

Working Group Report on High Blood Pressure in Pregnancy

Editor's Note

Last year a report entitled "High Blood Pressure in Pregnancy" was published in *The American Journal of Obstetrics and Gynecology* (2000;183:SI-S22). A distinguished group of physicians, which included internists, family practitioners, and obstetricians/gynecologists, were brought together by the National Heart, Lung, and Blood Institute to reach a consensus on the management of hypertension in pregnancy. Their report reviews available information on the pathophysiology, classification, and management of hypertensive disorders in pregnancy. Opinions differ concerning the approach to this problem; the report attempts to clarify the issues.

The following are excerpts from this report. A full discussion of pathophysiology, the use of anesthesia for delivery, and other technical information, which may be of more interest to obstetricians/gynecologists than to family practitioners, internists, and cardiologists, will be found in the original report. The full report also contains more than 200 references.

Several comments in this report may be somewhat confusing to family physicians, internists, and cardiologists, who are often called upon to review the treatment of women with pre-existing hypertension who become pregnant. The 1997 Joint National Committee on Prevention, Detection, Evaluation, and Treatment of Hypertension (JNC VI) report stated, "Chronic hypertension is high blood pressure that is present and observable before pregnancy or that is diagnosed before the 20th week of gestation. The goal of treatment for women with chronic hypertension in pregnancy is to minimize the short-term risks of elevated blood pressure to the mother

while avoiding therapy that compromises the well-being of the fetus. If taken before pregnancy, diuretics and most other antihypertensive drugs, except angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers, may be continued." This seems to be a reasonable approach.

Statements from the present report suggest that medication may be stopped in patients with pre-existing hypertension and no evidence of target organ involvement, and that therapy should be restarted if blood pressures exceed 150/100–160/110 mm Hg. These levels are relatively higher in a pregnant than in a nonpregnant woman (most women maintain blood pressures of <130/80 mm Hg throughout pregnancy). Although caution should be exercised in lowering blood pressure in a pregnant woman so as not to reduce placental flow, there are many physicians who believe that therapy should be reinstituted if blood pressures rise to >140/90 mm Hg. There is little to no evidence that this approach will prevent pre-eclampsia. On the other hand, lowering blood pressures from these levels may help to prevent hypertensive complications in the mother. As noted, antihypertensive agents that were used prior to pregnancy may be used, with the exception of ACE inhibitors or angiotensin receptor blockers. It may be necessary to lower the dosage of the medication, especially during the first trimester and early second trimester, when pressures tend to be lower as a result of vasodilation. Medication should be discontinued only if blood pressures are too low. Certainly, as the report indicates, these patients should be followed carefully.

—Marvin Moser, MD
Editor in Chief

This report updates the 1990 National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy and focuses on classification, pathophysiology, and management of the hypertensive disorders of pregnancy. Using evidence-based medicine and consensus, this report updates contemporary approaches to hypertension control during pregnancy by expanding on recommendations made in the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI). The recommendations to use K5 for determining diastolic pressure and to eliminate edema as a criterion for diagnosing pre-eclampsia are discussed. In addition, the use of blood pressure increases of 30 mm Hg systolic or 15 mm Hg diastolic as a diagnostic criterion has not been recommended, as available evidence shows that women in this group are not likely to suffer increased adverse outcomes. Management considerations are made between chronic hypertension that is present before pregnancy and those occurring as part of the pregnancy-specific condition preeclampsia, as well as management considerations in women with comorbid conditions. A discussion of the pharmacologic treatment of hypertension in pregnancy includes recommendations for specific agents. The use of low-dose aspirin, calcium, or other dietary supplements in the prevention of pre-eclampsia is described, and expanded sections on counseling women for future pregnancies and recommendations for future research are included. Once again we thank Dr. Ray Gifford, Jr., and his committee for volunteering their time to produce this important report. We hope it helps the busy clinician prevent and manage a very important problem.—Claude Lenfant, MD, Director, National Heart, Lung, and Blood Institute, and Chair, National High Blood Pressure Education Program Coordinating Committee

Hypertensive disorders during pregnancy are the second leading cause, after embolism, of maternal mortality in the United States, accounting for almost 15 percent of such deaths. Hypertensive disorders occur in 6%–8% percent of pregnancies and contribute significantly to still-births and neonatal morbidity and mortality. Expectant mothers with hypertension are predisposed to the development of potentially lethal complications, notably abruptio placentae, disseminated intravascular coagulation, cerebral hemorrhage, hepatic failure, and acute

renal failure. The etiology of most cases of hypertension during pregnancy, particularly pre-eclampsia, remains unknown.

The purpose of the *National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy* is to provide guidance to practicing clinicians on managing 1) patients with hypertension who become pregnant; and 2) patients who develop hypertensive disorders during gestation. The members of the working group recognize that the responsible clinician's judgment of the individual patient's needs remains paramount. Therefore, this national guideline should serve as a tool to be adapted and implemented in individual situations. Using evidence-based medicine and consensus, the report updates contemporary approaches to hypertension control during pregnancy. This report expands and updates recommendations made in *The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI)*.

CLASSIFICATION OF THE HYPERTENSIVE DISORDERS OF PREGNANCY

The most important consideration in the classification of diseases in which blood pressure rises abnormally is differentiating hypertensive disorders that antedate pregnancy from a potentially more ominous disease peculiar to pregnancy: pre-eclampsia. Pre-eclampsia is a pregnancy-specific syndrome of reduced organ perfusion secondary to vasospasm and activation of the coagulation cascade. Although our understanding of this syndrome has increased, the criteria used to identify the disorder remain a subject of confusion and controversy. This doubtless reflects the fact that pre-eclampsia is a syndrome and that attempts at definition use arbitrarily selected markers rather than changes of pathophysiologic importance.

In chronic hypertension, elevated blood pressure is the cardinal pathophysiologic feature, whereas in pre-eclampsia, increased blood pressure is important primarily as a sign of the underlying disorder and is a potential cause of maternal morbidity. As might be expected, the impact of the two conditions on mother and fetus is different, as is their management. Attempts to differentiate the two conditions have led to confusion in terminology worldwide. We have modified the ACOG [American College of Obstetrics and Gynecology] classification slightly by adding the term "gestational hypertension" for the woman who has hypertension without proteinuria during pregnancy, reserving "transient hypertension" for a definitive diagnosis made postpartum.

