The illustration above may appear a bit amusing, but this actually mirrors various practices that I've encountered during my training and career. Several years ago, the ICU at Genius General Hospital transitioned from using normal saline to using mostly Lactated Ringers (spoiler alert: it was neither difficult nor dramatic). More recently, the use of pH-guided resuscitation has become increasingly common.

Fluid choice probably doesn't make much difference for most patients. However, fluid therapy is an extremely common intervention. When leveraged over the high number of patients receiving fluid, even small differences in efficacy can be important (e.g. NNT of 30 or 50). Finally, for occasional patients with significant pre-existing hyperkalemia or metabolic acidosis, fluid choice may be extremely important.
crystalloids versus colloids

role of colloids (albumin)?

- The crystalloid vs. colloid debate will likely continue indefinitely, but it is dying down a bit. Despite theoretical support for albumin, there's no real evidentiary support. In practice, crystalloid is generally preferred because it is cheaper and more readily available.
- Currently, albumin seems to be indicated primarily for the purpose of supporting renal function among patients with cirrhosis, including:
  - Management of spontaneous bacterial peritonitis.
  - Management of hepatorenal syndrome.
  - Prophylaxis against hepatorenal syndrome after large volume paracentesis.

hetastarch is poison

- Hetastarch is a cheap, synthetic colloid.
- Numerous large high-quality RCTs have shown that it causes renal failure and may increase mortality in sepsis.
- Strangely, this continues to be sold by pharmaceutical companies and remains on formulary at many hospitals.
- There is no medicolegal or evidence-based justification for using hetastarch.

step I: balanced crystalloid

rationale for transitioning from normal saline to balanced crystalloids

- (1) There was never any physiologic rationale to use normal saline in the first place. Most reasons offered to support the use of saline aren't based on physiology or evidence (e.g. "it's cheap" or "it's what we're used to using").
- (2) Normal saline exacerbates acidosis. This may be problematic – especially in patients who are severely acidic to begin with (which isn't uncommon among critically ill patients).
- (4) In animal models, normal saline causes significant harm compared to balanced crystalloid (e.g. greater acidosis, impaired cardiac function, coagulopathy, impaired renal function, and mortality) (Kellum 2004 (https://www.ncbi.nlm.nih.gov/pubmed/14718447), Orbegozo 2016 (https://www.ncbi.nlm.nih.gov/m/pubmed/27655180/)). In humans, two RCTs have shown that saline may cause hemodynamic instability, compared to balanced crystalloids (Potura 2015 (https://www.ncbi.nlm.nih.gov/pubmed/25185593), Pfortmueller 2018 (https://www.ncbi.nlm.nih.gov/pubmed/29406176)).
• (5) Hyperchloremia caused by normal saline may cause renal vasoconstriction, increasing the risk of kidney injury. This has been shown in a variety of studies, most recently the SALT-ED RCT (https://www.ncbi.nlm.nih.gov/pubmed/29485926).

• Interestingly, the SALT-ED trial showed benefit from balanced crystalloids, despite most patients’ receiving relatively little fluid.

