IV Fluid Safety

The FAQ below answers common questions about safely using IV fluids.

Clinical Question	Answer/Pertinent Information
What is meant by "isotonic" and "isosmotic?"	• Osmo***LAR***ity is the number of osmotically active particles **per L** of solution.[1] • Osmo***LAL***ity is the number of osmotically active particles **per kg** of solution.[1] • Osmo***LAL***ity is the same or slightly less than osmo***LAR***ity.[1] Generally, "osmolality" is used when talking about body fluids, and "osmolarity" when talking about IV fluids. • The normal osmolality of body fluids is 280 to 295 mOsm/kg.[16] • Isosmotic/isotonic fluids have an osmolarity that approximates the osmolality of human extracellular fluid (e.g., blood).[4,15,26] • "Hyperosmotic/hypertonic" or "hypoosmotic/hypotonic" solutions have osmolarities that are higher or lower, respectively, than the osmolality of blood (e.g., ≥375 mOsm/L or <250 mOsm/L, respectively).[7,26] • Osmolarity is often used as a synonym for "tonicity," but this is not always correct.[26] This is because tonicity depends on osmolarity and whether the solutes in the solution (e.g., glucose, sodium) will enter the cells.[26] ○ D5W is an example of an isosmotic solution that behaves like a hypotonic solution once administered.[26] • A cell will neither swell nor shrink in an isotonic solution, will swell in a hypotonic solution, and will shrink in a hypertonic solution.[26]
What is the approximate osmolarity of some common IV fluids? *Continued…*	The osmolarity of IV solutions is usually printed on the bag. The bag might also state that the solution is isotonic, hypertonic, or hypotonic/hemolytic. Here are some examples of approximate osmolarities of common IV fluids: **Isosmotic/Isotonic**: • 0.9% saline (NS): 308 mOsm/L[1] • LR: 275 mOsm/L[1] (The osmo***lal***ity of LR is 252 to 255 mOsm/kg due to incomplete dissociation of some ions, and so it is **slightly hypotonic**.[1,4]) • D5W: 278 mOsm/L[1] (acts as a **hypotonic** solution once administered because glucose enters cells and is unavailable to keep the water in the vascular space)[26] • Dextrose 5% in 0.225% saline (D5 1/4 NS): 329 mOsm/L • 5% albumin: 290 mOsm/L[1]

<table>
<tr><th>Clinical Question</th><th colspan="3">Answer/Pertinent Information</th></tr>
<tr><td>Approximate osmolarity of some common IV fluids, continued</td><td colspan="3">Hypoosmotic/Hypotonic:
• 0.45% saline: (half-normal saline; 1/2 NS): 154 mOsm/L[1]

Very Hypoosmotic/Hypotonic
• Sterile water: 0 mOsm/L[23]
• 0.225% saline (quarter normal saline; 1/4 NS): 77 mOsm/L[23]
• Sodium bicarbonate drip using 1 “amp” (50 mEq added to 1 L sterile water): 100 mOsm/L[31]

Hyperosmotic/Hypertonic:
• 3% saline: 1026 mOsm/L[1]
• Dextrose 5% in 0.9% saline (D5NS): 561 mOsm/L[1]
• Dextrose 5% in Lactated Ringer’s (D5LR): 525 mOsm/L[1]
• Dextrose 5% in 0.45% saline (D5 1/2 NS): 405 mOsm/L[1]</td></tr>
<tr><td>What is considered an isotonic fluid, and when is it used?</td><td colspan="3">• Examples of isotonic solutions include NS, LR, and D5W.[1,4,7]
o LR is often considered isotonic, but it is actually slightly hypotonic.[28]
o Although D5W is isotonic in the bag, once administered, the dextrose is metabolized, providing free water that mostly distributes out of the vascular space.[7,12] Therefore, unlike NS or LR, D5W is not useful for fluid resuscitation.[1,12]
• Isotonic, sodium-containing solutions are safer maintenance IV fluids than hypotonic solutions in regard to hyponatremia risk, especially in pediatrics.[2,5,15,25] However, use of isotonic solutions in children poses a risk of hypernatremia that is similar to the risk of hyponatremia conferred by hypotonic solutions.[24]</td></tr>
<tr><td>How do the isotonic solutions (e.g., normal saline, Lactated Ringer’s) compare?
Continued…</td><td>Fluid/
cost per liter[a]</td><td>Balanced Fluids (not all-inclusive)
(LR [~$4], Isolyte S pH 7.4 [$5.87], Normosol-R pH 7.4 [$5.25], Plasma-Lyte 148 [$10.78])</td><td>Normal saline
(0.9% Sodium Chloride)</td></tr>
</table>

Clinical Question	**Answer/Pertinent Information**		

How do the isotonic solutions (e.g., normal saline, Lactated Ringer's) compare?
 	