*National Institutes of Health, National Heart, Lung, and Blood Institute, National High Blood Pressure Education Program, NIH Publication No. 003029
Originally printed 1990, revised July 2000*

Classification

- Chronic hypertension
- Pre-eclampsia-eclampsia
- Pre-eclampsia superimposed upon chronic hypertension
- Gestational hypertension: (1) transient hypertension of pregnancy if pre-eclampsia is not present at the time of delivery and blood pressure returns to normal by 12 weeks postpartum (a retrospective diagnosis) or (2) chronic hypertension if the elevation persists.

Chronic Hypertension

Chronic hypertension is defined as hypertension that is present and observable before pregnancy or that is diagnosed before the 20th week of gestation. Hypertension is defined as a blood pressure equal to or greater than 140 mm Hg systolic or 90 mm Hg diastolic (5th K sound disappearance). Hypertension that is diagnosed for the first time during pregnancy and that does not resolve postpartum is also classified as chronic hypertension.

Pre-eclampsia-Eclampsia

The pregnancy-specific syndrome usually occurs after 20 weeks of gestation (or earlier with trophoblastic diseases such as hydatidiform mole or hydrops). It is determined by increased blood pressure (gestational blood pressure elevation) accompanied by proteinuria. *Gestational blood pressure elevation* is defined as a blood pressure greater than 140 mm Hg systolic or 90 mm Hg diastolic in a woman normotensive before 20 weeks. In the absence of proteinuria the disease is highly suspect when increased blood pressure appears accompanied by the symptoms of headache, blurred vision, and abdominal pain, or with abnormal laboratory tests, specifically, low platelet counts and abnormal liver enzymes. In the past it has been recommended that an increment of 30 mm Hg systolic or 15 mm Hg diastolic blood pressure be used as a diagnostic criterion, even when absolute values are below 140/90 mm Hg. This definition has not been included in our criteria because the only available evidence shows that women in this group are not likely to suffer increased adverse outcomes. Nonetheless, it is the collective clinical opinion of this panel that women who have a rise of 30 mm Hg systolic or 15 mm Hg diastolic blood pressure warrant close observation, especially if proteinuria and hyperuricemia (uric acid [UA] greater than or equal to 6 mg/dL) are also present. Diastolic blood pressure is determined as the disappearance of sound (Korotkoff 5). Measuring the blood pressure successively may result in very different readings. It

is recommended that gestational blood pressure elevation be defined on the basis of at least two determinations. The repeat blood pressure should be performed in a manner that will reduce the likelihood of artifact and/or patient anxiety.

Proteinuria is defined as the urinary excretion of 0.3 g protein or greater in a 24-hour specimen. This will usually correlate with 30 mg/dL ("1+ dipstick") or greater in a random urine determination with no evidence of urinary tract infection. However, because of the discrepancy between random protein determinations and 24-hour urine protein in pre-eclampsia (which may be either higher or lower), it is recommended that the diagnosis be based on a 24-hour urine if at all possible or a timed collection corrected for creatinine excretion if this is not feasible. Pre-eclampsia always presents potential danger to mother and baby. Other conditions may increase blood pressure and even result in proteinuria; thus, as the certainty of the diagnosis increases, the requirements for careful assessment and consideration for delivery also increase. The following findings increase the certainty of the diagnosis of the pre-eclampsia syndrome and indicate such follow-up:

- Blood pressure of 160 mm Hg or more systolic, or 110 mm Hg or more diastolic.
- Proteinuria of 2.0 g or more in 24 hours (2+ or 3+ on qualitative examination). *The proteinuria should occur for the first time in pregnancy and regress after delivery.*
- Increased serum creatinine (>1.2 mg/dL unless known to be previously elevated).
- Platelet count less than 100,000 cells/mm³ and/or evidence of microangiopathic hemolytic anemia (with increased lactic acid dehydrogenase).
- Elevated hepatic enzymes (alanine aminotransferase [ALT] or aspartate aminotransferase [AST]).
- Persistent headache or other cerebral or visual disturbances.
- Persistent epigastric pain. Eclampsia is the occurrence, in a woman with pre-eclampsia, of seizures that cannot be attributed to other causes. Edema occurs in too many normal pregnant women to be discriminant and has been abandoned as a marker in this and other classification schemes.

Pre-eclampsia Superimposed upon Chronic Hypertension

There is ample evidence that pre-eclampsia may occur in women already hypertensive (i.e., who have chronic hypertension) and that the prognosis for mother and fetus is much worse than with either condition alone. Distinguishing superimposed pre-eclampsia from worsening chronic hyperten-

sion tests the skills of the clinician. For clinical management, the principle of high sensitivity and unavoidable overdiagnosis is appropriate. The suspicion of superimposed pre-eclampsia mandates close observation, with delivery indicated by the overall assessment of maternal-fetal well-being rather than any fixed end point. The diagnosis of superimposed pre-eclampsia is highly likely with the following findings:

- In women with hypertension and no proteinuria early in pregnancy (<20 weeks), new-onset proteinuria, defined as the urinary excretion of 0.3 g protein or greater in a 24-hour specimen.
- In women with hypertension and proteinuria before 20 weeks' gestation.
- Sudden increase in proteinuria.
- A sudden increase in blood pressure in a woman whose hypertension has previously been well controlled.
- Thrombocytopenia (platelet count <100,000 cells/mm³).
- An increase in ALT or AST to abnormal levels.

Gestational Hypertension

The woman who has blood pressure elevation detected for the first time after midpregnancy, without proteinuria, is classified as having gestational hypertension. This nonspecific term includes women with the pre-eclampsia syndrome who have not yet manifested proteinuria as well as women who do not have the syndrome. The hypertension may be accompanied by other signs of the syndrome, which will influence management. The final differentiation that the woman does not have the pre-eclampsia syndrome is made only postpartum. If pre-eclampsia has not developed and blood pressure has returned to normal by 12 weeks postpartum, the diagnosis of transient hypertension of pregnancy can be assigned. If blood pressure elevation persists, the woman is diagnosed as having chronic hypertension. Note that the diagnosis of gestational hypertension is used during pregnancy only until a more specific diagnosis can be assigned postpartum.

CLINICAL IMPLICATIONS OF CLASSIFICATION

The clinical spectrum of pre-eclampsia ranges from mild to severe forms. In most women, progression through this spectrum is slow, and the disorder may never proceed beyond mild pre-eclampsia. In others, the disease progresses more rapidly, changing from mild to severe in days or weeks. In the most serious cases, progression may be fulminant, with mild pre-eclampsia evolving to severe pre-

eclampsia or eclampsia within days or even hours. Thus, for clinical management, pre-eclampsia should be overdiagnosed, because a major goal in managing pre-eclampsia is the prevention of maternal and perinatal morbidity and mortality, primarily through timing of delivery.

