both (Table 56-12). **Major contraindications to thrombolytic therapy** include intracranial disease, uncontrolled hypertension at presentation, recent major surgery or trauma (past 3 weeks), and metastatic cancer. Any patient with head trauma from syncope should have a CT scan prior to therapy to detect hemorrhage.

Alteplase (tissue plasminogen activator) is the only currently approved agent for PE, dosed at 100 milligrams IV over 2 hours. Either enoxaparin (1 milligram/kg SC) or unfractionated heparin (80 units/kg IV bolus followed by 18 units/kg/h) is the anticoagulant, with the activated partial thromboplastin time kept at <120 seconds for unfractionated heparin. Heparin or low-molecular-weight heparin is typically started after the thrombolytic infusion. Use of 50 mg of alteplase may reduce bleeding risk with similar outcomes as 100 mg of alteplase, although the safety and efficacy of this approach remain controversial.[81,82] For further discussion of fibrinolytic agents, see Chapter 239, "Thrombotics and Antithrombotics."

CATHETER-DIRECTED THROMBOLYSIS

Recent systematic reviews suggest that catheter-directed fibrinolysis for intermediate-risk PE produces good hemodynamic improvements and an intracranial bleeding rate <2%.[83-86] Catheter-directed thrombolysis for PE requires a far lower dose of alteplase (approximately 10 milligrams total), which may confer a lower bleeding risk. Catheter-directed thrombolysis is an option for patients over 65 years old, in whom intracranial bleeding risk is highest.[87] Because of the time delay needed to activate the vascular intervention suite, intrapulmonary fibrinolytic delivery should not be used in most patients with massive PE.[88]

SURGICAL EMBOLECTOMY

If available, surgical embolectomy is an option in young patients with large, proximal PE accompanied by hypotension. Because surgical embolectomy is often delayed, the reported mortality rate is approximately 30%. The amount of clot that can be extracted is often extensive, and removal may help limit later cardiopulmonary complications.

SPECIAL POPULATIONS

PREGNANCY

The clinical assessment of VTE in pregnant women is difficult because many signs and symptoms suggestive of VTE are seen in normal pregnancy.[89-91] Fewer than 2% of pregnant women with Wells' score ≤4 had PE in prior retrospective studies.[92,93] In one prospective study, the revised Geneva score resulted in a stepwise increase in probability of PE (7 of 192 [3.6%] in the low–pretest probability group, 18 of 200 [9.0%] in the intermediate-probability group, and 3 of 3 [100%] in the high-probability group).[94] The PE rule-out criteria rule has not been adequately tested in pregnant patients to recommend its use in isolation to exclude PE.

The D-dimer has low specificity in pregnant patients; by the third trimester, almost all healthy pregnant women have a positive D-dimer.[95,96] Studies that have examined the diagnostic sensitivity of the D-dimer have been hampered by low numbers and problems with D-dimer measurements made after systemic anticoagulation, which degrades test sensitivity.[97] Some have advocated for sequentially increasing the cutoff by approximately 50% for the D-dimer per trimester (first trimester, 750 nanograms/mL; second trimester, 1000 nanograms/mL; third trimester, 1250 nanograms/mL), although this approach has not been tested in a management study.[96,98-100]

The diagnostic accuracy of US for DVT appears to be similar to that of nonpregnant patients.[101,102] The best choice of pulmonary vascular imaging in pregnancy is controversial and uncertain.[103] Both a normal CT pulmonary angiogram and V̇/Q̇ scanning have shown 100% diagnostic sensitivity for technically adequate studies.[91] MRI has not been adequately tested in pregnancy to provide any basis for recommendation, but it had too low of a sensitivity (78%) to rule out PE in nonpregnant patients.[91,104]

Pregnant patients diagnosed with VTE in the ED should be anticoagulated with low-molecular-weight heparin. In the case of massive PE, options include systemic fibrinolysis, catheter-directed fibrinolysis, or the use of cardiopulmonary venoarterial extracorporeal membrane oxygenation. Current literature suggests a >80% probability of survival of both mother and fetus with the use of systemic fibrinolytics in the setting of massive PE.[105] For additional discussion, see Chapter 99, "Comorbid Disorders in Pregnancy."

ISOLATED SUBSEGMENTAL PULMONARY EMBOLISM

Isolated subsegmental PE is a filling defect seen in one small pulmonary artery, usually <3 mm in diameter and in the absence of DVT; radiologists often do not agree when viewing these images separately. The optimal treatment of subsegmental PE remains uncertain. Pooled data suggest that patients without high risk of recurrence (e.g., prior unprovoked VTE, active cancer, or other major active risk factor) may not benefit from anticoagulation.[106] However, no randomized trial has been performed to test this hypothesis. The author's choice is to treat subsegmental PE as an outpatient with apixaban or rivaroxaban and check a D-dimer in 1 month and, if normal, stop anticoagulation. It is best to discuss the risks and benefits of treatment of subsegmental PE with patients and their physicians to help make the best decision about anticoagulation.

CANCER PATIENTS WITH VENOUS THROMBOEMBOLISM

Current data and guidelines recommend treatment of patients with active cancer with low-molecular-weight heparin for at least 6 months.[107] One randomized trial suggested that rivaroxaban can be used in patients with active cancer, with a reduction in VTE recurrence but increased risk of bleeding.[108]

REFERENCES

The complete reference list is available online at www.TintinalliEM.com.

CHAPTER 57

Systemic Hypertension

Brigitte M. Baumann

INTRODUCTION AND EPIDEMIOLOGY

Hypertension affects approximately 40% of the U.S. population, and 1% to 6% of all ED patients present with severe hypertension.[1-5] Of the latter, between one quarter and one half will have end-organ damage.[2-5] Risk factors for the development of acute hypertensive events include obesity, cigarette smoking, older age, lack of access to health care, and noncompliance with antihypertensive medications.[6]

Chronic hypertension is categorized into three classifications: prehypertension, stage 1 hypertension, and stage 2 hypertension (**Table 57-1**).[7]

Hypertensive crisis is an acute elevation of blood pressure, where the systolic blood pressure is >180 mm Hg and/or the diastolic blood pressure is >120 mm Hg. There are two forms of hypertensive crisis.

Hypertensive emergency is a hypertensive crisis (systolic blood pressure >180 mm Hg and/or diastolic blood pressure >120 mm Hg) *with concomitant* end-organ damage; the targeted end organs include the brain, heart, aorta, kidneys, or eyes (**Table 57-2**).[7]

Hypertensive urgency is a controversial term—some believe it does not exist distinctly apart from severe hypertension—denoting a marked and acutely elevated blood pressure *without* acute or worsening target organ dysfunction.[7] Often, an arbitrary blood pressure of >180/120 mm Hg is cited as an indication for rapid pharmacologic intervention (typically parenteral) to reduce blood pressure within hours. There is no clinical

TABLE 57-1 Categories of Blood Pressure in Adults*

BP Category	Systolic BP (mm Hg)		Diastolic BP (mm Hg)
Normal	<120	*and*	<80
Elevated	120–129	*and*	<80
Hypertension			
Stage 1	130–139	*or*	80–89
Stage 2	≥140	*or*	≥90

Abbreviation: BP = blood pressure.

**Data adapted from:* 2017 High Blood Pressure Clinical Practice Guideline: Executive Summary, where BP is based on an average of ≥2 careful readings obtained on ≥2 occasions.[7]

benefit of such treatment (hence the concern about the term *urgency*), and precipitous drops in blood pressure can be harmful.[7-9] Current recommendations for patients with hypertensive urgency are reinstitution or intensification of oral antihypertensive therapy and prompt outpatient follow-up.[7] Gradual blood pressure reduction should occur over days to weeks.