## comparison of normal saline versus balanced crystalloids – a survey of the evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Very brief description of finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kellum JA 2004 14711847*</td>
<td>Animal sepsis study: Pedrena hypochloremic metabolic acidosis causes hypotension.</td>
</tr>
<tr>
<td>O'Malley CH 20051584578</td>
<td>RCT during kidney transplant surgery: Normal saline cause greater degree of hyperkalemia than LR.</td>
</tr>
<tr>
<td>Kellum JA 2006 17035425</td>
<td>Rat sepsis model: Hypochloremic metabolic acidosis increases levels of pro-inflammatory cytokines.</td>
</tr>
<tr>
<td>Khogali MR 2008 18559939</td>
<td>RCT during kidney transplant surgery: Normal saline cause greater degree of hyperkalemia than LR.</td>
</tr>
<tr>
<td>Wu 2011 21044062</td>
<td>RCT in pancreatitis: Normal saline results in higher levels of inflammation compared to LR.</td>
</tr>
<tr>
<td>Mod MP 2012 22237327</td>
<td>RCT during kidney transplant surgery: Normal saline cause greater degree of hyperkalemia than LR.</td>
</tr>
<tr>
<td>Chowdhury AH 2012 22590984</td>
<td>RCT of human volunteers: Saline results in decreased renal perfusion compared to plasmalyte.</td>
</tr>
<tr>
<td>Yunnef NP 2012</td>
<td>Before-after study: Transition to balanced crystalloids in critically ill patients appeared to decrease kidney injury.</td>
</tr>
<tr>
<td>Zhao F 2014 24335448</td>
<td>Rat sepsis model: Saline results in greater kidney injury and some short-term survival versus LR.</td>
</tr>
<tr>
<td>Futura E 2015 25169599</td>
<td>RCT during renal transplant surgery: Saline resuscitation causes more resuscitation versus balanced crystalloids.</td>
</tr>
<tr>
<td>SPLIT 2015 26444962</td>
<td>RCT of critically ill patients: No differences found in rates of acute kidney injury or dialysis comparing NS vs. plasmalyte.</td>
</tr>
<tr>
<td>Orbegozo D 2016 27055189</td>
<td>Sheep sepsis model: Saline resuscitation reduces cardiac &amp; renal function, and hastens death (versus LR).</td>
</tr>
<tr>
<td>Steinberg L 2017 29123262</td>
<td>RCT during kidney transplant surgery: Normal saline cause greater degree of hyperkalemia than plasmalyte.</td>
</tr>
<tr>
<td>Plotnicker CA 2018 29403116</td>
<td>RCT during abdominal surgery: Study stopped early due to harm (saline was causing hypotension vs balanced crystalloids).</td>
</tr>
<tr>
<td>De-Medina E 2018 29435333</td>
<td>RCT in pancreatitis: Normal saline results in more patients displaying SIRS criteria compared to LR.</td>
</tr>
<tr>
<td>SALT-ED 2018 29405592</td>
<td>Cluster-randomized trial of patients in emergency department: Normal saline increases renal injury versus LR.</td>
</tr>
<tr>
<td>SMART 2018 29485926</td>
<td>Cluster-randomized trial of critically ill patients: NS increases the composite of death or kidney injury versus balanced fluid.</td>
</tr>
</tbody>
</table>

Very brief summary of evidentiary base supporting the use of balanced crystalloids. Due to the large number needed to treat (LNT), it’s difficult to definitively prove benefit from balanced crystalloid within a RCT. However, on the whole there is a substantial volume of basic science and clinical evidence indicating that normal saline (and in consequence, non-ionic-glycine metabolic acidosis) may be harmful. On the flip side, there is essentially no evidence that saline is superior to balanced crystalloid.

---


### arguments for using saline & why they lack merit

• "Normal saline is cheaper."
  • Lactated Ringers is only ~25 cents more expensive per liter, and the cost difference of Plasmalyte/Normosol isn’t much greater. These differences simply aren’t relevant in the context of a patient’s hospital bill which will range in the thousands of dollars. Additionally, use of a balanced fluid may avoid the need for IV bicarbonate and/or dialysis – which would save a considerable amount of money.

• "I will give two liters of saline and then switch to a balanced fluid."
  • First, nobody does that. Human beings aren’t that well organized. If physicians and nurses in your unit are used to giving saline and a patient crashes, they’re going to give saline. They’re not going to check first to see how much saline the patient received.
  • Second, the SALT-ED (https://www.ncbi.nlm.nih.gov/pubmed/29485926) trial suggested that clinical benefits from balanced crystalloid may occur even if only small volumes are used.

• "Lactated Ringers isn’t safe in hyperkalemia."
  • Lactated Ringers is fine in hyperkalemia. In fact, it is actually normal saline which is contraindicated in hyperkalemia (more on this [here](https://emcrit.org/pulmcrit/myth-busting-lactated-ringers-is-safe-in-hyperkalemia-and-is-superior-to-ns/)).