Pre-eclampsia is a syndrome with both maternal and fetal manifestations. The maternal disease is characterized by vasospasm, activation of the coagulation system, and perturbations in many humoral and autocrine systems related to volume and blood pressure control. Oxidative stress and inflammatory-like responses may also be important in the pathophysiology of pre-eclampsia. The pathologic changes in this disorder are primarily ischemic in nature and affect the placenta, kidney, liver, and brain. Of importance, and distinguishing pre-eclampsia from chronic or gestational hypertension, is that pre-eclampsia is more than hypertension; it is a systemic syndrome, and several of its "nonhypertensive" complications can be life-threatening when blood pressure elevations are quite mild.

PATHOPHYSIOLOGY OF THE MATERNAL MANIFESTATIONS OF PRE-ECLAMPSIA

Blood Pressure in Pre-eclampsia

Women with pre-eclampsia do not usually develop frank hypertension until the second half of gestation, but vasoconstrictor influences may be present earlier. For instance, alterations in vascular reactivity may be detected by gestational week 20, and numerous surveys suggest that women destined to develop pre-eclampsia have slightly higher "normal" blood pressure (e.g., diastolic levels >70 mm Hg) as early as the second trimester, confirmed by ambulatory blood pressure monitoring techniques.

High blood pressure in pre-eclampsia is due mainly to a reversal of the vasodilation characteristic of normal pregnancy, replaced by marked increases in peripheral vascular resistance. Normally, the vasculature of normotensive gravidas manifests a decreased pressor responsiveness to several vasoactive peptides and amines, especially to angiotensin II (AII). The vessels of women with pre-eclampsia, however, become hyper-responsive to these hormones, and in the case of AII, such changes may occur months before the appearance of overt disease, although this has not been observed by all investigators. Hypertension in pre-eclampsia can be labile and may be accompanied by a blunting and even reversal of normal circadian blood pressure rhythms. Blood pressure normalizes postpartum, usually within the first few days of the puerperium, but may take as long as 2–4 weeks, especially in severe cases. The mechanisms underlying vasocon-

striction and altered vascular reactivity in pre-eclampsia remain obscure.

The Heart

The heart is usually unaffected in pre-eclampsia, the decrements in cardiac performance representing a normally contracting ventricle against a markedly increased afterload. Cardiac decompensation may complicate this disorder; however, this is most often due to the presence of pre-existing heart disease.

The Kidney

The renal lesion that is characteristic of pre-eclampsia is termed "glomerular endotheliosis." The glomeruli are enlarged and swollen but not hypercellular, due primarily to hypertrophy of the intracapillary cells (mainly endothelial but mesangial as well), which encroach on the capillary lumina, giving the appearance of a bloodless glomerulus. Both glomerular filtration rate (GFR) and renal blood flow decrease in pre-eclampsia, the former more so than the latter, leading to a decrease in filtration fraction. The decrement is usually modest (25%) even when morphological changes are pronounced. Since renal function normally rises 35%–50% during pregnancy, creatinine levels in women with pre-eclampsia may still be below the upper limits of normal for pregnancy (0.8 mg/dL). Renal insufficiency is rarely severe, but acute tubular or cortical necrosis has been linked to pre-eclampsia. Fractional urate clearance decreases, producing hyperuricemia, which is an important marker of pre-eclampsia. Proteinuria may appear late in the clinical course and tends to be nonselective. Pre-eclampsia is associated with hypocalciuria, in contrast with the increased urinary calcium excretion observed during normal pregnancy. Sodium excretion may be impaired in pre-eclampsia, although this is variable. Some of the severest forms of the disease occur in the absence of edema. Even when edema is marked, plasma volume is lower than that of normal gestation, and there is evidence of hemoconcentration, believed to be due in part to extravasation of albumin into the interstitium. In addition, central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) are often low or low normal. The reductions in intravascular volume and the lack of evidence for elevations in central pressures, along with decrements in placental perfusion, are major reasons to avoid diuretic therapy in women with pre-eclampsia.

The Coagulation System

Thrombocytopenia, rarely severe, is the most commonly found hematologic abnormality in pre-

eclampsia. Platelet counts below 100,000 cells/mm signal serious disease, and if delivery is delayed, levels may continue to fall precipitously. Although platelet counts have not been correlated with maternal hemorrhagic complications, very low platelet counts would be expected to increase the risk of bleeding. The cause of the thrombocytopenia is also unclear. It has been ascribed to platelet deposition at sites of endothelial damage and to an immunologic process. There is no firm evidence that the fetuses born to women with severe pre-eclampsia-eclampsia will develop thrombocytopenia, despite severe maternal thrombocytopenia.

The Liver

Liver damage accompanying pre-eclampsia may range from mild hepatocellular necrosis with serum enzyme abnormalities (aminotransferase and lactate dehydrogenase) to the ominous hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, with markedly elevated enzyme levels and even subcapsular bleeding or hepatic rupture. The latter syndrome represents serious disease and is associated with significant maternal morbidity.

The Central Nervous System

Eclampsia, the convulsive phase of pre-eclampsia, remains a significant cause of maternal mortality. Other central nervous system manifestations include headache and visual disturbances, including blurred vision, scotomata, and, rarely, cortical blindness. Occasionally, focal neurologic signs may develop, which should prompt radiologic investigation. The pathogenesis of eclampsia remains disputed and has been attributed both to coagulopathy and fibrin deposition, as well as hypertensive encephalopathy. The latter explanation is difficult to reconcile with the clinical observations that many women develop convulsions with only mild or moderate hypertension. However, vasoconstriction in eclampsia may be selective, and the results of studies using ultrasonographic Doppler techniques suggest that severe cerebral vasospasm may occur even when peripheral vasoconstriction is less evident.

Decisions regarding hospitalization and delivery that have significant impact on maternal and fetal health are often based on whether the patient is believed to have pre-eclampsia or a more benign form of high blood pressure, such as chronic or gestational hypertension. The correct diagnosis is important when counseling patients regarding future pregnancies.

The period in gestation when hypertension is first documented is helpful in determining the correct diagnosis. Documentation of hypertension before

conception, or before gestational week 20, favors a diagnosis of chronic hypertension (either essential or secondary). High blood pressure presenting at midpregnancy (weeks 20–28) may be due either to early pre-eclampsia (rare before 24 weeks), transient hypertension, or unrecognized chronic hypertension. Concerning the latter, blood pressure normally falls in the initial trimesters, and this “physiologic” decrement may even be exaggerated in patients with essential hypertension, masking the diagnosis in pregnancy. Hypertension may be noted later in pregnancy, however, as part of the normal third trimester rise in blood pressure or when superimposed pre-eclampsia occurs.