TABLE 57-2 Hypertensive Emergencies

Diagnostic Category	Signs and Symptoms	Evidence of Acute End-Organ Damage
Acute aortic dissection	Chest pain, back pain Unequal blood pressures (>20 mm Hg difference) in upper extremities	Abnormal CT angiogram of chest and abdomen/pelvis or transesophageal echocardiogram of the aorta
Acute pulmonary edema	Shortness of breath	Interstitial edema on chest radiograph
Acute myocardial infarction	Chest pain, nausea, vomiting, diaphoresis	Changes on ECG or elevated levels of cardiac biomarkers
Acute coronary syndrome	Chest pain, nausea, vomiting, diaphoresis	Clinical diagnosis, changes on ECG, or elevated levels of cardiac biomarkers
Acute renal failure	May have systolic or diastolic abdominal bruit	Elevated serum creatinine level, proteinuria
Severe pre-eclampsia, eclampsia	Seizures, shortness of breath, headache, or vision abnormalities (blurred vision, flashing lights, scotomata)	Proteinuria (no longer required for the diagnosis of preeclampsia), low platelet count, renal insufficiency, elevated liver enzyme levels, pulmonary edema
Hypertensive retinopathy	Blurred vision	Retinal hemorrhages and cotton-wool spots (**Figure 57-1**), hard exudates, and sausage-shaped veins
Hypertensive encephalopathy	Altered mental status, nausea, vomiting, headache	May see papilledema or arteriolar hemorrhage or exudates on funduscopic examination, may note cerebral edema with a predilection for the posterior white matter of the brain on MRI
Subarachnoid hemorrhage	Headache, focal neurologic deficits	Abnormal CT of the brain; red blood cells on lumbar puncture
Intracranial hemorrhage	Headache, new neurologic deficits	Abnormal CT of the brain
Acute ischemic stroke	New neurologic deficits	Abnormal MRI or CT of the brain
Acute perioperative hypertension	Bleeding unresponsive to direct pressure	Clinical diagnosis; manifestations of other hypertensive emergencies
Sympathetic crisis*	Anxiety, palpitations, tachycardia, diaphoresis	Clinical diagnosis in the setting of sympathomimetic drug use (i.e., cocaine or amphetamines) or pheochromocytoma (24-h urine assay for catecholamines and metanephrine or plasma fractionated metanephrines)

*In this syndrome, acute end-organ dysfunction may not be measurable, but complications affecting the brain, heart, or kidneys may occur in the absence of acute treatment.

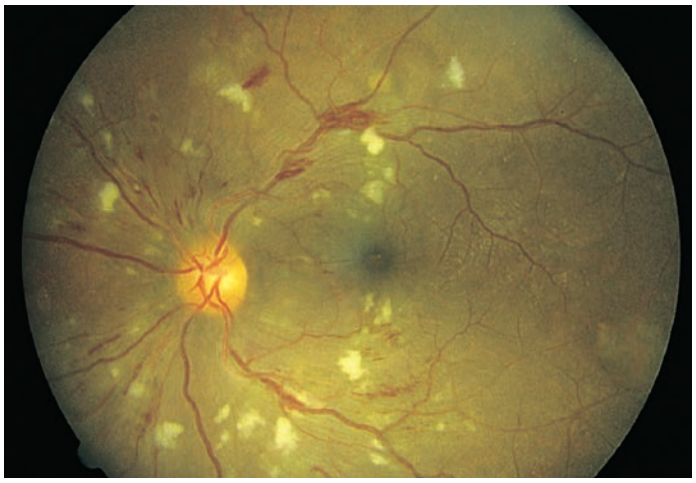

FIGURE 57-1. Hypertensive retinopathy. Scattered flame (splinter) hemorrhages and cotton-wool spots (nerve fiber layer infarcts) in a patient with headache and a blood pressure of 234/120 mm Hg.

PATHOPHYSIOLOGY

At baseline, chronic hypertensive patients have biochemical and structural changes in the arterial walls that shift the vascular autoregulatory curve, requiring higher arterial pressures to maintain end-organ blood flow, notably in the brain.[10-12] Eventually, the ability to adapt is passed. The resultant mechanical wall stress and endothelial injury lead to increased permeability and hyperperfusion of the cerebral, cardiac, and renal vascular beds. This may be followed by activation of the coagulation cascade and platelets, and deposition of fibrin results in fibrinoid necrosis of the arterioles. Clinically, this produces hematuria (involvement of the renal vasculature), arterial hemorrhages, or exudates on funduscopic examination.[12] Further contributing to the damage are prostaglandins, free radicals, cytokines, and mitogenic, chemoattractant, and proliferation factors, causing endothelial damage, smooth muscle proliferation, and thrombosis.[10,12] The renin-angiotensin system may also be activated, which leads to vasoconstriction. Pressure natriuresis occurs, leading to volume depletion, prompting additional release of vasoconstrictors from the kidney. These combined effects produce hypoperfusion, ischemia, and dysfunction of end organs. Endothelial dysfunction from such crises can persist for years after the acute event.[13]

CLINICAL FEATURES

Measure blood pressure in both arms in a narrow time interval while the patient is quietly resting. Check blood pressure several times before starting antihypertensive therapy. Blood pressure differences between extremities can result from aortic dissection, coarctation, peripheral vascular disease, and some unilateral neurologic and musculoskeletal abnormalities. Interarm blood pressure differences exist in some normal individuals, particularly the elderly, due to the loss of vascular elasticity or asymmetrical atheromatous narrowing of subclavian or brachial arteries. Although no guidelines regarding blood pressure disparities exist, an interarm difference >10 to 20 mm Hg is meaningful and increases long-term risks of cardiovascular events and mortality.[14,15] **When an interarm blood pressure difference is detected, treat the higher blood pressure and ensure that subsequent measurements are made on the same arm.**[15] Avoid wrist oscillometric devices as these give lower readings than upper arm measurements.[16]

A modest drop (up to 12 mm Hg) in systolic and diastolic blood pressures can occur absent therapy in patients presenting with elevated blood pressures. Conversely, do not discount a diagnosis of hypertensive

TABLE 57-3 Specific Diseases Associated With Elevated Blood Pressures

Disease	Threshold Value Raising Risk	% of Patients With Elevated Pressures
Subarachnoid hemorrhage[19]	≥140 mm Hg SBP	100%
Ischemic stroke[19,20]	≥140 mm Hg SBP	77%–82%
	≥160 mm Hg SBP	47%–54%
Intracerebral hemorrhage[19]	≥140 mm Hg SBP	75%
	≥160 mm Hg SBP	27%
Type B aortic dissection[21,22]	≥140 mm Hg SBP or ≥90 mm Hg DBP	67%–77%
Type A aortic dissection[23]	>150 mm Hg SBP	36%–74%
Acute heart failure[24,25]	>140 mm Hg SBP	52%–54%
NSTEMI-ACS[24,26]	≥140 mm Hg SBP	57%–59%
	≥160 mm Hg SBP	31%

Abbreviations: DBP = diastolic blood pressure; NSTEMI-ACS = non–ST-segment elevation myocardial infarction acute coronary syndrome; SBP = systolic blood pressure.

emergency in patients with no prior history of elevated blood pressure[17,18] because up to 16% have no history of hypertension.[4]

Table 57-3 lists the proportion of patients who present with elevated blood pressure by stroke subtypes, aortic dissection subtypes, heart failure, and acute coronary syndrome. Although elevations in blood pressure accompany most of these presentations, note that **severe** elevations of blood pressure are *far less common* in presentations typically labeled as hypertensive emergencies.

CHEST PAIN AND SEVERE HYPERTENSION

Rapid identification of acute aortic dissection is critical because delays in management increase mortality. Differentiating aortic dissection from the more common acute coronary syndromes is imperative given that blood pressure control differs in these two disorders and anticoagulation can prove catastrophic in acute aortic dissection.[27]

Acute aortic dissection presents with abrupt, sudden onset of pain, usually in the chest, often described as tearing or ripping, and radiating to the interscapular region[22,23,28-30] (see Chapter 59, "Aortic Dissection and Related Aortic Syndromes," for more discussion).

ACUTE NEUROLOGIC SYMPTOMS AND SEVERE HYPERTENSION

Elevated blood pressure, headache, and focal neurologic deficits are associated with either ischemic or hemorrhagic strokes (see Chapter 167, "Stroke Syndromes") (**Figure 57-2**).

