
بسم الله الرحمن الرحيم

Specific Circumstances

- Resistant Hypertension
- Secondary Hypertension
- Hypertension in Pregnancy
- Hypertension in Breastfeeding
- Hypertension Emergency
- Hypertension in elderly
- Hypertension in pediateric

Resistant Hypertension

Definition:

- Seated office BP >140/90 mmHg (above goal)
- In a patient **treated with three or more** antihypertensive medications of different classes
- Medications should be at **optimal (or maximally tolerated)** doses
- One of the medications should be a **diuretic**

affects around 10% of hypertensive individuals

Risk factors

- higher baseline blood pressure (particularly systolic)
- presence of left ventricular hypertrophy (especially by echocardiogram)
- older age
- obesity
- African-American race
- chronic kidney disease
- diabetes
- medications
- Extracellular volume expansion

Drugs and other substances with potential to induce or exacerbate elevated blood pressure and hypertension[1]

Nonsteroidal antiinflammatory drugs (NSAIDs)
Oral contraceptives
Antidepressants (eg, tricyclic antidepressants, selective serotonin reuptake inhibitors)
Corticosteroids (including glucocorticoids and mineralocorticoids)
Decongestants (eg, phenylephrine, pseudoephedrine)
Some weight loss medications (eg, phentermine, diethylpropion)
Sodium-containing antacids
Erythropoietin
Cyclosporine or tacrolimus
Cocaine or methamphetamine
Stimulants (eg, methylphenidate, amphetamines)
Atypical antipsychotics (eg, clozapine, olanzapine)
Angiogenesis inhibitors (eg, bevacizumab)
Tyrosine kinase inhibitors (eg, sunitinib, sorafenib)

References:

What is the problem?

- has a negative impact on well-being
- higher risk of:

✓coronary artery disease

✓chronic HF

✓Stroke

✓end-stage renal disease

✓all-cause mortality

Differential Diagnosis

- Secondary hypertension
- Substance/drug-induced hypertension
- Pseudoresistance **(uncontrolled hypertension):**

✓Poor BP measurement technique

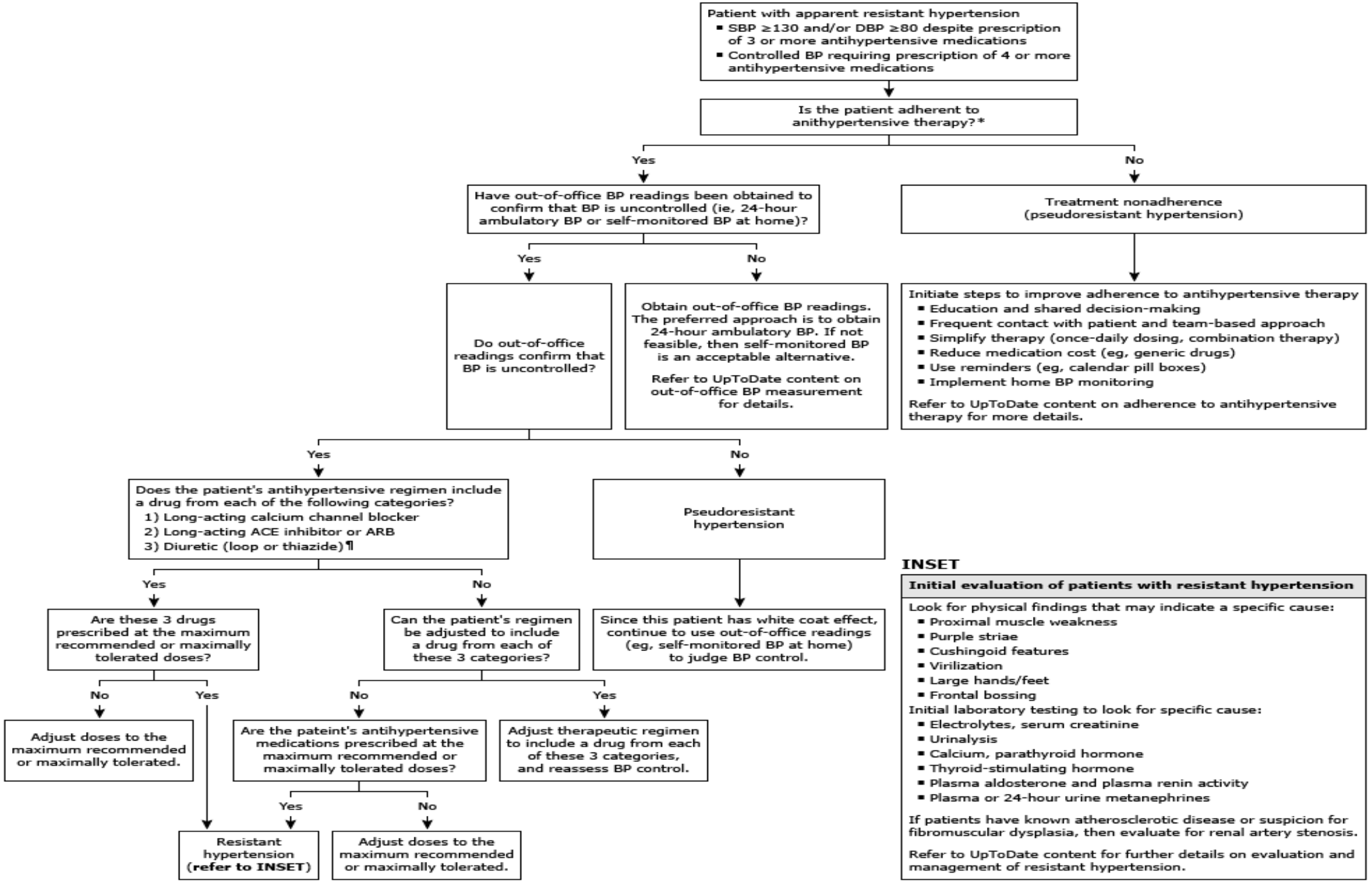
✓ white coat effect

✓ medication nonadherence

✓ suboptimal choices in antihypertensive therapy

Approximately **50%** of patients diagnosed with resistant hypertension have pseudoresistance rather than true resistant hypertension.

