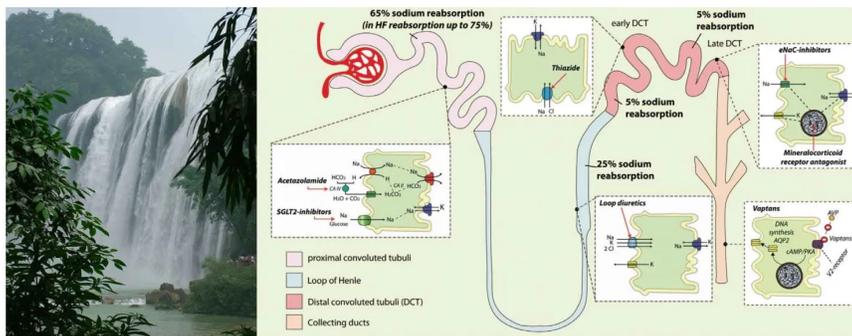
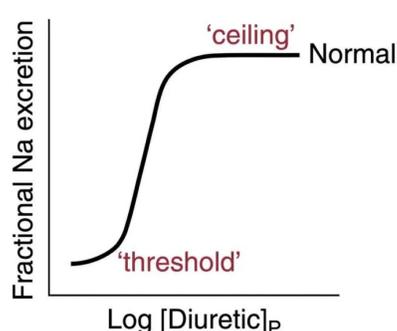


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The Internet Book of Critical Care

Deresuscitation: Dominating the Diuresis

January 9, 2020 by [Josh Farkas](#)

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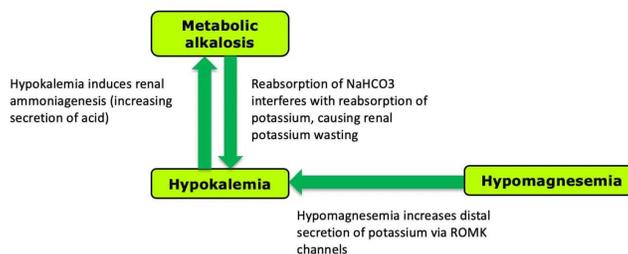
intro

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rationale for this chapter

- There is increasing evidence that volume overload is detrimental to critically ill patients.
- It is common to encounter patients in the ICU who are massively volume overloaded. For example:
 - Iatrogenic volume overload following 1-2 weeks of ICU care without attention to volume control.
 - Volume overload due to cor pulmonale with systemic congestion.
- Simply giving furosemide is generally fine for removing a few liters in patients with normal electrolytes. However, removing larger volumes of fluid without causing electrolyte abnormalities generally requires a more sophisticated diuretic strategy.
 - Electrolyte abnormalities induced by diuresis may reinforce themselves, in a vicious spiral (figure below).
- This chapter explores how to achieve large-volume diuresis, while limiting iatrogenic complications.

electrolyte problems induced by diuresis may be self-reinforcing



Diuresis often causes several electrolyte abnormalities, which reinforce one another, rendering them harder to treat. This calls for an organized and aggressive approach to electrolyte maintenance in patients undergoing large-volume diuresis.

-The Internet Book of Critical Care, by @PulmCrit

are diuretics nephrotoxic?

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diuretics are *not* intrinsically nephrotoxic

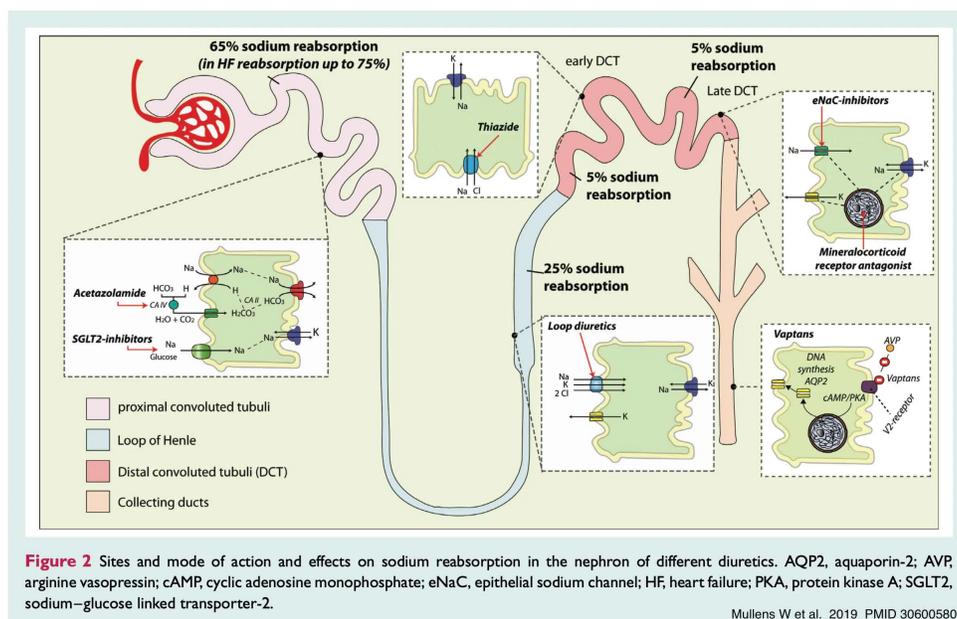
- Diuretics don't seem to directly cause harm to the kidneys (with the possible exception of triamterene).
- Diuretics often block various ion channels in the renal tubules. This actually *reduces* the amount of energy expended by the nephron, thereby decreasing oxygen consumption. This may theoretically *protect* the kidneys in situations with poor perfusion.

diuretics can induce renal failure

- If sufficient diuretics are administered to provoke *volume depletion* (e.g. hypovolemic shock), then this can surely cause renal failure.
- Therefore:
 - (1) Diuretics can cause renal failure. But they do this indirectly (via induction of hypovolemia) – not directly.
 - (2) Close attention to volume status and hemodynamics during diuresis should reduce the risk of kidney injury.

diuretics can *improve* renal function

- *Systemic venous congestion* can impair renal function, via several mechanisms (“congestive nephropathy”). For example:
 - Impaired renal perfusion pressure: the blood pressure gradient across the kidneys is equal to the mean arterial pressure (MAP) minus the central venous pressure. Elevating the central venous pressure chokes off blood flow through the kidneys.
 - Venous congestion can cause intra-renal interstitial edema, which can cause a compartment syndrome within the kidney!
- In patients with venous congestion, diuresis may relieve this congestion and thereby improve renal function.
- In the [FACTT trial \(https://www.wikijournalclub.org/wiki/FACTT\)](https://www.wikijournalclub.org/wiki/FACTT), of patients with ARDS, patients randomized to the conservative fluid arm received *higher* doses of diuretics (mostly loop diuretics) and had *improved* renal outcomes. This was mediated by maintenance of an even fluid



mechanism of action & physiologic effects

- The primary effect is blockade of the Na/K/Cl channel, which is located predominantly on the thick ascending loop of Henle. Consequences include:
 - (1) Increased magnesium, and calcium wasting.
 - Mg and Ca are reabsorbed between cells in the thick ascending loop of Henle, driven by a lumen-positive electrochemical gradient. Loop diuretics reduce this electrochemical gradient.
 - Furosemide was once used as a treatment for hypercalcemia, but this has largely *fallen out of favor* (<https://emcrit.org/ibcc/hypercalcemia/#treatment>).
 - (2) Contraction alkalosis.
 - (3) Blockade of NaCl entry into the macula densa (which normally occurs via the NKCC2 channel). Consequences of this are:
 - Blockage of tubulo-glomerular feedback. This ultimately leads to renal vasodilation, which is potentially beneficial (via increases in prostaglandin E2).
 - Increased renin production:
 - This increases Angiotensin II levels (which may increase blood pressure and potentially defend the glomerular perfusion).
 - This also increases aldosterone levels (which may increase sodium retention by the distal nephron, potentially impairing further diuresis).
- Note: Patients with an allergy to sulfa *antibiotics* can safely receive loop diuretics (14573734 (<https://www.ncbi.nlm.nih.gov/pubmed/14573734>)).

pharmacokinetics & dosing

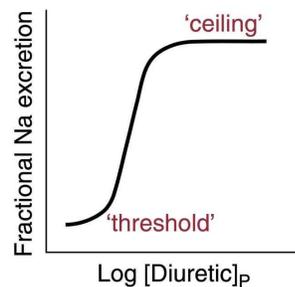
- Oral bioavailability
 - Furosemide averages ~50% oral bioavailability, but is *widely variable* from 10-100% (so IV to PO conversion is very roughly 1:2).
 - Bumetanide and torsemide have oral bioavailability >80% (so IV to PO conversion is 1:1).
 - Peak drug concentrations are reached within 0.5-2 hours (30936153 (<https://www.ncbi.nlm.nih.gov/pubmed/30936153>)).
- Following an intravenous dose, peak action occurs after 30 minutes (for both furosemide and bumetanide).
- Half-life:
 - Furosemide has a longer half-life than bumetanide, which may be a major advantage of furosemide.
 - Furosemide is metabolized by the kidney, whereas bumetanide is metabolized in the liver. This results in an extended half-life of furosemide in renal dysfunction, whereas bumetanide's half-life is extended in hepatic dysfunction.
- Entry into the tubule
 - Loop diuretics have high albumin binding (>90%), so they aren't freely filtered into the tubule. In order to enter the nephron lumen, they must be actively *secreted* in the proximal tubule via organic anion transporters (OATs).
 - Secretion is impaired in uremia due to *competition* for organic anion transporters with other organic anions which accumulate in renal failure. Additionally, metabolic acidosis impairs tubular secretion.