Hypertensive encephalopathy is a clinical diagnosis made after excluding focal ischemia or bleeding. Patients with this condition have altered mental status, headache, vomiting, seizures, or visual disturbances, and most patients will have papilledema. When MRI findings demonstrate reversible edema that is predominantly posterior (occipital), the **posterior reversible encephalopathy syndrome** (**Figure 57-3**) exists, which carries a poor prognosis.

ACUTE RENAL FAILURE, PERIPHERAL EDEMA, AND SEVERE HYPERTENSION

Patients with new-onset renal failure may have peripheral edema, oliguria, loss of appetite, nausea and vomiting, orthostatic changes, or confusion. However, some patients have few or no specific symptoms (see Chapter 88, "Acute Kidney Injury"). Elevated serum creatinine confirms the diagnosis, and urinary sediment is also abnormal.

PREECLAMPSIA AND ECLAMPSIA

Preeclampsia presents with elevated blood pressure (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg) on two occasions at least 4 hours apart in pregnant patients beyond the 20th week

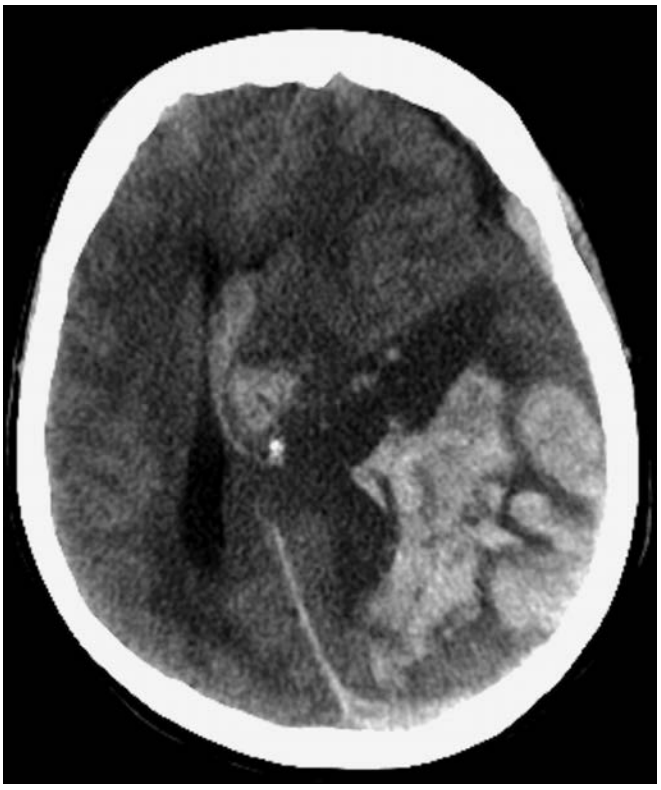

FIGURE 57-2. Intracerebral hypertensive hemorrhage. Noncontrast head CT scan with acute intraparenchymal hemorrhage, mass effect, midline shift, and intraventricular extension. [Image used with permission of Todd Siegal, MD.]

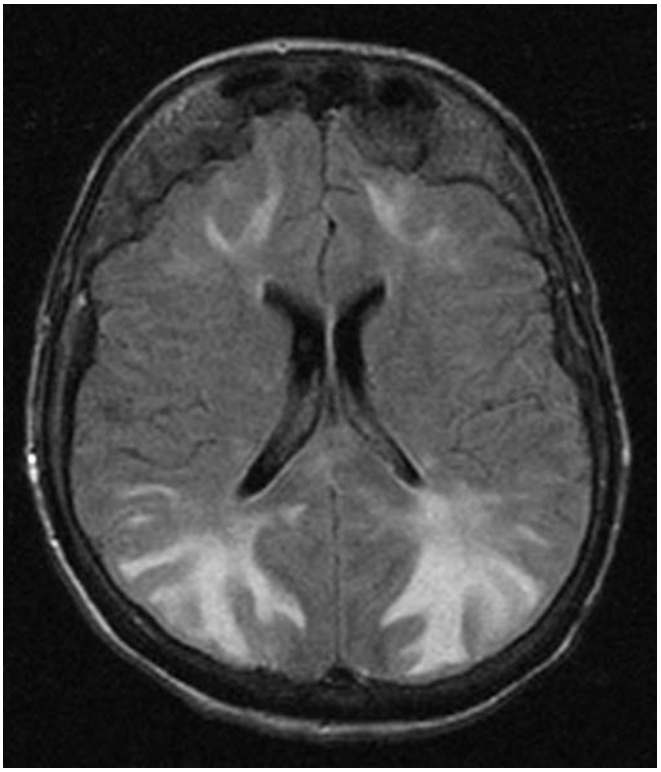

FIGURE 57-3. Axial fluid-attenuated inversion recovery MRI showing white matter hyperintensity in the occipital lobes bilaterally consistent with posterior reversible encephalopathy syndrome. The patient's confusion improved with blood pressure control. Repeat MRI after several days of therapy demonstrated remarkable improvement. [Image used with permission of Michael Farner, MD.]

of gestation. **Eclampsia** is the progression of preeclampsia to new-onset grand mal seizures in the absence of other neurologic conditions that could account for the seizure[31] (see Chapter 100, "Maternal Emergencies After 20 Weeks of Pregnancy and in the Peripartum Period").

SYMPATHETIC CRISIS AND SEVERE HYPERTENSION

There are four settings in which an excess of catecholamines can result in a hypertensive emergency. An acute catecholaminergic syndrome may occur with abrupt discontinuation of oral or transdermal **clonidine**. This withdrawal syndrome is potentiated by concomitant β-blocker therapy due to unopposed α-mediated vasoconstriction.

Pheochromocytoma is rare, and between 5% and 20% of tumors are malignant. Patients may experience life-threatening hypertension.[32] Signs and symptoms of pheochromocytoma include asymptomatic periods punctuated by episodic headache, elevated blood pressure, tachycardia, and diaphoresis.

Sympathomimetic drugs such as cocaine, amphetamines, phencyclidine hydrochloride, and lysergic acid diethylamide can precipitate a hypertensive emergency, with tachycardia, diaphoresis, chest pain, and mental status changes.[33] Patients receiving **monoamine oxidase inhibitors** who consume tyramine-containing foods may develop a hyperadrenergic state.[34]

Autonomic dysfunction due to spinal cord or severe head injury or abnormalities such as spina bifida may also present as a hypertensive emergency, with the diagnosis made clinically. Often, the associated blood pressure measurements are marginally elevated in this condition; do not let "near normal" values falsely exclude this diagnosis.

ASYMPTOMATIC PATIENTS WITH SEVERE HYPERTENSION

Formal recommendations for the *evaluation* of an ED patient presenting with asymptomatic but severe hypertension do not exist.[9] Commonly ordered tests include basic metabolic panel, ECG, chest radiograph, and urinalysis, but in the asymptomatic population, abnormal results attributable to acute hypertensive target organ injury are found in <6% of patients.[3,35] Until more data are available, base ED evaluation on the patient complaint, history, and review of systems, and perform selected testing.

TREATMENT

Patients presenting with a hypertensive emergency should be admitted to a critical care setting for continuous monitoring of blood pressure and target organ function. Use parenteral antihypertensive agents to reduce systolic blood pressure no more than 25% in the first hour; if stable, then reduce to 160/100 mm Hg over the next 2 to 6 hours and then to normal over the following 24 to 48 hours. Balance the reduction of blood pressure with avoidance of hypoperfusion of cerebral, coronary, and renovascular beds, which can exacerbate end-organ damage. **More aggressive blood pressure control is needed** for acute aortic dissection, pheochromocytoma crisis, severe preeclampsia or eclampsia, and acute intracerebral hemorrhage.[7] **Table 57-4** lists agents used in the management of hypertensive emergencies categorized by diagnosis. In selecting therapy, be familiar with the administration of the selected agent and establish a target range for blood pressure reduction.

