Diagnosis and Management of Preeclampsia

LANA K. WAGNER, M.D., *First Choice Community Healthcare, Albuquerque, New Mexico*

Preeclampsia is a pregnancy-specific multisystem disorder of unknown etiology. The disorder affects approximately 5 to 7 percent of pregnancies and is a significant cause of maternal and fetal morbidity and mortality. Preeclampsia is defined by the new onset of elevated blood pressure and proteinuria after 20 weeks of gestation. It is considered severe if blood pressure and proteinuria are increased substantially or symptoms of end-organ damage (including fetal growth restriction) occur. There is no single reliable, cost-effective screening test for preeclampsia, and there are no well-established measures for primary prevention. Management before the onset of labor includes close monitoring of maternal and fetal status. Management during delivery includes seizure prophylaxis with magnesium sulfate and, if necessary, medical management of hypertension. Delivery remains the ultimate treatment. Access to prenatal care, early detection of the disorder, careful monitoring, and appropriate management are crucial elements in the prevention of preeclampsia-related deaths. (Am Fam Physician 2004;70:2317-24. Copyright© 2004 American Academy of Family Physicians.)

See page 2252 for definitions of strength-of-recommendation labels.

Preeclampsia is a pregnancy-specific, multisystem disorder that is characterized by the development of hypertension and proteinuria after 20 weeks of gestation. The disorder complicates approximately 5 to 7 percent of pregnancies,[1] with an incidence of 23.6 cases per 1,000 deliveries in the United States.[2]

Complications of hypertension are the third leading cause of pregnancy-related deaths, superseded only by hemorrhage and embolism.[3] Preeclampsia is associated with increased risks of placental abruption, acute renal failure, cerebrovascular and cardiovascular complications, disseminated intravascular coagulation, and maternal death.[3] Consequently, early diagnosis of preeclampsia and close observation are imperative.

Diagnostic criteria for preeclampsia include new onset of elevated blood pressure and proteinuria after 20 weeks of gestation.

Diagnosis

Diagnostic criteria for preeclampsia include new onset of elevated blood pressure and proteinuria after 20 weeks of gestation. Features such as edema and blood pressure elevation above the patient's baseline no longer are diagnostic criteria.[4,5] Severe preeclampsia is indicated by more substantial blood pressure elevations and a greater degree of proteinuria. Other features of severe preeclampsia include oliguria, cerebral or visual disturbances, and pulmonary edema or cyanosis *(Table 1)*.[4,5]

Diagnosis becomes less difficult if physicians understand where preeclampsia "fits" into the hypertensive disorders of pregnancy. These disorders include chronic hypertension, preeclampsia-eclampsia, preeclampsia superimposed on chronic hypertension, and gestational hypertension *(Figure 1)*.[5]

Chronic hypertension is defined by elevated blood pressure that predates the pregnancy, is documented before 20 weeks of gestation, or is present 12 weeks after delivery.[5] In contrast, preeclampsia-eclampsia is defined by elevated blood pressure and proteinuria that occur after 20 weeks of gestation. Eclampsia, a severe complication of preeclampsia, is the new onset of seizures in a woman with preeclampsia. Eclamptic seizures are relatively rare and occur in less than 1 percent of women with preeclampsia.[1]

Preeclampsia superimposed on chronic

TABLE 1
Diagnostic Criteria for Preeclampsia*

Preeclampsia
Blood pressure: 140 mm Hg or higher systolic or 90 mm Hg or higher diastolic after 20 weeks of gestation in a woman with previously normal blood pressure
Proteinuria: 0.3 g or more of protein in a 24-hour urine collection (usually corresponds with 1+ or greater on a urine dipstick test)
Severe preeclampsia
Blood pressure: 160 mm Hg or higher systolic or 110 mm Hg or higher diastolic on two occasions at least six hours apart in a woman on bed rest
Proteinuria: 5 g or more of protein in a 24-hour urine collection or 3+ or greater on urine dipstick testing of two random urine samples collected at least four hours apart
Other features: oliguria (less than 500 mL of urine in 24 hours), cerebral or visual disturbances, pulmonary edema or cyanosis, epigastric or right upper quadrant pain, impaired liver function, thrombocytopenia, intrauterine growth restriction

**—For the diagnosis of preeclampsia, both hypertension and proteinuria must be present.*

Information from references 4 and 5.

