HYPERTENSIVE CRISIS

- generally considered to be a ***diastolic pressure >120 mmHg*** **(>180/120 mmHg)**

✓ hypertensive emergencies

✓ and hypertensive urgencies

Definition

JNC7

- **Hypertensive urgencies** are those situations associated with severe elevations in BP **without progressive target organ dysfunction**

Definition

JNC7

- Hypertensive **emergencies** are characterized by severe elevations in BP complicated by evidence of **impending or progressive target organ dysfunction**.

Definition

- **25 percent** of all patient visits to busy urban **emergency rooms**.(76% urgencies, 24% emergencies)

Epidemiology

- **Without antihypertensive therapy** approximately **7% of patient** with hypertension would **progress to hypertensive crisis**
- **Effective management** of chronic hypertension has lowered this rate to **<1%**

Epidemiology

- **One-year** and **5-year mortality** following untreated hypertensive emergency are **70% to 90%** and **100%**, respectively.
- With **adequate blood pressure control**, these mortality rates decrease to **25%** and **50%**, respectively.

MORTALITY

History of hypertension

- In several studies of patients with hypertensive emergency, **a history of hypertension** was previously diagnosed in **>90% of the patients**, suggesting that hypertensive emergencies are **almost entirely preventable**

ETIOLOGY

- **Aortic dissection**
- **Aortic coarctation**
- **Autonomic hyperactivity** (guillain barre syndrom)
- **Burns**
- **Cerebrovascular condition** (e.g., hypertensive encephalopathy, ischemic stroke, intracerebral hemorrhage, head injury)

Etiology

- **Drug induced hypertension**

  (e.g.,cocaine,amphetamines,MAOI,abrupt withdrawal of clonidine)

- **Endocrine** (e.g., pheochromocytoma, Cushing syndrome,primary aldestronism,excess glucocortioids)

- **Postoperative HTN**

Etiology

- **Pregnancy (**eclampsia, pre-eclampsia)
- **Renal disease (**e.g., acute glomeronephritis,renal artery stenosis, macroscopic polyarteritis, post renal transplantation)
- **Vasculatis**
- **Head injury**

Etiology

- **Drug–drug interactions** (including herbal medications)
- **Erythropoietin administration**
- **Drug–food interactions** (i.e., patients receiving monoamine oxidase inhibitors who ingest foods rich in tyramine)

Etiology

- The pathophysiology of HC is **not well carectrized**
- **Renin-angiotension-aldestrone system**

Pathophysiology

CLINICAL PRESENTATION OF HYPERTENSIVE URGENCY

- The **most frequently reported symptoms** included:

- **Headache (42%)** and **dizziness (30%)**
- Other symptoms include **visual changes**, **chest discomfort**, **nausea**, **epistaxis**, **fatigue**, and **psychomotor agitation**

- It should be noted that  **not all patients** presenting with a hypertensive urgency **will have symptoms**

TREATMENT

- ✓ “hypertensive urgency” → “uncontrolled blood pressure”
- **Avoid rapidly lowering blood pressure hypotension** and **subsequent morbidity**
- Reduction of BP to a safe level can occur more slowly over **24 to 48 hours**.
- **Oral** Versus Parenteral Therapy

HYPERTENSIVE URGENCIES

- **Captopril**, **enalapril**, **sublingual NTG**, **nifedipine**, **IV furosemide**, **losartan**
- **What's your idea?**

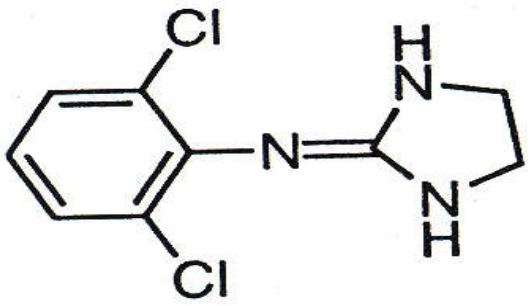
- **Clonidine**, **Labetalol**, **Minoxidil**, and **Captopril** have all been used to lower BP acutely