A practical approach to evaluating apparent resistant hypertension

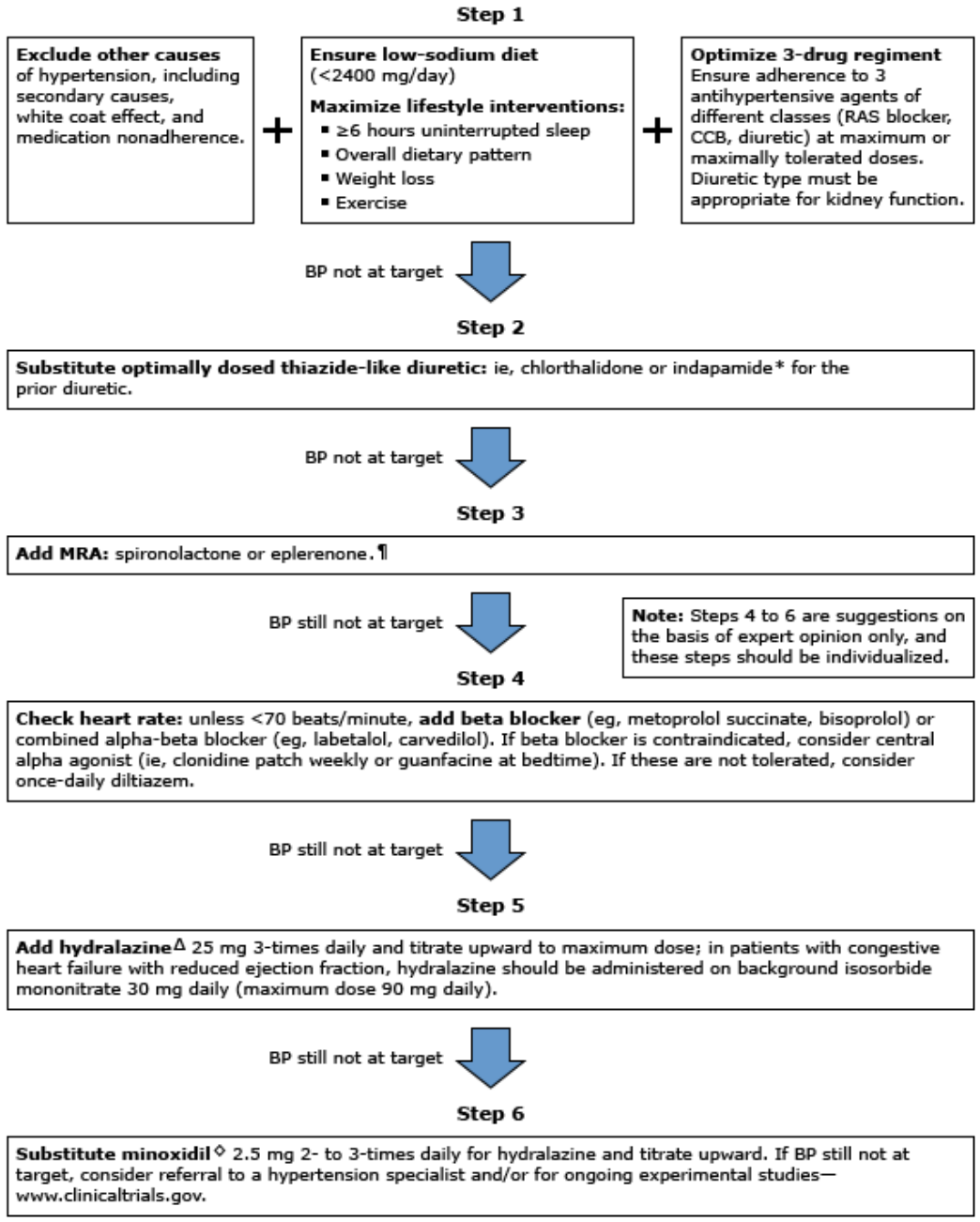


Treatment

Optimize the current treatment regimen:

- health behavior change (eg, weight loss, exercise, eating a healthy diet)
- Stop medications that raise blood pressure
- Optimize diuretic-based treatment
- ✓ maximally tolerated doses of diuretics
- ✓ use of thiazide-like rather than thiazide diuretics
- ✓ initiation of loop diuretics for eGFR <30 ml/min/1.73m2 or clinical volume overload.
- Add a low dose of **spironolactone** (K<4.5 mmol/L and eGFR >45 ml/min/1.73m2)
- **amiloride, doxazosin, eplerenone, clonidine, and beta-blockers** or any available antihypertensive class not already in use are alternatives.

Overall management approach of resistant hypertension in adults



Refractory hypertension

- **Refractory hypertension:** was defined as the inability to achieve blood pressure control (by office or ambulatory blood pressure monitoring) despite maximum tolerated doses of at least five antihypertensive medications, including chlorthalidone and spironolactone.

the authors suggested that treatment failure in such patients may be due to **neurologic mechanisms** (eg, sympathetic overactivity). This contrasts with the conventional thinking that resistant hypertension is largely due to persistent **hypervolemia**.

Secondary Hypertension

- Secondary cause can be identified in **5%–10%** of hypertensive patients.
- Early diagnosis and appropriate targeted treatment have the potential to:

✓ cure hypertension in some patients

✓ improve BP control/reduce antihypertensive medications

When suspect?

it is not cost effective to perform a complete evaluation for secondary hypertension in every hypertensive patient, it is important to be aware of the clinical clues:

1) patients with early onset hypertension (<30 years of age) in particular in the absence of hypertension risk factors (obesity, metabolic syndrome, familial history etc.)
2) those with resistant hypertension
3) individuals with sudden deterioration in BP control
4) hypertensive urgency and emergency

Secondary causes of resistant hypertension

Common
Obstructive sleep apnea
Renal parenchymal disease
Primary aldosteronism
Renal artery stenosis
Uncommon
Pheochromocytoma
Cushing's disease
Hyperparathyroidism
Aortic coarctation

Table 11. Features of Secondary Hypertension

Secondary Hypertension	Clinical History and Physical Examination	Basic Biochemistry and Urine Analysis	Further Diagnostic Tests
Renal parenchymal disease	• Personal/familial history of CKD	• Proteinuria, hematuria, leukocyturia on dipstick urine analysis • Decreased estimated GFR	• Kidney ultrasound
Primary aldosteronism	• Symptoms of hypokalemia (muscle weakness, muscle cramps, tetany)	• Spontaneous hypokalemia or diuretic-induced hypokalemia on blood biochemistry (50%–60% of patients are normokalemic). • Elevated plasma aldosterone-renin activity ratio	• Confirmatory testing (eg, intravenous saline suppression test) • Imaging of adrenals (adrenal computed tomography) • Adrenal vein sampling
Renal artery stenosis	• Abdominal bruit • Bruits over other arteries (ie, carotid and femoral arteries) • Drop in estimated GFR >30% after exposure to ACE-inhibitors/ARBs • For suspected atherosclerotic RAS, history of flash pulmonary edema or history of atherosclerotic disease or presence of cardiovascular risk factors • For suspected fibromuscular dysplasia, young women with onset of hypertension <30 years	• Decrease in estimated GFR	• Imaging of renal arteries (duplex ultrasound, abdominal computed tomography or magnetic resonance angiograms depending on availability and patient's level of renal function)

