

# ACOG *PRACTICE BULLETIN*

CLINICAL MANAGEMENT GUIDELINES FOR  
OBSTETRICIAN–GYNECOLOGISTS

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This Practice Bulletin was developed by the ACOG Committee on Practice Bulletins—Obstetrics with the assistance of Larry C. Gilstrap III, MD, and Susan M. Ramin, MD. The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.



## Diagnosis and Management of Preeclampsia and Eclampsia

*Hypertensive disease occurs in approximately 12–22% of pregnancies, and it is directly responsible for 17.6% of maternal deaths in the United States (1, 2). However, there is confusion about the terminology and classification of these disorders. This bulletin will provide guidelines for the diagnosis and management of hypertensive disorders unique to pregnancy (ie, preeclampsia and eclampsia), as well as the various associated complications. Chronic hypertension has been discussed elsewhere (3).*

### Background

#### Definition

The National High Blood Pressure Education Program Working Group (hereafter referred to as the “Working Group”) has recommended that the term “gestational hypertension” replace the term “pregnancy-induced hypertension” to describe cases in which elevated blood pressure without proteinuria develops in a woman after 20 weeks of gestation and blood pressure levels return to normal postpartum (4). According to the criteria established by the Working Group, in pregnant women, hypertension is defined as a systolic blood pressure level of 140 mm Hg or higher or a diastolic blood pressure level of 90 mm Hg or higher that occurs after 20 weeks of gestation in a woman with previously normal blood pressure (4). As many as one quarter of women with gestational hypertension will develop proteinuria, ie, preeclampsia (5).

Preeclampsia is a syndrome defined by hypertension and proteinuria that also may be associated with myriad other signs and symptoms, such as edema,

visual disturbances, headache, and epigastric pain. Laboratory abnormalities may include hemolysis, elevated liver enzymes, and low platelet counts (HELLP syndrome). Proteinuria may or may not be present in patients with HELLP syndrome. Proteinuria is defined as the presence of 0.3 g or more of protein in a 24-hour urine specimen. This finding usually correlates with a finding of 1+ or greater but should be confirmed using a random urine dipstick evaluation and a 24-hour or “timed” collection (4). See the box for the criteria for diagnosing preeclampsia. Many practitioners have traditionally used these criteria to diagnose preeclampsia, although they have not been substantiated by research, and other definitions exist. These also are the criteria frequently used in research protocols. Severe preeclampsia is defined in the box.

In the past, hypertension indicative of preeclampsia has been defined as an elevation of more than 30 mm Hg systolic or more than 15 mm Hg diastolic above the patient’s baseline blood pressure; however, this definition has not proved to be a good prognostic indicator of outcome (6, 7). The so-called “30–15 rule” is not part of the criteria for preeclampsia established by the Working Group (4). According to the Working Group, however, women who demonstrate an elevation of more than 30 mm Hg systolic or more than 15 mm Hg diastolic above baseline “warrant close observation.”

Eclampsia is defined as the presence of new-onset grand mal seizures in a woman with preeclampsia. Other causes of seizures in addition to eclampsia include a bleeding arteriovenous malformation, ruptured aneurysm, or idiopathic seizure disorder. These diagnoses may be more likely in cases in which new-onset seizures occur after 48–72 hours postpartum.

The diagnostic criteria for superimposed preeclampsia include “new-onset proteinuria” in a woman with hypertension before 20 weeks of gestation, a sudden increase in proteinuria if already present in early gestation, a sudden increase in hypertension, or the develop-

### Diagnosis of Severe Preeclampsia

Preeclampsia is considered severe if one or more of the following criteria is present:

- Blood pressure of 160 mm Hg systolic or higher or 110 mm Hg diastolic or higher on two occasions at least 6 hours apart while the patient is on bed rest
- Proteinuria of 5 g or higher in a 24-hour urine specimen or 3+ or greater on two random urine samples collected at least 4 hours apart
- Oliguria of less than 500 mL in 24 hours
- Cerebral or visual disturbances
- Pulmonary edema or cyanosis
- Epigastric or right upper-quadrant pain
- Impaired liver function
- Thrombocytopenia
- Fetal growth restriction

ment of HELLP syndrome (4). Women with chronic hypertension who develop headache, scotomata, or epigastric pain also may have superimposed preeclampsia.

