.)

Timing of delivery — For patients managed conservatively, delivery is indicated at 37+0 weeks of gestation or as soon as they develop preeclampsia with severe features (table 2) or eclampsia, whether or not the cervix is favorable. (See 'Term pregnancies: Delivery' above and 'General approach: Delivery' above.)

Earlier delivery is indicated if standard indications arise, such as abnormal antepartum testing, preterm labor, preterm prelabor rupture of membranes, or abruption [1].

INTRAPARTUM MANAGEMENT

Route of delivery — The route of delivery is based on standard obstetric indications. Observational data suggest that the decision to expedite delivery, even in the setting of preeclampsia with features of severe disease, does not mandate immediate cesarean birth [1,36,37]; no randomized trials have been performed [38]. Cervical ripening agents can be used prior to induction if the cervix is not favorable [39]. (See "Induction of labor: Techniques for preinduction cervical ripening".)

However, we believe that a prolonged induction and inductions with a low likelihood of success are best avoided. Identifying patients at high risk for these outcomes is subjective and made on a case-by-case basis. For example, we may suggest cesarean delivery to a nulliparous woman with preeclampsia with severe features who is <32 weeks of gestation and has an unfavorable cervix, given the relatively high frequency of abnormal intrapartum fetal heart rate tracings and low likelihood of a successful vaginal delivery (less than 40 percent) [39-42].

Intrapartum monitoring — Continuous maternal-fetal monitoring is indicated intrapartum to identify worsening hypertension; deteriorating maternal hepatic, renal, cardiopulmonary, neurologic, or hematologic function; abruptio

placentae; or an abnormal fetal heart rate tracing. There are no evidence-based standards for the optimal approach.

Routine invasive maternal hemodynamic monitoring (arterial catheterization, central venous catheter placement) is not recommended, even in the setting of preeclampsia with severe features. Most women can be managed without these invasive tools and should not be exposed to the risks associated with them.

However, information from an arterial or central venous catheter may be useful in select complicated patients, such as those with severe cardiac disease, severe renal insufficiency, oliguria, refractory hypertension, or pulmonary edema. Consultation with a maternal-fetal specialist and the anesthesia team is advised. Randomized trials of the utility of invasive monitoring in patients with complicated preeclampsia have not been performed [43]. (See "Anesthesia for the patient with preeclampsia", section on 'Hemodynamic monitoring'.)

Fluids — The ideal fluid management approach for women with preeclampsia is unclear, despite meta-analysis of several randomized trials comparing different strategies [44]. Fluid balance (input versus urine output plus estimated insensible losses [usually 30 to 50 mL/hour]) should be monitored closely to avoid excessive fluid administration, since women with preeclampsia are at risk for pulmonary edema and significant third-spacing, especially those at the severe end of the disease spectrum. A maintenance infusion of a balanced salt or isotonic saline solution at approximately 80 mL/hour is often adequate for a patient who is nil by mouth and has no ongoing abnormal fluid losses, such as bleeding [45].

Oliguria that does not respond to a modest fluid bolus (eg, a 300 mL fluid challenge) suggests renal insufficiency and should be tolerated to reduce the potential for iatrogenic pulmonary edema [45]. In patients with renal insufficiency, it is important to revise the maintenance infusion rate to account for the volume of fluid used to infuse intravenous medications.

Management of hypertension — Severe hypertension in labor should be treated promptly with intravenous labetalol (avoid in patients with asthma) or hydralazine or, less commonly, oral nifedipine to prevent stroke (table 3). Antihypertensive medications do not prevent eclampsia. Drugs and doses are reviewed in detail separately. (See "Treatment of hypertension in pregnant and postpartum women", section on 'Acute therapy of severe hypertension'.)

Seizure prophylaxis

Candidates for seizure prophylaxis — We administer intrapartum and postpartum seizure prophylaxis to all women with preeclampsia, based on data from randomized trials that demonstrated that magnesium sulfate treatment reduced the risk of eclampsia (see 'Drug of choice: Magnesium sulfate' below). Although seizure is an infrequent occurrence in women without severe features of preeclampsia and not receiving seizure prophylaxis, we feel the benefit of treatment is justifiable given the low cost and toxicity of the treatment of choice: magnesium sulfate, and the relatively small number of patients that need to be treated to prevent one seizure. In the MAGPIE trial (magnesium sulfate for prevention of eclampsia trial), which included 10,000 patients and is the largest randomized placebo-controlled trial that evaluated outcomes by severity of disease, the frequency of eclampsia in women with preeclampsia without severe features was 0.7 percent with prophylaxis versus 1.6 percent without prophylaxis (RR 0.42, 95% CI 0.26-0.67); approximately 100 women with preeclampsia without severe features and approximately 60 women with preeclampsia with severe features would need to be treated to prevent one seizure [46]. Although not statistically significant, prophylaxis also reduced the risk of maternal death in women without severe features of preeclampsia (RR 0.54, 95% CI 0.20-1.45; 6/3758 [0.16 percent] versus 11/3710 [0.30 percent] without treatment).

It is important to emphasize that seizure prophylaxis does not prevent progression of disease unrelated to convulsions. Approximately 10 to 15 percent of women in labor with preeclampsia without severe features will develop signs/symptoms of preeclampsia with severe features (eg, severe hypertension, severe headache, visual disturbance, epigastric pain, laboratory abnormalities) or abruptio placentae, whether or not they receive magnesium sulfate therapy [47,48].

We do not administer seizure prophylaxis to women with only gestational hypertension (pregnancy-related hypertension without proteinuria or end-organ dysfunction), as the seizure risk in the latter group is less than 0.1 percent [49]. (See "Gestational hypertension".)

The American College of Obstetricians and Gynecologists (ACOG) has opined that the "clinical decision of whether to use magnesium sulfate for seizure prophylaxis in patients with preeclampsia without severe features should be determined by the physician or institution, considering patient values or preferences, and the unique risk-benefit trade-off of each strategy" [1]. Magnesium sulfate should be used for the prevention of seizures in women with preeclampsia with severe features.

Drug of choice: Magnesium sulfate — Major medical organizations worldwide consistently recommend magnesium sulfate as the drug of choice for the prevention of eclampsia [1,9,50]. In a meta-analysis of randomized trials of women with preeclampsia (any severity), magnesium sulfate was more effective for prevention of a first seizure than placebo/no treatment (RR 0.41, 95% CI 0.29-0.58; six trials, 11,444 women), phenytoin (RR 0.08, 95% CI 0.01-0.60; three trials, 2291 women), or an antihypertensive drug alone (nimodipine, RR 0.33, 95% CI 0.14-0.77; one trial, 1650 women) [51]. Compared with placebo/no treatment, magnesium sulfate resulted in a nonstatistical but potential clinically important reduction in maternal death (RR 0.54, 95% CI 0.26-1.10) and a slight increase in cesarean deliveries (RR 1.05, 95% CI 1.01-1.10), with no clear difference in stillbirth or neonatal death (RR 1.04, 95% CI 0.93-1.15) or serious maternal morbidity (RR 1.08, 95% CI 0.89-1.32).

In meta-analyses of randomized trials involving eclamptic women, magnesium sulfate was safer and more effective for prevention of recurrent seizures than phenytoin, diazepam, or lytic cocktail (ie, chlorpromazine, promethazine, and pethidine). These data provide additional indirect evidence of its effectiveness in preeclampsia [52-54]. (See "Eclampsia", section on 'Prevention of recurrent seizures'.)

The mechanism for the anticonvulsant effects of magnesium sulfate has not been clearly defined [55]. The primary effect is thought to be central. Hypotheses include raising the seizure threshold by its action at the n-methyl d-aspartate (NMDA) receptor, membrane stabilization in the central nervous system secondary to its actions as a nonspecific calcium channel blocker, as well as decreasing acetylcholine transmission in motor nerve terminals [56,57]. Another theory is that it promotes vasodilatation of constricted cerebral vessels by opposing calcium-dependent arterial vasospasm, thereby reducing cerebral barotrauma [58].

