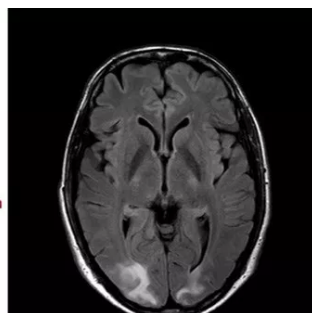
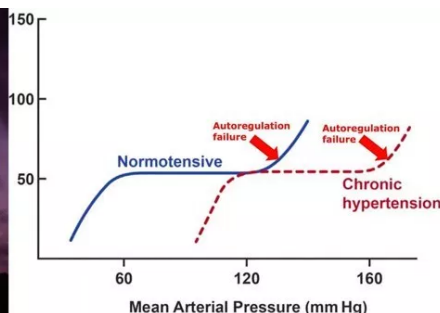


The Internet Book of Critical Care

Hypertensive emergency

November 11, 2016 by [Josh Farkas](#)



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Preamble: Use the MAP

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Before getting started, it will be useful to define our preferred measurement of blood pressure: the mean arterial pressure (MAP). The MAP is the average arterial pressure, which can be estimated as follows:

$$\text{MAP} = [2(\text{diastolic Bp}) + \text{Systolic Bp}] / 3$$

There are several reasons that MAP is the preferred measurement of blood pressure, as follows:

Reason #1: MAP is what the automated Bp cuff is actually measuring

- Automated oscillometric Bp cuffs measure the MAP directly (whereas the systolic and diastolic Bp are *estimated* using proprietary algorithms).
- This could make the MAP the most accurate measurement.

Reason #2: MAP may be most closely related to the risk of hypertensive emergency

- We tend to focus on the *systolic* blood pressure ("she had a systolic of 250!!"). However, the risk of hypertensive emergency seems overall be more closely related to the *diastolic* pressure than the systolic pressure.
- MAP is probably the single parameter most closely related to the risk of hypertensive emergency.

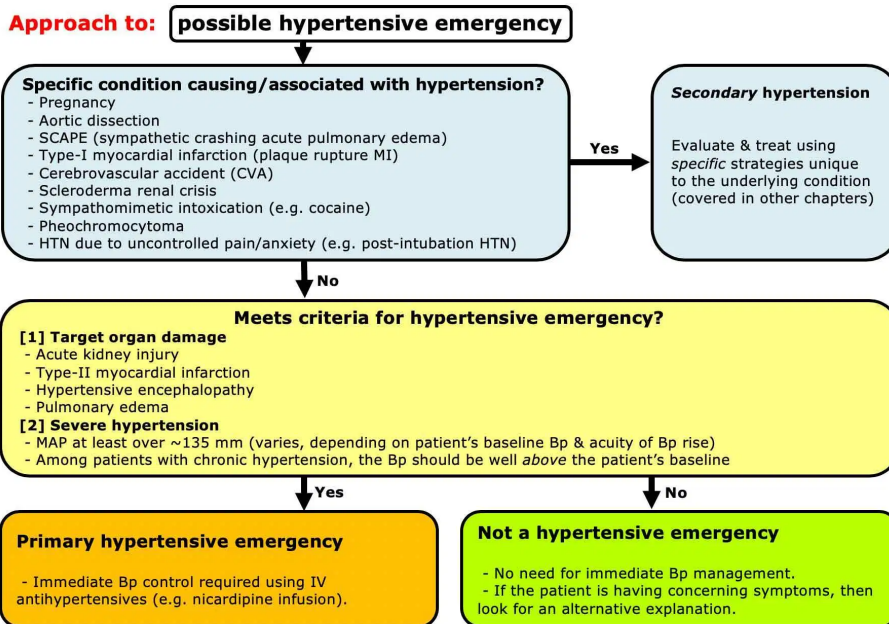
Reason #3: MAP is useful in guiding therapy

- The dosing of any antihypertensive drug can be titrated only against a *single* variable. The best way to titrate antihypertensive drugs in a logical fashion is to target a specific MAP.
- Trying to titrate an antihypertensive infusion against systolic *and* diastolic blood pressure simultaneously is often impossible and confusing (for example, what happens if the systolic target is reached but not the diastolic?).



diagnosis & definition

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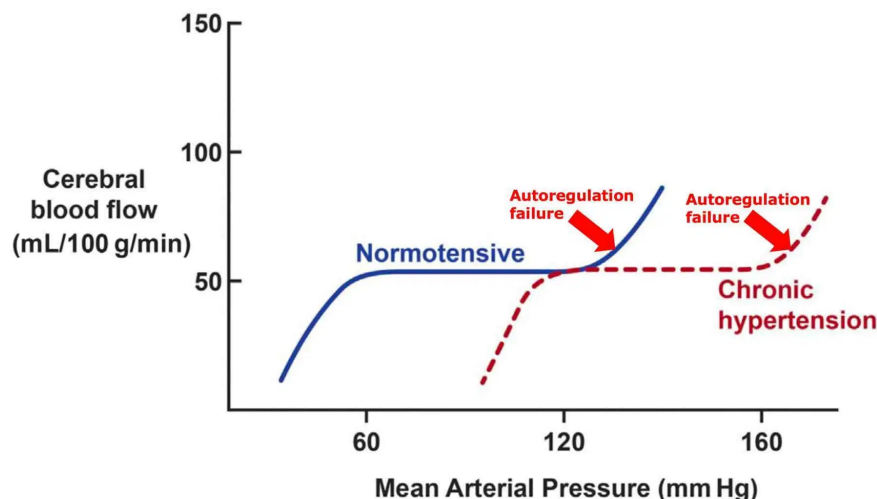


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"secondary hypertension"

- Secondary hypertension is used here to refer to HTN which is a result of some other primary process. In most cases, the primary process will be more obvious clinically, dominating the initial clinical presentation (e.g. aortic dissection, sympathetic crashing acute pulmonary edema, cocaine intoxication).

- Treatment will vary widely, depending on the specific context. This will be covered in other chapters regarding these individual conditions.
- Please note that the remainder of this chapter *doesn't necessarily apply* to secondary hypertension (for example, *do not* use this as a guide to pregnancy-associated hypertension and pre-eclampsia, which requires an entirely different approach).



