APPENDIX 12
Composition of 1000 mL (1 litre) of Crystalloid Intravenous Fluids

Plasma Normal Range	COMMON NAME	Normal Saline[1]	Hartmann's[2]	Plasma-Lyte[3]	D5W[4]	D10W	0.9% Saline with 5% Glucose	0.45% Saline with 5% Glucose	0.18% Saline with 4% Glucose	3% Saline
	CHEMICAL NAME	0.9% Sodium Chloride	Compound Sodium Lactate	PL 148	5% Dextrose	10% Dextrose				
135-145	**Na**	154	129	140	0	0	154	77	31	513
3.5-5.3	**K**	0	5	5	0	0	0	0	0	0
95-105	**Cl**	154	109	98	0	0	0	77	31	513
2.2-2.6	**Ca**	0	2	0	0	0	0	0	0	0
0.8-1.2	**Mg**	0	0	1.5	0	0	0	0	0	0
24-32	**Bic**	0	29 (as lactate)	27 (acetate) 23 (gluconate)	0	0	0	0	0	0
3.5-5.5	**Gluc**	0	0	0	50 g	100g	50 g	50 g	40 g	0
7.35-7.45	**pH**	4.5-7.0	5.0-7.0	7.4	3.2-6.5	3.2-6.5	3.5-6.5	3.5-6.5	4.5	5.0
	Theoretical Osmolality	308	255	295	278	505	560	406	284	1027
275-295	**In-vivo Osmolality**	286	278	271	290/0					
	Tonicity vs Plasma	Isotonic	Isotonic	Isotonic	Iso/ hypotonic[4]	Iso/ hypotonic[4]	Hypertonic	Hypertonic	Isotonic	Hypertonic
	Energy (kJ)	0	38	67	711	1422	711	711	569	0
	Cost (NZ$) (April 2023)	$1.26	$1.80	$2.27	$1.68	$6.11 (500 mL)	$14.50	$13.60	$13.61	$7.60

All values expressed in millimoles per litre (mmol/L) unless otherwise stated, except pH (no units) & osmolality (Osm/kg H_2O).
For monovalent ions (Na^+, K^+, Cl^-, $HCO3^-$), 1 milliequivalent (mEq) is equal to 1 mmol. For divalent ions (Ca^{2+}, Mg^{2+}), 1 mEq is equal to 0.5 mmol.

Notes:

1) 'Normal' or 'physiological' saline is approximately isotonic to plasma because:

- The molecular weight of sodium chloride (NaCl) is 58.4 gm per mole
- 0.9% saline means 0.9 gm NaCl in 100 mL = 9 gm in 1000 mL
- The milliequivalent of NaCl in 1000 mL is therefore 9 gm/58.4 = 0.154 mole per 1000 mL
- NaCl dissociates into two separate ions: Na^+ & Cl^-, meaning 1 **molar** NaCl is 2 **osmolar**
- 0.9% saline contains 154 mEq/L Na^+ & 154 mEq/L Cl^-, giving a total calculated osmolarity of 154+154 = 308 mOsm/L
- Plasma osmolarity is between 275-295 mOsmol/Kg, making 'normal' saline hypertonic with respect to plasma
- When correcting for non-ideal solutions using the osmotic coefficient (which for NaCl is 0.93), measured tonicity is reduced to 286 which is equivalent to plasma. This is used to justify the epithet 'normal'

The terms 'osmo**larity**' & 'osmo**lality**' are often used interchangeably. **Osmolarity** is an indirect calculation from laboratory data of measured electrolytes in solutions (using the Dorwart and Chalmers formula), and has the units **mOsm/L**. **Osmolality** refers to direct measurements from an osmometer in a clinical laboratory and has the units **mOsm/kg.** In humans they are mostly equivalent as 1 L plasma weighs approximately 1 kg.

Tonicity refers to the effect of a solution on a cell's volume if the cell was placed in that solution and allowed to equilibrate. Tonicity is a behaviour, not a measure, and depends on the osmolarity of the solution and, more importantly, whether solutes in the solution can enter the cell. An isotonic solution is one that, when administered intravenously, means that water neither enters nor leaves cells. A hypotonic solution will cause water to enter cells; a hypertonic solution will cause water to leave. Iso-osmotic does not mean isotonic; both D5W & normal saline are iso-osmotic at administration but glucose enters cells causing water to follow by osmosis. The cell increases in volume so D5W is hypotonic. This glucose is then metabolised by aerobic respiration (producing carbon dioxide & water).

