HYPERTENSIVE CRISIS

Hypertensive Crisis

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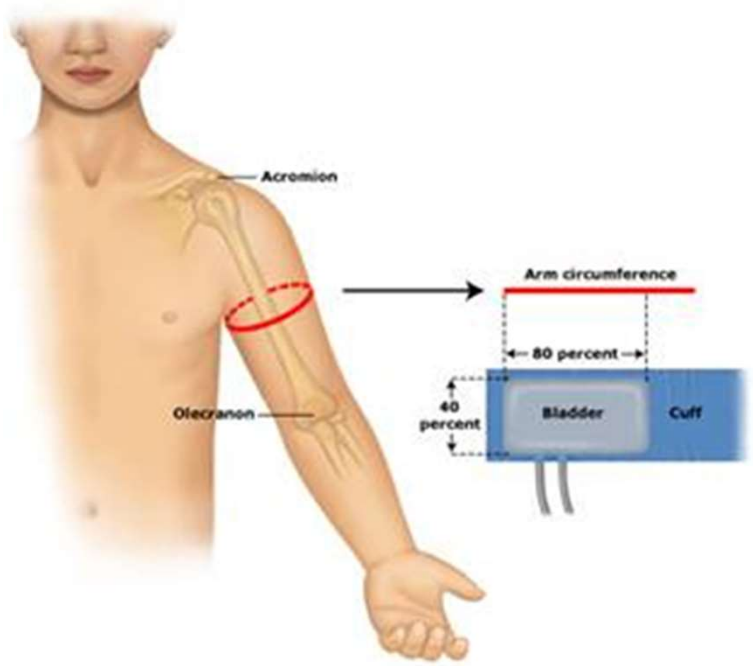
Accurate Measurement of BP in the Office

Step 1: Properly prepare the patient

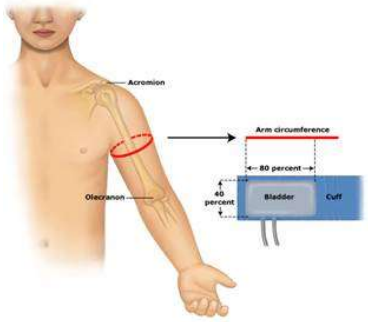
1. Have the patient relax, sitting in a chair (feet on floor, back supported) for >5 min.
2. The patient should avoid caffeine, exercise, and smoking for at least 30 min before measurement.
3. Ensure patient has emptied his/her bladder.
4. Neither the patient nor the observer should talk during the rest period or during the measurement.
5. Remove all clothing covering the location of cuff placement.
6. Measurements made while the patient is sitting or lying on an examining table do not fulfill these criteria.

Step 2: Use proper technique for BP measurements

1. Use a BP measurement device that has been validated, and ensure that the device is calibrated periodically.*
2. Support the patient's arm (e.g., resting on a desk).
3. Position the middle of the cuff on the patient's upper arm at the level of the right atrium (the midpoint of the sternum).
4. Use the correct cuff size, such that the bladder encircles 80% of the arm, and note if a larger- or smaller-than-normal cuff size is used (**Table 9**).
5. Either the stethoscope diaphragm or bell may be used for auscultatory readings (S4.1-5,S4.1-6).


Acromion
Olecranon
Arm circumference
80 percent
40 percent
Bladder
Cuff

2. **CUFF:** An appropriately sized cuff should be used. The internal inflatable bladder width should be at least 40% and the bladder length and cover at least 80% of the upper arm circumference. The cuff should be wrapped snugly around the arm with the center of the bladder over the brachial artery.



3. **MONITOR:** Measurements should be taken with a correctly calibrated mercury sphygmomanometer, an aneroid manometer, or a validated electronic device.

