

Hypertensive Emergency and Severe Hypertension: What to Treat, Who to Treat, and How to Treat

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Hypertensive emergency is a clinical syndrome of rapidly progressive end-organ damage associated with a significant elevation of blood pressure. The immediate reduction of blood pressure using potent intravenous (IV) agents is indicated to reduce the mortality rate, which ranges historically as high as 90%. Virtually all episodes of hypertensive emergency are associated with a diastolic blood pressure (DBP) > 120 mm Hg; however, most patients who present with severe hypertension do not have a hypertensive emergency. It is crucial to recognize that not only will these patients not benefit from aggressive normalization of blood pressure but also there can be substantial morbidity caused by overly rapid decreases in blood pressure in patients who do not have rapidly evolving end-organ damage. Distinguishing between these two groups of patients is the first step in the safe management of significantly hypertensive patients. A thorough history, physical examination, and assessment of readily available laboratory tests will efficiently identify the minority of patients who need intensive treatment. Unfortunately, unclear terminology for clinically describing these patients is often a source of confusion and can present a barrier to correct management. As medical therapy grows more powerful, the attendant risks also grow in consequence. Definitions that served in the past now need refinement, based on the available evidence of the benefits and risks of therapy.

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Definitions

Hypertensive crisis is traditionally defined as an elevation of diastolic blood pressure > 120 mm Hg. This category includes patients who have hypertensive emergency, hypertensive urgency, and severe hypertension. The term "crisis" suggests a need for immediate intervention, which is often contraindicated in these latter groups. For this reason, the use of this term should be de-emphasized.

Hypertensive emergency is defined by acute and rapidly evolving end-organ damage associated with significant hypertension, usually a DBP > 120 mm Hg. Controlling blood pressure within hours is desirable and requires admission to a critical care setting.

Hypertensive urgency is defined as a DBP > 120 mm Hg that requires improvement in blood pressure control over a period of 24 to 48 hours. This definition is problematic because, in the absence of evolving end-organ damage, there is little evidence of clinical benefit with the control of blood pressure over this period. Often the urgency is more in the mind of the treating physician than in the body of the patient. There are certainly occasions when improved short-term blood pressure control is needed, such as the imminent need for a procedure under anesthesia, but the clinician must carefully weigh the benefits of blood pressure control against the known risks of achieving it. Hypertensive urgency as a general descriptive term poses many of the same drawbacks as hypertensive crisis and therefore likewise should be de-emphasized.

Severe hypertension is defined usually as systolic blood pressure (SBP) > 180 mm Hg or DBP > 110 mm Hg, with some variability from study to study. The key definition of severe hypertension is the lack of rapidly evolving end-organ damage and a concomitant indication to gradually control the blood pressure.

The Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [1,2] has changed the classification of hypertension between the sixth and seventh report (Table 1).

Table 1
Changes in Joint National Committee classification of hypertension

JNC report no. [Ref. no.] and stages	SBP/DBP range (mm Hg)
<i>JNC VI</i> [1]	
High normal	130–139/85–89
Stage 1	140–153/90–99
Stage 2	160–179/100–109
Stage 3	180+/110+
<i>JNC VII</i> [2]	
Prehypertension	120–139/80–89
Stage 1	140–159/90–99
Stage 2	160+/100+

Malignant hypertension is an older term no longer in wide usage. It referred originally to elevated pressure associated with group IV Keith-Wagener-Barker retinopathy, papilledema, retinal hemorrhages and exudates, and is sometimes used to describe hypertensive emergency associated with central nervous system findings. Accelerated hypertension is another older term applied originally to hypertension associated with group III Keith-Wagener-Barker retinopathy and retinal hemorrhages and exudates. It has since been demonstrated that the Keith-Wagener-Barker classification of retinopathy does not accurately assess the severity of hypertension [3] or the clinical outcome [4,5], and these terms are no longer considered useful.

Demographics of hypertension and hypertensive emergency

According to the JNC VII [2], hypertension is the most common primary diagnosis in the United States (35 million office visits per year) affecting almost 25% of the population. Thirty percent of the population is unaware they have hypertension, and control rates for patients known to have hypertension still fall short of 50%. The consequences of hypertension are well described in JNC VII:

- In persons older than 50 years of age, systolic blood pressure greater than 140 mm Hg is a much more important cardiovascular disease (CVD) risk factor than diastolic blood pressure.
- The risk of CVD beginning at 115/75 mm Hg doubles with each increment of 20/10 mm Hg.

