

Severely Increased Blood Pressure in the Emergency Department

Philip H. Shayne, MD
Stephen R. Pitts, MD, MPH

*From the Department of
Emergency Medicine, Emory
University School of Medicine,
Atlanta, GA.*

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See commentary, p. 530.

Patients with severely increased blood pressure often present to the emergency department. Emergency physicians evaluate and treat hypertension in various contexts, ranging from the compliant patient with well-controlled blood pressure to the asymptomatic patient with increased blood pressure to the critically ill patient with increased blood pressure and acute target-organ deterioration. Despite extensive study and national guidelines for the assessment and treatment of chronically increased blood pressure, there is no clear consensus on the acute management of patients with severely increased blood pressure. In this article, we examine the broad spectrum of disease, from the asymptomatic to critically ill patient, and the dilemma it creates for the emergency physician in deciding how and when in the process to intervene.

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INTRODUCTION

Is severely increased blood pressure an emergency? Patients with severely increased blood pressure often present to the emergency department.¹⁻⁴ Emergency physicians evaluate and treat hypertension in a variety of contexts, ranging from the compliant patient with well-controlled blood pressure to the asymptomatic patient with increased blood pressure to the critically ill patient with increased blood pressure and acute target-organ deterioration. Despite extensive study and national guidelines for the assessment and treatment of increased blood pressure,⁵ there is no clear consensus on the acute management of patients with severely increased blood pressure. The broad spectrum of disease, from asymptomatic to critically ill, creates a dilemma for the emergency physician in deciding how and when in the process to intervene.

MANAGEMENT DILEMMAS

The following fictional case highlights the difficulties in the management of hypertension in the ED. A 50-year-old man with a long history of hypertension presents to the ED with the complaints of headache and malaise for 2 days. He has not taken his antihypertensive medications in more than a year and does not remember their names. His physical examination is remarkable only for a persistent blood pressure of 210/120 mm Hg and grade I retinopathy. Questions for the emergency physician include the following: Is this patient stable? Is further workup indicated, and if so, what? Does the patient require immediate intervention, and if so, what should be done? Does the patient require admission or monitoring, or if discharged, how soon should he be seen in follow-up?

The emergency physician functions to both stabilize acute disease and to assess the potential for further deterioration. Stabilization might require immediate reduction of severely increased blood pressure to arrest the progressive deterioration of brain, heart, or kidney function by using the broad range of pharmacologic agents and treatment options available. Assessing the potential for deterioration involves knowledge of the near-term

risk to the patient from increased blood pressure balanced against the risks, benefits, and costs of initiating therapy. It has been firmly established that prolonged and severely increased blood pressure causes cerebral, cardiovascular, and renal disease and that both morbidity and mortality can be improved with treatment.^{6,7} But what is the implication of an isolated episode of high blood pressure during an unplanned visit to the ED? Rapidly decreasing blood pressure might cause more harm than good.⁵ In our scenario, can a patient who has been out of his medication for a year wait a few more days to see a primary care provider who will be making the long-term management decisions? Or is there an unacceptable risk to the patient of having an adverse event within that time? Is that risk better managed by initiating outpatient medical therapy from the ED, by urgently decreasing the patient's blood pressure in the ED, or by admitting the patient for inpatient care?

The emergency physician also faces public health considerations. Although all patients should be encouraged to seek a primary care provider, for many, the ED is their only contact with the medical world.⁸ Because many in the general population have inadequately treated hypertension,⁹ an ED visit might be the only opportunity to emphasize their need for longitudinal care.

BACKGROUND

The importance of hypertension as a cause rather than a consequence of kidney disease was first championed by Mahomed of Guy's Hospital in London in 1879 on the basis of personal observations and intuitive arguments.¹⁰ Practical measurement of blood pressure by clinicians came after the invention of the now familiar pneumatic arm cuff by Riva-Rocci of Torino in 1896 and its subsequent adoption and popularization by the visiting American neurosurgeon Harvey Cushing.¹¹ The benefits of treating chronic hypertension were clearly identified by the historic placebo-controlled VA Cooperative Study published in 1967, showing that blood pressure-decreasing drugs markedly reduce cardiovascular morbidity and mortality.⁶ Recognition of the massive potential public health effect of treating this highly prevalent condition led to the creation of the federally

funded National High Blood Pressure Education Program in 1972. This program and other educational interventions led to a progressive increase in public awareness and treatment.⁵

The evidence base for treating chronic hypertension continues to evolve. One principle is that overall morbidity and mortality improve with treatment. The recent population-based Hypertension Optimal Treatment study of more than 19,000 patients randomized to varying intensities of treatment found that treatment benefit did not plateau until diastolic pressures as low as 83 mm Hg were achieved.¹² However, not all antihypertensive agents demonstrate consistent benefit across the spectrum of patients, and greater attention has been directed toward individualizing antihypertensive treatment on the basis of overall cardiac risk rather than treating absolute levels of blood pressure.^{5,13} For example, long-term use of nifedipine (not the extended-release preparation) was shown to increase the risk of myocardial infarction and probably all-cause mortality.^{14,15} In the Hypertension Optimal Treatment trial, however, there was no excess cardiac mortality with another calcium-channel blocker, felodipine.¹² Furthermore, the African American Study of Kidney Disease demonstrated that in black hypertensive patients with baseline proteinuria, the calcium-channel blocker amlodipine was significantly less effective than ramipril in protecting from further loss of renal function.¹⁶ In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, a randomized comparison of several initial treatment strategies, the doxazosin limb was dropped after an interim analysis because of increased cardiovascular events. This casts doubt on the relative safety of yet another category of antihypertensives, the central α -blockers.¹⁷ A recent systematic review concluded that β -blockers and diuretics are the only first-line antihypertensive drugs shown to clearly reduce the incidence of cardiovascular disease in patients with chronic hypertension.¹⁸

