



PACU

PHARMACY & ACUTE CARE UNIVERSITY

Hypertensive Urgency and Emergency

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A Pharmacy and Acute Care University Live Webinar

Goals of this Session

- Discuss pros and cons of common drugs used
- Recognize and evaluate hypertensive urgency/emergency
- Differentiate between urgency and emergency
- Select appropriate treatment given the indication
- Analyze data supporting ideal medication choice

Medications for Hypertensive Urgency & Emergency

(Underlined = common in my practice)

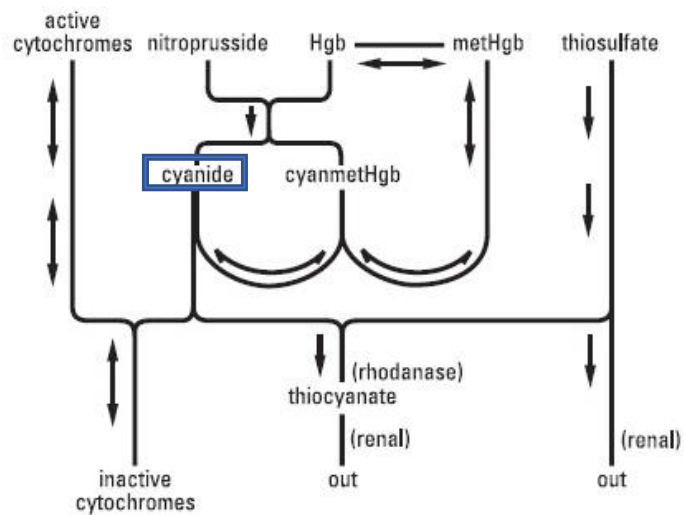
Vasodilators



- Hydralazine – Interferes with calcium transport, causing vasodilation
 - Pros: PO/IV Push, rapid onset, short duration
 - Cons: Multiple doses, lupus-like syndrome, no use in CHF exacerbation
- Nitroglycerin – Forms NO which is broken down, resulting in vasodilation
 - Pros: Multipurpose (HTN, CHF, ACS), cheap, quickly titratable
 - Cons: Watch for PDE-5 inhibitors, continuous infusion not always ideal

Vasodilators

Metabolism of Sodium Nitroprusside

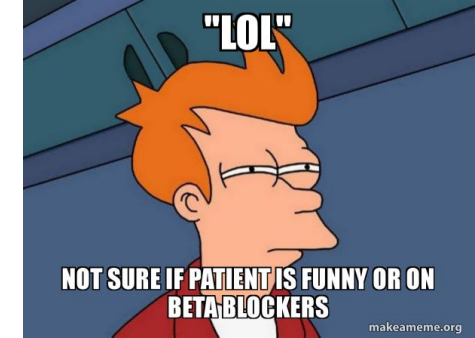


- Nitroprusside – Contains NO, which results in vasodilation
 - Pros: Multipurpose (HTN, CHF), rapidly titratable (seconds vs. mins with nitroglycerin)
 - Cons: Cyanide toxicity!!!, methemoglobinemia, elevated ICP

Calcium Channel Blockers

- Nicardipine – Inhibits calcium ion from entering during repolarization, relaxing vascular smooth muscle
 - Pros: Quickly titratable, widely available, small titration range (5-15mg/hr)
 - Cons: Effects 8 hours after end, negative inotrope, caution in renal dysfunction
- Clevidipine – Calcium channel inhibition potentially specific in arterial smooth muscle
 - Pros: Rapidly titratable, fast on/off, no renal/hepatic cautions
 - Cons: Egg/Soy allergy, relatively expensive, wide titration range (1-32mg/hr), negative inotrope, hypertriglyceridemia, tubing change Q12H (infection)

Beta Blockers



- Labetalol – Nonselective Beta-1 and Beta-2 receptor antagonist, minor alpha blocking activity
 - Pros: PO/IV Push/Cont. Infusion, more-peripheral BB, quick onset
 - Cons: Not for CHF or $> 1^{\text{st}}$ degree AV block, caution in bronchospastic disease
- Metoprolol – Selective Beta-1 receptor antagonist
 - Pros: Inexpensive, rapid onset, great for ACS or maintenance in CHF
 - Cons: Hepatic metabolism, HR effect $>$ BP effect

Beta Blockers

- Esmolol – Beta-1 receptor antagonist with little effects on Beta-2 receptors, *except at high doses*
 - Pros: Rapid on/off, rapidly titratable, ideal for aortic dissection, can give with/without bolus, no renal/hepatic caution
 - Cons: IV only, vesicant, hyperkalemia, rebound tachycardia