These demographics and the consequences of hypertension are well outlined in this report [2] and throughout the medical literature. In marked contrast, the prevalence and incidence of hypertensive emergency, crisis, and urgency are far from clear. There are several reasons for this, and reviewing them introduces the reader to the complexities of managing these conditions.

First, the lack of a consistent definition of hypertension extremes has resulted in variable data collection in published studies, making comparisons difficult. Second, much of the literature on hypertensive crisis and associated conditions is older. Although hypertension management is far from perfect now, there have been tremendous strides during the last 4 decades, and much of the cited literature is now 2 to 4 decades old. Third, hypertensive emergency is a heterogeneous condition probably resulting from a tiny percentage of poorly controlled essential hypertensive cases and even rarer cases of secondary hypertension. The acquisition of meaningful statistics describing such uncommon occurrences is problematic and susceptible to multiple biases such as enrollment in primary health care, socioeconomic status of the population, and referral bias in tertiary care centers. With these caveats in mind, the interpretation of the widely quoted incidence of hypertensive crisis of 1% of all hypertensive cases would suggest that as many

as 500,000 Americans present for evaluation yearly, giving weight to the importance of correct diagnosis and management of this condition [6].

Pathophysiology of hypertensive emergency

The striking rapidity of end-organ damage and severity of blood pressure elevation at the time of presentation of hypertensive emergency are attributed to the failure of the normal autoregulatory function and to abrupt increases in systemic vascular resistance. There is concurrent endovascular injury, with fibrinoid necrosis of arterioles. The ensuing cycle of ischemia, platelet deposition, and further failure of autoregulation caused by the release of vasoactive substances accelerates the patient's clinical deterioration [7,8].

The specific triggers for this dramatic process usually are unknown and may well vary among the heterogeneous causes of the underlying hypertensive process. In any event, the bedside management of the patient is addressed usually to mitigating damage to whichever organ system is manifesting the most disease, rather than to modifying the underlying autoregulatory function.

Under normal conditions, tissue perfusion in the brain, heart, and kidneys remains relatively constant, despite normal fluctuations in blood pressure. In the presence of severe hypertension, this ability to autoregulate shifts upward to protect the exposed organ from excessive pressure. In both the normal situation and when upwardly shifted, the lower threshold of autoregulation (the threshold for hypoperfusion) is approximately 20% to 25% lower than the prevailing blood pressure [8]. This physiologic observation has been translated into a clinical recommendation to limit the initial lowering of blood pressure to 20% below pretreatment values.

Conditions associated with extremes of hypertension

Severe hypertension is seen disproportionately in association with secondary hypertension, and many causes of secondary hypertension are known to result in blood pressure lability, further disposing toward hypertensive crisis. **Box 1** lists some of these conditions.

Although these conditions can underlie a hypertensive crisis, given the relative prevalence of essential hypertension, it is not surprising that this diagnosis accounts for most presentations of severe hypertension and hypertensive emergency. Many asymptomatic patients who have severe hypertension are unaware of their condition; however, most patients who experience a hypertensive emergency are aware of their condition [9] and have a history of inadequate treatment or of abrupt medication withdrawal. Centrally acting agents such as clonidine are often implicated in medication withdrawal, but rapid end-organ damage can result from the abrupt discontinuation of any potent regimen, and patients on high doses and multiple drug regimens need to understand the importance of avoiding the sudden discontinuation of medications.

Box 1. Causes of secondary hypertension*Neurologic conditions*

- Autonomic hyperactivity (spinal cord injury, Guillain-Barré syndrome, and other causes)
- Baroreflex failure
- Cardiovascular accident
- Head trauma

Hormonal conditions

- Pheochromocytoma
- Renin- or aldosterone-secreting tumors

Pregnancy-associated conditions

- Eclampsia
- Preeclampsia

Immune conditions

- Scleroderma and other collagen vascular disease
- Vasculitis

Renal conditions

- Parenchymal renal disease, such as glomerulonephritis
- Renovascular disease

Drug-related conditions

- Drug interaction (eg, interactions of monamine oxidase inhibitor with tyramine, tricyclics, or sympathomimetics)
- Sympathomimetics (eg, cocaine, amphetamine, and phencyclidine)