Contraindications — Magnesium sulfate is contraindicated in women with myasthenia gravis since it can precipitate a severe myasthenic crisis. Alternative anticonvulsant drugs should be used. (See "Management of myasthenia gravis in pregnancy", section on 'Treatment issues'.)

Although at least one guideline considers pulmonary edema a contraindication to use of magnesium sulfate [59], the authors administer the drug cautiously to patients with pulmonary edema, with attention to fluid restriction, diuresis, and oxygen supplementation. (See "Acute respiratory failure during pregnancy and the peripartum period", section on 'Pulmonary edema'.)

Regimen — There is no consensus on the optimal magnesium regimen, when it should be started and terminated, or route of administration [60]. Commonly used regimens are described below.

Timing — Magnesium sulfate for seizure prophylaxis is usually initiated at the onset of labor or induction, or prior to and throughout the duration of a cesarean delivery [1,61,62]. It is usually not administered to stable antepartum patients, but is sometimes given to women with preeclampsia with severe features while they are being considered for expectant management. Prolonged antepartum therapy (more than five to seven days) should be avoided as it has been associated with adverse effects on fetal bones when it was administered for long-term tocolysis [63]. (See "Expectant management of preterm preeclampsia with severe features".)

Dosing — The most common magnesium sulfate regimen, and the one that we use, is:

- Loading dose of 6 g of a 10% solution intravenously over 15 to 20 minutes followed by 2 g/hour as a continuous infusion [48,62,64].
- An alternative regimen is 5 g of a 50% solution intramuscularly into each buttock (total of 10 g) followed by 5 g intramuscularly every four hours (may be mixed with 1 mL of xylocaine 2% solution to reduce pain).

These regimens generally result in similar magnesium levels; however, intramuscular administration results in more fluctuation and is associated with more side effects, particularly pain at the injection site [65]. Published dose regimens for magnesium sulfate vary, with loading doses of 4 to 6 g intravenously over 20 to 30 minutes and maintenance doses of 1 to 2 g/hour (and up to 3 g/hour) [1].

Dosing in renal insufficiency — Magnesium sulfate is excreted by the kidneys. Women with renal insufficiency should receive a standard loading dose, since their volume of distribution is not altered, but a reduced maintenance dose. If the serum creatinine is >1.1 and <2.5 mg/dL (110 to 221 micromol/L), we suggest a maintenance dose of 1 g/hour; if the serum creatinine is ≥2.5 mg/dL (221 micromol/L) or magnesium toxicity is suspected, we suggest no maintenance dose. We also monitor serum magnesium levels. (See 'When to check magnesium levels' below.)

ACOG suggests a loading dose of 4 to 6 g followed by a maintenance dose of 1 g/hour for patients with mild renal insufficiency (serum creatinine 1.0 to 1.5 mg/dL [88 to 133 micromol/L]) or oliguria (less than 30 mL urine output per hour for more than four hours) [1].

Clinical assessment and adjusting maintenance therapy — Clinical assessment for magnesium toxicity should be performed every one to two hours (see 'Signs of magnesium toxicity' below). The maintenance dose is only given when a patellar reflex is present (loss of reflexes is the first manifestation of symptomatic hypermagnesemia), respirations exceed 12 breaths/minute, and urine output exceeds 100 mL over four hours.

In women with normal renal function, following serum magnesium levels is not required as long as the woman's clinical status is closely monitored for signs and symptoms of potential magnesium toxicity and no abnormalities are noted.

When to check magnesium levels — We obtain a serum magnesium level as an adjunct to clinical assessment in patients who have:

- A seizure while receiving magnesium sulfate.
- Renal insufficiency (creatinine >1.1 mg/dL [110 micromol/L]). Serum magnesium levels are checked every four to six hours as an adjunct to clinical assessment for magnesium toxicity.
- Clinical signs/symptoms suggestive of magnesium toxicity (see 'Signs of magnesium toxicity' below). If magnesium toxicity is suspected, the maintenance dose should be decreased or eliminated, and the magnesium level should be checked. If the serum level is >9.6 mg/dL (8 mEq/L), the infusion should be stopped and serum magnesium levels should be determined at two-hour intervals [1]. The infusion can be restarted at a lower dose when the serum level is <8.4 mg/dL (7 mEq/L).

It is not necessary to routinely check for a therapeutic drug level in all patients as there does not appear to be a clear threshold concentration for ensuring the prevention of seizures. A therapeutic range of 4.8 to 8.4 mg/dL (2.0 to 3.5 mmol/L) has been recommended based on retrospective data [66]. Loading doses less than 6 g are more likely to result in subtherapeutic magnesium levels (less than 4.5 mg/dL) [64,67]. This may be particularly important in obese patients as higher maternal weight increases the time required to reach steady state levels [68].

Maternal side effects — Rapid infusion of magnesium sulfate can cause diaphoresis, flushing, and warmth, probably related to peripheral vasodilation and a drop in blood pressure. Nausea, vomiting, headache, muscle weakness, visual

disturbances, and palpitations can also occur. Dyspnea or chest pain may be symptoms of pulmonary edema, which is a rare side effect. (See "Hypermagnesemia: Causes, symptoms, and treatment", section on 'Symptoms of hypermagnesemia'.)

Although magnesium sulfate is often administered as a tocolytic agent, labor duration does not appear to be affected by its administration [69]. The risk of postpartum hemorrhage, possibly related to uterine atony from magnesium's tocolytic effects, appears to be increased in observational studies (odds ratio [OR] 2.96, 95% CI 1.10-7.99), but a clear increase has not been confirmed in randomized trials (OR 1.53, 95% CI 0.65-3.58) [70]. More data are needed.

Magnesium therapy results in a transient reduction of total and ionized serum calcium concentration due to rapid suppression of parathyroid hormone release [71]. Rarely, hypocalcemia becomes symptomatic (myoclonus, delirium, electrocardiogram abnormalities). Cessation of magnesium therapy will restore normal serum calcium levels. However, calcium gluconate administration may be required for patients with significant symptoms (calcium gluconate 10 to 20 mL of a 10 percent solution). (See "Hypermagnesemia: Causes, symptoms, and treatment", section on 'Hypocalcemia' and "Hypermagnesemia: Causes, symptoms, and treatment", section on 'Treatment'.)

Signs of magnesium toxicity — Magnesium toxicity is uncommon in women with good renal function [72]. Toxicity correlates with the serum magnesium concentration [73]:

- Loss of deep tendon reflexes occurs at 7 to 10 mEq/L (8.5 to 12.0 mg/dL or 3.5 to 5.0 mmol/L)
- Respiratory paralysis at 10 to 13 mEq/L (12 to 16 mg/dL or 5.0 to 6.5 mmol/L)
- Cardiac conduction is altered at >15 mEq/L (>18 mg/dL or >7.5 mmol/L)
- Cardiac arrest occurs at >25 mEq/L (>30 mg/dL or >12.5 mmol/L)

Antidote — Calcium gluconate 15 to 30 mL of a 10 percent solution (1500 to 3000 mg) intravenously over 2 to 5 minutes is administered to patients in cardiac arrest or with severe cardiac toxicity related to hypermagnesemia [74]. A starting dose of 10 mL of a 10 percent solution (1000 mg) is used for patients with less severe, but life-threatening, cardiorespiratory compromise. Concomitant intravenous administration of furosemide accelerates urinary excretion of magnesium [1].

Calcium chloride 5 to 10 mL of a 10 percent solution (500 to 1000 mg) intravenously over two to five minutes is an acceptable alternative, but is more irritating and more likely to cause tissue necrosis in the event of extravasation.

Fetal and neonatal effects from magnesium sulfate — Magnesium freely crosses the placenta; as a result, the cord blood concentration approximates the maternal serum concentration. Maternal therapy causes a decrease in baseline fetal heart rate, which generally remains within the normal range, and a decrease in fetal heart rate variability, which may be absent or minimal [75]. The biophysical profile score and nonstress test reactivity are not significantly altered [76].

A meta-analysis of randomized trials of antenatal magnesium sulfate administration found no clear adverse outcomes in the neonate [77].