THE EVIDENCE BASE FOR MANAGEMENT OF HYPERTENSIVE CRISES

We searched the MEDLINE database since 1966 and found only 43 randomized trials indexed by the medical

subject heading “hypertension” combined with the text words “emergency/ies” or “crisis/es” in the title or abstract, excluding pregnancy-related and perioperative hypertension. Most of these trials compared antihypertensive drug regimens, including several trials that were dose-ranging studies. None of these studies used morbidity or mortality as the primary outcome, instead focusing either on blood pressure control itself or on future compliance with antihypertensive treatment. Safety was often cited as an outcome, but the median sample size was 45, ranging from 13 to 204, which is far too small to detect even very large differences in the rate of adverse events. If near-term adverse events occur in as many as 5% of patients with severe hypertension, a randomized trial of treatment with approximately 1,000 patients in each limb would be needed to demonstrate a reduction in relative risk by half, given conventional 5% α and 20% β error thresholds (Arcus Quickstat software, Biomedical version 1.1, build 137, StatsDirect, Sale, United Kingdom). If the baseline risk was as low as 1%, demonstrating the same reduction in risk would require 5,000 patients in each limb. These calculations assume that treatment of severe hypertension is beneficial, but similar projections apply if one assumes that immediate treatment results in net harm because the baseline event rate is probably low in either case. The Cochrane Database of Systematic Reviews has recently published their protocol for systematic analysis of the literature comparing pharmacologic interventions for hypertensive emergencies or urgencies, but the full review is not completed.¹⁹

In this review, we use evidence from understanding the pathophysiology of hypertension, identifying descriptive clinical studies, and assessing clinical experience rather than from large-scale randomized trials to provide clinical direction.

PATHOGENESIS

Uncontrolled chronic hypertension might complicate all facets of atherosclerotic vascular disease and shorten life expectancy by 10 to 20 years.²⁰ Hypertension primarily affects the heart, brain, kidneys, and large arteries, referred to as the “target organs.”

Most patients who present to the ED with increased blood pressure have chronic hypertension. Chronic hypertension results in a rightward shift of the pressure-flow autoregulation curve, which has best been described with cerebrovascular perfusion.²¹ When blood pressure decreases, cerebral vasodilation occurs, and when blood pressure increased, cerebral vasoconstriction occurs, so that cerebral perfusion pressure remains constant despite fluctuations in mean arterial pressure (MAP). In normal individuals, cerebral blood flow remains fairly constant for a MAP from approximately 60 mm Hg to up to 150 mm Hg. When the MAP decreased to less than the lower limits of autoregulation, the brain becomes hypoperfused and cerebral hypoxia occurs, with symptoms such as dizziness, nausea, and syncope. In chronically hypertensive individuals, the lower limit of autoregulation has increased, and autoregulation might fail at MAPs that are well tolerated in nonhypertensive individuals. This model suggests that chronically hypertensive patients cannot tolerate a rapid return to normal blood pressure. Indeed, there are reports of adverse outcomes with acutely decreasing the blood pressure in hypertensive patients by using short-acting nifedipine.²²⁻²⁵ The observation that the lower limit of the autoregulation curve tends to be approximately 25% of MAP has led to the general recommendation that the MAP be acutely decreased by no more than 20% to 25%.

JOINT NATIONAL COMMITTEE-VI GUIDELINES

Many clinicians rely on the National High Blood Pressure Education Program reports for guidance on hypertension management. The introduction to the most recent report explains “The purpose of the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI) is to provide guidance for *primary care clinicians* [emphasis added]. The committee recognizes that the responsible clinician’s judgment of the individual patient’s needs remains paramount. Therefore, this national guideline should serve as a tool to be adapted

and implemented in local and individual situations.”⁵ The JNC-VI is the sixth report of the National High Blood Pressure Education Program since it first published guidelines in 1972 and provides the most aggressive recommendations to date for reducing risk in hypertensive patients. The report stages hypertension by severity, identifies cardiovascular risk factors, and suggests treatment strategies on the basis of a combination of disease severity and end-organ risk. The most severe stage of hypertension (stage 3) is classified as a systolic blood pressure (SBP) of greater than 180 mm Hg or a diastolic blood pressure (DBP) of greater than 110 mm Hg (Table 1). The report makes recommendations for follow-up intervals on the basis of initial blood pressure measurements (Table 2) and suggests initial drug choices on the basis of the patient’s history (Figure 1). These recommendations might help emergency physicians develop appropriate discharge plans for a patient with an increased blood pressure. The benefits of antihypertensive therapy were clearly identified by the VA Cooperative Study, one of the few to compare placebo with drug treatment for hypertension in patients with DBPs of between 115 and 130 mm Hg. This study found that 27 (39%) of 70 patients treated with placebo and 2 (3%) of 73 patients treated with antihypertensive drugs experienced adverse events within 20 months (absolute risk reduction=36%, 95%

Table 1.
Classification of blood pressure for adults aged 18 years and older.*

Category	SBP, mm Hg		DBP, mm Hg
Optimal	<120	and	<80
Normal	<130	and	<85
High normal	130–139	or	85–89
Hypertension			
Stage 1 (mild)	140–159	or	90–99
Stage 2 (moderate)	160–179	or	100–109
Stage 3 (severe)	≥180	or	≥110

From the National High Blood Pressure Education Program.⁵

*Results are based on the average of ≥2 readings taken at each of ≥2 visits after an initial screening.

confidence interval [CI] 24% to 48%; number needed to treat=3, 95% CI 2 to 4).⁶

Unfortunately, the JNC-VI provides little guidance for the management of severely increased blood pressure in acute care settings. The JNC-VI recommendation for the follow-up of a patient with a high blood pressure (stage 3; ≥ 180 mm Hg systolic or ≥ 110 mm Hg diastolic) is to “evaluate or refer to source of care immediately or within 1 week depending on the clinical situation.” Brief recommendations suggest parenteral drugs for emergencies in which there is target-organ deterioration and oral medications for loosely defined urgencies. Of note is a statement placed in the JNC-VI in bold: “Elevated blood pressure alone, in the absence of symptoms or new or progressive target organ damage, rarely requires emergency therapy.”

STRATIFICATION OF HYPERTENSIVE CRISES

The presence or risk of progressive target-organ deterioration determines the urgency with which severely increased blood pressure needs to be controlled. Despite the common practice of treating severely increased blood pressure in asymptomatic ED patients, we find no evidence to support this approach. Any given person’s risk of a near-term complication of an increased blood pressure is multifactorial; age, chronicity of disease, rapidity of blood pressure increase, and type of previous

end-organ disease are more important considerations than the actual severity of hypertension. By convention, patients with DBPs of greater than 115 to 120 mm Hg or SBPs of greater than 180 mm Hg are categorized as having a hypertensive crisis.^{20,26-32} Despite the loose use of this term, many of these patients are not likely to experience a near-term adverse event, and therefore, the term “crisis” is misleading. We prefer the term “severely increased blood pressure” and suggest that clinical scenarios be stratified as “hypertensive emergencies,” “hypertensive urgencies,” and “uncontrolled severe hypertension.” Because there are no studies that clearly demonstrate sizable rates of near-term adverse events to validate these terms, our stratification is based on conventional wisdom rather than empiric data.