### Epidemiology and Risk Factors

The exact incidence of preeclampsia is unknown but it has been reported to be approximately 5–8% (8, 9). Preeclampsia is primarily a disorder of first pregnancies. Other risk factors include multifetal gestations, preeclampsia in a previous pregnancy, chronic hypertension, pregestational diabetes, vascular and connective tissue disease, nephropathy, antiphospholipid antibody syndrome, obesity, age 35 years or older, and African-American race (1, 8, 10–12).

The precise role of genetic and environmental factors on the risk and incidence of preeclampsia is unclear, although emerging data suggest the tendency to develop preeclampsia may have a genetic basis (13–15). Women with thrombophilias also may have a genetic predisposition to preeclampsia.

### Pathophysiology

The etiology of preeclampsia is unknown, although much of the literature has focused on the degree of trophoblastic invasion by the placenta (4). In cases of preeclampsia, invasion by the trophoblast appears to be incomplete (16–18). Moreover, the severity of hypertension may be related to the degree of trophoblastic invasion (19). Preeclampsia also may be associated with significant alterations in the immune response (4).

### Criteria for Diagnosis of Preeclampsia\*

- Blood pressure of 140 mm Hg systolic or higher or 90 mm Hg diastolic or higher that occurs after 20 weeks of gestation in a woman with previously normal blood pressure
- Proteinuria, defined as urinary excretion of 0.3 g protein or higher in a 24-hour urine specimen

\*Preeclampsia is a pregnancy-specific syndrome that usually occurs after 20 weeks of gestation.

Data from Report of the National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol* 2000;183:S1–S22

## **Vascular Changes**

Hemoconcentration, in addition to hypertension, is a significant vascular change, because women with the preeclampsia-eclampsia syndrome may not develop the normal hypervolemia of pregnancy (20). Changes in vascular reactivity may be mediated by prostaglandins (21, 22). The interaction of various vasoactive agents, such as prostacyclin (vasodilator), thromboxane A<sub>2</sub> (potent vasoconstrictor), nitric oxide (potent vasodilator), and endothelins (potent vasoconstrictors) cause another pathophysiologic change seen in preeclampsia: intense vasospasm. The vasospasm and subsequent hemoconcentration are associated with contraction of the intravascular space. Because of capillary leak and decreased colloid oncotic pressure often associated with this syndrome, attempts to expand the intravascular space in these women with vigorous fluid therapy may result in elevation of the pulmonary capillary wedge pressure and even pulmonary edema. A study using invasive hemodynamic monitoring in women with preeclampsia found that before aggressive intravenous fluid therapy, the women had hyperdynamic ventricular function with low pulmonary capillary wedge pressure (23). However, after aggressive fluid therapy, the pulmonary capillary wedge pressure increased significantly above normal levels (23).

## **Hematologic Changes**

Various hematologic changes also may occur in women with preeclampsia, especially when the preeclampsia is severe. Both thrombocytopenia and hemolysis may occur as part of the HELLP syndrome, although the etiology is unknown. Interpretation of hematocrit levels in the face of severe preeclampsia should take into consideration that hemolysis or hemoconcentration or both may occur. Thus, the hematocrit level may be very low because of hemolysis or very high secondary to hemoconcentration in the absence of hemolysis. Lactate dehydrogenase is present in erythrocytes in high concentration. A disproportionate elevation of levels of lactate dehydrogenase in serum may be a sign of hemolysis.

## **Hepatic Changes**

Hepatic function may be significantly altered in women with severe preeclampsia. Alanine aminotransferase and aspartate aminotransferase may be elevated. Hyperbilirubinemia may occur, especially in the presence of hemolysis. Hepatic hemorrhage, which usually manifests as a subcapsular hematoma, also may occur, especially in women with preeclampsia and upper abdominal pain (24). Rarely, hepatic rupture, which is associated with a high mortality rate, occurs (25).

## **HELLP Syndrome**

Women with severe preeclampsia and hepatic involvement may develop HELLP syndrome. In one study, HELLP syndrome occurred in approximately 20% of women with severe preeclampsia (26). As with severe preeclampsia, HELLP syndrome is associated with an increased risk of adverse outcomes, including placental abruption, renal failure, subcapsular hepatic hematoma, recurrent preeclampsia, preterm delivery, and even fetal or maternal death (26–30).