MAP associated with hypertensive emergency? Normally, autoregulation allows the brain to achieve a stable perfusion across a range of MAP values (*flat* portion of the above curves). Hypertensive emergency occurs when the blood pressure is so high that autoregulation fails, leading to cerebral edema (red arrows above). In a previously *normotensive* person with relatively acute hypertension, this may occur at a MAP as low as ~135 mm. In a chronically *hypertensive* person, hypertensive emergency won't occur until the MAP is much higher.
(Suneja M & Sanders ML 2017 PMID 28372707)

criteria required to diagnose hypertensive emergency

- (1) Severe hypertension
 - Usually a MAP of at least >140 mm is needed to cause a hypertensive emergency.
 - This may vary considerably depending on the patient's baseline Bp. Hypertensive emergency can occur at lower MAPs in previously normotensive patients who have acute hypertension (e.g. pregnant women with preeclampsia).¹ Alternatively, patients with chronic hypertension may have extremely elevated Bp without hypertensive emergency.
- (2) Target organ damage, such as:
 - **Acute kidney injury** (often with microscopic hematuria)
 - **Myocardial ischemia** (type-II myocardial ischemia).
 - This should be a true myocardial infarction, not solely an elevated troponin (more on the definition of myocardial infarction [here](https://emcrit.org/ibcc/troponin/) (<https://emcrit.org/ibcc/troponin/>)).
 - **Pulmonary edema**
 - **Hypertensive encephalopathy** (visual disturbance, seizure, delirium). In situations where this is unclear, the presence of increased optic nerve sheath diameter on ultrasonography might support the diagnosis of hypertensive encephalopathy with increased intracranial pressure.
 - (Note: Epistaxis, proteinuria, or chronic renal failure *don't* qualify as target organ damage.)

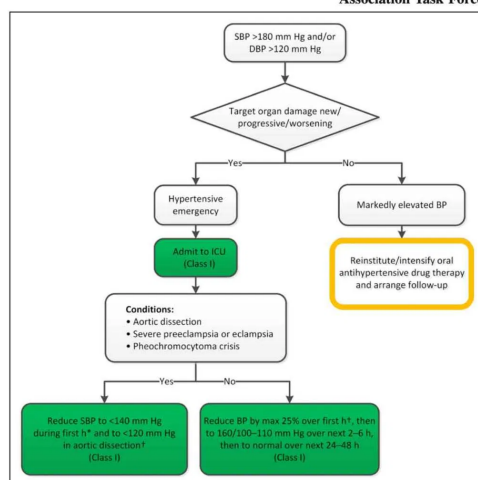
if there's no target organ damage, it's not an emergency!

- Without target organ damage, *it's not a hypertensive emergency and there is no need for hospital admission*.
 - (So, there's certainly no reason to admit the patient to the ICU!)
- In case there is any doubt about this, the following is a verbatim statement of the AHA/ACC guidelines 📄 (29133354 (<https://www.ncbi.nlm.nih.gov/pubmed/29133354>)).

Clinical Practice Guideline

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines



In contrast, hypertensive urgencies are situations associated with severe BP elevation in otherwise stable patients without acute or impending change in target organ damage or dysfunction. Many of these patients have withdrawn from or are noncompliant with antihypertensive therapy and do not have clinical or laboratory evidence of acute target organ damage. These patients should not be considered as having a hypertensive emergency and instead are treated by reinstitution or intensification of antihypertensive drug therapy and treatment of anxiety as applicable. There is no indication for referral to the emergency department, immediate reduction in BP in the emergency department, or hospitalization for such patients.

Guidelines do not recommend hospital or ICU admission for hypertensive urgency.

-Whelton PK et al. Hypertension, 71:1269, PMID 29133354
(The Internet Book of Critical Care, by @PulmCrit)

what is causing the hypertensive emergency?

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causes of hypertensive emergency

- Hypertensive emergency is often due to non-adherence to antihypertensive medications.
 - Especially withdrawal from clonidine
- If there is no clear trigger for the hypertensive emergency, the possibility of a *secondary* hypertensive emergency should be considered.

Causes include:

- Sympathomimetic drugs (e.g. cocaine, over-the-counter decongestants)
- Other medications (e.g. cyclosporine, tacrolimus, erythropoietin, steroid, NSAIDs)
- CNS event (e.g. ischemic stroke, intracranial hemorrhage)
- Sympathetic crashing acute pulmonary edema (SCAPE)
- Aortic dissection
- Preeclampsia
- Endocrinopathy (e.g. pheochromocytoma, hyperaldosteronism, Cushing's syndrome, hyperthyroidism)
- Renal (scleroderma renal crisis, acute glomerulonephritis)
- Volume overload
- Pain, anxiety, urinary obstruction

evaluation for the cause

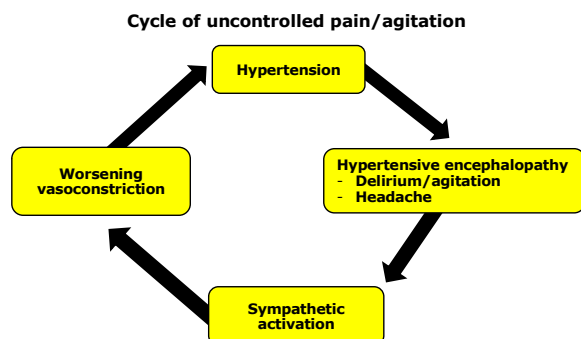
- EKG
- Bedside ultrasonography
 - ? Volume status
 - ? Evidence of aortic dissection
 - ? Evidence of left ventricular hypertrophy
 - ? Pulmonary edema on lung ultrasonography
- Labs
 - Basic labs (chemistries, CBC, coagulation studies)
 - Troponin (only if EKG/clinical evidence to support MI)
 - Urinalysis
 - Urine toxicology screen may be considered.
- Non-contrast head CT if presentation is worrisome for possible intracranial hemorrhage

Rx #1- remove exacerbating factors

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Blood pressure can be affected by a myriad of factors. Before initiation of antihypertensives, consider some simple interventions which may be highly effective in reducing the blood pressure. Overlooking these factors may eventually lead to *overshoot hypotension* (e.g. if pain is driving the hypertension but you initiate therapy with antihypertensives first, when the pain eventually resolves the patient may develop *overshoot hypotension*).

control agitation and/or pain



Uncontrolled pain/agitation may promote a vicious cycle of delirium and hypertension.