IV furosemide vs. IV bumetanide?

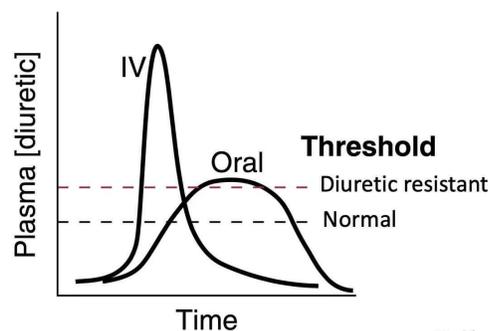
- These are similar agents. There doesn't seem to be any definitive data comparing them, to determine if one is superior to the other.
 - 1 mg IV bumetanide is roughly equivalent to 40 mg IV furosemide. In renal failure, the half-life of furosemide *increases*, making furosemide last longer (so the ratio may decrease, such that 1 mg IV bumetanide is roughly equivalent to 20 mg IV furosemide).
- The longer half-life of furosemide could theoretically make furosemide superior for *intermittent* dosing.
- The shorter half-life of bumetanide could theoretically make this superior for administration as a continuous infusion.
- Overall, furosemide seems to be a more widely used agent in critical care – so we will focus a bit more on it here. However, the same general concepts apply to both medications.

practical furosemide dosing 101

Loop diuretic pharmacology



- Below the threshold concentration, there is zero efficacy.
- Above ceiling concentration, there is no added efficacy (although pharmacokinetically, the dose may have a longer duration of efficacy)



- Diuretic effect depends on the *duration* of time that drug concentrations are above the threshold concentration.
- IV administration achieves higher levels, but may lead to a shorter duration of action.

Modified from Ellison DH. CJASN 14:1248 PMID 30936153

• [1] Determine an effective dose

- Furosemide exhibits a *ceiling effect*, meaning that beyond a certain dose additional drug won't increase the diuretic effect (although higher doses might have a more *prolonged* effect).
- Higher doses are generally required in renal failure and in patients chronically exposed to furosemide.
- The starting dose doesn't particularly matter. Reasonable choices might be:
 - Patients on chronic oral furosemide: give an IV dose equal to or a bit higher than the patient's home oral furosemide dose.
 - Patients not on chronic furosemide: give a dose between 20-80 mg IV depending on the renal function & acuity of the situation.
- The key is *empiric dose titration*. If there is no result in 30-60 minutes, *keep doubling the dose* until the patient responds (or until you reach a dose of ~240 mg furosemide)([29141174](https://www.ncbi.nlm.nih.gov/pubmed/29141174) (<https://www.ncbi.nlm.nih.gov/pubmed/29141174>)). This rapid dose-titration should empirically define an effective furosemide dose.
 - The target urine output following an effective dose is >100-150 ml/hour ([30600580](https://www.ncbi.nlm.nih.gov/pubmed/30600580) (<https://www.ncbi.nlm.nih.gov/pubmed/30600580>)).

• [2] Determine the proper dosing interval

- Furosemide will typically cause diuresis for <6 hours ("LASIX" was so named because it **LA**sts **SIX** hours – but this is based on oral pharmacokinetics). After the furosemide wears off, the kidney generally *retains* sodium. So, giving furosemide once daily will often achieve relatively little (6 hours of diuresis, 18 hours of sodium retention).
- More effective diuresis generally depends on giving furosemide more *frequently* (rather than necessarily in higher doses). Depending on the clinical scenario, this may involve giving the furosemide q6hr, q8hr, or q12hr. Alternatively, an infusion can be used (section below).
- Co-administration of a long-acting thiazide (e.g. indapamide or metolazone) may help prevent sodium retention when the furosemide wears off, thereby facilitating effective diuresis.

maximal effective doses of diuretics in specific diseases

	Furosemide	Bumetanide	Torsemide
Normal	40 mg	1 mg	15-20 mg
Chronic kidney disease	160-200 mg	8-10 mg	50-100 mg
Heart failure	40-80 mg	2-3 mg	20-50 mg
Cirrhosis	40 mg	1 mg	15-20 mg
Nephrotic syndrome	120 mg	3 mg	50 mg

Loop diuretics have a *ceiling effect* – after a certain dose, additional drug has no further effect. Thus, the key to more effective diuresis is often using more frequent doses, rather than higher doses (once you've found an effective dose of the diuretic). The numbers here aren't based on hard data, but rather are intended to provide a general concept of effective doses in various situations.

Table data from Lachance P and Bagshaw SM in Critical Care Nephrology 3rd Ed.

continuous infusion of loop diuretic

- General concept:
 - One pitfall of loop diuretics is that they last for a finite period of time (<6 hours for furosemide, less for bumetanide). In between diuretic doses, the kidney will retain sodium. If diuretic doses are spaced too far apart (e.g. q12hr or q24hr), this may defeat the effectiveness of diuresis.
 - Continuous infusion of a diuretic could avoid the kidney's ever escaping the effect of the loop diuretic.
- Evidence:
 - Multiple RCTs have compared the efficacy of intermittent boluses versus continuous infusions of loop diuretic. There is no definitive evidence that either strategy is superior.
 - Ototoxicity does appear to be lower with the use of continuous infusions of loop diuretics. However, this difference becomes manifest only when the dose of diuretics is massive (e.g. individual boluses of furosemide up to 2,000 mg)(8800113 (<https://www.ncbi.nlm.nih.gov/pubmed/8800113>)).
- Bottom line?
 - Choice of infusion vs. bolus diuretic depends largely on *logistics* (neither strategy is intrinsically superior).
 - The primary advantage of a diuretic infusion is that it may be titrated continuously by the nurse at the bedside. This may lead to a greater amount of attention to the amount of urine output (ensuring that the patient truly meets their diuretic goals).
 - Diuretic infusions are useful only in patients who have responded to a bolus of loop diuretic (if the patient is refractory to large bolus doses, they will similarly be refractory to an infusion!).

thiazides & thiazide-like diuretics

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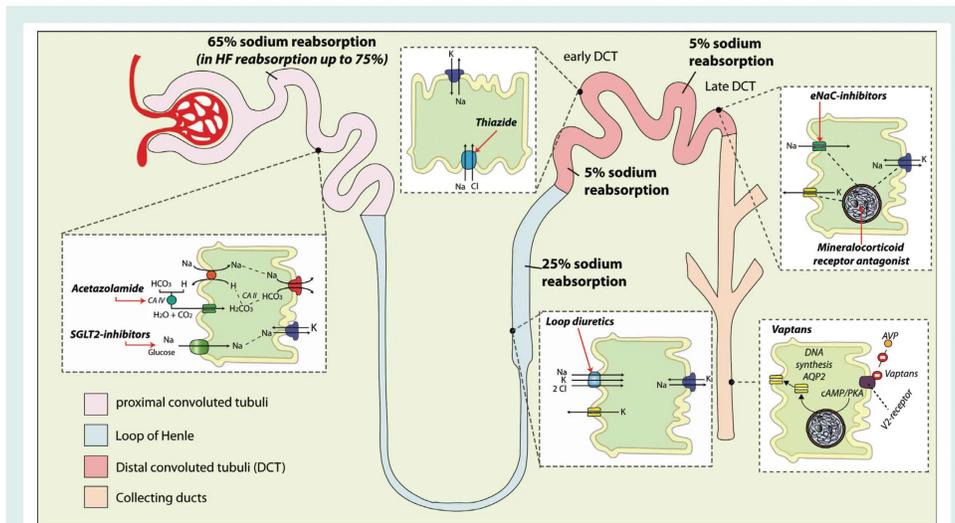


Figure 2 Sites and mode of action and effects on sodium reabsorption in the nephron of different diuretics. AQP2, aquaporin-2; AVP, arginine vasopressin; cAMP, cyclic adenosine monophosphate; eNaC, epithelial sodium channel; HF, heart failure; PKA, protein kinase A; SGLT2, sodium–glucose linked transporter-2.