Preeclampsia as a Hypertensive Disorder of Pregnancy

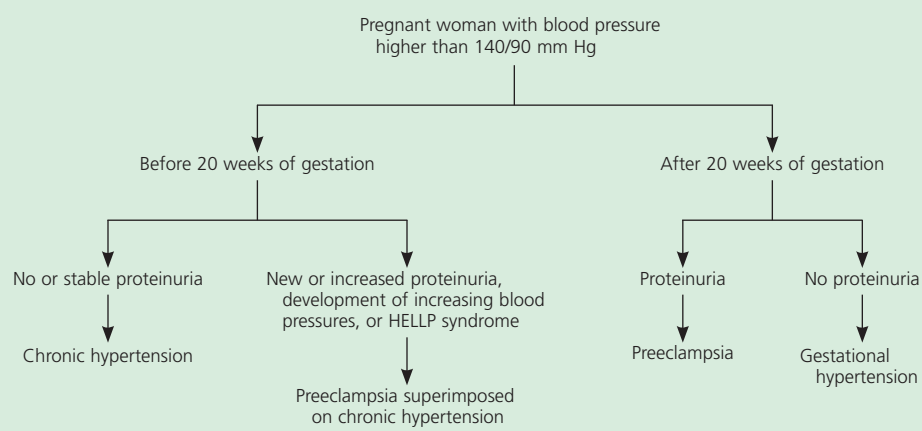

Figure 1. An algorithm for differentiating among hypertensive disorders in pregnant women. (HELLP = ***h***emolysis, ***e***levated ***l***iver enzymes, ***l***ow ***p***latelet count)

Information from reference 5.

hypertension is characterized by new-onset proteinuria (or by a sudden increase in the protein level if proteinuria already is present), an acute increase in the level of hypertension (assuming proteinuria already exists), or development of the HELLP (***h***emolysis, ***e***levated ***l***iver enzymes, ***l***ow ***p***latelet count) syndrome.[4]

Gestational hypertension is diagnosed when elevated blood pressure without proteinuria develops after 20 weeks of gestation and blood pressure returns to normal within 12 weeks after delivery.[4] One fourth of women with gestational hypertension develop proteinuria and thus progress to preeclampsia.[6,7]

TABLE 2
Risk Factors for Preeclampsia

Pregnancy-associated factors
Chromosomal abnormalities
Hydatidiform mole
Hydrops fetalis
Multifetal pregnancy
Oocyte donation or donor insemination
Structural congenital anomalies
Urinary tract infection
Maternal-specific factors
Age greater than 35 years
Age less than 20 years
Black race
Family history of preeclampsia
Nulliparity
Preeclampsia in a previous pregnancy
Specific medical conditions: gestational diabetes, type I diabetes, obesity, chronic hypertension, renal disease, thrombophilias
Stress
Paternal-specific factors
First-time father
Previously fathered a preeclamptic pregnancy in another woman

Information from references 4 and 8.

Risk Factors

Risk factors for preeclampsia include medical conditions with the potential to cause microvascular disease (e.g., diabetes mellitus, chronic hypertension, vascular and connective tissue disorders), antiphospholipid antibody syndrome, and nephropathy.[4,8] Other risk factors are associated with pregnancy itself or may be specific to the mother or father of the fetus *(Table 2)*.[4,8]

Pathophysiology

Although the exact cause of preeclampsia remains unclear,[4,5] many theories center on problems of placental implantation and the level of trophoblastic invasion.[9,10] It is important to remember that although hypertension and proteinuria are the diagnostic criteria for preeclampsia, they are only symptoms of the pathophysiologic changes that occur in the disorder. One of the most striking physiologic changes is intense systemic vasospasm, which is responsible for decreased perfusion of virtually all organ systems.[11] Perfusion also is diminished because of vascular hemoconcentration and third spacing of intravascular fluids. In addition, preeclampsia is accompanied by an exaggerated inflammatory response and inappropriate endothelial activation.[10] Activation of the coagulation cascade and resultant microthrombi formation further compromise blood flow to organs.[11]

Up to 40 percent of eclamptic seizures occur before delivery; approximately 16 percent occur more than 48 hours after delivery.