LABORATORY TESTS

Laboratory tests recommended to diagnose or manage hypertension in pregnancy serve primarily to distinguish pre-eclampsia from either chronic or transient hypertension. They are also useful in assessing the severity of disease, particularly in the case of pre-eclampsia, which is usually associated with laboratory abnormalities that deviate significantly from those of normal pregnant women. These same measurements are usually normal in women with uncomplicated chronic or transient hypertension. Efforts to identify an ideal screening or predictive test for pre-eclampsia have not been successful to date. Several parameters, such as midpregnancy blood pressure, ambulatory blood pressure monitoring, serum β -HCG, AII sensitivity, urinary calcium excretion, urinary kallikrein, uterine artery Doppler, plasma fibronectin, and platelet activation, have been shown to be statistically valid early markers of disease; however, they have not been demonstrated to have sufficient predictive value or practical utility for application to individual patients.

High-Risk Patients Presenting with Normal Blood Pressure

Pregnant women whose gestations are considered “high risk” for pre-eclampsia (e.g., history of increased blood pressure before conception or in a previous gestation, especially before week 34, or when the subject is multiparous; women with diabetes, collagen vascular disease, or underlying renal vascular or renal parenchymal disease; and those with a multifetal pregnancy) will benefit from a database of laboratory tests performed in early gestation. Tests that by later comparison will help establish an early diagnosis of pre-eclampsia (pure or superimposed) include hematocrit, hemoglobin, and platelet count as well as serum creatinine and uric acid levels. Observation of 1+ protein by rou-

tine urine analysis, documented by a clean-catch specimen, should be followed by a 24-hour collection for measurement of protein as well as creatinine content (to determine accuracy of collection and to permit calculation of the creatinine clearance). High-risk patients require accurate dating and assessment of fetal growth. If conditions are not optimal for clinical dating, sonographic dates should be established as early in pregnancy as possible. A baseline sonogram for evaluating fetal growth should be considered at 25–28 weeks in these circumstances.

Patients Presenting with Hypertension Before Gestation Week 20

Most women presenting with hypertension before gestation week 20 have, or will develop, essential hypertension; their management is discussed in the next section. Some may be already under the care of primary physicians and screened for secondary hypertension. Young women with pre-existing or early gestational hypertension are among the population in which secondary hypertension is more apt to be found (e.g., renal disease, renovascular hypertension, primary aldosteronism, Cushing’s syndrome, and pheochromocytoma). Thus, further evaluation with noninvasive testing may be warranted, especially when there is suspicion of those forms of secondary hypertension that are associated with more maternal and fetal complications.

The same database described above (high-risk women presenting with normal blood pressure) is helpful in determining whether further increments in pressure in the third trimester represent the “physiologic” increments or the onset of superimposed pre-eclampsia. Since these fetuses are at higher risk for the development of intrauterine growth restriction, early baseline sonography for dating and fetal size is also indicated for these patients.

Patients Presenting with Hypertension after Midpregnancy

The Table summarizes the laboratory tests that are recommended in the evaluation of women with hypertension after midpregnancy and the rationale for testing them biweekly or more often if clinical circumstances lead to hospitalization of the patient. Not only do such tests help to distinguish pre-eclampsia from chronic and transient hypertension, but they are useful in assessing disease progression and severity. It is important to recognize that in women with pre-eclampsia, one or more abnormalities may be present even when blood pressure elevation is minimal. If there is a life-threatening abnormality, such as coagulopathy or abnormal

hepatic or renal function, it may be necessary to terminate the pregnancy despite only mild hypertension.

PREPREGNANCY COUNSELING

Women with hypertension should be evaluated before pregnancy to define the severity of their hypertension and to facilitate planning for potential lifestyle changes that a pregnancy may require. As recommended in *JNC VI*, the diagnosis should be confirmed by multiple measurements and may incorporate home or other out-of-office blood pressure readings. If hypertension is confirmed and particularly if it is severe (stage 3: systolic pressure ≥ 180 mm Hg or diastolic pressure ≥ 110 mm Hg), a woman should be evaluated for potentially reversible causes. Angiotensin-converting enzyme inhibitors and AII receptor antagonists should be discontinued.

Women with a history of hypertension for several years should be evaluated for target organ damage, including left ventricular hypertrophy, retinopathy, and renal disease. If damage is present, the woman should be advised that pregnan-

cy may exacerbate the condition. Women with chronic hypertension are at higher risk for adverse neonatal outcomes independent of the development of pre-eclampsia, if proteinuria is present early in pregnancy. The risks of fetal loss and accelerated deterioration of maternal renal disease are increased if serum creatinine is above 1.4 mg/dL at conception, although it may be difficult to separate the effects of the pregnancy from progression of the underlying renal disease. In patients with impaired renal function, relative risk of fetal loss has been reported to be increased 10-fold when hypertension is present and not controlled at conception, compared with pregnancy without hypertension or with well controlled hypertension.

Chronic hypertension before pregnancy requires planning for lifestyle changes. For example, pregnant women with hypertension may need to restrict their activities at work and home and refrain from vigorous exercise. Although regular exercise is beneficial for hypertensive individuals who are not pregnant and may be safe for normotensive pregnant women, there are no data on

TABLE. LABORATORY EVALUATION AND ITS RATIONALE FOR WOMEN WHO DEVELOP HYPERTENSION AFTER MIDPREGNANCY

Test	Rationale
Hemoglobin and hematocrit	Hemoconcentration supports diagnosis of pre-eclampsia and is an indicator of severity. Values may be decreased, however, if hemolysis accompanies the disease.
Platelet count	Thrombocytopenia suggests severe pre-eclampsia.
Quantification of protein excretion	Pregnancy hypertension with proteinuria should be considered preeclampsia (pure or superimposed) until it is proved otherwise.
Serum creatinine level	Abnormal or rising serum creatinine levels, especially in association with oliguria, suggest severe pre-eclampsia.
Serum uric acid level	Increased serum uric acid levels suggest the diagnosis of pre-eclampsia.
Serum transaminase levels	Rising serum transaminase values suggest severe pre-eclampsia with hepatic involvement.
Serum albumin, lactic acid	For women with severe disease, these values indicate the extent of endothelial leak (hypoalbuminemia), presence of hemolysis (lactic acid dehydrogenase level increase, schizocytosis, spherocytosis), and possible coagulopathy, including thrombocytopenia.

safety in the setting of chronic hypertension and pregnancy. *The committee therefore recommended that hypertensive women not engage in vigorous aerobic exercise until more data are available.*

Weight reduction during pregnancy, even in obese women, is not recommended. Although obesity may be a risk factor for superimposed pre-eclampsia, there is no evidence that limiting weight gain reduces its occurrence. Although the evidence is sparse in pregnant women, many experts recommend restriction of sodium intake to the same 2.4 g sodium intake recommended for essential hypertension. Women who already follow a more restricted sodium intake may continue to follow that dietary approach.