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- Severe pain: manage this immediately (e.g. with IV fentanyl).
- Agitation: agitated delirium itself may lead to sympathetic activation and hypertension. If the patient is severely agitated, treat this immediately (e.g. with intravenous antipsychotic or dexmedetomidine).
 - (Hint: Dexmedetomidine is a *sympatholytic* drug, so it will tend to decrease blood pressure and heart rate. It's a nice choice for agitated delirium with excessive sympathetic activity.)

volume removal

- Volume overload may cause hypertension, which is relatively difficult to treat using conventional antihypertensives.
- This is most often seen in the following situations:
 - Recovery phase following critical illness that was managed with excessive fluid administration.
 - Chronic renal insufficiency with accumulation of volume (especially in patients on chronic dialysis).
- Diagnosis of volume overload is based on a combination of clinical history and bedside ultrasonography.
- The preferred treatment is volume removal (either diuresis or dialysis).
 - For dialysis patients, a high-dose nitroglycerine infusion may be used as a *temporizing* measure until hemodialysis is available. As volume is removed with dialysis, the nitroglycerine is weaned off.

Rx #2- IV antihypertensive

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blood pressure goal?

- There isn't solid evidence behind this. The following approach seems reasonable & consistent with guidelines ([29133354](https://www.ncbi.nlm.nih.gov/pubmed/29133354) (<https://www.ncbi.nlm.nih.gov/pubmed/29133354>)).
 - (#1) The initial goal is to decrease the MAP by ~10-20% within 1-2 hours.
 - (#2) If this reduction is tolerated, then decrease the MAP to ~120 mm (e.g. ~160/110 mm) over the next 2-6 hours.
 - (#3) The blood pressure may subsequently be gradually decreased further over a period of days, as clinically tolerated.
- These general recommendations may not hold for every patient. Consider what the patient's baseline pressure is, and how rapid the increase in pressure was.
 - For a patient with chronic hypertension, a more gradual approach to lowering the Bp may be wise.

- For a patient with very acute development of hypertension (e.g. postoperatively or due to an acute ingestion), more rapid reduction of Bp may be reasonable.
- Whenever possible, try to clearly define the baseline Bp (e.g. obtain multiple Bp readings in both arms before starting antihypertensives). Lack of a definite baseline Bp leads to uncertainty regarding all downstream Bp targets.

useful intravenous antihypertensive agents

Agent	Pro	Con	Contraindication/caution	Onset & duration	Dose
Nicardipine	- Good for most situations. - Seems more powerful than most other agents.	- Can get reflex tachycardia. - Longish half-life may give the infusion a tendency to accumulate and cause hypotension.	- Cirrhosis (cleared by liver)	Onset ~15 min. Lasts 1-2 hours.	- Start at 5 mg/hr. - Increase by 2.5 mg/hr every 5 min, to a maximum rate of 15 mg/hour. - When Bp reaches target, consider <i>reducing</i> the infusion to 5 mg/hr to prevent accumulation. - If Bp falls below target, decrease infusion to 2.5 mg/hr or stop entirely.
Clevidipine	- Like nicardipine, but shorter half-life makes it easily titratable.	- Expensive, unavailable at many hospitals.	- Hypersensitivity to egg/soy (technically) - Hyperlipidemia, lipoid nephrosis, or acute pancreatitis.	Onset 2 min. Lasts 10 min.	- Start at 1-2 mg/hour - Double every 2 minutes until Bp begins approaching target, then titrate by smaller increments every 5-10 minutes. - Dose range is 1-32 mg/hour (use low-end dose range in elderly patients)
Labetalol	- Good for most situations - Might be preferred to nicardipine if concurrent MI	- Can cause bradycardia. - Nonselective beta-blocker, so it may cause hyperkalemia.	- Bradycardia - Heart block or sick sinus syndrome - Cardiogenic pulmonary edema - Asthma exacerbation - Acute cocaine/sympathomimetic intoxication	Onset 5-15 min. Lasts 3-6 hours.	- Load with sequential pushes of 20mg, 40mg, 80mg, 80mg, 80mg (q15 min PRN). If a total dose of 300mg doesn't work, switch to another agent. - Once Bp controlled, may use intermittent boluses to keep in range (e.g. 10-20 mg IV q10 minutes PRN).
Esmolol	- More easily titrated than labetalol - 1 st line agent for aortic dissection	- Not very powerful by itself.	- Bradycardia - Heart block or sick sinus syndrome - Cardiogenic pulmonary edema - Asthma exacerbation - Acute cocaine/sympathomimetic intoxication	Onset one minute. Lasts 10-20 min.	- Loading dose = 0.5 mg/kg - Start infusion at 50 mcg/kg/min. - For persistent hypertension, re-load and increase infusion by 50 mcg/kg/min. Up-titrate as needed to a max dose of 200 mcg/kg/min.
Nitroglycerine	- Agent of choice for acute cardiogenic pulmonary edema - Coronary vasodilation may be helpful in myocardial ischemia	- Headache	- Phosphodiesterase inhibitors use (e.g. sildenafil) within 48 hours - Elevated intracranial pressure	Onset 2 minutes. Lasts 10 min.	- 0-300 mcg/min

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preamble on hypertensive infusions: titratable vs. quasi-titratable vs. bolus

- In general:
 - *Continuous infusions* are used for drugs with a short half-life (e.g. norepinephrine). The short half-life means that the drug needs to be infused continuously. It also makes the drug easily titratable.
 - Intermittent boluses are used for drugs with longer half-lives (most drugs).
- Anti-hypertensive drugs can be classified into roughly three groups:
- **(1) Truly titratable agents**
 - Duration of action is <<30 minutes.
 - The drug *must* be given as a continuous infusion. It is fairly easy to titrate.
 - Examples: Nitroglycerine, nitroprusside, esmolol, clevidipine.
- **(2) Quasi-titratable agents**
 - Duration of action is <1-2 hours.
 - The drug is generally given as a continuous infusion, but it's a bit sluggish to titrate.
 - Examples: Nicardipine, diltiazem.
- **(3) Bolus agents**
 - Duration of action is >1-2 hours
 - The easiest way to give the drug is as intermittent bolus doses. If an infusion is used, it will tend to accumulate and be rather difficult to titrate.
 - Examples: Labetalol, metoprolol.