Mullens W et al. 2019. PMID 30600580

mechanism of action & physiologic effects

- Thiazides inhibit sodium reabsorption in the distal convoluted tubule.

- Thiazide monotherapy has a relatively weak diuretic effect (because not much sodium is generally reabsorbed in the distal convoluted tubule).
- Patients being treated with loop diuretics will tend to reabsorb more sodium in the distal convoluted tubule. Thus, adding a thiazide in combination with a loop diuretic may substantially augment the efficacy of the loop diuretic.
- Other physiologic effects include:
 - (1) Thiazides tend to reduce the serum sodium level (due to increases in sodium excretion and reduction in the excretion of water).
 - (2) Thiazides increase potassium wasting (due to stimulation of aldosterone & increased distal tubule flow).

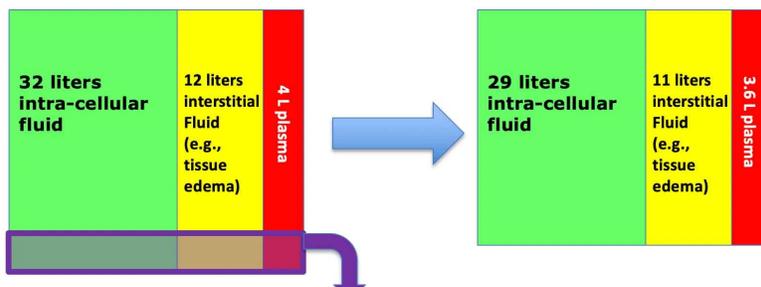
pharmacokinetics & dosing

- Like loop diuretics, thiazides are bound to albumin and secreted into the tubule via organic anion transporters.
- Secretion into the tubule is delayed in renal failure, reducing diuretic efficacy.

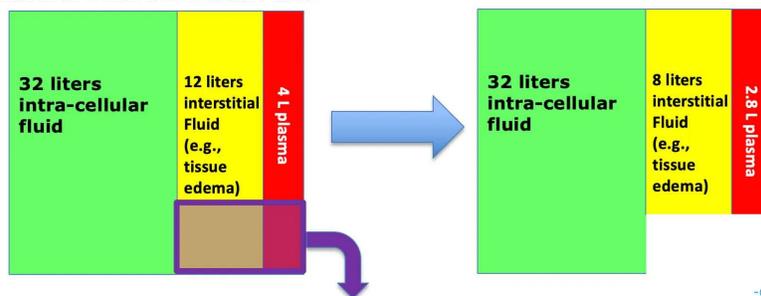
benefits of using a thiazide diuretic as a 2nd line agent (in combination with a loop diuretic)

- (1) Avoiding hyponatremia: Loop diuretic therapy by itself tends to promote excretion of dilute, hypotonic urine. This frequently leads to hyponatremia, which eventually must be treated by administering free water (which largely eliminates the volume loss). Addition of a thiazide diuretic to a loop diuretic promotes excretion of sodium (natriuresis), leading to more effective volume loss (discussed further [here](https://emcrit.org/pulmcrit/occult-diuretic-resistance/) (<https://emcrit.org/pulmcrit/occult-diuretic-resistance/>)).
- (2) Improved responsiveness to furosemide: Addition of a thiazide diuretic may prevent or reverse *resistance* to loop diuretics.
 - Chronic furosemide use leads to up-regulation of sodium reabsorption in the distal convoluted tubule – which impairs furosemide's effectiveness. Administration of a thiazide may restore responsiveness to furosemide.
- (3) Avoidance of sodium retention: A long-acting thiazide (e.g. metolazone or indapamide) can act *continuously* to prevent sodium retention (even in-between doses of loop diuretic).

Removal of 5 liters of *electrolyte-free water*



Removal of 5 liters of *isotonic fluid*



Top: Water removal doesn't cause effective diuresis because this mostly removes fluid from the intracellular space. This doesn't cause effective decongestion. Furthermore, water removal often causes hyponatremia, which must be treated with administration of water (reversing volume losses). A similar (albeit less severe) problem is encountered with loop diuretic monotherapy, as this often causes production of relatively *dilute* urine (leading to hyponatremia and free water loss).

Bottom: Removal of isotonic fluid (water plus sodium) is generally needed to achieve effective reduction of plasma volume and tissue edema. Combining a loop diuretic and thiazide may promote loss of more isotonic urine.

-@PulmCrit

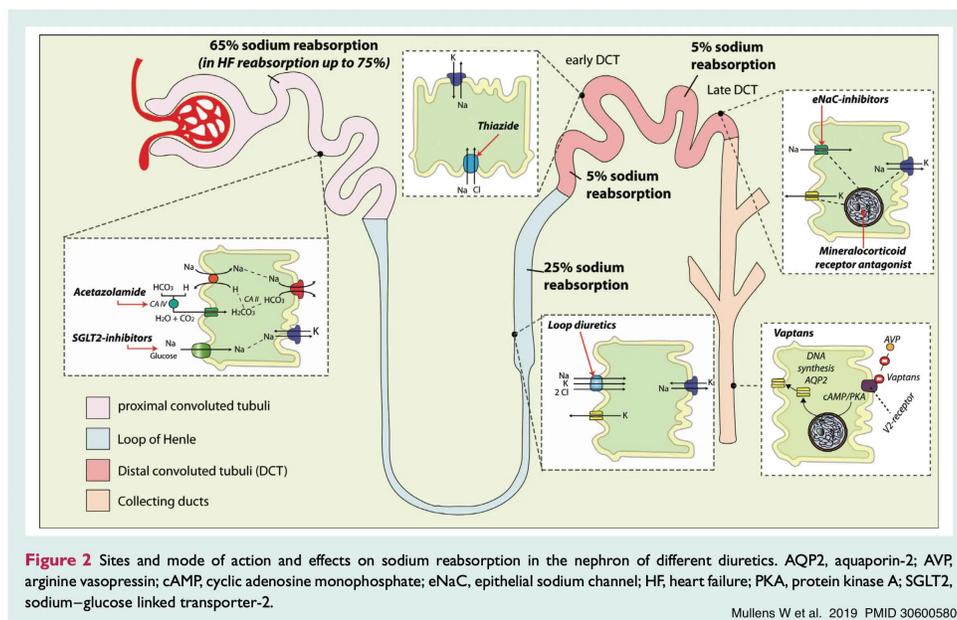
which thiazide to choose?

- **Intravenous chlorothiazide**
 - This is the only intravenous thiazide available, so it's the only option for patients who are NPO.
 - Intravenous chlorothiazide has the fastest onset, so it's preferred in extremely emergent situations (e.g. critical hyperkalemia).
 - Limitations of IV chlorothiazide include being more expensive, and having a relatively short half-life (~2 hours).
- **Oral indapamide or metolazone**

- These agents have longer half-lives (~24 hours for indapamide, ~12 hours for metolazone). This may be useful to promote ongoing diuretic pressure (preventing the kidneys from retaining sodium in between doses of diuretic).
- Metolazone is supported by more evidence in acute decompensated heart failure (5 mg PO daily or BID is a classic dose used in the AVOID-HF trial, CARESS-HF, and the 3T trial)(26519995, 23131078 (<https://www.ncbi.nlm.nih.gov/pubmed/23131078>), 23131078).
- Indapamide was shown to be effective in one ICU RCT (26948252). Indapamide appears to have renoprotective properties, which could make it especially useful (28460782, 23488823).
- There is no solid data comparing these two agents. Metolazone may be a bit more powerful (especially when used at higher doses, such as 10 mg BID). However, the renoprotective properties of indapamide are intriguing, potentially making indapamide a preferred choice as a gentle add-on agent for de-resuscitation in the ICU.
- Oral hydrochlorothiazide could also be used, but there is less evidence regarding its use in critical care.

spironolactone

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mechanism of action & physiologic effects

- Spironolactone is a mineralocorticoid inhibitor, which will impair the effects of aldosterone on the distal tubule in conditions of elevated aldosterone activity. This will tend to promote sodium excretion, potassium retention, and cause a non-anion-gap metabolic acidosis.