AORTIC DISSECTION

The therapeutic goal in acute aortic dissection is a systolic blood pressure between 100 and 120 mm Hg and a heart rate ≤60 beats/min, ideally within the first hour of presentation.[7,22,36] The resultant reduction in tachycardia decreases the shearing forces and aortic wall stress, limiting the progression of the dissection.[36] Pain control with opioids helps decrease sympathetic tone.

ACUTE HYPERTENSIVE PULMONARY EDEMA

Tailor the treatment of hypertensive pulmonary edema to the underlying pathophysiology. Most patients have existing poorly controlled hypertension with cardiac remodeling and left ventricular hypertrophy, stiffness, and diastolic dysfunction. With an acute rise in blood pressure, there is an increase in afterload and a decrease in venous capacitance. This leads to fluid shifts from the splanchnic and peripheral vascular beds into the pulmonary circulation. Interventions that improve forward flow, via afterload reduction, tend to work better than diuresis. Other causes of acute hypertensive pulmonary edema include transient left ventricular systolic or diastolic dysfunction, acute dyssynchrony, or ischemic mitral regurgitation.[39] For these reasons, one must provide individualized management.

The mainstay of therapy is vasodilators, predominantly **nitrates**.[39] IV, sublingual, and topical nitrates reduce blood pressure, decrease myocardial oxygen consumption, and improve coronary blood flow.[39,40] If adding diuretics, be careful using loop diuretics in combination with **nesiritide** because together these might worsen renal function.[40,41,60] In patients with systolic dysfunction, IV **nicardipine** or clevidipine may help by increasing both stroke volume and coronary blood flow.[7,61,62]

ACUTE MYOCARDIAL INFARCTION

Patients presenting with severely elevated blood pressure and ischemic changes on ECG should be treated with sublingual or IV **nitrates**.[7,42,43] Currently, IV β-blockade is only recommended for patients presenting with severe hypertension. Oral β-blockade in patients presenting with ST-segment elevation myocardial infarctions and non–ST-segment elevation myocardial infarctions remains part of early care, but this route may not provide sufficient or rapid enough blood pressure control in a hypertensive emergency.[42,43]

ACUTE SYMPATHETIC CRISIS

Manage patients in acute sympathetic crisis due to either cocaine or amphetamines with an IV **benzodiazepine**, such as lorazepam or diazepam, to decrease adrenergic stimulation.[33,44] Monitor patients for respiratory depression and sedation. If benzodiazepines are not effective, add **nitroglycerin or phentolamine**. A calcium channel blocker can serve as a third-line agent.[42,44] β-blockers can result in unopposed α-blockade, which then can worsen coronary vasoconstriction and increase blood pressure.[44] If a β-blocker is selected, labetalol, due to its α-adrenergic blocking effects, should be used in conjunction with a vasodilator.[42]

IV phentolamine is the first-line agent for patients with pheochromocytoma and a hypertensive emergency. Intramuscular administration is an option if venous access is absent.[32] Second-line agents include clevidipine and nicardipine.[7] Phenoxybenzamine, a long-acting oral adrenergic α-receptor blocker, is used only in the preoperative setting in patients who are hypertensive but not in crisis.

Patients with monoamine oxidase inhibitor toxicity often respond to an IV benzodiazepine; if more therapy is needed, use phentolamine, nitroglycerin, or nitroprusside. Nitroglycerin is the preferred agent for these hypertension events associated with chest pain or cardiac ischemia. Monitor patients closely after reaching a targeted blood pressure because the hypertensive phase is often followed by a hypotensive one.

ACUTE RENAL FAILURE

Fenoldopam, nicardipine, and clevidipine are all suitable for acute hypertension-induced isolated renal failure, because they reduce systemic vascular resistance while preserving renal blood flow.[7] Fenoldopam improves natriuresis and creatinine clearance in patients with elevated blood pressure and impaired renal function.[45]

ECLAMPSIA AND PREECLAMPSIA

Obstetrical hypertensive emergencies can occur well below the blood pressure threshold for other hypertensive emergencies. Hydralazine and labetalol have good safety profiles in pregnancy. Another option is oral nifedipine.[31] (See Chapter 100, "Maternal Emergencies After 20 Weeks of Pregnancy and in the Peripartum Period," for further details.)

NEUROLOGIC EMERGENCIES

Hypertensive encephalopathy (defined as a change in sensorium or seizure from the blood pressure elevation) warrants rapid and uniform

TABLE 57-4 Treatment of Hypertensive Emergencies by Diagnosis

Diagnosis	Therapy Goals	Agents	Risks	Comments
Aortic dissection	Reduce shear forces by ↓ BP and PR Lower SBP to 100–120 mm Hg ↓ PR ≤60 beats/min[7,36]	**Esmolol*** IV bolus, then continuous infusion[7,36,37] OR **Labetalol*** IV bolus or continuous infusion[7,36,37] **Nicardipine** IV continuous infusion (after β-blocker)[7,38] **Nitroprusside** continuous infusion (after β-blocker)[7]	**β-blockers:** Respiratory distress in asthma, COPD patients; test dose of esmolol recommended, switch to diltiazem if esmolol intolerant	Measure BP in both arms and treat higher BP Always use β-blocker prior to vasodilators; nitroprusside alone increases wall stress from reflex tachycardia; cyanide and thiocyanate toxicity in patients with reduced renal function or therapy >24–48 h
Acute hypertensive pulmonary edema	Reduce BP by 20%–30%; diuresis through vasodilation; symptomatic relief[39]	**Nitroglycerin*** SL, topical, or IV continuous infusion[7,39,40] **Clevidipine** IV continuous infusion[7] **Nitroprusside** IV continuous infusion[7,39,40] **Enalaprilat** IV[40] **Nicardipine** IV continuous infusion[7] **Nesiritide** IV[41]	**ACE inhibitors**, can worsen renal function **ACE inhibitors:** Avoid hypotension and use with caution; some patients experience a negative inotropic effect **Nitroprusside:** Cyanide and thiocyanate toxicity in patients with reduced renal function or therapy >24–48 h	**IV nitrates** dilate capacitance vessels at low doses; higher doses dilate arterioles and lower BP Mixed outcomes (favorable and unfavorable) with **nesiritide**, with most recent ASCEND-HF trial showing no difference in dyspnea and mortality when compared to placebo[4]
Acute myocardial infarction	Reduce ischemia; avoid ≤25% reduction of MAP[7]	**Nitroglycerin*** SL, aerosol, or IV continuous infusion[7,42,43] **Esmolol*** IV continuous infusion[7] **Labetalol or metoprolol** IV bolus[7,42,43]	Do not give **nitrates** in patients who have taken phosphodiesterase inhibitors for erectile dysfunction ≤24 h for sildenafil and 48 h for tadalafil[42] Do not give **β-blockers** in CHF, low-output states, or other contraindications to β-blockers	**β-blockers:** Monitor for hypotension; consider RV infarct and volume depletion if this occurs SBP >180 mm Hg or DBP >110 mm Hg is a relative contraindication for thrombolytics[43]
Acute sympathetic crisis (cocaine, amphetamines, MAOI toxicity)	Reduce excessive sympathetic drive and symptomatic relief Aim for SBP <140 mm Hg in the first hour[7]	**Benzodiazepine*** IV bolus[33,44] **Nitroglycerin** SL, topical, or IV continuous infusion[42,44] **Phentolamine*** IV or IM[32] **Nicardipine or clevidipine** IV continuous infusion[7]	**Benzodiazepines** may induce respiratory depression; monitor patients closely **Labetalol** remains controversial, especially for cocaine-induced hypertension; if given, administer along with a nitrate[44]	**Benzodiazepines** are first-line agents for cocaine-induced hypertension **Phentolamine** is first-line therapy for pheochromocytoma **Calcium channel blockers** in cocaine-induced hypertension are considered third-line agents, after benzodiazepines and nitroglycerin[44]
Acute renal failure	Reduce BP by no more than 20% acutely	**Fenoldopam** IV continuous infusion[7,45] **Nicardipine** IV continuous infusion[7,45] **Clevidipine** IV continuous infusion[7]		Avoid **nitroprusside**, as it results in cyanide and thiocyanate toxicity Avoid **ACE inhibitors** acutely
Eclampsia, preeclampsia	Aim for SBP <140 mm Hg in the first hour[7]	**Hydralazine*** IV bolus[31] **Labetalol*** IV bolus[31] **Nifedipine*** oral[31]	**Hydralazine** can lead to reflex tachycardia and hypotension **Labetalol** may cause fetal bradycardia, and there is risk in patients with asthma, COPD, and heart failure **Nifedipine** may cause maternal tachycardia and overshoot hypotension	**Hydralazine, labetalol,** and **nifedipine** are all considered first-line agents. **Nifedipine** is ideal if IV access cannot be established **Contraindicated:** ACE inhibitors, ARBs, renin inhibitors, and nitroprusside
Hypertensive encephalopathy	Decrease MAP 20%–25% in the first hour of presentation[46]; more aggressive lowering may lead to ischemic infarction	**Labetalol** IV bolus or continuous infusion[7] **Nicardipine** IV continuous infusion[47] **Clevidipine** IV continuous infusion[47]	Avoid **β-blockers** in sympathetic crisis from drugs	Autoregulation of cerebral perfusion may be significantly impaired, so avoid rapid BP lowering to prevent cerebral hypoperfusion Do not give **nitroglycerin**[48] as it may worsen cerebral autoregulation
Subarachnoid hemorrhage	SBP <160 mm Hg to prevent rebleeding BP parameters have not yet been defined[49,50]	**Nicardipine** IV continuous infusion[49,51] **Labetalol** IV bolus, 10–20 milligrams IV, or continuous infusion[49,52] **Esmolol** IV bolus, then continuous infusion **Clevidipine** IV continuous infusion[49]	Avoid hypotension to preserve cerebral perfusion	**Nimodipine** is used to decrease mortality. BP control is not its primary goal, but some decrease in BP may be seen[49] **Clazosentan** is used with success in lieu of nimodipine and has similar hypotensive effects[53]