Drug interactions — Neuromuscular blockade and hypotension due to concurrent use of magnesium sulfate and calcium channel blockers have been described in case reports, but the risk appears to be minimal [78]. See Lexicomp drug interactions tool.

Postpartum patients receiving both magnesium sulfate and opioids are at a higher risk for cardiopulmonary depression. (See 'General postpartum care' below.)

Duration of therapy — Magnesium sulfate is usually continued for 24 hours postpartum [1,62]. Timing of drug discontinuation has been arbitrary; there are no high-quality data to guide therapy. In most women who have preeclampsia without severe features, therapy can be safely discontinued after 12 hours [79]. In women with preeclampsia with severe

features or eclampsia, seizure prophylaxis is generally continued for 24 to 48 hours postpartum, after which the risk of recurrent seizures is low.

It is probably reasonable to extend the duration of magnesium sulfate therapy in women whose disease has not begun to improve postpartum and shorten the duration of therapy in women who are clearly improving clinically (eg, diuresis of ≥100 mL/hour for two consecutive hours, absence of symptoms [headache, visual changes, epigastric pain], and absence of severe hypertension) [80-83]. Diuresis (greater than 4 L/day) is believed to be the most accurate clinical indicator of resolution of preeclampsia/eclampsia, but is not a guarantee against the development of seizures [84].

Although a multicenter trial in women with severe antepartum preeclampsia randomly assigned to continue the infusion for 24 hours postpartum versus stopping it immediately after delivery did not detect a statistically significant reduction in seizure occurrence when magnesium sulfate was maintained (eclampsia 1/555 [0.18 percent] with postpartum treatment versus 2/558 [0.35 percent] without postpartum treatment) [85], the trial was underpowered to exclude a modest benefit.

In women with persistent renal impairment postpartum, it is important to be cautious when prolonging the magnesium sulfate infusion since these patients are at increased risk for magnesium toxicity and need close monitoring, as described above.

Management of thrombocytopenia — The risk of bleeding due to thrombocytopenia is generally considered to increase only when the platelet count is below 100,000/microL, and the risk increases substantially only with platelet counts below 50,000/microL. Platelet transfusion should not be used to normalize the platelet count in nonbleeding patients, as long as the platelet count is above 10,000 to 20,000/microL. However, platelets should not be withheld from a patient with potentially life-threatening bleeding or one who requires a higher platelet count to prevent bleeding in a high-risk setting, such as surgery. (See "Thrombocytopenia in pregnancy".)

Although a platelet count >50,000/microL is generally considered safe for delivery (vaginal or cesarean) [86,87], achievement of a specific platelet threshold does not substitute for clinical judgment in preparation for and management of delivery. For severely thrombocytopenic patients (platelet count <20,000/microL), the author notifies the blood bank and has platelets readily available in the delivery room for transfusion in case excessive bleeding develops at vaginal delivery or excessive oozing is observed at the time of the skin incision at cesarean. Excessively bleeding patients are transfused.

The decision for prophylactic platelet transfusion in women with severe preeclampsia-related thrombocytopenia but no excessive bleeding depends on patient-specific factors; consultation with the hematology service may be helpful. Patient-specific factors that may influence the author's decision to initiate prophylactic platelet transfusion include a rapidly falling platelet count, recent use of low-dose aspirin, coexistent abruption, and severe hypertension, because all of these factors may impact the risk of clinical bleeding or cerebrovascular accident.

ACOG has not made a specific recommendation [88] but cites an AABB guideline that recommends platelet transfusion to increase the maternal platelet count to >50,000/microL before major planned non-neuraxial surgery (weak recommendation based on very low-quality evidence) [89].

The minimum platelet count before placement of neuraxial anesthesia is controversial, depends on factors in addition to platelet concentration, and is institution-dependent. (See "Adverse effects of neuraxial analgesia and anesthesia for obstetrics", section on 'Neuraxial analgesia and low platelets'.)

Glucocorticoid therapy does not appear to be effective for significantly raising the platelet count in women with preeclampsia, although available data are limited [90]. We do not administer glucocorticoids to raise the platelet count in patients with preeclampsia.

Analgesia and anesthesia — Neuraxial techniques are generally safe and effective in women with preeclampsia [91]. In preeclampsia, the two major anesthesia-related concerns with use of neuraxial techniques are (1) the potential for a large drop in blood pressure due to the combination of depleted intravascular volume and sympathetic blockade and (2)

peridural hematoma in women with severe thrombocytopenia. The former can be minimized by appropriate adjustments in preprocedure hydration, drug choice, drug dosing, and drug delivery by the anesthesiologist; however, as discussed above, a low platelet count may preclude neuraxial anesthesia. The platelet count necessary to safely perform neuraxial anesthesia is unknown [92], and practice varies. Early placement of an epidural catheter should be considered if there is concern about a falling platelet count. (See "Anesthesia for the patient with preeclampsia".)

The major concerns associated with general anesthesia (for cesarean delivery) are difficult or failed intubation because of oropharyngeal edema, a transient spike in blood pressure during intubation as a response to noxious stimuli, and hypotension from anesthetic-induced reduction in cardiac output and systemic vascular resistance. Given these issues, early patient assessment by the anesthesia team is desirable. (See "Anesthesia for the patient with preeclampsia".)

Cranial imaging — Most patients with symptoms associated with the severe spectrum of the disease respond to treatment with antihypertensive and analgesic medications. For those with either unremitting headache or neurologic signs/symptoms, we consult the neurology service. The decision of whether or not to proceed with neuroimaging should be made in conjunction with the neurology consultant. In general, we would perform neuroimaging in patients with persistent focal central nervous system symptoms or signs, and those who experience an atypical eclamptic seizure (eg, lasting more than 10 minutes, occurring while on magnesium sulfate seizure prophylaxis, or recurrent).

POSTPARTUM CARE

General postpartum care — There are no evidence-based standards for the optimal approach to postpartum maternal monitoring and follow-up. We monitor vital signs every two hours while the patient remains on magnesium sulfate, and we repeat laboratory tests (eg, platelet count, creatinine, liver transaminases) daily until two consecutive sets of data are normal or trending to normal.

Postpartum patients receiving both magnesium and opioids are at a higher risk for cardiopulmonary depression. Pain should be controlled with the minimally effective dose of opioid while recognizing the possible synergy between the two drugs with respect to respiratory depression. Vital signs are closely monitored, ideally in association with pulse oximetry. It may be necessary to reduce the dose of one or both drugs, and patients with serious toxicity may require an antidote (calcium gluconate, naloxone). (See "Overview of the postpartum period: Normal physiology and routine maternal care", section on 'Pain management' and "Pain control in the critically ill adult patient", section on 'Type and management of side effects'.)

Persistent severe hypertension should be treated; some patients will have to be discharged on antihypertensive medications, which are discontinued when blood pressure returns to normal. Although nonsteroidal anti-inflammatory drugs (NSAIDs) sometimes exacerbate hypertension, NSAIDs should be used preferentially over opioid analgesics [1]. Management of postpartum hypertension is reviewed separately. (See "Treatment of hypertension in pregnant and postpartum women", section on 'Postpartum hypertension'.)

We suggest frequently monitoring blood pressure in the hospital or at home for the first 72 hours postpartum and if it is in an acceptable range, then blood pressure is measured at a follow-up visit 7 to 10 days postdelivery. Some patients will require longer monitoring; continued follow-up is needed until all of the signs and symptoms of preeclampsia have resolved. Alternative diagnoses should be sought in those with persistent abnormal findings after three to six months [93]. (See "Overview of hypertension in adults".)

Women with preeclampsia receiving gentamicin were at significantly increased risk of acute kidney injury (RR 2.00, 99% CI 1.61-2.48) in one study, but the absolute risk was low (1.6 versus 0.3 percent with no antibiotics) [94]. (See "Pathogenesis and prevention of aminoglycoside nephrotoxicity and ototoxicity".)