general properties of spironolactone

- Spironolactone will have the greatest efficacy in contexts where the renin-angiotensin-aldosterone system is highly activated (e.g. cirrhosis and heart failure). Alternatively, in situations where the basal aldosterone tone is low, spironolactone may have little clinical effect.
- Spironolactone takes 1-2 days to have maximal effect, which limits its utility in emergent situations. This also makes it difficult to perform any rapid dose-titration.
- Spironolactone is a “potassium-sparing” diuretic. In patients undergoing large-volume diuresis, addition of spironolactone may reduce hypokalemia and contraction alkalosis.

clinical utility may include:

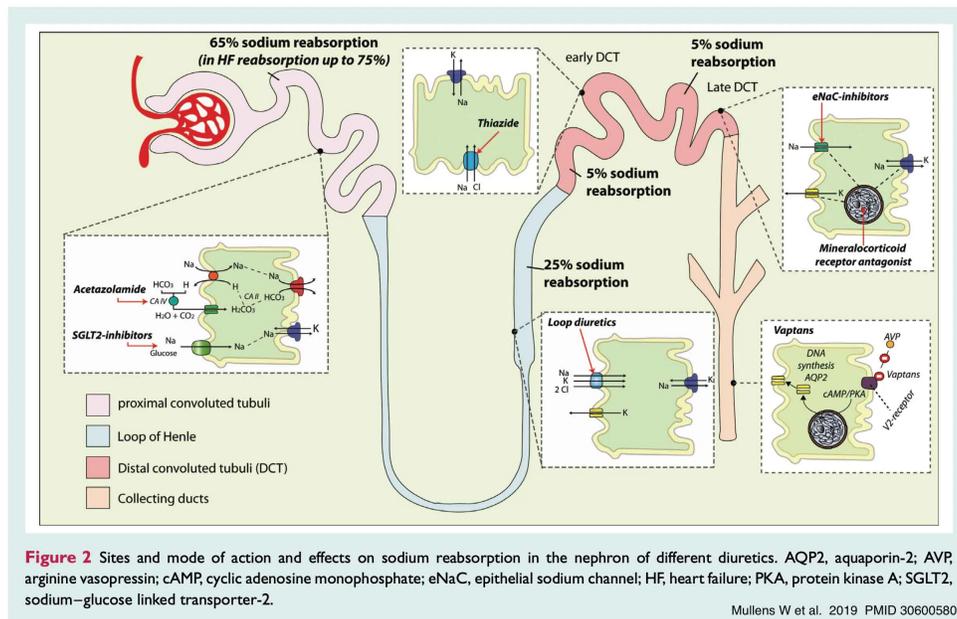
- (1) Volume removal in cirrhosis.
- (2) Counteracting neurohormonal activation in patients with heart failure and reduced ejection fraction (the dose is limited to 50 mg/day when used *solely* for this indication).
- (3) Adjunctive diuretic in patients with ongoing diuresis (with an anticipated duration of diuretic therapy >1-2 days).

dosing ?

- Current guidelines for cirrhosis suggest use with furosemide in a ratio of 100 mg spironolactone : 40 mg furosemide. The maximal recommended dose of spironolactone is 400 mg daily ([23463403](https://www.ncbi.nlm.nih.gov/pubmed/23463403) (<https://www.ncbi.nlm.nih.gov/pubmed/23463403>)).
- In the ATHENA-HF trial, 100 mg spironolactone daily failed to affect plasma potassium concentration in patients with heart failure, raising the possibility that fairly high doses of spironolactone may be needed to modulate diuresis (29141174).

amiloride

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mechanism of action & physiologic effects

- Amiloride acts predominantly via blocking the ENaC channel in the distal nephron. This has the following consequences:
 - Increases serum potassium ("potassium-sparing diuretic").
 - Decreases the serum bicarbonate level (either causing a non-anion-gap metabolic acidosis, or treating a metabolic alkalosis).
 - Reduces urinary excretion of calcium and magnesium.

triamterene (and why to avoid it)

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Triamterene has the same mechanism of action as amiloride, blocking passive potassium efflux out of the distal nephron (via the ENaC channel). As such, it is a potassium-sparing diuretic. Triamterene is a weak diuretic on its own, so its main role is to reduce potassium wasting (and thus reduce the amount of potassium replacement the patient requires).

Unfortunately, triamterene has a variety of unique nephrotoxic properties. Triamterene can cause nephrolithiasis, interstitial nephritis, and acute renal failure (due to effects on the prostaglandin system) ([2662034](https://www.ncbi.nlm.nih.gov/pubmed/2662034) (<https://www.ncbi.nlm.nih.gov/pubmed/2662034>), [6589647](https://www.ncbi.nlm.nih.gov/pubmed/6589647) (<https://www.ncbi.nlm.nih.gov/pubmed/6589647>)). In fairness, these nephrotoxicities are *mild* (many patients are chronically maintained on triamterene with no ill effects). However, the risk of nephrotoxicity just doesn't seem worth the benefit of using triamterene in the ICU:

- ICU patients are at increased risk of nephrotoxicity.
- Replacement of potassium in the ICU is reasonably easy to do.

Amiloride seems to be a superior drug compared to triamterene (with similar efficacy, but less toxicity).

- If you have access to amiloride, then amiloride seems to be a safe option for potassium-sparing diuresis.
- If you don't have access to amiloride, then it's probably safer to just accept that the patient will lose potassium (and you will need to give them more potassium to keep up with ongoing losses). For patients with prolonged diuresis, spironolactone may be used to limit potassium

loss (more on this above).

osmotic diuretics (mannitol & urea)

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Osmotic diuretic agents function as aquaretics – that is, they stimulate the loss of electrolyte-free water. These agents are primarily useful for patients with hyponatremia. They are generally not used for management of volume overload, but might be considered for patients with hyponatremia plus refractory volume overload (who are failing to respond to conventional therapies).

mechanism of action & physiologic effect of osmotic diuretics

- Osmotic diuretics are filtered freely through the glomerulus. They remain in the tubule and are eventually excreted. Their passage through the nephron obligates the body to excrete water along with them, so the ultimate result is loss of water.
 - These agents will increase the sodium concentration. In hyponatremia this may be beneficial.
 - For patients with diuretic resistance due to hyponatremic hypochloremia, osmotic diuretics could theoretically re-establish normal chloride concentrations, which might theoretically improve diuretic responsiveness.
- Osmotic diuretics are somewhat unique among diuretics in that they don't require active transport into the renal tubule. Thus, these agents might theoretically be expected to work in some patients with kidney disease who have impaired functionality of the organic anion transporters (and thus difficulty transporting other diuretics across the tubule).
- If the kidneys are unable to excrete mannitol, this may lead to volume overload and dilutional hyponatremia (but since the serum osmolarity is normal or high, this is classified as *pseudohyponatremia*).

intravenous mannitol: pharmacokinetics & dosing

- Half-life depends on GFR (may vary from 1 – 36 hours).
- May be infused in daily doses of 50-200 grams.
- Should be reserved for truly dire situations, where other options aren't available.

oral urea: pharmacokinetics & dosing

- Half-life depends on GFR (with normal GFR, its half-life is ~1 hour). An orally administered dose of urea will generally be eliminated in <12 hours.
- The initial dose is usually 15-30 grams orally. More on urea [here \(https://emcrit.org/pulmcrit/aquaresis/\)](https://emcrit.org/pulmcrit/aquaresis/).

volume removal from the pleura or peritoneum

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Be careful about trying to use large-volume diuresis to remove fluid from the pleura or peritoneum! There is often a limit to the amount of volume which can be removed from these spaces...

diuresis to remove fluid from the pleura

- Diuresis is effective only in patients with *transudative, cardiogenic effusions*.
 - Exudative effusions can't be diuresed off at all.
- Fluid removal occurs gradually.
- For patients in extremis from a pleural effusion, thoracentesis may be the only strategy which achieves rapid resolution.

diuresis to remove ascites fluid

- This can be achieved only in transudative effusions due to cirrhosis.
- The maximum amount of fluid which can be drained into systemic circulation per day may be ~ 300-900 ml ([4910836 \(https://www.ncbi.nlm.nih.gov/pubmed/4910836\)](https://www.ncbi.nlm.nih.gov/pubmed/4910836)). Diuresis at a faster rate may lead to intravascular volume depletion.
- For patients with very tense ascites, this may increase intra-abdominal pressure and cause a compartment syndrome. Such patients may not respond well to diuresis, due to renal dysfunction. Appropriate management of tense ascites causing organ failure is therapeutic paracentesis.