A hypertensive emergency involves rapid and progressive decompensation or damage of vital organ function caused by severely increased blood pressure. Hypertensive urgencies “are those situations in which it is desirable to reduce blood pressure within a few hours” (JNC-VI).⁵ Uncontrolled hypertension refers to the vast majority of patients with hypertension who need timely and appropriate long-term management but do not require acute intervention.

Table 2.
Recommendations for follow-up on the basis of initial blood pressure measurements for adults.

Initial Screening Blood Pressure, mm Hg		Follow-up Recommended
SBP	DBP	
<130	<85	Recheck in 2 y
130–139	85–89	Recheck in 1 y
140–159	90–99	Confirm in 2 mo
160–179	100–109	Evaluate or refer to a source of care within 1 mo
≥ 180	≥ 110	Evaluate or refer to a source of care immediately or within 1 wk depending on clinical situation

From the National High Blood Pressure Education Program.⁵

Figure 1.
Recommendations for initial antihypertensive drug therapy. ACE, Angiotensin-converting enzyme. From the National High Blood Pressure Education Program.⁵

Initial drug choices
Use unless contraindicated: start with a low dose of a long-acting once daily drug and titrate dose: low-dose combinations might be appropriate.

- Uncomplicated hypertension
 - Diuretics
 - β -Blockers
- Diabetes mellitus (type 1) with proteinuria
 - ACE inhibitors
- Heart failure
 - ACE inhibitors
 - Diuretics
- Isolated systolic hypertension (older persons)
 - Diuretics preferred
 - Long-acting dihydropyridine calcium antagonist
- Myocardial infarction
 - β -Blockers (without intrinsic sympathomimetic activity)
 - ACE inhibitors (with systolic dysfunction)

In practical terms, hypertensive emergencies are thought to require immediate (within 1 to 2 hours) decreasing of the blood pressure, hypertensive urgencies require initiation of a strategy to decrease and monitor the blood pressure over 24 to 48 hours, and uncontrolled severe hypertension should have therapy initiated to decrease blood pressure within a week. The difficulty arrives in determining where a given patient falls within this scheme because stratification often depends on outcome rather than initial presentation (eg, Was the chest pain really angina?). Another scheme for classifying severe hypertension by using plasma renin levels has been proposed, but this information is usually not available in the ED.³³ Thus, stratification involves a careful clinical evaluation and understanding of target-organ disease and treatment strategies.

A hypertensive emergency is the rapid decompensation of vital organ function caused by an inappropriate increased blood pressure requiring immediate blood pressure reduction. Physicians are less likely to encounter hypertensive emergencies in the current era of improved awareness, improved disease management, and widely accessible dialysis for renal failure. Figure 2 lists clinical situations consistent with hypertensive emergency.

There is little consensus on what constitutes a hypertensive urgency or even if such a condition exists. The term “hypertensive urgency” has been used to describe all patients with severely increased blood pressure (DBP >115 to 120 mm Hg), including those not having an acute event.²⁶ Increasingly, however, reliance on blood pressure measurement alone is considered inadequate.³⁴ The vast majority of ED patients found to have a very high blood pressure have no symptoms referable to hypertension and do not have rapidly progressive end-organ disease in the short term. The absolute risk of development of a myocardial infarction or stroke in the near term in such patients is small; the VA Cooperative Trial noted no adverse outcomes within the first 3 months among the 143 patients who had a DBP of between 115 and 130, irrespective of whether they received treatment or placebo (95% CI 0% to 2.55%).⁶

We propose that a better definition for hypertensive urgency is severely increased blood pressure in a patient at high risk for rapidly progressive end-organ damage but without evidence of new injury. In our opinion, high risk would include patients with a history of prior target-organ disease, such as congestive heart failure, unstable angina, coronary artery disease, renal insufficiency, transient ischemic attack, or stroke. Patients in this category should receive an increased level of scrutiny greater than that of most asymptomatic hypertensive patients. An increased level of care does not necessarily mean immediate treatment, admission, or both, but it does imply a heightened responsibility on the part of the emergency physician to develop a plan for blood pressure control. By convention, urgencies also encom-

Figure 2.

Scenarios considered as hypertensive emergencies when associated with an increased blood pressure.

Cerebrovascular

Hypertensive encephalopathy
Intracerebral hemorrhage
Subarachnoid hemorrhage
Atherothrombotic brain infarction with extreme hypertension

Cardiovascular

Acute aortic dissection
Acute left ventricular failure
Acute myocardial infarction or unstable angina
Accelerated-malignant hypertension
Symptomatic aortic aneurysm

Renovascular

Acute glomerulonephritis
Renal crises from collagen vascular disease
Severe hypertension after kidney transplantation

Catecholaminergic

Pheochromocytoma crisis
Food or drug interaction with monoamine oxidase inhibitors
Sympathomimetic drug use
Rebound hypertension after sudden cessation of antihypertensive drugs

Autonomic hyperreflexia after spinal cord injury

Eclampsia/preeclampsia

Surgical

Severe hypertension in patients requiring immediate surgery
Postoperative hypertension
Postoperative bleeding from vascular suture sites
After cardiac bypass surgery

Severe body burns

Severe epistaxis

pass patients with severe perioperative hypertension and the hypertensive pregnant patient without proteinuria or signs of preeclampsia.

As seen in the VA Cooperative Study, very few asymptomatic patients with markedly increased blood pressure will experience a near-term adverse event. Very high blood pressures might be seen in chronic hypertensive patients as a consequence of discontinuing prior therapy or as a result of other easily reversible causes, such as anxiety, pain, drug use, or dietary change. There is no evidence that the absolute level of a patient's blood pressure warrants immediate or aggressive treatment.