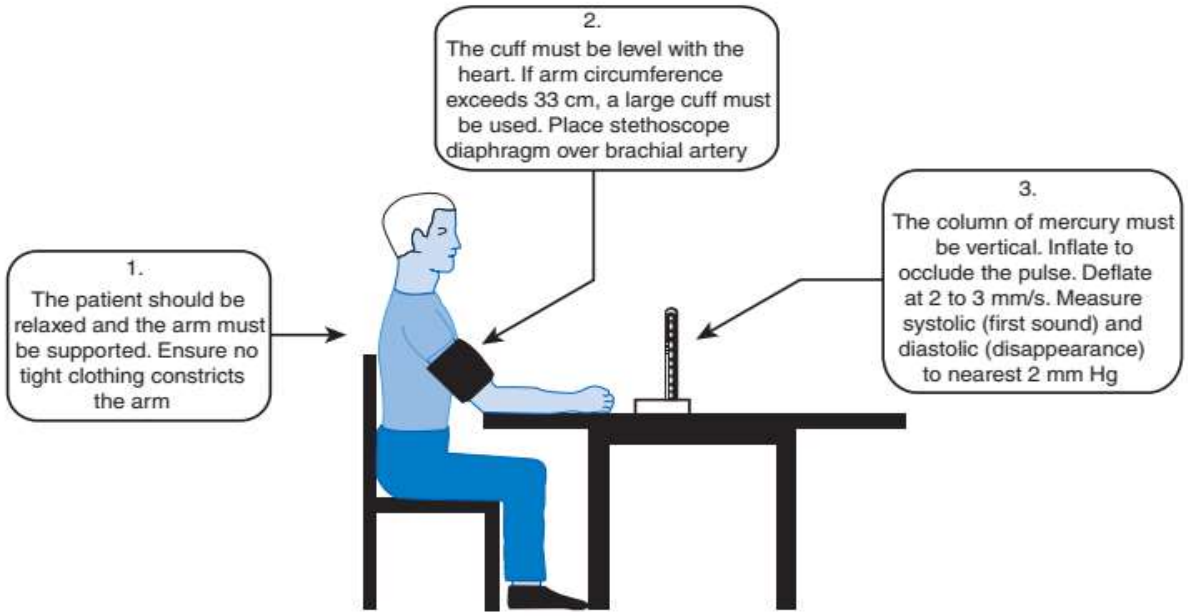


FIGURE 2-8 • Technique of BP measurement recommended by the British Hypertension Society. (From British Hypertension Society. Standardization of blood pressure measurement. *J Hypertens* 1985;3:29–31. Reproduced with permission)

- **Wrist** or **finger** devices that measure BP are generally not accurate and **should not be routinely used**.

Instructions on HBPM procedures:

- **Remain still:**
  - Avoid smoking, caffeinated beverages, or exercise within 30 min before BP measurements.
  - Ensure ≥5 min of quiet rest before BP measurements.
- **Sit correctly:**
  - Sit with back straight and supported (on a straight-backed dining chair, for example, rather than a sofa).
  - Sit with feet flat on the floor and legs uncrossed.
  - Keep arm supported on a flat surface (such as a table), with the upper arm at heart level.
- Bottom of the cuff should be placed directly above the antecubital fossa (bend of the elbow).
- **Take multiple readings:**
  - Take at least 2 readings 1 min apart in morning before taking medications and in evening before supper. Optimally, measure and record BP daily. Ideally, obtain weekly BP readings beginning 2 weeks after a change in the treatment regimen and during the week before a clinic visit.
- **Record all readings accurately:**
  - Monitors with built-in memory should be brought to all clinic appointments.
  - BP should be based on an average of readings on ≥2 occasions for clinical decision making.

The information above may be reinforced with videos available online.

Hypertensive crisis

- 62 yo M with a history of hypertension, normally on Lisinopril, presents to PCP for routine check-up. Patient with no complaints.
  - BP found to be **224/130 on check** in clinic.
  - PE normal.
  - Referred to ED for “hypertensive crisis”.

Case 1

- Patient had run out of Lisinopril and been off it for more than a week.
  - In ED, remained asymptomatic. Repeat BP 210/120.
  - PE normal.

Case 1

- Restarted on Lisinopril, referred back to PCP in a week for bp check
- In clinic later that week, BP 150/92.
- Started on second anti-hypertensive.

Case 1

- 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.