Oral Drugs Commonly Used in the Treatment of Hypertensive Urgencies

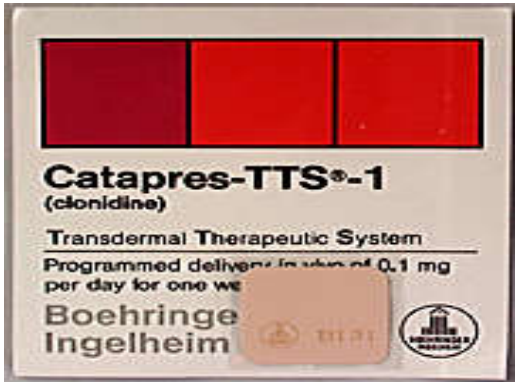
Drug[a] (Brand Name)	Dose/Route	Onset of Action	Duration of Action	Major Side Effects[a]	Mechanism of Action	Avoid or Use Cautiously in Patients With These Conditions
Captopril[b] (Capoten) 12.5-, 25-, 50-, 100-mg tablets	6.5–50 mg PO	15 minutes	4–6 hours	Hyperkalemia, angioedema, increased BUN if dehydrated, rash, pruritus, proteinuria, loss of taste	ACE inhibitor	Renal artery stenosis, hyperkalemia, dehydration, renal failure, pregnancy
Clonidine (Catapres) 0.1-, 0.2-, 0.3-mg tablets	0.1–0.2 mg PO initially, then 0.1 mg/h up to 0.8 mg total	0.5–2 hours	6–8 hours	Sedation, dry mouth, constipation	Central α_2-agonist	Altered mental status, severe carotid artery stenosis
Labetalol (Normodyne, Trandate) 100-, 200-, 300-mg tablets	200–400 mg PO repeated every 2–3 hours	30 minutes–2 hours	4 hours	Orthostatic hypotension, nausea, vomiting	α- and β-adrenergic blocker	Heart failure, asthma, bradycardia
Minoxidil (Loniten) 2.5-, 10-mg tablets	5–20 mg PO	30–60 minutes; maximum response in 2–4 hours	12–16 hours	Tachycardia, fluid retention	Arterial and venous vasodilator	Angina, heart failure

[a] All may cause hypotension, dizziness, and flushing.
[b] Other oral ACE inhibitors too slow in onset to be useful but should be used for maintenance therapy to improve adherence as captopril requires multiple daily doses
ACE, angiotensin-converting enzyme; BUN, blood urea nitrogen; PO, orally.

- Effective **first-line** therapy for hypertensive urgency
- Guanabenz → document is lacking in this seting



Clonidine



CLONIDINE

- Oral **loading dose** (**0.1–0.2 mg**)
- Followed by repeated doses of **0.1 mg/hour** → desired response or cumulative dose of **0.5 to 0.8 mg**
- Significant reduction in BP → within **1 hour**, MAP → ↓ **25%** in most patients after several hours

Dosing

- sequential loading doses ⟹ **caution**
  - **lack of benefit over placebo** and the potential for **unpredictable adverse effects**, particularly **abrupt occurrences of hypotension**.

- The **acute response to oral clonidine loading** is **not predictive of the daily dose** required to maintain acceptable BP control.

- **2-3 times daily** dosing → due to the short half-life.

- **reduce loading doses** → **volume depletion**, **recent use of other antihypertensive drugs**, and the **elderly**

ADVERSE EFFECTS

- Orthostatic hypotension
- Bradycardia
- Sedation
- Dry mouth
- Dizziness

- Clonidine **should not be used** in patients in whom **mental status** is an important monitoring parameter
- Can **decrease cerebral blood flow** by up to 28%, it **should not be used** in patients with severe **cerebrovascular disease**

- should be **avoided** in:
  - patients with **HF**, **bradycardia**, **sick sinus syndrome**, or **cardiac conduction defects**
  - as well as patients at risk for medication **nonadherence**

- **Orally** or **sublingually?**
- Can be used **orally** and **sublingually**
- May be given sublingually, but **no therapeutic advantage demonstrated**

- **Peaks** → **30 to 90 minutes** after ingestion
- **Onset** → **within 10 to 15 minutes**

- effects **persisting** for **<u>2 to 6 hours</u>**

- Sublingual captopril → as effective as nifedipine in acutely reducing MAP in both urgent and emergent conditions
- Caution → renal insufficiency or volume depletion

- First-dose hypotension → high renin levels → volume depletion or diuretics therapy → initial doses should not exceed 12.5 mg

- Oral ACE inhibitors, **other than captopril**, are **not useful** for acutely lowering BP because their **onset of action** is too slow?

- **Onset of action is slower** than that of **clonidine** or **captopril**
- **β-blockers** and loop diuretics generally must be used concomitantly ?

