Chronic hypertension in pregnancy is defined by the American College of Obstetrics and Gynecology (ACOG) as blood pressure ≥140 mmHg systolic and/or 90 mmHg diastolic before pregnancy or, in recognition that many women seek medical care only once pregnant, before 20 weeks of gestation, use of antihypertensive medications before pregnancy, or persistence of hypertension for >12 weeks after delivery. Chronic hypertension needs to be distinguished from new-onset hypertensive complications of pregnancy such as preeclampsia (elevated blood pressure and proteinuria often accompanied by evidence of maternal organ injury and fetal compromise from placental dysfunction) and gestational hypertension (elevated blood pressure alone after 20 weeks of gestation and most commonly in the mid to late third trimester without evidence or history of hypertension before pregnancy; Table 1).

Epidemiology
Chronic hypertension is estimated to be present in 3% to 5% of pregnancies and is increasingly more commonly encountered. Factors contributing to the increase in prevalence include 2 major risk factors for hypertension, obesity and older age, which are of increasing prevalence in pregnancy. These shifts in risk and childbearing have resulted in an increased number of women who will require counseling on the risks of chronic hypertension in pregnancy and management of their antihypertensive medications both in anticipation of and during pregnancy. Because many pregnancies are unplanned, all women with chronic hypertension should receive regular counseling so that they can anticipate any issues that may arise if they become pregnant and optimize their health and care to temper risk. Because blacks have a higher prevalence of chronic hypertension and onset occurs at younger ages, it is more common to encounter chronic hypertension in blacks during pregnancy. Despite its increasing prevalence, the majority of women with chronic hypertension do well in pregnancy, but as we discuss below, some women develop complications such as superimposed preeclampsia, fetal growth restriction, placental abruption, preterm birth, and cesarean section (Table 2). As part of family planning before conception, they should be counseled about these risks and the anticipated need for surveillance and management of any incident complications during pregnancy.

Physiological Changes in Blood Pressure During Pregnancy
Women who are normotensive entering pregnancy typically experience a decrease in blood pressure toward the end of the first trimester. This decrease is thought to be secondary to the marked vasodilatation that occurs despite the increase in plasma volume that comes with pregnancy. Blood pressure usually falls by 5 to 10 mmHg and remains at this lower level throughout pregnancy until the third trimester, when it rises to return to preconceptional values. For the majority of women with chronic hypertension, blood pressure changes also follow this same pattern. As a result, some hypertensive women become normotensive during pregnancy, and others who remain hypertensive can have their antihypertensive medications tapered. These physiological changes may confuse the diagnosis of chronic hypertension when a woman presents for prenatal care or the first time in the second trimester once the physiological decrease has occurred and is now normotensive. In such cases, the increase to preconceptional values in the third trimester may suggest gestational hypertension. It may not be until elevated blood pressures persist beyond 12 weeks postpartum that, in retrospect, the correct diagnosis of chronic hypertension is recognized.

Pregnancy Complications in Women With Chronic Hypertension
Although many women with chronic hypertension do well in pregnancy, they are at increased risk for several pregnancy complications, including superimposed preeclampsia, fetal growth restriction, placental abruption, preterm birth, and cesarean section (Table 2). As part of family planning before conception, they should be counseled about these risks and the anticipated need for surveillance and management of any incident complications during pregnancy.

Preeclampsia
The most prevalent complication in pregnancy in women with chronic hypertension is the development of preeclampsia. In the general population, the risk of preeclampsia is 3% to 5%, yet among women with chronic hypertension, 17% to 25% develop superimposed preeclampsia. In a study of 763 women with chronic hypertension that reported a 25% rate of superimposed preeclampsia, rates were higher in women with >4-year duration of hypertension and with diastolic blood pressures of 100 to 110 mmHg compared with <100 mmHg. In a more recent study of 822 women with chronic hypertension enrolled in a trial of antioxidants for the prevention of preeclampsia, the risk of superimposed preeclampsia was 22%. Of note, 44% of this 22% developed superimposed...
Table 1. Classification of Hypertension in Pregnancy