ACE-Inhibitors

- Captopril – Inhibits angiotensin converting enzyme
 - Pros: Quick onset for PO (15mins), inexpensive
 - Cons: PO only, wide half-life range, renal impairment caution, angioedema warning
- Enalaprilat – Inhibits angiotensin converting enzyme
 - Pros: Quick onset (15-30mins), PO/IV Push, inexpensive
 - Cons: Long duration (12-24 hours), renal dose adjustment, angioedema warning



Hypertensive Urgency

Guidance

Hypertensive Urgency: Evaluation

- Blood pressure > 180/110mmHg
- Lack of end-organ system damage
 - Will be discussed in more detail later on
- Largely asymptomatic
 - Can still have headache/lightheadedness, nausea, shortness of breath
 - Not considered end-organ system damage

A spike in blood pressure

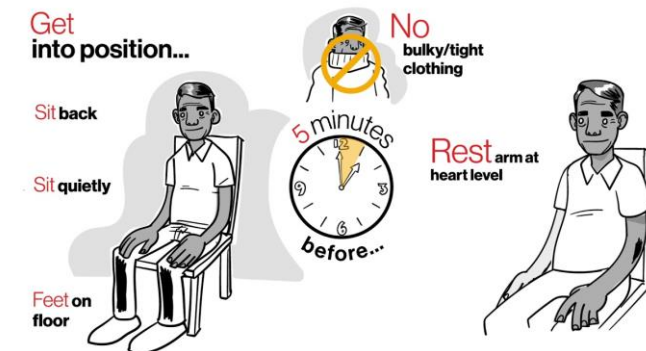


Hypertensive Urgency: Evaluation

- Patient history is important
- Previously diagnosed hypertension?
 - Compliance with medication regimen
- Other personal risk factors:
 - CAD, CHF, diabetes, smoker status, obesity, illicit drug use
- Family history of:
 - Hypertension, CKD

Hypertensive Urgency: Diagnosis

- At least two blood pressure readings that average to $> 180/110\text{mmHg}$
- Proper technique
 - Resting with legs uncrossed for 5 minutes
 - Arm resting on table/surface, heart level
 - Empty bladder
 - Consider white coat hypertension
- Evaluate for hypertensive emergency
 - Discussed later



Hypertensive Urgency: Management Overview

- Goal: Reduce BP by 25% within first 2-4 hours
 - Reducing more rapidly can produce myocardial infarction, ischemic stroke, or AKI
- Treatment modality depends on environment
 - Outpatient/Ambulatory vs. emergency room
 - Mainly time constraint-oriented

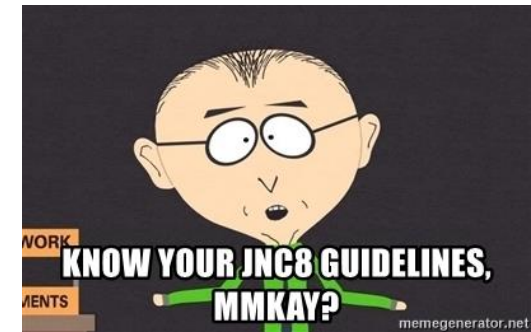
Hypertensive Urgency: Treatment

- Approach 1: Reduction over period of hours
 - Use rapid-onset, short-acting oral agents: Clonidine, captopril, hydralazine
 - Reassess in 2-4 hours
- Approach 2: Reduction over period of days
 - Long-acting medications: JNC8 guideline-directed therapy
 - Follow-up appointment with PCP in 1-2 days
- Assess compliance with home regimen (if applicable)
 - If non-adherent, restart home regimen at appropriate dose

1. Gauer, R. Severe Asymptomatic Hypertension: Evaluation and Treatment. *American Family Physician*: Leawood, KS. April 15, 2017.

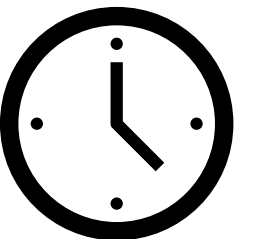
2. Handler, J. Hypertensive Urgency. *J Clin Hypertens*: Oxford, UK. January 31, 2007.