Women with postpartum onset of preeclampsia — Some women are diagnosed with preeclampsia for the first time after delivery. We suggest administration of magnesium sulfate to those with (1) new-onset hypertension and headache or blurred vision or (2) severe hypertension. Antihypertensive therapy is also administered to women with severe hypertension to prevent stroke. (See "Treatment of hypertension in pregnant and postpartum women", section on 'Acute therapy of severe hypertension'.)

PROGNOSIS

Prognostic issues include the risk of recurrent preeclampsia and related complications in subsequent pregnancies and long-term maternal health risks.

Recurrence — A 2015 meta-analysis of individual patient data from over 75,000 women with preeclampsia who became pregnant again found that 16 percent developed recurrent preeclampsia and 20 percent developed hypertension alone in a subsequent pregnancy [95].

However, the recurrence risk varies with the severity and time of onset of the initial episode [96]. Women with early-onset, severe preeclampsia are at greatest risk of recurrence (as high as 25 to 65 percent) [97-99]. The risk of preeclampsia in a second pregnancy is much lower (5 to 7 percent) for women who had preeclampsia without severe features in their first pregnancy and less than 1 percent in women who had a normotensive first pregnancy (excluding abortions) [97,100-105].

Among women with a history of severe preeclampsia in the second trimester, 21 percent of subsequent pregnancies are complicated by recurrent severe preeclampsia in the second trimester [97]. If any severity of preeclampsia is considered, approximately one-third of recurrences develop at ≤27 weeks, one-third at 28 to 36 weeks, and one-third at ≥37 weeks.

Recurrent preeclampsia is more likely following a singleton pregnancy with preeclampsia than a twin pregnancy with preeclampsia [106]. The recurrence risk in women with HELLP syndrome (who may develop either HELLP or preeclampsia in a subsequent pregnancy) is discussed separately. (See "HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets)", section on 'Recurrence in subsequent pregnancies'.)

Prevention of recurrence — Low-dose aspirin therapy during pregnancy modestly reduces the risk of preeclampsia in women at high risk for developing the disease. Selection of candidates for prophylaxis, drug dosing, and evidence of efficacy are reviewed in detail separately. (See "Preeclampsia: Prevention", section on 'Low-dose aspirin'.)

Available evidence does not support use of heparin or low molecular weight heparin to prevent recurrence [107]. Heparin or low molecular weight heparin may be used selectively in women with antiphospholipid syndrome in cases of aspirin failure or when placental examination shows extensive decidual inflammation and vasculopathy and/or thrombosis. (See "Preeclampsia: Prevention", section on 'Anticoagulation' and "Antiphospholipid syndrome: Pregnancy implications and management in pregnant women", section on 'Preterm delivery related to uteroplacental insufficiency'.)

Risk of related obstetric complications — Preeclampsia, growth restriction, preterm delivery, abruptio placentae, and stillbirth can be sequelae of inadequate placentation. Women with pregnancies complicated by one of these disorders are at increased risk of developing one or more of the other disorders in future pregnancies [108,109]. Early-onset preeclampsia is more likely to be associated with one of these adverse events in a subsequent pregnancy, even if normotensive, than late-onset preeclampsia [110,111].

Long-term maternal risks of pregnancy-associated hypertension — Women with pregnancy-related hypertensive disorders appear to be at increased risk for hypertension, cardiovascular disease (CVD, including coronary heart disease, stroke, and heart failure), and renal disease later in life, as well as early all-cause mortality and some cause-specific mortality (ischemic heart disease, stroke, diabetes). The risk is particularly high if two or more pregnancies were affected [112] or early-onset preeclampsia necessitated delivery before 34 weeks [113].

Cardiovascular disease — The American Heart Association considers a history of preeclampsia or pregnancy-induced hypertension a major risk factor for development of CVD [114], based on consistent findings from case-control and cohort studies. The future risk of cardiovascular morbidity and mortality appears to be related to the severity of preeclampsia, the gestational age when delivery was required, and the number of disease recurrences [115,116]. Women with early-onset/severe preeclampsia with preterm delivery are at highest risk of CVD later in life, including during the premenopausal period (table 4). Because women and their primary care providers may be unaware of the long-term risk of CVD associated with preeclampsia, it may be beneficial for the obstetric provider to discuss this risk with the patient postpartum [117,118].

The relationship between preeclampsia and CVD has been illustrated in multiple systematic reviews of controlled studies that evaluated the risk of late cardiovascular events in women with and without a history of preeclampsia [119-121]. For example:

- A systematic review of 22 studies including >6.4 million women, of whom >258,000 had preeclampsia, reported the following. Compared with women with no history of preeclampsia, women with preeclampsia were at increased risk for future [121]:

  - Heart failure (RR 4.19, 95% CI 2.09-8.38)
  - Coronary heart disease (RR 2.50, 95% CI 1.43-4.37)
  - Death from CVD (RR 2.21, 95% CI 1.83-2.66)
  - Stroke (RR 1.81, 95% CI 1.29-2.55)

  These relationships persisted after adjustment for age, body mass index, and diabetes mellitus. The difference in relative risk compared with unaffected women was attenuated 10 years after the affected pregnancy, which the authors attributed to an increasing frequency of these disorders as the control group became older and the low number of events. The authors also noted that prepregnancy cardiovascular risk factor profiles were not available in the majority of the included studies, but where available, pregestational hypertension appeared to account for the increased risk of future coronary heart disease.

- Another systematic review illustrated the graded relationship between severity of preeclampsia and risk of future CVD [120]:

  - Mild preeclampsia (RR 2.00, 95% CI 1.83-2.19)
  - Moderate preeclampsia (RR 2.99, 95% CI 2.51-3.58)
  - Severe preeclampsia (RR 5.36, 95% CI 3.96-7.27)

  In this review, preeclampsia was defined as "mild" if the pregnancy had an uncomplicated course, "moderate" if preeclampsia was complicated by fetal growth restriction or maternal seizures, and "severe" if preeclampsia was complicated by preterm delivery or fetal demise.

In addition, preeclampsia is a known risk factor for cardiomyopathy, both peripartum (see "Peripartum cardiomyopathy: Etiology, clinical manifestations, and diagnosis") and years after delivery. In a retrospective population-based cohort study, women with a history of preeclampsia or gestational hypertension were at increased risk of cardiomyopathy for >5 years after delivery compared with women without such a history [122]. Eleven percent of all cardiomyopathy events in the cohort occurred among women with a history of preeclampsia or gestational hypertension and approximately 50 percent of the association was related to postpregnancy chronic hypertension. However, the absolute risk of cardiomyopathy was small: 14.6 to 17.3 cases/100,000 person-years.

Some epidemiologic data suggest that the increased risk of late cardiovascular morbidity/mortality in a previously preeclamptic woman can be attributed to underlying genetic factors and risk factors that are common to both disorders [123-126]. In this model, pregnancy is a cardiovascular stress test in the same way that it is a metabolic stress test for future

development of diabetes. It is also possible that preeclampsia-induces physiologic and metabolic changes associated with CVD, such as endothelial dysfunction [127-130], insulin resistance, sympathetic overactivity, proinflammatory activity, and abnormal lipid profile [131], that remain after delivery, leading to late CVD [132-136] and other disorders associated with these abnormalities. In one study, 20 percent of women with both preeclampsia and a growth-restricted newborn met criteria for metabolic syndrome when evaluated several months postpartum [137].

Prevention — The American College of Cardiology/American Heart Association (ACC/AHA) guidelines on management of hypertension and hyperlipidemia utilize the individual's predicted CVD risk in their recommendations: For nonpregnant individuals, they recommend initiating antihypertensive drug treatment for those with stage I hypertension (ie, >130/80 mmHg) and 10-year CVD risk ≥10 percent; initiation of a moderate or high intensity statin in individuals with hyperlipidemia is based on 10-year CVD risk ≥7.5 percent [138,139]. The 2019 ACC/AHA primary prevention guideline codified a history of a hypertensive disorder of pregnancy as a risk-enhancing factor to guide the prescription of statins for primary atherosclerotic CVD (ASCVD) prevention among woman at intermediate risk (7.5 to 20.0 percent 10-year ASCVD risk) by conventional risk calculation [140]. (See "Cardiovascular disease risk assessment for primary prevention: Risk calculators".)