<table>
<thead>
<tr>
<th>Classification</th>
<th>Criteria Met</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>After 20 wk of gestation, SBP ≥140 mm Hg or DBP ≥90 mm Hg in a previously normotensive woman</td>
</tr>
<tr>
<td></td>
<td>Proteinuria (excretion of ≥0.3 g protein in a 24-h urine collection) or with other systemic manifestations</td>
</tr>
<tr>
<td>Gestational hypertension</td>
<td>Elevated BP (SBP ≥140 mm Hg or DBP ≥90 mm Hg) after 20 wk of gestation in a previously normotensive woman</td>
</tr>
<tr>
<td>Chronic hypertension</td>
<td>SBP ≥140 mm Hg and/or DBP ≥90 mm Hg before pregnancy or before 20 wk of gestation</td>
</tr>
<tr>
<td>Chronic hypertension with superimposed preeclampsia</td>
<td>New onset of proteinuria in the setting of hypertension before 20 wk of gestation</td>
</tr>
<tr>
<td></td>
<td>An increase in proteinuria (if present earlier)</td>
</tr>
<tr>
<td></td>
<td>An increase in blood pressure</td>
</tr>
<tr>
<td></td>
<td>Onset of HELLP syndrome</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; DBP, diastolic blood pressure; HELLP, hemolysis, elevated liver enzymes, low platelets; and SBP, systolic blood pressure.

Preeclampsia before 34 weeks of gestation, a rate that stands in contrast to patterns seen in women without chronic hypertension, who more commonly develop preeclampsia closer to term.13 Preeclampsia is more commonly observed in blacks than whites, but whether this is due to the greater prevalence of underlying chronic hypertension in blacks or to a greater underlying propensity for preeclampsia is controversial.14,15 Preeclampsia is a major contributor to preterm birth and cesarean delivery in women with chronic hypertension because of its association with induced early delivery, placental abruption, and fetal growth abnormalities.10,13 Accordingly, women with chronic hypertension with superimposed preeclampsia have worse birth outcomes than women with chronic hypertension without superimposed preeclampsia.12,16

It can be challenging to diagnose preeclampsia in women with chronic hypertension because their blood pressures are already elevated and proteinuria may be present before pregnancy. In this population, superimposed preeclampsia should be considered if blood pressure increases in pregnancy and especially if there is new-onset proteinuria or worsening of prepregnancy proteinuria. Laboratory abnormalities (thrombocytopenia, elevated liver function tests, and increasing serum creatinine) will also often distinguish preeclampsia from worsening of underlying hypertension.

Because preeclampsia is managed differently from worsening chronic hypertension, it is important to distinguish these 2 entities. There is a continuing search for improved tests to both predict and diagnose preeclampsia. Chief among the candidate tests studied are angiogenic markers, including soluble fms-like tyrosine kinase 1 (sFlt-1) and placental growth factor. A post hoc analysis of blood collected as part of a study examining the utility of calcium supplementation to prevent recurrent preeclampsia demonstrated higher levels of sFlt-1 and reduced levels of placental growth factor in those women who developed preeclampsia compared with those who did not. sFlt-1, for example, was reported to be elevated as early as the second trimester in women who went on to develop preeclampsia.17 From these and other supportive results,18,19 sFlt-1 was proposed as a potential predictive marker for the development of preeclampsia. However, in a prospective study that excluded women with chronic hypertension, sFlt-1 measured in the first trimester had a poor positive predictive value (<10%) for the development of preeclampsia.20 On the basis of current data, these markers are not recommended for clinical use at this time.1 It is possible that future work and analyses may show that, although these markers do not appear to be useful in a general population, they may function more effectively as predictors of preeclampsia among a group whose risk for primary or recurrent preeclampsia is chronic hypertension.