Continued…
	Composition[b]	**Balanced Fluids**
		Electrolytes (for products listed above):
		• calcium (only in **LR**): ~2.7 mEq/L
		• chloride: 98 to 110 mEq/L
		• magnesium (not in LR): ~3 mEq/L
		• sodium:
		  ○ LR: ~130 mEq/L
		  ○ others ~140 to 141 mEq/L
		• phosphate: ~0 to 1 mEq/L
		• potassium: ~4 to 5 mEq/L
		Buffers (may contain one or more of the following):
		• acetate (not LR): ~27 mEq/L
		• gluconate (not LR): ~23 mEq/L
		• lactate (LR): ~29 mEq/L
			Normal saline
			Electrolytes
			• chloride: ~154 mEq/L
			• sodium: ~154 mEq/L

	Preferred Indications or Potential Benefits	**Balanced Fluids** • Hyperchloremic metabolic acidosis.[29] • Preferred by some as an initial resuscitation fluid in critically ill, burn, trauma, or surgical patients, or diabetic ketoacidosis.[4,28] • May **prevent one major adverse kidney event** in critically ill patients (NNT = 91) compared to NS [Evidence Level B-1].[29] Other studies show no difference in renal outcomes or mortality, perhaps due to differences in patient populations.[36,37] • May improve survival, reduce kidney injury, and reduce the length of time vasopressors are required in **pediatric patients with severe sepsis** compared to resuscitation with non-balanced fluids [Evidence Level B-3].[19]	**Normal saline** • Hypovolemic, hypochloremic metabolic alkalosis.[4,34] • Replacement of chloride from GI losses (e.g., diarrhea, excessive colostomy output, high output ileal stoma or fistula, jejunal stoma or fistula, pancreatic or biliary drainage).[8,34]

Clinical Question	Answer/Pertinent Information		
Comparison of isotonic solutions (e.g., normal saline, Lactated Ringer's), continued	**When to Avoid Use, or Possible Complications**	**Balanced Fluids** • LR provides 114 mL of free water/L; therefore, excessive amounts can cause hypotonicity.[4] Volumes more than 3 L can provide enough free water to increase intracranial pressure.[1] o May be associated with increased mortality when used prior to hospital admissions for traumatic brain injury compared to NS [Evidence Level B-1].[18] • Avoid LR (even if infusing through different lines) **in neonates ≤28 days old receiving ceftriaxone** due to potential for calcium precipitation.[31] ◦ Ceftriaxone and LR can be used together in patients older than 28 days as long as they are infused separately, and lines are properly flushed between infusions.[31]	**Normal saline** • May cause hyperchloremic metabolic acidosis.[20]
	Use in Patients with Kidney or Liver Impairment	**Balanced Fluids** • In **severe liver impairment** metabolism of buffers may be impaired. Alkalinizing effect of lactate may be impaired. Accumulation of gluconate or acetate may worsen alkalosis.[b]	**Normal Saline** • Consider limiting use of large volumes of NS in patients with **impaired renal function**, especially with concomitant heart failure, due to risk of sodium retention.[b]
	Impact on Potassium Levels	**Balanced Fluids** • The small amount of potassium in balanced fluids was not associated with a higher incidence of severe hyperkalemia in critically ill patients [Evidence level B-1].[11] • In acidosis, buffers in these solutions may help prevent the extracellular potassium shift and resultant hyperkalemia.[11]	**Normal Saline** • Does not contain any potassium, but can cause hyperchloremic metabolic acidosis, which increases potassium by causing extracellular potassium shift.[11]

Clinical Question	Answer/Pertinent Information

What are the concerns with hypotonic solutions, or D5W?	• Hypotonic saline or isotonic D5W may result in hyponatremia due to insufficient provision of sodium.[2,13]
	  o Risk of hyponatremia is highest within the first 24 hours.[25]
	• Hypotonic and sodium-free solutions provide free water.[1,2] This reduces plasma osmolality and reduces serum sodium.[1,2] If serum sodium falls quickly (e.g., the body cannot compensate, and the resultant osmotic gradient causes water to enter the brain, causing cerebral edema).[1,2] This can result in brainstem herniation with compression of the midbrain, and death.[2]
	  o Patients at particular risk include post-op patients, ICU patients, children, and patients with conditions or medications that promote antidiuretic hormone secretion or otherwise reduce serum sodium (e.g., diuretics; opioids; proton pump inhibitors; heparin; inhalational anesthetics; desmopressin; pain; nausea; stress; dehydration; pneumonia; central nervous system infections; or adrenal, renal, or hepatic insufficiency).[2]
	  o Children are at particular risk because their ability to maintain water balance is not robust, and they are more likely to develop syndrome of inappropriate antidiuretic hormone secretion (SIADH) post-op. Children develop cerebral edema at higher sodium levels than adults and have little extra room in their cranium to accommodate brain swelling.[2]
	• Because they are hypotonic, sterile water and 1/4 NS can cause hemolysis, kidney failure, and death.[23]