• "Lactated Ringers will elevate the lactate level."
  • A 30 cc/kg bolus of Lactated Ringers might possibly raise the lactate level by ~0.5 mM (30037514). Changes in lactate are minimal and will dissipate rapidly, because the liver is extremely adept at metabolizing lactate. If you’re making clinical decisions on the basis of tiny deviations in lactate level, then you’re using the lactate lab value wrong.

• "Lactated Ringers isn’t compatible with some drugs (e.g. ceftriaxone)."
  • This shouldn’t be a problem if the patient has adequate IV access. Furthermore, Plasmalyte doesn’t contain calcium, so it’s compatible with a wider variety of drugs.

• "Lactated Ringers isn’t compatible with blood."
  • This seems to be a myth. Lactated Ringers contains 1.5 mM of calcium. If this concentration of calcium caused blood to clot, then mild hypercalcemia would lead to lethal clotting problems (it doesn’t). Several studies have found that Lactated Ringers may be compatible with blood transfusion (9568658, 19340493, 1866680).

### ongoing studies on saline versus balanced crystalloids

[https://emcrit.org/ibcc/fluid/](https://emcrit.org/ibcc/fluid/)
Further studies are ongoing regarding the selection of saline versus balanced crystalloids. However, it’s dubious whether we really need any additional trials (Vincent 2016). 
- There is zero physiologic rationale for using saline in most patients.
- Nearly all available physiologic, animal, and clinical data suggests balanced crystalloids are superior.
- It’s well established that normal saline will cause acidosis and hyperchloremia (this is a fact).
- At this point, there are only two logically coherent strategies which exist, as shown below:

**Logically coherent approaches to saline vs. balanced crystalloid**

<table>
<thead>
<tr>
<th>Do you believe that pH, hyperchloremia, or acidosis matter?</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use balanced crystalloid</td>
<td>Use any fluid (e.g. normal saline)</td>
<td>Stop checking electrolytes</td>
</tr>
<tr>
<td>Stop checking any ABGs or VRGs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Saline causes acidosis and hyperchloremia. Thus, it’s logical to use normal saline and then worry about hyperchloremia or pH. 

- Sodium lactate
  - Historically, administration of lactate was feared (due to worsening of “lactic acidosis”). This isn’t possible, because sodium lactate isn’t an acid.
  - Lactate may function as a metabolic fuel for the heart, so if anything, lactate could be a good thing. Hypertonic sodium lactate infusion has been shown to improve cardiac function (Nalos 2014).
  - In vivo, lactate will be very rapidly metabolized into bicarbonate by the liver (unless the patient has fulminant hepatic failure).
- Sodium acetate
  - Rapidly metabolized into bicarbonate.

Vineet Lenin


Discussion of various anions

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- Lacks lactate's beneficial cardiac effects. Excessive acetate levels may cause vasodilation and hypotension, but this doesn't seem to be clinically relevant (acetate will be rapidly metabolized and only transiently present).
- Sodium gluconate
  - Although often believed to be metabolized into bicarbonate, this doesn't seem to be the case — so sodium gluconate does not function as an alkali (unlike sodium acetate and sodium lactate). This means that Plasmylate has the same exact pH effect as Lactated Ringers.
  - Sodium gluconate appears to be cleared unchanged from the kidneys. It could even function as an osmotic diuretic agent. **contraindications to Lactated Ringers**
  - These are not legitimate contraindications:
    - Hyperkalemia (more on this here [https://emcrit.org/pulmcrit/myth-busting-lactated-ringers-is-safe-in-hyperkalemia-and-is-superior-to-nsl/].)
    - Cirrhosis or liver injury (unless the patient has frank hepatic failure, it will be able to metabolize lactate).
  - Legitimate contraindications (all relative however):
    - Elevated intracranial pressure — Lactated Ringers could theoretically worsen this, because it is slightly hypotonic. Giving a liter of lactated ringer will have roughly the same effect as giving a liter of normal saline plus a dose of medication mixed in ~150 ml D5W. So this isn’t a huge issue, but it's not ideal either. For a patient with known elevation of intracranial pressure, plasmylate would be preferable.
    - Metformin-associated lactic acidosis — In this clinical scenario patients genuinely may have difficulty metabolizing the lactate. Note, however, that lactated ringer contains sodium lactate — so it will increase the lactate level without causing acidosis (more on this here [https://emcrit.org/ibcc/metformin/#volume_resuscitation]).
    - Severe hypercalcemia — Lactated Ringers has 1.5 mM of calcium, which won't worsen hypercalcemia (if anything it could decrease the calcium level, because this will be a lower calcium concentration than the patient's blood). However, this isn't the optimal fluid here (more on this here [https://emcrit.org/ibcc/hypercalcemia/#treatment]).
  - Overall, the contraindications to lactated ringers are generally uncommon and fairly mild. Outside of a neurological ICU, LR would be an excellent choice for ~95% of patients and a safe choice for nearly all patients.