Image: Meme Generator/Comedy Central



Hypertensive Urgency: Emergency Room Approach

- Goal of 25% reduction in 2-4 hours
- Allow appropriate time for onset to recheck
 - Captopril: 15min onset, 1 hour peak
 - Hydralazine: 30min onset
 - Clonidine: 30min onset, 2 hour peak
- If non-compliant, restart home regimen if appropriate



Hypertensive Urgency: Emergency Room Approach

- Appropriate initial doses:
 - Clonidine 0.1mg orally
 - Captopril 12.5-25mg orally
 - Hydralazine 10-25mg orally
- Repeat doses may be needed
 - Always allow reasonable time for first drug to work

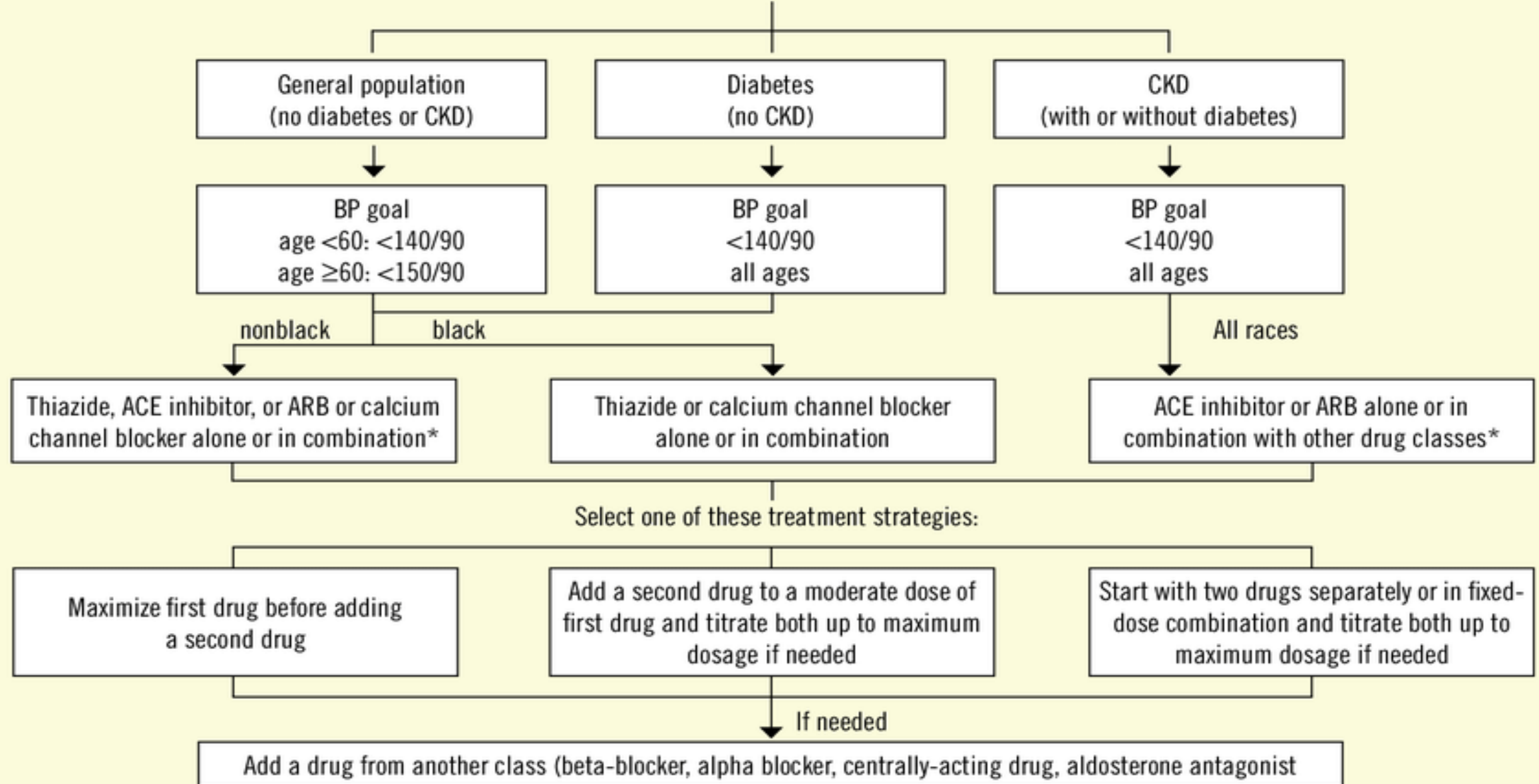
Hypertensive Urgency: Long-Term Management

- Restart home regimen (if applicable)
- Select appropriate new maintenance agent
 - JNC Algorithm



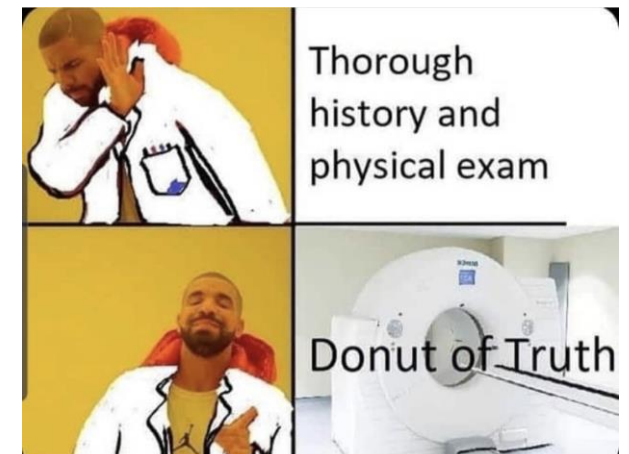
Image from ResearchGate

Lifestyle modification (throughout treatment)