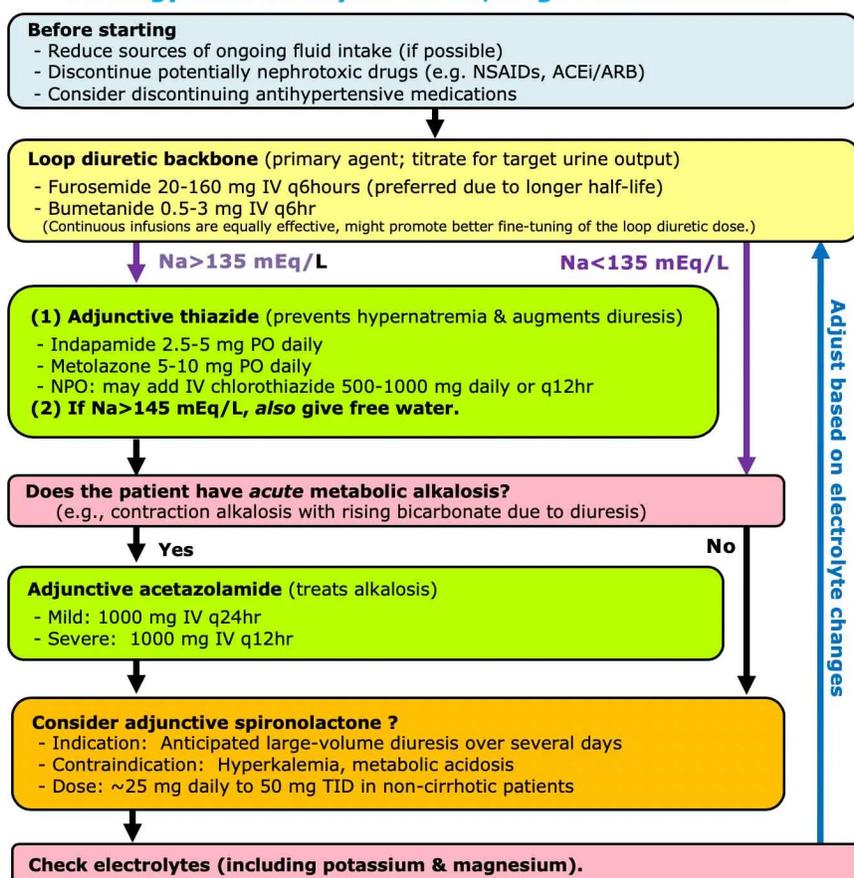
clinical approach to the patient with symptomatic pleural effusion or ascites

- Consider the following factors:
 - (1) Is the fluid removable via diuresis? (this requires the presence of a transudative process).
 - (2) How rapidly do you need to remove the fluid? (is this an emergency, or is gradual fluid removal acceptable).
 - (3) Is there simultaneous total body volume overload, or is there fluid accumulation solely in the pleura/peritoneum? Patients with total body volume overload may better tolerate large-volume diuresis, whereas patients without true hypervolemia may not.
- If emergent relief is needed, fluid removal via thoracentesis or paracentesis may be necessary.
- Beware of trying to remove fluid too aggressively (i.e., faster than the ascitis or pleural fluid can be reabsorbed).

overall strategy for large-volume diuresis

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This section is about a patient with gross volume overload (e.g. estimated fluid excess of several liters). The patient is diuretic-responsive, so you could probably use any diuretic(s) to eliminate fluid. The challenge here is fluid removal without causing electrolyte abnormalities.

strategy for electrolyte-neutral, large-volume diuresis

Without proper attention, large-volume diuresis will often cause substantial electrolyte shifts (typically, hypernatremia, metabolic alkalosis, hypomagnesemia, and hypokalemia). These shifts are entirely manageable with careful monitoring and early/aggressive treatment.

-The Internet Book of Critical Care, by @PulmCrit

o) avoid ongoing fluid inputs, if possible

- Continuous intravenous infusions may cause substantial sodium intake. Intermittent fluid administration with medications may contribute as well.
- Review all sources of fluid input. Curtail these as much as possible.
- (Remember: the goal is *net fluid loss* – not merely excretion of a large volume of urine).

1) IV loop diuretic

- This is the backbone of the diuretic regimen.
- Due to the relatively short half-life of loop diuretics (<6 hours), the IV loop diuretic is the most easily *titratable* agent:
 - Thiazides and spironolactone may be adjusted on a daily basis, but cannot be fine-tuned.
 - The loop diuretic dose is actively titrated to achieve daily fluid targets.

2) long-acting thiazide diuretic (e.g. indapamide or metolazone)

- This serves several purposes:
 - (1) Prevents hyponatremia (or assists in the correction of hyponatremia).
 - (2) Prevents sodium retention in between doses of loop diuretic.
 - (3) Indapamide may have nephroprotective properties.
- Long-acting thiazides are often very helpful.

3) acetazolamide PRN contraction alkalosis

- More on this in the section below on [contraction alkalosis \(#metabolic_alkalosis_\("contraction_alkalosis"\)\)](#).
- Acetazolamide alone is generally sufficient, but in severe cases additional therapies may also be needed.

4) potassium-sparing diuretic (if available)

- Potassium-sparing diuretics may help prevent hypokalemia, hypomagnesemia, and metabolic alkalosis.
- These aren't necessary in most cases, but may be useful (especially among patients who are requiring very high doses of potassium supplementation).
 - Amiloride is probably the most useful agent (it will work rapidly, and should be effective regardless of prevailing aldosterone levels).
 - Spironolactone could be useful if diuresis is anticipated to last for >1-2 days (spironolactone requires 1-2 days for full efficacy).

basic management for electrolyte problems encountered during ongoing diuresis

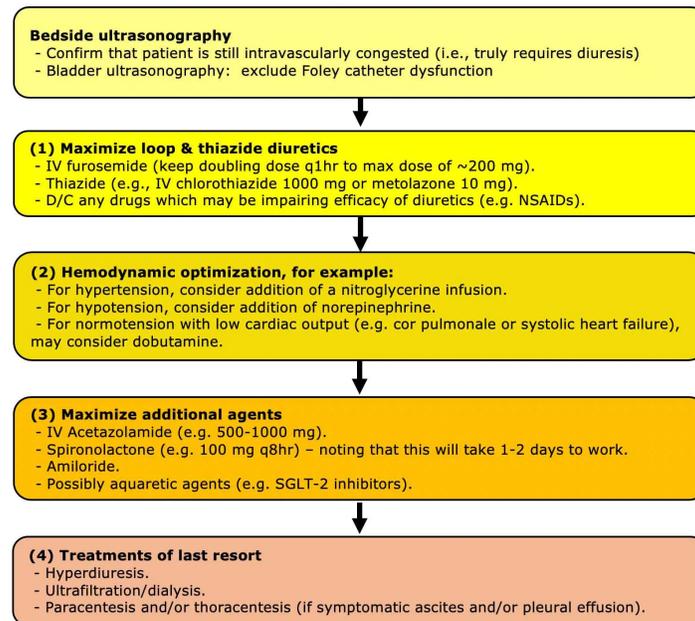
Hi	Low
↑ Bicarbonate <ul style="list-style-type: none"> • Common during diuresis (contraction alkalosis). • 1st line therapy = Add IV acetazolamide. • Other treatments: aggressive repletion of hypokalemia & hypomagnesemia, K-sparing diuretics (amiloride, spironolactone). 	↓ Bicarbonate <ul style="list-style-type: none"> • Uncommon during diuresis: look for other cause. • Stop any acetazolamide.
↑ Sodium <ul style="list-style-type: none"> • Treat with free water (either oral water or D5W intravenously). • Add thiazide diuretic. • May need to give additional doses of loop diuretic to prevent free water from causing the patient to gain weight. 	↓ Sodium <ul style="list-style-type: none"> • D/c thiazide diuretics, amiloride, and spironolactone. • Continue diuresis with furosemide (this may increase serum sodium). • Remove sources of free water if possible. • Ongoing administration of loop diuretics will generally increase Na. • Could consider adding oral Urea if refractory to above treatments.
↑ Potassium <ul style="list-style-type: none"> • D/c any potassium supplementation. • D/c potassium-sparing diuretics (e.g. amiloride, spironolactone). • Evaluate renal function (may be early sign of renal dysfunction). 	↓ Potassium <ul style="list-style-type: none"> • Supplement with potassium (and check/replete Mg as well). • Severe/ongoing: May add a potassium-sparing diuretic (e.g. amiloride, spironolactone).
↑ Magnesium <ul style="list-style-type: none"> • Discontinue magnesium supplementation. • Evaluate renal function (may be early sign of renal dysfunction). • Generally safe unless profound hypermagnesemia, should resolve over time. 	↓ Magnesium <ul style="list-style-type: none"> • Aggressive supplementation with IV magnesium sulfate.
↑ Chloride <ul style="list-style-type: none"> • Either due to elevated sodium or low bicarbonate. Treat these problems as above. 	↓ Chloride <ul style="list-style-type: none"> • Either due to reduced sodium or elevated bicarbonate. Treat these problems as above.
↑ Calcium <ul style="list-style-type: none"> • Rarely encountered during diuresis, look for other cause. • Consider discontinuation of thiazide. 	↓ Calcium <ul style="list-style-type: none"> • Moderately reduced calcium is common in critical illness, and generally of little significance. • Unless calcium is profoundly reduced or symptoms are present, the best approach is often to stop checking the calcium.

