Preeclampsia: Intrapartum and postpartum management and long-term prognosis

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INTRODUCTION

Preeclampsia is a multisystem progressive disorder characterized by the new onset of hypertension and proteinuria or other significant end-organ dysfunction in the last half of pregnancy or postpartum (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 patients for signs and symptoms of preeclampsia. If the diagnosis is made, the only definitive treatment is delivery to prevent development of maternal or fetal complications from disease progression. Delivery leads to eventual resolution of the disease, although end-organ dysfunction may worsen in the first one to three days postpartum. Timing of delivery is based on a combination of factors, including disease severity, maternal and fetal condition, and gestational age.

Low-dose aspirin can reduce the occurrence of preeclampsia in patients at high risk for the disease. Once the diagnosis has been made, antihypertensive therapy does not prevent disease progression but can prevent the occurrence of severe hypertension and its sequalae (such as stroke and placental abruption) and magnesium sulfate can prevent seizures (eclampsia).

Postpartum maternal monitoring is important to identify the minority of patients whose

blood pressure does not return to normal after giving birth. Long-term maternal surveillance is also important because patients with a history of preeclampsia are at increased risk for development of cardiovascular disease later in life.

This topic will discuss the intrapartum and postpartum management of pregnancies complicated by preeclampsia, as well as long-term prognosis. Other important issues related to this disease are reviewed separately.

- (See "Preeclampsia: Antepartum management and timing of delivery".)
- (See "Preeclampsia: Pathogenesis".)
- (See "Preeclampsia: Clinical features and diagnosis".)
- (See "Early pregnancy prediction of preeclampsia".)
- (See "Preeclampsia: Prevention".)
- (See "Preeclampsia with severe features: Expectant management remote from term".)

INTRAPARTUM MANAGEMENT

Route of birth — The route of birth 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 [1-3]; no randomized trials have been performed [4]. Cervical ripening agents can be used prior to induction if the cervix is unfavorable [5]. (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 birth to a nulliparous patient 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 birth (less than 40 percent) [5-8].

Intrapartum monitoring — Continuous maternal and fetal monitoring is indicated intrapartum to identify worsening hypertension; deteriorating maternal hepatic, renal, cardiopulmonary, neurologic, or hematologic function; abruption; 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 patients can be managed without these invasive tools and should not be exposed to the risks associated with them. Oxygen saturation can be monitored noninvasively by pulse oximetry and if low (oxyhemoglobin saturation <95 percent), supplemental oxygen should be administered and the patient evaluated for pulmonary edema and cardiomyopathy. This evaluation may include an electrocardiogram, chest radiograph, echocardiogram, and/or plasma brain natriuretic peptide (BNP). (See "Management of heart failure during pregnancy" and "Acute respiratory failure during pregnancy and the peripartum period", section on 'Pulmonary edema'.)

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 [9]. (See "Anesthesia for the patient with preeclampsia", section on 'Hemodynamic monitoring'.)

Fluids — The ideal approach to fluid management in patients with preeclampsia is unclear, despite meta-analysis of several randomized trials comparing different strategies [10]. 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 patients 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 not permitted any oral intake and has no ongoing abnormal fluid losses, such as bleeding [11].

Oliguria that does not respond to a modest fluid bolus (eg, a 300 mL fluid challenge) suggests renal insufficiency. In patients with renal insufficiency, it is important to adjust the maintenance infusion rate to account for the volume of fluid used to infuse intravenous medications, otherwise iatrogenic pulmonary edema may occur.

Management of hypertension — Severe hypertension confirmed with a repeat measurement within 15 minutes should be treated promptly (within 30 to 60 minutes)

with intravenous labetalol (avoid in patients with asthma or heart rate <50 beats/minute) or hydralazine or, less commonly, intravenous nicardipine or 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 patients", section on 'Acute therapy of severe hypertension'.)

Indications for 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).

Seizure prophylaxis

Candidates for seizure prophylaxis — We administer intrapartum and postpartum seizure prophylaxis to all patients with preeclampsia with severe features, based on data from randomized trials that demonstrated that magnesium sulfate treatment reduced the risk of developing eclampsia (see 'Drug of choice: Magnesium sulfate' below).