comments on preferred agents

Nicardipine

- Workhorse agent in hospitals that don't have clevidipine.
- Highly effective and applicable to most scenarios.
- Drawback is that it's a *quasi-titratable* agent, so it may accumulate over time and cause *overshoot hypotension*. One approach to avoid overshooting is to scale back the infusion rate once the target blood pressure is reached. One strategy to avoid this:

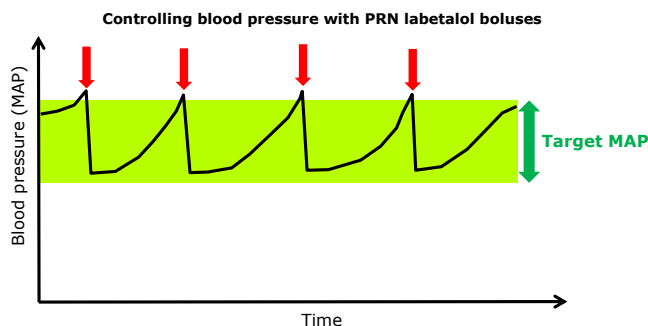
- If Bp is above target, increase infusion by 2.5 mg/hr every 5-15 minutes to a maximum rate of 15 mg/hour.
- After the blood pressure reaches target, drop the infusion down to 5 mg/hr.
- If the blood pressure falls below target, drop the infusion down to 2.5 mg/hr.
- If the blood pressure falls substantially below target, stop the infusion entirely.

Clevidipine

- Basically, a next-generation nicardipine with much shorter half-life. This makes clevidipine a *truly titratable* agent (as defined above).
- Clevidipine has been shown to be more successful than nicardipine at achieving tight blood pressure control.² It's easier to use than nicardipine, with a lower risk of overshoot hypotension.
- Clevidipine is unavailable at many hospitals due to cost considerations. If clevidipine could decrease in cost to become competitive with nicardipine, it would probably replace nicardipine as a front-line agent for antihypertensive emergency.

Labetalol

- Good option, especially if you're trying to drop the Bp by only a moderate amount (e.g. 10-30 mm). For profound hypertension, labetalol may be less effective than nicardipine.
- Labetalol lasts ~2-4 hours, so it doesn't make sense to give it as a continuous infusion (a continuous infusion will gradually accumulate and eventually cause overshoot hypotension). Although some references recommend using labetalol as a continuous infusion, it may be more of a *bolus agent* (as defined above).
- One strategy for using labetalol:
 - 1) A PRN bolus dose must be found which is sufficient to cause an effective drop in Bp (yet not an excessive drop). The dose varies between patients and must be determined empirically (start with 10 mg and up-titrate as needed until an effective dose is determined).
 - 2) The blood pressure must be monitored carefully, with repeat PRN doses used as necessary (figure below).
- Escalating boluses of labetalol can be useful to achieve rapid control of severe hypertension at the bedside if this is needed (e.g. acute Bp spike which requires immediate control).



Given the relatively long half-life of labetalol, the best way to dose it might be as PRN boluses (red arrows) when the blood pressure exceeds the target range. A PRN-bolus strategy prevents drug accumulation (which could lead to overshoot hypotension).

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(<https://emcrit.org/wp-content/uploads/2016/11/prnlabetalol.svg>), **Esmolol**

- Esmolol has a very short half-life, making it a truly titratable agent. This is a potential advantage compared to labetalol.
- Unfortunately, as a pure beta-blocker esmolol lacks the power of nicardipine or labetalol. Thus, esmolol infusion alone may be inadequate for severe hypertension.
 - The classic use of esmolol is as a *second* agent in combination with a vasodilator, to prevent reflex tachycardia.

Nitroglycerine

- Causes predominantly venodilation at lower doses, but causes arterial vasodilation at higher doses.
- Mostly used for patients with myocardial ischemia, heart failure, or volume overload.
- It is a safe agent with a short half-life, which makes it easy to titrate.

drugs which aren't preferred

Nitroprusside

- Reasons not to use nitroprusside:
 - (1) Can increase the intracranial pressure.
 - (2) Can cause cyanide toxicity and lactic acidosis – which may create a confusing picture if the patient deteriorates.
 - (3) Tends to cause wide swings in the blood pressure (requires continuous close attention and meticulous titration).
 - (4) Coronary vasodilation can cause a steal phenomenon that promotes myocardial ischemia.
- Generally, another agent will be equally effective and safer.
- Given lack of any high-quality evidence that tight Bp control improves outcomes, it's challenging to justify the risks involved with using nitroprusside.

Intravenous hydralazine

- Reasons not to use IV hydralazine
 - (1) Effect is unpredictable (sometimes minimally effective, sometimes causes precipitous Bp drop)
 - (2) Impossible to titrate (works for 2-4 hours)
- Most situations, another agent will be equally effective and safer (one potential exception is preeclampsia with refractory hypertension).

is an arterial line needed?

- No good data on this.
- Indications for an arterial line might include:
 - Discrepant blood pressures in different extremities (in this situation consider aortic dissection)
 - Very labile blood pressures
 - Profound hypertension (too high to be real?)
 - Clinical deterioration despite noninvasive management
 - Use of nitroprusside (which, as discussed above, is generally a bad idea)
- My opinion is that an arterial line is unnecessary in most cases of hypertensive emergency.
 - The pain of arterial line insertion can exacerbate hypertension.
 - No prospective evidence exists to show that this procedure is beneficial or necessary.
 - Bp targets are arbitrary and poorly defined. It's illogical to tightly chase an arbitrary target:



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@PulmCrit

goose-chase principle: if there is no solid evidence regarding a therapeutic goal (e.g. pH in ARDS), don't go crazy trying to chase it with high accuracy.