Guide to basic strategies for electrolyte management during large-volume diuresis. For severe or persistent abnormalities, see the individual chapters regarding each abnormality. The most commonly encountered abnormalities are highlighted in yellow.

-Internet Book of Critical Care, by @PulmCrit

diuretic resistance

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potential approach to critically ill patient with diuretic resistance

-The Internet Book of Critical Care, by @PulmCrit

Diuretic resistance refers to patients who fail to produce urine in response to diuretics. A potential approach to this is shown above, although there is overall little evidence to support steps #3-4. Perhaps the most important aspect is to consider why the patient isn't responding to diuretics:

causes of diuretic resistance in the ICU

- Excessive fluid & sodium intake
 - Continuous infusions and various intravenous medications.
- Inadequate dosing/schedule of diuretics
 - Dose is below the diuretic threshold.
 - Dosing interval is too long.
 - Oral route is used in patients with bowel edema or dysfunction (especially with furosemide).
- Medications that interfere with diuretic
 - NSAIDs impair diuretic responsiveness.
 - Some medications may compete with diuretics for entry into the renal tubule (e.g. probenecid).
- Hemodynamics: Impaired renal perfusion
 - Shock of any etiology.
 - Systemic congestion (which reduces renal perfusion pressure).
 - Hypovolemia (e.g. a patient with lymphedema who has already been excessively diuresed).
- Renal failure
 - Post-renal (e.g. ureter or bladder obstruction).
 - Intrinsic renal failure (e.g. acute tubular necrosis).
- Endogenous homeostatic mechanisms tend to limit ongoing diuresis ("diuretic braking")
 - Blood pressure reduction may reduce urine output directly.
 - Renin-angiotensin-aldosterone activation increases sodium retention.
 - Sympathetic nervous system activation increases sodium retention.
 - Anti-diuretic hormone (ADH) increases water reabsorption.
 - Hypertrophy of renal tubular segments downstream to the action of the diuretic (e.g. the distal convoluted tubule).

evaluation of diuretic resistance

- Review the medication list for any agents that may hinder diuresis.
- Review the input/output balance (are there sources of fluid and sodium which can be curtailed?).
- Bedside echocardiogram and fluid assessment: Is the patient truly volume overloaded and in need of further diuresis?

- Note that peripheral edema by itself isn't an indication for diuresis. Some patients with compensated heart failure will require somewhat elevated filling pressures (and some peripheral edema) to sustain adequate perfusion.

hyperdiuresis ?

- This involves a combination of hypertonic saline plus a loop diuretic.
- Hyperdiuresis is a controversial technique, which may be considered in patients who don't have other great therapeutic options (e.g. patients who would otherwise require dialysis).
 - Further discussion of hyperdiuresis [here](https://emcrit.org/pulmcrit/pulmcrit-hyperdiuresis-using-hypertonic-saline-to-facilitate-diuresis/) (https://emcrit.org/pulmcrit/pulmcrit-hyperdiuresis-using-hypertonic-saline-to-facilitate-diuresis/).

Hyperdiuresis strategy

- **Candidate for Hyperdiuresis**
 - Heart failure with definite volume overload, which is refractory to standard diuretic therapies (i.e. persistent congestion and inadequate urine response to diuretics).
 - No acute hypertension.
 - No baseline hypernatremia or hyperchloremia.
- **Treatment**
 - Infuse a combination of 150 ml 3% NaCl plus a large dose of IV furosemide (e.g. ~160-250 mg) over an hour. Note that 3% saline is safe for peripheral infusion.
 - If effective, may repeat this twice daily until volume goals are reached. (Alternatively, if the patient *fails* to respond, do *not* give additional doses.)
 - Follow electrolytes and renal function. (If hypernatremia occurs, further doses should be withheld).

Based on numerous studies, but particularly Larmenier G et al 2017 PMID 28932357.
-The Internet Book of Critical Care, by @PulmCrit

furosemide stress test

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definition of a furosemide stress test

- Administration of a defined dose of furosemide:
 - 1 mg/kg for patients who are furosemide naive.
 - 1.5 mg/kg for patients with prior exposure to furosemide.
- Monitoring urine output
 - >200 ml within two hours indicates adequate response.

significance

- Failure to respond to a furosemide stress test suggests renal failure (with an increased risk of requiring hemodialysis).
- Please note that failure to respond doesn't exclude the possibility of renal recovery – especially if other resuscitative steps are available to improve renal function (e.g. improvement in blood pressure and/or perfusion).

clinical utility of a furosemide stress test?

- (1) The oliguric patient: Will additional hemodynamic manipulation help?
 - A furosemide stress test may be useful to obtain a concept of whether the patient has intractable intrinsic renal failure.
 - Failure to respond to furosemide implies that the kidneys are less likely to respond to hemodynamic manipulation (e.g. volume administration) and more likely to progress towards dialysis. Thus, a fluid-conservative strategy might be more beneficial.
 - Response to a furosemide stress test reveals that the kidneys are functional. Therefore, hemodynamic manipulations to maintain urine output (e.g. volume administration, inotropes, vasopressors) may be more likely to succeed.
- (2) A patient who requires diuresis anyway

- Using the dose of furosemide prescribed in the furosemide stress test can help interpret the patient's response in a more rigorous fashion.

More on the furosemide stress test [here](https://emcrit.org/pulmcrit/furosemide-stress-test/) (<https://emcrit.org/pulmcrit/furosemide-stress-test/>).

kaliuresis

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kaliuresis basics

- The easiest and safest way to remove potassium from the body in patients with hyperkalemia is often via the urine (kaliuresis).
- In mild-moderate cases, a loop diuretic alone is sufficient. For more severe situations, a combination of multiple potassium-wasting diuretics may be used (e.g. loop diuretic, thiazide diuretic, and possibly even acetazolamide).

conservative kaliuresis

- For patients with normal renal function, kaliuresis is fairly easy to accomplish with moderate doses of potassium-wasting diuretics (e.g. furosemide). If the patient is euvolemic, then fluid should be administered to prevent volume depletion (e.g. IV Lactated Ringers administration to match urine output).
 - And yes, Lactated Ringers is [safe](https://emcrit.org/pulmcrit/myth-busting-lactated-ringers-is-safe-in-hyperkalemia-and-is-superior-to-ns/) (<https://emcrit.org/pulmcrit/myth-busting-lactated-ringers-is-safe-in-hyperkalemia-and-is-superior-to-ns/>) in hyperkalemia.

aggressive kaliuresis (the nephron bomb)

- For patients with severe renal failure and severe hyperkalemia, the question is whether the patient will respond to diuretics or whether the patient will require hemodialysis. To emergently determine whether hemodialysis is required, it may be reasonable to administer *maximal* doses of diuretics.
 - If the patient responds to this with good urine output, then dialysis can often be avoided.
 - If there is no dramatic urine output, then immediate dialysis is required.
- A typical diuretic bomb regimen would be as follows:
 - i) Maximal dose of IV loop diuretic (e.g. ~200 mg IV furosemide).
 - ii) Maximal dose of IV thiazide (e.g. 1000 mg IV chlorothiazide).
 - iii) Maximal dose of IV acetazolamide (1000 mg IV).
- Mannitol isn't generally recommended here, but in the most desperate situation it might be an option (e.g. critical hyperkalemia and hemodialysis isn't available).

hypernatremia

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management of hypernatremia

- Iatrogenic hypernatremia is common in ICU patients, particularly patients undergoing large-volume diuresis (furosemide tends to cause this).
- If the sodium starts trending up, this should be managed aggressively in a pro-active fashion (if ignored, it will almost always continue to increase).
- Hypernatremia or up-trending sodium should be treated as follows:
 - (1) Thiazide diuretic should be added, if not already in use.
 - (2) Free water should be aggressively provided. As described in the [hypernatremia chapter](https://emcrit.org/ibcc/hypernatremia/#treatment:.free_water_replacement) (https://emcrit.org/ibcc/hypernatremia/#treatment:.free_water_replacement), this should be based on a calculation of the free water deficit.
 - (3) When administering free water, the dose of furosemide may need to be *increased* in order to achieve a net negative fluid balance.
- Using the above approach, it is generally possible to simultaneously fix the hypernatremia while maintaining a negative fluid balance.