Drug withdrawal conditions

- Abrupt discontinuation of antihypertensive medications
- Alcohol withdrawal

The role of chronic, progressive hypertension as a cause of hypertensive emergency is hard to specify in an age of widespread hypertension screening and treatment. Most patients are identified and at least partially treated well below the threshold for hypertensive emergency. Messerli [10] reviews the case of former President Franklin D. Roosevelt, with further editorial observations by Calhoun and Oparil [11], which throws light on the threshold for hypertensive emergency in chronically hypertensive patients and on the possible role played by secondary causes of hypertension in the extremes of hypertension. When hypertension was regarded medically as an “essential” adaptation to underlying vascular disease, President Roosevelt developed hypertension in his 50s, and within 10 years, he died of cerebral hemorrhage,

with a final blood pressure of 300 mm Hg systolic and 190 mm Hg diastolic. Fig. 1 shows the time course of Roosevelt's hypertension.

Masserli [10] indicates that this 10-year time course is atypically rapid for essential hypertension, because the age of onset was late and the progression to death was relatively swift. As summarized by Calhoun and Oparil [11] in the associated editorial, the onset of essential hypertension in the fourth decade of life with an untreated survival of 20 years was more typical in the pretreatment era. This observation suggests that the long duration of asymptomatic severe hypertension, whether essential or secondary, before hypertensive disease manifests as hypertensive emergency.

Recognizing hypertensive emergency

Significant elevation of blood pressure is a common thread in the diagnosis of hypertensive emergency, but the key symptomatic manifestations of the syndrome vary widely, depending on the target organ involvement. The major target organs in hypertensive emergency are the brain, heart and great vessels, kidney, and the gravid uterus. One recent study by Zampaglione and colleagues [9] found single-organ involvement in 83%, two-organ involvement in 14%, and three or more organ involvement in only 3% of hypertensive emergencies. The relative frequency of end-organ involvement in hypertensive emergency is summarized in Table 2.

The initial assessment of hypertensive crisis is straightforward. A history and physical examination rapidly direct further investigation to the involved

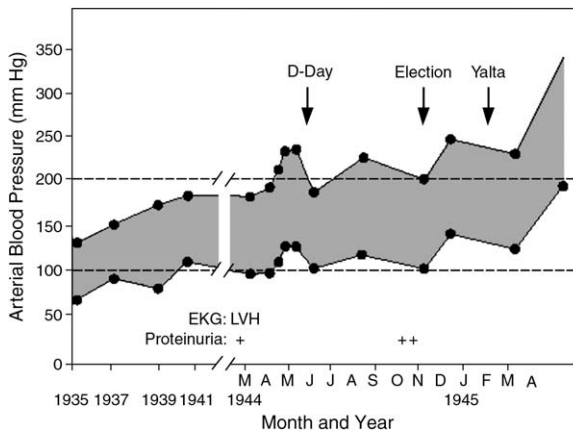


Fig. 1. Diastolic and systolic arterial pressure of Franklin D. Roosevelt from 1935 until his death on April 12, 1945. LVH, left ventricular hypertrophy. Data are from the diary of Dr. Howard G. Bruenn. (From Messerli FH. This day 50 years ago. *N Engl J Med* 1995;332:1038-9. © 1995 Massachusetts Medical Society; with permission.)

Table 2
Types of end-organ damage associated with hypertensive emergency

End-organ damage type	Cases (%)
Cerebral infarction	24.5
Intracerebral or subarachnoid bleed	4.5
Hypertensive encephalopathy	16.3
Acute pulmonary edema	22.5
Acute congestive heart failure	14.3
Acute myocardial infarction or unstable angina	12.0
Aortic dissection	2.0
Eclampsia	2.0

Data from Zampaglione B, Pascale C, Marchisio M, et al. Hypertensive urgencies and emergencies. Prevalence and clinical presentation. Hypertension 1996;27:144-7.

organs. Appropriate chemistry measurements and EKG are available widely. Urine toxicology for cocaine metabolites is helpful in select populations. Plain chest radiographs are useful for assessing volume status and cardiac size and are a first screen for aortic dissection. In patients whose condition is highly suspicious for aortic dissection (those who experience severe or ripping chest or abdominal pain, especially radiating to the back), further diagnostic studies with CT scanning of the chest with contrast is warranted. Unfortunately, renal function is often marginal and carefully balancing risks and benefits is called for. It bears repeating that aortic dissection accounted for only 2% of hypertensive emergencies in the above-cited series. With this in mind, CT screening for dissection in the emergent setting is not indicated routinely. This careful balancing of risk and benefit is not an issue concerning head CT for patients who display neurologic symptoms because these scans are performed initially without contrast, usually after the first control of blood pressure is achieved.