Fetal Growth Restriction

American, Canadian, and New Zealand population data demonstrate a 10% to 20% prevalence of fetal growth restriction, defined as absolute or estimated weight less than the 10th percentile for gestational age–based population norms, in pregnancies in women with chronic hypertension.4,9,10 A similar association remained even after adjustment for age, body mass index, smoking, parity, and diabetes mellitus in an analysis of the Danish National Birth Cohort. In that analysis, “definite chronic hypertension” was associated with a 5.5- and 1.5-fold risk for preterm and term small-for-gestational-age birth, respectively (95% confidence intervals [CIs], 3.2–9.4 and 1.0–2.2).21 A more recent analysis using growth curves customized for fetal sex and maternal height, weight, parity, and ethnicity suggests that the risk may be higher, 41% and 21% among women with and without superimposed preeclampsia, respectively.13

Placental Abruption

Because fetal growth abnormalities are often thought of as manifestations of placental dysfunction,22 it is interesting to note that placental abruption—premature separation of the placenta from the underlying myometrium resulting in pain, bleeding, and, potentially, clinical significant interruption of fetal gas and nutrient exchange—is more common in women with chronic hypertension. National Center for Health Statistics data from 1995 to 2002 demonstrated that women with chronic hypertension had a frequency of placental abruption of 1.56% compared with 0.58% in nonhypertensive women (adjusted relative risk, 2.4; 95% CI, 2.3–2.5).23 In the Sibai et al12 study of women with chronic hypertension mentioned above, the overall rate of abruption was 1.5%, with higher rates in those with superimposed preeclampsia (3%) than those without (1%). A more recent analysis of a large Swedish birth registry found rates of abruption of 1.1% versus 0.4% when women with and without chronic hypertension, respectively, were compared.24

Table 2. Complications of Chronic Hypertension in Pregnancy

<table>
<thead>
<tr>
<th>Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superimposed preeclampsia</td>
</tr>
<tr>
<td>Fetal growth restriction</td>
</tr>
<tr>
<td>Placental abruption</td>
</tr>
<tr>
<td>Preterm birth</td>
</tr>
<tr>
<td>Caesarian section</td>
</tr>
</tbody>
</table>
Preterm Birth and Cesarean Delivery

The individual pregnancy complications discussed above contribute to an increased risk for preterm delivery among women with chronic hypertension because, faced with such problems, early delivery may be judged as unavoidable, necessary, or better than continued expectant management. Rates of preterm delivery range from 12% to 34% among all women with chronic hypertension but as high as 62% to 70% in women with severe hypertension, defined as 2 blood pressure readings \( \geq 170/110 \) mm Hg measured at least 24 hours apart. These rates contrast with a preterm delivery rate of 10% to 12% for the US population as a whole. An Israeli study noted odds ratios for preterm delivery of 1.89 and 3.23 for treated and untreated chronic hypertension, respectively, with 22.9% of those in the group who received a prescription for antihypertensives (treated group) delivering at <37 weeks of gestation compared with just 8% of the control group with no diagnosis of chronic hypertension. Such early deliveries are often the result of the decisions patients make with their obstetric providers when worsening maternal or fetal health argues for induction at an early gestational age. Prematurity certainly contributes to the recognized increased risk of perinatal mortality among pregnancies in women with chronic hypertension. Zetterström and colleagues conducted an analysis of >800,000 Swedish birth records, including those in 4749 women with chronic hypertension, and reported an odds ratio of 2.71 (95% CI, 1.96–3.73) for intrauterine demise (stillbirth) and an odds ratio of 2.89 (95% CI, 1.95–4.83) for neonatal death among the group with chronic hypertension. Importantly, this risk appears to be independent of but may be augmented by the development of superimposed preeclampsia.\(^{27}\) These rates contrast with a preterm delivery rate of 10% to 12% for the US population as a whole. An Israeli study noted odds ratios for preterm delivery of 1.89 and 3.23 for treated and untreated chronic hypertension, respectively, with 22.9% of those in the group who received a prescription for antihypertensives (treated group) delivering at <37 weeks of gestation compared with just 8% of the control group with no diagnosis of chronic hypertension. Such early deliveries are often the result of the decisions patients make with their obstetric providers when worsening maternal or fetal health argues for induction at an early gestational age. Prematurity certainly contributes to the recognized increased risk of perinatal mortality among pregnancies in women with chronic hypertension. Zetterström and colleagues conducted an analysis of >800,000 Swedish birth records, including those in 4749 women with chronic hypertension, and reported an odds ratio of 2.71 (95% CI, 1.96–3.73) for intrauterine demise (stillbirth) and an odds ratio of 2.89 (95% CI, 1.95–4.83) for neonatal death among the group with chronic hypertension. Importantly, this risk appears to be independent of but may be augmented by the development of superimposed preeclampsia.\(^{27}\) Such early deliveries are often the result of the decisions patients make with their obstetric providers when worsening maternal or fetal health argues for induction at an early gestational age. Prematurity certainly contributes to the recognized increased risk of perinatal mortality among pregnancies in women with chronic hypertension. Zetterström and colleagues conducted an analysis of >800,000 Swedish birth records, including those in 4749 women with chronic hypertension, and reported an odds ratio of 2.71 (95% CI, 1.96–3.73) for intrauterine demise (stillbirth) and an odds ratio of 2.89 (95% CI, 1.95–4.83) for neonatal death among the group with chronic hypertension. Importantly, this risk appears to be independent of but may be augmented by the development of superimposed preeclampsia.\(^{27}\)