Many clinicians no longer administer seizure prophylaxis to patients with preeclampsia without severe features. Seizure is an infrequent occurrence in these patients; however, some clinicians and patients believe the benefit of treatment is justifiable given the low cost and low 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 [12]:

- The frequency of eclampsia in patients with preeclampsia without severe features was 0.8 percent (40 out of 5055) with magnesium sulfate prophylaxis versus 1.9 percent (96 out of 5055) without prophylaxis (RR 0.42, 95% CI 0.29-0.60); approximately 100 patients with preeclampsia without severe features and approximately 60 patients with preeclampsia with severe features would need to be

treated to prevent one seizure.

- The risk of abruption was also reduced with magnesium sulfate prophylaxis (2.0 versus 3.2 percent; RR 0.67, 99% CI 0.45-0.89).
- Although not statistically significant, magnesium sulfate prophylaxis reduced the risk of maternal death in those without severe features of preeclampsia (RR 0.54, 95% CI 0.20-1.45; 6 out of 3758 [0.16 percent] versus 11 out of 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 patients 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 abruption, whether or not they receive magnesium sulfate prophylaxis [13,14].

We do not administer seizure prophylaxis to patients with only gestational hypertension (pregnancy-related nonsevere hypertension without proteinuria or end-organ dysfunction), as the seizure risk in these patients is less than 0.1 percent [15]. (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" [3]. Magnesium sulfate should be used intrapartum and postpartum for the prevention of seizures in patients 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 [3,16,17]. In a meta-analysis of randomized trials of patients 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 patients), phenytoin (RR 0.08, 95% CI 0.01-0.60; three trials, 2291 patients), or an antihypertensive drug alone (nimodipine, RR 0.33, 95% CI 0.14-0.77; one trial, 1650 patients) [18]. 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 patients, magnesium sulfate was safer and more effective for preventing recurrent seizures than phenytoin, diazepam, or lytic cocktail (ie, chlorpromazine, promethazine, and pethidine). These data provide additional indirect evidence of its effectiveness in preeclampsia [19-21]. (See "Eclampsia", section on 'Prevention of recurrent seizures'.)

The mechanism for the anticonvulsant effects of magnesium sulfate has not been clearly defined [22]. 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 [23,24]. Other theories are that it promotes vasodilatation of constricted cerebral vessels by opposing calcium-dependent arterial vasospasm, thereby reducing cerebral barotrauma [25] and that it prevents disruption of the blood-brain barrier caused by circulating small extracellular vesicles secreted into the plasma of patients with preeclampsia [26].

Contraindications — Magnesium sulfate is contraindicated in patients with myasthenia gravis since it can precipitate a severe myasthenic crisis. Alternative antiseizure medications (eg, levetiracetam, valproic acid) 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 [27], the author of this topic administers 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 [28]. 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 birth [3,29,30]. Usually, it is not administered to stable antepartum patients, but is sometimes given to patients 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 administered for long-term tocolysis [31]. (See "Preeclampsia with severe features: Expectant management remote from term".)

Dosing — The most common magnesium sulfate regimen in patients with normal renal function is:

- Loading dose 4 to 6 g of a 10% solution intravenously over 15 to 20 minutes followed by 1 to 2 g/hour as a continuous infusion [3,14,30,32].
- If intravenous access is not available, 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). Intramuscular administration results in more fluctuation in magnesium levels and is associated with more side effects, particularly pain at the injection site [33].

The author's preference is a 6 g intravenous loading dose and 2 g/hour infusion since this regimen is most likely to quickly achieve a serum magnesium level in the so-called therapeutic range derived from early studies (4.8 to 8.4 mg/dL [2.0 to 3.5 mmol/L] [33,34]) and maintain the level in this range, but he acknowledges that these serum levels were measured retrospectively and the effective therapeutic range has not been clearly established. Loading doses less than 6 g are more likely to result in subtherapeutic magnesium levels (less than 4.5 mg/dL) [32,35], which may be particularly important in patients with obesity, especially body mass index ≥40 kg/m^2, as higher maternal weight increases the time required to reach steady state levels [36].