Hypertensive Urgency: Further Evaluation

- Based on physical exam/history, screen for hypertensive emergency
- Basic metabolic panel, cardiac enzymes, urinalysis, CT imaging
 - All tests can be appropriate in certain circumstances



Hypertensive Emergency

Emergency

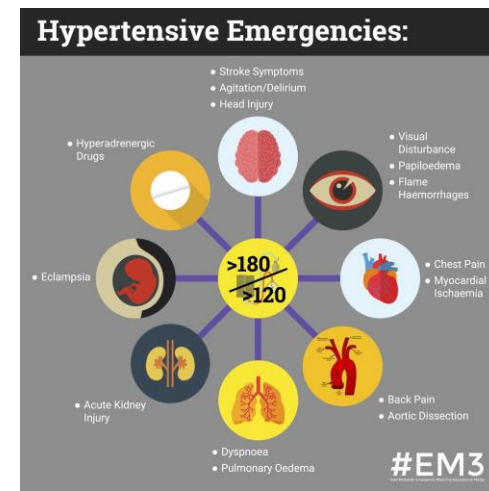
Hypertensive Emergency: Evaluation

- Extremely elevated blood pressure with presence of end-organ system damage
- BP > 180/110mmHg
- End organ-system damage
 - Motor/sensory deficits
 - Pulmonary edema
 - Peripheral pulse abnormalities
 - JVD
 - Arrhythmia or other cardiac abnormalities
 - AKI

1. Benken, S. T. Hypertensive Emergencies. *American College of Clinical Pharmacy*: Lenexa, KS. 2018.

2. Peixoto, A. J. Acute Severe Hypertension. *N Engl J Med*: Boston, MA. 2019.

Image: East Midlands Emergency Medicine Educational Media



Hypertensive Emergency: Management Overview

- Reduction of 10-20% in first hour
- Further reduction by 5-15% over subsequent 23 hours
- We do NOT aim for immediate normotensive state
 - Could precipitate MI, acute ischemic stroke, etc

Me: ***Lowers BP too quick***

All of my patient's organs:



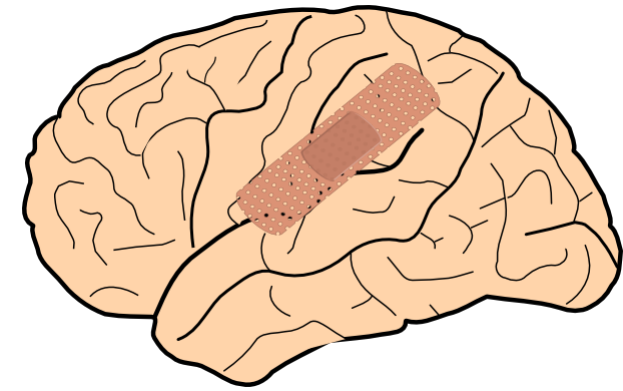
Hypertensive Emergency: Management Overview



- Notable exceptions to our reduction goals:
 - Acute ischemic stroke – different guidelines/reperfusion therapy/permissive hypertension
 - Aortic dissection – RAPID titration to systolic 100-120mmHg
 - Intracranial hemorrhage – Usual rapid lowering to systolic < 140mmHg
- Other exceptions exist but these 3 most notable

Hypertensive Emergency: Manifestations

- Evaluate end-organ system affected:
 - Neurologic
 - Cardiovascular
 - Renal
 - Hepatic
 - Ocular
 - Vascular
- Treatment modalities in-detail to follow



Hypertensive Emergency: Neurologic Damage

- Manifestations:
 - Acute ischemic stroke
 - Intracranial/subarachnoid hemorrhage (ICH/SAH)
 - Hypertensive encephalopathy

1. Benken, S. T. Hypertensive Emergencies. *American College of Clinical Pharmacy*: Lenexa, KS. 2018.

2. Peixoto, A. J. Acute Severe Hypertension. *N Engl J Med*: Boston, MA. 2019.

Image: Medical Dialogues : Brain Damage

Hypertensive Emergency: Neurologic Damage

- Acute ischemic stroke – Lower rapidly only if indicated for reperfusion (IV labetalol/hydralazine)
 - Otherwise, generally want permissive hypertension
- Hemorrhagic stroke (ICH/SAH) – Generally goal < 140mmHg
 - Drips of rapidly titratable agents preferred: nicardipine, clevidipine
 - Occasionally labetalol
- Hypertensive encephalopathy – Standard treatment goal: 10-20% first hour, 5-15% next 23 hours
 - Diagnosis of exclusion
 - Usual resolution with BP correction
 - Drips: nicardipine, clevidipine