However, the first study to evaluate the clinical utility of including past history of a hypertensive disorder of pregnancy and parity in a standard risk prediction model reported that, although predictive of CVD risk, inclusion did not enhance discrimination or risk reclassification [141], possibly because much of the link between hypertensive disorders of pregnancy and CVD is mediated by traditional risk factors. More research is needed regarding use of pregnancy history in CVD risk prediction and risk reduction interventions.

Nevertheless, clinicians should consider informing women about the link between preeclampsia and future CVD and be more aggressive about advising them about healthy behaviors, such as extended lactation (which decreases risk of maternal hypertension [142-144] and CVD [145-152]), achieving an optimal body mass index, smoking cessation, healthy diet, and regular exercise. Increased awareness about her CVD risk may increase the woman's motivation to reduce modifiable risk factors, if present. There is no consensus as to how these women should be followed in the years after the affected pregnancy, including the type and frequency of screening for CVD [153]. (See "Overview of cardiovascular risk factors in women" and "Cardiovascular disease risk assessment for primary prevention in adults: Our approach".)

Diabetes mellitus — Women with a history of preeclampsia or gestational hypertension may be at increased risk of developing diabetes [154-157]; however, the available evidence does not support a change in standard screening guidelines. (See "Screening for type 2 diabetes mellitus", section on 'Screening recommendations by expert groups'.)

In a population-based retrospective cohort study including over one million women, preeclampsia or gestational hypertension in the absence of gestational diabetes mellitus (GDM) was associated with a twofold increase in the incidence of diabetes during 16.5 years of postdelivery follow-up, after controlling for several confounding variables (but the authors did not control for obesity) [154]. In women who had preeclampsia or gestational hypertension and GDM, the risk of future diabetes increased 16- to 18-fold, which was above the already elevated 13-fold increase in risk associated with GDM alone. Previous studies have reported similar findings [155-157].

Chronic and end-stage kidney disease — Preeclampsia has been associated with an increased risk for developing chronic kidney disease, particularly within five years of the affected pregnancy [158-161]. Moreover, women with preeclampsia may be at increased risk for developing end-stage kidney disease (ESKD) later in life, but the absolute risk is small, and evaluation of asymptomatic women is not warranted [159,160]. A study that linked four decades of data from the Norwegian national birth and ESKD registries found that women with preeclampsia in their first pregnancy had a fourfold increase in risk of ESKD compared with women without preeclampsia (RR 4.7, 95% CI 3.6-6.1) after adjusting for known confounders, but the absolute risk of ESKD was less than 1 percent within 20 years [159]. Similarly, a study using claims data from the Taiwan National Health Insurance Program noted that women with preeclampsia/eclampsia were at significantly higher risk of developing ESKD over time than women without hypertensive disorders during pregnancy (incidence 5.33 versus 0.34 per 10,000 person-years) [160].

Although women who went on to develop ESKD may have had subclinical renal disease during pregnancy, it is also possible that as yet undefined risk factors predisposed these women to both preeclampsia and ESKD. It is less likely that preeclampsia damages the kidney, thereby initiating a process of chronic deterioration.

Subclinical hypothyroidism — In a nested case-control study, nulliparous women who developed preeclampsia were twice as likely to develop subclinical hypothyroidism during pregnancy and remote from delivery compared with matched normotensive controls [162]. The risk was highest in women with recurrent preeclampsia and without thyroid peroxidase antibodies, suggesting an autoimmune mediated mechanism of hypothyroidism was not involved. In a study including 25,000 pregnant women, women with subclinical hypothyroidism identified during pregnancy were at increased risk of developing severe preeclampsia compared with euthyroid women (odds ratio 1.6, 95% CI 1.1-2.4), after adjustment for risk factors for preeclampsia [163]. Abnormal levels of thyroid hormones appear to damage endothelial cells, potentially leading to preeclampsia and long-term cardiovascular sequelae.

All patients with symptoms of hypothyroidism should be evaluated for hypothyroidism. Screening of asymptomatic individuals is controversial and reviewed separately. (See "Diagnosis of and screening for hypothyroidism in nonpregnant adults", section on 'Candidates for screening'.)

Cancer — A systematic review of prospective and retrospective cohort studies found no significant association between preeclampsia and later development of cancer [119]. Antiangiogenesis is a key characteristic of preeclampsia. Because antiangiogenesis is also important for restricting tumor growth, it has been hypothesized that women with preeclampsia may be at reduced risk of future development of solid cancers.

Long-term risks in offspring — Pregnancy-related hypertension has been associated with higher blood pressures in offspring compared with offspring of women who remain normotensive during pregnancy, in a systematic review [164]. The association has been attributed to shared genetic background, familial behaviors, and environmental exposures, but a physiological component cannot be excluded.

An association between preeclampsia and autism spectrum disorder (ASD) has also been observed [165,166]. Further research is warranted regarding ASD and other potential adverse neurodevelopmental outcomes [167].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Hypertensive disorders of pregnancy".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Preeclampsia (The Basics)" and "Patient education: High blood pressure and pregnancy (The Basics)" and "Patient education: HELLP syndrome (The Basics)")

- Beyond the Basics topics (see "Patient education: Preeclampsia (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

General principles

- The definitive treatment of preeclampsia is delivery to prevent development of maternal or fetal complications from disease progression. Timing of delivery is based upon gestational age, the severity of preeclampsia, and maternal and fetal condition (algorithm 1). (See 'Introduction' above.)

- Preeclampsia with features of severe disease (table 2) is generally regarded as an indication for delivery, regardless of gestational age, given the high risk of serious maternal morbidity. However, prolonged antepartum management in a tertiary care setting or in consultation with a maternal-fetal medicine specialist is an option for selected women remote from term (<34 weeks of gestation). (See 'Preeclampsia with features of severe disease' above.)

- Antihypertensive therapy is indicated for treatment of persistent severe hypertension (defined as systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg) to prevent stroke (table 3); it does not prevent eclampsia. Antihypertensive therapy to control mild hypertension does not alter the course of preeclampsia or diminish perinatal morbidity or mortality, and should be avoided in most patients. (See "Treatment of hypertension in pregnant and postpartum women".)

Timing of delivery

- For women at term (≥37+0 weeks) with preeclampsia without features of severe disease, we suggest delivery rather than expectant management (**Grade 2B**). Delivery reduces the risk of maternal complications and is associated with a low risk of neonatal morbidity at this gestational age. (See 'Term pregnancies: Delivery' above.)

- For women with early preterm (<34 weeks) and late preterm (34+0 to 36+6 weeks) preeclampsia without features of severe disease, we suggest expectant management with delivery when the pregnancy has reached 37+0 weeks of gestation (**Grade 2C**). Earlier delivery is indicated for standard obstetric indications (eg, nonreassuring fetal testing, preterm premature rupture of membranes). (See 'Preterm pregnancies: Expectant management' above.)

Components of expectant management

- Expectant management of women with preeclampsia without features of severe disease consists of frequent laboratory monitoring (platelet count, liver and renal function tests), assessment of maternal blood pressure and symptoms, and evaluation of fetal growth and well-being. In most patients, antihypertensive therapy is not indicated for systolic blood pressure <160 mmHg or diastolic blood pressure <110 mmHg. (See 'Components of expectant management' above.)

- For women with a viable fetus and preeclampsia <34+0 weeks of gestation, we recommend a course of antenatal glucocorticoids (betamethasone) (**Grade 1A**). Use of steroids at 34 to 36 weeks is controversial. (See "Antenatal corticosteroid therapy for reduction of neonatal respiratory morbidity and mortality from preterm delivery", section on 'Candidates for a first ACS course by gestational age'.)