**Management of the Woman With Chronic Hypertension**

**Prepregnancy Care**

Prenatal care of women with chronic hypertension should begin before pregnancy to provide counseling about the pregnancy risks discussed above and to optimize antihypertensive regimens before conception. The majority of women who enter pregnancy with chronic hypertension have hypertension of unknown origin. Evaluation for secondary causes of hypertension should follow recommendations of the Seventh Report of the Joint National Commission\(^ {8}\) and, when indicated, should occur before pregnancy because such evaluation may involve radiation exposure or require surgical intervention. Women with chronic hypertension should also be evaluated as indicated according to Seventh Report of the Joint National Commission for end-organ damage before pregnancy because end-organ damage may affect pregnancy outcomes or help stratify the risk of developing specific obstetric complications. A 24-hour urine collection for protein determination before pregnancy may assist in the diagnosis of superimposed preeclampsia and provides prognostic information because women with prepregnancy proteinuria have an increased risk for fetal growth restriction.\(^ {11}\) Finally, as discussed below, antihypertensive agents may need to be changed to another class before conception.

**Lifestyle Modification**

Lifestyle modifications such as sodium restriction, weight reduction, and implementation of the Dietary Attempts to Stop Hypertension (DASH) diet\(^ {29}\) have been demonstrated to improve blood pressure control in many nonpregnant individuals. Given the need for volume expansion in pregnancy, strict sodium restriction in hypertensive women planning pregnancy is of concern, and new dietary sodium restriction is not recommended by the Canadian guidelines. However, both weight reduction and the DASH diet are reasonable to recommend for such women. ACOG recommends weight reduction in overweight/obese women with hypertension before pregnancy. Whether such recommendations implemented before pregnancy, however prudent, result in improved pregnancy outcomes among hypertensive women is unknown, however, and needs to be studied.