In the United Kingdom, the National Institute for Health and Care Excellence (NICE) recommends a loading dose of 4 g intravenously over 5 to 15 minutes, followed by an infusion of 1 g/hour maintained for 24 hours, as used in the MAGPIE trial [37]. A maintenance infusion of 1 g/hour results in fewer side effects than the 2/g hour dose but generally produces concentrations below the level considered therapeutic [33,38]. No difference in seizure rates has been documented with the lower dose, possibly because

eclampsia is uncommon and the minimum effective serum magnesium concentration for eclampsia prophylaxis may be lower than the generally accepted level.

Dosing in renal insufficiency — Magnesium sulfate is excreted by the kidneys. Patients 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. Extreme caution is advised when treating patients with reduced GFR (<30 mL/min). We monitor serum magnesium levels in patients with renal insufficiency, in addition to frequent assessment for signs and symptoms of magnesium toxicity. (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) [3].

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 or continued 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 patients with normal renal function, following serum magnesium levels is not required as long as the patient'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 [3]. 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. If the level is checked, 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 [39].

Maternal side effects — Side effects occur in approximately 25 percent of patients [12]. 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 [40]. 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) [41]. 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 [42]. Rarely, hypocalcemia becomes symptomatic (myoclonus, delirium, electrocardiogram abnormalities). Cessation of magnesium therapy will restore normal serum calcium levels. However, administration of calcium gluconate (10 percent solution) may be required for patients with significant symptoms. (See 'Antidote' below and "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 patients with

good renal function [43]. Toxicity correlates with the serum magnesium concentration [44]:

- 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 occurs 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 [45]. 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 [3].

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 [46]. The biophysical profile score and nonstress test reactivity are not significantly altered [47].

A meta-analysis of randomized trials of antenatal magnesium sulfate administration found no clear adverse outcomes in the neonate [48].

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 [49]. Consult the Lexicomp drug interactions tool for further information.

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 [3,30]. Timing of drug discontinuation has been arbitrary; there are no high-quality data to guide therapy. In most patients who have preeclampsia without severe features, therapy can be safely discontinued after 12 hours [50]. In patients 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 patients whose disease has not begun to improve postpartum and shorten the duration of therapy in patients 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) [51-54]. 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 [55].

Although a multicenter trial in patients with severe antepartum preeclampsia randomly assigned to continue the infusion for 24 hours postpartum versus stopping it immediately after giving birth did not detect a statistically significant reduction in seizure occurrence when magnesium sulfate was maintained (eclampsia 1 out of 555 [0.18 percent] with postpartum treatment versus 2 out of 558 [0.35 percent] without postpartum treatment) [56], the trial was underpowered to exclude a modest benefit. Continuing treatment prolonged the duration of side effects, as well as the time to starting ambulation and lactation (by six to seven hours), which are potential harms of treatment. This is the largest trial that has evaluated duration of therapy postpartum.

In patients 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. (See 'Clinical assessment and adjusting maintenance therapy' above and 'When to check magnesium levels' 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 when giving birth (vaginal or cesarean) [57,58], achievement of a specific platelet threshold does not substitute for clinical judgment in preparation for and management of the birth. For severely thrombocytopenic patients (platelet count <20,000/microL), the author notifies the blood bank and has platelets readily available for transfusion in the birthing room in case excessive bleeding develops at vaginal birth 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 patients 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 [59] but cites an Association for the Advancement of Blood & Biotherapies 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) [60].

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 patients with preeclampsia, although available data are limited [61]. 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 patients with preeclampsia [62]. In these patients, 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 patients with severe thrombocytopenia. The former can be minimized by appropriate adjustments in preprocedure hydration, drug choice, drug dosing, and drug administration 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 [63], 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 birth) 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".)

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 (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'.)

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 [3]. Management of postpartum hypertension is reviewed separately. (See "Treatment of hypertension in pregnant and postpartum patients", section on 'Postpartum hypertension'.)