(*Continued*)

TABLE 57-4 Treatment of Hypertensive Emergencies by Diagnosis (*Continued*)

Diagnosis	Therapy Goals	Agents	Risks	Comments
Intracerebral hemorrhage	If SBP >220 mm Hg, consider aggressive management with IV infusion[54] If SBP 150–220 mm Hg, IV boluses of antihypertensive medications should be used to acutely lower SBP to 140 mm Hg[54]	**Labetalol** IV bolus or continuous infusion[52,55] **Nicardipine** IV continuous infusion[52,55] **Esmolol** IV bolus, then continuous infusion		Drops in SBP <150 mm Hg are not associated with increased morbidity[56] Early hemorrhage growth often occurs in first 6 h. Recent data suggest that at this time, aggressive BP control (SBP 130–139 mm Hg) diminishes hematoma growth, morbidity, and mortality[56-58]
Acute ischemic stroke, rtPA candidate (BP ≤185/110 mm Hg)	If fibrinolytic therapy planned, treat if BP remains >185/110 mm Hg after 3 measurements[59] The following antihypertensive recommendations (agents section) are for immediate BP control prior to reperfusion; BP management during and after reperfusion therapy is outlined in comments section	**Labetalol*** 10–20 milligrams IV over 1–2 min; may repeat once[55] **Nicardipine*** 5 milligrams/h IV infusion, titrate up by 2.5 milligrams/h every 5–15 min until desired BP is reached; maximum 15 milligrams/h[59] **Clevidipine*** 1–2 milligrams/h IV infusion, double the dose every 2–5 min until desired BP is reached; maximum 21 milligrams/h **Nitroprusside** may be used if BP is not controlled with above agents or DBP >140 mm Hg[59]	Excess BP lowering may worsen ischemia	**Management of BP during and after reperfusion therapy** If SBP >180–230 mm Hg or DBP >105–120 mm Hg, then consider: **Labetalol** 10 milligrams IV bolus followed by continuous IV infusion 2–8 milligrams/min **Nicardipine** 5 milligrams/h IV infusion, titrate up by 2.5 milligrams/h every 5–15 min to desired effect; maximum 15 milligrams/h **Clevidipine** 1–2 milligrams/h IV infusion; titrate up by doubling the dose every 2–5 min to desired effect; maximum 21 milligrams/h
Acute ischemic stroke, hypertension excludes reperfusion therapy	Treat if ≥220/120 mm Hg on third of 3 measurements, spaced 15 min apart; BP should be reduced by ~15% in the first 24 h[59] Early treatment of hypertension is indicated if required by other comorbid conditions (i.e., acute coronary syndrome, aortic dissection, preeclampsia/eclampsia). Lowering by 15% acutely is probably safe[59]	Same agents and doses as above acute ischemic stroke rtPA candidate	Be careful with BP control efforts in patients taking oral β-blockers or clonidine; antihypertensive withdrawal syndrome may occur.	Do not lower SBP by >15% in first 24 h[59] BP that is lower during the acute ischemic stroke than the premorbid pressure could be considered hypotension

Abbreviations: ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BP = blood pressure; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; DBP = diastolic blood pressure; MAP = mean arterial pressure; MAOI = monoamine oxidase inhibitor; PR = pulse rate; rtPA= recombinant tissue-type plasminogen activator; RV = right ventricular; SBP = systolic blood pressure; SL = sublingual.

*Preferred agents.

blood pressure reduction once other neurologic emergencies, notably ischemic or hemorrhagic stroke, are excluded.[46,63]

Management includes cessation of inciting agents, such as chemotherapy and immunosuppressants, and blood pressure control in hypertensive patients with IV nicardipine, clevidipine, labetalol, or fenoldopam.[7,47,64] Avoid nitroglycerin because it dilates cerebral arteries and alters both global and regional blood flow, which may worsen the autoregulation failure.[48]

The ideal targets for blood pressure control in subarachnoid hemorrhage and ischemic stroke are not clear and should be balanced to avoid worsening ischemia or rebleeding. For **subarachnoid hemorrhage**, recommended agents include IV labetalol, nicardipine, nitroprusside, and clevidipine, with no superior agent identified to date.[49] Oral nimodipine is a good choice for those with modest blood pressure elevations because it lowers blood pressure and reduces vasospasm and subsequent cerebral infarction rates, improving neurologic outcomes.[49,50,65] High-dose clazosentan can also decrease the incidence of vasospasm-related delayed ischemic neurologic deficits and has similar blood pressure–lowering effects as nimodipine.[53] If an anticonvulsant that can also reduce blood pressure is used, such as IV phenytoin or a benzodiazepine, be cautious with additional blood pressure reduction attempts.

The treatment of hypertension in patients with **intracerebral hemorrhage** includes labetalol, nicardipine, and esmolol.[52,55,66] Enalaprilat may also be used, but due to concerns of precipitous blood pressure drop, start with a smaller test dose (0.625 mg).[66] Lowering systolic blood pressures from >180 mm Hg to 130 to 160 mm Hg may improve clinical outcomes.[54-58]

In **ischemic stroke**, moderately elevated blood pressure may be beneficial in preserving cerebral perfusion of ischemic areas. Conversely, it may also worsen edema and contribute to hemorrhagic transformation. Ideal blood pressure ranges for ischemic stroke subtypes have not yet been determined. For the treatment of ischemic stroke, labetalol, nicardipine, and clevidipine are the recommended agents; however, the route and degree of blood pressure reduction depend on whether the patient is a candidate for reperfusion therapy (Table 57-4).[59] **Fibrinolytic therapy is contraindicated in patients with ongoing blood pressure >185/110 mm Hg *after* antihypertensive therapy**. In patients who maintain blood pressures ≤185/110 mm Hg (with or without antihypertensive therapy) and undergo fibrinolytic therapy, blood pressure goal is ≤180/105 mm Hg for the first 24 hours. Monitor blood pressure closely from the start of recombinant tissue plasminogen activator therapy for 24 hours.