**Management During Pregnancy**

**Blood Pressure Goals in Pregnancy**

Studies suggest that the primary benefit of antihypertensive treatment of hypertension pregnancy is the reduction of maternal morbidity by limiting episodes of severe hypertension.\(^ {32}\) Antihypertensive treatment has not been shown to reduce superimposed preeclampsia, placental abruption, or growth restriction or to improve neonatal outcome.\(^ {32}\) There is concern that overly aggressive antihypertensive treatment may decrease fetoplacental perfusion and increase the risk for fetal growth restriction. A large meta-analysis, for example, suggests that treatment of hypertension in pregnancy may be associated with increased fetal growth restriction.\(^ {33}\) As a result, blood pressure goals are higher during pregnancy than they are outside of pregnancy, and medication dosages may need to be adjusted downward, particularly in the second trimester when pregnancy-associated nadirs of blood pressure are typically encountered. The exact goal ranges for blood pressures during pregnancy in women with chronic hypertension are not established because, at this point, there are no randomized studies to support one goal over another. As a result, blood pressure goals for pregnancy for women with chronic hypertension are often not specified in guidelines or differ among guidelines. ACOG recommends that blood pressures in women with uncomplicated hypertension be maintained between 120/80 and 160/105 mm Hg.\(^ {3}\) The Society of Obstetricians and Gynaecologists of Canada clinical practice guidelines target systolic blood pressure of 130 to 155 mm Hg and diastolic blood pressure of 80 to 105 mm Hg in women without comorbid conditions and systolic blood pressure of 130 to 139 mm Hg and diastolic blood pressure of 80 to 89 mm Hg in women with comorbid conditions (such as type 1 diabetes mellitus). Some experts recommend stopping antihypertensives
during pregnancy, as long as pressures fall below these thresholds. For women with chronic hypertension who enter pregnancy not on antihypertensive treatment, ACOG recommends initiating antihypertensive treatment when blood pressures are consistently >160 mm Hg systolic and/or >105 mm Hg diastolic.\(^1\) The Society of Obstetric Medicine of Australia and New Zealand guidelines indicate a definitive recommendation for antihypertensive treatment when blood pressure is ≥160 mm Hg systolic or ≥100 mm Hg diastolic and that treatment of blood pressure between 140 and 159 mm Hg systolic or 90 and 99 mm Hg diastolic is common practice with good outcomes.\(^2\) Thus, there is variability in goal range for blood pressure in pregnancy. When blood pressures fall below these ranges, there is a recommendation to taper the antihypertensive and eventually to stop the antihypertensive if blood pressure remains within the goal range. There are no evidence-based regimens for tapering antihypertensive medications in pregnancy. Thus, the tapering regimen needs to take into consideration factors related to the particular medication used, dose, and timing in pregnancy (ie, keeping in mind the physiological decrease in blood pressure at the end of the first trimester.) We recommend tapering antihypertensives when blood pressures consistently fall below 130/80 mm Hg, a threshold consistent with Canadian guidelines.\(^3\)

As indicated above, prospective studies randomizing women to different levels of blood pressure and pregnancy outcomes are lacking. The Control of Hypertension in Pregnancy Study (CHIPS; NCT01192412) is ongoing and randomizing women to “less tight” (target diastolic blood pressure, 100 mm Hg) or “tight” (target diastolic blood pressure, 85 mm Hg) control and will determine maternal, fetal, and neonatal outcomes of the different goals. Results from CHIPS are not available at this time; study completion is anticipated in 2014.

### Antihypertensive Medications

The Food and Drug Administration provides classification of medications in pregnancy\(^4\) based on the level of the data available to support safety (Table 3). Because of a lack of randomized, controlled studies, no antihypertensives are categorized as “class A: controlled human studies have demonstrated no fetal risk.” Instead, commonly used antihypertensives in pregnancy are classified as class B (α-methyldopa or labetalol), class C (labetalol, β-blockers, calcium channel blocker, and thiazide diuretics), class D (angiotensin-converting enzyme inhibitors (ACEIs) are considered class C in the first trimester and class D in the second and third trimesters. In contrast to nonpregnant individuals with hypertension for whom good data exist, there are no randomized trials to guide how race and other comorbidities should influence the choice of antihypertensive therapy during pregnancy.

Commonly used antihypertensive agents in pregnancy and their class are depicted in Table 4. Of note, there is a lack of randomized, placebo-controlled trials of antihypertensives in pregnancy looking at the important maternal and fetal/neonatal outcomes. As a result, many of the data on antihypertensive use in pregnancy are from reviews and meta-analyses of small, retrospective studies. The majority of studies compare 1 antihypertensive with no treatment, so comparative efficacy and safety data to guide choices between alternative antihypertensives are generally absent. Even among those studies that compare agents head to head, allocation was generally not blinded, raising concerns for possible biases in and confounding of the data. α-Methyldopa is considered a first-line\(^5\) or co-first-line drug\(^6\) by many guideline groups on the basis of pregnancies exposed to α-methyldopa noted no adverse developmental effects up to 7.5 years of age.\(^7\) However, α-methyldopa may not be well tolerated by women because of the common side effect of somnolence.