<table>
<thead>
<tr>
<th>Contraindications</th>
<th>Lactated Ringers (LR)</th>
<th>Plasmalyte (note: identical to normosol)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effect on pH</strong></td>
<td>- Both fluids have equivalent effect on pH.</td>
<td>- Metformin-induced lactic acidosis** (&lt;br&gt;(No strong contraindications))</td>
</tr>
<tr>
<td><strong>Effect on sodium</strong></td>
<td>- Extremely weak effect, may tend to pull sodium gently towards ~130 mmol/L.</td>
<td>- Extremely weak effect, may tend to pull sodium gently towards ~140 mmol/L.</td>
</tr>
<tr>
<td><strong>Effect on potassium</strong></td>
<td>- Both fluids are safe in hyperkalemia (and preferred to NS).</td>
<td>- May tend to very gently pull potassium towards a normal level.</td>
</tr>
<tr>
<td><strong>Effect on magnesium</strong></td>
<td>- Lacks magnesium</td>
<td>- Slightly supraphysiologic Mg concentration, which may help avoid hypomagnesemia.</td>
</tr>
<tr>
<td><strong>Effect on calcium</strong></td>
<td>- Slightly supraphysiologic Ca concentration, which may help avoid hypocalcemia.</td>
<td>- Lacks calcium (arguably the crystalloid of choice for patients with hypercalcemia).</td>
</tr>
<tr>
<td><strong>Compatibility with various drugs</strong></td>
<td>- Calcium causes incompatibility with some medications.</td>
<td>- Doesn't contain calcium, which may improve compatibility with drugs (compared to LR).</td>
</tr>
<tr>
<td><strong>Anion quality</strong></td>
<td>- Sodium lactate is a physiologic anion which may improve cardiac function. Arguably the better choice for anion.</td>
<td>- Sodium acetate &amp; gluconate aren't terrific anions, but this may not be important (acetate is rapidly metabolized into bicarbonate).</td>
</tr>
<tr>
<td><strong>Cost &amp; availability</strong></td>
<td>- Cheaper (small difference)</td>
<td>- Slightly more expensive</td>
</tr>
<tr>
<td><strong>Evidence basis</strong></td>
<td>- No comparative trials showing benefit of one over the other.</td>
<td>- Availability more variable</td>
</tr>
</tbody>
</table>

Currently lactated ringers and plasmylate both seem like very good balanced crystalloids, without any clear evidence regarding which might be better. This table focuses on differences, but for the vast majority of patients these fluids are interchangeable.

*Metformin-induced lactic acidosis may interfere with the metabolism of both sodium lactate and sodium acetate. See that chapter for further discussion of fluid selection.

The Internet Book of Critical Care, by @PulmCrit
- Differences between various balanced crystalloids are minor and probably of minimal clinical significance.
- Lactated Ringers is generally an outstanding choice as it is inexpensive, widely available, and physiologically sound (the choice of lactate as an anion is arguably superior to gluconate/acetate).
- Plasmalyte is also an excellent choice, which may be superior in situations where Lactated Ringers is relatively contraindicated (listed above).

