OBG MANAGEMENT

Controlling chronic hypertension in pregnancy

How to identify women at highest risk, and select treatment during pregnancy and after delivery

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One unhappy effect of the obesity epidemic and the increasing age of women at childbirth is the rising prevalence of chronic hypertension, which climbed from 4.6% to 22.3% in women aged 30 to 39 years, and from 0.6% to 2.0% in women aged 18 to 29 years, according to the National Health and Nutrition Examination Survey for 1988–1991. These trends are expected to continue, and so are the rates of chronic hypertension in pregnancy, with its increased possibility of superimposed preeclampsia.

This article outlines diagnosis and management, including:

- how to tell when drug therapy is needed
- how to detect superimposed preeclampsia
- when to discontinue drug regimens
- which drugs and doses should be used during pregnancy and after delivery.

When is hypertension "chronic"?

Hypertension is *chronic* if the elevated blood pressure was documented before pregnancy. If prepregnancy blood pressure is unknown, the patient is thought to have chronic hypertension if it is consistently elevated before 20 weeks of gestation.

Blood pressure is *elevated* if systolic pressure is at least 140 mm Hg or diastolic pressure is at least 90 mm Hg. These blood pressure ranges should be documented on at least 2 occasions at least 4 hours apart.[1]

Diagnosis may be difficult in women with previously undiagnosed chronic hypertension who begin prenatal care after 16 weeks' gestation, because a physiologic decrease in blood pressure usually begins at that time. These women are more likely to be erroneously diagnosed as having gestational hypertension.[2]

Chronic hypertension is *primary* (essential) in approximately 80% to 90% of cases, and, in 10% to 20% of cases, *secondary* to collagen vascular disease, or renal, endocrine, or vascular disorders.

Outside of pregnancy, hypertension is categorized into 3 stages: prehypertension, stage 1 hypertension, and stage 2 hypertension.[3]

Mild vs severe, low-risk vs high-risk

During pregnancy, chronic hypertension is classified according to its severity, depending on the systolic and diastolic blood pressures. Systolic pressures of at least 160 mm Hg and/or diastolic pressures of at least 110 mm Hg constitute severe hypertension (Korotkoff phase V). The diagnosis requires documented evidence of hypertension before pregnancy and/or before 20 weeks' gestation.

Korotkoff phase V readings are more precise. This phase occurs when the sound disap-

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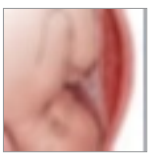


TABLE 1

Low- and high-risk criteria

LOW RISK	HIGH RISK
Uncomplicated essential hypertension	Secondary hypertension
	Target organ damage*
No previous perinatal loss	Previous perinatal loss
Systolic pressure <160 mm Hg and diastolic pressure <110 mm Hg	Maternal age >40 years
	Systolic pressure ≥160 mm Hg or diastolic pressure ≥110 mm Hg

*Left ventricular dysfunction, retinopathy, dyslipidemia, microvascular disease, or stroke.

***FAST** TRACK*

Use blood pressure at the initial visit to classify risk as low or high

pears, as opposed to phase IV, in which the sound is muffled. Phase V is more accurate because it correlates with actual intra-arterial pressure. Moreover, phase IV cannot be recorded in at least 10% of gravidas because of hemodynamic changes of pregnancy.

Low vs high risk. For management and counseling purposes, chronic hypertension in pregnancy also is classified as low- or high-risk (**TABLE 1**). A gravida has a low risk when she has mild essential hypertension without any organ involvement.

Blood pressure criteria are based on measurements at the initial visit regardless of whether the patient is taking antihypertensive drugs. For example, if the patient has blood pressure of 140/80 mm Hg and is taking antihypertensive agents, she is nevertheless classified as low-risk. Her medications are discontinued, and blood pressure is monitored very closely. If readings reach severe levels, she is then classified as high-risk and managed as such.

Risk classification may change. A woman initially classified as low-risk early in pregnancy may become high-risk if preeclampsia or severe hypertension develops.

Risk factors for preeclampsia

Pregnancies complicated by chronic hypertension carry a heightened risk of superimposed preeclampsia, which is associated with high rates of adverse maternal and perinatal outcomes.[4] Sibai and colleagues[4] documented the rate of superimposed preeclampsia among 763 women with chronic hypertension who were followed prospectively at several medical centers in the United States. The overall rate of superimposed preeclampsia was 25%. **Specific characteristics** affected the risk of preeclampsia: age, previous preeclampsia, duration of hypertension, diastolic blood pressure, thrombophilia, diabetes, proteinuria, multifetal gestation, and use of assisted reproductive technology (**TABLE 2**).