The combined α- and β-blocker labetalol is often recommended as an alternative first-line\(^8\) or second-line agent\(^9\) for the treatment of hypertension in pregnancy. Labetalol compared with α-methyldopa or no treatment was studied in a population of 300 women with chronic hypertension. Both labetalol and α-methyldopa effectively lowered blood pressure. Exposure to labetalol (n=86) or α-methyldopa (n=88) compared with no antihypertensive (n=90) was associated with no increased risk of congenital malformations, but neither were there any differences in risk for superimposed preeclampsia, placental abruption, or preterm delivery compared with no antihypertensive treatment.\(^10\) β-Blockers are used less commonly in pregnancy because of concerns about fetal growth restriction raised in retrospective studies examining the outcomes of pregnancies in which atenolol was used.\(^11\) Some organizations recommend that atenolol be avoided in pregnancy.

Data are sparse for the use of calcium channel blockers in pregnancy to control blood pressure (as opposed to short-term use for the treatment of preterm contractions/preterm labor), and most data are available for long-acting nifedipine. In a prospective study in which a mixed population of 283 women with chronic hypertension or new-onset hypertension during pregnancy (diastolic blood pressure, 90–110 mm Hg) were randomized to long-acting nifedipine versus no medication at 12 to 34 weeks of pregnancy, there were no differences among the pregnancy outcomes of preterm delivery, caesarean section, or birth weight.\(^12\) A study of nifedipine use in the first trimester does not suggest an increase in major birth defects.\(^13\) Although there has been theoretical concern that calcium

<table>
<thead>
<tr>
<th>Table 3. FDA Classification of Drugs in Pregnancy(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Category A:</strong> controlled studies in pregnant women have demonstrated no risk of fetal abnormalities.</td>
</tr>
<tr>
<td><strong>Category B:</strong> reproduction studies in animal indicate no fetal risk, but there are no adequate and well-controlled studies in pregnant women; or animal reproduction studies have shown an adverse effect of the drug but not in well-controlled studies in pregnant women.</td>
</tr>
<tr>
<td><strong>Category C:</strong> animal reproduction studies have shown an adverse effect of the drug but no adequate human or animal studies; or animal reproduction studies have not been conducted and it is not known whether the drug can cause fetal harm when administered to a pregnant woman.</td>
</tr>
<tr>
<td><strong>Category D:</strong> evidence of human fetal risk, but benefits outweigh risks. Women taking this drug during pregnancy should be informed of potential fetal risk.</td>
</tr>
<tr>
<td><strong>Category X:</strong> evidence of human fetal risk. Drug is contraindicated in women who are pregnant or who may become pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.</td>
</tr>
</tbody>
</table>

\(^4\) FDA indicates Food and Drug Administration.
Table 4. Antihypertensive Therapies Commonly Used in Pregnancy*

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dose Range</th>
<th>FDA Classification</th>
<th>Potential Side Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-Methyldopa</td>
<td>Often used as first line</td>
<td>250 mg–1.5 g orally twice a day</td>
<td>B</td>
<td>Lethargy</td>
<td>Data on offspring up to 7.5 y of age demonstrating long-term safety</td>
</tr>
<tr>
<td>Labetalol</td>
<td>Often used as first line</td>
<td>100–1200 mg orally twice a day</td>
<td>C</td>
<td>Exacerbation of asthma</td>
<td>Widely used in pregnancy</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Second line or alternative first line (nifedipine)</td>
<td>Varies according to drug used</td>
<td>C</td>
<td>Concern for synergy with magnesium sulfate for neuromuscular depression</td>
<td></td>
</tr>
<tr>
<td>β-Blockers</td>
<td>Second line</td>
<td>Varies according to drug used</td>
<td>C</td>
<td>Exacerbation of asthma</td>
<td>Some recommend avoiding atenolol during pregnancy and lactation</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>Second line</td>
<td>12.5–50 mg orally once a day</td>
<td>C</td>
<td>Volume depletion and hypokalemia</td>
<td></td>
</tr>
</tbody>
</table>

FDA indicates Food and Drug Administration.

*Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are contraindicated in the second and third trimesters of pregnancy and are class D.