Minoxidil

- Minoxidil should be used only in patients presenting with hypertensive urgency who are **not responding to other antihypertensive therapies** or who have **previously been taking this agent**

- The **most appropriate dosing regimen?**
- **Initial doses** of **100 to 300 mg** may provide a sustained response for **up to 4 hours**.Labetalol (200 mg given at hourly intervals to a maximum dose of 1,200 mg) was **comparable to oral clonidine** in reducing mean arterial pressure

Oral Labetalol

- An alternative regimen using **300 mg initially** followed by **100 mg** at **2-hour intervals** to a **maximum** of **500 mg** was also successful in acutely lowering BP.[54] However, **Wright et al** were **unable** to **achieve** an **adequate BP response** in a small series of patients using a single loading dose of **200** to **400** mg

- ✓ Orthostatic hypotension → supine position
- ✓ Before ambulation → check for orthostasis
- ✓ Should be avoided in patients with **ASTHMA**, **BRADYCARDIA**, or **ADVANCED HEART BLOCK**

- Nifedipine → "bite and swallow"
- peripheral vasodilation. This reduces coronary perfusion, induces a **reflex tachycardia**, and increases myocardial oxygen consumption → **ischemia, MI, and stroke**

✓ Decreases cerebral blood flow

Rapidly Acting Calcium Channel Blockers

- Elderly patients with underlying coronary or cerebrovascular disease
  - volume depletion
  - concurrent use of other antihypertensive drugs

Predisposing Factors

HYPERTENSIVE EMERGENCIES

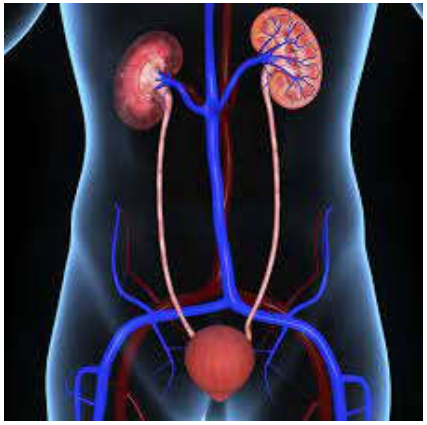
- **Similar to hypertensive urgencies**, hypertensive emergencies **rarely develop in patients without a previous history of hypertension**

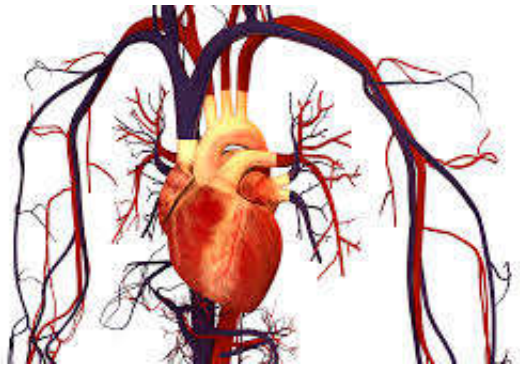
- **History of hypertension** was previously diagnosed in ***more than 90% of the patients***, suggesting that hypertensive emergencies are **almost entirely preventable**

- The **primary sites of damage** are the **central nervous system**, **heart**, **kidneys**, and **eyes**

TARGET ORGAN DYSFUNCTION

- The **CNS**, **Cardiovascular** and **Renal system** are most affected





End Organ Dysfunction

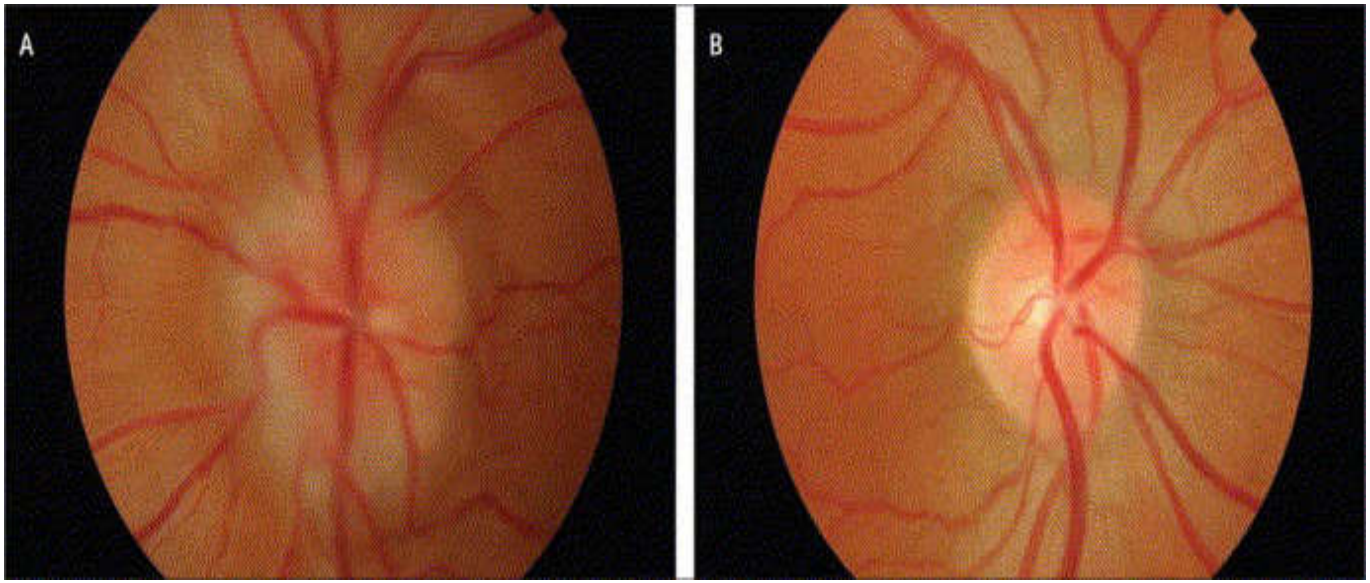
- central nervous system (CNS) abnormalities were the **most frequently** reported:
- Cerebral infarctions were noted in 24%
- encephalopathy in 16%
- intracranial or subarachnoid hemorrhage in 4% of patients.