metabolic alkalosis

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management of contraction alkalosis

- Contraction alkalosis is common with large-volume diuresis. This can be problematic, because the metabolic alkalosis will impair the effectiveness of loop diuretics ([9616263](https://www.ncbi.nlm.nih.gov/pubmed/9616263) (<https://www.ncbi.nlm.nih.gov/pubmed/9616263>)).
- Contrary to popular belief, metabolic alkalosis doesn't necessarily reflect anything about the patient's volume status. Specifically, it is possible for patients to develop contraction alkalosis well before they have reached a euvolemic state. Thus, development of contraction alkalosis shouldn't be misinterpreted to mean that the patient cannot tolerate further diuresis.
- Contraction alkalosis may be challenging to treat in patients who are continuing to undergo active diuresis. In such patient, a relatively aggressive strategy may be required to control this issue (and, in particular, to avoid a worsening alkalosis).
 - Attempting to continue diuresis *without* actively managing the alkalosis will predictably make the alkalosis worse.

management

- (1) Hypokalemia and hypomagnesemia may contribute to metabolic alkalosis, so these should be treated aggressively if present.
 - Of course, these should be repleted anyway – especially in patients undergoing active diuresis (where levels are likely to fall further).
- (2) Acetazolamide is the front-line agent for contraction alkalosis.
 - It takes a while for acetazolamide to work, so for patients undergoing large-volume diuresis it may be desirable to start some acetazolamide when the bicarbonate starts rising (rather than waiting until the patient has a severe metabolic alkalosis).
 - Acetazolamide may continue to work for ~24 hours after the last dose. Thus, when the bicarbonate has fallen to a near-normal level acetazolamide should be discontinued to prevent overshoot.
 - A reasonable acetazolamide dose may be 500-1,000 mg IV q12hr. The dose depends on the severity of the alkalosis and how briskly the patient is being diuresed (since ongoing diuresis will predictably make the alkalosis worse). In the [DABOLO study](http://jamanetwork.com/journals/jama/fullarticle/2484684) (<http://jamanetwork.com/journals/jama/fullarticle/2484684>), patients with alkalosis and ongoing diuresis were treated with acetazolamide 1000 mg IV q12hr (most patients won't require such a high dose, but the study demonstrates that high doses are safe).
- (3) Potassium-sparing diuretics will also tend to improve the metabolic alkalosis (spironolactone and amiloride).
- For more on treatment of metabolic alkalosis (including additional treatment modalities), see the chapter on [metabolic alkalosis](https://emcrit.org/ibcc/metabolic-alkalosis/) (<https://emcrit.org/ibcc/metabolic-alkalosis/>).

electrolyte repletion

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hypomagnesemia

- Both loop diuretics and thiazides cause magnesium wasting, so hypomagnesemia is extremely common in patients undergoing large-volume diuresis.
- Hypomagnesemia is problematic for a few reasons:
 - (a) Hypomagnesemia may contribute to hypokalemia (i.e. it may be impossible to achieve control of hypokalemia until the hypomagnesemia is treated)
 - (b) Hypomagnesemia may synergize with hypokalemia to cause Torsades de pointes. Thus, the presence of hypomagnesemia will make hypokalemia more dangerous.
- Management
 - Hypomagnesemia should be treated aggressively with IV magnesium sulfate.
 - It might be rational to target slightly higher magnesium levels than usual in a patient with ongoing aggressive diuresis, in anticipation of the possibility of hypokalemia and the likelihood of ongoing magnesium loss.
- More on hypomagnesemia [here](https://emcrit.org/ibcc/hypomagnesemia/) (<https://emcrit.org/ibcc/hypomagnesemia/>).

hypokalemia

- Potassium wasting is caused by loop diuretics, thiazides, and acetazolamide. Thus, patients on combination diuretic regimens can easily become severely hypokalemic.
- Management
 - (a) Potassium should be aggressively repleted. This should be done orally if possible, based on the estimated potassium deficit as well as anticipated potassium losses (due to ongoing diuresis). If renal function is intact, scheduling multiple doses of enteral potassium may be a useful strategy to maintain adequate potassium levels.

- (b) Check the magnesium level and replete aggressively (discussed above).
- (c) For ongoing, problematic hypokalemia a potassium-sparing diuretic could be considered (e.g. spironolactone or amiloride).
- More on hypokalemia [here \(https://emcrit.org/ibcc/hypokalemia/\)](https://emcrit.org/ibcc/hypokalemia/).

hypotension

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hypotension

- Hypotension may occur. This may or may not be related to diuresis, so it should be evaluated in the usual fashion (e.g. see the chapter on [approach to undifferentiated shock \(https://emcrit.org/ibcc/shock/\)](https://emcrit.org/ibcc/shock/)).
- For patients who are severely volume overloaded, it may be reasonable to pursue a “squeeze-and-diurese” strategy:
 - Low-dose vasopressor is used to maintain an adequate MAP.
 - Gradual diuresis is continued with close monitoring of hemodynamics.
- A squeeze-and-diurese strategy could be sensible in the following situations:
 - (a) A patient with cor pulmonale and severe intravascular volume overload, in whom volume overload is causing excessive dilation of the right ventricle with compression of the left ventricle. In this scenario, removal of volume may eventually *improve* the blood pressure.
 - (b) A patient with abdominal compartment syndrome, in whom excess intra-abdominal volume may be impairing hemodynamics (discussed further [here \(https://emcrit.org/pulmcrit/abdominal-hypertension/\)](https://emcrit.org/pulmcrit/abdominal-hypertension/)).
 - (c) Low-dose vasopressors are occasionally required to balance out the effect of vasodilating sedatives (e.g. propofol). Thus, the patient isn't severely hemodynamically unstable.
- If a squeeze-and-diurese strategy is taken, close attention should be paid to hemodynamics and vasopressor requirements:
 - Ongoing volume removal with a relatively stable and low vasopressor requirement suggests that the strategy is working.
 - Escalating vasopressor requirements suggests that the strategy is failing and may be promoting hypoperfusion.
 - There is no high-quality evidence supporting this practice, so be sure to monitor patients very carefully and make sure they are responding well to the treatment.

rising creatinine

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- Rising creatinine following initiation of diuresis is challenging. As with any creatinine rise in the ICU, this has a broad differential diagnosis, for example:
 - (1) Diuretic-induced hypovolemic shock causing renal hypoperfusion.
 - (2) Random daily fluctuations in creatinine.
 - (3) Acute kidney injury due to other medications or sepsis.
- If the creatinine elevation is substantial, then it should be evaluated similarly to that of any other patient with acute kidney injury (more on this [here \(https://emcrit.org/ibcc/acute-kidney-injury/\)](https://emcrit.org/ibcc/acute-kidney-injury/)).
- At a minimum, hemodynamic re-evaluation should occur (e.g. ultrasonography to image the heart and assess for systemic venous congestion).
- Whether or not diuretics should be held is ultimately a clinical decision, for example:
 - If the patient clearly remains congested, then continuing diuresis may be beneficial. Some patients with congestive nephropathy will have minor elevation in creatinine with diuresis, but this recovers with ongoing decongestion. Likewise, some studies of heart failure have correlated small elevations in creatinine with *better* outcomes (perhaps because these reflected patients who were being effectively diuresed)([20606118 \(https://www.ncbi.nlm.nih.gov/pubmed/20606118\)](https://www.ncbi.nlm.nih.gov/pubmed/20606118)).
 - If the patient isn't definitely congested, then holding diuretics may be sensible. This is particularly true if diuresis appears to cause hypotension.