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if the blood pressure plummets, evaluate for hypovolemia and volume resuscitate if necessary

- Patients often have a combination of:
 - (1) Excessive vasoconstriction, which is driving their hypertension.
 - (2) Hypovolemia due to the diuretic effect of hypertension ("pressure diuresis").
- When treated with vasodilation, these patients may develop hypotension (due to unmasking of their hypovolemia). Overall this may lead to wide fluctuations in blood pressure, which is difficult to control. Stabilizing these patients requires addressing *both* problems:
 - (1) Control hypertension with vasodilation.
 - (2) Volume replete to manage hypovolemia (e.g. with guidance of echocardiography).



Patients with a combination of hypovolemia and vasoconstriction may develop highly labile Bp if treated only with vasodilation. Both problems must be addressed to stop the cycle.

Rx #3- Transition to oral antihypertensives

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when to start oral titration

- Patient has stabilized and improved on IV antihypertensives for several hours.
- Initiate oral antihypertensive agent and wean off the IV infusion (or PRN boluses if you're using labetalol).

preamble on oral antihypertensives & dose-stacking

- The key concern with oral antihypertensive agents is how rapidly they take effect. As in any other situation where you're up-titrating medications (e.g. procedural sedation), it's important to allow one dose of medication to take effect *before* you escalate the dose.
 - If doses are escalated *before* the last dose has taken effect, this may eventually lead to an excessive drop in blood pressure.
- The ideal oral antihypertensive will take effect in under ~2 hours. This allows for a fairly prompt up-titration of oral doses, which allows rapid weaning of the IV antihypertensive agent.

oral anti-hypertensives with relative fast onset of action

Agent	Pro	Con	Contraindication & caution	Onset & duration	Dose
Labetalol	- Usually preferred oral antihypertensive. - More effective than most beta-blockers (e.g. metoprolol)	- Can cause bradycardia	- Bradycardia - Heart block or sick sinus syndrome - Cardiogenic pulmonary edema - Asthma exacerbation - Cocaine/sympathomimetic toxicity	Onset in ~2 hr Duration ~10 hr	Start 200 mg q12hr Max dose 1000 mg q12hr
Isradipine	- Good for most situations. - Similar to amlodipine, but faster acting.	- Relatively expensive		Onset in ~2 hr Duration ~10 hr	Start 2.5 mg q12hr Max 5 mg q12hr
Nifedipine, extended release	- Similar to amlodipine but faster acting	- Cannot be crushed for administration via feeding tube		Onset in ~4 hr Duration ~24 hr	Starting dose 60 mg daily Max 120 mg daily
Captopril	- Reduction of preload and afterload may be useful in heart failure. - Faster onset & shorter half-life than other ACEi makes this the most titratable ACEi.	- Can promote renal failure, should be avoided if there is acute kidney injury or other nephrotoxic medications. - Not great long-term agent (requires frequent dosing)	- Hyperkalemia - Renal failure (but not chronic ESRD on hemodialysis) - Prior cough due to ACEi	Onset in 15-30 min Duration ~6 hr	Start 12.5 mg q8hr Max dose 50 mg q8hr
Losartan Telmisartan	- Alternative to ACEi in patients unable to tolerate ACEi.	- Overall similar to ACEi above. - Less titratable than captopril.	- Hyperkalemia - Renal failure (but not chronic ESRD on hemodialysis)	Max effect at 4-6 hours Duration ~24 hours (Telmisartan has faster onset; losartan slower if administered with food)	Telmisartan Start 40 mg daily Max dose 80 mg daily Losartan Start 50 mg daily Max dose 100 mg daily
Hydralazine monotherapy	- Afterload reduction may be useful in patients with heart failure.	- Not great long-term agent (can cause drug-induced SLE) - May cause reflex tachycardia - Cerebral vasodilation could increase ICP - Renal clearance may cause unexpected kinetics in acute kidney injury	- HOCM or LV outflow tract obstruction	Onset ~1 hour Duration ~6 hours	Start 25 mg q8hr Max dose 100 mg q8hr
Prazosin	- Not usually preferred. Could be beneficial in patients with benign prostatic hypertrophy (BPH).	- Can cause reflex tachycardia and headache (similar physiologic effect compared to hydralazine)		Onset ~2 hours Duration ~12 hours	Start 1-2 mg q12 hr Max dose 10 mg q12 hr
Isosorbide dinitrate	- Preload reduction may be useful in patients with heart failure. - Generally used in combination with hydralazine. This combination reduces preload & afterload similar to an ACEi, but without nephrotoxicity.	- Not great for long-term therapy (requires frequent dosing) - Tolerance can develop			
Clonidine	- May provide some anxiolysis.	- Not good medication for chronic use (risk of rebound hypertension).	- May cause somnolence	Onset ~1 hour Duration ~12 hr	Start 0.2 mg PO q12hr Max dose 1.2 mg PO q12hr
Furosemide	- Excellent if volume overload is cause of HTN.	- Only useful in patients with volume overload.	- Will decrease potassium, magnesium levels. - Should never be used in patients with euvoolemia or hypovolemia.	Onset: 1-2 hours Duration: Indefinite	Titrated doses with a goal of achieving euvoolemia. Stop as soon as patient is euvolemic.

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<https://emcrit.org/wp-content/uploads/2016/11/oralonset.svg> comments on specific agents

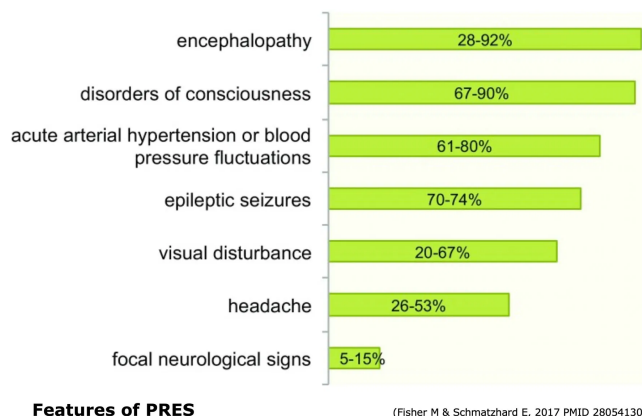
- Labetalol and isradipine are preferred agents, which take effect rapidly and can be used in most situations.
 - Extended release nifedipine is a reasonable option, especially if you don't have access to isradipine.
 - Carvedilol is an alpha/beta blocker, similar to labetalol. It's a reasonable choice, but with a half-life of 6-10 hours it takes a few doses to reach steady state. This precludes the ability to perform rapid oral dose-titration.
- Other agents can be useful in specific situations:
 - Clonidine can be useful in patients with anxiety/agitation.
 - ACEi, ARB, or nitrate/hydralazine may be useful in patients with heart failure (especially if there is a history of sympathetic crashing acute pulmonary edema).
- These agents aren't necessarily optimal for chronic use. Once the patient has been stabilized for some days, they may be transitioned to a better oral regimen for chronic outpatient use.
- Agents to avoid:
 - Amlodipine takes forever to work – this drug is an absolute slug and has no role here.
 - Metoprolol drops heart rate, but is relatively ineffective for controlling blood pressure.