Hypertensive Emergency: Cardiovascular Damage



- Acute CHF and pulmonary edema – Standard treatment goal
 - IV loop diuretics ± nitroglycerin drip
 - AVOID hydralazine and labetalol (and other agents that decrease CO/contractility)
- Acute coronary syndrome – Standard treatment goal
 - Many different IV agents appropriate: Nitroglycerin, nicardipine, metoprolol, clevidipine, esmolol, etc
 - Usually facility-focused protocol or provider preference

Hypertensive Emergency: Renal Damage



- Acute kidney injury – Standard treatment goal
 - Findings: Elevated serum creatinine (SCr), hematuria (microscopic hematuria)
- Correction of hypertensive emergency can initially worsen renal function
 - May return to normal with long-term control

Hypertensive Emergency: Hepatic Damage

- Usually associated with HELLP/preeclampsia – Different treatment guidelines
- Preeclampsia: Complication of pregnancy resulting in possible organ system damage from hypertension
- Severe hypertension in pregnancy: BP > 160/110mmHg
 - Reduce 25% over 2 hours
 - Preferred medications: IV hydralazine or labetalol (refractory: nicardipine drip)

Hypertensive Emergency: Hepatic Damage

- HELLP → Hemolysis, Elevated LFTs, and Low Platelets
- Criteria: Serum bilirubin > 1.2mg/dL, ALT or AST > 2 times ULN, and platelets < 100,000
- Treat hypertension as per previous slide
 - Reduce risk of stroke/bleeding – coagulopathies
- Have yet to see at my practice
 - Awareness is key

HELLP
SYNDROME MNEMONIC

HELLP SYNDROME

H - Hemolysis (Elevated LDH)

EL - Elevated Liver Enzymes (AST, ALT)

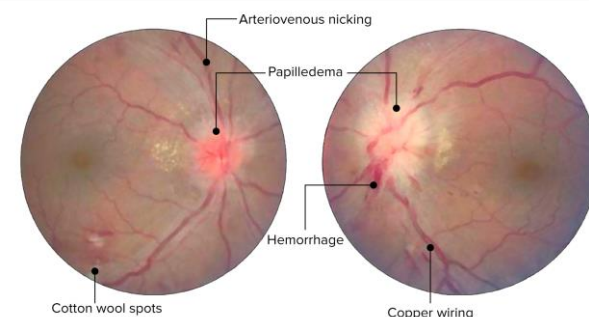
LP - Low platelets (Thrombocytopenia)

+

Pregnant Woman with Hypertention

Hypertensive Emergency: Ocular Damage

- Hypertensive retinopathy – usually from long-term uncontrolled hypertension
 - Retinal hemorrhage/exudate and papilledema
- Standard treatment goals
 - 10-20% in first hour
 - 5-15% in subsequent 23 hours
- Retinal hemorrhage – Bleeding of vessels in retina
- Retinal exudate – Lipid residue being excreted from eye, result of breakdown of blood-retina barrier
- Papilledema – Swelling around optic nerve due to increase in pressure



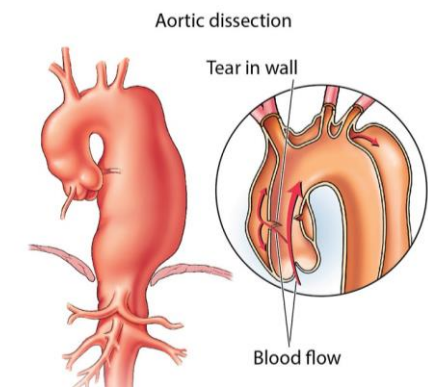
1. Benken, S. T. Hypertensive Emergencies. *American College of Clinical Pharmacy*: Lenexa, KS. 2018.