**step II: pH-guided resuscitation**

- The transition from normal saline to balanced crystalloids (Step I, above) is focused largely on the avoidance of harm from fluid (e.g. hyperchloremia). However, we can take this concept a step further to use crystalloids to improve the pH status of selected patients.
  - Fluid should be viewed as a drug.
  - Just as we wouldn't give the patient "any antibiotic" we shouldn't give "any fluid" – the fluid should be selected to maximize benefit.
- Fluid resuscitation is a limited opportunity to manipulate pH status.
  - Large volumes of fluid can be used to affect the patient's pH status.
  - After the patient is volume resuscitated, this opportunity will be lost (because large volumes of fluid can no longer be given without causing volume overload).

**pH abnormalities treatable with crystalloid**

- **(1) Non-anion-gap metabolic acidosis (NAGMA)**
  - This essentially represents a bicarbonate deficit (whether bicarbonate has been lost in the stool or urine).
  - Patients with normal kidneys will eventually re-generate bicarbonate, but this takes time. Furthermore, critically ill patients frequently have renal insufficiency or renal tubular acidosis, which prolong recovery from NAGMA.
  - Exogenous bicarbonate administration is a physiologically logically and reasonably well-accepted treatment for NAGMA.

- **(2) Uremic metabolic acidosis**
  - Most forms of anion-gap metabolic acidosis (e.g. lactic acidosis or ketoacidosis) don't respond favorably to IV bicarbonate. One exception to this rubric may be uremic metabolic acidosis.
  - Exogenous bicarbonate has long been used by nephrologists in efforts to improve pH and avoid dialysis. This practice was recently validated in the BICAR-ICU trial, wherein bicarbonate administration decreased the requirement for dialysis in uremic patients (more on this here).

- **(3) Acute metabolic alkalosis**
  - Most forms of metabolic alkalosis seen in the ICU are chronic (e.g. chronic compensatory metabolic alkalosis in response to chronic respiratory acidosis). Compensatory alkalosis should be left alone.
  - Very rarely, acute metabolic alkalosis may be seen. For example, this may be caused by ingestion of large quantities of alkali, large volume diuresis (contraction alkalosis), or gastric losses (vomiting, continuous NG suction).
Fluid selection & pH-guided fluid resuscitation - EMCrit Project

- Normal saline is a rational therapy for acute metabolic alkalosis, because it will reduce the serum bicarbonate level back towards normal.
- Note that the following abnormalities are not treatable with crystalloid:
  - Chronic metabolic alkalosis which is compensatory for a chronic respiratory acidosis.
  - Anion-gap metabolic acidoses other than uremia (e.g. lactic acidosis or ketoacidosis).

**pH-guided resuscitation**


- This is pretty simple – it largely amounts to thinking about the patient’s pH status and whether choice of IV fluid could improve it.
- When giving bicarbonate, the bicarbonate deficit may be a useful guide:
  - Bicarbonate deficit (in mEq) can be estimated [this calculator](https://www.mdcalc.com/bicarbonate-deficit) from MDCalc.
  - Each liter of isotonic bicarbonate contains 150 mEq of bicarbonate (more on this below).
  - Generally, avoid giving the patient more than roughly ~80% of their bicarbonate deficit, to prevent over-correction of the metabolic acidosis.
- During a bicarbonate shortage, sodium acetate can be used in its place.