Overview of treatment of hypertensive emergency

After developing a high index of clinical suspicion of rapidly evolving end-organ damage, the clinician needs to initiate therapy in a timely fashion, keeping in mind the following:

- Promptly initiate goal-directed pharmacologic therapy with readily available agents, often before the diagnostic workup is completed.
- Ensure that the involved critical staff is familiar with dose ranges, infusion techniques, blood pressure monitoring requirements, and side effects of the medications used.
- Be mindful of practical considerations influencing the choice of pharmacologic therapy, including the need to transport the patient to multiple locations (emergency department, diagnostic radiology, operating room, catheterization lab, and intensive care unit). It is often difficult to maintain continuous IV infusions and even more difficult to maintain continuous intra-arterial pressure monitoring during this process.

- Always remember to “first, do no harm.” Do not hypoperfuse already ischemic organs; avoid rapid swings of blood pressure beyond the already dysfunctional range of autoregulation of tissue perfusion. Consider contraindications to and side effects of specific medications. Coordinate the choice of pharmacotherapy among the many medical specialists involved in the care of the patient because each must share in the therapeutic goals and be familiar with the treatments used.

This article does not provide specific medication dosing guidelines. Rather, Table 3 summarizes therapeutic goals, suggested classes of agents used in various clinical scenarios, risks, caveats, and clinical “pearls” as they apply to the common clinical presentations of hypertensive emergency.

Hypertensive urgency and severe hypertension

Significant hypertension, typically SBP > 180 mm Hg or DBP > 110 mm Hg corresponding to stage III hypertension in JNC VI [1], without acutely evolving end-organ damage is a much more common presentation than a hypertensive emergency. This condition is described traditionally as a hypertensive urgency; however, this terminology represents a psychologic “framing effect” [12] that presumes this condition needs to be treated urgently. In fact, there is a substantial body of evidence that the rapid control of asymptomatic hypertension often results in adverse effects. Faced with a patient whose initial history and physical examination do not suggest emergent end-organ damage, consider the following points before initiating therapy.

First, assess the accuracy of the blood pressure reading. To meet JNC VII [2] criteria for accuracy, two readings must be taken at least 5 minutes apart with the patient at rest in a seated position. Keep in mind that with any measurement there is a statistical tendency for repeat measurements to regress toward the mean. This mathematical principle has been validated in a study of 195 consecutive hypertensive patients in an emergency department that documented a mean decline of 11.6 mm Hg in repeated diastolic blood pressure readings [13]. Remember also to repeat unexpectedly high blood pressure readings as a measurement error that can arise from the misapplication of the sphygmomanometer cuff, use of an undersized cuff, or operator error [14]. Even in the most technologically sophisticated settings, there is still a need for a manual sphygmomanometer with a variety of cuff sizes.

Second, consider whether the hypertension is reactive. If the hypertension is caused by anxiety, pain, use of sympathomimetics as innocent as decongestants or as risky as cocaine, or by withdrawal states such as alcohol or discontinuation of antihypertensive medication, addressing the underlying condition is the first priority.