Clinical Presentation

The clinical presentation of preeclampsia may be insidious or fulminant. Some women may be asymptomatic at the time they are found to have hypertension and proteinuria; others may present with symptoms of severe preeclampsia, such as visual disturbances, severe headache, or upper abdominal pain. From 4 to 14 percent of women with preeclampsia present with superimposed HELLP syndrome.[12] HELLP syndrome may be a variant of preeclampsia or a separate entity, but its development is ominous because mortality or serious morbidity occurs in 25 percent of affected women.[13]

Preeclampsia-eclampsia may develop before, during, or after delivery. Up to 40 percent of eclamptic seizures occur before delivery; approximately 16 percent occur more than 48 hours after delivery.[1] Death associated with preeclampsia-eclampsia may be due to cerebrovascular events, renal or hepatic failure, HELLP syndrome, or other complications of hypertension.[3]

Diagnostic Evaluation

HISTORY

As part of the initial prenatal assessment, pregnant women should be questioned about potential risk factors for preeclampsia. They should be asked about their obstetric history, specifically the occurrence of hypertension or preeclampsia during previous pregnancies. A thorough medical history should be obtained to identify medical conditions that

increase the risk for preeclampsia, including diabetes mellitus, hypertension, vascular and connective tissue disease, nephropathy, and antiphospholipid antibody syndrome.

During prenatal visits after 20 weeks of gestation, pregnant women should be asked about specific symptoms, including visual disturbances, persistent headaches, epigastric or right upper quadrant pain, and increased edema. Questions about these symptoms are included in many standardized prenatal documentation forms.

PHYSICAL EXAMINATION

Blood pressure should be measured at each prenatal visit. As mentioned previously, increases above the patient's baseline (greater than 30 mm Hg systolic or 15 mm Hg diastolic) are no longer considered to be criteria for the diagnosis of preeclampsia. However, such increases warrant close observation.[5] To ensure accurate readings, an appropriate-size blood pressure cuff should be used, and blood pressure should be measured after a rest period of 10 minutes or more. During the blood pressure measurement, the patient should be in an upright or left lateral recumbent position with the arm at the level of the heart.[4]

There currently is no single reliable, cost-effective screening test for preeclampsia.

Fundal height should be measured at each prenatal visit because size less than dates may indicate intrauterine growth retardation or oligohydramnios. These conditions may become apparent long before diagnostic criteria for preeclampsia are met. Increasing maternal facial edema and rapid weight gain also should be noted because fluid retention often is associated with preeclampsia. Although these symptoms (e.g., facial edema, rapid weight gain) are not unique to preeclampsia, it is wise to follow affected patients for hypertension and proteinuria.[5] Edema involving the lower extremities frequently occurs during normal pregnancy and therefore is of less concern.

LABORATORY EVALUATION

There currently is no single reliable, cost-effective screening test for preeclampsia.[4] The serum uric acid level once was used as an indicator of preeclampsia but has been found to lack sensitivity and specificity as a diagnostic tool.[14] However, an elevated serum uric acid level may be of some use in identifying pregnant women with chronic hypertension who have an increased likelihood of having superimposed preeclampsia.[14]

A baseline laboratory evaluation should be performed early in pregnancy in women who are at high risk for preeclampsia. Tests should include a hepatic enzyme level, a platelet count, a serum creatinine level, and a 12- to 24-hour urine collection for total protein measurement. Once the diagnosis of preeclampsia has been made, an expanded set of laboratory tests should be performed *(Table 3)*.[15] In women who have preeclampsia with no suspected progression, all laboratory tests should be conducted weekly.[4,5] If progression of eclampsia is suspected, the tests should be repeated more frequently.