Diagnostic criteria

In women with hypertension only, superimposed preeclampsia is diagnosed when there is proteinuria of at least 500 mg in 24 hours or thrombocytopenia or abnormal liver enzymes (**TABLE 3**).

In women with hypertension and proteinuria (renal disease or class F diabetes), new onset of persistent symptoms (severe headache, visual changes) and/or thrombocytopenia, and/or elevated liver enzymes makes the diagnosis of preeclampsia.

Risk of abruption and other complications

Gravidas with chronic hypertension also have an increased risk for abruptio placentae.

In addition, women with high-risk chronic hypertension are at increased risk for life-threatening maternal complications such as pulmonary edema, hypertensive encephalopathy, retinopathy, cerebral hemorrhage, and acute renal failure.[5] These risks are particularly acute in women with uncontrolled severe hypertension, renal dysfunction early in pregnancy, or left ventricular dysfunction prior to conception. The risk of these and other complications increases further when superimposed preeclampsia develops (**TABLE 4**).

Fetal and neonatal complications in women with chronic hypertension are 3 to 4 times more likely than in the general obstetric population.[1] These complications include

premature delivery and small-for-gestational-age infants (**TABLE 5**).

Benefits vs risks of drug treatment

Although long-term blood pressure control greatly reduces stroke, cardiovascular morbidity, and mortality in nonpregnant persons,[3] hypertension in pregnancy is different because the duration of therapy is shorter. In people with mild to moderate hypertension, the benefit is achieved after at least 5 years of treatment.[2] In pregnancy, the benefits to the mother may not be obvious during the short time of treatment, and exposure to drugs includes both mother and fetus.[6] Thus, in pregnancy, one must balance the potential short-term maternal benefits against possible short- and long-term benefits and risks to the fetus and infant.[1,5,6]

Low-risk: No benefit

We lack compelling evidence that short-term antihypertensive therapy is beneficial in these women except for a reduction in the exacerbation of hypertension.[5,7]

High-risk: Drug therapy is needed

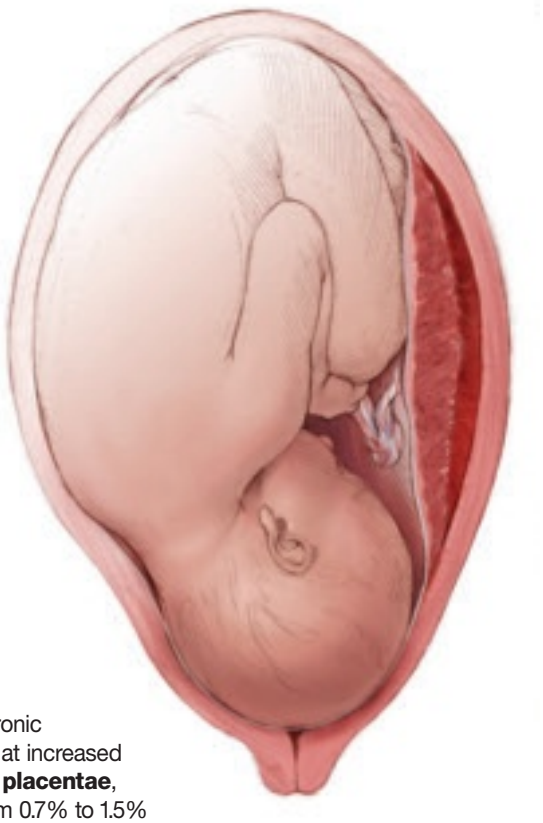
We lack placebo-controlled trials of antihypertensive therapy in gravidas with severe hypertension, and none are likely to be performed because of the potential risks of untreated severe hypertension.

In these women, drug therapy reduces the acute risk of stroke, congestive heart failure, and renal failure.[2] Control of severe hypertension may also prolong the pregnancy and thereby improve perinatal outcome. However, there is no evidence that control of severe hypertension reduces the rates of superimposed preeclampsia or abruptio placentae.[2,4,5]

Adverse effects

The potential adverse effects of the most commonly prescribed antihypertensive agents are poorly established or unclearly quantified.[1] In general, we have limited and selective information about teratogenicity except in laboratory animals, and minimal data on the benefits and risks of most antihypertensive drugs when used during pregnancy. Nevertheless, the limited data available suggest that some drugs carry the potential for adverse fetal effects and should be avoided (**TABLE 6**).