End Organ Dysfunction

- ❑ acute heart failure and pulmonary edema were seen in 36% of patients
- acute myocardial infarction and unstable angina in 12% of patients.
- Acute dissection was noted in 2%
- eclampsia in 4.5% of patients.

End Organ Dysfunction

- **Accelerated-malignant hypertension with papilloedema**



Hypertensive Emergencies Versus Urgencies

Emergencies	Urgencies
Severely elevated blood pressure (diastolic >120 mm Hg)[a]	Severely elevated blood pressure (diastolic >120 mm Hg)[a]
Potentially life-threatening	Not acutely life-threatening
End-organ damage acute or progressing	Chronic end-organ damage that is not progressing
CNS (dizziness, N/V, encephalopathy, confusion, weakness, intracranial or subarachnoid hemorrhage, stroke)	Optic disc edema
Eyes (ocular hemorrhage or funduscopic changes, blurred vision, loss of sight)	
Heart (left ventricular failure, pulmonary edema, MI, angina, aortic dissection)	
Renal failure or insufficiency	
Requires immediate pressure reduction	Treated for several hours to days
Requires IV therapy (Table 21-2)	Oral therapy (Table 21-3)

[a] Degree of blood pressure elevation less diagnostic than rate of pressure rise and presence of concurrent diseases or end-organ damage. See Chapter 14, Essential Hypertension, for staging of hypertension.

CNS, central nervous system; IV, intravenous; MI, myocardial infarction; N/V, nausea and vomiting.

- Immediate hospitalization, generally in an ICU,
- Oral Versus Parenteral Therapy?

Principles of Treatment

- Effective therapy greatly improves the prognosis, reverses symptoms, and arrests the progression of end organ damage.

- Treatment **reverses the vascular changes** in the eyes and slows or arrests the progressive **deterioration in renal function**

Principles of Treatment

- Whether treatment can completely reverse end organ damage is related to two factors:

I. how soon treatment is begun

II. and the extent of damage at the initiation of therapy.

Principles of Treatment

- There are two fundamental concepts in the management of hypertensive emergencies:

- **FIRST**: immediate and intensive therapy

- **SECOND**: the choice of drugs will depend on how their time course of action and hemodynamic and metabolic effects meet the needs of a crisis situation.

Principles of Treatment

- ✓ If encephalopathy, acute left ventricular failure, dissecting aortic aneurysm, eclampsia, or other serious conditions are present, the BP should be lowered promptly with rapid-acting, parenteral antihypertensive medications