Pheochromocytoma	• Headaches • Palpitations • Perspiration • Pallor • History of labile hypertension	• Increased plasma levels of metanephrines • Increased 24-hour urinary fractional excretion of metanephrines and catecholamines	• Abdominal/pelvic computational tomography or MRI
Cushing's syndrome and disease	• Central obesity • Purple striae • Facial rubor • Signs of skin atrophy • Easy bruising • Dorsal and supraclavicular fat pad • Proximal muscle weakness	• Hypokalemia • Increased late-night salivary cortisol	• Dexamethasone suppression tests[118] • 24 hour urinary free cortisol • Abdominal/ pituitary imaging
Coarctation of the aorta	• Higher blood pressure in upper than lower extremities • Delayed or absent femoral pulses		• Echocardiogram • Computational tomography angiogram • Magnetic resonance angiogram
Obstructive sleep apnea	• Increased BMI • Snoring • Daytime sleepiness • Gasping or choking at night • Witnessed apneas during sleep • Nocturia		• Home sleep apnea testing (eg, level 3 sleep study) • Overnight polysomnography testing
Thyroid disease	• Symptoms of hyperthyroidism: heat intolerance, weight loss, tremor, palpitations • Symptoms of hypothyroidism: cold intolerance, weight gain, dry brittle hair	• TSH, Free T4	

Hypertension in Pregnancy

- Preexisting hypertension
- Gestational hypertension
- Preexisting hypertension plus gestational hypertension
- Preeclampsia
- Eclampsia
- HELLP syndrome

Risks of chronic hypertension in pregnancy[1-3]

Maternal	Fetal/neonatal
▪ Severe hypertension ▪ Superimposed preeclampsia ▪ Abruption ▪ Cesarean delivery ▪ Postpartum hemorrhage ▪ Renal insufficiency/failure ▪ Stroke ▪ Myocardial infarction ▪ Pulmonary edema ▪ Death	▪ Fetal growth restriction/small for gestational age infant ▪ Preterm delivery ▪ Congenital anomalies ▪ Stillbirth ▪ Neonatal death

Definitions for the hypertensive disorders of pregnancy

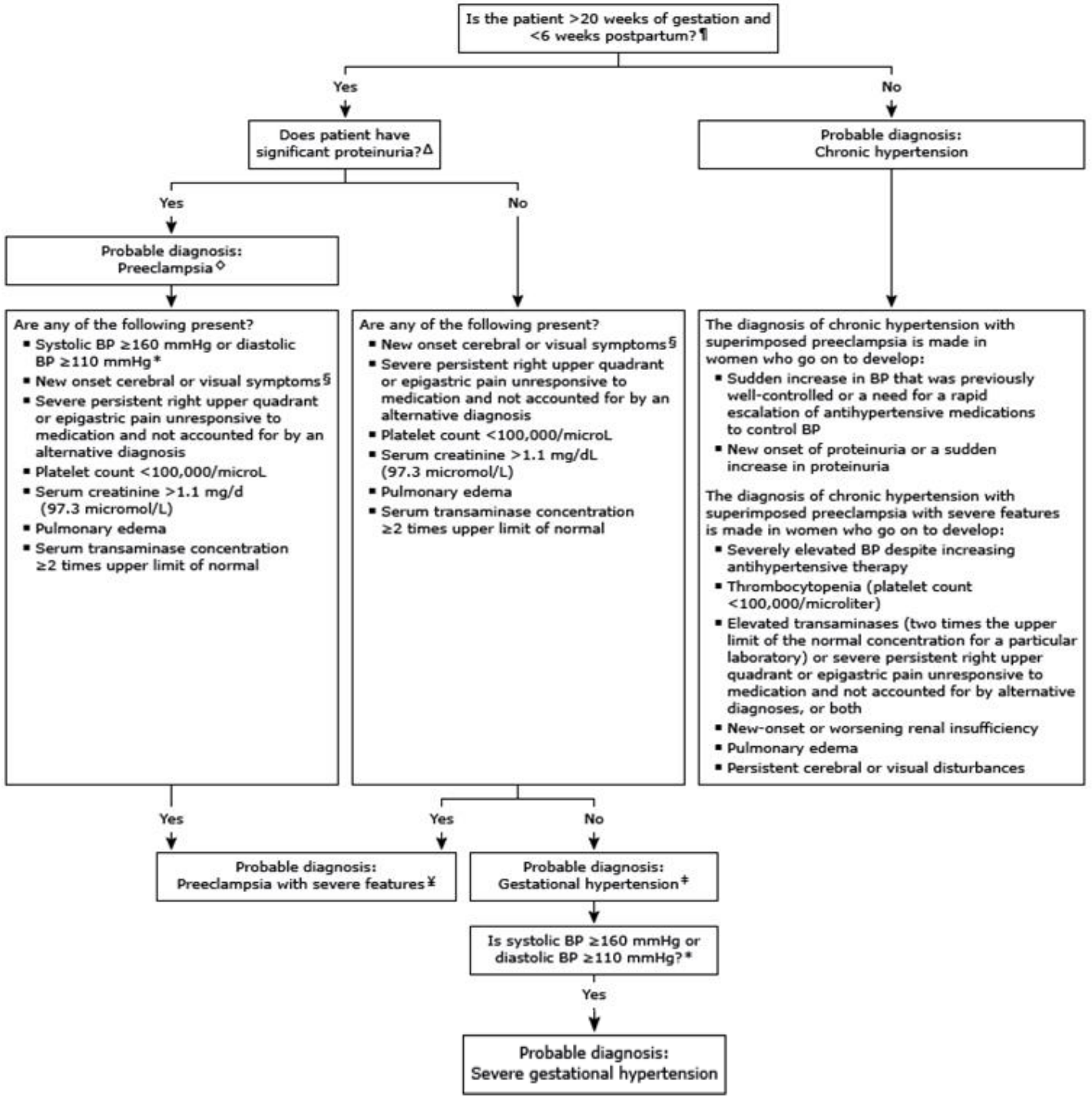
Gestational hypertension	▪ New onset of systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on at least 2 occasions 4 hours apart after 20 weeks of gestation in a previously normotensive woman **And:** ▪ No proteinuria ▪ No severe features of preeclampsia (thrombocytopenia, renal insufficiency, elevated liver transaminases, pulmonary edema, cerebral or visual symptoms)
Preeclampsia	▪ New onset of systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on at least 2 occasions at least 4 hours apart after 20 weeks of gestation in a previously normotensive woman **or** systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy **And:** ▪ Proteinuria (≥300 mg per 24-hour urine collection [or this amount extrapolated from a timed collection], or protein:creatinine ratio ≥0.3, or urine dipstick reading ≥1+ [if other quantitative methods are not available]) **Or, in the absence of proteinuria, new-onset hypertension with the new onset of any of the following:** ▪ Thrombocytopenia (platelet count <100,000/microL) ▪ Renal insufficiency (serum creatinine of >1.1 mg/dL [97 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal disease) ▪ Impaired liver function as indicated by liver transaminase levels at least twice the normal concentration ▪ Pulmonary edema ▪ Persistent cerebral or visual symptoms
Preeclampsia with severe features	**Any of these findings in a patient with preeclampsia:** ▪ Systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg on 2 occasions at least 4 hours apart while a patient is on bed rest (unless antihypertensive therapy is initiated before this time) ▪ Thrombocytopenia (platelet count <100,000/microL) ▪ Impaired liver function as indicated by liver transaminase levels at least twice the normal concentration or severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both ▪ Progressive renal insufficiency (serum creatinine concentration >1.1 mg/dL [97 micromol/L] or a