2. Peixoto, A. J. Acute Severe Hypertension. *N Engl J Med*: Boston, MA. 2019.

Image: Lecturio Hypertensive Retinopathy

Hypertensive Emergency: Vascular Damage

- Aortic dissection – Surgical emergency, RAPID lowering to goal 100-120mmHg systolic (20mins from diagnosis)
 - IV beta blocker (esmolol > labetalol, propranolol, or metoprolol) for goal HR < 60
 - Plus or minus vasodilator (nicardipine, clevidipine) for goal BP
- Recent vascular surgery – Usually rapid reduction in BP
 - No real-world evidence to support rapid > gradual approach
 - Severe hypertension → compromised closures/sutures, etc



1. Benken, S. T. Hypertensive Emergencies. *American College of Clinical Pharmacy*: Lenexa, KS. 2018.

2. Peixoto, A. J. Acute Severe Hypertension. *N Engl J Med*: Boston, MA. 2019.

Image: Cleveland Clinic – Aortic Dissection: Causes, Symptoms & Treatments

Hypertensive Emergency: Other Etiologies

- Medication withdrawal: Clonidine and beta-blockers
 - Clonidine: Restart therapy
 - Beta-blockers: May have delayed onset, possibly bridge with IV agents
- Pheochromocytoma – Neuroendocrine tumor that secretes catecholamines
 - Extremely rare
 - Management complicated (alpha blockade, then beta blockade, followed by surgery)
 - Generally outside scope of hypertensive emergency
 - Just be aware

surgeon: *prescribes propranolol to a patient with heart failure*
cardiologist: are you nuts? use bisoprolol!
surgeon:



Hypertensive Emergency: Other Etiologies

- Sympathomimetic ingestion, usually illicit compounds – Amphetamines, cocaine, etc
- My strategy – Benzos first
 - Controls agitation, leads to control of HR and BP
- By the book: IV phentolamine or nitroglycerin plus benzos
 - Definitive solution to control BP and agitation
 - Somewhat unrealistic – difficult to attain control of situation oftentimes

When the Pyxis asks if you're going to administer the entire dose of Ativan

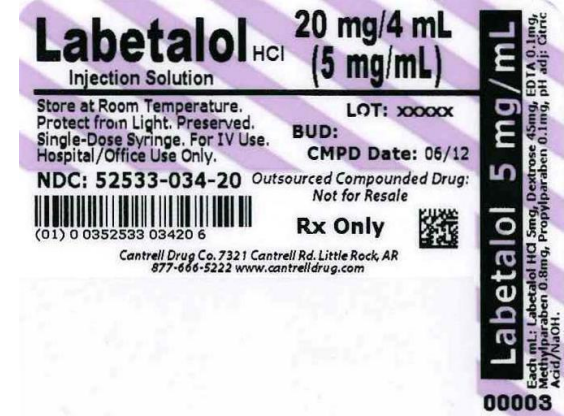


**What medication is
the best?**

**What does the data
say?**

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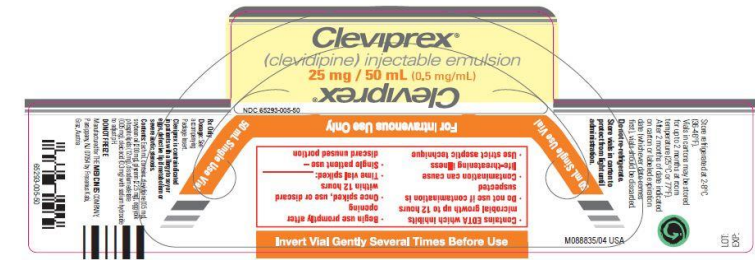
Labetalol



- Personal mainstay of IV Push antihypertensive therapy for emergency
- Labetalol vs. competitors:
 - Vs. Nicardipine: 30min BP attainment goal hit more often in nicardipine group (91.7%) vs. labetalol (82.5%); % of timer in goal MAP range was lower (worse) in labetalol group (58%) than nicardipine (78%)
 - Vs. Hydralazine: No difference in SBP, DBP, or MAP goal attainment in two studies

Clevidipine

- New(ish) kid on the block
- Clevidipine vs. competitors:
 - Vs. Nitroglycerin: Greater time in BP goal range with clevidipine than nitroglycerin ($p=0.0006$) in cardiac surgery patients
 - Vs. Nitroprusside: No difference in MAP control ability or number of total dose adjustments to achieve control
 - Vs. Nicardipine: Trend to lower time to target SBP with clevidipine (30mins) than nicardipine (46mins), not statistically significant ($p=0.13$) in neuro ICU study