**pH-guided resuscitation is most important in uremic metabolic acidosis**

- This is probably the most common situation where pH-guided resuscitation is beneficial.
- Isotonic bicarbonate may improve the pH and help avoid dialysis. Alternatively, if the patient is resuscitated to a euvolemic state without isotonic bicarbonate, it will become impossible to provide them with an adequate amount of bicarbonate (these patients are often oliguric, so further fluid could provoke pulmonary edema).
- These patients are often hyperkalemic – a process which will also be alleviated by isotonic bicarbonate (discussed further in the chapter on [hyperkalemia](https://emcrit.org/bcc/hyperkalemia/#Rx_severe_hyperkalemia_Temporizing_measures)).
- Overall, there is a subset of patients with acute kidney injury, uremic metabolic acidosis, and hyperkalemia who will respond very favorably to isotonic bicarbonate with resolution of their electrolytic problems. This may buy them some time for their kidneys to recover, potentially avoiding the need for dialysis.
Isotonic bicarbonate is generally prepared by combining a liter of D5W with three 50-mEq ampules of sodium bicarbonate. This creates a roughly isotonic solution (~150 mEq/L).

**what is isotonic bicarbonate?**

- Isotonic bicarbonate is generally formulated by adding 150 mEq of sodium bicarbonate to a liter of D5W (above).
- Although the bag of fluid will be hypertonic, glucose doesn't function as an effective osmole (since it readily enters cells). Therefore, in vivo this solution will behave as an isotonic fluid.
- D5W is used as the base solution because most hospitals don't have IV sterile water available. If your hospital does have IV sterile water, this would be preferable to D5W to produce a pure isotonic solution of bicarbonate.

<table>
<thead>
<tr>
<th>Isotonic Bicarbonate (150 mEq/L)</th>
<th>Hypertonic bicarbonate (1 mEq/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% NaHCO₃ by weight</td>
<td>~1.3% NaHCO₃</td>
</tr>
<tr>
<td>Tonicity</td>
<td>300 mOsm</td>
</tr>
<tr>
<td>General properties</td>
<td>2,000 mOsm</td>
</tr>
<tr>
<td></td>
<td>- Doesn't cause hypernatremia</td>
</tr>
<tr>
<td></td>
<td>- Large volume required to increase bicarb.</td>
</tr>
<tr>
<td></td>
<td>- Will decrease potassium concentration.</td>
</tr>
<tr>
<td>Use</td>
<td>- Metabolic acidosis in patient with acidosis</td>
</tr>
<tr>
<td></td>
<td>- Emergency treatment of hypernatremia</td>
</tr>
<tr>
<td></td>
<td>- Emergency treatment of cerebral edema</td>
</tr>
<tr>
<td>Cautions</td>
<td>- Excess may cause volume overload and hypokalemia</td>
</tr>
<tr>
<td></td>
<td>- Excess will cause hypernatremia</td>
</tr>
<tr>
<td></td>
<td>- Administer slowly to avoid significant pCO₂ rise</td>
</tr>
</tbody>
</table>


- The most commonly used forms of bicarbonate are hypertonic bicarbonate (undiluted ampules) and isotonic bicarbonate, as compared above.
- The amount of hypertonic bicarbonate which can be given is limited by the sodium concentration. Each 50-ml ampule of bicarbonate will increase the sodium concentration by roughly ~1-1.5 mEq/L. Caution needs to be exercised with repeated ampules, as eventually this may cause hypernatremia.
- The amount of isotonic bicarbonate which can be given is generally limited by volume overload. Each 150 mEq of bicarbonate comes along with a liter of volume.

**dissolved CO₂ & how rapidly can isotonic bicarbonate be given?**
Intravenous bicarbonate contains both bicarbonate and dissolved CO₂. For example, the concentration of pCO₂ in an ampule of bicarbonate may be ~100 mm.

Following administration:
- Dissolved CO₂ will transiently increase the patient's pCO₂. Over time, this will be breathed off and the patient will return to their prior pCO₂ level. This will happen even if the patient is on mechanical ventilation (administered pCO₂ increases the gradient driving CO₂ out of the body – which increases CO₂ clearance and eventually returns the patient to their baseline pCO₂). The only situation where CO₂ doesn't return to baseline is if the patient has died (e.g. cardiac arrest, with minimal effective circulation).
- Bicarbonate will persist longer, after the pCO₂ has been exhaled. This explains the alkalinizing effect of IV bicarbonate.
- Fun fact: the pH of an ampule of bicarbonate is only 8. It's not that alkaline in the bottle (which contains both pCO₂ and bicarbonate).
- The reason it causes alkalinization in vivo is because pCO₂ is breathed off while bicarbonate remains.