Eclampsia	▪ In a patient with preeclampsia, generalized seizures that cannot be attributed to other causes
HELLP syndrome (hemolysis, elevated liver enzymes, low platelets)	▪ Presence of HELLP syndrome in a pregnant woman; hypertension may be present (HELLP in such cases is often considered a variant of preeclampsia)
Chronic (preexisting) hypertension	▪ Hypertension diagnosed or present before pregnancy or before 20 weeks of gestation. Hypertension that is first diagnosed during pregnancy and persists at least 12 weeks post-delivery is also considered chronic hypertension. • The blood pressure criteria are systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or both. Ideally, this diagnosis is based on at least 2 elevated blood pressure measurements taken at least 4 hours apart. In the setting of severe hypertension, the diagnosis can be confirmed in a shorter interval to facilitate timely treatment.
Chronic hypertension with superimposed preeclampsia*	**Any of these findings in a patient with chronic hypertension:** ▪ A sudden increase in blood pressure that was previously well-controlled or an escalation of antihypertensive therapy to control blood pressure ▪ New onset of proteinuria or sudden increase in proteinuria in a patient with known proteinuria before or early in pregnancy
Chronic hypertension with superimposed preeclampsia with severe features	**Any of these findings in a patient with chronic hypertension and superimposed preeclampsia:** ▪ Systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg despite escalation of antihypertensive therapy ▪ Thrombocytopenia (platelet count <100,000/microL) ▪ Impaired liver function as indicated by liver transaminase levels at least twice the normal concentration or severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both ▪ New-onset or worsening renal insufficiency ▪ Pulmonary edema ▪ Persistent cerebral or visual disturbances

Comparison of the major hypertensive disorders that occur in pregnant women

	Normotension before pregnancy	Hypertension during pregnancy (%)	Proteinuria	Thrombocytopenia and/or increased transaminases
Preeclampsia	Yes	100	Usually present	Variable, depending on whether preeclampsia is at the severe end of the disease spectrum
HELLP	Yes	82 to 88	Usually present	100%
Gestational hypertension	Yes	100	No	No
Chronic hypertension	No	100	Variable	No
Preeclampsia superimposed on chronic hypertension	No	100	Usually present	Variable, depending on whether preeclampsia is at the severe end of the disease spectrum

HELLP: hemolysis, elevated liver enzymes, low platelets.


Is the patient >20 weeks of gestation and <6 weeks postpartum?¶
Yes
No
Does patient have significant proteinuria?Δ
Probable diagnosis: Chronic hypertension
Yes
No
Probable diagnosis: Preeclampsia◇
Are any of the following present?
Systolic BP ≥160 mmHg or diastolic BP ≥110 mmHg*
New onset cerebral or visual symptoms§
Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis
Platelet count <100,000/microL
Serum creatinine >1.1 mg/d (97.3 micromol/L)
Pulmonary edema
Serum transaminase concentration ≥2 times upper limit of normal
Are any of the following present?
New onset cerebral or visual symptoms§
Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis
Platelet count <100,000/microL
Serum creatinine >1.1 mg/dL (97.3 micromol/L)
Pulmonary edema
Serum transaminase concentration ≥2 times upper limit of normal
The diagnosis of chronic hypertension with superimposed preeclampsia is made in women who go on to develop:
Sudden increase in BP that was previously well-controlled or a need for a rapid escalation of antihypertensive medications to control BP
New onset of proteinuria or a sudden increase in proteinuria
The diagnosis of chronic hypertension with superimposed preeclampsia with severe features is made in women who go on to develop:
Severely elevated BP despite increasing antihypertensive therapy
Thrombocytopenia (platelet count <100,000/microliter)
Elevated transaminases (two times the upper limit of the normal concentration for a particular laboratory) or severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both
New-onset or worsening renal insufficiency
Pulmonary edema
Persistent cerebral or visual disturbances
Yes
Yes
No
Probable diagnosis: Preeclampsia with severe features¥
Probable diagnosis: Gestational hypertension‡
Is systolic BP ≥160 mmHg or diastolic BP ≥110 mmHg?*
Yes
Probable diagnosis: Severe gestational hypertension

Prevention of Preeclampsia

High risk Women

- hypertension in previous pregnancy
- CKD
- autoimmune disease
- Diabetes
- Chronic hypertension

Moderate risk Women

- first pregnancy in a woman >40 years
- pregnancy interval >10 years
- BMI >35 kg/m2
- family history of preeclampsia
- multiple pregnancies

- Aspirin 75–162 mg at weeks 12–36
- calcium supplementation of 1.5–2 g/day in women with low dietary intake (<600 mg/day).

Management

Mild hypertension:

Drug treatment at persistent BP>150/95 mmHg in all women.

Drug treatment at persistent BP >140/90 mm Hg in gestational hypertension, preexisting hypertension with superimposed gestational hypertension; hypertension with subclinical HMOD at any time during pregnancy.

First choices: methyldopa, beta-blockers (labetalol), and dihydropyridine-calcium channel blockers (DHP-CCBs) (nifedipine [not capsular], nicardipine).

Contraindicated: RAS blockers (ACE-I, ARB, direct renin inhibitors) due to adverse fetal and neonatal outcomes.

Drug doses for oral treatment of hypertension in pregnancy

Drug	Class	Initial dose	Usual effective dose range	Maximum suggested total daily dose	Comments
Labetalol	Combined alpha and beta blocker	100 mg 2 times daily, increase by 100 mg twice daily every 2 to 3 days as needed	200 to 800 mg in 2 divided doses	2400 mg	Can cause bronchoconstriction. Avoid in women with asthma, chronic obstructive lung disease, heart failure, bradycardia, or greater than first-degree heart block.
Hydralazine **NOTE:** Due to reflex tachycardia, monotherapy with oral hydralazine is not recommended; hydralazine may be combined with methyldopa or labetalol if needed as add-on therapy	Peripheral vasodilator	Begin with 10 mg 4 times per day, increase by 10 to 25 mg/dose every 2 to 5 days	50 to 100 mg in 2 to 4 divided doses	200 mg*	
Nifedipine extended release¶	Calcium channel blocker	30 to 60 mg once daily as an extended release tablet, increase at 7 to 14 day intervals	30 to 90 mg once daily	120 mg	Do not administer sublingually.
Methyldopa	Centrally acting alpha agonist	250 mg 2 to 3 times daily, increase every 2 days as needed[Δ]	250 to 1000 mg in 2 to 3 divided doses	3000 mg	Sedation is a common side effect.

Management

Severe hypertension: At BP >170 mm Hg systolic and/or >110 mm Hg diastolic: immediate hospitalization is indicated (emergency).