Magnesium sulfate management

- For women with preeclampsia and features of severe disease, we recommend intrapartum and postpartum seizure prophylaxis (**Grade 1A**). The benefit of seizure prophylaxis is less clear in women without severe hypertension or preeclampsia symptoms; however, we also suggest intrapartum and postpartum prophylaxis for these women (**Grade 2B**). We recommend the use of magnesium sulfate as a first-line agent for seizure prophylaxis in preeclampsia (**Grade 1A**). (See 'Seizure prophylaxis' above.)

- We give a loading dose of 6 g magnesium sulfate intravenously over 15 to 20 minutes followed by 2 g/hour as a continuous infusion. The maintenance dose is only given when a patellar reflex is present (loss of reflexes is the first manifestation of symptomatic hypermagnesemia), respirations exceed 12 breaths/minute, and urine output exceeds 100 mL over four hours. (See 'Dosing' above.)

- The maintenance dose (but not the loading dose) should be adjusted in women with renal insufficiency. We use 1 g/hour if the serum creatinine is >1.2 and <2.5 mg/dL (106 to 221 micromol/L) and no maintenance dose if the serum creatinine is ≥2.5 mg/dL (221 micromol/L). (See 'Dosing in renal insufficiency' above.)

- Magnesium toxicity is uncommon in women with good renal function. Toxicity is related to serum magnesium concentration: loss of deep tendon reflexes occurs at 7 to 10 mEq/L (8.5 to 12 mg/dL or 3.5 to 5.0 mmol/L), respiratory paralysis at 10 to 13 mEq/L (12 to 16 mg/dL or 5.0 to 6.5 mmol/L), cardiac conduction is altered at >15 mEq/L (>18 mg/dL or >7.5 mmol/L), and cardiac arrest occurs at >25 mEq/L (>30 mg/dL or >12.5 mmol/L). (See 'Signs of magnesium toxicity' above.)

- Clinical assessment for magnesium toxicity should be performed every one to two hours. We obtain serum magnesium levels every six hours as an adjunct to clinical assessment in patients who have a seizure while receiving magnesium sulfate, clinical signs/symptoms suggestive of magnesium toxicity, or renal insufficiency. (See 'When to check magnesium levels' above.)

- Calcium gluconate 15 to 30 mL of a 10 percent solution intravenously over 2 to 5 minutes is administered to women with cardiac arrest or severe cardiac toxicity related to hypermagnesemia. A starting dose of 10 mL of a 10 percent solution is used for patients with less severe but life-threatening cardiorespiratory compromise. (See 'Antidote' above.)

Delivery

- Preeclampsia is not an indication for cesarean delivery. Most patients with preeclampsia with or without severe features can be delivered vaginally. Cesarean delivery should be reserved for usual obstetric indications. (See 'Route of delivery' above.)

- For severely thrombocytopenic patients (platelets <50,000/microL), we notify the blood bank and have platelets readily available for transfusion in case excessive bleeding develops at vaginal delivery or excessive oozing is observed at the time of skin incision at cesarean. The decision for prophylactic platelet transfusion in women with severe preeclampsia-related thrombocytopenia but no excessive bleeding depends on patient-specific factors; consultation with the hematology service may be helpful. (See 'Management of thrombocytopenia' above.)

- Fluid balance should be monitored closely to avoid excessive administration, which can lead to pulmonary edema. A maintenance infusion of a balanced salt or isotonic saline solution at approximately 80 mL/hour is often adequate. Oliguria that does not respond to a modest trial of increased fluids (eg, a 300 mL fluid challenge) suggests renal insufficiency and should be tolerated to reduce the potential for iatrogenic pulmonary edema. (See 'Fluids' above.)

Prognosis

- There is an increased risk of preeclampsia recurrence in subsequent pregnancies. Early-onset preeclampsia with severe features has a higher risk of recurrence than milder disease with onset at term. (See 'Prognosis' above.)

- The American Heart Association considers a history of preeclampsia or pregnancy-induced hypertension a major risk factor for development of cardiovascular disease (coronary heart disease, stroke, and heart failure) (see 'Cardiovascular disease' above). Routine well-woman care should include assessment of cardiovascular risk factors, including history of pregnancy-related hypertension, with appropriate patient monitoring and risk reduction interventions, when indicated. (See "Overview of primary prevention of cardiovascular disease".)

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GRAPHICS

Criteria for the diagnosis of preeclampsia

Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on at least 2 occasions at least 4 hours apart after 20 weeks of gestation in a previously normotensive patient AND the new onset of 1 or more of the following*:
▪ Proteinuria ≥0.3 g in a 24-hour urine specimen or protein/creatinine ratio ≥0.3 (mg/mg) (30 mg/mmol) in a random urine specimen or dipstick ≥2+ if a quantitative measurement is unavailable
▪ Platelet count <100,000/microL
▪ Serum creatinine >1.1 mg/dL (97.2 micromol/L) or doubling of the creatinine concentration in the absence of other renal disease
▪ Liver transaminases at least twice the upper limit of the normal concentrations for the local laboratory
▪ Pulmonary edema
▪ New-onset and persistent headache not accounted for by alternative diagnoses and not responding to usual doses of analgesics¶
▪ Visual symptoms (eg, blurred vision, flashing lights or sparks, scotomata)

Preeclampsia is considered superimposed when it occurs in a woman with chronic hypertension. It is characterized by worsening or resistant hypertension (especially acutely), the new onset of proteinuria or a sudden increase in proteinuria, and/or significant new end-organ dysfunction after 20 weeks of gestation in a woman with chronic hypertension.

* If systolic blood pressure is ≥160 mmHg or diastolic blood pressure is ≥110 mmHg, confirmation within minutes is sufficient.
¶ Response to analgesia does not exclude the possibility of preeclampsia.

Adapted from: American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin No. 222: Gestational Hypertension and Preeclampsia. Obstet Gynecol 2020; 135:e237.

Graphic 79977 Version 36.0

In a patient with preeclampsia, the presence of one or more of the following indicates a diagnosis of "preeclampsia with severe features"

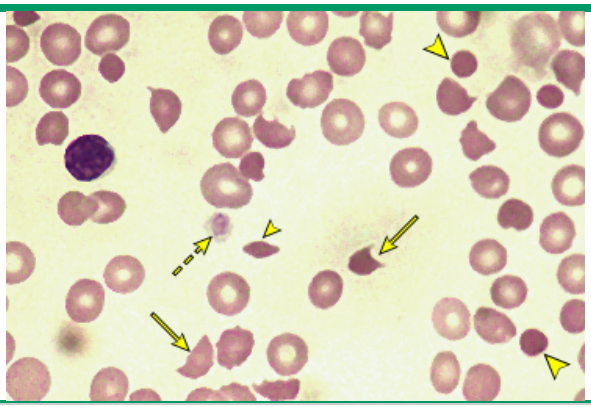
Severe blood pressure elevation:
Systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg on 2 occasions at least 4 hours apart while the patient is on bedrest (antihypertensive therapy may be initiated upon confirmation of severe hypertension, in which case criteria for severe blood pressure elevation can be satisfied without waiting until 4 hours have elapsed)
Symptoms of central nervous system dysfunction:
New-onset cerebral or visual disturbance, such as: ▪ Photopsia, scotomata, cortical blindness, retinal vasospasm ▪ Severe headache (ie, incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy and not accounted for by alternative diagnoses
Hepatic abnormality:
Impaired liver function not accounted for by another diagnosis and characterized by serum transaminase concentration >2 times the upper limit of the normal range or severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis
Thrombocytopenia:
<100,000 platelets/microL
Renal abnormality:
Renal insufficiency (serum creatinine >1.1 mg/dL [97.2 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal disease)
Pulmonary edema

Reference:

1. American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin No. 222: Gestational Hypertension and Preeclampsia. Obstet Gynecol 2020; 135:e237.