The use of alcohol and tobacco during pregnancy should be strongly discouraged. Both have a deleterious effect on the fetus and the mother. Excessive consumption of alcohol can cause or aggravate maternal hypertension. Tobacco is associated with a substantive risk for placental abruption and fetal growth restriction.

TREATMENT OF CHRONIC HYPERTENSION

The majority of women with chronic hypertension in pregnancy have stage 1–2 hypertension (defined as systolic blood pressure of 140–179 mm Hg or diastolic blood pressure of 90–109 mm Hg) and are at low risk for cardiovascular complications within the short time frame of pregnancy. Among women with stage 1–2 preexisting essential hypertension and normal renal function, most pregnancies will have good maternal and neonatal outcomes. These women are candidates for nondrug therapy because, to date, there is no evidence that pharmacologic treatment results in improved neonatal outcomes. Since blood pressure usually falls during the first half of pregnancy, hypertension may be easier to control with less or no medication.

The value of continued administration of antihypertensive drugs to pregnant women with chronic hypertension continues to be an area of debate. Although it may be beneficial for the mother with hypertension to reduce her blood pressure, lower pressure may impair uteroplacental perfusion and thereby jeopardize fetal development. Although it is not generally agreed whether antihypertensive therapy is beneficial or detrimental to pregnancy outcome, several studies offer some clinical guidance. Over the past 30 years, at least seven studies have compared antihypertensive therapy with either no medication or a placebo in pregnant women with mild chronic hypertension. Higher fetal losses during the second trimester were noted among untreated women in several early trials, but this finding

was not confirmed. Indeed, overall prevalence rates of these adverse outcomes were very low. Rey and Couturier retrospectively evaluated the course of 298 pregnant women with chronic hypertension whose antihypertensive medications had been discontinued or whose doses were reduced early in pregnancy. Treatment did not decrease the frequency of superimposed pre-eclampsia, preterm delivery, abruptio placentae, or perinatal death when compared with untreated groups. Much uncertainty about the benefits of lowering blood pressure in pregnant women with mild chronic hypertension stems from published trials that are too small to detect modest reductions in obstetrical complications.

Most of the increased risk associated with chronic hypertension occurs in the setting of superimposed pre-eclampsia. Pre-eclampsia is more common in women with chronic hypertension and complicates almost 25% of such pregnancies. The incidence is even higher if the high blood pressure is associated with renal insufficiency, the presence of hypertension for at least 4 years, and a history of hypertension in a previous pregnancy.

On the basis of available data, some centers currently manage women with chronic hypertension by stopping antihypertensive medications under close observation. In patients with hypertension for several years, with evidence of target organ damage, or on multiple antihypertensive agents, medications may be tapered on the basis of blood pressure readings but should be continued if needed to control blood pressure. End points for reinstituting treatment include exceeding threshold blood pressure levels of 150–160 mm Hg systolic or 100–110 mm Hg diastolic or the presence of target organ damage, such as left ventricular hypertrophy or renal insufficiency. Methyldopa is preferred by most practitioners. Alternatively, women who are well controlled on antihypertensive therapy before pregnancy may be kept on the same agents (with the exception of angiotensin-converting enzyme inhibitors and AII receptor antagonists) during pregnancy.

ANTIHYPERTENSIVE DRUG SELECTION

While the goal of treating chronic hypertension is to reduce maternal risk, the agents selected must be efficacious and safe for the fetus, especially in regard to acute and long-range neurologic effects. Methyldopa is preferred by many physicians as first-line therapy, on the basis of reports of stable uteroplacental blood flow and fetal hemodynamics, and one follow-up study after 7.5 years, in a limited number of infants, showed no long-term adverse effects on development of children exposed

to methyldopa in utero. Methyldopa causes somnolence in many individuals. If this agent cannot be tolerated, alternatives such as labetalol are selected based on more limited clinical experience. If methyldopa is ineffective, alternatives can be substituted (see below) based on rational considerations of mechanisms of action. In the latter respect, salt retention may cause refractoriness to vasodilator therapy, in which case a diuretic added to the regimen restores blood pressure control and permits prolongation of the pregnancy.

β Blockers. Most of the published experience with other agents comes from trials using adrenergic-blocking drugs, including β blockers and the α-β blocker labetalol. There is a suggestion that β-blockers prescribed early in pregnancy, specifically atenolol, may be associated with growth restriction. On the other hand, none of these agents has been associated with any consistent ill effects; however, long-term follow-up studies are lacking.

Calcium Channel Blockers. Experience with calcium antagonists is limited, with most reported uses being late in pregnancy. A multicenter prospective cohort study of first trimester drug exposures reported no increase in major teratogenicity from these agents. A recent multicenter study randomizing patients to slow-release nifedipine or no treatment beginning in the second trimester reported neither benefits nor evidence of harm from nifedipine treatment.

Diuretics. The use of diuretic agents in pregnancy is controversial. The primary concern is theoretical. It is known that pre-eclampsia is associated with a reduction of plasma volume and that fetal outcome is worse in women with chronic hypertension who fail to expand plasma volume. Whether this is a cause-and-effect relationship is not clearly established. Nonetheless, women using diuretics from early pregnancy do not increase their blood volume to the degree usually occurring in normal pregnancy. Because of the theoretical concerns, diuretics are usually not used as first-line drugs. A meta-analysis of nine randomized trials involving more than 7000 subjects receiving diuretics revealed a decrease in the tendency of the women to develop edema and/or hypertension and confirmed no increased incidence of adverse fetal effects. They are safe and efficacious agents, can markedly potentiate the response to other antihypertensive agents, and are not contraindicated in pregnancy except in settings where uteroplacental perfusion is already reduced (pre-eclampsia and intrauterine growth restriction).

Although data concerning the use of diuretics in pregnant women with essential hypertension are sparse, this working group concluded that gestation does not preclude use of diuretic drugs to reduce or control blood pressure in women whose hypertension predated conception or manifested before midpregnancy.

ACE Inhibitors. Angiotensin-converting enzyme inhibitors are contraindicated during pregnancy because of associations with fetal growth restriction, oligohydramnios, neonatal renal failure, and neonatal death. Although no data are available on human use of angiotensin II receptor antagonists, adverse effects are likely to be similar to those reported with angiotensin-converting enzyme inhibitors, and these agents should be avoided.