- Treatment with **intravenous labetalol** (alternative: intravenous nicardipine, esmolol, hydralazine,), oral methyldopa or DHP-CCBs (nifedipine [not capsular] nicardipine).
- Add magnesium (hypertensive crisis to prevent eclampsia).
- In pulmonary edema: nitroglycerin intravenous infusion.
- Sodium nitroprusside should be avoided due to the danger of fetal cyanide poisoning with prolonged treatment.

Antihypertensive agents used for urgent blood pressure control in pregnancy

Drug	Initial dose	Follow-up
Labetalol	20 mg IV gradually over 2 minutes.	Repeat BP measurement at 10-minute intervals: ▪ If BP remains above target level at 10 minutes, give 40 mg IV over 2 minutes. ▪ If BP remains above target level at 20 minutes, give 80 mg IV over 2 minutes. ▪ If BP remains above target level at 30 minutes, give 80 mg IV over 2 minutes. ▪ If BP remains above target level at 40 minutes, give 80 mg IV over 2 minutes. Cumulative maximum dose is 300 mg. If target BP is not achieved, switch to another class of agent.
	A continuous IV infusion of 1 to 2 mg/minute can be used instead of intermittent therapy or started after 20 mg IV dose. Requires use of programmable infusion pump and continuous noninvasive monitoring of blood pressure and heart rate.	Adjust dose within this range to achieve target blood pressure. Cumulative maximum dose is 300 mg. If target BP is not achieved, switch to another class of agent.
Hydralazine	5 mg IV gradually over 1 to 2 minutes.* Adequate reduction of blood pressure is less predictable than with IV labetalol.	Repeat BP measurement at 20-minute intervals: ▪ If BP remains above target level at 20 minutes, give 5 or 10 mg IV over 2 minutes, depending on the initial response. ▪ If BP remains above target level at 40 minutes, give 10 mg IV over 2 minutes, depending on the previous response. Cumulative maximum dose is 30 mg. If target BP is not achieved, switch to another class of agent.
Nifedipine extended release	30 mg orally.	If target BP is not achieved in 1 to 2 hours, another dose can be administered. If target BP is not achieved, switch to another class of agent.
Nicardipine (parenteral)	The initial dose is 5 mg/hour IV by infusion pump and can be increased to a maximum of 15 mg/hour. Onset of action is delayed by 5 to 15 minutes; in general, rapid titration is avoided to minimize risk of overshooting dose. Requires use of a programmable infusion pump and continuous noninvasive monitoring of blood pressure and heart rate.	Adjust dose within this range to achieve target BP.
Nifedipine immediate release*	10 mg orally. May be associated with precipitous drops in BP in some women, with associated FHR decelerations for which emergency cesarean delivery may be indicated. As such, this regimen is not typically used as a first-line option and is usually reserved only for women without IV access. If used, FHR should be monitored while administering short-acting nifedipine.	Repeat BP measurement at 20-minute intervals: ▪ If BP remains above target at 20 minutes, give 10 or 20 mg orally, depending on the initial response. ▪ If BP remains above target at 40 minutes, give 10 or 20 mg orally, depending on the previous response. If target BP is not achieved, switch to another class of agent.

American College of Obstetricians and Gynecologists (ACOG)

- recommends not initiating medication therapy for mild chronic hypertension in pregnancy (>140/90 mmHg and <160/110 mmHg) given the limited evidence for a clear benefit and safety of treatment.
- ecommends considering discontinuing medication in women with mild hypertension who become pregnant and recommending lifestyle modifications (diet, exercise).
- Pharmacologic therapy is recommended for pregnant women with severe hypertension (systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥105 to 110 mmHg. A lower threshold for initiation of medications (≥150/100 mmHg) is recommended for women with end-organ involvement, such as cardiac or renal disease.
- For most women, the blood pressure target is systolic blood pressure ≥120 and <160 mmHg and diastolic blood pressure ≥80 and <110 mmHg.

Delivery

ISH: in gestational hypertension or preeclampsia:

- At week 37 in asymptomatic women.
- Expedite delivery in women with visual disturbances, hemostatic disorders.

ACOG suggested the following approach for delivery of women with chronic hypertension :

- ≥38+0 to 39+6 weeks of gestation for women not requiring medication
- ≥37+0 to 39+0 weeks for women with hypertension controlled with medication
- 34+0 to 36+6 weeks for women with severe hypertension that is difficult to control

Postpartum management

- **Acetaminophen** as first-line medication for pain management. NSAIDs should be used preferentially over opioid analgesics, when possible.
- If hypertension persists, any of recommended drugs except methyldopa (**postpartum depression**)
- Postpartum visits for a blood pressure check within 3 to 10 days after delivery or home blood pressure monitoring is recommended as severe hypertension can develop after hospital discharge

Breastfeeding

All antihypertensives excreted into breast milk at low concentrations.

Avoid: atenolol, propranolol, nifedipine (high concentration in milk).

Prefer: long acting CCBs.

Hypertensive Emergency

association of substantially elevated BP with acute hypertension-mediated organ damage. Target organs include:

- ✓**Retina**
- ✓**Brain**
- ✓**Heart**
- ✓**large arteries**
- ✓**kidneys**

There is no specific BP threshold to define a hypertensive emergency.

clinical presentations

- The clinical presentation can vary and is mainly determined by the organ(s) acutely affected.
- **Malignant hypertension:** Severe BP elevation (commonly >200/120 mm Hg) associated with advanced bilateral retinopathy (hemorrhages, cotton wool spots, papilledema).
- **Hypertensive encephalopathy**: Severe BP elevation associated with lethargy, seizures, cortical blindness and coma in the absence of other explanations.
- **Hypertensive thrombotic microangiopathy:** Severe BP elevation associated with hemolysis and thrombocytopenia in the absence of other causes and improvement with BP-lowering therapy.
- Other presentations of hypertensive emergencies include severe BP elevation associated with cerebral hemorrhage, acute stroke, acute coronary syndrome, cardiogenic pulmonary edema, aortic aneurysm/dissection, and severe preeclampsia and eclampsia.

Diagnostic Workup

- Medical history:

✓ preexisting hypertension

✓ onset and duration of symptoms

✓ potential causes (nonadherence with prescribed antihypertensive drugs, lifestyle changes, concomitant use of BP elevating drugs [NSAIDS, steroids, immunesuppressants, sympathomimetics, cocaine, antiangiogenic therapy])

Management

The overall therapeutic goal in patients presenting with hypertensive emergencies is a controlled BP reduction to safer levels to prevent or limit further hypertensive damage while avoiding hypotension and related complications.

There is a lack of randomized controlled trial data to provide clear cut guidance on BP targets and times within which these should be achieved. Most recommendations are based on expert consensus.

The type of acute HMOD is the main determinant of the preferred treatment choice.

The timeline and magnitude of BP reduction is strongly dependent on the clinical context.

Availability of drugs and local experience with individual drugs are likely to influence the choice of drugs.