schema

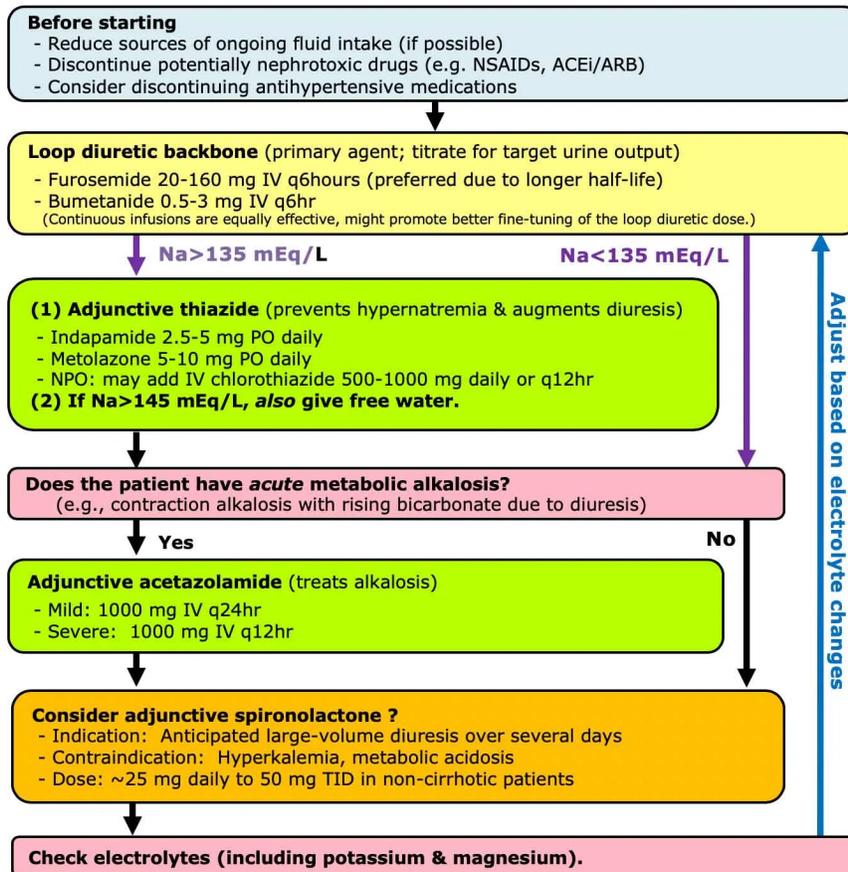
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thumbnail guide to diuretics in critical care

	Acetazolamide	Loop diuretics	Thiazides	Spironolactone	Amiloride
Physiologic effect					
pH effect	Lowers bicarb	Increases bicarb	Increases bicarb	Lowers bicarb	Lowers bicarb
Effect on serum Na (typical)		Increases Na	Lowers Na		
Effect on serum K	Lowers K	Lowers K	Lowers K	Increases K	Increases K
Effect on serum Mg		Decreases Mg	Acute: Increases Mg Chronic: Decrease Mg	Increases Mg	Increases Mg
Effect on serum Ca		Decreases Ca	Acute effects variable Chronic: increases calcium	Decreases Ca	Increases Ca
Pharmacology					
Commonly used agents in critical care	Acetazolamide	Furosemide (IV) Bumetanide (PO or IV) Torsemide (PO)	Oral-only agents Indapamide Metolazone (Hydrochlorothiazide) Intravenous thiazides Chlorothiazide	Spironolactone	Amiloride
Typical dose to facilitate diuresis in critically ill patients	500-1000 mg IV, q12-q24	Intermittent boluses (up to q6hr) Furosemide 20-240 mg IV Bumetanide 0.5-10 mg IV Continuous infusion Start with loading bolus, then... Furosemide: ~5-30 mg/hr Bumetanide: ~0.5-1 mg/hr Usual max daily dose Furosemide: ~ 600 mg Bumetanide: ~15 mg	Indapamide 5-10 mg PO QD Metolazone 5 mg PO daily to 10 mg PO BID Chlorothiazide 500-1000 mg IV q12 Hydrochlorothiazide : 25 mg daily to 100 mg PO BID.	Usual dose is 25 mg PO BID up to 100 mg BID (but can increase to 100 mg PO q6hr, especially in cirrhosis). Typical dose in cirrhosis is 2.5 times higher than furosemide dose (e.g. 40 mg furosemide plus 100 mg spironolactone).	Amiloride 2.5-10 mg PO BID
Equipotent doses of different agents		40 mg IV furosemide = 1 mg IV bumetanide = 20 mg PO torsemide (In renal failure, furosemide lasts longer, so 20 mg furosemide ~ 1 mg bumetanide)	2.5 mg indapamide = 5 mg metolazone = 500 mg chlorothiazide = 50 mg hydrochlorothiazide		
Half-life	Half-life ~10 hours. Duration of effect may last longer (~24 hrs)	Furosemide: 1.5-3 hours (prolonged in renal failure) Bumetanide: 1-1.5 hours Torsemide: 3-6 hours	Indapamide: 14-24 hours Metolazone: 8-14 hours Chlorothiazide: ~2 hours Hydrochlorothiazide: 6-15 hours	Active metabolites. Overall biological half-life is long (perhaps ~20 hours)	Normal GFR: 6-9 hr GFR <50 ml/min: 21-144 hr (accumulates in renal failure, use caution).
Oral bioavailability	~100% (may decrease with higher doses however)	Furosemide: 10-100% Bumetanide 80-100% Torsemide 80-100%	Indapamide ~93% Metolazone ~70% Chlorothiazide: ~70%	~90%	30-90%
Time to onset	15-60 minutes (IV)	5-10 minutes (IV)	IV chlorothiazide: 30 minutes PO ~1-2.5 hours	~48-72 hours	2 hours

-The Internet Book of Critical Care, by @PulmCrit

strategy for electrolyte-neutral, large-volume diuresis



Without proper attention, large-volume diuresis will often cause substantial electrolyte shifts (typically, hypernatremia, metabolic alkalosis, hypomagnesemia, and hypokalemia). These shifts are entirely manageable with careful monitoring and early/aggressive treatment.

-The Internet Book of Critical Care, by @PulmCrit

basic management for electrolyte problems encountered during ongoing diuresis

Hi	Low
<p>↑ Bicarbonate</p> <ul style="list-style-type: none"> Common during diuresis (contraction alkalosis). 1st line therapy = Add IV acetazolamide. Other treatments: aggressive repletion of hypokalemia & hypomagnesemia, K-sparing diuretics (amiloride, spironolactone). 	<p>↓ Bicarbonate</p> <ul style="list-style-type: none"> Uncommon during diuresis: look for other cause. Stop any acetazolamide.
<p>↑ Sodium</p> <ul style="list-style-type: none"> Treat with free water (either oral water or D5W intravenously). Add thiazide diuretic. May need to give additional doses of loop diuretic to prevent free water from causing the patient to gain weight. 	<p>↓ Sodium</p> <ul style="list-style-type: none"> D/c thiazide diuretics, amiloride, and spironolactone. Continue diuresis with furosemide (this may increase serum sodium). Remove sources of free water if possible. Ongoing administration of loop diuretics will generally increase Na. Could consider adding oral Urea if refractory to above treatments.
<p>↑ Potassium</p> <ul style="list-style-type: none"> D/c any potassium supplementation. D/c potassium-sparing diuretics (e.g. amiloride, spironolactone). Evaluate renal function (may be early sign of renal dysfunction). 	<p>↓ Potassium</p> <ul style="list-style-type: none"> Supplement with potassium (and check/replete Mg as well). Severe/ongoing: May add a potassium-sparing diuretic (e.g. amiloride, spironolactone).
<p>↑ Magnesium</p> <ul style="list-style-type: none"> Discontinue magnesium supplementation. Evaluate renal function (may be early sign of renal dysfunction). Generally safe unless profound hypermagnesemia, should resolve over time. 	<p>↓ Magnesium</p> <ul style="list-style-type: none"> Aggressive supplementation with IV magnesium sulfate.
<p>↑ Chloride</p> <ul style="list-style-type: none"> Either due to elevated sodium or low bicarbonate. Treat these problems as above. 	<p>↓ Chloride</p> <ul style="list-style-type: none"> Either due to reduced sodium or elevated bicarbonate. Treat these problems as above.
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Guide to basic strategies for electrolyte management during large-volume diuresis. For severe or persistent abnormalities, see the individual chapters regarding each abnormality. The most commonly encountered abnormalities are highlighted in yellow.

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podcast

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The Podcast Episode

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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/diurese/) (<https://emcrit.org/pulmcrit/diurese/>).



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

- Ignoring hypernatremia or metabolic alkalosis until these are severe. Both of these issues will very predictably get worse if they aren't managed actively, so they should be treated *early* in an expectant fashion.
- Interpreting a metabolic alkalosis or hypernatremia to mean that the patient has been diuresed adequately, and/or that the patient cannot tolerate further diuresis. This is incorrect: these are *iatrogenic complications* due to a poor diuretic strategy. Often patients will develop these complications despite persistent volume overload.

- Failure to replete magnesium.

The Internet Book of Critical Care is an online textbook written by Josh Farkas (@PulmCrit), an associate professor of Pulmonary and Critical Care Medicine at the University of Vermont.

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