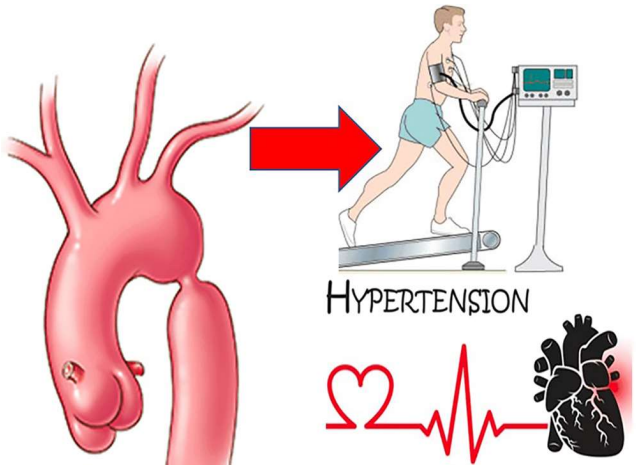
MORTALITY

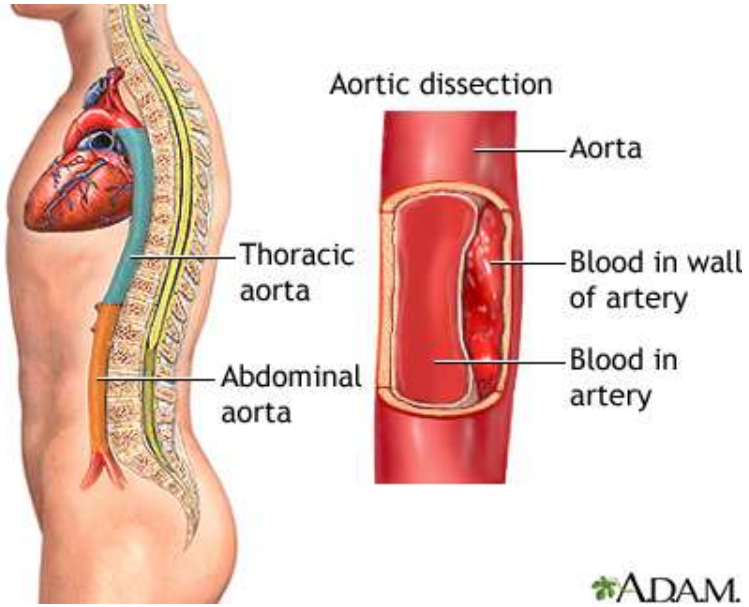
History of Hypertension

- 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**





Etiology

- **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

RRAS

- 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**

Hypertensive urgencies

- Reduction of BP to a safe level can occur more slowly over **24 to 48 hours**.
- **Oral** Versus Parenteral Therapy?

Hypertensive urgencies

- In adults with severe asymptomatic hypertension, the shorter-term goal of management is to reduce the blood pressure to ≤160/≤100 mmHg. However, the mean arterial pressure should not be lowered by **more than 25 to 30 percent over the first several hours**

- Patients judged to be at high risk for imminent cardiovascular events due to severe hypertension, including those with known **aortic or intracranial aneurysms**, should have their blood pressure lowered over a period of hours

- Captopril, enalapril, sublingual NTG, nifedipine, IV furosemide, losartan

- What's your idea?

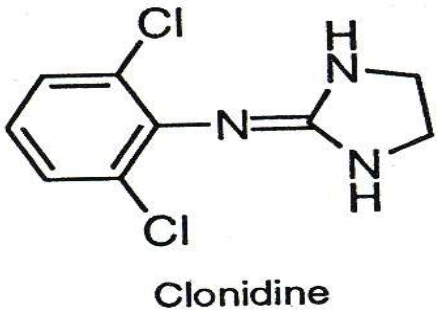
- Clonidine, Labetalol, Minoxidil, and Captopril have all been used to lower BP acutely

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



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**

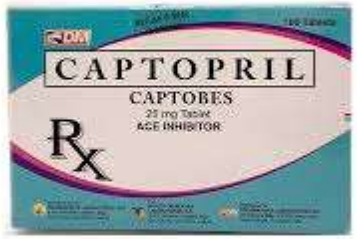
ADVERSE EFFECTS

- 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**



CAPTOPRIL

Captopril

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

- Effects **persisting** for **2 to 6 hours**

Captopril

- **Sublingual captopril** → as effective as **nifedipine** in acutely reducing MAP in both urgent and emergent conditions

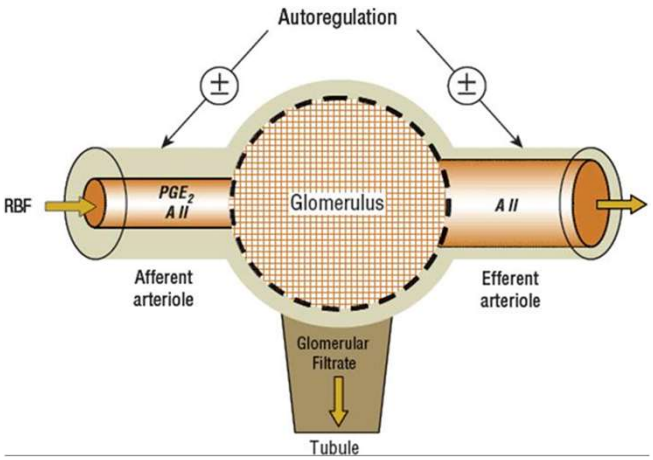
- **Caution** → **renal insufficiency** or **volume depletion**

Captopril

- First-dose hypotension or AKI → ?