PHARMACOLOGIC AGENTS

Parenteral agents used for hypertensive emergencies, including dosage, mechanisms, and warnings, are listed in Table 57-4 and **Table 57-5**. See Chapter 19, "Pharmacology of Antiarrhythmics and Antihypertensives," for detailed discussion of individual agents.

TABLE 57-5 IV Agents Used for Hypertensive Emergencies

Drug	Dosage	Mechanism/Comments	Warnings
β-Blockers			
Labetalol	Bolus: 10–20 milligrams (0.25 milligram/kg for an 80-kg patient) IV over 2 min; may administer 40–80 milligrams at 10-min intervals, up to 300 milligrams total dose. Continuous infusion: initially, 2 milligrams/min; titrate to response up to 300 milligrams total dose, if needed.	Combined selective α_1-adrenergic and non-selective β-adrenergic receptor blocker with an α- to β-blocking ratio of 1:7.[67] Effect in 2–5 min, peaking by 15 min, duration 2–4 h. Renal, cerebral, and coronary blood flow maintained; minimal placental transfer. **Safe in pregnancy.**	Avoid use in patients with bradycardia, greater than first-degree heart block, uncompensated cardiac failure, or active bronchospasm, and in patients receiving IV verapamil or diltiazem. Caution in patients with liver impairment (effects may be prolonged); the elderly have a less predictable response and more toxicity.
Esmolol	Loading dose: 250–500 micrograms/kg infused over 1–3 min IV, follow with: Maintenance infusion: 50 micrograms/kg/min IV over 4 min; if adequate effect not observed, repeat loading dose and increase infusion rate using increments of 50 micrograms/kg/min IV (for 4 min). This regimen can be repeated for 4 bolus doses and to an infusion rate of 300 micrograms/kg/min.	Ultra-short-acting, cardioselective, β-adrenergic receptor blocker. Onset within 60 s, duration 10–20 min. Ideal for use in patients at risk for complications from β-blockers, especially patients with mild to moderately severe left ventricular dysfunction or peripheral vascular disease. Duration 10–20 min; easily stopped.	Avoid use in patients with bradycardia, heart block, cardiogenic shock, decompensated cardiac failure, or active bronchospasm, and in patients receiving IV verapamil or diltiazem. Caution in patients with asthma, COPD, uncompensated cardiac failure; extravasation can lead to skin necrosis and sloughing; anemic patients will have a prolonged half-life, because drug is metabolized by red blood cell esterases.
Calcium Channel Blockers			
Nicardipine	Continuous infusion: start at rate of 5 milligrams/h. If target BP not achieved in 5–15 min, increase dose by 2.5 milligrams/h every 5–15 min until target pressure or the maximum dose of 15 milligrams/h is reached.	Second-generation dihydropyridine calcium channel blocker with vascular selectivity for the cerebral and coronary arteries. Onset of action is 5–15 min; duration is 1–4 h.	Avoid in patients with advanced aortic stenosis. Caution in decompensated heart failure. Avoid in patients receiving IV β-blockers. Common side effects are headache, hypotension, vomiting, and tachycardia.
Clevidipine	Continuous infusion: initiate infusion at 1–2 milligrams/h. Dose titration: double dose at short (90-s) intervals initially. As BP approaches goal, increase dose by less than doubling and lengthen time between dose adjustments to every 5–10 min. Maximum dose 32 micrograms/h; maximum duration is 72 h.	Very rapid onset and offset of effect due to its ultra-short half-life, approximately 2–4 min. Clevidipine is rapidly hydrolyzed to its inactive metabolite in blood and extravascular tissues. It exerts a selective vasodilating action on arteriolar resistance vessels but has no effect on venous capacitance vessels. Its metabolism is independent of the kidney or liver.	Cautions: Clevidipine contains approximately 0.2 gram of lipid per mL (2.0 kcal). Lipid restrictions may be necessary for patients with significant disorders of lipid metabolism. Clevidipine may produce hypotension and reflex tachycardia. Contraindicated in patients with severe aortic stenosis and egg or soy hypersensitivity. Use caution and lower doses in elderly.
Vasodilators			
Hydralazine	10 milligrams slow IV infusion (maximum initial dose is 20 milligrams). Repeat every 4–6 h as needed.	Potent direct arteriolar vasodilator with minimal effect on venous circulation. Onset begins at 10–30 min (can be sooner and precipitous); duration is 2–4 h. **Safe in pregnancy.**	Avoid in patients with myocardial ischemia, pulmonary edema, and aortic dissection. Reflex tachycardia increases myocardial demand.
Nitroglycerin	Sublingual: 0.4 milligram. Paste: 1–2 in. Continuous infusion: start 5 micrograms/min, increase by 5 micrograms/min every 3–5 min to 20 micrograms/min; if no response at 20 micrograms/min, increase by 10 micrograms/min every 3–5 min, up to 200 micrograms/min (note: many clinicians initiate with a higher infusion rate).	Potent venodilator and only affects arterial tone at high doses. Onset begins at 2 min; duration is 10–20 min (paste duration 3–4 h, unless removed). Reduces BP by reducing preload and cardiac output. Decreases coronary vasospasm and cardiac workload.	Avoid in cases of compromised cerebral and renal perfusion; avoid concurrent use (within past 24–48 h) with phosphodiesterase-5 inhibitors (sildenafil, tadalafil, or vardenafil). Caution: may cause hypotension with reflex tachycardia, which is exacerbated by volume depletion.
Nitroprusside	Continuous infusion: 0.3–0.5 microgram/kg/min IV initial infusion, increase in increments of 0.5 microgram/kg/min; titrate to desired effect. Rates >2 micrograms/kg/min may lead to cyanide toxicity. Use lowest possible dose. For infusions ≥4–10 micrograms/kg/min, institute a thiosulfate infusion.	Arterial and venous vasodilator due to its interaction with oxyhemoglobin to produce nitric oxide. It decreases preload and afterload. Onset of action is in seconds; duration is 1–2 min. Cerebral blood flow is decreased, whereas ICP is increased.	Avoid in patients with kidney or hepatic failure, arteriovenous shunts, hereditary optic nerve atrophy (increases nerve ischemia), or elevated ICP. Caution: intra-arterial monitoring is recommended; must be protected from light. Nitroprusside is recommended only when other agents fail. Coronary steal syndrome may occur.
Other Agents			
Phentolamine	Bolus load: 1–5 milligrams IV; may repeat every 10 min. Continuous infusion: 0.2–0.5 milligram/min.	α_1- and α_2-adrenergic blocking agent; effective for pheochromocytoma and hypercatecholaminergic-induced hypertension.	Myocardial infarction, cerebrovascular spasm, and cerebrovascular occlusion have occurred after administration.
Fenoldopam	Continuous infusion: start 0.1–0.3 microgram/kg/min, titrate by 0.05–0.1 microgram/kg/min every 15 min to desired BP. Maximum infusion rate: 1.6 microgram/kg/min.	Dopamine 1 receptor agonist. Onset of action in 5 min; peak effect at 15 min; duration 30–60 min. Metabolized by liver, without P450 system. Improves creatinine clearance, urine flow, and sodium excretion.	Caution: causes reflex tachycardia at higher dosages. Concurrent use of acetaminophen may increase fenoldopam levels. May cause flushing, dizziness, vomiting. Caution in patients with increased ocular pressures and ICP; caution in patients who have sulfite sensitivity (it is contained in a solution of sodium metabisulfite).

(*Continued*)

TABLE 57-5 IV Agents Used for Hypertensive Emergencies (*Continued*)

Drug	Dosage	Mechanism/Comments	Warnings
Enalaprilat	Bolus: 1.25 milligrams IV over 5 min every 4–6 h; titrate at increments of 1.25 milligrams every 12–24 h, with a maximum of 5 milligrams every 6 h.	Angiotensin-converting enzyme inhibitor. Test dose of 0.625 milligram recommended when concern for first-dose hypotension exists.[66] **AVOID in pregnancy.**	Avoid in pregnancy and those with myocardial ischemia or bilateral renal artery stenosis. Caution: first-dose hypotension is common, especially in high-renin states; may cause dizziness and headache.