Small studies[16-18] have shown that random

TABLE 3
Laboratory Tests

Women at high risk for eclampsia
Hemoglobin level
Hematocrit
Platelet count
Urine protein collection (12 or 24 hour)
Serum creatinine level
Serum uric acid level
Women developing hypertension after 20 weeks of gestation
Same tests as in women at high risk
Serum transaminase levels
Serum albumin level
Lactic acid dehydrogenase level
Peripheral blood smear
Coagulation profile

Adapted from National High Blood Pressure Education Program. Working Group on High Blood Pressure in Pregnancy. Working group report on high blood pressure in pregnancy. Bethesda, Md.: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute, 2000; NIH publication no. 00-3029. Accessed online November 8, 2004, at http://www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_preg.pdf.

urinary protein-to-creatinine ratios predict the 24-hour urine total protein level and may provide a faster, simplified method of estimating proteinuria, providing that the protein values are less than 1 g in 24 hours.[19] The urinary protein-to-creatinine ratio is not sensitive enough to differentiate mild and severe preeclampsia if significant proteinuria exists. However, a ratio of less than 0.2 effectively excludes the presence of significant proteinuria.[20] A cutoff ratio of greater than 0.19 is a good predictor of significant proteinuria, with a sensitivity of 90 percent and a specificity of 70 percent. The negative predictive value of the urinary protein-to-creatinine ratio is 87 percent.[17]

OTHER STUDIES

A baseline sonogram should be considered at 25 to 28 weeks of gestation to evaluate fetal growth in pregnant women at high risk for preeclampsia.[5] In women who have already been diagnosed with preeclampsia, antepartum testing with a nonstress test, a biophysical profile, or both should be performed on a weekly basis starting at the time of diagnosis.[5] If intrauterine growth retardation or oligohydramnios is suspected, the tests should be performed at least twice weekly, and delivery should be contemplated if there are any signs of fetal compromise.[4,5] Immediate antepartum testing or delivery is indicated for suspected placental abruption and nonreassuring fetal surveillance.[5]

Treatment

Delivery remains the ultimate treatment for preeclampsia.[4,5] Although maternal and fetal risks must be weighed in determining the timing of delivery, clear indications for delivery exist *(Table 4)*.[15] When possible, vaginal delivery is preferable to avoid the added physiologic stressors of cesarean delivery.[5] If cesarean delivery must be used, regional anesthesia is preferred because it carries less maternal risk.[5] In the presence of coagulopathy, use of regional anesthesia generally is contraindicated.[5]

Women with preeclampsia and preterm pregnancy can be observed on an outpatient basis, with frequent assessment of maternal and fetal well-being. Women who are noncompliant, who do not have ready access to medical care, or who have progressive or severe preeclampsia should be hospitalized. Women whose pregnancy is remote from term should be cared for in a tertiary care setting or in consultation with an obstetrician or family physician who is experienced in the management of high-risk pregnancies.[4]

A baseline sonograph should be considered at 25 to 28 weeks of gestation to evaluate fetal growth in pregnant women at high risk for preeclampsia.

During labor, the management goals are to prevent seizures and control hypertension.[4] Magnesium sulfate is the medication of choice for the prevention of eclamptic seizures in women with severe preeclampsia and for the treatment of women with eclamptic seizures.[1,21] One commonly used regimen is a 6-g loading dose of magnesium

TABLE 4
Indications for Delivery in Preeclampsia

Fetal indications
Severe intrauterine growth restriction
Nonreassuring fetal surveillance
Oligohydramnios
Maternal indications
Gestational age of 38 weeks or greater*
Platelet count below 100×10^3 per mm^3 (100×10^9 per L)
Progressive deterioration of hepatic function
Progressive deterioration of renal function
Suspected placental abruption
Persistent severe headache or visual changes
Persistent severe epigastric pain, nausea, or vomiting
Eclampsia

**—Delivery should be based on maternal and fetal conditions as well as gestational age.*

Adapted from National High Blood Pressure Education Program. Working Group on High Blood Pressure in Pregnancy. Working group report on high blood pressure in pregnancy. Bethesda, Md.: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute, 2000; NIH publication no. 00-3029. Accessed online July 19, 2004, at http://www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_preg.pdf.