## **Neurologic and Cerebral Manifestations**

Eclampsia remains a cause of maternal mortality (31, 32), usually in association with intracranial hemorrhage (33). Although uncommon, temporary blindness (lasting a few hours to up to a week) also may accompany severe preeclampsia and eclampsia (34). Other nervous system manifestations include headache, blurred vision, scotomata (4), and hyperreflexia.

## **Renal Changes**

As a result of vasospasm, the normal expected increase in glomerular filtration rate and renal blood flow and the expected decrease in serum creatinine may not occur in women with preeclampsia, especially if the disease is severe. Oliguria, commonly (albeit arbitrarily) defined as less than 500 mL in 24 hours, also may occur secondary to the hemoconcentration and decreased renal blood flow. Rarely, persistent oliguria may reflect acute tubular necrosis, which may lead to acute renal failure (8).

## **Fetal Changes**

As a result of impaired uteroplacental blood flow or placental infarction, manifestations of preeclampsia also may be seen in the fetal placental unit. These include intrauterine growth restriction, oligohydramnios, placental abruption, and nonreassuring fetal status demonstrated on antepartum surveillance.

# **Clinical Considerations and Recommendations**

### **► Are there effective methods for identifying women at risk for preeclampsia?**

No single screening test for preeclampsia has been found to be reliable and cost-effective (35–37). Uric acid is one of the most commonly used tests but it has a positive predictive value of only 33% and has not proved useful in predicting preeclampsia (38). Doppler velocimetry of the uterine arteries was reported not to be a useful test for

screening pregnant women at low risk for preeclampsia (35, 39).

► ***How should the blood pressure be taken?***

According to the Working Group, the diastolic blood pressure is that pressure at which the sound disappears (Korotkoff phase V) (4). To reduce inaccurate readings, an appropriate size cuff should be used (length 1.5 times upper arm circumference or a cuff with a bladder that encircles 80% or more of the arm). The blood pressure level should be taken with the patient in an upright position, after a 10-minute or longer rest period. For patients in the hospital, the blood pressure can be taken with either the patient sitting up or in the left lateral recumbent position with the patient's arm at the level of the heart (40). The patient should not use tobacco or caffeine for 30 minutes preceding the measurement (37, 41). Although validated electronic devices can be used, a mercury sphygmomanometer is preferred because it is the most accurate device (37, 41).

► ***What is the optimal treatment for preeclampsia?***

The decision to deliver a patient with preeclampsia must balance both the maternal and fetal risks. Continued observation is appropriate for the woman with a preterm fetus only if she has mild preeclampsia (4). Such therapy consists of fetal and maternal evaluation. No randomized trials have determined the best tests for fetal evaluation. The Working Group recommends weekly nonstress tests, biophysical profiles, or both, which should be repeated as indicated according to maternal condition. Testing is recommended twice weekly for suspected fetal growth restriction or oligohydramnios. Daily fetal movement assessment also may prove useful. The Working Group also recommends ultrasound examination for fetal growth and amniotic fluid assessment every 3 weeks (4).

Maternal evaluation consists primarily of frequent evaluation for worsening preeclampsia. Initial laboratory tests consist of evaluation of platelet count, liver enzymes, and renal function and a 12-hour to 24-hour urine collection for protein (4). With mild disease and no progression, these tests can be repeated weekly. The tests should be repeated sooner if disease progression is questionable.

The management of a woman with severe preeclampsia remote from term is best accomplished in a tertiary care setting or in consultation with an obstetrician-gynecologist with training, experience, and demonstrated competence in the management of high-risk pregnancies, such as a maternal-fetal medicine subspecialist (4, 42–44). Laboratory evaluation and fetal surveillance may be indicated on a daily basis depending on the severity and progression of the disorder (4).

No large randomized clinical trials have compared conservative versus aggressive management of women with HELLP syndrome. Considering the serious nature of this complication, it seems reasonable to conclude that women with HELLP syndrome should be delivered regardless of their gestational age. Expectant management of this syndrome in women before 32 weeks of gestation should be undertaken only in tertiary care centers or as part of randomized clinical trials with appropriate safeguards and consent (4).