PREGNANCY, HYPERTENSION, AND RENAL DISEASE

Among pregnant women with mild renal disease (serum creatinine less than 1.4 mg/dL), fetal survival is moderately reduced, and the underlying disease does not generally worsen. Women with renal diseases that tend to progress should be encouraged to complete their childbearing while their renal function is well preserved. The presence of hypertension before conception or early in pregnancy increases the incidence of maternal and fetal complications, with a 10-fold higher relative risk of fetal loss.

Moderate or severe renal insufficiency may accelerate during pregnancy and jeopardize fetal survival. Hypertension occurs in more than half of these pregnancies. A decrease in birthweight correlates directly with rising maternal serum creatinine concentration. As renal failure progresses, the hypertension has a component of volume overload and may require sodium restriction, use of loop diuretics, or dialysis. Recognition of superimposed pre-eclampsia may be difficult because proteinuria commonly increases in women with glomerular disease during pregnancy. Chronic dialysis during pregnancy is associated with significant maternal morbidity, and conception should be discouraged. Infant survival rates are higher in pregnancies where dialysis is started after conception (74%–80%) than in those women who conceived while on maintenance dialysis (40%–50%), presumably because the former are women with greater residual renal function. Infant survival may improve with greater duration of dialysis each week. Although low birth weight and preterm delivery are the rule, prognosis appears to be improving.

Clinical Note. Magnesium sulfate is hazardous in women with severe renal failure, and maintenance doses must be reduced. The usual loading dose can be given as this distributes to total body water and is not influenced by renal function. Then magnesium should be administered at 1 gram per hour maintenance, with therapy guided by hourly to 2-hourly magnesium levels until steady state is reached. Phenytoin may be considered as an alternative.

TREATING HYPERTENSION THAT PERSISTS POSTPARTUM

Women with chronic hypertension can develop encephalopathy, heart failure and pulmonary edema, and renal failure in the postpartum period. Risk factors include underlying cardiac disease, chronic renal disease, superimposed pre-eclampsia in the second trimester, placental abruption complicated by disseminated intravascular coagulation, and requirement for multiple antihypertensive agents. Acute hypertensive changes induced by pregnancy usually dissipate rapidly, within the first several days after delivery. Resolution of hypertension is more rapid in patients with gestational hypertension and may lag in those with pre-eclampsia, especially those with longer duration of pre-eclampsia and greater extent of renal impairment. This delay in resolution may reflect the time needed for endothelial recovery.

Oral antihypertensive agents may be required after delivery to help control maternal blood pressure, in particular, for women who were hypertensive before pregnancy. If prepregnancy blood pressures were normal or unknown, it is reasonable to stop oral medication after 3–4 weeks and observe the blood pressure at 1- to 2-week intervals for 1 month, then at 3- to 6-month intervals for 1 year. If hypertension recurs, it should be treated.

TREATING HYPERTENSION DURING LACTATION

Breast feeding should be encouraged and can be done safely with certain limits on antihypertensive drug choices. In mildly hypertensive mothers who wish to breast feed for a few months, the clinician may consider withholding medication, with close monitoring of blood pressure. After discontinuation of nursing, antihypertensive therapy can be reinstituted. For patients with more severe blood pressure elevation and taking a single antihypertensive agent, the clinician may consider reducing the dosage, then closely observing both the mother and the infant. The available data suggest that all studied antihypertensive agents are excreted into human breast milk, although differences in the milk/plasma

ratio are related to lipid solubility and extent of ionization of the drug at physiologic pH. No short-term adverse effects have been reported from exposure to methyldopa or hydralazine. Although the Committee on Drugs considers atenolol compatible with breast feeding, this β blocker, as well as metoprolol and nadolol, appears to be concentrated in breast milk. This property is not shared by propranolol or labetalol; for that reason these agents have been recommended if a β blocker is indicated. No data on calcium channel blockers and lactation have been reported. Diuretics may reduce milk volume and suppress lactation. Angiotensin-converting enzyme inhibitors and angiotensin receptor antagonists should be avoided on the basis of reports of adverse fetal and neonatal renal effects. Given the scarcity of data, breast-fed infants of mothers taking antihypertensive agents should be closely monitored for potential adverse effects.

PREVENTION OF PRE-ECLAMPSIA

The ability to prevent pre-eclampsia is limited by lack of knowledge of its underlying cause. Prevention has focused on identifying women at higher risk, followed by close clinical and laboratory monitoring to recognize the disease process in its early stages. These women can then be selected for more intensive monitoring or delivery. Although these measures do not prevent pre-eclampsia, they may be helpful for preventing some adverse maternal and fetal sequelae.

Use of Low-Dose Aspirin to Prevent Pre-eclampsia

Benefits of low-dose aspirin prophylaxis are unproven for most women, including nulliparas. The prevailing opinion is that women without risk factors do not benefit from treatment, despite earlier prospective studies that suggested that aspirin administration reduced the incidence of pre-eclampsia. The basis for this opinion is the results of eight large trials in different populations around the world.

Calcium Supplementation

There are no data indicating that dietary supplementation with calcium will prevent pre-eclampsia in low-risk women in the United States. Certainly, a diet that provides 1000 mg elemental calcium daily is recommended for general health. Whether an enriched calcium diet beyond this amount may have benefit is unproven. Randomized trials of calcium supplementation in nulliparous women considered at *high risk* demonstrated significant reductions in incidence of pre-eclampsia.

Other Dietary Supplements

Prophylactic magnesium supplementation has not been shown to be beneficial in preventing pre-eclampsia.

The results of three randomized trials of fish oil supplementation in women at high risk for pre-eclampsia revealed no reduction in incidence of pre-eclampsia. A recent study showing the benefits of vitamins C and E to prevent pre-eclampsia was encouraging but needs further confirmation.