Ampules of sodium bicarbonate generally shouldn't be pushed over a few seconds. This may cause rapid pH shifts, including elevated pCO₂. Thus, ampules of hypertonic bicarbonate should generally be pushed slowly over ~5-10 minutes if possible.

Isotonic bicarbonate can be infused at rates similar to other crystalloids (e.g. 75-1,000 ml/hr). Given the lower concentration of CO₂ in isotonic bicarbonate, rapidly loading the patient with CO₂ isn't an issue here.

**effect on potassium concentration**

Three factors are in play here:
- (1) Hypertonicity causes potassium to shift out of cells (a process known as solute drag).
- (2) Bicarbonate increases the pH, which shifts potassium into cells.
- (3) Volume load of isotonic bicarbonate may directly dilute out potassium, thereby decreasing the potassium concentration.

Hypertonic bicarbonate
- Factors #1 & #2 cancel each other out.
- Several RCTs have shown that hypertonic bicarbonate does not affect potassium level.

Isotonic bicarbonate
- Factors #2 & #3 both serve to reduce the potassium level.
- Available data shows that isotonic bicarbonate decreases the potassium level among patients with metabolic acidosis (Blumberg 1992, Fraley 1977, Gutierrez 1991).
- Clinical significance depends on what you're trying to achieve:
  - Hyperkalemia: If you're trying to reduce the potassium level, you need to use isotonic bicarbonate.
  - Hypokalemia: If you're trying to increase the pH without dropping the potassium, then hypertonic bicarbonate could have an advantage here. Alternatively you could use isotonic bicarbonate with simultaneous potassium supplementation.

**hypocalcemia**

Increases in pH will tend to decrease the ionized calcium level (essentially removal of protons stuck to albumin renders albumin more negatively charged, leading to an increase in calcium-albumin binding).

Increasing the pH to a normal range shouldn't cause hypocalcemia, but it may exacerbate pre-existing hypocalcemia.

**common errors with bicarbonate**

In general, it's desirable to standardize this fluid in order to avoid medication errors:
- (a) Don't mix up a solution with two ampules of bicarbonate. If you want to give the patient some additional D5W, it's preferable to run two simultaneous infusions (one with D5W and another with true isotonic bicarbonate).
- (b) Don't mix up 3 ampules of bicarbonate in a liter of normal saline!

Don't be afraid to run isotonic bicarbonate at the rate you need. For example, in a severely hypovolemic patient who needs fluid and bicarbonate, you may wish to run the isotonic bicarbonate at 250-1,000 ml/hr (to provide both volume and bicarbonate).

Don't slam in an ampule of hypertonic bicarbonate (unless there is a really good reason, such as profound tricyclic intoxication).

Don't use hypertonic bicarbonate to treat hyperkalemia (proven not to work).

Don't bolus hypertonic bicarbonate for a patient in cardiac arrest (unless you suspect a toxicologic etiology).

Don't use bicarbonate to treat lactic acidosis or ketoacidosis (this doesn't work and gives bicarbonate a bad reputation).