PRES (Posterior reversible encephalopathy syndrome)

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basics

- Also known as RPLS (reversible posterior leukoencephalopathy syndrome).
- May occur within context of another disorder (e.g. preeclampsia).
- Reflects vasogenic edema occurring predominantly in the posterior brain.



hallmark findings include:

- Hypertension generally seen.
- Neurologic symptoms as shown above.
- Clinical deterioration is acute or sub-acute (may evolve over 1-2 days).

causes

- Hypertension is the most common cause (in which case this can be termed hypertensive encephalopathy).
 - Especially in association with pre-eclampsia or Guillain Syndrome.
 - PRES can occur as a *complication* of stroke, which triggers hypertension (stroke → HTN → PRES).
 - However, ~20% of patients lack documented hypertension.
- Systemic inflammation
 - Sepsis
 - Autoimmune diseases (lupus, scleroderma, Sjogren's disease, vasculitis)
- Immunosuppressive & chemotherapeutic medications
 - Calcineurin inhibitors (tacrolimus, cyclosporine)
 - Chemotherapy (vincristine, cisplatin, gemcitabine, bortezomib, cytarabine)
 - VEGF-inhibitors (sunitinib, bevacuzimab, sorafenib)
- Other risk factors
 - Renal failure
 - Hypomagnesemia, hypercalcemia

imaging

- MRI is more sensitive than CT
- The most common sites of involvement are the parieto-occipital areas. However, may also involve cerebellum, brainstem, basal ganglia, frontal lobes, or spinal cord.³
 - Edema is seen on T2-weighted sequences, such as fluid-attenuated inversion recovery (FLAIR).⁴
 - Restricted diffusion can be seen in diffusion-weighted images (DWI) in 15-30% of cases, which may correlate with worse prognosis. This can mimic ischemic stroke.⁴

lumbar puncture

- Not necessary to secure diagnosis (e.g. if other features don't suggest infection).
- Commonly see elevated protein with normal cell count.⁵

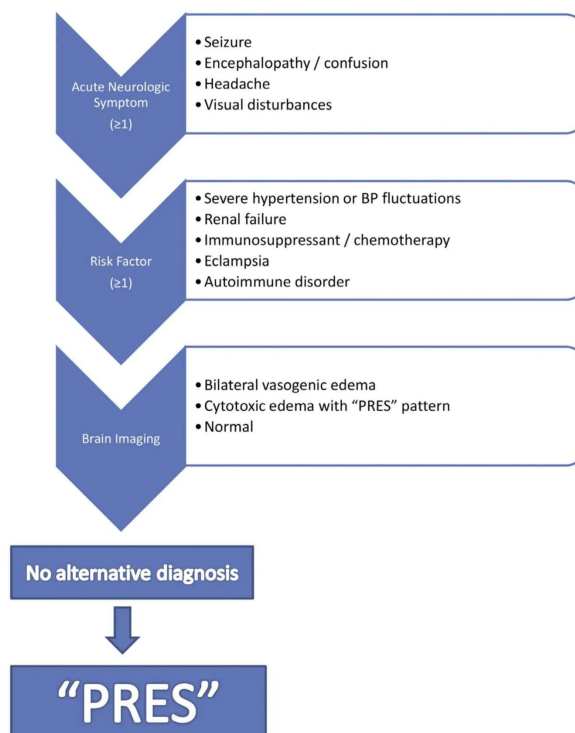


Fig. 26.7. Proposed algorithm for the diagnosis of posterior reversible encephalopathy syndrome (PRES). BP, blood pressure. (Reproduced with permission from Fugate and Rabinstein, 2015.)

diagnosis

- No single diagnostic test proves PRES (although MRI may be strongly suggestive).
- The above figure shows how this diagnosis is often approached, using a combination of clinical features, supportive evidence, and exclusion of other possibilities.⁴

treatment

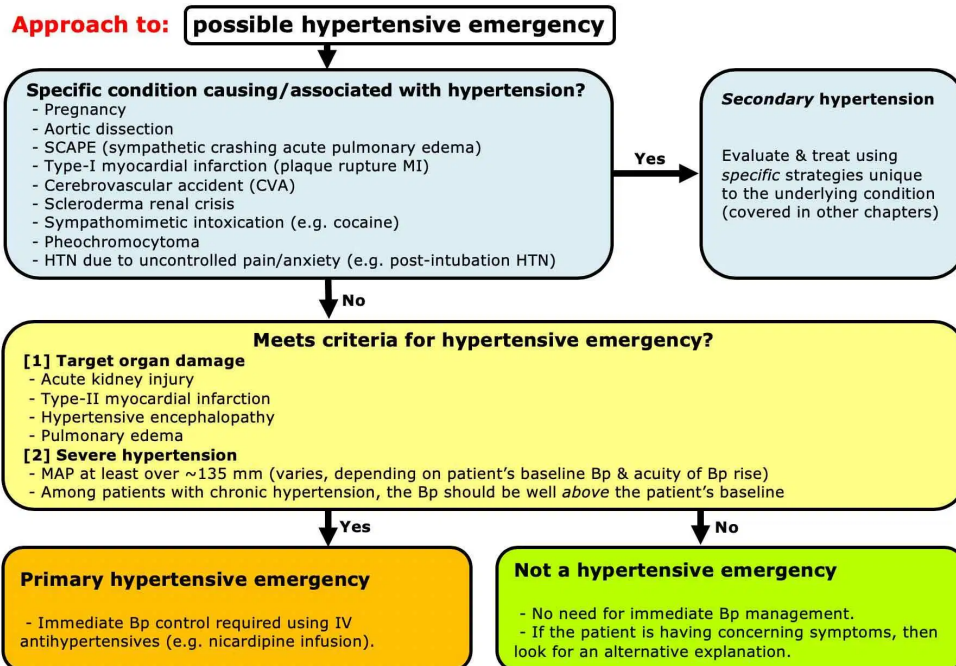
- (1) Blood pressure control
 - Same as for hypertensive emergencies in general (see [above \(#Rx_#1- IV_antihypertensives\)](#)).
- (2) Seizure management
 - Treatment of seizure or possible seizure (e.g. with levetiracetam).
 - Consider EEG for PRES patients with persistent and unexplained alteration in mental status.
- (3) Evaluation & removal of any causative factor
 - For example, certain immunosuppressive and chemotherapeutic agents may cause this (e.g. tacrolimus, cyclosporine, gemcitabine, bevacizumab)
 - Hypomagnesemia may be a contributing factor, so magnesium should be repleted aggressively.³
- (4) Intracranial pressure management
 - Rarely, severe swelling may cause obstructive hydrocephalus requiring temporary placement of an external ventricular drain.