1. Benken, S. T. Hypertensive Emergencies. *American College of Clinical Pharmacy*: Lenexa, KS. 2018.
 2. Aronson S., Dyke C. M., Stierer K. A., et al. The ECLIPSE trials: comparative studies of clevidipine to nitroglycerin, sodium nitroprusside, and nicardipine for acute hypertension treatment in cardiac surgery patients. *Anesth Analg*. 2008.
 3. Aronson S., Levy J, Lumb PD, et al. Impact of perioperative blood pressure variability on health resource utilization after cardiac surgery: an analysis of the ECLIPSE trials. *J Cardiothorac Vasc Anesth*. 2014.
 4. Peacock W. F., Chandra A., Char D., et al. Clevidipine in acute heart failure: results of the A Study of Blood Pressure Control in Acute Heart Failure-A Pilot Study (PRONTO). *Am Heart J*. 2014.
 5. Powroznyk A. V., Vuylsteke A., Naughton C., et al. Comparison of clevidipine with sodium nitroprusside in the control of blood pressure after coronary artery surgery. *Eur J Anaesthesiol*. 2003.
- Image: GNH India – Buy Clevidipine Fresenius Kabi Austria GmbH

Nicardipine



- Nicardipine vs. Competitors:
 - Vs. Nitroglycerin: in CABG patients BP decreased to goal sooner with nicardipine than nitroglycerin (7.7 vs. 1.9hrs) but no difference in clinical outcomes
 - Vs. Nitroprusside: in patients with hypertension + pulmonary edema, no time difference in BP reduction between groups. More rapid response with nicardipine (14mins) than nitroprusside (30mins) to goal in post-op cardiac surgery patients

1. Benken, S. T. Hypertensive Emergencies. *American College of Clinical Pharmacy*: Lenexa, KS. 2018.
2. Vecht R. J., Swanson K. T., Nicolaides E. P., et al. Comparison of intravenous nicardipine and nitroglycerin to control systemic hypertension after coronary artery bypass grafting. *Am J Cardiol*. 1989.
3. Suri M. F., Vazquez G., Ezzeddine M.A., et al. A multicenter comparison of outcomes associated with intravenous nitroprusside and nicardipine treatment among patients with intracerebral hemorrhage. *Neurocrit Care*. 2009.
4. Halpern N. A., Goldberg M., Neely C., et al. Postoperative hypertension: a multicenter, prospective, randomized comparison between intravenous nicardipine and sodium nitroprusside. *Crit Care Med*. 1992.
5. Yang H. J., Kim J. G., Lim Y. S., et al. Nicardipine versus nitroprusside infusion as antihypertensive therapy in hypertensive emergencies. *J Int Med Res*. 2004.

Image: Prescription(RX) Drugs – CARDENE I.V.

Hypertensive Urgency & Emergency: Summary

- Severe hypertension: BP > 180/110mmHg
- Presence of end-organ system damage indicates urgency vs. emergency
- Generally give oral meds for urgency
 - 25% reduction in 2-4 hours
 - Can also recheck outpatient in 1-2 days
 - Captopril, hydralazine, or clonidine
- Meds generally given IV for emergency
 - 10-20% over first hour, 5-15% over next 23 hours
 - IV Push: hydralazine, labetalol
 - IV Continuous Infusion: nicardipine, clevidipine

Hypertensive Urgency & Emergency: Summary

- Diagnoses with different treatment targets:
 - Ischemic stroke – Generally leave hypertensive
 - Hemorrhagic stroke – More rapid reduction
 - Aortic dissection – RAPID reduction, surgical emergency
 - Pregnancy – Severe hypertension at 160/110mmHg, 25% reduction over 2 hours

Hypertensive Urgency & Emergency: Summary

- End-organ system manifestations – also treat underlying disease state
 - CHF/Pulmonary edema? Loops \pm Nitroglycerin
 - Aortic dissection? Beta blocker \pm Vasodilator
 - Medication withdrawal? Restart medication
- Follow-up important
 - Follow JNC8 guidelines to initiate in someone likely to be lost to follow-up

Next are some comprehensive questions.

I will take any questions you may have after the comprehension questions.

Question 1:

PB is a 44 year old male coming into the general wellness clinic for his annual checkup. He is triaged by the nurse, and his vitals are as follows:

Pulse: 77

RR: 14

O2 saturation: 100%

BP: 194/115mmHg, 2 minute recheck of 190/113mmHg

PB has no history of hypertension and only takes 2 medications: OTC loratadine 10mg daily and OTC Tylenol sparingly for pain. He notes that his mother is alive but had two MI's in her 50's and his father has a history of hypertension. Which of the following is the most appropriate course of action at this time?