Patients with preeclampsia are not candidates for early discharge (within 24 hours of giving birth). 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. The American College of Obstetricians and Gynecologists (ACOG) suggests blood pressure evaluation within 72 hours of discharge in those with severe hypertension during pregnancy or postpartum and no later than 7 to 10 days postpartum for those with nonsevere hypertension [64]. 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 [65]. (See "Overview of hypertension in adults".)

In postpartum patients who are readmitted with preeclampsia with severe features, there is for a role for a second course of magnesium sulfate prophylaxis.

Patients 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) [66]. (See "Pathogenesis and prevention of aminoglycoside nephrotoxicity and ototoxicity".)

Patients with postpartum onset of preeclampsia — Some patients are diagnosed with preeclampsia for the first time after giving birth. We suggest administration of magnesium sulfate to those with (1) new-onset nonsevere hypertension with headache or blurred vision or (2) severe hypertension with or without other signs of preeclampsia with severe features. Antihypertensive therapy is administered to patients with severe hypertension to prevent stroke. (See "Treatment of hypertension in pregnant and postpartum patients", section on 'Acute therapy of severe hypertension'.)

Magnesium sulfate is usually continued empirically for 24 hours. It is reasonable to extend the duration of therapy for up to an additional 24 hours in patients whose disease has not

begun to improve clinically within 24 hours or shorten the duration of therapy in those who are clearly improving clinically (eg, diuresis of ≥100 mL/hour for two consecutive hours, resolution of symptoms [headache, visual changes, epigastric pain], and resolution of severe hypertension). (See 'Duration of therapy' above.)

PROGNOSIS

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

Recurrence — In a meta-analysis of individual patient data from 22 studies including nearly 100,000 patients with a hypertensive disorder of pregnancy (HDP) who had a subsequent pregnancy, the recurrence rate of an HDP was 20.7 percent (95% CI 20.4–20.9) and recurrence manifested as preeclampsia in 13.8 percent, gestational hypertension in 8.6 percent, and HELLP syndrome in 0.2 percent [67]. Among the over 75,000 patients with preeclampsia who became pregnant again, 20.4 percent developed HDP, 16 percent developed recurrent preeclampsia, 6 percent developed gestational hypertension, and 0.2 percent developed HELLP.

However, the recurrence risk varies with the severity and time of onset of the initial episode [68]. Patients with early-onset, severe preeclampsia are at greatest risk of recurrence (as high as 25 to 65 percent) [69-71]. The risk of preeclampsia in a second pregnancy is much lower (5 to 7 percent) for patients who had preeclampsia without severe features in their first pregnancy and less than 1 percent in patients who had a normotensive first pregnancy (excluding abortions) [69,72-77]. Among patients 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 [69]. 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 after a twin pregnancy with preeclampsia [78]. The recurrence risk in patients 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 patients 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 [79]. Heparin or low molecular weight heparin may be used selectively in some patients with antiphospholipid syndrome. (See "Preeclampsia: Prevention", section on 'Anticoagulation' and "Antiphospholipid syndrome: Obstetric implications and management in pregnancy", section on 'Preterm delivery related to uteroplacental insufficiency'.)

Weight loss in patients who are overweight or have obesity may reduce the risk of recurrence. Exercise may also be helpful. Using techniques to avoid multiple gestation in patients undergoing assisted reproduction may also reduce the risk of recurrence in this population. (See "Preeclampsia: Prevention", section on 'Effective interventions'.)

Risk of related obstetric complications — Preeclampsia, growth restriction, preterm birth, abruption, and stillbirth can be sequelae of inadequate placentation. Patients with pregnancies complicated by one of these disorders are at increased risk of developing one or more of the other disorders in future pregnancies [80,81]. 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 [82,83].

Long-term maternal risks of pregnancy-associated hypertension — Patients with pregnancy-related hypertensive disorders (preeclampsia, gestational hypertension) appear to be at increased risk for hypertension, cardiovascular disease (CVD, including coronary heart disease, stroke, and heart failure), and kidney 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 [84] or early-onset preeclampsia necessitated delivery before 34 weeks [85].

