Hypertension Before, During, and After Pregnancy

This FAQ addresses questions about treating hypertension before, during, and after pregnancy.

Question	Answer/Pertinent Information
Which **antihypertensive meds should be avoided** in patients planning to become pregnant, those at risk of an unplanned pregnancy, or those who are pregnant?	• The RAAS plays a role in the development of the fetal kidney and other organs.[16,22] Medications that affect the RAAS are generally not recommended to be used during pregnancy.[21] **Antihypertensives not recommended during pregnancy include**: o **ACEIs** and **ARBs** ▪ ACEI or ARB use in the second and third trimesters has been associated with fetal demise, preterm birth, skull defects, lung dysplasia, and limb deformities, possibly due to oligohydramnios.[16,22,24] ▪ Cardiovascular malformations have been reported, even with first trimester exposure, perhaps due to inhibition of angiogenesis.[22] o **direct renin inhibitors** (aliskiren [*Tekturna*, generic, US; *Rasilez*, Canada]) ▪ Human data (from ACEI and ARBs) suggest risk with use of aliskiren in second and third trimesters.[10] o **aldosterone antagonists** (e.g., spironolactone, eplerenone [*Inspra*, generics]) • There is limited human data with these agents, but animal data suggest risk with spironolactone.[10,14] o Spironolactone has anti-androgen effects and has demonstrated feminization in male animal fetuses.[10]
BEFORE pregnancy: About 50% of all pregnancies are unplanned.[4] Exposure to meds prior to two weeks post-conception (i.e., before patients even know they are pregnant) usually has an all-or-none impact, meaning either no impact on the embryo or there is loss of the pregnancy.[5] For patients with hypertension planning to become pregnant or are at risk of an unplanned pregnancy, it is important to plan ahead, use effective contraception, or use antihypertensives with the most acceptable safety profile in pregnancy.	
Which **contraceptive** is the best choice for patients with chronic hypertension?	• Generally, for patients of childbearing potential with chronic hypertension: o Nonhormonal options (e.g., copper IUD) are safe.[1] o The levonorgestrel IUD, implant, and progestin-only pill are safe options if BP is <160 mm Hg/100 mm Hg and can be used with caution in other patients.[1] o Depot medroxyprogesterone acetate can be used with caution provided that BP is <160 mm Hg/100 mm Hg. o Reserve estrogen-containing contraceptives for healthy patients ≤35 years of age with well-controlled BP in whom safer options have been tried.
Which **antihypertensives are preferred** for patients planning to become pregnant or at risk of an unplanned pregnancy?	• Antihypertensives considered to have the most acceptable safety profile in pregnancy include (see section below for more about their use during pregnancy):[10,21] o labetalol (human data suggest low risk). o long-acting nifedipine (human data suggest low risk). o methyldopa (compatible with pregnancy, but less effective and tolerable).