- A. Labetalol 10mg IV, goal of 10-20% reduction in first hour
- B. Captopril 12.5mg orally, goal of 10-20% reduction in first hour
- C. Amlodipine 5mg orally, goal of 25% reduction in 2-4 hours
- D. Hydralazine 10mg orally, goal of 25% reduction in 2-4 hours

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- D. Hydralazine 10mg orally, goal of 25% reduction in 2-4 hours**

A – IV not appropriate for urgency, 10-20% reduction is goal for emergency not urgency

B – Appropriate dose and agent, but 10-20% reduction is goal for emergency not urgency

C – Appropriate dose and agent, would be appropriate goal but amlodipine is delayed-onset and long acting. This would only be appropriate for a follow-up in 1-2 days while taking amlodipine



Question 2:

PB's blood pressure improved with hydralazine after a recheck in 4 hours. He is sent home with a prescription for Lisinopril 5mg PO daily for long-term control of his blood pressure. You are working a shift in the local emergency department and PB comes in with a chief complaint of "chest pain/shortness of breath." His vitals in triage are as follows:

Pulse: 115

RR: 16

O2 Saturation: 89%

BP: 202/123mmHg, 2 minute recheck of 200/119mmHg

PB has some labs done and his cardiac enzymes come back with an elevated troponin. The attending would like to treat the hypertension as well as for CHF with pulmonary edema. What is the most appropriate diagnosis and what is the most appropriate course of action at this time?

- A. Hypertensive emergency, 40mg furosemide IV plus IV nitroglycerin drip
- B. Hypertensive emergency, 10mg labetalol IV
- C. Hypertensive urgency, 40mg furosemide IV
- D. Hypertensive urgency, 12.5mg captopril PO plus 100mg labetalol PO

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- B. Hypertensive emergency, 10mg labetalol IV
- C. Hypertensive urgency, 40mg furosemide IV
- D. Hypertensive urgency, 12.5mg captopril PO plus 100mg labetalol PO

B – Correct diagnosis, labetalol not appropriate for patients with elements of acute heart failure

C – Incorrect diagnosis, loop diuretic appropriate though

D – Incorrect diagnosis, not appropriate drug choices for acute heart failure – need diuretics plus IV vasodilators

Question 3:

AS is a 73 year old female with a history of dementia, cardiovascular disease, hypertension, and atrial fibrillation. She is presenting to the wellness clinic for a chief complaint of “elevated blood pressure.” Vitals in triage are as follows:

Pulse: 80

RR: 13

O2 Saturation: 100%

BP: 224/130mmHg, 2 minute recheck of 224/131mmHg

She hands you a medication list prepared by her partner which reads: Donepezil 10mg daily, Memantine 10mg daily, Clopidogrel 75mg daily, Losartan 100mg daily, and Xarelto 20mg daily. On exam, she states she has no complaints and just wanted to have her blood pressure evaluated. Additionally, she admits she is getting more forgetful, and often forgets to take her medications. What is the most appropriate course of action at this time?

- A. Administer 25mg oral hydralazine and follow-up in 2 days
- B. Administer 10mg IV labetalol and recheck in 2-4 hours
- C. Administer home dose of losartan and follow-up in 1 day
- D. Administer nitroglycerin continuous IV infusion and recheck in 2-4 hours

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- B. Administer 10mg IV labetalol and recheck in 2-4 hours
- C. Administer home dose of losartan and follow-up in 1 day**
- D. Administer nitroglycerin continuous IV infusion and recheck in 2-4 hours

A – Acceptable drug choice, should recheck in 2-4 hours though

B – IV administration not preferred in ambulatory setting, follow-up is appropriate though

D – Continuous IV infusion not feasible in ambulatory setting, continuous monitoring would be required

Question 3:

PM is an 88 year old female who is presenting to the emergency room via EMS after somebody noticed stroke-like symptoms. Not much history is able to be obtained, but ER staff was able to confirm that she has a history of atrial fibrillation on apixaban. She has a noticeable left facial droop, minor slurring of words, and left-sided extremity weakness. Vitals are as follows:

Pulse: 89

RR: 13

O2 Saturation: 98%

BP: 188/108mmHg, 2 minute recheck of 190/113mmHg

She is sent for a CT scan which reveals an intracranial hemorrhage. The attending physician would like to get her blood pressure under control. What is the most appropriate agent and blood pressure goal at this time?

- A. Clevidipine IV continuous infusion, goal < 140mmHg systolic rapidly
- B. Nicardipine IV continuous infusion, goal 20% reduction in 1st hour
- C. Captopril 25mg orally, goal 25% reduction in 2-4 hours
- D. Hydralazine 10mg IV, goal 20% reduction in 1st hour

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- C. Captopril 25mg orally, goal 25% reduction in 2-4 hours
- D. Hydralazine 10mg IV, goal 20% reduction in 1st hour

B – Acceptable drug choice, ICH is an exception to standard goal of 20% reduction in first hour

C – IV mandatory in this case, though good follow-up window for captopril if indicated

D – Could get away with hydralazine, but need rapid reduction to <140 systolic

Thank you!

Any questions?

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Hypertensive Urgency and Emergency

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A Pharmacy and Acute Care University Live Webinar