Table 12. Hypertensive Emergencies Requiring Immediate BP Lowering

Clinical Presentation	Timeline and Target BP	First Line Treatment	Alternative
Malignant hypertension with or without TMA or acute renal failure	Several hours, MAP −20% to −25%	Labetalol Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediate, MAP −20% to −25%	Labetalol Nicardipine	Nitroprusside
Acute ischaemic stroke and SBP >220 mm Hg or DBP >120 mm Hg	1 h, MAP −15%	Labetalol Nicardipine	Nitroprusside
Acute ischaemic stroke with indication for thrombolytic therapy and SBP >185 mm Hg or DBP >110 mm Hg	1 h, MAP −15%	Labetalol Nicardipine	Nitroprusside
Acute hemorrhagic stroke and SBP >180 mm Hg	Immediate, 130<SBP<180 mm Hg	Labetalol Nicardipine	Urapidil
Acute coronary event	Immediate, SBP <140 mm Hg	Nitroglycerine Labetalol	Urapidil
Acute cardiogenic pulmonary edema	Immediate, SBP <140 mm Hg	Nitroprusside or nitroglycerine (with loop diuretic)	Urapidil (with loop diuretic)
Acute aortic disease	Immediate, SBP <120 mm Hg and heart rate <60 bpm	Esmolol and nitroprusside or nitroglycerine or nicardipine	Labetalol or metoprolol
Eclampsia and severe preeclampsia/ HELLP	Immediate, SBP <160 mm Hg and DBP <105 mm Hg	Labetalol or nicardipine and magnesium sulphate	

Adapted from van den Born et al.[127]

Management

- Labetalol and nicardipine are generally safe to use in all hypertensive emergencies and should be available wherever hypertensive emergencies are being managed.
- Nitroglycerin and nitroprusside are specifically useful in hypertensive emergencies including the heart and the aorta.

Parenteral drugs for treatment of hypertensive emergencies in adults*

Drug	Dose range	Onset of action (minutes)	Duration of action (minutes)	Adverse effects¶	Role△
Vasodilators					
Clevidipine	Initially 1 to 2 mg/hour as IV infusion with rapid titration. Most patients respond to 4 to 6 mg/hour and are treated with maximum doses of 16 mg/hour or less. NOTE: Delivered in lipid emulsion. 1000 mL maximum per 24 hours (equivalent to 21 mg/hour) due to lipid load.	2 to 4	5 to 15	Atrial fibrillation, nausea, lipid formulation contains potential allergens (eg, soy, egg)	Hypertensive emergencies including postoperative hypertension.
Enalaprilat	1.25 to 5 mg every six hours IV	15 to 30	approximately 6 to >12 hours	Precipitous fall in pressure in high-renin states; variable response, headache, dizziness	Acute left ventricular failure. Due to slow onset and long duration of effect, rarely used. Avoid use in AMI, renal impairment, or pregnancy.
Fenoldopam	Initially 0.1 mcg/kg per minute◇ as IV infusion titrated to a maximum of 1.6 mcg/kg per minute	5 to 10	30 to 60	Tachycardia, headache, nausea, flushing	Most hypertensive emergencies. Use caution or avoid with glaucoma or increased intracranial pressure.
Hydralazine	10 to 20 mg IV	10 to 20 IV	1 to ≥4 hours IV	Sudden precipitous drop in blood pressure, tachycardia, flushing, headache, vomiting, aggravation of angina	In general, hydralazine should be avoided due to its prolonged and unpredictable hypotensive effect. Labetalol and nicardipine are generally preferred choices for treatment of eclampsia.
	10 to 20 mg IM (40 mg maximum per labeling)	20 to 30 IM	4 to 6 hours IM		
Nicardipine	5 to 15 mg/hour as IV infusion. Some patients may require up to 30 mg/hour.	5 to 15	approximately 1.5 to ≥4 hours	Tachycardia, headache, dizziness, nausea, flushing, local phlebitis, edema	Most hypertensive emergencies, including pregnancy induced. Avoid use in acute heart failure. Caution with coronary ischemia.

Nitroglycerin (glyceryl trinitrate)	5 to 100 mcg/minute as IV infusion	2 to 5	5 to 10	Hypoxemia, tachycardia (reflex sympathetic activation), headache, vomiting, flushing, methemoglobinemia, tolerance with prolonged use	Potential adjunct to other IV antihypertensive therapy in patients with coronary ischemia (ACS) or acute pulmonary edema.
Nitroprusside	0.25 to 10 mcg/kg per minute as IV infusion. To minimize risk of cyanide toxicity, infusion duration should be as short as possible and not exceed 2 mcg/kg per minute. Patients who receive higher doses (ie, >500 mcg/kg at a rate exceeding 2 mcg/kg per minute) should receive sodium thiosulfate infusion to avoid cyanide toxicity.	0.5 to 1	1 to 10	Elevated intracranial pressure, decreased cerebral blood flow, reduced coronary blood flow in CAD, cyanide and thiocyanate toxicity, nausea, vomiting, muscle spasm, flushing, sweating	In general, nitroprusside should be avoided due to its toxicity. Nitroprusside should be avoided in patients with AMI, CAD, CVA, elevated intracranial pressure, renal impairment, or hepatic impairment.
Adrenergic inhibitors					
Esmolol	250 to 500 mcg/kg loading dose over one minute; then initiate IV infusion at 25 to 50 mcg/kg per minute; titrate incrementally up to maximum of 300 mcg/kg per minute	1 to 2	10 to 30	Nausea, flushing, bronchospasm, first-degree heart block, infusion-site pain; half-life prolonged in setting of anemia	Perioperative hypertension. Avoid use in acute decompensated heart failure.
Labetalol	Initial bolus of 20 mg IV followed by 20 to 80 mg IV bolus every 10 minutes (maximum 300 mg) **or** 0.5 to 2 mg/minute as IV loading infusion following an initial 20 mg IV bolus (maximum 300 mg)	5 to 10	2 to 4 hours	Nausea/vomiting, paresthesias (eg, scalp tingling), bronchospasm, dizziness, nausea, heart block	Most hypertensive emergencies including myocardial ischemia, hypertensive encephalopathy, pregnancy, and postoperative hypertension. Avoid use in acute decompensated heart failure. Use cautiously in obstructive or reactive airway.
Metoprolol	Initially 1.25 to 5 mg IV followed by 2.5 to 15 mg IV every three to six hours	20	5 to 8 hours	Refer to labetalol	Myocardial ischemia, perioperative hypertension. Avoid use in acute decompensated heart failure.
Phentolamine	5 to 15 mg IV bolus every 5 to 15 minutes	1 to 2	10 to 30	Tachycardia, flushing, headache, nausea/vomiting	Alternative option for catecholamine excess (eg, adrenergic crisis secondary to pheochromocytoma or cocaine overdose).

: intravenous injection; AMI: acute myocardial infarction; IM: intramuscular injection; ACS: acute coronary syndrome; CAD: coronary artery disease; CVA: cerebrovascular accident.