**therapeutic alkalization to augment permissive hypercapnia**

https://emcrit.org/fbcc/fluid/
## Basic Concept

- Occasionally, intubated patients who are encountered who are extremely difficult to ventilate (typically due to status asthmaticus or severe ARDS).
- The safest approach to these patients may be to administer exogenous bicarbonate, with a goal of increasing the bicarbonate level to ~30-35 mEq/L.
  - Note that the normal level of bicarbonate in blood is 22-28 mEq/L. Thus, a serum bicarbonate level of 30-35 mEq/L isn’t terribly high.
  - This will generally amount to shifting patients from a state of mild metabolic acidosis (most patients start off with a bicarbonate of ~20 mEq/L) to mild metabolic alkalosis. Higher serum bicarbonate makes it easier to safely ventilate patients (targeting a pH >7.15-7.20).
- Bicarbonate administration may be safer than increasing the respiratory rate or tidal volume (maneuvers which will increase mechanical force delivered to the lungs and may also increase the risk of pneumothorax).
  - Note that the development of a pneumothorax in a patient with profound ARDS or asthma may be a catastrophic event.
- Left to their own devices, patients with ARDS or status asthmaticus will often eventually compensate for their respiratory acidosis by mounting a compensatory metabolic alkalosis. Exogenous bicarbonate administration aims to achieve the same thing, merely accelerating this normal adaptation process.
- There is no high-quality evidence on this topic. The use of exogenous bicarbonate to balance out severe respiratory acidosis is a longstanding practice in critical care (e.g. utilized in the classic ARMA trial on ARDS). Unfortunately there is no clear data to guide the speed and magnitude of alkalization which may be optimal.

### How to Achieve Therapeutic Alkalization

- Depending on the patient’s weight and baseline bicarbonate, this will generally involve administration of ~150-300 mEq sodium bicarbonate to target a serum bicarbonate level of ~30-35 mEq/L. This should generally be achieved gradually over a period of several hours.
- **Hypertonic bicarbonate**: Some or all of this exogenous bicarbonate may be administered in the form of hypertonic sodium bicarbonate (8.4%, described above). Hypertonic bicarbonate has the advantage of limiting added volume, but it will eventually cause hypernatremia.
- **Isotonic bicarbonate**: This may be useful in patients with hypovolemia or hypernatremia. In a patient with euvolemia and high-normal sodium, isotonic bicarbonate could be combined with diuretics (e.g. furosemide and thiazide diuretics) to achieve alkalinization without causing volume overload.
  - A thiazide diuretic may be useful here to promote sodium excretion and avoid hypernatremia (more on this [here](https://emcrit.org/pulmcrit/occult-diuretic-resistance/)). Furosemide alone tends to cause excretion of dilute urine – so the combination of furosemide plus isotonic bicarbonate may still tend to increase the patient’s sodium level.
- The optimal rate of alkalization is unknown, and likely varies depending on the individual patient scenario. In most cases, gradual alkalization (e.g. 25-100 mEq bicarbonate per hour) is sufficient.
- Bicarbonate administration will cause a transient increase in pCO2 during its administration, which will cause a transient reduction in pH. However, once completed, pCO2 will decrease to baseline and the added bicarbonate will increase the pH.
  - If bicarbonate is administered more slowly, then transient pCO2 elevations are smaller. Of course, it will take longer to get to target pH.
  - This issue of dissolved CO2 is discussed further in the above section in IV bicarbonate.

![Serum bicarbonate level required to achieve pH > 7.2](image-url)
Don't use normal saline as your default resuscitative fluid. There are many reasons for this, but one salient one is as follows: eventually you will wind up giving liters of saline to a hyperkalemic and acidic patient, thereby pushing them off a pH cliff.

Don't be afraid to use Lactated Ringers in patients with hyperkalemia or liver dysfunction. Don't be afraid to use Plasmalyte in any patient (there don't seem to be any legitimate contraindications to Plasmalyte).

Don't miss opportunities to fix your patient's pH abnormalities using pH-guided resuscitation (especially for patients with uremic metabolic acidosis).

Not understanding how to use various forms of bicarbonate.

Talk on pH-guided resuscitation at the Hospitalist & Resuscitationist Conference 2018 (by far the best part of this video is the baby babbling in the background who – I think – really likes the presentation).
Going further:

- LR is safe in hyperkalemia (https://emcrit.org/pulmcrit/myth-busting-lactated-ringers-is-safe-in-hyperkalemia-and-is-superior-to-ns/)
- Is hyperchloremic acidosis bad? (https://emcrit.org/pulmcrit/is-correcting-hyperchloremic-acidosis-beneficial/)
- SMART trial & nine reasons to stop using saline for resuscitation (https://emcrit.org/pulmcrit/smart/)