HYPERTENSIVE URGENCY/EMERGENCY

Hypertensive urgency = ↑↑BP alone

Hypertensie emergency = ↑↑BP + end-organ damage

Subcategory defns...
- malignant htn: retinal hemorrhages, exudates, or papilledema)
- malignant nephrosclerosis: renal involvement
- htnsive encephalopathy: signs of cerebral edema (from breakthru hyperperfusion)

End organs that can be involved...

Eye	- retinal hemorrhages, exudates - papilledema (Si of ↑ICP)
Brain	- ↑ICP d/t cerebral edema: presents as h/a -> n/v -> delta MS - stroke/bleed - seizure
Lung	- pulm edema (Si of CHF)
Heart/vessel	- MI - Ao dissection - CHF
Kidney	- ARF -> acute ↑Cr, hematuria, proteinuria
Blood	- hemolytic anemia (MAHA)

Acute management

1. Cardiac monitor; consider step-down bed or unit, particularly if emergency (consider a-line if emergency)

2. If DBP >110, lower by 10-15% or to 110 mmHg

3. Lower MAP by max 25% in the 1st 24 hrs (any faster risks cerebral hypoperfusion)
   - lower *over minutes* if emergency (start with IV meds)
   - lower *over hours* if urgency (can start with either PO or IV meds)

4. Options for acute treatment...

B-blockers	CCB	Nitrates	ACEi	Other
metop po or IVP labetolol IVP or gtt esmolol gtt	nifedipine XL po nicardipine gtt	NTG gtt (not as effective at ↓BP)	captopril po enalapralit gtt	clonidine po fenoldopam IV
⇓	⇓	⇓	⇓	
good for ↑HR, CP, ACS, h/o CAD, hypertensive encephalopathy	good for ARF, hypertensive encephalopathy	good for active CP, ACS, pulm edema (along with lasix & nitroprussside)	consider in low EF, AR, MR, but avoid in ARF	

Note: in Ao dissection, use labetolol (or nitroprusside + esmolol); in eclampsia, use hydralazine, labetolol, or nicardipine

5. After BP controlled on IV's, start transitioning to PO meds

Chronic management

Consider work-up for secondary causes of hypertension if not already done & cause unclear.

Hypertensive Urgency / Emergency

Hypertensive emergencies are acute, life-threatening, and usually associated with marked increases in blood pressure. There are two major clinical syndromes induced by the severe hypertension:

- Malignant hypertension is marked hypertension with retinal hemorrhages, exudates, or papilledema. There may also be renal involvement, called malignant nephrosclerosis.
- Hypertensive encephalopathy refers to the presence of signs of cerebral edema caused by breakthrough hyperperfusion from severe and sudden rises in blood pressure.

MECHANISMS OF VASCULAR INJURY — With mild to moderate elevations in blood pressure, the initial response to hypertension is arterial and arteriolar vasoconstriction. This autoregulatory process both maintains tissue perfusion at a relatively constant level and prevents the increase in pressure from being transmitted to the smaller, more distal vessels.

With increasingly severe hypertension, however, autoregulation eventually fails. The ensuing rise in pressure in the arterioles and capillaries leads to damage to the vascular wall. Disruption of the vascular endothelium then allows plasma constituents (including fibrinoid material) to enter the vascular wall, thereby narrowing or obliterating the vascular lumen. Within the brain, the breakthrough vasodilation from failure of autoregulation leads to the development of cerebral edema and the clinical picture of hypertensive encephalopathy.

CLINICAL MANIFESTATIONS — Malignant hypertension most often occurs in patients with long-standing uncontrolled hypertension, many of whom have discontinued antihypertensive therapy. Underlying renal artery stenosis is also commonly present, particularly in white patients.

In addition to marked elevation in BP, the major clinical manifestations include:

- Retinal hemorrhages and exudates (representing both ischemic damage and leakage of blood and plasma from affected vessels) and papilledema.
- Malignant nephrosclerosis, leading to acute renal failure, hematuria, and proteinuria. Renal biopsy reveals fibrinoid necrosis in the arterioles and capillaries, producing histologic changes that are indistinguishable from any of the forms of the hemolytic-uremic syndrome. The renal vascular disease in this setting leads to glomerular ischemia and activation of the renin-angiotensin system, possibly resulting in exacerbation of the hypertension.
- Neurologic symptoms due to intracerebral or subarachnoid bleeding, lacunar infarcts, or hypertensive encephalopathy. The last problem, which is related to cerebral edema, is characterized by the insidious onset of headache, nausea, and vomiting, followed by nonlocalizing neurologic symptoms such as restlessness, confusion, and, if the hypertension is not treated, seizures and coma. Magnetic resonance imaging (particularly with T2-weighted images) may reveal edema of the white matter of the parieto-occipital regions, a finding termed posterior leukoencephalopathy.

These neurologic symptoms differ from the abrupt onset of focal neurologic symptoms typically seen with a stroke or hemorrhage. Nevertheless, a CT scan should be obtained to exclude these disorders, which usually are not treated with aggressive BP reduction.

PARENTERAL DRUGS —

Nitroprusside — Nitroprusside dilates both arterioles and veins and is generally considered to be the most effective parenteral drug for most hypertensive emergencies. Nitroprusside, administered by intravenous infusion, begins to act within seconds and its effects disappear within minutes, thereby minimizing the risk of hypotension. Constant monitoring of the blood pressure is required. Nitroprusside and other nitrovasodilators (such as nitroglycerin) that provide nitric oxide appear to induce vasodilatation via generation of cyclic GMP which then activates calcium-sensitive potassium channels in the cell membrane.