MANAGEMENT OF PRE-ECLAMPSIA

Rationale for Treatment

The objectives of therapy for pre-eclampsia are based on a philosophy of management arising from the knowledge of the pathology, pathophysiology, and prognosis of the disorder for mother and baby. The following three important tenets underlie management schemes:

1. Delivery is always appropriate therapy for the mother but may not be so for the fetus. For maternal health, the goal of therapy is to prevent eclampsia as well as other severe complications of pre-eclampsia. These disorders are completely reversible and usually begin to abate with delivery. Thus, if only maternal well-being was considered, the delivery of all women with pre-eclampsia, regardless of the severity of pre-eclampsia or duration of gestation, would be appropriate. Conversely, delivery induction is not indicated for a preterm fetus with no evidence of fetal compromise in women with mild disease. There are two important corollaries of this statement. First, any therapy for pre-eclampsia other than delivery must have as its successful end point the reduction of perinatal morbidity and mortality. Second, the cornerstone of obstetric management of pre-eclampsia is based on whether the fetus is more likely to survive without significant neonatal complications in utero or in the nursery.
2. The pathophysiologic changes of severe pre-eclampsia indicate that poor perfusion is the major factor leading to maternal physiologic derangement and increased perinatal morbidity and mortality. Attempts to treat pre-eclampsia by natriuresis or by lowering blood pressure may exacerbate the important pathophysiologic changes.
3. The pathogenic changes of pre-eclampsia are present long before clinical diagnostic criteria are manifest. Several studies indicate that changes in vascular reactivity, plasma volume,

and renal tubular function antedate—in some cases by weeks—the increases in blood pressure, protein excretion, and sodium retention. These findings suggest that irreversible changes affecting fetal well-being may be present before the clinical diagnosis. If there is a rationale for management other than delivery, it would be to palliate the maternal condition to allow fetal maturation and cervical ripening.

NONPHARMACOLOGIC MANAGEMENT

Fetal Evaluation

Fetal surveillance is indicated for the woman with pre-eclampsia. For all women with pre-eclampsia, daily fetal movement assessment is a useful screening assessment. Further testing is indicated if movements are not normal, and should be performed periodically with even normal fetal activity. The frequency of testing will be dictated by the clinical condition. Although weekly to biweekly assessment will usually suffice, for women with severe pre-eclampsia who are being managed expectantly, daily testing is appropriate.

If possible fetal compromise is indicated by fetal surveillance, then decision-making for delivery requires judgment heavily weighted by fetal age.

Maternal Evaluation

Antepartum monitoring has two goals. The first is to recognize pre-eclampsia early; the second is to observe progression of the condition, both to prevent maternal complications by delivery and to determine whether fetal well-being can be safely monitored with the usual intermittent observations.

At present, clinical management of pre-eclampsia is directed by overt clinical signs and symptoms. Although rapid weight increase and facial edema may indicate the fluid and sodium retention of pre-eclampsia, they are neither universally present nor uniquely characteristic of pre-eclampsia.

These signs are, at most, a reason for closer monitoring of blood pressure and urinary protein. Early recognition of impending pre-eclampsia is based primarily on blood pressure increases in the late second and early third trimesters. Once blood pressure starts to rise (this may be the first sign of developing pre-eclampsia), a repeat examination within 1–3 days is recommended. In selected patients, blood pressure and urinary protein may be checked at home. In either case, the woman should be evaluated for symptoms suggestive of pre-eclampsia—headaches, blurred vision, right upper quadrant or epigastric pain—and should undergo laboratory testing for platelet count, renal function, and liver enzymes. Quantification of a 12- to

24-hour urine sample for proteinuria is recommended. These measures determine how fast the condition is progressing to ensure that it is not following a fulminant course. The frequency of subsequent observations is determined by the initial observations and the ensuing clinical progression. If the condition appears stable, weekly observations may be appropriate. The initial appearance of proteinuria is an especially important sign of progression and dictates frequent observations. 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 pre-eclampsia is diagnosed, as determined by laboratory findings, symptoms, and clinical signs, hospitalization is indicated.

Hospitalization for the duration of pregnancy is indicated for preterm onset of severe gestational hypertension or pre-eclampsia. The decision to prolong the pregnancy in these women is determined day by day. The women should receive intensive maternal and fetal surveillance, usually at a tertiary care facility. Laboratory studies are performed at frequent intervals and include serial determinations of platelet count, serum liver enzyme levels, renal function, and urinary protein. Assiduous attention is given for worsening hypertension; evidence of central nervous system involvement that includes severe headache, disorientation, or visual symptoms; and hepatic involvement indicated by epigastric pain and tenderness.

Antepartum Management of Pre-eclampsia

There is little to suggest that any therapy alters the underlying pathophysiology of pre-eclampsia. Therapeutic efforts that may be palliative, slow progression of the disorder, and permit continuation of pregnancy have not been shown to reverse the underlying disorder. Restricted activity is a usual and reasonable recommendation for women with pre-eclampsia, although its efficacy is not clearly established. Strict sodium restriction and diuretic therapy appear to have no role in management. Finally, results of several randomized trials suggest that antihypertensive therapy for women with gestational hypertension or pre-eclampsia does not improve perinatal outcomes.

Indications for Delivery

Delivery is the only definitive treatment for pre-eclampsia. All women with this diagnosis should be considered for delivery at 40 weeks' gestation. Delivery may be indicated for women with mild disease and a favorable cervix for induction at 38 weeks' gestation and should be considered in women who

have severe pre-eclampsia beyond 32–34 weeks' gestation. At gestational week 33–34, the fetus may benefit from corticosteroid administration.

Prolonged antepartum management in women with severe pre-eclampsia is possible in a select group of women with fetal gestational age between 23 and 32 weeks. Delivery in these preterm pregnancies is indicated by worsening maternal symptoms, laboratory evidence of end organ dysfunction, or fetal deterioration.

Route of Delivery

Vaginal delivery is preferable to cesarean delivery for women with pre-eclampsia, thus avoiding the added stress of surgery to multiple physiologic aberrations. The aggressive approach to induction includes a clear end point for delivery, usually within 24 hours of the decision to induce labor. Most experts recommend a trial of induction regardless of cervical condition. If vaginal delivery cannot be effected within a reasonable time, cesarean delivery is considered and is also performed for other usual obstetrical indications.

Anticonvulsive Therapy

Anticonvulsive therapy is usually indicated either to prevent recurrent convulsions in women with eclampsia or to prevent convulsions in women with pre-eclampsia. There is universal agreement that women with eclampsia should receive anticonvulsive therapy. Several randomized studies indicate that parenteral magnesium sulfate reduced the frequency of eclampsia more effectively than phenytoin in a mixed group of gestational hypertensive and preeclamptic women. Parenteral magnesium sulfate is given during labor, delivery, and for variable durations postpartum. There is not clear agreement concerning the use of prophylactic magnesium sulfate for women with pre-eclampsia.

Treatment of Acute Hypertension

Antihypertensive therapy is indicated when blood pressure is dangerously high or rises suddenly in women with pre-eclampsia, especially intrapartum. When treatment is required, the ideal drug that reduces pressures to a safe level should act quickly, reduce pressure in a controlled manner, not lower cardiac output, reverse uteroplacental vascular constriction, and result in no adverse maternal or fetal effects.