Captopril

First-dose hypotension or AKI



↓

High renin levels

↓

Volume depletion or diuretics therapy

↓

Initial doses should not exceed **12.5 mg**

Other ACEIs

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

- The **most appropriate dosing regimen?**
- **Initial doses** → **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.
  - 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

Warnings and precautions

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

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

- 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**

Nifedipine

- Nifedipine → **“bite and swallow”**

Nifedipine

- Peripheral vasodilation. This reduces coronary perfusion, induces a **reflex tachycardia**, and increases myocardial oxygen consumption → **ischemia, MI, and stroke**

✓ Decreases cerebral blood flow

Nifedipine

- 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

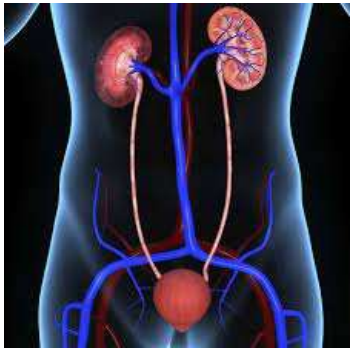
- **History of hypertension** was previously diagnosed in ***more than 90% of the patients***, suggesting that hypertensive emergencies are **almost entirely preventable**

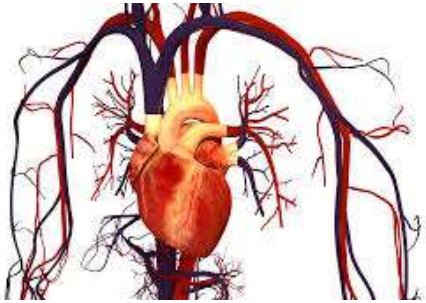
History of Hypertension in more than 90% of patients

- 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:**

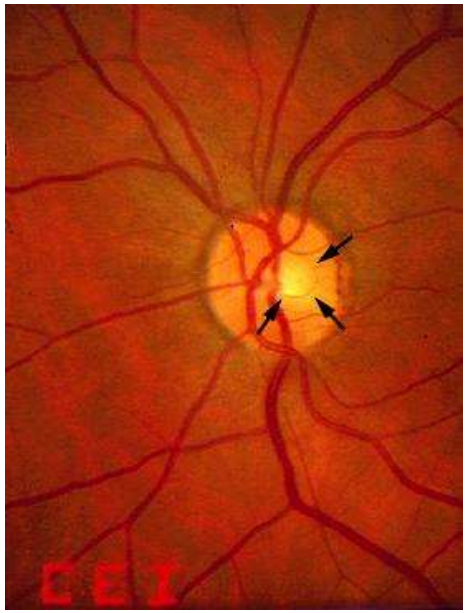
- Cerebral infarctions were noted in 24%
- Encephalopathy in 16%
- Intracranial or subarachnoid hemorrhage in 4% of patients.

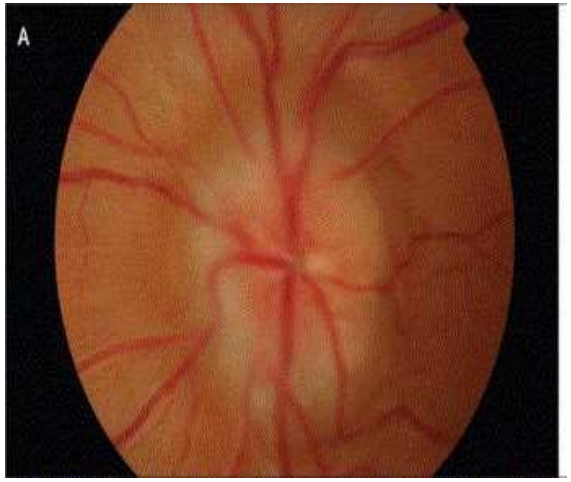
End Organ Dysfunction

- 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. 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** is required

- **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

The BP should be lowered promptly

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.