► ***Is there a role for outpatient management in women with preeclampsia?***

According to the Working Group (4):

“Hospitalization is often initially recommended for women with new-onset preeclampsia. After maternal and fetal conditions are serially assessed, subsequent management may be continued in the hospital, at a day-care unit, or at home on the basis of the initial assessment. Prolonged hospitalization for the duration of pregnancy allows rapid intervention in case of fulminant progression to hypertensive crisis, eclampsia, or abruptio placentae. These complications are rare in compliant women who have mild [disease].... Ambulatory management at home or at a day-care unit has been evaluated as an option for monitoring women with mild gestational hypertension or preeclampsia remote from term. A number of observational and randomized studies suggest a place for ambulatory management of selected women. If day care or home management is selected, it should include frequent maternal and fetal evaluation and access to health care providers. If worsening of preeclampsia is diagnosed, as determined by laboratory findings, symptoms, and clinical signs, hospitalization is indicated.”

Women who have difficulty with compliance, including logistic barriers, who manifest signs of disease progression or who have severe preeclampsia should be hospitalized.

► ***Is medical management beneficial during labor and delivery in women with preeclampsia?***

The two main goals of management of women with preeclampsia during labor and delivery are prevention of seizures or eclampsia and control of hypertension. Although there is no unanimity of opinion regarding the prophylactic use of magnesium sulfate for the prevention of seizures in women with mild preeclampsia or gestational hypertension, a significant body of evidence attests to the efficacy of magnesium sulfate in women with severe preeclampsia and eclampsia. A randomized, con-

trolled trial of 822 women with severe preeclampsia (699 evaluated) receiving either intravenous magnesium sulfate or placebo reported one case (0.3%) of eclampsia among the 345 women in the magnesium group versus 11 (3.2%) of 340 in the placebo group (relative risk, 0.09; 95% confidence interval, 0.01–0.69;  $P = 0.003$ ) (45). A review of the literature on magnesium sulfate therapy in women with either preeclampsia or eclampsia identified 19 randomized controlled trials, five retrospective studies, and eight observational studies (46). In the randomized controlled trials of women with eclampsia, recurrent seizures occurred in 23% of 935 women who received either phenytoin or diazepam compared with 9.4% of 932 women who received magnesium sulfate. In the randomized trials of women with severe preeclampsia, seizures occurred in 2.8% of 793 women treated with antihypertensives compared with only 0.9% in women treated with magnesium sulfate. Thus, the data support the use of magnesium sulfate to prevent seizures in women with severe preeclampsia or eclampsia (31, 45–47).

Although no large randomized clinical trials have compared treatment with placebo, antihypertensive therapy is generally recommended for diastolic blood pressure levels of 105–110 mm Hg or higher (4, 8, 48). Hydralazine and labetalol are the two agents most commonly used for this purpose (see box).

► ***What is the optimal mode of delivery for women with preeclampsia?***

For mild preeclampsia, vaginal delivery at term is preferred. No randomized clinical trials have evaluated the optimal method of delivery for women with severe preeclampsia or eclampsia. Two retrospective studies comparing induction of labor with cesarean delivery in women with severe preeclampsia remote from term concluded that induction of labor was reasonable and was not “harmful” to low-birth-weight infants (49, 50). The decision to perform cesarean delivery should be individualized.

**Antihypertensive Treatment for Preeclampsia**

Hydralazine: 5–10-mg doses intravenously every 15–20 minutes until desired response is achieved\*

Labetalol: 20-mg intravenous bolus dose followed by 40 mg if not effective within 10 minutes; then, 80 mg every 10 minutes to maximum total dose of 220 mg†

\*Cunningham FG, Gant NF, Leveno KJ, Gilstrap LC III, Hauth JC, Wenstrom KD. Hypertensive disorders in pregnancy. In: Williams obstetrics. 21st ed. New York: McGraw-Hill, 2001:567–618

†Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000;183:S1–S22

► ***Is anesthesia contraindicated during labor and delivery in women with preeclampsia?***

With improved techniques over the past two decades, regional anesthesia has become the preferred technique for women with severe preeclampsia and eclampsia—both for labor and delivery (4). A secondary analysis of women with severe preeclampsia in the National Institute of Child Health and Human Development’s Maternal–Fetal Medicine Units Network trial of low-dose aspirin reported that epidural anesthesia was not associated with an increased rate of cesarean delivery, pulmonary edema, or renal failure (51). Moreover, general anesthesia carries more risk to pregnant women than does regional anesthesia (52). However, regional anesthesia is generally contraindicated in the presence of a coagulopathy because of the potential for hemorrhagic complications.