TABLE 21-2

Parenteral Drugs Commonly Used in the Treatment of Hypertensive Emergencies

Drug (Brand Name)	Class of Drug	Dose/Route	Onset of Action	Duration of Action
Clevidipine (Cleviprex) 0.5 mg/mL	Arterial vasodilator (calcium-channel blocker)	Initial: 1–2 mg/h; titrate dose to desired BP or to a max of 16 mg/h	2–4 minutes	10–15 minutes after D/C
Enalaprilat[a] (Vasotec IV) 1.25 mg/mL, 2.5 mg/2 mL	ACE inhibitor	0.625–1.25 mg IV every 6 hours	15 minutes (max, 1–4 hours)	6–12 hours
Esmolol[b] (Brevibloc) 100 mg/10 mL, 2,500 mg/10 mL concentrate	β-adrenergic blocker	250–500 mcg/kg for 1 minute, then 50–300 mcg/kg/min	1–2 minutes	10–20 minutes
Fenoldopam (Corlopam) 10 mg/mL, 20 mg/2 mL, 50 mg/5 mL	Dopamine-1 agonist	0.1–0.3 mcg/kg/min	<5 minutes	30 minutes
Hydralazine[c] (generic) 20 mg/mL	Arterial vasodilator	10–20 mg IV	5–20 minutes	2–6 hours
Labetalol[d] (Normodyne) 20 mg/4 mL, 40 mg/8 mL, 100 mg/20 mL, 200 mg/20 mL	α- and β-adrenergic blocker	2 mg/min IV or 20–80 mg every 10 minutes up to 300 mg total dose	2–5 minutes	3–6 hours
Nicardipine[e] (Cardene IV) 25 mg/10 mL	Arterial vasodilator (calcium-channel blocker)	IV loading dose 5 mg/h increased by 2.5 mg/h every 5 minutes to desired BP or a max of 15 mg/h every 15 minutes, followed by maintenance infusion of 3 mg/h	2–10 minutes (max, 8–12 hours)	40–60 minutes after D/C infusion
Nitroglycerin[f] (Tridil, Nitro-Bid IV, Nitro-Stat IV) 5 mg/mL, 5 mg/10 mL, 25 mg/5 mL, 50 mg/10 mL, 100 mg/20 mL	Arterial and venous vasodilator	IV infusion pump 5–100 mcg/min	2–5 minutes	5–10 minutes after D/C infusion
Nitroprusside[g] (Nitropress), 50 mg/2 mL (most commonly used)	Arterial and venous vasodilator	IV infusion.[a] Start: 0.5 mcg/kg/min Usual: 2–5 mcg/kg/min Max: 8 mcg/kg/min	Seconds	3–5 minutes after D/C infusion
Phentolamine (Regitine)	α-adrenergic blocker	1–5 mg IV initially, repeat as needed	Immediate	10–15 minutes

TABLE 21-4

Treatment Recommendations for Hypertensive Emergency

Clinical Presentation	Recommendation	Rationale
Aortic dissection	Nitroprusside, nicardipine, or fenoldopam plus esmolol or IV metoprolol; labetalol; trimethaphan. Avoid inotropic therapy.	Vasodilator will decrease pulsatile stress in aortic vessel to prevent further dissection expansion. β-blockers will prevent vasodilator-induced reflex tachycardia.
Angina, myocardial infarction	Nitroglycerin plus esmolol or metoprolol; labetalol. Avoid nitroprusside.	Coronary vasodilation, decreased cardiac output, myocardial workload, and oxygen demand. Nitroprusside may cause coronary steal.
Acute pulmonary edema, left ventricular failure	Nitroprusside, nicardipine, or fenoldopam plus nitroglycerin and a loop diuretic. Alternative: enalaprilat. Avoid nondihydropyridines, β-blockers.	Promotion of diuresis with venous dilatation to decrease preload. Nitroprusside, enalaprilat decrease afterload. Nicardipine may increase stroke volume.
Acute kidney injury	Nicardipine or fenoldopam. Avoid nitroprusside, enalaprilat.	Peripheral vasodilation without renal clearance. Fenoldopam shown to increase renal blood flow.
Cocaine overdose	Nicardipine, fenoldopam, verapamil, or nitroglycerin. Alternative: labetalol. Avoid β-selective blockers.	Vasodilation effects without potential unopposed α-adrenergic receptor stimulation. CCBs control overdose-induced vasospasm.
Pheochromocytoma	Nicardipine, fenoldopam, or verapamil. Alternatives: phentolamine, labetalol. Avoid β-selective blockers.	Vasodilation effects without potential unopposed α-adrenergic receptor stimulation.
Hypertensive encephalopathy, intracranial hemorrhage, subarachnoid hemorrhage, thrombotic stroke	Nicardipine, fenoldopam, or labetalol. Avoid nitroprusside, nitroglycerin, enalaprilat, hydralazine.	Vasodilation effects without compromised CBF induced by nitroprusside and nitroglycerin. Enalaprilat and hydralazine may lead to unpredictable BP changes when carefully controlled BP management is required.

- The rate of BP lowering must be **individualized**
- Elderly and patients with severely defective autoregulatory mechanisms (autonomic dysfunction or fixed sclerotic stenosis of cerebral or neck arteries) → hypotension complications
- chronically elevated BP → hypertensive encephalopathy, cerebral hypoperfusion may occur if the mean BP is reduced by >40%

Principles of Treatment

- initially by no more than 25% (within minutes to 1 hour), then if stable → 160/100 mmHg within 2 to 6 hours and gradual reduction to normal → over the next 8 to 24 hours.