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Question	Answer/Pertinent Information
DURING pregnancy: Hypertension during pregnancy has been associated with poor fetal growth, preterm birth, need for neonatal intensive care, and fetal death.[21] The use of antihypertensives reduces the risk of progression to severe hypertension by about 50%, but **has not been shown to prevent preeclampsia, preterm birth, or infant mortality**.[15] As with most medications in pregnancy, antihypertensives have not been evaluated in robust, randomized, controlled trials and much of the data available are limited and conflicting. Caution is warranted during pregnancy, weighing the risks of uncontrolled hypertension against the risks of antihypertensives.	
What are the different **definitions for hypertension disorders** during pregnancy?	• **Hypertension in pregnancy**: SBP ≥140 mm Hg, DBP ≥90 mm Hg, or both measured on two occasions at least four hours apart (average of at least two measurements taken at least 15 minutes apart [Canada]).[2,21] o chronic hypertension: diagnosed **before pregnancy or before 20 weeks' gestation**. o gestational hypertension: diagnosed **after 20 weeks' gestation**. o severe hypertension: SBP ≥160 mm Hg, DBP ≥110 mm Hg, or both. • **Preeclampsia** (can lead to premature birth): gestational hypertension AND one of the following: o proteinuria: ≥300 mg per 24-hour urine (either measured or extrapolated from a timed collection).[2,20] o protein/creatinine ratio: ≥0.3 mg/dL (26.5 umol/L).[20] o urine protein dipstick reading of 2+ (should only be used if other quantitative methods are not able to be used).[20] **OR without proteinuria** with gestational hypertension and development of ≥1 target organ complication:[2,20] o thrombocytopenia (platelet count <100,000/mm^3).[20] o impaired kidney function (serum creatinine >1.1 mg/dL [97.2 umol/L] or doubling in the absence of other kidney disease).[20] o impaired liver function (liver transaminases at least twice the upper limit of normal).[20] o pulmonary edema.[20] o new onset headache not responding to meds and not attributed to another diagnosis or visual symptoms.[20] • **Eclampsia**: Convulsive expression of hypertension in pregnancy displayed as new onset seizures (tonic-clonic, focal, or multifocal) in the absence of other causes (e.g., epilepsy, cerebral ischemia, intracranial hemorrhage).[20] • **H**emolysis **E**levated **L**iver enzymes and **L**ow **P**latelets (HELLP syndrome): Syndrome involves damaged or destroyed red blood cells, impaired blood clotting, and possible bleeding in the liver, causing chest or abdominal pain. HELLP syndrome is a medical emergency. Management of HELLP syndrome is beyond the scope of this document.
What hypertension-related symptoms should pregnant patients watch for?	• Chronic hypertension and gestational hypertension can both progress to preeclampsia or eclampsia.[2,21] • Signs and symptoms of preeclampsia include swelling (especially in face and hands), severe headaches, vision changes, severe upper abdominal pain, nausea or vomiting, or shortness of breath.[25] o Pregnant patients should alert their obstetrician right away or go to an emergency room if they develop severe headaches, blurred vision or other visual disturbance, severe abdominal pain, or significant shortness of breath.[25]

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Question	Answer/Pertinent Information
During pregnancy, continued	
How should a patient with **chronic hypertension** be treated if she becomes pregnant?	• Patients who become pregnant while taking an ACEI, ARB, aliskiren, spironolactone, or eplerenone should be switched to an antihypertensive compatible with pregnancy.[11,19,21] • Based on the results of the CHAP trial [Evidence Level B-1], the Society for Maternal-Fetal Medicine and the American College of Obstetrics and Gynecology recommend that patients with mild chronic hypertension (BP 140/90 mm Hg to <160/105 mm Hg) should be treated, or have their current antihypertensive titrated, at a threshold of 140/90 mm Hg.[11,13] o Treatment reduces the risk of maternal and perinatal morbidity without increasing the risk of SGA.[11] • Hypertension Canada and the Society of Obstetricians and Gynaecologists of Canada recommend: o Treating SBP ≥140 mm Hg or DBP ≥90 mm Hg with a target DBP of 85 mm Hg [Evidence Level B-1].[2,19] ▪ Recommendations are based in part on data suggesting a target DBP of 85 mm Hg (compared to a target DBP of 100 mm Hg) decreases the progression to severe hypertension, which may lower the risk of pregnancy loss, high-level neonatal care, preterm birth, or low-birth weight.[2,18]
Which **antihypertensive medications** are used to treat chronic hypertension during pregnancy?	• **Labetalol**[2,19,21] o Some beta-blockers have been reported to impair fetal growth.[10] Labetalol does not affect uteroplacental blood flow, possibly because it has both alpha- and beta-blocking activity.[10] ▪ Other beta-blockers that can be considered include pindolol, acebutolol, metoprolol, and propranolol.[2,19] ▪ Avoid atenolol. Human data suggest risk with atenolol in the second and third trimesters due to risk of fetal growth restriction.[10] • **Long-acting nifedipine**[2,19,21] o Use during pregnancy is not linked to significant adverse outcomes in infants.[10] o Less data are available with amlodipine, verapamil, and diltiazem during pregnancy.[10] • **Methyldopa** has a long history of safety in pregnancy. May be less effective compared to labetalol and long-acting nifedipine.[21] o Use of methyldopa during pregnancy may be limited by adverse reactions (e.g., sedation, dizziness).[21] • **Thiazides** are a second-line or third-line option.[2,19,21] o Thiazides do not appear to be teratogenic.[10] o There is a theoretical concern for fetal growth restriction or oligohydramnios due to intravascular volume depletion.[21] ▪ Volume depletion occurs mostly during the first two weeks of treatment, then gradually returns toward baseline due to compensatory mechanisms.[27] o Some experts suggest continuing thiazides if they were started prior to pregnancy.[26] • Hypertension Canada also considers **clonidine** and **hydralazine** second-line options.[2]