CLINICAL EVALUATION

The clinical evaluation should determine the nature, severity, and management of patients in hypertensive crisis. The JNC-VI guidelines recommend that patients with blood pressure persistently increased to 180/110 mm Hg or higher (JNC-VI stage 3) receive an "immediate or within a week evaluation."⁵ When such a patient presents to the ED, accurate measurement of blood pressure is the first step. Initially increased ED blood pressures frequently decrease spontaneously by the time a second reading is obtained. Most of the time this is not the result of reduced stress but of regression to the mean, a property of all extreme observations.³⁶ For this reason alone, interventions should be based on the composite of several separate blood pressure determinations in the ED. Taking an average of at least 2 blood pressure measurements reduced the number of patients presenting to our ED with a DBP of greater than 120 mm Hg by half.³⁶ To obtain an accurate measurement, a patient should be seated with the arm at the level of the heart, and the cuff bladder should cover at least 80% of the arm circumference.²⁰ Blood pressure should be evaluated in both arms. Blood pressure measurement with an automated cuff is inaccurate in patients with atrial fibrillation and other heart rhythm irregularities.⁵ Appropriate pain management and relief of underlying causes (eg, hypoxia, bladder dis-

attention) might resolve hypertension. Other medications, over-the-counter preparations, or illicit drugs might exacerbate or mitigate blood pressure (Figure 3).

If the patient's blood pressure is persistently increased, the history should start with an assessment of symptoms that might be consistent with target-organ compromise. Details include the duration and severity of preexisting hypertension, the degree of previous success with blood pressure control, and the presence of target-organ disease (cardiovascular, cerebrovascular, renovascular, and great vessels). The physical examination should be directed toward identifying signs of target-organ damage. A fundoscopic examination demonstrating the presence of retinal hemorrhage or papilledema is sufficient to diagnose accelerated-malignant hypertension.²⁰ The cardiovascular examination should focus on identifying signs of heart failure (eg, increased jugular venous pressure, pulmonary rales, S3 heart sound). The neurologic examination should assess the level of consciousness, visual fields, and the presence of focal motor and sensory deficits.

Few studies have assessed the prognostic value of abnormal laboratory findings in patients with severe asymptomatic hypertension. Because renal failure is silent, measurement of serum creatinine is reasonable.³⁷ The incremental value of obtaining a chest radiograph in the ED patient without relevant symptoms is generally likely to be low.^{38,39} A recent study

Figure 3.

Drugs that can increase blood pressure or interfere with the effectiveness of antihypertensive agents.

Oral contraceptives
Steroids
Nonsteroidal anti-inflammatory drugs
Nasal decongestants
Cold remedies
Appetite suppressants
Tricyclic antidepressants
Monoamine oxidase inhibitors

demonstrated unexpected and presumably new ECG abnormalities have been observed in 22% of asymptomatic ED patients with a DBP of greater than 115 mm Hg, although the clinical relevance is unclear given the lack of a comparison group or adverse outcome rate.³⁷ An ECG is probably reasonable in the patient with asymptomatic hypertension, although no clinical trials demonstrate more benefit than harm. When renovascular disease or hypercortisolism are suspected causes of hypertension, a serum tube for plasma renin activity and aldosterone should be drawn before medications are administered.³³ A urine screen for cocaine and amphetamines might help confirm common causes of hypertension.

PHARMACOLOGIC AGENTS

The ideal drug for treating hypertensive emergencies would have a rapid onset, rapid maximal effect, and rapid offset for easy titration of blood pressure. These characteristics are only found in parenteral agents. The most common of this group are summarized in Table 3 from the JNC-VI, and reviews of these agents are common in the medical literature.^{32,40-42}

Nitroprusside remains the mainstay of treatment for patients with hypertensive emergencies.⁴³ In aortic dissection, β -blockers should be added to nitroprusside to avoid the potential adverse effects of reflex tachycardia. Labetalol is a unique parenteral agent that achieves its

Table 3.
Parenteral drugs for treatment of hypertensive emergencies.

Drug	Dose*	Onset of Action	Duration of Action	Adverse Effects†	Special Indications
Vasodilators					
Sodium nitroprusside	0.25–10 g/kg per min as IV infusion‡ (maximal dose for 10 min only)	Immediate	1–2 min	Nausea, vomiting, muscle twitching, sweating, thiocyanate and cyanide intoxication	Most hypertensive emergencies; caution with high intracranial pressure or azotemia
Nicardipine hydrochloride	5–15 mg/h IV	5–10 min	1–4 h	Tachycardia, headache, flushing, local phlebitis	Most hypertensive emergencies except acute heart failure; caution with coronary ischemia
Fenoldopam mesylate	0.1–0.3 g/kg per min IV infusion	<5 min	30 min	Tachycardia, headache, nausea, flushing	Most hypertensive emergencies; caution with glaucoma
Nitroglycerin	5–100 g/min IV infusion‡	2–5 min	3–5 min	Headache, vomiting, methemoglobinemia, tolerance with prolonged use	Coronary ischemia
Enalaprilat	1.25–5 mg every 6 h IV	15–30 min	6 h	Precipitous decrease in pressure in high-renin states; response variable	Acute left ventricular failure; avoid in acute myocardial infarction
Hydralazine hydrochloride	10–20 mg IV; 10–50 mg IM	10–20 min; 20–30 min	3–8 h	Tachycardia, flushing, headache, vomiting, aggravation of angina	Eclampsia
Diazoxide	50–100 mg IV bolus repeated or 15–30 mg/min infusion	2–4 min	6–12 h	Nausea, flushing, tachycardia, chest pain	Now obsolete: when no intensive monitoring available
Adrenergic inhibitors					
Labetalol hydrochloride	20–80 mg IV bolus every 10 min; 0.5–2.0 mg/min IV infusion	5–10 min	3–6 h	Vomiting, scalp tingling, burning in throat, dizziness, nausea, heart block, orthostatic hypotension	Most hypertensive emergencies except acute heart failure
Esmolol hydrochloride	250–500 g/kg per min for 1 min, then 50–100 g/kg per min for 4 min; may repeat sequence	1–2 min	10–20 min	Hypotension, nausea	Aortic dissection, perioperative
Phentolamine	5–15 mg IV	1–2 min	3–10 min	Tachycardia, flushing, headache	Catecholamine excess

From the National High Blood Pressure Education Program.⁵

IV, Intravenous; IM, intramuscular.

*These doses might vary from those in the *Physicians' Desk Reference*, 51st ed.