Rate of BP lowering

- 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:**

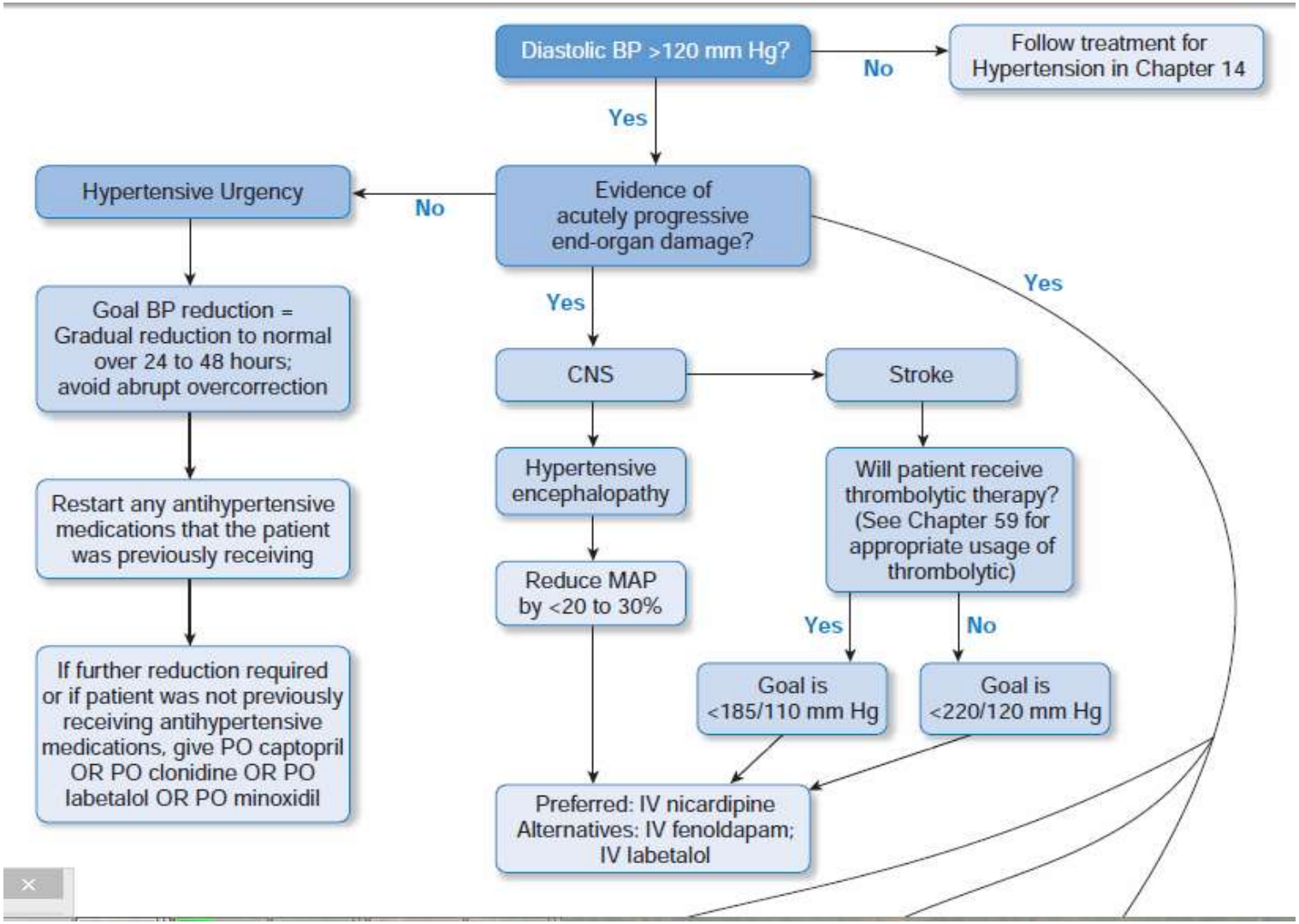
✓ **Two exception:**

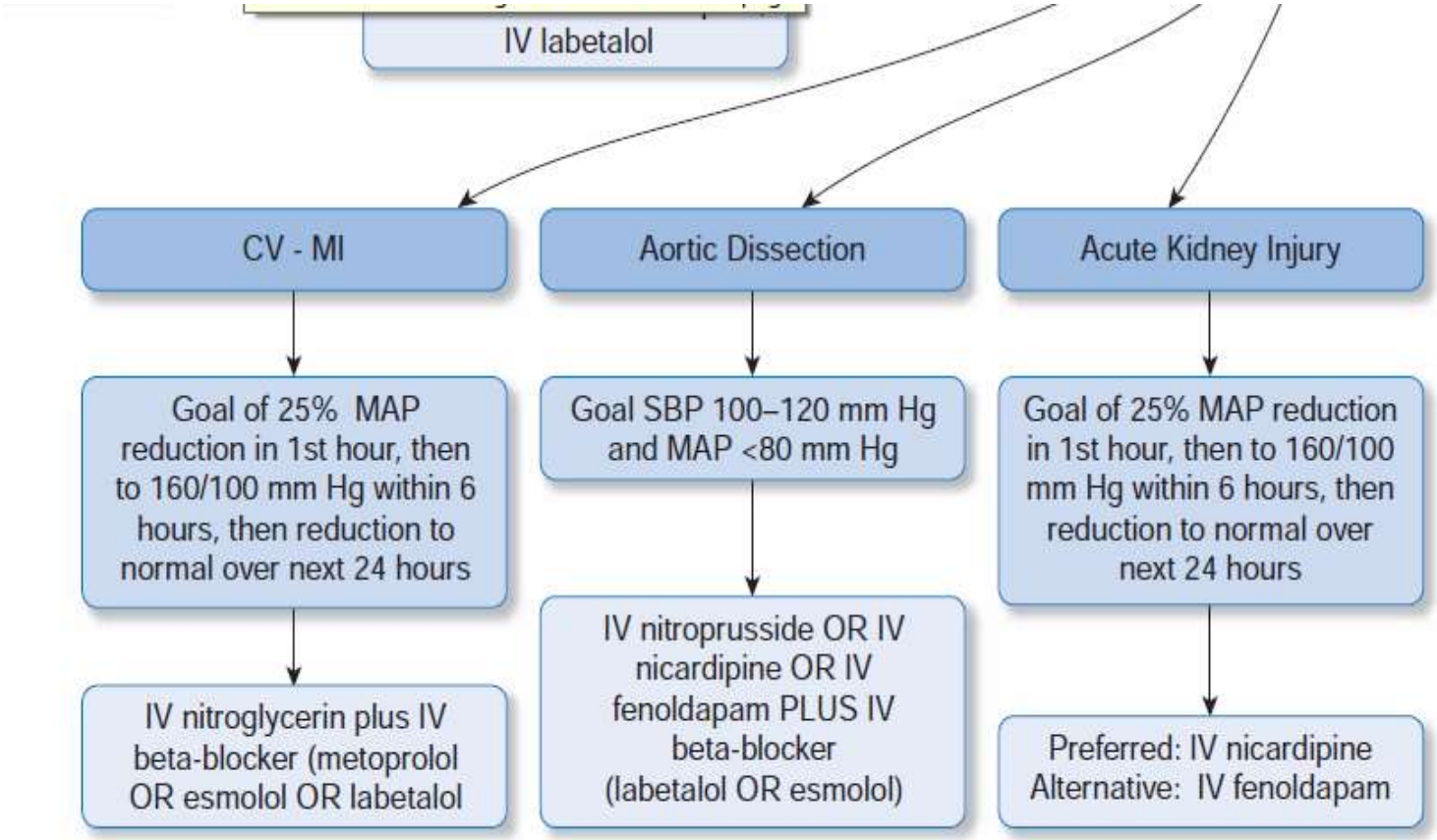
I. Aortic Dissection

Lower pressures may be indicated

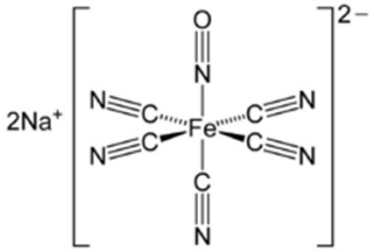
II. Acute Cerebrovascular Accidents:

- 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


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
IV nitroglycerin plus IV beta-blocker (metoprolol OR esmolol OR labetalol
Goal SBP 100–120 mm Hg and MAP <80 mm Hg
IV nitroprusside OR IV nicardipine OR IV fenoldapam PLUS IV beta-blocker (labetalol OR esmolol)
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
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.

- ✓ easily titratable
- ✓ *Onset of Action* ⟹ Sec
- ✓ *Duration of Action* ⟹ 3–5 min after D/C infusion
- ✓ Low cost
- ➢ cyanide or thiocyanate toxicity

- extreme potency ⟹ exact concentrations precisely calculated rates using a controlled infusion device ⟹ BP must be closely monitored

- the solution should be shielded with an opaque sleeve but It is **not necessary** to protect the **tubing** from light

- Reconstituted solutions are stable for 24 hours at room temperature
- A change in the solution's color  discarded

- infusion rates range from 0.25 to 10 mcg/kg/minute
  - Cyanide toxicity → infusion rates >2 to 3 mcg/kg/minute
  - Start → 0.25 mcg/kg/minute
  - ✓ The dose should be increased slowly by 0.25 mcg/kg/minute every 5 minutes
  - Maximum → 10 mcg/kg/minute or 8 mcg/kg/minute?
- No response after 10 min post max infusion rate → D/C

- Hypotension ⟹ nitroprusside should be discontinued and M.R. should be placed in the Trendelenburg position, where the head is kept lower than the trunk

- Relatively **ineffective** in the acute treatment of hypertension except in patients with concomitant volume overload or HF

  - Renal failure aggravation and profound hypotension

  - ✓ **Venodilation or diuresis?**

Concurrent Use of Diuretics

- cyanide toxicity and mortality associated with nitroprusside exceed 3,000 and 1,000 cases per year, respectively 44% of nitroprusside by weight ⇒ prussic acid (hydrogen cyanide)
- mitochondrial rhodanese system converts cyanide to thiocyanate
- Elimination rate ⇒ 2 mcg/kg/minute