What can be done to reduce harm associated with hypotonic solutions?	• Some hospitals have policies prohibiting or restricting use of solutions with osmolarity <154 mOsm/L.
	• STERILE WATER WITHOUT ADDITIVES IS NOT FOR DIRECT INFUSION.[3]
	  • It is recommended that institutions:
	  o remove the "IV route" from computer order entry system as an option for sterile water, so prescribers cannot order it.[3]
	  o in the pharmacy, do not allow sterile water to leave the sterile compounding area.[3]
	  o stock sterile water only in 2 L bags, bottles, or vials to help distinguish it from 1 L bags of fluids for direct IV administration.[3,10]
	  o label sterile water for use as respiratory humidification with "For Respiratory Equipment-Not for Use" on the bag and on the end of the tubing closest to the patient.[22]
	• Prohibit compounding of <0.45% saline (less than half-normal saline; <1/2 NS).[23]
	• Prohibit use of 1/4 NS, and instead use Dextrose 5% in 0.225% saline (D5 1/4 NS).
	  o Ease concerns about dextrose in the solution; the risk of hyperglycemia is low and manageable, and less than the risks of administering a hypotonic solution.[23] Each 100 mL provides only 17 kcals of glucose.
	• Standardize orders for sodium bicarbonate drips so that very hypotonic solutions (e.g., sodium bicarbonate 50 mEq/L sterile water) are avoided.
	• Reserve IV treatment of hypernatremia for patients who cannot take fluids orally or enterally, or for those who are hemodynamically unstable.[23]

Clinical Question	Answer/Pertinent Information
When might a sodium-free (D5W) or lower-sodium solution be appropriate?	• For dilution of drugs, when compatible (**D5W**), to prevent hypernatremia in critical care patients [Evidence Level B-3].[30] • To keep peripheral venous catheters patent (i.e., KVO rate) (**D5W**) to prevent hypernatremia in critical care patients.[27] • For treatment of hypovolemic hypernatremia (**D5W**), **after** initial fluid resuscitation.[4,23] • For treatment of diabetic ketoacidosis (**1/2 NS**), **after** initial fluid resuscitation.[9] • For treatment of isovolemic hypernatremia (**D5W**).[33] • Maintenance IV fluid in most stable adults (**D5 1/2 NS**).[32] • Maintenance or replacement in stable patient with slight hypernatremia **(D5 1/4 NS)**.[32] • Replacement of certain GI losses (e.g., vomiting, nasogastric tube output, diarrhea) or insensible losses (**1/2 NS**).[8,34]
What are some concepts regarding safe use of hypertonic solutions?	• Examples of hypertonic solutions include 3% saline, and dextrose concentrations >5% (e.g., D10W, D50W).[7] • Hypertonic solutions can cause phlebitis.[17] The cut-off for peripheral vs central administration is generally considered 900 mOsm/L.[17] Some hospitals allow peripheral administration of 3% sodium chloride short-term.[6] If a peripheral line must be used for administration, experts recommend using the largest peripheral vein available (avoiding a flexion site if feasible) and monitoring the site for redness, swelling, pain, and tenderness.[14] Canadian labeling suggests changing the site every 24 hours.[21] • Keep in mind that like D5W, D10W is a sodium-free source of free water, and although hypertonic, is not useful for fluid resuscitation because most of the water distributes out of the vascular space.[12] • To minimize errors with hypertonic saline, it has been suggested that hospitals stick with commercially available concentrations (as opposed to compounding) and standardize dosing for specific uses. Special storage, use of warning stickers, and pharmacist oversight are also suggested.[17] • The safety of hypertonic (3%) saline for fluid resuscitation is unclear.[4]

What steps can be taken to ensure that patients don't receive unnecessary IV fluids?	• Determine if fluids can be given orally or enterally.[8]
	• The purpose of maintenance IV fluids/electrolytes is to replacement of insensible losses, maintenance of normal volume status, and ensure kidney function.[38] Needs in adults are generally 25 to 30 mL/kg/day, but should be individulaized.[8,38]
	• Follow daily weights and fluid balance to guide discontinuation or adjustment of fluids.[38]
	• Look for all sources of fluids and subtract these in the daily requirement, including:[35]
	  o enteral or parenteral nutrition
	  o continuous infusions (e.g., pressors, sedatives)
	  o piggybacks(e.g., larger volumes or given frequently)
	• If the patient is getting excess fluids, consider:[35]
	  o switching IV meds to the oral or subcutaneous route (e.g., heparin to apixaban or enoxaparin).
	  o concentrating continuous infusions.
	  o switching from IV infusions to IV push (e.g., antibiotics).

Abbreviations: D5W = dextrose 5% in water; GI = gastrointestinal; IV = intravenous; LR = Lactated Ringer's; NS = normal saline.

a. Wholesale acquisition cost (WAC). Medication pricing by Elsevier, accessed July 2022.
b. Information from US product labeling unless otherwise indicated: Lactated Ringer's (Baxter, October 2019); *Isolyte S pH 7.4* (October 2019); *Normosol-R pH 7.4* (April 2018); *Plasma-Lyte 148* (August 2019); sodium chloride 0.9% injection (Baxter, March 2018).

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56.
https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

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