Abbreviations: BP = blood pressure; COPD = chronic obstructive pulmonary disease; ICP = intracranial pressure.

β-BLOCKERS

Labetalol is unique among commonly used β-blockers because it also has modest selective α_1-inhibitory effects, with an α- to β-blocking ratio of 1:7.[67,68] It is recommended for nearly all hypertensive emergencies with the exception of cocaine intoxication and systolic dysfunction in association with decompensated heart failure. In the latter, nicardipine and clevidipine are preferred when nitroglycerin fails. Oral **metoprolol** use is common in patients presenting with acute coronary syndromes. Oral β-blockers improve survival, whereas mortality data are conflicting with IV formulations.[42,43] However, if blood pressure control is needed in a patient with acute coronary syndrome, use the IV formulation first, then change later. Esmolol has a short duration of action and is titratable, an advantage in patients at risk for the adverse effects of β-blockers, such as those with severe asthma and chronic obstructive pulmonary disease.

CALCIUM CHANNEL BLOCKERS

Clevidipine is a third-generation dihydropyridine calcium channel blocker with ultra-short-acting selective arteriolar vasodilator properties.[68-70] Its advantage is its ability to be titrated with a half-life less than a minute. **Nicardipine** has a rapid onset of action and can be titrated at 5- to 15-minute intervals. It is safe and effective in neurologic hypertensive emergencies and has a favorable effect on myocardial oxygen balance, increasing both stroke index and coronary blood flow. Compared to labetalol, nicardipine achieves physician-specified targeted blood pressure goals more often within 30 minutes of therapy.[67] Use **oral nifedipine** (10 milligrams) only in peripartum patients.[31]

VASODILATORS

Hydralazine is a potent vasodilator with a rapid onset of action that can have an unpredictable effect on blood pressure, which may not always be dose dependent. A potentially adverse effect is reflex tachycardia, which can worsen myocardial ischemia. Given the availability of other, more easily titratable agents, it is limited to pregnancy-related care. **Nitroglycerin** is a potent venodilator, showing arterial dilatation only at very high doses. Use may cause hypotension and reflex tachycardia, both worsened by the volume depletion characteristic of hypertensive emergencies. **Nitroglycerin is a first-line agent only in the treatment of heart failure and acute coronary syndromes** due to its favorable effects on coronary blood flow and cardiac workload.[7] Its hypotensive effects are due to its reduction of preload and cardiac output, which makes it a poor choice in other hypertensive emergencies.

Sodium nitroprusside is best used when other agents fail. It requires invasive monitoring to prevent "overshoot" in blood pressure control and has demonstrated higher mortality rates in cardiac surgery patients when compared to clevidipine.[7,71] Concerns about cyanide toxicity, heightened in patients with renal or hepatic insufficiency, and the potential for tachyphylaxis curtail use.[7] Combination therapy is the most common current use, as in aortic dissection patients who also receive esmolol to achieve blood pressure targets at lower doses.

OTHER AGENTS

Fenoldopam is a unique peripheral dopaminergic-1 receptor agonist, and due to its ability to promote diuresis, natriuresis, and creatinine clearance, it is useful in renal hypertensive emergencies.[68] **Phentolamine** is used successfully in cocaine-, amphetamine-, and pheochromocytoma-related hypertensive emergencies and also to counteract soft tissue catecholamine injection extravasation and ischemia (by injecting in the same area).[32,68,72] **Enalaprilat**, the only available IV angiotensin-converting enzyme inhibitor, has special application in patients with heart failure or acute coronary syndrome, but monitor carefully because of first-dose hypotension.[66]

Clonidine, a central α_2-agonist, generally does not have a role in the treatment of patients with hypertensive emergencies except for those who have recently stopped taking the drug. The resultant rebound hypertension may be difficult to control with other agents. When used, 0.2-0.3 mg PO clonidine is a common start, with blood pressure reduction starting within 30 to 60 minutes and peaking at 2 to 4 hours.[68] In patients who are unable to take oral medications, a clonidine patch for dermal delivery is an option, although the onset of action may be delayed by 2 to 3 days and titration is challenging. For maximum absorption, apply the patch to the chest or upper arm.[68,73] Although abrupt cessation of either clonidine or a β-blocker may result in rebound hypertension, clonidine withdrawal tends to be more severe and often will not respond to therapy without reinstitution.

TREATMENT OF ASYMPTOMATIC SEVERE HYPERTENSION

Acute treatment of asymptomatic severe hypertension does *not* prevent or reduce short-term patient morbidity or mortality.[8] However, uncorrected hypertension is associated with an eventual increased risk of cardiovascular events and renal dysfunction.[74] In addition, if severe hypertension is not addressed in the ED setting, patients may not seek further outpatient blood pressure management. These considerations support initiating outpatient blood pressure reduction regimens prior to ED discharge. **Table 57-6** lists oral agents commonly used for hypertension. The drugs listed are chosen for their relatively rapid onset of action and their potential use for ongoing control of chronic hypertension. Choosing an agent that can be used once daily and is inexpensive is often an ideal plan (e.g., generic hydrochlorothiazide, started at 25 milligrams daily). If choosing an angiotensin-converting enzyme inhibitor or angiotensin II receptor antagonist, check the patient's creatinine and potassium first.

DISPOSITION AND FOLLOW-UP OF ASYMPTOMATIC HYPERTENSION

Table 57-7 provides a summary of the 2017 blood pressure management recommendations from the American Heart Association.[7] Although the American Heart Association recommendations are comprehensive, they fall short of providing common ED guidance and management of patients who present with severe hypertension with no prior history of hypertension. In all cases, reinforce the need for outpatient follow-up, with or without ED-initiated oral therapy, even if elevated blood pressure was not part of the chief complaint.[7,75]

Table 57-8 lists indications for recommended oral antihypertensive classes based on trial data and consensus guidelines.[7,75]

Be sure to inform patients about potential adverse effects when prescribing an antihypertensive medication. The most common side effects stratified by drug class are provided in **Table 57-9**. Pediatric regimens are in **Table 57-10**; start these in close consultation with a pediatrician.

TABLE 57-6 Oral Agents for Hypertensive Urgencies

Agent	Mechanism of Action	Dosage	Onset of Action	Duration	Contraindications	Adverse Effects
Carvedilol	α_1-, β-Adrenergic blocker	6.25 milligrams PO	30–60 min	7–10 h	Asthma, chronic obstructive pulmonary disease, bradycardia, heart block, heart failure, hepatic impairment	Hypotension, bradycardia, syncope, dizziness
Labetalol	α_1-, β-Adrenergic blocker	200–400 milligrams PO, repeat every 2–3 h	30–120 min	6–12 h	Asthma, chronic obstructive pulmonary disease, bradycardia, heart block, heart failure	Bronchoconstriction, bradycardia, hyperkalemia
Metoprolol	β-Adrenergic blocker	50 milligrams PO	Oral (IR): ≤1 h	3–4 h	Asthma, chronic obstructive pulmonary disease, bradycardia, heart block, heart failure	Bronchoconstriction, bradycardia, heart block, weight gain, hyperglycemia
Captopril	Angiotensin-converting enzyme inhibitor	12.5–25 milligrams PO	15–30 min	4–6 h	Renal artery stenosis, pregnancy	Acute renal failure, angioedema, side effect of chronic cough
Losartan	Angiotensin II antagonist	50 milligrams PO	60 min	12–24 h	Second and third trimesters of pregnancy	Allergic reaction (rare)
Hydrochlorothiazide **Ideal first choice medication in most patients, but onset of action is delayed**	Thiazide diuretic	25 milligrams PO	2 h; peak effect at 4 h	24 h	Renal insufficiency, pregnancy Caution in diabetics; may raise glucose levels	Hypokalemia, dehydration, increased uric acid levels (may precipitate gout attacks)
Nifedipine (extended release) **Indicated for preeclampsia only**	Calcium channel blocker	10 milligrams PO, may repeat every 30–60 min	5–15 min	3–6 h	Angina, acute hypertension	Myocardial infarction, cerebrovascular accident, syncope, heart block, CHF
Clonidine **Primary indication for rebound hypertension**	Central α_2-agonist	0.1–0.2 milligram PO	30–60 min	6–8 h	CHF, second- or third-degree heart block Would not recommend as a new or singular antihypertensive agent	Drowsiness, sedation, tachycardia, dry mouth

Abbreviation: CHF = congestive heart failure; IR = immediate release.