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Question	Answer/Pertinent Information
During pregnancy, continued	
How should a patient with **gestational hypertension or preeclampsia** be managed?	• Avoid approaching gestational hypertension with a lower level of concern compared to concern with preeclampsia. BOTH gestational hypertension and preeclampsia are associated with negative outcomes. In fact, gestational hypertension may not truly be a separate entity from preeclampsia.[20] • Use proper technique and equipment to ensure accurate BP measurements.[20] Keep in mind that cuff size may change as pregnancy progresses. • American College of Obstetricians and Gynecologists recommends:[20] o Weekly (or more frequently if progression is a concern) monitoring for patients with gestational hypertension or preeclampsia should include assessment of symptoms (e.g., abdominal pain, edema, headaches, vision changes, shortness of breath) BP (office measurement), platelet count, serum creatinine, and liver enzymes. Assess for proteinuria weekly in patients with gestational hypertension to assess for preeclampsia. ▪ In addition to office BP checks (at least weekly) patients may also monitor BP at home. o Outpatient management may be appropriate for patients with BP readings <160/110 mm Hg or preeclampsia WITHOUT severe features (e.g., severe headache, vision changes, abdominal pain, shortness of breath, abnormal labs), as long as patients are willing and able to adhere to frequent monitoring. o Inpatient management is needed for patients with BP >160/110 mm Hg or WITH severe features (e.g., severe headache, vision changes, abdominal pain, shortness of breath, abnormal labs) and for patients in whom adherence to frequent monitoring is a concern. • Hypertension Canada and the Society of Obstetricians and Gynaecologists of Canada recommend: o Treat SBP ≥140 mm Hg or DBP ≥90 mm Hg with a target DBP of 85 mm Hg [Evidence Level B-1] for patients with gestational hypertension (can consider target DBP of 85 mm Hg for patients with preeclampsia).[2,19] • For patients with gestational hypertension, medications may need to be continued postpartum.[19] o Gestational hypertension usually resolves by about six weeks to three months after delivery.[19] o If the gestational hypertension or preeclampsia was severe, it may take up to six to 12 months to resolve postpartum.[19]