Cardiovascular disease, kidney disease, type 2 diabetes — The American Heart Association considers a history of preeclampsia or pregnancy-induced hypertension a major risk factor for development of CVD [86], 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 [87,88]. Patients with early-onset severe preeclampsia with preterm birth are at highest risk of CVD later in life, including during the premenopausal period (table 4). Because patients 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 [89,90].

The relationship between preeclampsia and CVD has been illustrated in multiple meta-analyses of controlled studies that evaluated the risk of late cardiovascular events in previously pregnant patients with and without a history of preeclampsia [91-94]. For example:

- In a meta-analysis of cohort and case-control studies of adverse cardiovascular outcome in patients with a history of preeclampsia in a first pregnancy compared with those with a previous normal pregnancy (50 studies, >10 million participants), patients with preeclampsia had increased long-term risks for [94].

  - Composite adverse cardiovascular outcome (2.57 versus 0.97 percent; adjusted pooled odds ratio [OR] 1.99, 95% CI 1.79-2.22)
  - Cardio- or cerebrovascular disease (1.20 versus 0.56 percent; aOR 1.79, 95% CI 1.61-2.01)
  - Cardiovascular death (2.39 versus 1.12 percent; aOR 2.18, 95% CI 1.79-2.66)
  - Hypertension (8.84 versus 3.32 percent; aOR 3.74, 95% CI 2.87-4.87)
  - Type 2 diabetes (3.55 versus 1.88 percent; aOR 2.28, 95% CI 1.58-3.28)
  - Acute or chronic kidney disease and end-stage kidney disease (0.38 versus 0.15 percent; aOR 3.35, 95% CI 2.25-5.00)
  - Metabolic syndrome (20.6 versus 4.2 percent; aOR 4.05, 95% CI 2.42-6.77)
  - Dyslipidemia (66.3 versus 54.6 percent; aOR 2.54, 95% CI 0.81-2.95)

  Patients with early-onset preeclampsia had higher long-term risks than those with late-onset preeclampsia compared with controls with previous normal pregnancies. Early and late onset were defined as preeclampsia requiring delivery before or after 34 weeks of gestation, respectively.

  - For the composite adverse cardiovascular outcome:

  - Early onset (3.22 versus 1.44 percent; OR 3.79, 95% CI 2.70-5.31)
  - Late onset (3.77 versus 1.51 percent; OR 1.89, 95% CI 1.53-2.33)

- For cardiovascular death:

  - Early onset (1.77 versus 0.92 percent; OR 5.12, 95% CI 3.22-8.12)
  - Late onset (1.06 versus 0.49 percent; OR 1.65, 95% CI 1.46-1.86)

In addition, preeclampsia is a known risk factor for cardiomyopathy, both peripartum (see "Peripartum cardiomyopathy: Etiology, clinical manifestations, and diagnosis") and years after giving birth. In a retrospective population-based cohort study, patients with a history of preeclampsia or gestational hypertension were at increased risk of cardiomyopathy for >5 years after giving birth compared with patients without such a history [95]. Eleven percent of all cardiomyopathy events in the cohort occurred among patients 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 patient can be attributed to underlying genetic factors and risk factors that are common to both disorders [96-99]. 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 [100-103], insulin resistance, sympathetic overactivity, proinflammatory activity, and abnormal lipid profile [104], that remain after giving birth, leading to late CVD [105-109] and other disorders associated with these abnormalities. In one study, 20 percent of patients with both preeclampsia and a growth-restricted newborn met criteria for metabolic syndrome when evaluated several months postpartum [110].

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

Prevention of cardiovascular disease — 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.

- (See "Overview of hypertension in adults", section on 'Who should be treated with pharmacologic therapy?'.)
- (See "Management of elevated low density lipoprotein-cholesterol (LDL-C) in primary prevention of cardiovascular disease", section on 'Initial drug therapy'.)
- (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 [111], possibly because much of the link between hypertensive disorders of pregnancy and CVD is mediated by traditional risk factors. Others have also observed that the high future risk of developing hypertension in patients with history of a hypertensive disorder of pregnancy was no longer statistically significant when adjusted for established risk factors [112]. More research is needed regarding use of pregnancy history in CVD risk prediction and risk reduction interventions.