Urgency?

- **ISA:** Patients with substantially elevated BP who lack acute HMOD are not considered a hypertensive emergency and can typically be treated with **oral antihypertensive therapy.**
- **Uptodate:** relatively asymptomatic or completely asymptomatic patient with a blood pressure in the "severe" range **(ie, ≥180/≥120 mmHg),** often a mild headache, but **no** signs or symptoms of acute end-organ damage. This entity of severe asymptomatic hypertension is sometimes called **hypertensive urgency** and occurs more frequently among patients who have been nonadherent with either their chronic antihypertensive drug regimen or their low-sodium diet.
- The most important aspect of the initial assessment of the patient with severely elevated blood pressure is to exclude acute, ongoing, target-organ damage, which would indicate a diagnosis of hypertensive emergency rather than severe asymptomatic hypertension

Management

- We suggest lowering the blood pressure **over a period of hours to days.** The rapidity with which blood pressure should be brought to safe levels is controversial and **not** based upon high-quality medical evidence. This suggestion stems from and seeks to balance two major concerns:

-**The risk of adverse events** (eg, stroke or myocardial infarction) that may occur if the blood pressure is lowered too rapidly or to a level below the ability for autoregulation to maintain adequate tissue perfusion.

-**The potential risk of imminent cardiovascular events** that may result from severe hypertension if the blood pressure is not quickly and sufficiently reduced.

Lowering BP over a period of hours

- Patients judged to be at high risk for imminent cardiovascular events due to severe hypertension, including those with **known aortic or intracranial aneurysms**, should have their blood pressure lowered over a period of hours.
- The blood pressure should usually be **lowered to <160/<100 mmHg**.
- The mean arterial pressure should not be lowered by more than 25 to 30 percent over the first 2-4 hours.
- All patients should be provided a quiet room in which to rest. This may produce a fall in blood pressure **≥20/10 mmHg** in approximately one-third of adults. If this is not effective, antihypertensive drugs

Pharmacotherapy

- A wide variety of therapeutic modalities have been used to lower blood pressure over this short period of time, including oral **nifedipine, nitrates, captopril**, or oral **clonidine** or **hydralazine** However, sublingual nifedipine is contraindicated in this setting and should not be used.
- Oral clonidine (but not intended as long-term therapy) at a dose of 0.1 to 0.2 mg
- Oral captopril (if the patient is not volume overloaded) at a dose of 6.25 or 12.5 mg
- Otherwise, many clinicians prefer long-acting drugs (eg, amlodipine, chlorthalidone) and a follow-up primary care office visit in the next one to two days.

elderly

- The prevalence of HTN in age greater than 60 to 65 years: as high as **70 to more than 80%**
- Isolated systolic hypertension is common in older adults: **SBP ≥140 mm Hg and DBP <90 mm Hg**
- aiming for control within **three to six months**, orthostatic (postural) and/or postprandial hypotension is common among older hypertensive patients.

Management

- **lifestyle modification**: dietary salt restriction and weight loss in obese patients
- initial monotherapy with a **thiazide-type diuretic, long-acting CCBs, ACE inhibitor/ARB.**
- **A long-acting dihydropyridine or a thiazide diuretic** is generally preferred because of increased blood pressure-lowering efficacy in this population.
- Goal blood pressure: <140/80 mmHg

Pediaterics

- The prevalence: **4.2%**
- HTN in childhood and adolescence contributes to premature atherosclerosis and the early development of cardiovascular disease .
- The diagnosis of chronic childhood HTN is made when the auscultated BP values on three repeated and separate visits are **greater than the 95th percentile for the age, sex, and height of the patient, or is ≥130/80 mmHg even if <95th percentile**.
- For children without risk factors or conditions associated with HTN, BP is measured beginning at three years of age during **annual** health care supervision visits.
- For children <3 years of age with risk factors for HTN, BP is measured at each health supervision visit

Risk factors for hypertension in children <3 years

Check BP at health supervision visits for children with the following:*
Perinatal risk factors: ▪ Born at <32 weeks gestation ▪ Small for gestational age ▪ Birth weight <1500 g ▪ Neonatal complications that required intensive care or umbilical artery catheterization
Recurrent urinary tract infection, hematuria, or proteinuria
Renal disease or urologic malformation
Family history of congenital renal disease
Solid organ or hematopoietic cell transplant
Malignancy or other systemic illness associated with hypertension (eg, neurofibromatosis, tuberous sclerosis complex, sickle cell disease)
Treatment with drugs known to raise blood pressure (eg, caffeine, nonsteroidal anti-inflammatory drugs, glucocorticoids)
Evidence of elevated intracranial pressure

Blood pressure levels for boys by age and height percentile

BP (percentile)	Systolic BP (mmHg)							Diastolic BP (mmHg)						
	Height percentile or measured height							Height percentile or measured height						
	5%	10%	25%	50%	75%	90%	95%	5%	10%	25%	50%	75%	90%	95%
1 year														
Height (in)	30.4	30.8	31.6	32.4	33.3	34.1	34.6	30.4	30.8	31.6	32.4	33.3	34.1	34.6
Height (cm)	77.2	78.3	80.2	82.4	84.6	86.7	87.9	77.2	78.3	80.2	82.4	84.6	86.7	87.9
50th	85	85	86	86	87	88	88	40	40	40	41	41	42	42
90th	98	99	99	100	100	101	101	52	52	53	53	54	54	54
95th	102	102	103	103	104	105	105	54	54	55	55	56	57	57
95th + 12 mmHg	114	114	115	115	116	117	117	66	66	67	67	68	69	69
2 years														
Height (in)	33.9	34.4	35.3	36.3	37.3	38.2	38.8	33.9	34.4	35.3	36.3	37.3	38.2	38.8
Height (cm)	86.1	87.4	89.6	92.1	94.7	97.1	98.5	86.1	87.4	89.6	92.1	94.7	97.1	98.5
50th	87	87	88	89	89	90	91	43	43	44	44	45	46	46
90th	100	100	101	102	103	103	104	55	55	56	56	57	58	58
95th	104	105	105	106	107	107	108	57	58	58	59	60	61	61
95th + 12 mmHg	116	117	117	118	119	119	120	69	70	70	71	72	73	73

Who should be treated ?