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Question	Answer/Pertinent Information
During pregnancy, continued	
How should a pregnant patient with **severe hypertension** (chronic or gestational hypertension) be managed?	• Treat acute, persistent (≥15 minutes) SBP ≥160 mm Hg or DBP ≥110 mm Hg urgently (e.g., start antihypertensive within 30 to 60 minutes) to prevent congestive heart failure, myocardial ischemia, kidney damage, and stroke.[2,9,20] • Treatment options include IV labetalol (onset 1 to 2 minutes), IV hydralazine (onset 10 to 20 minutes), and short-acting PO nifedipine (onset 5 to 10 minutes).[20] o For patients already taking an antihypertensive, choose an agent from a different class.[19] o Patients who do not respond to the initial choice may respond to one of the others.[19] o Dosing algorithms are available from the American College of Obstetricians and Gynecologists at https://www.acog.org/community/districts-and-sections/district-ii/programs-and-resources/safe-motherhood-initiative/severe-hypertension. o Guidelines from the Society of Obstetricians and Gynaecologists of Canada also suggest PO labetalol 200 mg every hour x 3 as an option.[19] PO methyldopa has a delayed onset, and may require the addition of another agent.[19] • Transition meds from IV to PO for continued control.[20] Example regimen: start labetalol 200 mg PO every 12 hours. Titrate up to labetalol 800 mg PO every 8 to 12 hours for control (max dose: 2,400 mg/day).[20] Short-acting nifedipine (note: is tocolytic[8]) can be added if labetalol isn't enough or labetalol side effects limit use.[20]
When should **aspirin** be used in pregnant patients?	• Avoid aspirin in patients with a history of aspirin allergy (e.g., urticaria), hypersensitivity to salicylates or NSAIDs, nasal polyps, or asthma WITH a history of aspirin-induced broncospasm.[23] • Start low-dose aspirin (81 mg/day) in most **patients at high risk of preeclampsia**, between 12- and 28-weeks' gestation (preferably before 16 weeks' gestation and taken at bedtime [Canada]). Continue until delivery to reduce risk of preeclampsia and low birth weight.[9,19,23] Consider patients with ≥1 of the following high risk:[9,23] o history of preeclampsia (especially if associated with an adverse outcome). o Multifetal gestation (i.e., pregnant with twins, triplets, etc). o chronic hypertension. o type 1 or 2 diabetes. o kidney or autoimmune disease (e.g., lupus, antiphospholipid syndrome). • Can consider starting low-dose aspirin (81 mg/day) in **patients at moderate risk of preeclampsia** between 12- and 28 weeks' gestation and continued until delivery.[23] Patients with one or more of the following risk factors are considered moderate risk: nulliparity (never given birth); obesity (e.g., body mass index >30); family history of preeclampsia; sociodemographic characteristics (e.g., African American, low socioeconomic status); age 35 years or older; previous pregnancy history (i.e., infant small for gestational age or low birth weight, previous adverse pregnancy outcome, >10 years since last pregnancy). • Though the risks of aspirin use during pregnancy are not clearly defined, **avoid in patients at low risk of preeclampsia** as the benefits have not been clearly established.[23]

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Question	Answer/Pertinent Information
During pregnancy, continued	
How should **magnesium** be used in pregnant patients?	• Magnesium (to decrease seizure risk) is first-line to treat or prevent eclampsia in patients who develop gestational hypertension or preeclampsia WITH severe features (severe headache, visual changes, shortness of breath).[19,20] • Data are less clear, but magnesium can be considered, in patients with gestational hypertension or preeclampsia WITHOUT severe features.[19,20] • Magnesium dosing protocols vary widely. An example magnesium dosing strategy is: o **Loading dose**: Magnesium sulfate 4 to 6 g (4 g [Canada]) IV over 20 to 30 minutes, followed by a **maintenance infusion** of 1 to 2 g/hour (1 g/hour [Canada]).[19,20] Usually, continue infusions for 24 hours AFTER delivery.[20] ▪ Use a maintenance infusion of 1 g/hour (after normal loading dose) **for patients with mild kidney impairment** (e.g., serum creatinine between 1 and 1.5 mg/dL) or oliguria (i.e., <30 mL urine output/hour for more than 4 hours).[20] • Magnesium sulfate can be given intramuscularly (IM) with an initial dose of magnesium 5 g IM in each buttock, followed by magnesium 5 g IM every four hours into alternating buttocks, **if IV access is not available**.[6,20] Can be mixed with 2% lidocaine (1 mL) to reduce pain associated with IM injection.[20] Expect more adverse effects (e.g., pain or burning at the injection site, flushing) with IM administration.[3,20] • **Monitoring** for patients receiving magnesium sulfate:[20] o Monitor **deep tendon reflexes (DTRs)** and for **respiratory depression**. Reduced deep tendon reflexes or respiratory depression can be indicators that magnesium levels are too high, allowing for dosage reductions before more serious toxicity develops (e.g., cardiac arrest).[20] o Measure **urine output** and **kidney function**, because magnesium is primarily eliminated by the kidneys. o **In patients with kidney impairment**, monitor magnesium levels about every four hours. ▪ Stop magnesium infusions for magnesium levels >9.6 mg/dL (~7.9 mEq [mmol]/L). Increase the frequency of monitoring magnesium levels to every two hours. Restart the magnesium infusion once magnesium levels fall to <8.4 mg/dL (~6.9 mEq [mmol]/L).
After pregnancy: Data on the use of antihypertensive meds during the postpartum period are extremely limited. Data are largely based on real-world use instead of good quality evidence. In general, highly protein bound and low lipid soluble meds are less likely to be transferred in breast milk.[17]	
What are the **long-term considerations** in patients with gestational hypertension or preeclampsia?	• Gestational hypertension and preeclampsia increase the risk of developing chronic hypertension and/or cardiovascular (CV) disease.[2,20] • Educate patients and encourage follow-up to monitor and manage BP and address preventive strategies (e.g., healthy weight, exercise, dietary changes).[20]