Cyanide Toxicity

- mixture of 0.1% sodium nitroprusside plus 1% sodium thiosulfate → as effective as sodium nitroprusside alone and is substantially less toxic → no studies have assessed the chemical compatibility of nitroprusside and sodium thiosulfate

- in high-risk patients (e.g., those with malnutrition) or when large doses of nitroprusside are administered (>3 mcg/kg/minute)

- The presence of hepatic or renal failure
- occurs most commonly when large doses (total dose 1.5 mg/kg) of nitroprusside are administered rapidly to patients undergoing a surgical procedure that requires induction of hypotension
- increasing concern about cyanide toxicity ⇒ revision of the product label ⇒ infusions at the maximum recommended dose can overwhelm the body's ability to buffer the cyanide within 1 hour

- No clinical data are available to indicate that it reduces overall mortality → accumulation of thiocyanate, particularly → at high infusion rates or renal insufficiency

sodium thiosulfate

- Infusion ⟹ 25 mg/hour
- 2.4 g of hydroxocobalamin is required to neutralize the cyanide released from 100 mg of nitroprusside
- with the availability of safer alternatives (e.g., fenoldopam, IV labetalol, IV nicardipine) for use in high-risk patients, the use of hydroxocobalamin or thiosulfate is rarely required

Hydroxocobalamin

- The half-life of thiocyanate is 2.7 days with normal renal function and 9 days in patients with renal failure.
- When sodium nitroprusside is infused for several days at moderate dosages (2–5 mcg/kg/minute), toxic levels of thiocyanate can occur within 7 to 14 days in patients with normal renal function and 3 to 6 days in patients with severe renal disease

Thiocyanate Toxicity

- Neurotoxic syndrome → manifested by psychosis, hyperreflexia, confusion, weakness, tinnitus, seizures, and coma
- levels of thiocyanate → renal disease or when the duration of the nitroprusside infusion exceeds 3 or 4 days
- Discontinued → thiocyanate levels exceed 10 to 12 mg/dL.
- Life-threatening toxicity → levels exceed 20 mg/dL.
- In emergency cases, thiocyanate can be readily removed by hemodialysis

- peripheral dopamine-1 agonist
  - Renal blood flow ⟹ advantageous in patients with impaired renal function.
  - No document that this effect reduces morbidity and mortality in patients with severe hypertension

Fenoldopam

- more expensive than, sodium nitroprusside
- only as an alternative to nitroprusside in patients who are at high risk for cyanide or thiocyanate toxicity.

- ✓ Fenoldopam is administered as a continuous infusion (without a bolus dose)
- ✓ Start → 0.1 mcg/kg/minute
  increments of 0.05 to 0.1 mcg/kg/minute at 15-minute intervals
- Max dose: → 1.6 mcg/kg/minute
- *Onset of Action* → <5 min
- half-life → approximately 5 minutes
- *Duration of Action* → 30 min
- its use has been studied for up to 48 hours of therapy

- The vasodilating effect may also cause flushing, dizziness, and headache
- dose-dependent increase in intraocular pressure(IOP) ⟹ should be used cautiously in patients with glaucoma or intraocular hypertension

Adverse Effects

- Labetalol blocks both β- and α-adrenergic receptors and also may exert a direct vasodilator effect.
- The β-blockade is nonselective with α to β potency of **3:1 for oral** and **7:1 for IV** labetalol without causing reflex tachycardia does not significantly reduce cerebral blood flow

Labetalol

- Glucuronidation in the liver
- <5% excreted unchanged in the urine

- Uncontrolled HF
- Raynaud's syndrome
- **Mask** the symptoms of **hypoglycemia** in insulin-dependent diabetic patients

Precautions

- Asthma
- Heart block greater than first degree
- Sinus bradycardia

Contraindications

- However, because labetalol is primarily a β-blocker, paradoxical hypertension may occur in patients with **pheochromocytoma**?

- Older patients achieve a greater reduction in BP
  require smaller doses

- Failure to lower BP ?

- ✓ supine position
- ❑ Start:20 mg given over 2 minutes
- ❑ followed by: 40 to 80 mg every 10 to 15 minutes until the desired response is or a cumulative dose of 300 mg
- ❑ maximal effect occurs within 5 to 10 minutes, and the antihypertensive response may persist for >6 hours

- ✓ when supine diastolic BP increases by 10 mmHg
- ➢ There is no correlation between the oral maintenance dose and the total initial IV dose

Parenteral/Oral Conversion

- Postural hypotension and dizziness (dose related)
- before permitting ambulation orthostasis should be rule out

SUBLINGUAL NITROGLYCERIN?