Graphic 76975 Version 25.0

Peripheral smear in microangiopathic hemolytic anemia showing presence of schistocytes

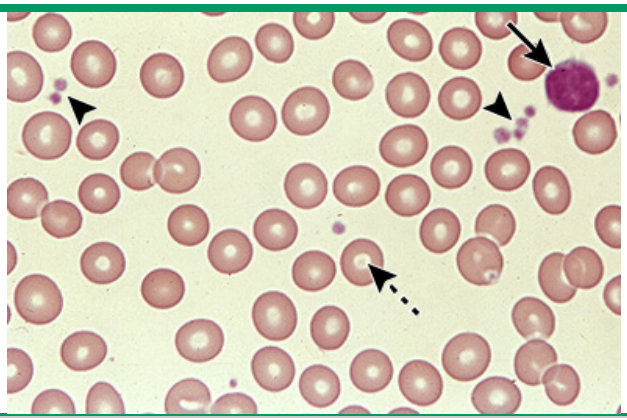


Peripheral blood smear from a patient with a microangiopathic hemolytic anemia with marked red cell fragmentation. The smear shows multiple helmet cells (arrows) and other fragmented red cells (small arrowhead); microspherocytes are also seen (large arrowheads). The platelet number is reduced; the large platelet in the center (dashed arrow) suggests that the thrombocytopenia is due to enhanced destruction.

Courtesy of Carola von Kapff, SH (ASCP).

Graphic 70851 Version 8.0

Normal peripheral blood smear

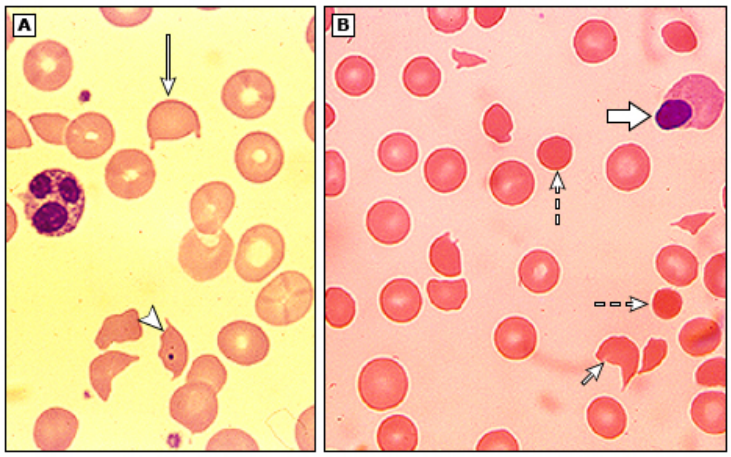


High-power view of a normal peripheral blood smear. Several platelets (arrowheads) and a normal lymphocyte (arrow) can also be seen. The red cells are of relatively uniform size and shape. The diameter of the normal red cell should approximate that of the nucleus of the small lymphocyte; central pallor (dashed arrow) should equal one-third of its diameter.

Courtesy of Carola von Kapff, SH (ASCP).

Graphic 59683 Version 5.0

Helmet cells in microangiopathic hemolytic anemia

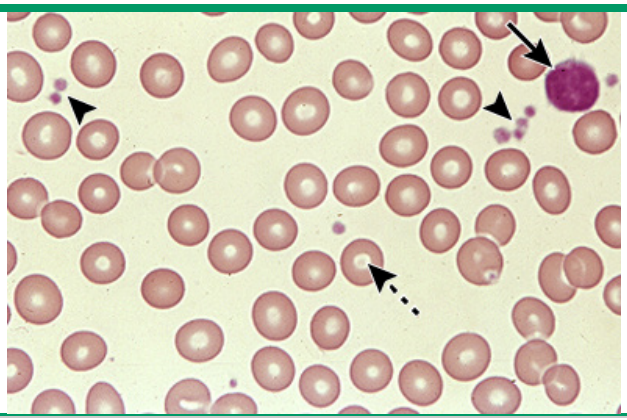


Peripheral smears from two patients with microangiopathic hemolytic anemia, showing a number of red cell fragments (ie, schistocytes), some of which take the form of combat (arrow), bicycle (arrowhead), or football (short arrow) "helmets." Microspherocytes are also seen (dashed arrows), along with a nucleated red cell (thick arrow).

Courtesy of Carola von Kapff, SH (ASCP).

Graphic 50715 Version 5.0

Normal peripheral blood smear



High-power view of a normal peripheral blood smear. Several platelets (arrowheads) and a normal lymphocyte (arrow) can also be seen. The red cells are of relatively uniform size and shape. The diameter of the normal red cell should approximate that of the nucleus of the small lymphocyte; central pallor (dashed arrow) should equal one-third of its diameter.

Courtesy of Carola von Kapff, SH (ASCP).

Graphic 59683 Version 5.0

Antihypertensive agents used for urgent blood pressure control in pregnancy

Drug	Initial dose	Follow-up
Labetalol	20 mg IV gradually over 2 minutes.	Repeat BP measurement at 10-minute intervals: ▪ If BP remains above target level at 10 minutes, give 40 mg IV over 2 minutes. ▪ If BP remains above target level at 20 minutes, give 80 mg IV over 2 minutes. ▪ If BP remains above target level at 30 minutes, give 80 mg IV over 2 minutes. ▪ If BP remains above target level at 40 minutes, give 80 mg IV over 2 minutes. Cumulative maximum dose is 300 mg. If target BP is not achieved, switch to another class of agent.
	A continuous IV infusion of 1 to 2 mg/minute can be used instead of intermittent therapy or started after 20 mg IV dose. Requires use of programmable infusion pump and continuous noninvasive monitoring of blood pressure and heart rate.	Adjust dose within this range to achieve target blood pressure. Cumulative maximum dose is 300 mg. If target BP is not achieved, switch to another class of agent.
Hydralazine	5 mg IV gradually over 1 to 2 minutes.* Adequate reduction of blood pressure is less predictable than with IV labetalol.	Repeat BP measurement at 20-minute intervals: ▪ If BP remains above target level at 20 minutes, give 5 or 10 mg IV over 2 minutes, depending on the initial response. ▪ If BP remains above target level at 40 minutes, give 10 mg IV over 2 minutes, depending on the previous response. Cumulative maximum dose is 30 mg. If target BP is not achieved, switch to another class of agent.
Nifedipine extended release	30 mg orally.	If target BP is not achieved in 1 to 2 hours, another dose can be administered. If target BP is not achieved, switch to another class of agent.
Nicardipine (parenteral)	The initial dose is 5 mg/hour IV by infusion pump and can be increased to a maximum of 15 mg/hour. Onset of action is delayed by 5 to 15 minutes; in general, rapid titration is avoided to minimize risk of overshooting dose. Requires use of a programmable infusion pump and continuous noninvasive monitoring of blood pressure and heart rate.	Adjust dose within this range to achieve target BP.
Nifedipine immediate release*	10 mg orally. May be associated with precipitous drops in BP in some women, with associated FHR decelerations for which emergency cesarean delivery may be indicated. As such, this regimen is not typically used as a first-line option and is usually reserved only for women without IV access. If used, FHR should be monitored while administering short-acting nifedipine.	Repeat BP measurement at 20-minute intervals: ▪ If BP remains above target at 20 minutes, give 10 or 20 mg orally, depending on the initial response. ▪ If BP remains above target at 40 minutes, give 10 or 20 mg orally, depending on the previous response. If target BP is not achieved, switch to another class of agent.

Labetalol and hydralazine are the preferred drugs.

IV: intravenous; BP: blood pressure; FHR: fetal heart rate.
* We caution against use of immediate-release oral nifedipine, although some obstetric guidelines have endorsed its use as a first-line option for emergency treatment of acute, severe hypertension in pregnancy or postpartum (other options were labetalol and hydralazine), particularly when IV access is not in place. In most cases, use of immediate-release oral nifedipine will be safe and well tolerated; however, there is a risk of an acute, precipitous fall in blood pressure, which may result in a reduction in uteroplacental perfusion. The immediate-release preparations are also associated with a higher incidence of headache and tachycardia. In nonpregnant adults, the package insert states that "nifedipine capsules should not be used for the acute reduction of blood pressure."