TABLE 57-7 Recommended Treatment Protocol for ED Patients With Increased Blood Pressure (BP)*

SBP (mm Hg)		DBP (mm Hg)	Follow-Up/Treatment
130–139	*or*	80–89 AND ASCVD† risk <10%	Lifestyle modification and outpatient follow-up
130–139	*or*	80–89 AND ASCVD† risk ≥10%	Lifestyle modification; initiate antihypertensive; follow-up in <1 month
140–179	*or*	>90–109	Lifestyle modification; initiate antihypertensive therapy (ideally 2 agents); follow-up in <1 month
≥180	*or*	≥110	Evaluation for target organ damage; initiate lifestyle modification and antihypertensive therapy (ideally 2 agents); prompt outpatient follow-up (within a week)

Abbreviations: ASCVD = atherosclerotic cardiovascular disease; DBP = diastolic blood pressure; SBP = systolic blood pressure.

*To assess 10-year risk, please refer to http://tools.acc.org/ASCVD-risk-estimator/.

†Use the lowest values for cholesterol, if unknown, to obtain a conservative risk value.

Data adapted from: Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.[7]

TABLE 57-8 Indications for Specific Antihypertensive Therapy

	Heart Failure	Post–Myocardial Infarction	High Coronary Artery Disease Risk	Recurrent Stroke Prevention	Diabetes	Chronic Kidney Disease
Blood pressure goal	<130/80 mm Hg	<130/80 mm Hg	<130/80 mm Hg	<140/90 mm Hg	<130/80 mm Hg	<130/80 mm Hg
First-line therapy	Diuretic with ACE inhibitor	β-Blocker, ACE inhibitor or ARB	β-Blocker, calcium channel blocker (if angina pectoris)	Thiazide diuretic with ACE inhibitor or ARB	Nonblack: Thiazide diuretic, ACE inhibitor, ARB, or CCB Black: Thiazide diuretic or CCB	ACE inhibitor or ARB
Second-line therapy	β-Blocker	Aldosterone antagonist	ACE inhibitor, calcium channel blocker, or diuretic	—	Above alone or in combination	Above alone or in combination with other drug class

Abbreviations: ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CCB = calcium channel blocker.

Data adapted from: Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.[7]

TABLE 57-9 Common Adverse Effects of Antihypertensive Drugs

Antihypertensive Class	Recommended Ancillary Testing Before Therapy	Most Common Adverse Effects
Diuretic	Chemistry panel: renal function and electrolytes	Hypokalemia, hypomagnesemia, hyperglycemia, hypercalcemia, hyperuremia, hyponatremia
Angiotensin-converting enzyme inhibitor	Chemistry panel: renal function and electrolytes Pregnancy test	Cough, hyperkalemia, acute renal failure, angioedema, myopathy, fetal abnormalities
Angiotensin receptor blocker	Chemistry panel: renal function and electrolytes Pregnancy test	Hyperkalemia, acute renal failure, angioedema, myopathy, fetal abnormalities
β-Blocker	ECG	Bronchospasm, bradycardia, depression, erectile dysfunction
Calcium channel blocker	ECG	Bradycardia, constipation, lower extremity edema
Aldosterone antagonist	Chemistry panel: renal function and electrolytes Pregnancy test	Hyperkalemia, gynecomastia, feminization of male fetuses

TABLE 57-10 Agents for Severely Hypertensive Pediatric Patients With Life-Threatening Symptoms

Agent	Dosage	Indications/Comments/Cautions
Esmolol	100–500 micrograms/kg/min IV infusion	Typically used in perioperative cardiac patients Risk of bradycardia
Hydralazine	0.1–0.2 milligram/kg per dose IV or IM; up to 0.4 milligram/kg per dose	Likely the most commonly used agent; caution with inadvertent overshooting of BP reduction Risk of tachycardia Give every 4 h if given as bolus
Labetalol	IV bolus: 0.2–1.0 milligrams/kg per dose; up to 40 milligrams per dose Infusion: 0.25–3.0 milligrams/kg/h	Rapid onset if given IV (2–5 min) Avoid in asthma and heart failure Risk of hypotension in children <24 months and concomitant ischemic or traumatic brain injury
Nicardipine	IV bolus: 30 micrograms/kg up to 2 milligrams per dose Infusion: 0.5–4 micrograms/kg/min	May need central access to avoid thrombophlebitis Risk of tachycardia; increases cyclosporine and tacrolimus levels
Nitroprusside	Starting: 0–3 micrograms/kg/min Maximum: 10 micrograms/kg per min	Significant experience in pediatric population Risk of cyanide poisoning after >48 h or earlier in renal/liver dysfunction patients
Oral Agents for Severely Hypertensive Pediatric Patients With Less Significant Symptoms and No Target Organ Damage		
Clonidine	2–5 milligrams/kg per dose up to 10 milligrams/kg per dose given every 6–8 h (PO)	Often used in patients with chronic hypertension and those refractory to other agents Risk of dry mouth, drowsiness
Fenoldopam	0.2–0.5 milligram/kg/min up to 0.8 milligram/kg/min IV infusion	Higher doses may lead to tachycardia without much more BP reduction
Hydralazine	0.25 milligram/kg per dose up to 25 milligrams per dose given every 6–8 h (PO)	Half-life varies with genetically determined acetylation rates
Isradipine	0.05–0.1 milligram/kg per dose up to 5 milligrams per dose given every 6–8 h (PO)	Exaggerated BP decrease in patients receiving azole antifungal agents
Minoxidil	0.1–0.2 milligram/kg per dose up to 10 milligrams per dose given every 8–12 h (PO)	Most potent oral vasodilator; long acting

Abbreviation: BP = blood pressure.

Data adapted from: Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents.[76-79]

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The complete reference list is available online at www.TintinalliEM.com.

CHAPTER 58

Pulmonary Hypertension

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INTRODUCTION AND EPIDEMIOLOGY

The pulmonary vascular system is normally a high-flow, low-resistance circuit, with a mean pulmonary arterial pressure that constitutes approximately 15% to 20% of the systemic circulation.[1] Normal pulmonary arterial systolic pressures range from 15 to 30 mm Hg, and diastolic pulmonary arterial pressures range from 4 to 12 mm Hg.[1] Pulmonary hypertension exists when a mean pulmonary arterial pressure is >25 mm Hg at rest or >30 mm Hg during exertion.[1,2]

Pulmonary hypertension classification uses measurements of pulmonary arterial pressure, pulmonary vascular resistance, and pulmonary capillary wedge pressure (**Table 58-1**).[1,3] Although echocardiography estimates pulmonary arterial pressure in a patient with suspected pulmonary hypertension, definitive diagnosis requires right heart catheterization.

Patients with group 1 pulmonary arterial hypertension have a mean pulmonary arterial pressure >25 mm Hg, a pulmonary vascular resistance >240 dynes/s/cm^5, and a pulmonary capillary wedge pressure <15 mm Hg.[2] Group 2 disease is caused by left heart disease and is the most common etiology.[2] Group 3 occurs with chronic hypoxemic lung disease. Chronic thromboembolic pulmonary hypertension, group 4, develops in up to 4% of patients with thromboembolic disease.[4-6] Regardless of the cause, pulmonary hypertension is associated with high rates of morbidity and mortality,[4,7] with a 5-year death rate for patients with idiopathic pulmonary arterial hypertension exceeding 30%.[8]