Safety in the first trimester is controversial; in this trimester, they are class C.

channel blockers could be synergistic with magnesium sulfate (used to prevent eclampsia in women with a diagnosis of preeclampsia), leading to neuromuscular depression, this concern was not borne out in a large retrospective study.41

The use of thiazide diuretics in the first trimester of pregnancy has not been associated with increased risk of major birth defects.42 However, because volume expansion is characteristic of healthy pregnancies, there has been long-standing concern about potential diuretic-related volume depletion. However, data do not support this concern,43 and continuing the use of diuretics in women with chronic hypertension is supported by some.1

Maternal exposure to ACEIs in the second and third trimesters has clearly been associated with adverse pregnancy outcomes, including impaired fetal renal function resulting in oligohydramnios, growth abnormalities, skull hypoplasia, and fetal death, as well as neonatal anuria and neonatal death.54,45 Similar fetal effects have been reported with exposure to angiotensin receptor blockers in the second half of pregnancy.56–58

The use of ACEIs in early pregnancy was previously thought to be safe, but a 2006 study raised the issue of a potential increase in fetal cardiovascular and central nervous system anomalies from such use and exposure. In that retrospective study, the risk ratio for birth defects among 209 infants exposed to ACEIs in the first trimester compared with those exposed to other antihypertensives was 4.04 (95% CI, 1.89–7.30) for cardiovascular defects and 5.45 (95% CI, 1.69–17.64) for central nervous system defects.5 Because this report was retrospective, differences between groups other than treatment class, including maternal body mass index, might explain the results. A subsequent study did not confirm these findings but instead suggested that the association of ACEIs with congenital malformation was confounded by the underlying diagnosis of hypertension and not explained by class of antihypertensive.59 Because of the clear contraindication of ACEIs/angiotensin receptor blockers in the second and third trimesters, the difficulty in dating pregnancies, and the large number of women who do not present for prenatal care until the second trimester, many caregivers avoid ACEIs and angiotensin receptor blockers in women planning to conceive or in women of childbearing age altogether, given that 50% of pregnancies are unplanned.

Lifestyle Modification for Blood Pressure Control During Pregnancy

Limiting weight gain is advisable in obese and overweight women during pregnancy, according to the Institute of Medicine.60 Whether limiting weight gain in chronic hypertensive women will lead to improved pregnancy outcomes, in particular lowered risk of superimposed preeclampsia, is not known, with data showing no benefit to limiting weight gain in nonhypertensive women.21 Whether implementing or continuing the DASH diet during pregnancy improves outcomes in women with chronic hypertension is also unknown and should be studied. Dietary sodium restriction during pregnancy has raised concerns that it would limit the volume expansion characteristic of normal pregnancy. Sodium restriction implemented after the first 12 weeks of pregnancy does not appear to be harmful in normotensive women, but there are no data to support that sodium restriction limits the occurrence of preeclampsia.64 ACOG recommends against the use of very low salt diets (<100 mEq/dy) to manage chronic hypertension in pregnancy.1

Acute Management of Severe Hypertension in Pregnancy

Because of concern for maternal morbidity, including cerebrovascular accidents, when blood pressure rises to severely elevated levels (≥160 mm Hg systolic or ≥110 mm Hg diastolic), intravenous antihypertensive medications are often used to promptly lower pressures below these thresholds. The majority of experience with the use of intravenous antihypertensive use in pregnancy is derived from their use in cases of severe preeclampsia.55,56 Commonly used intravenous antihypertensive agents in pregnancy include labetalol and hydralazine. A Cochrane review did not demonstrate superiority of one of these over the other or over other antihypertensive medications in the acute management of severe hypertension in pregnancy.54

Prevention of Preeclampsia

For women with chronic hypertension, superimposed preeclampsia is the major adverse pregnancy outcome; however, there currently are no effective preventive measures to decrease this risk. Large, randomized, placebo-controlled
studies have demonstrated that the use of calcium supplementation, low-dose aspirin, or antioxidant supplementation with vitamin C and E does not decrease the risk for preeclampsia.