Principles of Treatment

- A diastolic pressure of 100 to 110 mmHg is an appropriate initial therapeutic goal

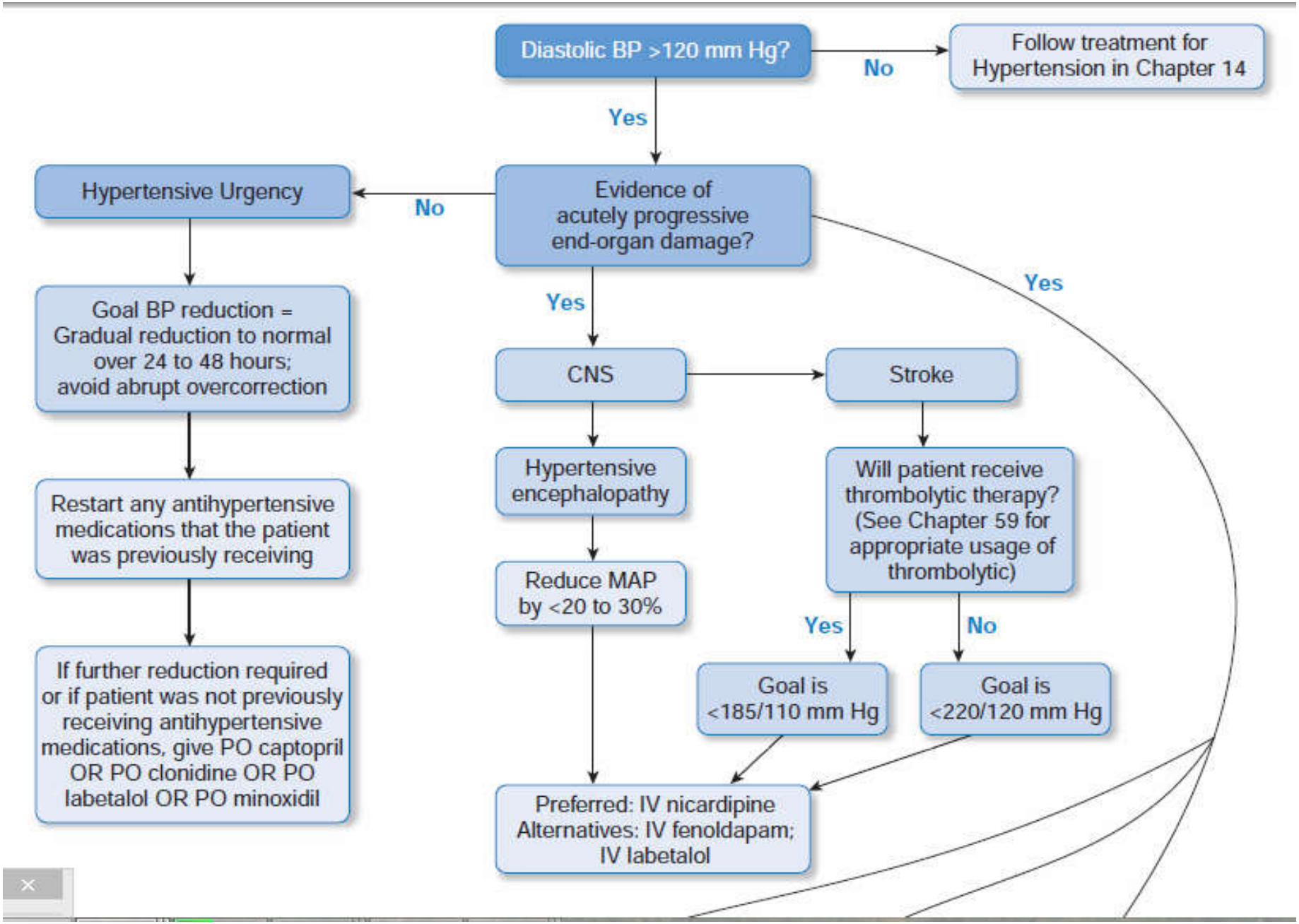
✓ **Two exception:**

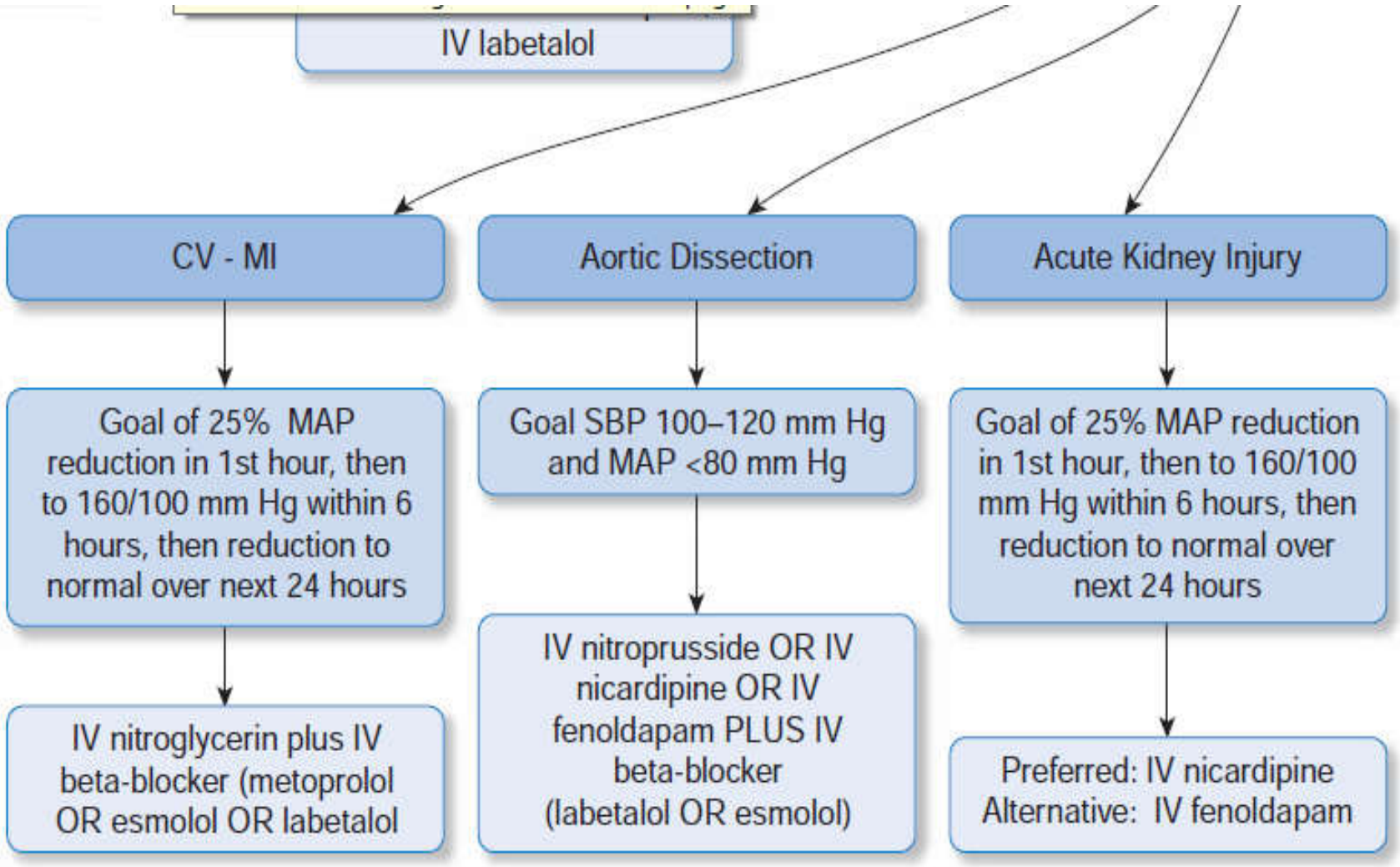
I. Aortic Dissection → Lower pressures may be indicated

II. Acute Cerebrovascular Accidents:

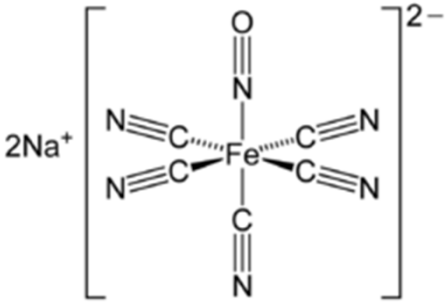
- following acute ischemic stroke in the presence of end organ damage if the blood pressure is <220/120 mmHg in patients ineligible for thrombolytic therapy or <185/110 mmHg in those who are candidates for thrombolytics.