Chronic hypertension heightens risk of placental abruption



Gravidas with chronic hypertension are at increased risk for **abruptio placentae**, which ranges from 0.7% to 1.5% in women with mild chronic hypertension, and from 5% to 10% in women with severe or high-risk hypertension. The rate increases to 30% with superimposed preeclampsia.

IMAGE: KIMBERLY MARTENS

Drug treatment of comorbidities

According to data from clinical trials in nonpregnant subjects, selected comorbidities can be treated as follows:

- **Ischemic heart disease.** Beta-blockers

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are the first line of treatment, particularly labetalol. Alternatively, calcium-channel blockers can be used.

- **Heart failure.** In asymptomatic gravidas, beta-blockers should be used. In symptomatic gravidas, both beta-blockers and diuretics are recommended.
- **Diabetes.** Two or more drugs are usually needed to control blood pressure in this population. Although angiotensin-converting enzyme (ACE) inhibitors have a beneficial effect outside of pregnancy, calcium-channel blockers and diuretics are safer for gravidas.
- **Chronic kidney disease** warrants aggressive management, typically with 3 or more medications. Again, while ACE inhibitors have a favorable effect outside of pregnancy, calcium-channel blockers, beta-blockers, and diuretics are better choices.

ACE inhibitors are contraindicated in pregnancy due to the risk of oligohydramnios, renal dysplasia, pulmonary hypoplasia, and intrauterine growth restriction.[8]

TABLE 2

Characteristics that affect risk of preeclampsia

CHARACTERISTIC	PREECLAMPSIA (%)
Age (yr)	
≤35	26
>35	25
Previous preeclampsia	
Yes	32
No	23
Duration of hypertension	
<4 years	23
≥4 years	32
Diastolic blood pressure (mm Hg)	
<100	24
100–109	25
≥110	40–50
Thrombophilia	40–50
Diabetes mellitus	30–40
Proteinuria	
No	25
Yes	27

Note: Risk is also increased in women with multifetal gestation and in those who have conceived using assisted reproductive technology.
Source: Sibai BM, et al[4]

Management goals

The primary objectives in managing chronic hypertension in pregnancy are to reduce maternal risks and achieve optimal perinatal survival. These objectives call for a rational approach that includes:

- preconception education and counseling,
- early antenatal care,
- frequent antepartum visits to monitor both mother and fetus,
- timely delivery with intensive intrapartum monitoring, and
- proper postpartum care.

Ideally, management should begin prior to pregnancy, with extensive evaluation and a complete workup to assess the cause and severity of the hypertension, determine whether other medical illnesses are present, and rule out target organ damage associated with longstanding hypertension (**TABLE 7**).

Low-risk hypertension

Stop drugs at first visit

Women with low-risk chronic hypertension without superimposed preeclampsia usually have pregnancy outcomes similar to those in the general obstetric population.[2,5,9]

Discontinuation of antihypertensive therapy early in pregnancy does not increase the rates of preeclampsia, abruptio placentae, and preterm delivery in these women.[2,9]

Our policy is to discontinue antihypertensive treatment in low-risk women at the first prenatal visit, because most of these women have good outcomes without such therapy.

Follow-up strategy

During subsequent visits, we educate the patient about nutritional requirements,

***FAST** TRACK*

We discontinue antihypertensive drugs in women at low risk, because outcomes are good without therapy

TABLE 3

Diagnosis of preeclampsia in women with preexisting conditions

PREEXISTING CONDITION	PREECLAMPSIA IS PRESENT IF SHE HAS…
Hypertension	Proteinuria ≥500 mg/24 hours or thrombocytopenia or abnormal liver enzymes
Proteinuria	New onset hypertension plus symptoms and/or thrombocytopenia or elevated liver enzymes
Hypertension plus proteinuria (renal disease or class F diabetes)	New onset of persistent symptoms (severe headache, visual changes) or thrombocytopenia or elevated liver enzymes

TABLE 4

Complication rates in women with superimposed preeclampsia vs women without hypertension*

COMPLICATION	WITHOUT HYPERTENSION (PER 1,000 CASES)	PREECLAMPSIA SUPERIMPOSED ON CHRONIC HYPERTENSION (PER 1,000 CASES)
Abruptio placentae	9.6	30.6
Thrombocytopenia	1.6	11.5
Disseminated intravascular coagulation	2.9	17.4
Pulmonary edema	0.2	6.4
Blood transfusion	1.5	16.3
Mechanical ventilation	0.2	17.0

*US women, 1988–1997
Source: Zhang J, et al[15]

weight gain, and sodium intake (maximum of 2.4 g sodium per day). We also remind them that alcohol use and smoking during pregnancy can aggravate maternal hypertension and cause adverse effects in the fetus such as fetal growth restriction and abruptio placentae.