- **Symptomatic HTN** (eg, headache, seizures, changes in mental status, focal neurologic complaints, visual disturbances, and cardiovascular complaints indicative of heart failure, such as chest pain, palpitations, cough, or shortness of breath).
- **Stage 2 HTN**
- Stage 1 HTN without any evidence of end-organ damage and that persists despite a trial of four to six months of nonpharmacologic therapy.
- **Hypertensive end-organ damage**, most often left ventricular hypertrophy (LVH)
- Any stage of HTN or elevated BP for patients with **chronic kidney disease (CKD)**
- Any stage of HTN for patients with **diabetes mellitus (DM)**

2017 American Academy of Pediatrics updated definitions for pediatric blood pressure categories

	For children aged 1 to <13 years	For children aged ≥13 years
Normal BP	Systolic and diastolic BP <90th percentile	Systolic BP <120 and diastolic BP <80 mmHg
Elevated BP	Systolic and diastolic BP ≥90th percentile to <95th percentile, **or** 120/80 mmHg to <95th percentile (whichever is lower)	Systolic BP 120 to 129 and diastolic BP <80 mmHg
Stage 1 HTN	Systolic and diastolic BP ≥95th percentile to <95th percentile+12 mmHg, **or** 130/80 to 139/89 mmHg (whichever is lower)	130/80 to 139/89 mmHg
Stage 2 HTN	Systolic and diastolic BP ≥95th percentile+12 mmHg, **or** ≥140/90 mmHg (whichever is lower)	≥140/90 mmHg

BP: blood pressure; HTN: hypertension.

Management

- For patients with primary HTN we suggest an agent that blocks the renin/angiotensin system (ie, **ACE inhibitor or ARB**), If the target BP goal is not met, add a **thiazide diuretic.**
- For sexually active females: **CCB** be used as the initial antihypertensive agent
- For patients with renovascular disease: **CCB** be used as the initial antihypertensive agent
- For patients with CKD: **ACE inhibitors or ARBs**
- For patients with either type 1 or type 2 DM: **ACE inhibitors or ARBs**

Antihypertensive drugs for outpatient management of chronic hypertension for infants, children, and adolescents

Drug	Age	Initial oral dose	Maximal oral dose per day	Dosing interval	Formulations
ACE inhibitors					
Contraindications: Pregnancy, angioedema. **Common adverse effects**: Cough, headache, dizziness, asthenia. **Severe adverse effects**: Hyperkalemia, acute kidney injury, angioedema, fetal toxicity.					
Benazepril	≥6 years*	0.2 mg/kg per day (up to 10 mg per day)	0.6 mg/kg (up to 40 mg)	Daily.	Tablet: 5, 10, 20, 40 mg (generic). Extemporaneous liquid: 2 mg/mL.
Captopril ¶	Infants	0.05 mg/kg per dose	6 mg/kg	Daily to 4 times a day.	Tablet: 12.5, 25, 50, 100 mg (generic). Extemporaneous liquid: 1 mg/mL.
	Children	0.5 mg/kg per dose	6 mg/kg	Three times a day.	
Enalapril	≥1 month*	0.08 mg/kg per day (up to 5 mg per day)	0.6 mg/kg (up to 40 mg)	Daily to twice a day.	Tablet: 2.5, 5, 10, 20 mg (generic). Solution: 1 mg/mL.
Fosinopril	≥6 years	0.1 mg/kg per day (up to 5 mg per day)	40 mg	Daily.	Tablet: 10, 20, 40 mg (generic).
	<50 kg				
	≥50 kg*	5 mg per day	40 mg		
Lisinopril	≥6 years*	0.07 mg/kg per day (up to 5 mg per day)	0.6 mg/kg (up to 40 mg)	Daily.	Tablet: 2.5, 5, 10, 20, 30, 40 mg (generic). Solution: 1 mg/mL.

ARBs					
Contraindications: Pregnancy. **Common adverse effects**: Headache, dizziness. **Severe adverse effects**: Hyperkalemia, acute kidney injury, fetal toxicity.					
Candesartan	1 to 5 years*	0.02 mg/kg per day (up to 4 mg per day)	0.4 mg/kg (up to 16 mg)	Daily to twice a day.	Tablet: 4, 8, 16, 32 mg. Extemporaneous liquid: 1 mg/mL.
	≥6 years*				
	<50 kg	4 mg per day	16 mg		
	≥50 kg	8 mg per day	32 mg		
Irbesartan	6 to 12 years	75 mg per day	150 mg	Daily.	Tablet: 75, 150, 300 mg (generic).
	≥13 years	150 mg per day	300 mg		
Losartan	≥6 years*	0.7 mg/kg (up to 50 mg)	1.4 mg/kg (up to 100 mg)	Daily.	Tablet: 25, 50, 100 mg (generic). Extemporaneous liquid: 2.5 mg/mL.
Olmesartan	≥6 years*	NA	NA	Daily.	Tablet: 5, 20, 40 mg. Extemporaneous liquid: 2 mg/mL.
	<35 kg	10 mg	20 mg		
	≥35 kg	20 mg	40 mg		
Valsartan	≥6 years*	1.3 mg/kg (up to 40 mg)	2.7 mg/kg (up to 160 mg)	Daily.	Tablet: 40, 80, 160, 320 mg (generic). Extemporaneous liquid: 4 mg/mL.

Thiazide diuretics					
Contraindications: Anuria. **Common adverse effects**: Dizziness, hypokalemia. **Severe adverse effects**: Cardiac dysrhythmias, cholestatic jaundice, new onset diabetes mellitus, pancreatitis.					
Chlorthalidone	Children	0.3 mg/kg	2 mg/kg (50 mg)	Daily.	Tablet: 25, 50, 100 mg (generic).
Chlorothiazide	Children*	10 mg/kg per day	20 mg/kg (up to 375 mg per day)	Daily to twice a day.	Tablet: 250, 500 mg (generic). Suspension: 250/5 mL. Extemporaneous liquid: 1 mg/mL.
Hydrochlorothiazide	Children*	1 mg/kg per day	2 mg/kg (up to 37.5 mg)	Daily to twice a day.	Tablet: 12.5, 25, 50 mg.
Calcium channel blockers					
Contraindications: Hypersensitivity to CCBs. **Common adverse effects**: Flushing, peripheral edema, dizziness. **Severe adverse effects**: Angioedema.					
Amlodipine	1 to 5 years	0.1 mg/kg	0.6 mg/kg (up to 5 mg)	Daily.	Tablet: 2.5, 5, 10 mg. Extemporaneous liquid: 1 mg/mL.
	≥6 years*	2.5 mg	10 mg		
Felodipine	≥6 years	2.5 mg	10 mg	Daily.	Tablet (extended release): 2.5, 5, 10 mg (generic).
Isradipine	Children	0.05 to 0.1 mg/kg	0.6 mg/kg (up to 10 mg)	Capsule: Twice daily to 3 times a day. Tablet (extended release): Daily.	Capsule: 2.5, 5 mg. Tablet (extended release): 5, 10 mg.

References

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- uptodate: Evaluation of secondary hypertension
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- uptodate: Treatment of hypertension in pregnant and postpartum women
- uptodate: Management of severe asymptomatic hypertension (hypertensive urgencies) in adults
- uptodate: Drugs used for the treatment of hypertensive emergencies
- uptodate: Evaluation and treatment of hypertensive emergencies in adults
- Uptodate: Treatment of hypertension in older adults, particularly isolated systolic hypertension
- uptodate: Definition and diagnosis of hypertension in children and adolescents
- uptodate: Nonemergent treatment of hypertension in children and adolescents

THANK YOU
for your
ATTENTION!