TABLE 5
Antihypertensive Drugs Commonly Used in the Treatment of Severe Preeclampsia

Hydralazine (Apresoline)*
Initial dose: 5 mg IV or 10 mg IM
When blood pressure is controlled, repeat initial dose as needed (usually about every 3 hours; maximum, 400 mg per day).
If blood pressure is not controlled in 20 minutes, repeat initial dose every 20 minutes until maximum dosage is reached, or go immediately to next step.
If blood pressure is not controlled with a total of 20 mg IV or 30 mg IM, consider using a different antihypertensive drug (labetalol,† nifedipine [Procardia], sodium nitroprusside [Nitropress]).
Labetalol (Normodyne, Trandate)*
Initial dose: 20 mg in IV bolus
If blood pressure is not controlled, give 40 mg 10 minutes after initial dose and then 80 mg every 10 minutes for two additional doses (maximum: 220 mg).
If blood pressure is not controlled, use a different antihypertensive drug (hydralazine, nifedipine, sodium nitroprusside).

IV = intravenous; IM = intramuscular.

**—In managing hypertensive emergencies, IV administration is safer than IM or oral administration because it is easier to combat inadvertent hypotension by stopping an IV injection or infusion.*

†—Labetalol should not be used in women with asthma or congestive heart failure.

Adapted from National High Blood Pressure Education Program. Working Group on High Blood Pressure in Pregnancy. Working group report on high blood pressure in pregnancy. Bethesda, Md.: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute, 2000; NIH publication no. 00-3029. Accessed online November 8, 2004, at http://www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_preg.pdf.

sulfate followed by a continuous infusion at a rate of 2 g per hour.[1] Magnesium sulfate has been shown to be superior to phenytoin (Dilantin) and diazepam (Valium) for the treatment of eclamptic seizures.[1] Although magnesium sulfate commonly is used in women with preeclampsia, studies to date have been inadequate to show that it prevents progression of the disorder.[22,23]

Antihypertensive drug therapy is recommended for pregnant women with systolic blood pressures of 160 to 180 mm Hg or higher[24] and diastolic blood pressures of 105 to 110 mm Hg or higher[4,5,25] The treatment goal is to lower systolic pressure to 140 to 155 mm Hg and diastolic pressure to 90 to 105 mm Hg. To avoid hypotension, blood pressure should be lowered gradually.[5]

Although evidence about the potential adverse effects of most antihypertensive drugs has been poorly quantified, use of many of these agents is contraindicated during pregnancy.[7] Hydralazine (Apresoline) and labetalol (Normodyne, Trandate) are the antihypertensive drugs most commonly used in women with severe preeclampsia *(Table 5)*.[15] Nifedipine (Procardia) and sodium nitroprusside (Nitropress) are potential alternatives, but significant risks are associated with their use.[5] Note that labetalol therapy should not be used in women with asthma or congestive

The Author

LANA K. WAGNER, M.D., practices family medicine at First Choice Community Healthcare, Albuquerque, where she is clinical director of the North Valley Clinic. Previously, she was assistant professor in the Department of Family and Preventive Medicine at Emory University School of Medicine, Atlanta, and co-medical director of the Emory Family Medicine Clinic in Dunwoody, Ga. Dr. Wagner earned her medical degree and completed a family medicine residency at the University of New Mexico School of Medicine, Albuquerque.

Address correspondence to Lana K. Wagner, M.D., First Choice Community Healthcare, 1231 Candelaria NW, Albuquerque, NM 87107. Reprints are not available from the author.

heart failure.[5] Use of angiotensin-converting enzyme inhibitors is contraindicated in pregnant women.