Principles of Treatment


Diastolic BP >120 mm Hg?
No
Follow treatment for Hypertension in Chapter 14
Yes
Hypertensive Urgency
No
Evidence of acutely progressive end-organ damage?
Yes
Goal BP reduction = Gradual reduction to normal over 24 to 48 hours; avoid abrupt overcorrection
Yes
CNS
Stroke
Restart any antihypertensive medications that the patient was previously receiving
Hypertensive encephalopathy
Will patient receive thrombolytic therapy? (See Chapter 59 for appropriate usage of thrombolytic)
If further reduction required or if patient was not previously receiving antihypertensive medications, give PO captopril OR PO clonidine OR PO labetalol OR PO minoxidil
Reduce MAP by <20 to 30%
Yes
No
Goal is <185/110 mm Hg
Goal is <220/120 mm Hg
Preferred: IV nicardipine
Alternatives: IV fenoldapam; IV labetalol


IV labetalol
CV - MI
Aortic Dissection
Acute Kidney Injury
Goal of 25% MAP reduction in 1st hour, then to 160/100 mm Hg within 6 hours, then reduction to normal over next 24 hours
Goal SBP 100–120 mm Hg and MAP <80 mm Hg
Goal of 25% MAP reduction in 1st hour, then to 160/100 mm Hg within 6 hours, then reduction to normal over next 24 hours
IV nitroglycerin plus IV beta-blocker (metoprolol OR esmolol OR labetalol
IV nitroprusside OR IV nicardipine OR IV fenoldapam PLUS IV beta-blocker (labetalol OR esmolol)
Preferred: IV nicardipine
Alternative: IV fenoldapam

- Nitroprusside is the drug of choice for acute hypertensive emergencies



Nitroprusside

Table 20-4 Treatment Recommendations for Hypertensive Crises

Clinical Presentation	*Recommendation*	*Rationale*
Aortic dissection	Nitroprusside, nicardipine, or fenoldopam plus esmolol or IV metoprolol; labetalol; trimethaphan. Avoid inotropic therapy.	Vasodilator will decrease pulsatile stress in aortic vessel to prevent further dissection expansion. β-blockers will prevent vasodilator-induced reflex tachycardia.
Angina, myocardial infarction	Nitroglycerin plus esmolol or metoprolol; labetalol. Avoid nitroprusside.	Coronary vasodilation, decreased cardiac output, myocardial workload, and oxygen demand. Nitroprusside may cause coronary steal.
Acute pulmonary edema, left ventricular failure	Nitroprusside, nicardipine, or fenoldopam plus nitroglycerin and a loop diuretic. Alternative: enalaprilat. Avoid nondihydropyridines, β-blockers.	Promotion of diuresis with venous dilatation to decrease preload. Nitroprusside, enalaprilat decrease afterload. Nicardipine may increase stroke volume.
Acute renal failure	Nicardipine or fenoldopam. Avoid nitroprusside, enalaprilat.	Peripheral vasodilation without renal clearance. Fenoldopam shown to increase renal blood flow.
Cocaine overdose	Nicardipine, fenoldopam, verapamil, or nitroglycerin. Alternative: labetalol. Avoid β-selective blockers.	Vasodilation effects without potential unopposed α-adrenergic receptor stimulation. CCBs control overdose-induced vasospasm.
Pheochromocytoma	Nicardipine, fenoldopam, or verapamil. Alternatives: phentolamine, labetalol. Avoid β-selective blockers.	Vasodilation effects without potential unopposed α-adrenergic receptor stimulation.
Hypertensive encephalopathy, intracranial hemorrhage, subarachnoid hemorrhage, thrombotic stroke	Nicardipine, fenoldopam, or labetalol. Avoid nitroprusside, nitroglycerin, enalaprilat, hydralazine.	Vasodilation effects without compromised CBF induced by nitroprusside and nitroglycerin. Enalaprilat and hydralazine may lead to unpredictable BP changes when carefully controlled BP management is required.

- relatively ineffective in the acute treatment of hypertension except in patients with **concomitant volume overload** or **HF**
  - Renal failure aggravation and profound hypotension
- ✓ HF ⟹ venodilation or diuresis?

Concurrent Use of Diuretics

SUBLINGUAL NITROGLYCERIN?

Nitroglycerin

- ✓ Nicardipine, Verapamil, or IV Nitroglycerin
- ❑ Calcium channels blockers and IV nitroglycerin are preferred in patients with active myocardial ischemia because they have both been shown to reverse cocaine-induced hypertension and vasoconstriction
- ❑ Fenoldopam and Nitroprusside can be used as alternative agents

Cocaine-induced Hypertension

- Benzodiazepines ⟹ can attenuate the effect of cocaine on the cardiac system

Benzodiazepines

THANK YOU