Nevertheless, clinicians should consider informing patients 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 [113-115] and CVD [116-123]), achieving an optimal body mass index, smoking cessation, healthy diet, and regular exercise. Increased awareness about their CVD risk may increase the patient's motivation to reduce modifiable risk factors, if present. There is no consensus as to how these patients should be followed in the years after the affected pregnancy, including the type and frequency of screening for CVD [124]. (See "Overview of atherosclerotic cardiovascular risk factors in females" and "Atherosclerotic cardiovascular disease risk assessment for primary prevention in adults: Our approach".)

Long-term risks in offspring — Pregnancy-related hypertension was associated with higher blood pressures in offspring compared with offspring of patients who remain normotensive during pregnancy, in a systematic review [125]. The association has been attributed to shared genetic background, familial behaviors, and environmental exposures, but a physiological component cannot be excluded.

Associations between preeclampsia and autism spectrum disorder (ASD) and possibly attention-deficit/hyperactivity disorder have also been observed [126-128]. Further research is warranted regarding ASD and other potential adverse neurodevelopmental outcomes [129].

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

- **Seizure prophylaxis** – For patients with preeclampsia with features of severe

disease, we recommend intrapartum and postpartum seizure prophylaxis with magnesium sulfate (**Grade 1A**). Seizure is an infrequent occurrence in patients without severe features of preeclampsia; however, some clinicians and patients may feel the benefit of treatment is justifiable given the low cost and toxicity of the treatment. (See 'Seizure prophylaxis' above.)

- **Initial and maintenance** magnesium sulfate **dosing** – The most common dose is 4 to 6 g magnesium sulfate intravenously over 15 to 20 minutes followed by 1 to 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 patients 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** – Magnesium toxicity is uncommon in patients 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.)

- **Management of toxicity** – Calcium gluconate 15 to 30 mL of a 10 percent solution intravenously over 2 to 5 minutes is administered to patients 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**
  - **Route** – 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 birth' above.)
  - **Patients with thrombocytopenia** – 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 patients 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** – 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. (See 'Fluids' above.)
- **Prognosis**
  - **Recurrence in future pregnancies** – 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.)
  - **Risk for development of cardiovascular disease** – 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, kidney disease, type 2 diabetes' above). Routine well-patient 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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Topic 139247 Version 4.0

GRAPHICS

Criteria for the diagnosis of preeclampsia

Systolic blood pressure ≥140 mmHg and/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.

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* If systolic blood pressure is ≥160 mmHg and/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 37.0

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 and/or diastolic blood pressure ≥110 mmHg on 2 occasions at least 4 hours apart while the patient is on bedrest; however, antihypertensive therapy generally should 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 with acetaminophen 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 27.0

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 5 to 10 mg IV over 2 minutes,

		depending on the previous response. Cumulative maximum dose is 20 to 30 mg per treatment event. If target BP is not achieved, switch to another class of agent.
Nicardipine (parenteral)	The initial dose is 5 mg/hour IV by continuous infusion titrated up to 15 mg/hour to achieve target BP 130 to 150/80 to 100 mmHg. The effect of dose titrations may not be observed for 5 to 15 minutes; rapid titration should be 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 birth 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.
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.

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. Gestational hyertension and preeclampsia. Practice Bulletin, Number 222. Obstet Gynecol 2020; 135:e237.*
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 13.0

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

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Errol R Norwitz, MD, PhD, MBA Patent Holder: Bayer [Prediction test for preeclampsia]. Consultant/Advisory Boards: Cognitive Care/Early Detect[AI platform for early risk detection and quantification];Illumina [Minimally invasive genetic testing for fetal and pregnancy-related disorders]. Other Financial Interest: NICHD [Board of Scientific Counselors]. All of the relevant financial relationships listed have been mitigated. **Charles J Lockwood, MD, MHCM** No relevant financial relationship(s) with ineligible companies to disclose. **Vanessa A Barss, MD, FACOG** No relevant financial relationship(s) with ineligible companies to disclose.

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