During the remainder of the pregnancy, we observe the gravida very closely for appropriate fetal growth and early signs of preeclampsia.

Fetal evaluation should include an ultrasound examination at 16 to 20 weeks' gestation, to be repeated at 32 to 34 weeks and monthly thereafter until term. In addition, all women with low-risk hypertension should undergo growth scans starting at 32 to 34 weeks, especially obese women in whom fundal height measurements are unreliable, because of the increased risk of intrauterine growth restriction.

If severe hypertension develops before term, start either nifedipine or labetalol (**TABLE 6**).

Immediate fetal testing with the nonstress test or biophysical profile is necessary if severe hypertension, preeclampsia, abnormal fetal growth, or evidence of oligohydramnios develops.

Hospitalization and delivery are necessary if severe hypertension, fetal growth restriction documented by ultrasound, or superimposed preeclampsia develops at or beyond 37 weeks.

If none of these complications is present, pregnancy can continue until 40 weeks' gestation.[5]

High-risk hypertension

The frequency and nature of maternal-fetal adverse effects depends on the cause of the hypertension and the extent of target organ damage.

Realistic preconception counseling

Women with substantial renal insufficiency (ie, serum creatinine >1.4 mg/dL), diabetes with vascular involvement (class R/F), severe collagen vascular disease, cardiomyopathy, or coarctation of the aorta should be advised that the pregnancy might exacerbate their condition. These patients should be made aware of the potential for congestive heart failure, acute renal failure requiring dialysis, and even death. In addition, perinatal loss and neonatal complications are markedly increased in these women.

Refer or consult a specialist

All women with severe hypertension should be managed in consultation with a subspecialist in maternal-fetal medicine, as well as any other specialists who may be indicated.

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TABLE 5

Adverse pregnancy outcomes in women with mild chronic hypertension

OBSERVATIONAL STUDY	PREECLAMPSIA (%)	ABRUPTIO PLACENTAE (%)	DELIVERY AT <37 WEEKS (%)	SMALL FOR GESTATIONAL AGE (%)
Sibai et al[2] (n=211)	10.0	1.4	12.0	8.0
Rey and Couturier[16] (n=337)	21.0	0.7	34.4	15.5
McCowan et al[17] (n=142)	14.0	Not reported	16.0	11.0
Sibai et al[4] (n=763)	25.0	1.5	33.3	11.1
August et al[18] (n=110)	34.0	Not reported	Not reported	8.0

They also should be observed and delivered at a tertiary care center with adequate maternal-neonatal care facilities.[5]

Management strategy

Our policy is to hospitalize women with high-risk hypertension at the time of the first prenatal visit to evaluate their cardiovascular and renal status and regulate antihypertensive medications, as well as other prescribed drugs (eg, insulin, cardiac drugs, thyroid drugs). Women receiving atenolol, ACE inhibitors, or angiotensin II receptor antagonists should have these medications discontinued under close observation.

In women without target organ damage, the aim of antihypertensive therapy is to keep systolic pressure between 140 and 150 mm Hg and diastolic pressure between 90 and 100 mm Hg.

In women with target organ damage and mild hypertension, antihypertensive therapy is also indicated, because there are short-term maternal benefits to lowering blood pressure. We recommend keeping systolic pressure below 140 mm Hg and diastolic pressure below 90 mm Hg.

Early, frequent visits. Women with high-risk chronic hypertension need close observation throughout pregnancy and may require serial evaluation of 24-hour urine protein excretion and a complete blood count with a metabolic profile at least once every trimester. Further laboratory testing depends on the clinical progress of the pregnancy. At each visit, remind the woman about the adverse effects of smoking and alcohol use, and counsel her about the importance of diet and minimal salt intake.[5]

Fetal surveillance includes ultrasound, growth scans, and nonstress testing (**TABLE 8**).

Hospitalization is warranted if uncontrolled severe hypertension, preeclampsia, or evidence of fetal growth restriction develops, so that more frequent evaluation of maternal and fetal well-being can be performed.