In women with preeclampsia, blood pressure usually normalizes within a few hours after delivery but may remain elevated for two to four weeks.[26] As previously noted, a diagnosis of chronic hypertension is made if blood pressure remains elevated at 12 weeks postpartum.[5]

Women with preeclampsia should be counseled about future pregnancies. In nulliparous women with preeclampsia before 30 weeks of gestation, the recurrence rate for the disorder may be as high as 40 percent in future pregnancies.[5] Multiparous women have even higher rates of recurrence.[5]

Prevention

There currently are no well-established measures for preventing preeclampsia.[4,8] Both low-dose aspirin therapy and daily calcium supplementation have been studied as preventive measures but have not been shown to be beneficial in the general pregnant population and are not recommended for primary prevention of preeclampsia.[4,5] Some evidence does support the use of low-dose aspirin therapy and daily calcium supplementation in certain high-risk women. Calcium supplementation has been shown to produce modest blood pressure reductions in pregnant women who are at above-average risk for hypertensive disorders of pregnancy and in pregnant women with low dietary calcium intake.[27] An optimum calcium dosage for these women has not been established.[27] Low-dose aspirin therapy (100 mg per day or less) has been shown to reduce the incidence of preeclampsia in women who were found to have an abnormal uterine artery on Doppler ultrasound examination performed in the second trimester.[28]

Research on the use of antioxidants in the prevention of preeclampsia is promising.[29] However, further study is needed, and antioxidant therapy currently is not recommended.[4,5,29]

Although preeclampsia is not preventable, many deaths from the disorder can be prevented. Women who do not receive prenatal care are seven times more likely to die from complications related to preeclampsia-eclampsia than women who receive some level of prenatal care.[3] Some studies indicate that preeclampsia-related fatalities occur three times more often in black women than in white women.[3] Although the precise reasons for the racial differences remain elusive, the differences may be indicative of disparities in health status, as well as access to, and quality of, prenatal care.[3] To decrease preeclampsia-related mortality, appropriate prenatal care must be available to all women. Early detection, careful monitoring, and treatment of preeclampsia are crucial in preventing mortality related to this disorder.[3,8]

The author indicates that she does not have any conflicts of interest. Sources of funding: none reported.

Members of various medical faculties develop articles for "Practical Therapeutics." This article is one in a series coordinated by the Department of Family and Preventive Medicine at Emory University School of Medicine, Atlanta. Guest editor of the series is Timothy L. Clenney, M.D.

REFERENCES

1. Witlin AG, Sibai BM. Magnesium sulfate therapy in preeclampsia and eclampsia. Obstet Gynecol 1998;92:883-9.
2. Samadi AR, Mayberry RM, Zaidi AA, Pleasant JC, McGhee N Jr, Rice RJ. Maternal hypertension and associated pregnancy complications among African-American and other women in the United States. Obstet Gynecol 1996;87:557-63.
3. Mackay AP, Berg CJ, Atrash HK. Pregnancy-related mortality from preeclampsia and eclampsia. Obstet Gynecol 2001;97:533-8.
4. ACOG Committee on Obstetric Practice. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. No. 33, January 2002. American College of Obstetricians and Gynecologists. Obstet Gynecol 2002;99:159-67.
5. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000;183:S1-22.
6. Saudan P, Brown MA, Buddle ML, Jones M. Does gestational hypertension become pre-eclampsia? Br J Obstet Gynaecol 1998;105:1177-84.
7. Sibai BM. Chronic hypertension in pregnancy. Obstet Gynecol 2002;100:369-77.
8. Dekker G, Sibai B. Primary, secondary, and tertiary prevention of pre-eclampsia. Lancet 2001;357:209-15.
9. Postovit LM, Adams MA, Graham CH. Does nitric oxide play a role in the aetiology of pre-eclampsia? Placenta 2001;22(suppl A);S51-5.
10. Dekker GA, Sibai BM. Etiology and pathogenesis of preeclampsia: current concepts. Am J Obstet Gynecol 1998;179:1359-75.