†Hypotension can occur with all agents.

‡Requires special delivery system.

maximal effect within minutes and then remains effective for several hours. This allows titration with small boluses, thus avoiding the constant monitoring and increased cost required with nitroprusside. Because labetalol does not dilate cerebral capacitance vessels, it is theoretically attractive in intracerebral disorders. Fenoldopam holds some promise as being equivalent to nitroprusside in efficacy without the rare side effects associated to nitroprusside's cyanide moiety and perhaps with less overshoot hypotension, but at present, its cost is often prohibitive.⁴⁴ Compared with nitroprusside, fenoldopam might improve outcomes in patients with hypertension and acute renal failure.⁴³

Oral agents have been promoted for treatment of some hypertensive emergencies as requiring less vigilance than an intravenous infusion, being easier to administer, and having a longer duration of action than intravenous agents.²⁰ They have been used in encephalopathy, malignant hypertension, angina, congestive heart failure, pheochromocytoma, and aortic dissection (Table 4). Caution is advised for the following reasons:

1. Studies of the use of these drugs for hypertensive emergencies are few and small. Most are not confined to true hypertensive emergencies.
2. Oral agents can cause a precipitous decrease in blood pressure, which might be harmful, is difficult to blunt, and is difficult to reverse.

3. Failure rates with oral agents are reported to be as high as 10% to 20%, necessitating multidrug therapy.

4. Oral drugs are not easily titrated or discontinued. Nifedipine capsules, taken both orally and sublingually, were once widely used by office practitioners and emergency physicians to rapidly decrease the blood pressure of hypertensive patients. Their use was discontinued when case reports suggested that they might precipitate vascular disasters, such as stroke and heart attack.^{22-25,45,46}

TREATMENT STRATEGIES

Most hypertensive emergencies require immediate blood pressure reduction. The important exception is cerebrovascular emergencies, in which a rapid decrease in cerebral blood flow might be harmful. Two entities are specific to hypertension and occur only with severely increased blood pressures: accelerated-malignant hypertension and hypertensive encephalopathy.

Accelerated-malignant hypertension occurs most commonly in young black men with underlying renal parenchymal disease or renovascular disease.²⁰ When endothelial vasodilator responses are overwhelmed, endothelial decompensation causes further hypertension and endothelial damage, resulting in an inflammatory vasculopathy.³¹ The diagnosis is based on a marked

Table 4.

Oral medications for the treatment of hypertensive emergencies.

Drug	Dose	Duration	Advantages	Caveats
Captopril	3.125–25 mg SL/PO; onset 15 min; peak 60 min	2–8 h	Positive effects on cerebral autoregulation and regional myocardial perfusion, excellent for congestive heart failure	Fine control not possible, avoid in renal artery stenosis and with immunosuppressive drugs
Clonidine	0.05–0.2 mg PO; onset 30–60 min; peak 2–4 h	3–12 h	Decreases heart rate, no increase in cardiac oxygen consumption	Sedation, orthostatic hypotension, large decrease in cerebral blood pressure, avoid in congestive heart failure and with heart block
Labetalol	300 mg PO; peak 20 min–4 h	8–12 h	Favorable cardiac and central nervous system effects	Avoid in heart failure, reactive airway disease, and heart block
Nifedipine (not extended release)	5–10 mg SL/PO; onset 5–20 min; peak 30–60 min	2–6 h	Rapid onset, dilates coronary arteries and relieves spasm	Reflex tachycardia lasting 1 h; can precipitate angina in patients with high-grade stenosis, nonhomogeneous cerebral perfusion, fine control is not possible; large initial blood flow

SL, Sublingual; PO, orally.

increase of blood pressure and characteristic eye-ground findings. Flame-shaped hemorrhages occur around the optic disk caused by high intravascular pressures, and soft exudates are caused by ischemic infarction of the nerve fibers after occlusion of supplying arterioles. Papilledema is considered by many to be the sine qua non of malignant hypertension. For this reason, accelerated hypertension has been used to describe the same condition (hemorrhages and exudates) without papilledema. Because absence of papilledema does not connote different clinical features or a better prognosis, the term “accelerated-malignant hypertension” is now recommended.²⁰

Common symptoms include headache (85%), visual blurring (55%), nocturia (38%), and weakness (30%). Laboratory evidence includes azotemia, proteinuria, hematuria, hypokalemia, and metabolic alkalosis. Accelerated-malignant hypertension is most commonly found in patients with long-standing hypertension and usually occurs without encephalopathy. Since the 1950s, the long-term prognosis of accelerated-malignant hypertension has improved from a 1-year survival rate of 10% to a 5-year survival rate of more than 75%.⁴⁷

Treatment for accelerated-malignant hypertension should begin immediately. Any of the potent parenteral antihypertensive agents are appropriate. In the absence of marked azotemia, nitroprusside is an excellent choice.

Cerebrovascular hypertensive emergencies include hypertensive encephalopathy, ischemia, and hemorrhage. An understanding of cerebrovascular physiology is helpful in determining the best treatment strategy.⁴⁸ Cerebral blood flow is a function of the cerebral perfusion pressure, which is equal to the MAP minus the intracranial pressure (Cerebral perfusion pressure = MAP - Intracranial pressure). Cerebral blood flow is maintained by means of vasoconstriction and vasodilation of the cerebral vasculature. However, cerebral autoregulation fails at approximately 25% more than or less than the MAP. In addition, changes in intracranial pressure or brain injury can result in loss of the brain's ability to autoregulate blood flow. Increased intracranial pressure, commonly seen with hemorrhage or edema, decreases the cerebral perfusion pres-

sure, making the brain more vulnerable to changes in MAP.