prognosis

- PRES can cause irreversible brain injury, but overall it is generally reversible.
- Patients can look pretty horrific (e.g. due to brainstem involvement), yet subsequently recover.
- Predictors of incomplete recovery:
 - Secondary intracranial hemorrhage in addition to PRES.
 - Restricted diffusion, suggestive of cerebral infarction.

Algorithm & drug tables

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useful intravenous antihypertensive agents

Agent	Pro	Con	Contraindication/caution	Onset & duration	Dose
Nicardipine	<ul style="list-style-type: none"> - Good for most situations. - Seems more powerful than most other agents. 	<ul style="list-style-type: none"> - Can get reflex tachycardia. - Longish half-life may give the infusion a tendency to accumulate and cause hypotension. 	<ul style="list-style-type: none"> - Cirrhosis (cleared by liver) 	Onset ~15 min. Lasts 1-2 hours.	<ul style="list-style-type: none"> - Start at 5 mg/hr. - Increase by 2.5 mg/hr every 5 min, to a maximum rate of 15 mg/hour. - When Bp reaches target, consider <i>reducing</i> the infusion to 5 mg/hr to prevent accumulation. - If Bp falls below target, decrease infusion to 2.5 mg/hr or stop entirely.
Clevidipine	<ul style="list-style-type: none"> - Like nicardipine, but shorter half-life makes it easily titratable. 	<ul style="list-style-type: none"> - Expensive, unavailable at many hospitals. 	<ul style="list-style-type: none"> - Hypersensitivity to egg/soy (technically) - Hyperlipidemia, lipid nephrosis, or acute pancreatitis. 	Onset 2 min. Lasts 10 min.	<ul style="list-style-type: none"> - Start at 1-2 mg/hour - Double every 2 minutes until Bp begins approaching target, then titrate by smaller increments every 5-10 minutes. - Dose range is 1-32 mg/hour (use low-end dose range in elderly patients)
Labetalol	<ul style="list-style-type: none"> - Good for most situations - Might be preferred to nicardipine if concurrent MI 	<ul style="list-style-type: none"> - Can cause bradycardia. - Nonselective beta-blocker, so it may cause hyperkalemia. 	<ul style="list-style-type: none"> - Bradycardia - Heart block or sick sinus syndrome - Cardiogenic pulmonary edema - Asthma exacerbation - Acute cocaine/sympathomimetic intoxication 	Onset 5-15 min. Lasts 3-6 hours.	<ul style="list-style-type: none"> - Load with sequential pushes of 20mg, 40mg, 80mg, 80mg, 80mg (q15 min PRN). If a total dose of 300mg doesn't work, switch to another agent. - Once Bp controlled, may use intermittent boluses to keep in range (e.g. 10-20 mg IV q10 minutes PRN).
Esmolol	<ul style="list-style-type: none"> - More easily titrated than labetalol - 1st line agent for aortic dissection 	<ul style="list-style-type: none"> - Not very powerful by itself. 	<ul style="list-style-type: none"> - Bradycardia - Heart block or sick sinus syndrome - Cardiogenic pulmonary edema - Asthma exacerbation - Acute cocaine/sympathomimetic intoxication 	Onset one minute. Lasts 10-20 min.	<ul style="list-style-type: none"> - Loading dose = 0.5 mg/kg - Start infusion at 50 mcg/kg/min. - For persistent hypertension, re-load and increase infusion by 50 mcg/kg/min. Up-titrate as needed to a max dose of 200 mcg/kg/min.
Nitroglycerine	<ul style="list-style-type: none"> - Agent of choice for acute cardiogenic pulmonary edema - Coronary vasodilation may be helpful in myocardial ischemia 	<ul style="list-style-type: none"> - Headache 	<ul style="list-style-type: none"> - Phosphodiesterase inhibitors use (e.g. sildenafil) within 48 hours - Elevated intracranial pressure 	Onset 2 minutes. Lasts 10 min.	<ul style="list-style-type: none"> - 0-300 mcg/min

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oral anti-hypertensives with relative fast onset of action