Third, determine whether the elevation represents ongoing severe hypertension or a temporary perturbation. A study of patients who were hypertensive during an emergency department visit showed that, at follow-up clinic visits, only 69% of those with initial readings of 140 to 159 mm Hg SBP or 90 to

Table 3
Common presenting scenarios of hypertensive emergency

Modes of comparison	Hypertensive encephalopathy, cardiovascular accident, intracranial hemorrhage	Acute congestive heart failure or pulmonary edema	Acute myocardial infarction or acute coronary syndrome	Aortic dissection	Acute cocaine or sympathomimetic intoxication
Therapeutic goal	<ul style="list-style-type: none"> • First do no harm, avoid hypoperfusion • Do not exceed 20% reduction of BP 	<ul style="list-style-type: none"> • Reduction of BP, especially by vasodilatation • Promote diuresis 	<ul style="list-style-type: none"> • Reduction of BP • Decrease myocardial oxygen demand 	<ul style="list-style-type: none"> • Reduction of shear forces by reduction of BP and tachycardia 	<ul style="list-style-type: none"> • Reduction of excessive sympathomimetic drive
Suggested agents	<ul style="list-style-type: none"> • Nicardipine: reduces cerebral ischemia • Consider ultra short acting agents (esmolol or nitroprusside) 	<ul style="list-style-type: none"> • IV nitroglycerin • Morphine • IV angiotensin converting enzyme inhibitor • IV diuretic 	<ul style="list-style-type: none"> • IV β blocker • IV nitroglycerin 	<ul style="list-style-type: none"> • IV labetalol • IV β blocker • Nitroprusside 	<ul style="list-style-type: none"> • Benzodiazepine • IV nitroglycerin • IV labetalol
Risk of therapy	<ul style="list-style-type: none"> • Cerebral autoregulation is disrupted in the ischemic brain • Patients demonstrate marked lability of BP with any agent, and hypoperfusion of the brain can occur 	<ul style="list-style-type: none"> • Diuretics and angiotensin converting enzyme inhibitor can exacerbate renal dysfunction 	<ul style="list-style-type: none"> • β Blockade can exacerbate left ventricular failure 	<ul style="list-style-type: none"> • Nitroprusside is extremely potent and requires continuous intra-arterial BP monitoring 	<ul style="list-style-type: none"> • Unopposed β blockade can cause alpha storm and increase cocaine toxicity
Pearls	<ul style="list-style-type: none"> • There is no clear evidence of benefit with intensive control of BP in the setting of stroke 	<ul style="list-style-type: none"> • Diuretics are slow to work • Angiotensin converting enzyme inhibitor has rapid onset of action • IV nitrates dilate capacitance vessels at low doses, higher doses dilate arterioles and lower BP 	<ul style="list-style-type: none"> • β Blockade also reduces mortality associated with ventricular arrhythmia 	<ul style="list-style-type: none"> • Avoid volume depletion in patients requiring IV dye or going for general anesthesia 	<ul style="list-style-type: none"> • Measure core temperature and treat hyperthermia if present • Consider the possibility of multidrug use

99 mm Hg DBP remained hypertensive but 100% correlation of subsequent readings in patients who had >180 mm Hg SBP or >110 mm Hg DBP [15].

If all of the above criteria are met, the presence of severe hypertension is confirmed, but the issue of urgency remains. At this juncture, many patients are referred for urgent evaluation, including EKG, urinalysis, blood glucose and hematocrit, serum potassium, creatinine (or estimated glomerular filtration rate), and calcium, as recommended in the JNC VII report [2]. The results of this testing are used to identify compelling indications for the use of individual drug classes. That this testing is appropriate is indisputable; that it identifies urgency is doubtful. Many patients who have significant hypertension will have chronic EKG abnormalities such as left ventricular hypertrophy, a strain pattern or T-wave inversion, but in the absence of symptoms, these findings seldom warrant acute intervention. Likewise, many of these patients will have a degree of renal impairment, usually found to be chronic and without the need for immediate intervention. These patients should be treated, according to JNC guidelines for stage II hypertension, with two oral agents, as described in Table 4.

Thus far in this discussion of severe hypertension, the issue of urgency remains unresolved. Are there symptoms or situations that differentiate urgency from severe asymptomatic hypertension? In terms of symptoms, concern arises over patients who present with nonspecific headache, without other signs of central nervous system emergency. There are no studies that document headache alone, which can be mitigated by immediate treatment, as a risk factor for further complication. Although many clinicians take advantage of the patient's perception of the need to treat headache in the setting of severe hypertension, it is preferable to initiate treatment with a regimen consistent with long-term use. In a large study [16] of nonemergent severe hypertension in an emergency department setting, 269 of 11,531 (2.3%) of patients had systolic blood pressure >180 mm Hg or diastolic blood pressure >110 mm Hg. The most frequent chief complaints were musculoskeletal pain in 18% and headache in 12%. Only 56 of the 269 were treated acutely, usually with a calcium channel-blocking drug.