Adapted from:

1. *American College of Obstetricians and Gynecologists Committee on Obstetric Practice. Committee Opinion No. 767: Emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. Obstet Gynecol 2019.*
2. *Bernstein PS, Martin JN Jr, Barton JR, et al. National Partnership for Maternal Safety: Consensus Bundle on Severe Hypertension During Pregnancy and the Postpartum Period. Obstet Gynecol 2017; 130:347.*

Graphic 110261 Version 8.0

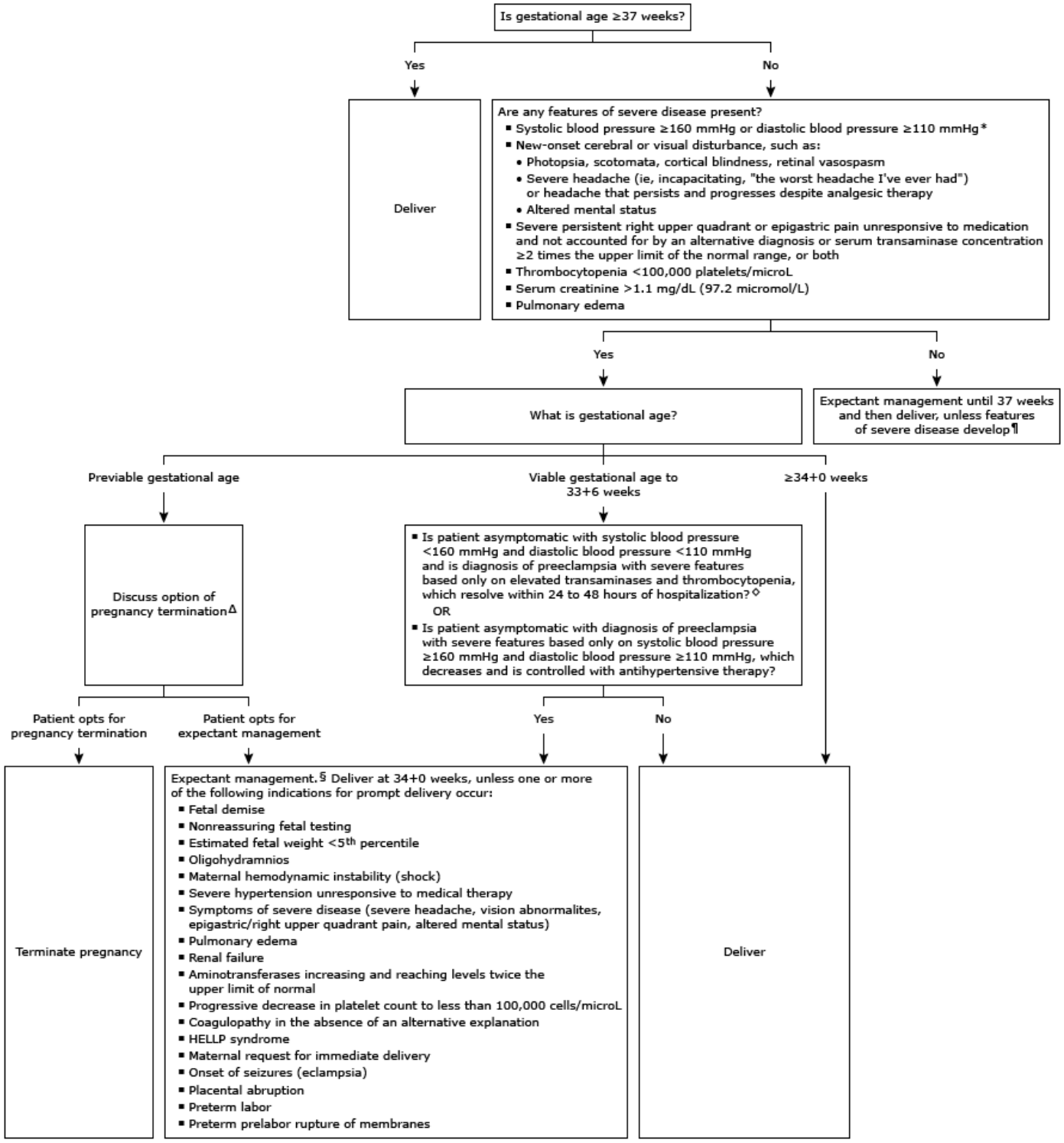
Deaths from cardiovascular causes

Population	Relative hazard rate (95% CI)
No preeclampsia, term delivery	1
No preeclampsia, preterm delivery	2.95 (2.12-4.11)
Preeclampsia, term delivery	1.65 (1.01-2.70)
Preeclampsia, preterm delivery	8.12 (4.31-15.33)

Data from: Irgens HU, Reisaeter L, Irgens LM, Lie RT. Long term mortality of mothers and fathers after pre-eclampsia: population based cohort study. BMJ 2001; 323:1213.

Graphic 76674 Version 4.0

Timing of delivery in women with preeclampsia



Women with suspected preeclampsia should be admitted to the hospital to confirm the diagnosis; assess severity; closely monitor maternal and fetal status; initiate supportive, therapeutic, and prophylactic therapies (eg, antihypertensive drugs for treatment of severe hypertension, antenatal corticosteroids, magnesium sulfate to prevent maternal seizures and, in some cases, fetal/neonatal neuroprotection); and either undergo delivery or expectant management in the hospital until delivery. Refer to UpToDate topics on Preeclampsia: Management and prognosis and Expectant management of preterm preeclampsia with severe features.

HELLP: hemolysis, elevated liver enzymes, low platelet count; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

* Blood pressure should be evaluated on at least 2 occasions at least 4 hours apart. However, if systolic pressure is ≥160 mmHg or diastolic pressure is ≥110 mmHg, confirmation after a short interval, even within a few minutes, is acceptable to facilitate timely initiation of antihypertensive therapy.

¶ In patients with no severe features of preeclampsia, guidelines from major medical organizations generally recommend expectant management before 34 weeks of gestation. There is less consensus about the optimum approach at 34+0 to 36+6 weeks. Although there are serious maternal risks with expectant management, we believe it is reasonable in fully informed patients because the absolute maternal risk of an adverse outcome is low and, although there is no benefit to the mother of continuing the pregnancy, the neonatal benefits from the additional time for in utero growth and maturation are substantial.

Δ If onset of preeclampsia with severe features is at a previable gestational age, we offer termination of pregnancy to reduce the mother's risk of developing life-threatening morbidity (eg, cerebrovascular hemorrhage) and to prevent the birth of an infant at the limit of viability and thus at high risk of death or severe permanent disability. Factors critical in making

this decision are the estimated fetal weight, actual gestational age, presence of growth restriction, and the neonatologist's judgment of the neonatal prognosis.

◊ In otherwise asymptomatic or mildly hypertensive women with features of severe disease by laboratory criteria, it is reasonable to delay delivery, administer antenatal corticosteroids, and repeat the laboratory tests (AST, ALT, platelet count) every 6 to 8 hours while the patient is on the labor unit to see if they improve. We would promptly deliver patients with worsening liver chemistries or falling platelet counts and those who develop other signs of preeclampsia with severe features. We often continue expectant management if the initially abnormal laboratory test results remain stable, but this decision is made on a case-by-case basis.

§ These patients should be hospitalized and cared for by, or in consultation with, a maternal-fetal medicine specialist. Such an approach should be undertaken only at facilities with adequate maternal and neonatal intensive care resources. After initial observation on the labor unit, these patients are closely monitored on an antepartum unit. See UpToDate topic on Expectant management of preterm preeclampsia with severe features.

Graphic 119146 Version 3.0

Contributor Disclosures

Errol R Norwitz, MD, PhD, MBA Grant/Research/Clinical Trial Support: Illumina [Preeclampsia]. Consultant/Advisory Boards: Illumina [Minimally invasive genetic testing for fetal and pregnancy-related disorders]. Patent Holder: Bayer [Prediction test for preeclampsia]. Equity Ownership/Stock Options: 1908 Brands/Bundle Organics [Nutritional supplements for pregnancy]. **Charles J Lockwood, MD, MHCM** Nothing to disclose **Vanessa A Barss, MD, FACOG** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

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