► ***How should women with eclampsia be managed?***

Women with eclampsia require prompt intervention. When an eclamptic seizure occurs, the woman should be medically stabilized. First, it is important to control convulsions and prevent their recurrence with intravenous or intramuscular magnesium sulfate (8). One protocol is a 4-g to 6-g loading dose diluted in 100 mL fluid and administered intravenously for 15–20 minutes, followed by 2 g per hour as a continuous intravenous infusion (8). Antihypertensive medications should be used for women with diastolic blood pressure levels of 105–110 mm Hg or higher.

The patient with eclampsia should be delivered in a timely fashion. Fetal bradycardia frequently occurs during an eclamptic seizure; usually, this can be managed by maternal treatment, and cesarean delivery is not necessary. Once the patient is stabilized, the method of delivery should depend, in part, on factors such as gestational age, fetal presentation, and the findings of the cervical examination.

► ***Is there a role for invasive hemodynamic monitoring?***

Most women with severe preeclampsia or eclampsia can be managed without invasive hemodynamic monitoring. A review of 17 women with eclampsia reported that use of a pulmonary artery catheter aided in clinical management decisions (53). However, no randomized trials support their routine use in women with severe preeclampsia. Invasive hemodynamic monitoring may prove beneficial in preeclamptic women with severe cardiac disease, severe renal disease, refractory hypertension, oliguria, or pulmonary edema (8, 54–56).



### ► *Can preeclampsia be prevented?*

Much of the obstetric research in the past several decades has been directed at finding ways to prevent preeclampsia and eclampsia. Recent studies have focused on low-dose aspirin, calcium supplementation, and antioxidant therapy. Most evidence suggests that low-dose aspirin therapy is of little, if any, benefit in preventing preeclampsia in low-risk women (4, 57–60).

Although there is some controversy regarding the use of calcium supplementation to prevent preeclampsia, large, randomized, controlled trials have shown no benefit (58, 61, 62). Recently, antioxidant therapy with 1,000 mg per day of vitamin C and 400 mg per day of vitamin E has shown promise in preventing preeclampsia (63). These results need to be confirmed in larger randomized trials.

## Summary of Recommendations

*The following recommendations are based on good and consistent scientific evidence (Level A):*

- Magnesium sulfate should be used for the prevention and treatment of seizures in women with severe preeclampsia or eclampsia.
- If analgesia/anesthesia is required, regional or neuraxial analgesia/anesthesia should be used because it is efficacious and safe for intrapartum management of women with severe preeclampsia in the absence of coagulopathy.
- Low-dose aspirin has not been shown to prevent preeclampsia in women at low risk and, therefore, is not recommended.
- Daily calcium supplementation has not been shown to prevent preeclampsia and, therefore, is not recommended.

*The following recommendations are based on limited or inconsistent scientific evidence (Level B):*

- The management of a woman with severe preeclampsia remote from term is best accomplished in a tertiary care setting or in consultation with an obstetrician–gynecologist with training, experience, and demonstrated competence in the management of high-risk pregnancies, such as a maternal–fetal medicine subspecialist.
- Practitioners should be aware that although various laboratory tests may be useful in the management of women with preeclampsia, to date there is no reliable predictive test for preeclampsia.

- Invasive hemodynamic monitoring should be considered in preeclamptic women with severe cardiac disease, renal disease, refractory hypertension, pulmonary edema, or unexplained oliguria.

*The following recommendations are based primarily on consensus and expert opinion (Level C):*

- Women should be considered as having severe preeclampsia if they have blood pressure levels of 160 mm Hg systolic or higher or 110 mm Hg diastolic or higher on two occasions at least 6 hours apart while the patient is on bed rest, proteinuria of 5 g or higher in a 24-hour urine specimen or 3+ or greater on two random urine samples collected at least 4 hours apart, oliguria of less than 500 mL in 24 hours, cerebral or visual disturbances, pulmonary edema or cyanosis, epigastric or right upper-quadrant pain, elevated liver enzymes, thrombocytopenia, or fetal growth restriction.
- Expectant management should be considered for women remote from term who have mild preeclampsia.
- Antihypertensive therapy (with either hydralazine or labetalol) should be used for treatment of diastolic blood pressure levels of 105–110 mm Hg or higher.

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The MEDLINE database, the Cochrane Library, and ACOG's own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and January 2001. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician-gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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