- Iso-osmotic solutions are **not always** isotonic
- Hyperosmotic solutions are **not always** hypertonic
- Hypo-osmotic solutions are **always** hypotonic

2) The lactate in Hartmann's solution is metabolised by two pathways that produce a relative excess of bicarbonate ions, contributing to alkalosis. These pathways are:
- **Oxidation** (30% of metabolism): mostly hepatic, some renal, cardiac/skeletal muscle. Lactate is oxidised to H_2O & CO_2, using H^+ & generating HCO_3^-
- **Gluconeogenesis** (70% of metabolism): lactate is converted to pyruvate then oxaloacetate then glucose. This process is mostly hepatic with some renal contribution

Production of bicarbonate from lactate has a half-life of around 10-15 minutes, taking around 1 hour to be completed; as such a steady amount of alkali is generated after administration of Hartmann's solution. If there is no acidosis to correct, the bicarbonate is renally excreted (assuming adequate renal function). Although Hartmann's contains lactate, it does not increase total body acid content as no extra hydrogen ions are added (it is a conjugate base). Rapid infusion causes a transient increase in serum lactate levels without a drop in pH. Hartmann's will only cause acidosis in the total absence of any liver function, a condition which, by itself, is non-survivable.

Despite both Hartmann's & Plasma-Lyte containing 5 mEq/L of K^+ and 0.9% sodium chloride containing none, Hartmann's and Plasma-Lyte are likely to **lower** serum potassium concentration whilst 0.9% sodium chloride will **raise** it. The rapid administration of chloride ions in high concentrations in saline causes hyperchloraemia with a resulting non-anion gap metabolic acidosis. This acidosis both relocates intracellular K^+ into the extracellular space (in exchange for H^-) and decreases both K^+ secretion and increased reabsorption in the kidney. Conversely, the bicarbonate generated from the metabolism of lactate (Hartmann's) and acetate/gluconate (Plasmalyte) will cause K^+ to shift into cells, decreasing hyperkalaemia.

3) Unlike Hartmann's, Plasma-Lyte contains no calcium and is therefore compatible with stored blood products. The gluconate content may cause patients tested for the galactomannan antigen (as a biomarker for pulmonary aspergillosis) to record a false positive result. This may last up to 24 hours after receiving Plasma-Lyte. Modern assays have reduced this likelihood. Although isotonic with respect to serum, Plasma-Lyte is hypotonic with respect to 0.9% sodium chloride. As such, it should be avoided in patients with traumatic brain injury or at risk of cerebral oedema.

4) The terms 'dextrose' & 'glucose' are often used interchangeably and confusingly with regard to intravenous fluids. Both are monosaccharides with the chemical formula $C_6H_{12}O_6$. Glucose contains both dextro (D-glucose) & levo (L-glucose) rotatory enantiomers (mirror images that rotate polarised light to both the right (D) & left (L)). Dextrose only contains the dextro-rotatory

(D) isomer of glucose. It is named from '*dextr*' (for its light rotation property), with an '-ose' suffix meaning 'sugar'. It is the only form used in IV fluids and is made from the hydrolysis of starch. Dextrose solutions are **hyper**tonic at administration; subsequent metabolism of sugar content leaves free water, making them **hypo**tonic. Dextrose is added to sodium chloride solutions that contain less than 0.9% (9 gm per 1000 mL) to increase the tonicity and prevent red cell lysis on administration although, as described above, the effect of giving D5W is the same as giving pure water as the dextrose is metabolised. Administering intravenous carbohydrate (in the form of dextrose) may help reduce liver glycogen depletion and have a protein-sparing action. Any dextrose administered intravenously is oxidated to water and carbon dioxide in all body tissues (but especially the liver).

When metabolised, dextrose provides around 3.4 kCal/gm. A 5% solution contains 5 grams in 100 mL, meaning 1000 mL contains 50 grams. The calorific content of 1000 mL of 5% dextrose solution is therefore 50 x 3.4 = 170 kCal (= 0.17 kCal/ml). As 1 kCal = 4.184 kJ, 1000 mL of 5% dextrose provides 711 kJ of energy

References:

Plasma-Lyte 148: A clinical review. World J Crit Care Med. 2016 Nov 4; 5(4):235-250

Intravenous fluid therapy in adults in hospital, NICE clinical guideline 174 (December 2013. Last update December 2016)

Isosmotic is not always isotonic. Adv Physiol Educ. 2016 Dec

Is Hartmann's the solution? Anaesthesia. 1997 May;52(5)

The role of bicarbonate precursors in balanced fluids during haemorrhagic shock with and without compromised liver function. BJA. 2016 117(4):521-8

Response to 1L of Hartmann's compound sodium lactate. Deranged Physiology.

A comparative study of impact of infusion of Ringer's Lactate solution versus normal saline on acid-base balance and serum electrolytes during live related renal transplantation. Saudi J Kidney Dis Transpl. 2012 Jan;23(1):135-7