Agent	Pro	Con	Contraindication & caution	Onset & duration	Dose
Labetalol	- Usually preferred oral antihypertensive. - More effective than most beta-blockers (e.g. metoprolol)	- Can cause bradycardia	- Bradycardia - Heart block or sick sinus syndrome - Cardiogenic pulmonary edema - Asthma exacerbation - Cocaine/sympathomimetic toxicity	Onset in ~2 hr Duration ~10 hr	Start 200 mg q12hr Max dose 1000 mg q12hr
Isradipine	- Good for most situations. - Similar to amlodipine, but faster acting.	- Relatively expensive		Onset in ~2 hr Duration ~10 hr	Start 2.5 mg q12hr Max 5 mg q12hr
Nifedipine, extended release	- Similar to amlodipine but faster acting	- Cannot be crushed for administration via feeding tube		Onset in ~4 hr Duration ~24 hr	Starting dose 60 mg daily Max 120 mg daily
Captopril	- Reduction of preload and afterload may be useful in heart failure. - Faster onset & shorter half-life than other ACEi makes this the most titratable ACEi.	- Can promote renal failure, should be avoided if there is acute kidney injury or other nephrotoxic medications. - Not great long-term agent (requires frequent dosing)	- Hyperkalemia - Renal failure (but not chronic ESRD on hemodialysis) - Prior cough due to ACEi	Onset in 15-30 min Duration ~6 hr	Start 12.5 mg q8hr Max dose 50 mg q8hr
Losartan Telmisartan	- Alternative to ACEi in patients unable to tolerate ACEi.	- Overall similar to ACEi above. - Less titratable than captopril.	- Hyperkalemia - Renal failure (but not chronic ESRD on hemodialysis)	Max effect at 4-6 hours Duration ~24 hours (Telmisartan has faster onset; losartan slower if administered with food)	Telmisartan Start 40 mg daily Max dose 80 mg daily Losartan Start 50 mg daily Max dose 100 mg daily
Hydralazine monotherapy	- Afterload reduction may be useful in patients with heart failure.	- Not great long-term agent (can cause drug-induced SLE) - May cause reflex tachycardia - Cerebral vasodilation could increase ICP - Renal clearance may cause unexpected kinetics in acute kidney injury	- HOCM or LV outflow tract obstruction	Onset ~1 hour Duration ~6 hours	Start 25 mg q8hr Max dose 100 mg q8hr
Prazosin	- Not usually preferred. Could be beneficial in patients with benign prostatic hypertrophy (BPH).	- Can cause reflex tachycardia and headache (similar physiologic effect compared to hydralazine)		Onset ~2 hours Duration ~12 hours	Start 1-2 mg q12 hr Max dose 10 mg q12 hr
Isosorbide dinitrate	- Preload reduction may be useful in patients with heart failure. - Generally used in combination with hydralazine. This combination reduces preload & afterload similar to an ACEi, but without nephrotoxicity.	- Not great for long-term therapy (requires frequent dosing) - Tolerance can develop			
Clonidine	- May provide some anxiolysis.	- Not good medication for chronic use (risk of rebound hypertension).	- May cause somnolence	Onset ~1 hour Duration ~12 hr	Start 0.2 mg PO q12hr Max dose 1.2 mg PO q12hr
Furosemide	- Excellent if volume overload is cause of HTN.	- Only useful in patients with volume overload.	- Will decrease potassium, magnesium levels. - Should never be used in patients with euvoolemia or hypovolemia.	Onset: 1-2 hours Duration: Indefinite	Titrated doses with a goal of achieving euvoolemia. Stop as soon as patient is euvolemic.

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<https://emcrit.org/wp-content/uploads/2016/11/oralonset.svg>

podcast

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questions & discussion

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To keep this page small and fast, questions & discussion about this post can be found on another page [here \(https://emcrit.org/pulmcrit/hypertensive/\)](https://emcrit.org/pulmcrit/hypertensive/).



(<https://i0.wp.com/emcrit.org/wp-content/uploads/2016/11/pitfalls2.gif>)

- #1 most common mistake = overdiagnosis of hypertensive emergency among patients with scary high Bp but no target organ damage. This isn't a hypertensive emergency, please don't call the ICU for this. Thanks in advance.
- #2 most common mistake = treating hypertensive emergency too aggressively and dropping the Bp too much and too fast.
- #3 most common mistake = trying to transition from an antihypertensive infusion to an oral agent that takes a long time to have any effect on blood pressure (e.g. amlodipine). This causes patients to be stuck in the ICU on an infusion forever. It's also unpredictable when these drugs take effect, so there is a risk of *dose-stacking* (i.e. you keep up-titrating oral agents and eventually they all kick in simultaneously, causing hypotension).
- Generally avoid IV hydralazine; this has erratic effects and sometimes bottoms out the blood pressure.
- Don't use IV metoprolol for blood pressure control. Metoprolol isn't very effective for control of blood pressure, but it will slow down the heart rate. That actually makes matters worse, because then you can't use labetalol (since the patient is already bradycardic).

Going further:

- EMCrit 190: [Emergencies with a side of hypertension](https://emcrit.org/emcrit/hypertensive-emergencies/) (<https://emcrit.org/emcrit/hypertensive-emergencies/>)
- [Hypertensive emergencies](https://emergencymedicinecases.com/episode-41-hypertensive-emergencies/) (<https://emergencymedicinecases.com/episode-41-hypertensive-emergencies/>) (Emergency Medicine Cases, Anton Helman)
- [Hypertensive Emergency](https://wikem.org/wiki/Hypertensive_emergency) (https://wikem.org/wiki/Hypertensive_emergency) (WikEM)

References

1. Leiba A, Cohen-Arazi O, Mendel L, Holtzman E, Grossman E. Incidence, aetiology and mortality secondary to hypertensive emergencies in a large-scale referral centre in Israel (1991-2010). *J Hum Hypertens*. 2016;30(8):498-502. [[PubMed \(https://www.ncbi.nlm.nih.gov/pubmed/26674757\)](https://www.ncbi.nlm.nih.gov/pubmed/26674757)]
2. Aronson S, Dyke C, Stierer K, 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;107(4):1110-1121. [[PubMed \(https://www.ncbi.nlm.nih.gov/pubmed/18806012\)](https://www.ncbi.nlm.nih.gov/pubmed/18806012)]
3. Fischer M, Schmutzhard E. Posterior reversible encephalopathy syndrome. *J Neurol*. 2017;264(8):1608-1616. [[PubMed \(https://www.ncbi.nlm.nih.gov/pubmed/28054130\)](https://www.ncbi.nlm.nih.gov/pubmed/28054130)]
4. Toledano M, Fugate J. Posterior reversible encephalopathy in the intensive care unit. *Handb Clin Neurol*. 2017;141:467-483. [[PubMed \(https://www.ncbi.nlm.nih.gov/pubmed/28190431\)](https://www.ncbi.nlm.nih.gov/pubmed/28190431)]
5. Datar S, Singh T, Fugate J, Mandrekar J, Rabinstein A, Hocker S. Albuminocytologic Dissociation in Posterior Reversible Encephalopathy Syndrome. *Mayo Clin Proc*. 2015;90(10):1366-1371. [[PubMed \(https://www.ncbi.nlm.nih.gov/pubmed/26349950\)](https://www.ncbi.nlm.nih.gov/pubmed/26349950)]

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