Table 4
Compelling indications for individual drug classes

Compelling indication	Initial therapy options
Heart failure	THIAZ, BB, ACEI, ARB, ALDO ANT
Post-myocardial infarction	BB, ACEI, ALDO ANT
High CVD risk	THIAZ, BB, ACEI, CCB
Diabetes	THIAZ, BB, ACEI, ARB, CCB
Chronic kidney disease	ACEI, ARB
Recurrent stroke prevention	THIAZ, ACEI

Abbreviations: ACEI, angiotensin converting enzyme inhibitor; ALDO ANT, aldosterone antagonist; ARB, angiotensin receptor blocker; BB, β blocker; CCB, calcium channel blocker; THIAZ, thiazide.

The strongest correlation to decision to treat was not the symptoms but the severity of blood pressure reading. In most cases, the patient's home regimen was not altered. This typical pattern of care argues that most clinicians do not place special priority on the treatment of nonspecific headache.

In terms of situations that denote urgency, an argument for immediate treatment can be mounted if patients need urgent procedural evaluation or intervention. Patients who have uncontrolled hypertension are known to have labile blood pressures under general anesthesia, and IV pharmacotherapy will often be needed during anesthesia [17]; therefore, it makes sense to initiate control preprocedure. Preoperative β blockade has demonstrated benefit in lowering perioperative complications, especially in hypertensive patients who have other risk factors for cardiovascular disease [18]. In contrast to the absence of a proven benefit of emergent treatment of severe asymptomatic hypertension, there is substantial evidence of morbidity resulting from rapidly lowering blood pressure in the chronically hypertensive patient. Of particular concern are reports that demonstrate the occurrence of stroke with both aggressive [19,20] and moderately acute blood pressure reduction [20]. In addition, symptomatic hypotension, myocardial infarction, and even death have occurred from oral agents used to acutely lower blood pressure [21–23].

Because of the lack of proven benefit and substantial evidence of risk in rapid blood pressure lowering, the present authors suggest that most cases of severe hypertension should be treated according to JNC VII [2] guidelines for the selection of medication that produces timely but gradual improvement in blood pressure control. Instead of initiating rapid control of blood pressure, emergency care should emphasize the thoughtful initiation of long-term therapy and appropriate follow-up care. The widely accepted guidelines for acceptable timeline in hypertensive management have been adapted from JNC VI (Table 5) [1].

In an editorial, Matthews [24] addresses the urge to treat the asymptomatic hypertensive aggressively: "The principle 'FIRST, DO NO HARM' is applicable. The compulsive need to treat reaches the pathological in some physicians, especially during the early years in their careers. If the urge to treat asymptomatic hypertension becomes over whelming, use an agent

Table 5
Appropriate follow up and intervention for asymptomatic patients without major end-organ damage

BP (mm Hg)	Follow up
140–159/90–99	Observe and confirm within 2 mo
160–179/100–109	Confirm and treat within 1 mo
180–209/110–119	Confirm and treat within 1 wk
210+/120+	Confirm, evaluate, and initiate therapy immediately with close follow up

Data from National Heart, Lung, and Blood Institute. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Publication no. NIH 03-5233. Bethesda (MD): NIH; 2003.

that lowers blood pressure gradually over time and ensure the patient understands the need and has an opportunity for early and adequate follow-up. This approach should be safe for the patient and will satisfy the concern that you will be sued if you do nothing. For the majority of these patients, ensuring good follow-up as an outpatient will suffice.”

Summary

Remember to treat patients, not numbers. Use fast acting short-term medicines only when convincing evidence of rapidly evolving end-organ damage is present. For all patients, emergent or asymptomatic, the treatment goal is long-term control of hypertension. Potent IV agents for the immediate control of elevated blood pressure need to be used cautiously, bearing in mind both the side effects and the hazards of overly rapid control of hypertension. Conventional oral medication regimens demonstrated to modify the risks of chronic hypertension should be used whenever possible and as early as is practical to promote gradual control of hypertension. Whenever a patient presents for the evaluation of severe hypertension in an emergent setting, take the opportunity to encourage appropriate ongoing follow-up; after all, hypertension is not a single episode, it is an ongoing threat to good health.

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