The triad of severe hypertension, altered mental status, and (often) papilledema characterizes hypertensive encephalopathy. It can be accompanied by the acute or subacute onset of lethargy, confusion, headache, visual disturbances, and seizures. Retinopathy might or might not be present. The diagnosis is confirmed if cerebral function improves with decreasing of the blood pressure. The mechanism is cerebral overperfusion; in effect, the MAP overwhelms the brain's ability to autoregulate cerebral blood flow. Overperfusion results in vasodilation and increased permeability of cerebral blood vessels, leading in turn to the development of cerebral edema. If not adequately treated, hypertensive encephalopathy can progress to cerebral hemorrhage, coma, and death.²⁰

Hypertensive encephalopathy is most likely to occur in previously normotensive individuals who experience a rapid increase in blood pressure, such as children with acute glomerulonephritis and young women with preeclampsia or eclampsia. Chronic hypertensive patients usually experience a more gradual increase in blood pressure and therefore have a rightward shift in their pressure-perfusion autoregulation curve that makes cerebral decompensation less likely. Hypertensive encephalopathy produces characteristic findings on computed tomography (CT), which should be performed to exclude other causes of altered mental status, such as intracranial bleeding. Schwartz et al⁴⁹ have described a posterior leukoencephalopathy in hypertensive encephalopathy that predominantly affects the white matter of the parieto-occipital regions bilaterally.

The treatment of increased blood pressure in the setting of ischemic cerebrovascular accidents is controversial. When systemic blood pressure is reduced, cerebral autoregulation might fail, producing an ischemic penumbra surrounding the infarct, leading to stroke extension. Alternatively, infarction can lead to edema, increasing intracranial pressure and reducing cerebral blood flow further.^{31,32,48} Some believe that an increased MAP in the face of a stroke might be a protective measure. If true, decreasing the blood pressure might

lead to further ischemic damage. However, acute antihypertensive therapy was not associated with a worse outcome at 3 months among control patients in the large National Institute of Neurological Disorders and Stroke Recombinant Tissue Plasminogen Activator (NINDS rt-PA) stroke trial.⁵⁰ The current American Heart Association guidelines recommend decreasing the blood pressure with stroke only when the MAP is greater than 130 mm Hg or the SBP is greater than 220 mm Hg.⁵¹

Theoretically, treatment for increased blood pressure in hemorrhagic cerebrovascular accidents and subarachnoid hemorrhage should be more aggressive than for patients with ischemic strokes. The rationale is to decrease the risk of ongoing bleeding from ruptured small arteries and arterioles⁵²; however, the relationship between rebleeding and systemic blood pressure is unproven. As with ischemic cerebral vascular accidents, overly aggressive treatment of hypertension might worsen brain injury by decreasing cerebral perfusion pressure, especially when intracranial pressure is increased. The American Heart Association guidelines for blood pressure control with hemorrhagic stroke are similar to those with ischemic stroke, decreasing the blood pressure only when the MAP is greater than 130 mm Hg or the SBP is greater than 220 mm Hg. Nimodipine might be given to decrease the incidence of vasospasm and rebleeding after subarachnoid hemorrhages, but the drug is not recommended for blood pressure control.⁴⁸

Blood pressure control cerebrovascular hypertensive emergencies should be undertaken with parenteral drugs that have a short half-life and are easily titrated with minimal effect on cerebral vasculature. Esmolol and labetalol are appropriate when an increase in intracranial pressure is suspected.⁴⁸ Direct vasodilators, such as nitroprusside, should be used with caution in the setting of focal brain injury. Calcium-channel blockers have been linked to an increase in the intracranial pressure, and therefore, are not favored in patients with brain injury.

Hypertensive emergencies involving the heart and great vessels include congestive heart failure, acute coronary syndromes, and dissecting aortic aneurysm.

Blood pressure is frequently increased in patients with acute pulmonary edema, particularly when a high output state is the cause, as in volume-overloaded patients with renal failure, thyrotoxicosis, or severe anemia. Acute pulmonary edema with hypertension and congestive heart failure might be caused by transient diastolic dysfunction, which might or might not be a direct result of the increased blood pressure.⁵⁴ If the patient is critically ill, a nitroprusside infusion should be used. The goal is careful but rapid reduction of blood pressure to normal levels if necessary for symptom relief.

In both critical and noncritical cases of congestive heart failure, an angiotensin-converting enzyme (ACE) inhibitor might be helpful; captopril might be given orally or sublingually, or enalaprilat can be given intravenously if the patient cannot take oral medications.⁵⁴ Large doses of furosemide are still popular. Although we agree that diuresis should eventually be instituted, it might initially exacerbate the underlying pressure natriuresis and further stimulate the renin-angiotensin axis. Scanty empiric evidence suggests that furosemide might even worsen clinical outcome, at least initially.^{55,56} There are clearly patients with volume overload in whom a diuretic is helpful. β -Blockers have recently been found to improve survival in patients with chronic congestive heart failure⁵⁷; however, this observation should not be extended to patients with acute pulmonary edema because the negative inotropic effects and bradycardia of β -blockade might precipitate immediate worsening. Intravenous nesiritide improves hemodynamic function and symptoms in decompensated heart failure and has a modest antihypertensive effect.⁵⁸

Acute coronary syndromes are frequently accompanied by hypertension. Reducing myocardial work by decreasing the blood pressure and heart rate has been demonstrated to reduce infarct size in patients not receiving thrombolytic therapy.⁵⁹ The ideal pharmacologic approach involves use of nitroglycerin rather than nitroprusside because the former is a potent coronary artery dilator in addition to reducing both preload and afterload. The goal of treatment is reduction of blood pressure to normal levels or even less if evidence of ischemia persists. However, this reduction should occur

carefully, with the patient intensively monitored. Overly vigorous blood pressure decreasing can worsen ischemia because coronary perfusion depends on DBP.

Acute aortic dissection is thought to occur through aortic dilation or high blood pressures superimposed on a structural weakness of the arterial wall. The result is a tear of the intimal layer of the aorta.⁶⁰ Pulsatile pressure extends the dissection by separating the layers of the arterial wall. Historical series report a mortality of 1% to 2% per hour. The stresses that extend the dissection are thought to be related as much to the aortic pulse wave or pulse pressure (dp/dt) as it is to MAP. Factors that contribute to increased pulse pressure include heart rate, myocardial contractility, and MAP. An arterial dilator, such as nitroprusside, or a calcium-channel blocker alone might decrease the MAP while simultaneously increasing the pulse pressure through reflex tachycardia. β -Blocking agents can control myocardial contractility and tachycardia and thus ought to be included to prevent progression of the dissection.