Delivery is indicated if any of these complications develop at or beyond 34 weeks' gestation. If there are none of these complications, consider delivery at 36 to 37 weeks after documenting fetal lung maturity.[5]

Postpartum care

Women with high-risk chronic hypertension are at risk for postpartum complications such as pulmonary edema, hypertensive encephalopathy, and renal failure.[10,11] These risks are heightened in women with target organ involvement, superimposed preeclampsia, or abruptio placentae.[10]

Blood pressure must be closely controlled for at least 48 hours after delivery. Intravenous labetalol or hydralazine can be used as needed, and diuretics may be appropriate in women with circulatory congestion and pulmonary edema.[12] Oral

FAST TRACK

We hospitalize women with high-risk hypertension at the first visit, to evaluate cardiovascular and renal status and regulate medications

TABLE 6

Acute and long-term drug treatment

DRUG	STARTING DOSE	MAXIMUM DOSE	COMMENTS
ACUTE TREATMENT OF SEVERE HYPERTENSION			
Hydralazine	5–10 mg IV every 20 min	30 mg*	
Labetalol	20–40 mg IV every 10–15 min	220 mg*	Avoid in women with asthma or congestive heart failure
Nifedipine	10–20 mg orally every 30 min	50 mg*	
LONG-TERM TREATMENT OF HYPERTENSION			
Methyldopa	250 mg BID	4 g/day	Rarely indicated
Labetalol	100 mg BID	2,400 mg/day	First choice
Atenolol	50 mg/day	100 mg/day	Associated with intrauterine growth restriction
Propanolol	40 mg BID	640 mg/day	Use with associated thyroid disease
Hydralazine	10 mg TID	100 mg/day	Use in cases of left ventricular hypertrophy
Nifedipine	10 mg BID	120 mg/day	Use in women with diabetes
Diltiazem	120–180 mg/day	540 mg/day	
Thiazide diuretic	12.5 mg BID	50 mg/day	Use in salt-sensitive hypertension and/or congestive heart failure May be added as second agent Avoid if preeclampsia develops or intrauterine growth restriction is present
Angiotensin-converting enzyme inhibitors and **angiotensin receptor blockers**	—	—	Do not use after 16–18 weeks

*If desired blood pressure levels are not achieved, switch to another drug.

***FAST** TRACK*

Methyldopa is a reasonable first-line oral antihypertensive for breastfeeding women

therapy may be needed to control blood pressure after delivery. In some women, it may be necessary to switch to a new agent such as an ACE inhibitor, particularly in women who had pregestational diabetes or cardiomyopathy.

All antihypertensive drugs are found in breast milk, although differences in the milk-to-plasma ratio do occur. The long-term effects of maternal antihypertensive drugs on breastfeeding infants has not been studied. However, methyldopa appears to be a reasonable first-line oral therapy (if it is contraindicated, use labetalol). Milk concentrations of methyldopa appear to be low and are considered safe. Beta-blockers (atenolol and metoprolol) are concentrated in breast milk, whereas labetalol or propanolol have low concentrations.[13,14] Concentrations of diuretics in breast milk are low, but may diminish milk production.[13] Little is known about the transfer of calcium-channel blockers to

breast milk, but there are no apparent side effects. ACE inhibitors and angiotensin II receptor antagonists should be avoided because of their effects on neonatal renal function, even though their concentrations in breast milk appear to be low. ■

TABLE 7

How to evaluate gravidas with chronic hypertension

POPULATION	RECOMMENDED TESTS
All	• Urinalysis, urine culture and sensitivity • 24-hour urine evaluations for protein • Electrolytes • Complete blood count • Glucose tolerance test
Gravidas with longstanding hypertension, poor compliance, or poor control	• Electrocardiogram • Echocardiography • Ophthalmologic evaluation • Creatinine clearance

TABLE 8

Recommended antenatal testing

LEVEL OF RISK	TEST
Low (uncomplicated)	• Ultrasound at 16–18 weeks to confirm gestational age/anatomy scan • Ultrasound for fetal growth and fluid starting at 32–34 weeks • Growth scan 37–38 weeks • Nonstress testing weekly starting at 34 weeks • Biophysical profile if nonstress test is nonreactive
High (complicated)	• Ultrasound at 16–18 weeks to confirm gestational age/anatomy scan • Start testing at 26–28 weeks with nonstress testing 1–2 times/week • Biophysical profile if nonstress test is nonreactive • Serial testing as needed

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