Nitroglycerin

- myocardial oxygen consumption ⇒ Unstable angina or MI and coronary bypass surgery
- Nitroprusside? **coronary steal?**

Nitroglycerin

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BP, blood pressure; CBF, cerebral blood flow; CCB, calcium channel blocker; IV, intravenous.

- Rapid onset of action and a short duration
  - Start: 5 to 10 mcg/minute
  - usual dose → 40 to 100 mcg/minute
  - Headache and the development of tolerance → major limiting side effects

- should be used only in patients who:

I. Cannot tolerate labetalol (e.g., asthma or advanced heart block)

II. require a more gradual lowering of BP than that produced by nitroprusside

III. require a more rapid and certain drop in BP than that which can be produced by oral antihypertensive agents

Diazoxide

- ✓ Small bolus or by slow infusion because larger doses cause cerebral and cardiovascular hypoperfusion
- ❖ Single-dose injections of >150 mg should not be used
- ○ Major disadvantage → reflex tachycardia → can precipitate or worsen angina
- when tachycardia is dangerous → IV propranolol (0.2 mg/kg)

✓Eclampsia

- Direct vasodilator → effect on arterial smooth muscle
- antihypertensive response is less predictable → rarely used to treat hypertensive emergencies
- is not consistently effective in controlling crises associated with essential hypertension

Hydralazine

I. coronary heart disease → reflex tachycardia

II. aortic dissection → reflex cardiostimulating effect

Contraindications

- chronic renal failure → increase in cardiac output is accompanied by an increase in organ perfusion

- FDA approval for hypertension
- Only **60%** of the patients **respond** to BP reduction within 30 minutes
- Initial doses should not exceed 0.625 mg in patients receiving diuretics or hypovolemia
- cerebral hypoperfusion → may be useful

Enalaprilat

- cannot be recommended for the routine treatment of patients with hypertensive emergencies

- Postoperative hypertension, especially if associated with tachycardia
- In cardiac bypass surgery antihypertensive effect of esmolol was comparable to that of nitroprusside
- Hypotension ⟹ most commonly reported adverse event
- contraindication ⟹ asthma, advanced heart block and severe HF

- Limited data
- extreme caution in systolic HF

❑Intravenous Nicardipine

IV nicardipine is an alternative to sodium nitroprusside for the immediate treatment of severe and postoperative hypertension

reflex tachycardia → caution in coronary ischemia

Intravenous Calcium Channel Blockers

- ✓ hypertensive emergencies induced by catecholamine excess (pheochromocytoma)
- The onset of action is almost immediate and the duration of action is short (<15 minutes)
- IV infusions are not recommended → due to the risk of causing hypotension

Intravenous Phentolamine

- ✓ The treatment of choice → has classically been a vasodilatory agent (sodium nitroprusside, fenoldopam, or nicardipine) + a β-blocker titrated to a heart rate of 55 to 65 beats/minute
  - ○ Labetalol monotherapy → alternative

Aortic Dissection

- combination of IV sodium nitroprusside (0.5–2 mcg/kg/minute) plus IV esmolol (25–200 mcg/kg/minute)
- ✓ **TRIMETHAPHAN** → advantage over sodium nitroprusside → reduces both arterial pressure and its rate of increase → it does not require concurrent administration of β-blockers

- major disadvantages → tachyphylaxis , urinary retention, and ileus
- Diazoxide and Hydralazine should be avoided

✓surgical intervention

- BP ↓ maintenance of adequate renal, cerebral, and cardiac perfusion → the systolic BP should be lowered to 100 to 120 mmHg or a MAP<80 mmHg. →

✓ Ganglionic Blocking agent

❑ often necessary to elevate the head of the bed to achieve an optimal effect

- To correct hypotension → trimethaphan should be discontinued and the patient should be placed in the Trendelenburg position.
- constant infusion pump
- Therapy with oral antihypertensive agents should begin simultaneously, and an attempt should be made to discontinue the ganglionic blocker within 48 hours before significant tolerance renders the patient resistant to its action.

Trimethaphan

- prolonged use is limited by → tachyphylaxis and sympathoplegic side effects.
  - ✓ Urinary retention
  - ✓ Constipation
  - ✓ paralytic ileus
  - ✓ paralysis of visual accommodation

- ✓ 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

- β-blockers should be avoided in patients with hypertension or myocardial ischemia/MI with recent cocaine use → unopposed α-adrenergic → further elevation in BP and heart rate
- Labetalol → caution → ↑ seizure in animals
- does not alleviate cocaine-induced coronary vasoconstriction
- worsen BP when α-stimulation has been left unopposed in patients with pheochromocytoma

THANK YOU