The kidney is unique in being both a target organ and the cause of many hypertensive emergencies. Chronic hypertension causes 30% of cases of end-stage renal disease, making it the second most common cause after diabetes and the leading cause among black individuals.⁶¹ Chronic hypertensive patients might have nephrosclerosis after 10 to 15 years manifested by damage to the medial layer of capillaries, reduced kidney size, and nonnephrotic levels of proteinuria without hematuria. By contrast, malignant hypertension damages the intimal layer of the renal capillary bed and might result in enlarged kidneys, a cellular urinary sediment, hematuria, and severe proteinuria.⁶² The diagnostic and prognostic relevance of these observations to ED patients with severe hypertension has not been investigated. The absence of both protein (>1+) and hematuria on the urine dipstick was shown in 1 study of 143 ED patients with hypertension to rule out an acute creatinine increase (sensitivity 100%; 95% CI 83% to 100%).⁶³ Because this test is was not very specific (30% to 42% depending on threshold), it will only help make decisions in the minority of ED patients with severe hypertension.

Severe hypertension in a young patient should raise the possibility of intrinsic acute renal disease, such as glomerulonephritis. IgA nephropathy has surpassed poststreptococcal glomerulonephritis in frequency and, among children, Henoch-Schoenlein purpura is the most likely cause of acute glomerular disease.⁶⁴

Although malignant hypertension might precipitate acute renal failure by injuring the kidney's microvasculature, this causal chain is often reversed, with hypertension instead a manifestation of renal failure. Both nitroprusside and labetalol are excellent choices in this setting. Although ACE inhibitor drugs definitely improve prognosis among chronic hypertensive patients with mild proteinuria,¹⁶ they should be used cautiously in hyperkalemic patients with acute uremia.

Stenosis of the renal arteries is present in only 1% of unselected hypertensive patients but is present in 4% of black patients and 32% of white patients who have severe hypertension (DBP >125 mm Hg with retinopathy). It is also more common among patients who have a rapidly progressive course.⁶⁵ Most patients have atherosclerosis, but a minority are young women with medial fibroplasia of the renal arteries. An abdominal bruit is present in 46% of patients, and they are more likely to have the onset of hypertension after age 50 years. Treatment with an ACE inhibitor might reverse high blood pressure dramatically in patients with unilateral stenosis, but it might provoke acute renal failure and severe hyperkalemia in patients with bilateral stenosis, particularly if they are taking supplemental potassium or a potassium-sparing diuretic. This complication can be completely reversed by discontinuing the ACE inhibitor. Occasionally, because of intrarenal vasculitis, rare but devastating acute renal failure can occur. This is common in the setting of scleroderma and might be responsive to ACE inhibitors.

Women who are pregnant for the first time, who are between 20 weeks' gestation and 2 weeks postpartum, and who have any degree of hypertension accompanied by peripheral edema and proteinuria should be considered to have preeclampsia. Hypertension is important mainly as a symptom of the underlying disorder rather than as a cause. Preeclampsia is important to recognize

because it can progress suddenly to eclampsia defined by the occurrence of convulsions and can rapidly progress to coma or death. Magnesium infusion is more effective than other anticonvulsants in this setting.⁶⁶ Definitive treatment consists of delivery of the fetus, and therefore, the emergency physician usually collaborates with an obstetrician early in the patient's progress through the department. The mainstay of antihypertensive treatment in many institutions is hydralazine administered intravenously in boluses of 5 to 10 mg every 20 to 30 minutes. If treatment is refractory to hydralazine, second-line agents are diazoxide and β -blockers.⁶⁷ Calcium-channel blockers have been studied in chronic hypertension among pregnant patients, but they might not be effective with proteinuric hypertension.⁶⁸

Perioperative hypertension is usually managed by anesthesiologists and does not differ much from hypertension in other settings. However, some unique circumstances are worth noting: intraoperative manipulation of certain structures (eg, carotid artery, adrenal glands, kidneys) can occasionally precipitate severe hypertension. Conversely, surgery on an unanticipated pheochromocytoma can precipitate severe hypotension, requiring massive fluid resuscitation. Hypertension might also place recent vascular anastomoses at risk.

The most familiar drugs causing hypertension in EDs today are sympathomimetic drugs, such as phenylephrine, cocaine, and methamphetamine. Tyramine can induce a hypertensive crisis in patients taking a monoamine oxidase inhibitor drug, and hypertension can complicate withdrawal syndromes from alcohol, clonidine, and, less frequently, β -blockers. Pheochromocytomas can cause intermittent hypertensive crisis, usually accompanied by headache.

Patients with a pheochromocytoma can secrete a bewildering variety of catecholamines and even peptide hormones in either a constant or wildly intermittent pattern. They can produce many clinical findings in addition to hypertension, such as headache, sweating, palpitations, pallor, nausea, and (rarely) seizures. Some patients with pheochromocytomas have paroxysms of low blood pressure instead.

Patients with severe hypertension caused by pheochromocytoma are commonly treated with the pure β -blocker phentolamine administered intravenously. This might be accompanied by a β -blocker if needed for tachycardia. Administration of β -blockers alone in the setting of any sympathomimetic might leave the α -receptors open, with subsequent worsening of hypertension. Thus, an attractive alternative to β -blockers is labetalol, a β -blocker with some α -antagonist properties. However, the α - and β -blockade with labetalol might not be equally effective. Although several studies report reductions in blood pressure and heart rate when labetalol is given to patients with cocaine toxicity, case reports indicate that some individuals might get worse.⁶⁹⁻⁷¹ The clinical importance of the unopposed α effect of labetalol increasing blood pressure requires better evidence.

Most patients with a hypertensive emergency should be hospitalized in a unit in which vigilant monitoring is possible. It is often possible to rapidly stabilize these patients and switch from parenteral agents.

HYPERTENSIVE URGENCIES

As noted previously, we define hypertensive urgency as a severely increased blood pressure in a patient with known target-organ disease but without active compromise. Examples include a severely hypertensive patient with a previous history of myocardial infarction or stroke. The immediacy arises because the patient with target-organ disease might be considered at higher risk for a hypertension-related adverse event in the short term. This definition of hypertensive urgency is not universally recognized, and our position is based on deduction.