The most commonly used drug is hydralazine, administered as either intravenous (i.v.) or intramuscular (i.m.), which, if given cautiously, is successful in most instances. It has been shown to be effective against pre-eclamptic hypertension. Although this

drug is sometimes given as an intravenous infusion, the pharmacokinetics (maximal effect at 20 minutes, duration of action 6 to 8 hours) indicate intermittent bolus injections are more sensible. A 5 mg bolus is given intravenously over 1–2 minutes. After 20 minutes, subsequent doses are dictated by the initial response. Once the desired effect is obtained, the drug is repeated as necessary (frequently in several hours). Parenteral labetalol has been shown to be effective for the treatment of acute severe hypertension in pregnancy. The drug may be used as intravenous bolus injections of 20 mg or 40 mg, or as continuous intravenous infusion of 1 mg/kg as needed. Labetalol is usually used as a second-line drug. It should be avoided in women with asthma and in those with congestive heart failure.

The use of oral nifedipine has been described in a limited number of women with acute severe hypertension during pregnancy. Nifedipine acts rapidly, causing significant reduction in arterial blood pressure within 10–20 minutes of oral administration. Although it has favorable hemodynamic effects, physicians should be advised that rapidly acting nifedipine (in capsules containing the liquid form) has never been approved by the Food and Drug Administration for treating hypertension or hypertensive emergencies. The *JNC VI* has recommended that it not be used for this purpose because it has been associated with fatal and nonfatal untoward cardiovascular events, especially in older patients. Care should be exercised when using nifedipine or any calcium antagonist with magnesium sulfate. In the rare case, sodium nitroprusside may be indicated after the failure of hydralazine, nifedipine, and labetalol for acute hypertensive emergency.

Women who develop hypertension during pregnancy should be carefully re-evaluated during the immediate postpartum months and counseled with respect to future gestations and remote cardiovascular risks as well. Any laboratory abnormality or physical finding that has not returned to normal before postdelivery discharge should be reassessed at postpartum follow-up. The expectation is that hypertension and other signs or symptoms of organ dysfunction associated with pre-eclampsia will have remitted by the 6-week postpartum examination, but if abnormalities persist, the patients should be re-examined 6 weeks later, when persisting pathology will probably be chronic.

COUNSELING FOR FUTURE PREGNANCIES

Women who have had pre-eclampsia are more prone to hypertensive complications in subsequent pregnancies. Risk is best established for nulliparas

with a history of pre-eclampsia, the magnitude of the recurrence rate increasing the earlier the disease manifested during the index pregnancy. For instance, when pre-eclampsia presents clinically before gestational week 30, the recurrence rate may be as high as 40%. Pre-eclampsia reappearance rates may also be population-specific. For example, in white women with well defined disease after gestational week 36, recurrence is barely 10%, but it may be substantially greater in black patients. The recurrence rate for women with one episode of HELLP is almost 5%.

Recurrence rates are higher for those experiencing pre-eclampsia as multiparas compared with nulliparous women. Risk is also increased in multiparas who conceive with a new father even when their first pregnancy was normotensive, the incidence being intermediate between that of primiparous women and monogamous multiparous women who have not had a pre-eclamptic pregnancy.

REMOTE CARDIOVASCULAR PROGNOSIS

Pre-eclampsia-Eclampsia

The remote prognosis of women experiencing pre-eclampsia or eclampsia is best summarized as follows: The more certain the diagnosis is pre-eclampsia alone (e.g., nulliparity, especially if complicated by eclampsia or confirmed by renal biopsy), the lower the prevalence of remote cardiovascular disorders. Prevalence of remote hypertension, however, is increased in nulliparous women with pre-eclampsia or eclampsia manifesting hypertension in subsequent gestations, multiparas who develop the disorder, and women with severe early-onset disease of any parity. The literature further suggests that pre-eclampsia-eclampsia, by itself, is not a cause of essential hypertension. In essence, it is the hypertension in subsequent gestations, presence of pre-eclampsia in a multipara, or early-onset disease in any pregnancy that signals that the disease has occurred in a patient with an increased probability of essential hypertension later in life.

In summary, it is reasonable to counsel patients as follows: If pre-eclampsia occurred late in an initial gestation, there is no evidence of remote cardiovascular risk, but subsequent pregnancies will help us define risk more accurately. Women with early-onset disease, multiparous women with pre-eclampsia or only hypertension, and those manifesting gestational hypertension in any pregnancy are at increased cardiovascular risk—information of importance for long-term health care strategies. The best news, however, is that women experiencing normotensive births have a reduced risk for remote hypertension.

A complete listing of references and tables can be found in the full report, in The American Journal of Obstetrics and Gynecology 2000;183:S1–S22.

Appendix: The National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy.

Ray W. Gifford, Jr., MD, Chair Emeritus, Department of Nephrology and Hypertension, Cleveland Clinic Foundation, Cleveland, OH, Fountain Hills, AZ; Phyllis A. August, MD, Professor of Medicine, Obstetrics and Gynecology, Chief, Hypertension Division, Weill Medical College of Cornell University, New York Presbyterian Hospital, New York, NY; Gary Cunningham, MD, Professor and Chair, Department of Obstetrics and Gynecology, University of Texas Southwestern Medical Center, Dallas, TX; Lee A. Green, MD, MPH, Associate Professor and Assistant Chair, Department of Family Medicine, University of Michigan, Ann Arbor, MI; Marshall D. Lindheimer, MD, Professor of Medicine, Obstetrics and Gynecology, and Clinical Pharmacology, University of Chicago, Chicago, IL; Donald McNellis, MD, Special Assistant for Obstetrics Pregnancy and Perinatology Branch, Center for Research for Mothers and Children, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD; James M. Roberts, MD, Professor and Vice Chair (Research), Department of Obstetrics and Gynecology and Reproductive Sciences, University of Pittsburgh, Elsie Hilliard Hillman Chair in Women's and Infants' Health Research, Director, Magee-Women's Research Institute, Vice President for Research, Magee-Women's Hospital, Pittsburgh, PA; Edward J. Roccella, PhD, MPH, Coordinator, National High Blood Pressure Education Program, Office of Prevention, Education, and Control, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD; Baha M. Sibai, MD, FACOG, Professor and Chair, Department of Obstetrics and Gynecology, University of Cincinnati, Cincinnati, OH; Sandra J. Taler, MD, Assistant Professor of Medicine, Consultant, Division of Hypertension and Internal Medicine, Mayo Clinic, Rochester, MN.