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Question	Answer/Pertinent Information
After pregnancy, continued	
What are the considerations when treating hypertension in **breastfeeding patients**?	• **Beta-blockers**: Low levels of **labetalol**, **metoprolol**, and **propranolol** are transferred to breast milk, with no reported effects in infants.[12] Metoprolol concentrates in breast milk, so some experts suggest monitoring the infant for beta-blockade.[10,21] o **Atenolol**: There are reports of effects in infants, and higher amounts are transferred to breast milk than some other beta-blockers.[12] Avoid, especially in infants ≤ 3 months of age.[7,12] o **Acebutolol**: There are reports of effects in infants, and higher amounts are transferred to breast milk than some other beta-blockers. Other agents are preferred, especially if the infant is preterm or newborn.[12] o **Bisoprolol** and **carvedilol**. There are no published data. Based on their pharmacokinetics, they have a low (carvedilol) to moderately high (bisoprolol) risk of accumulation in the breastfed infant. Other agents may be preferred, especially if the infant is preterm or newborn.[12] • **Methyldopa**: Low levels of **methyldopa** are transferred to breast milk. It is unlikely to cause adverse effects in breastfed infants.[12] • **Calcium channel blockers**: Low amounts of **amlodipine, diltiazem**, **nifedipine**, and **verapamil** are transferred to breast milk. They are unlikely to cause adverse effects in newborns, especially in those older than 2 months.[12] o No information available abut **felodipine**. Other agents may be preferred.[12] • **Thiazide diuretics**: **Hydrochlorothiazide** doses ≤50 mg appear compatible with breastfeeding.[12] o Thiazides can theoretically decrease milk volume at large maternal doses.[12] o **Chlorthalidone** could accumulate based on its long half-life, and there is no information on **indapamide**. Other thiazides may be preferred.[12] • **ACEIs**: levels in breast milk are low, but avoid high doses.[21] o **Captopril** is considered compatible with breastfeeding.[10] o **Enalapril** and **quinapril** are probably compatible with breastfeeding based on limited human data. Amounts in breast milk are likely clinically insignificant to infants.[10] o No human data are available for **benazepril**, **fosinopril**, or **lisinopril**; probably compatible.[10] • **ARBs**: Candesartan milk levels are low; it is probably compatible.[10,12] There is no information for other ARBs.[12] • **Spironolactone** appears compatible with breastfeeding.[12]

Abbreviations: ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BP = blood pressure; DBP = diastolic blood pressure; IUD = intrauterine device; IV = intravenous; NSAID = nonsteroidal anti-inflammatory drug; PO = by mouth; RAAS = renin-angiotensin-aldosterone system; SBP = systolic blood pressure; SGA = small for gestational age.

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In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004 Feb 1;69(3):548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

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