In our opinion, these patients should have a treatment strategy initiated from the ED, although the blood pressure does not necessarily need to be decreased during the visit. Some degree of blood pressure reduction might occur spontaneously, without pharmacologic intervention. The patients most responsive to this approach are those with the most severe hypertension.³⁵ Initiating oral agents can treat most hypertensive

urgencies. Table 4 summarizes 4 oral antihypertensive agents commonly used with hypertensive urgencies. They are all highly effective at reducing blood pressure and have relatively good safety records. There is no evidence to support the practice of treating hypertension by reducing the blood pressure acutely in the ED, and 1 trial found no difference at 24 hours between groups of patients who had or had not received antihypertensive loading before initiation of maintenance therapy.⁷²

The key is to pick a therapeutic agent that suits the underlying pathology and minimizes the chances of exacerbating it. The best medication is usually one the patient can continue to take, ideally chosen with the concurrence of the patient's primary care physician. Resuming a previous regimen that the patient tolerated well is often the best choice. JNC-VI recommendations for the choice of initial agents for blood pressure control are listed in Figure 1.

In our opinion, the main distinction between hypertensive urgency and severe increase is the intensity of treatment and monitoring required. Patients classified as having hypertensive urgency might need to be held in a short-term observation unit if there is a question as to medication compliance or blood pressure monitoring. Many can go home with good follow-up instructions. Reasonable discharge criteria for patients with hypertensive urgencies are the following:

1. likely to be compliant with established primary care;
2. known to have hypertension;
3. reversible precipitating cause (eg, medication noncompliance or adverse drug effect);
4. able to resume a previously effective medication regimen; and
5. can be seen in follow-up within 7 days.

UNCONTROLLED HYPERTENSION

In the patient with asymptomatic increased blood pressure with no evidence of target-organ disease, the most important intervention is to ensure proper follow-up. The goal should be lifelong control of the blood pressure. When the increased blood pressure might be the

artifact of a systemic process, such as pain or infection, the best strategy is to refer the patient for reevaluation of the blood pressure once the primary problem has resolved. If the patient has discontinued his or her blood pressure medications, the regimen should be restarted, barriers to compliance should be evaluated, and a primary care physician should be contacted to ensure reevaluation in a week.

A patient with severely increased blood pressure and no history of previous treatment might be started on an initial agent. In principle, if there has never been a previous measurement of increased blood pressure, the blood pressure needs to be rechecked on another visit before the diagnosis of hypertension can be made. In 1 study, one third of patients with an ED DBP of greater than 95 mm Hg were found to be normotensive on follow-up.⁷³ In practice, many physicians start individuals with readings persistently greater than 180/110 mm Hg in the ED on first-line antihypertensive therapy. Ideally, the physician who will provide ongoing supervision should be the one to pick an initial agent he or she is comfortable managing. The best role of the emergency physician is to identify a primary physician for the patient and encourage that physician to select an initial antihypertensive agent and provide a follow-up appointment within the week.⁸

CASE MANAGEMENT

Returning to our fictional scenario: a 50-year-old man with a history of hypertension presented to the ED with the complaints of a headache and malaise for 2 days. He has not taken his hypertension medications in more than a year and does not remember what he was taking. His physical examination is remarkable for a persistent blood pressure of 210/120 mm Hg and is otherwise unremarkable, except for grade I retinopathy.

The first management step would be administration of a nonsedating analgesic (eg, ibuprofen) for the headache. Pain relief or simply regression to the mean might result in a subsequent decrease in the blood pressure. Concomitantly, the patient should be carefully evalu-

ated for evidence of acute target-organ disease. Laboratory tests should include a serum creatinine measurement, urinalysis, and perhaps an ECG. If the patient has findings in his history or physical examination suggesting significant central nervous system involvement, a head CT scan would be appropriate.

If the history or a head CT scan provide evidence of a prior stroke or cerebral vascular disease without evidence of an acute lesion, the patient qualifies as a hypertensive urgency under our stratification. This would justify cautious initiation of maintenance antihypertensive therapy. The best regimen is one previously known to be effective. In the absence of a known and previously successful antihypertensive regimen, the patient could be started on a diuretic and a β -blocker. If the patient can be reasonably expected to be able to comply with instructions, he might be discharged to follow-up in no more than a week. Given the potential risk of a recurrent stroke in a patient with severely increased blood pressure coupled with his previous noncompliance with therapy, it might be equally reasonable to admit him on observational status to establish blood pressure control. There is no compelling evidence in the literature to argue for either approach. However, a policy of routine hospitalization is likely to stress safety net health care systems in which hypertension is most prevalent.

If the clinical examination and workup results are negative and the blood pressure remains increased even after resolution of the headache, the patient can be stratified as having severe uncontrolled hypertension. Questioning should focus on barriers to care, reasons for medication noncompliance, and/or lack of a primary care physician. Ideally, a primary care physician should be contacted and allowed to recommend an initial treatment regimen. The patient should be counseled and every effort made to ensure that he begins therapy and complies with follow-up as planned. There is no evidence to suggest that the blood pressure must be decreased while in the ED.

In summary, patients presenting to the ED with severely increased blood pressure span the spectrum

from hypertensive emergencies requiring immediate intervention through hypertensive urgencies to uncontrolled hypertension. Hypertensive emergencies demonstrate rapidly progressive end-organ damage. Hypertensive urgencies are scenarios in which the blood pressure is severely increased and there is a history of end-organ disease, signaling an increased risk of further injury within a short time frame. The majority of patients presenting to the ED with severely increased blood pressure have poorly controlled hypertension, are asymptomatic, and simply need to be referred to a primary care physician. Treatment strategies should be tailored to the patient's presentation. In general, patients with hypertensive emergencies need parenteral medication and ICU admission, hypertensive urgencies can be managed by initiating oral medication and short-term follow-up or observation, and uncontrolled hypertension can be managed by means of patient education and referral for initiation of long-term treatment by a primary care provider.

In the course of preparing this review, we were struck by both the dearth and low quality of evidence relating to the most common and most important questions in the ED management of severely increased blood pressure. In contrast to the huge resources and amount of evidence devoted to chronic hypertension, including randomized trials of tens of thousands of patients, there are virtually no randomized trials of severe hypertension that used clinically important outcomes. In light of the frequency of this presentation and the significant resources committed to its management, emergency physicians urgently need to collaborate in explicitly defining the boundaries of this problem and its current costs to society. This would allow us to prioritize the clinical questions that should be answered by future research.

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Address for reprints: Philip Shayne, MD, Department of Emergency Medicine, Emory University School of Medicine, 69 Jesse Hill Jr. Drive SE, Atlanta, GA 30303; 404-616-6674, fax 404-616-0191; E-mail pshayne@emory.edu.

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