**Surveillance of Fetal Well-Being**

More frequent prenatal visits are recommended for pregnant women with chronic hypertension compared with healthy women. Such visits are designed to evaluate women for complications of chronic hypertension in pregnancy by following blood pressures, urine protein, fundal height, and maternal symptoms. Because these pregnancies are more likely to be complicated by growth abnormalities, ACOG indicates that “evaluation of fetal growth by ultrasound in women with chronic hypertension is warranted.” In practice, most undertake surveillance for fetal growth restriction with ultrasounds beginning in the third trimester and spaced at 2- to 4-week intervals, depending on maternal blood pressure, medications, complications, and findings on prior scans. With the recognition of the association between chronic hypertension and stillbirth, fetal testing is often recommended, although some restrict such testing to those pregnancies with complications such as growth restriction or preeclampsia. However, ACOG states that there is “no consensus on the most appropriate fetal surveillance test(s) or the interval and timing of testing in women with chronic hypertension.” Although no single protocol is of demonstrated superior utility, testing often includes daily fetal kick counts, fetal heart rate testing (nonstress testing), and ultrasound evaluation of amniotic fluid volume or fetal movements and tone (biophysical profile). The particular tests chosen, the frequency of testing, and the time for initiating surveillance are often based on individual patient characteristics, including degree and duration of hypertension, use of antihypertensives, evidence of underlying maternal organ compromise related to hypertension, suspicion for fetal growth restriction, and presence of pregnancy complications such as preeclampsia.

**Timing of Delivery in Women With Chronic Hypertension**

Because of the risks associated with chronic hypertension, delivery is often planned near the estimated due date, although the need for such intervention, if testing and growth are reassuring, is uncertain. A 2011 Eunice Kennedy Shriver National Institute of Child Health and Human Development and the Society for Maternal-Fetal Medicine workshop, Timing of Indicated Late Preterm and Early Term Deliveries, indicated that for chronic hypertension requiring no medications, delivery was recommended at 38 to 39 weeks of gestation. In contrast, for women with chronic hypertension on medications and for women whose hypertension was difficult to control, defined as requiring frequent medication adjustment, this expert group recommended delivery at 37 to 39 and 36 to 37 weeks of gestation, respectively. For cases in which there was superimposed preeclampsia, delivery was recommended at 37 weeks of gestation or earlier if markers of severe preeclampsia were present.

**Breast-Feeding**

Given the benefits of breast-feeding, women with chronic hypertension, including those on antihypertensive medications, should be encouraged to breast-feed. Although most antihypertensives are measurable in breast milk, levels are generally lower than in maternal plasma. From these data and observational data, the American Academy of Pediatrics has labeled most antihypertensives, including ACEIs, as usually compatible with breast-feeding. Higher breast milk levels and case reports of lethargy and bradycardia in newborns breast-fed by mothers on atenolol led the American Academy of Pediatrics to recommend that atenolol be used with caution. In addition, on the basis of the higher degree of excretion of atenolol into breast milk, the Drugs and Lactation Database of the National Library of Medicine indicates that agents other than atenolol may be preferable for newborns, preterm infants, and babies of mothers on high doses. The American Society of Hypertension recommends against the use of diuretics during breast-feeding because of the concern that they may decrease breast milk production.

**Summary**

Although the majority of women with chronic hypertension have healthy pregnancy outcomes, pregnancies among such women have increased risk of superimposed preeclampsia, fetal growth restriction, early delivery, and caesarian section. Women should be counseled about these risks before pregnancy and followed up for the potential development of these complications during pregnancy. Blood pressure goals are higher in pregnant compared with nonpregnant women because of the concern of adversely affecting fetoplacental perfusion with too large a decrease in maternal blood pressure. Therefore, during pregnancy, antihypertensive therapy can be tapered in many women. Labetalol and α-methyldopa are considered first-line therapies for those women who require medications during pregnancy. ACEIs and angiotensin receptor blockers are contraindicated for use in the second and third trimesters of pregnancy because of adverse effects of the fetus, and there is controversy over whether ACEIs are safe in the first trimester. Randomized studies comparing various antihypertensives for the management of chronic hypertension in pregnancy are limited, and as a result, the ideal range for blood pressure to optimize the health of the mother, fetus, and neonate remains unknown. It is important that these studies be undertaken and funded.

Thus, pregnancy in women with chronic hypertension needs to be carefully planned and managed. In our view, such care is best undertaken by comanagement among obstetricians, internists, and other medical specialists. It is our experience that such coordinated care will optimize pregnancy outcomes and the health of women with chronic hypertension during their reproductive years.

**Disclosures**

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**References**


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