Strength of Recommendations

Key clinical recommendation	Label	References
All pregnant women should be screened for preeclampsia at the first prenatal visit and periodically throughout the remainder of the pregnancy.	B	25
Pregnant women with diastolic blood pressure of 105 to 110 mm Hg or higher should receive antihypertension medication.	C	4, 5
Women at increased risk for preeclampsia who have low calcium intake should increase their calcium intake.	B	27

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, opinion, or case series.

11. Roberts JM, Cooper DW. Pathogenesis and genetics of pre-eclampsia. Lancet 2001; 357:53-6.
12. Sibai BM, Ramadan MK, Chari RS, Friedman SA. Pregnancies complicated by HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): subsequent pregnancy outcome and long-term prognosis. Am J Obstet Gynecol 1995;172(1 pt 1):125-9.
13. Padden MO. HELLP syndrome: recognition and perinatal management. Am Fam Physician 1999;60:829-36,839.
14. Lim KH, Friedman SA, Ecker JL, Kao L, Kilpatrick SJ. The clinical utility of serum uric acid measurements in hypertensive diseases of pregnancy. Am J Obstet Gynecol 1998;178:1067-71.
15. National High Blood Pressure Education Program. Working Group on High Blood Pressure in Pregnancy. Working group report on high blood pressure in pregnancy. Bethesda, Md.: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institutes, 2000; NIH publication no. 00-3029. Accessed online July 19, 2004, at: http://www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_preg.pdf.
16. Robert M, Sepandj RM, Liston RM, Dooley KC. Random protein-creatinine ratio for the quantitation of proteinuria in pregnancy. Obstet Gynecol 1997;90:893-5.
17. Rodriquez-Thompson D, Lieberman ES. Use of a random urinary protein-to-creatinine ratio for the diagnosis of significant proteinuria during pregnancy. Am J Obstet Gynecol 2001;185:808-11.
18. Neithardt AB, Dooley SL, Borensztajn J. Prediction of 24-hour protein excretion in pregnancy with a single voided urine protein-to-creatinine ratio. Am J Obstet Gynecol 2002;186:883-6.
19. Adelberg AM, Miller J, Doerzbacher M, Lambers DS. Correlation of quantitative protein measurements in 8-, 12-, and 24-hour urine samples for the diagnosis of preeclampsia. Am J Obstet Gynecol 2001;185:804-7.
20. Neithardt A, Dooley SL, Borensztajn J. Prediction of 24-hour protein excretion in pregnancy with a single voided urine protein-to-creatinine ratio. Am J Obstet Gynecol 2002;186:883-6.
21. Magpie Trial Collaboration Group. Do women with preeclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet 2002;359:1877-90.
22. Scott JR. Magnesium sulfate for mild preeclampsia [Editorial]. Obstet Gynecol 2003;101:213.
23. Livingston JC, Livingston LW, Ramsey R, Mabie BC, Sibai BM. Magnesium sulfate in women with mild preeclampsia: a randomized controlled trial. Obstet Gynecol 2003;101:217-20.
24. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. Obstet Gynecol 2003;102:181-92.
25. Guide to clinical preventive services: report of the U.S. Preventive Services Task Force. 2d ed. Washington, D.C.: U.S. Dept. of Health and Human Services, Office of Public Health and Science, Office of Disease Prevention and Health Promotion, 1996.
26. Ferrazzani S, DeCarolis S, Pomini F, Testa AC, Mastromarino C, Caruso A. The duration of hypertension in the puerperium of preeclamptic women: relationship with renal impairment and week of delivery. Am J Obstet Gynecol 1994;171:506-12.
27. Atallah AN, Hofmeyr GJ, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev 2004;(2): CD001059.
28. Coomarasamy A, Papaioannou S, Gee H, Khan KS. Aspirin for the prevention of preeclampsia in women with abnormal uterine artery Doppler: a meta-analysis. Obstet Gynecol 2001;98(5 pt 1):861-6.
29. Chappell LC, Seed PT, Briley AL, Kelly FJ, Lee R, Hunt B, et al. Effect of antioxidants on the occurrence of preeclampsia in women at increased risk: a randomised trial. Lancet 1999;354:810-6.