The major limitation to the use of nitroprusside is its metabolism to cyanide, possibly leading to the development of cyanide or rarely thiocyanate toxicity that may be fatal. This problem, which is manifested by clinical deterioration, altered mental status, and lactic acidosis, can be minimized by using the lowest possible dose and by careful patient monitoring. Treatment for a prolonged period (>24 to 48 hours), underlying renal insufficiency, and the use of doses that exceed the capacity of the body to detoxify cyanide (more than 2 µg/kg per min) increase the risk of cyanide accumulation. The current FDA

recommendation is that maximum doses of 10 µg/kg per minute should never be given for more than 10 minutes. An infusion of sodium thiosulfate can be used in affected patients to provide a sulfur donor to detoxify cyanide into thiocyanate.

The recommended starting dose of nitroprusside is 0.25 to 0.5 µg/kg per minute. This can be increased as necessary to a maximum dose of 8 to 10 µg/kg per minute, although use of these higher doses should generally be avoided or limited to a maximum duration of 10 minutes. Nitroprusside should not be given to pregnant women.

Nitroglycerin — Nitroglycerin is also administered by intravenous infusion and is similar in action to nitroprusside except that it produces relatively greater venodilation than arteriolar dilation. It may be most useful in patients with symptomatic coronary disease and in those with hypertension following coronary bypass.

The initial dose of nitroglycerin is 5 µg/min, which can be increased as necessary to a maximum of 100 µg/min. The onset of action is 2 to 5 minutes, while the duration of action is 5 to 10 minutes. Headache (due to direct vasodilation) and tachycardia (resulting from reflex sympathetic activation) are the primary side effects. Cyanide accumulation does not occur.

Nicardipine — Nicardipine is a dihydropyridine calcium channel blocker (like nifedipine) that can be given as an intravenous infusion. The initial dose is 5 mg/h and can be increased to a maximum of 15 mg/h. Initial experience with nicardipine has been very favorable when compared to nitroprusside. The major limitation is a longer half-time, which precludes rapid titration.

Fenoldopam — Fenoldopam is a peripheral dopamine-1 receptor agonist, and unlike other parenteral antihypertensive agents, maintains or increases renal perfusion while it lowers BP. It maintains most of its efficacy for 48 hours of constant rate infusion without rebound hypertension when discontinued. Fenoldopam can be safely used in all hypertensive emergencies, and may be particularly beneficial in patients with renal insufficiency. After a starting dose of 0.1 µg/kg per min, the dose is titrated at 15 min intervals, depending on the BP response. Fenoldopam is contraindicated in patients with glaucoma.

Labetalol — Labetalol is a combined beta-adrenergic and alpha-adrenergic blocker. Its rapid onset of action (5 minutes or less) makes it the only ß-blocker that is useful in the treatment of hypertensive emergencies. Labetalol is safe in patients with active coronary disease, since it does not increase the heart rate. On the other hand, labetalol should generally be avoided in patients with asthma, chronic obstructive lung disease, congestive heart failure, bradycardia, or greater than first-degree heart block. Labetalol can be given as an intravenous bolus or infusion. The bolus dose is 20 mg initially, followed by 20 to 80 mg every 10 minutes to a total dose of 300 mg. The infusion rate is 0.5 to 2 mg/min.

Esmolol — Esmolol, a relatively cardioselective beta blocker, is rapidly metabolized by blood esterases and has a short (about 9 minutes) half-life and total duration of action (about 30 minutes). Its effects begin almost immediately, and it has found particular use during anesthesia to prevent postintubation hemodynamic perturbations.

Hydralazine — Hydralazine is a direct arteriolar vasodilator with little or no effect on the venous circulation. Thus, precautions are needed in patients with underlying coronary disease or a dissecting aortic aneurysm, and a ß-blocker should be given concurrently to minimize reflex sympathetic stimulation. The hypotensive response to hydralazine is less predictable than that seen with other parenteral agents and its current use is primarily limited to pregnant women. Hydralazine is given as an intravenous bolus. The initial dose is 10 mg, with the maximum dose being 20 mg. The fall in blood pressure begins within 10 to 30 minutes and lasts 2 to 4 hours.

Enalaprilat — Enalaprilat is an intravenous preparation of the active form of the angiotensin converting enzyme (ACE) inhibitor enalapril. The response to enalaprilat is variable and not predictable, a reflection of the variable plasma volume and plasma renin activity in patients with a hypertensive emergency. As an example, hypovolemic patients with a high plasma renin activity may have an excessive hypotensive response. In addition, ACE inhibitors are generally contraindicated in pregnancy.

The usual initial dose is 1.25 mg. As much as 5 mg may be given every six hours as necessary. The onset of action begins in 15 minutes but the peak effect may not be seen for four hours. The duration of action ranges from 12 to 24 hours.

Phentolamine — Phentolamine is an alpha-adrenergic blocker, the use of which is limited to the treatment of severe hypertension due to increased catecholamine activity. Examples include pheochromocytoma and tyramine ingestion in a patient being treated with a monoamine oxidase inhibitor. Phentolamine is given as an intravenous bolus. The usual dose is 5 to 10 mg every 5 to 15 minutes as necessary.