
بسم الله الرحمن الرحیم

Which type of IV Fluid is better?

(Crystalloids, balanced, colloids)

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Outline

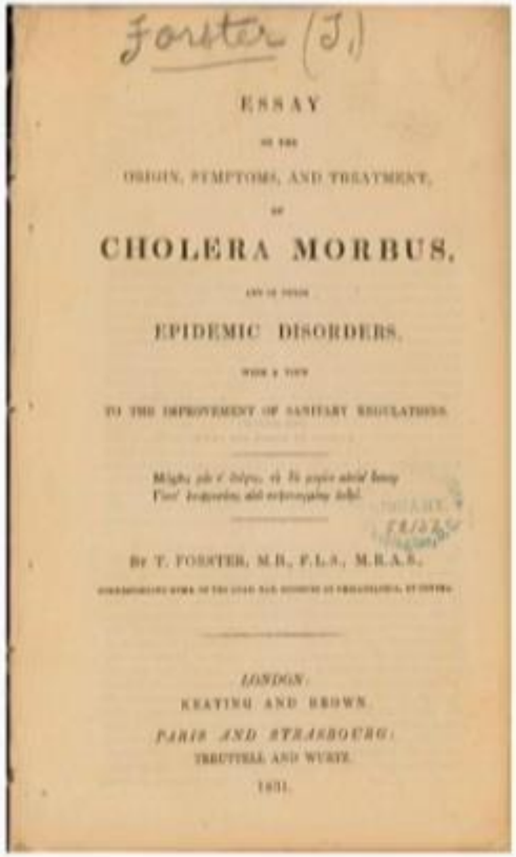
- **1. Principles of fluid therapy**

- **2. Crystalloids or Colloids : which is better?**

- **3. Whitin Crystalloids, are balanced solutions better than normal saline?**

History of intravenous fluids

1831-32 British Cholera Epidemic



Forster (J.)

ESSAY

ORIGIN, SYMPTOMS, AND TREATMENT,

CHOLERA MORBUS,

EPIDEMIC DISORDERS.

TO THE IMPROVEMENT OF SANITARY REGULATIONS

BY T. FORSTER, M.B., F.L.S., M.R.A.S.

LONDON:
KEATING AND BROWN.
PARIS AND STRASBOURG:
TREUTTEL AND WURTZ.
1831.

MacGillivray J Inf Prev 2009;10(1):4–6.

principles of fluid therapy

- **Fluids are drugs:**

- Fluids can correct hypovolemia .
- Fluids increase blood pressure .
- Fluids alter plasma osmolality .
- Fluids alter plasma electrolytes.
- Fluids have adverse effects .

Principles of fluid therapy

- 1. Does the patient need fluid?
- **2. Which fluid is better?**
- 3. How much fluids does the patient need?
- 4. What about volume status?
- 5. What about cardiac,kidney,liver function?
- 6. What is your estimation about ADH?
- 7.How do you evaluate fluid responsiveness?
- 8. How long should you continue fluid therapy?
- 9. Is your patient fluid overload?

TYPES OF I.V. FLUIDS

1. **Crystalloids vs. Colloids**

CRYSTALLOIDS	COLLOIDS
Normal (0.9%) saline	Human Albumin
Ringer's lactate solution (Hartmann's' solution)	Gelatin solutions (Haemaccel®,Gelafundin ®)
5% Dextrose	Dextran
	Hydroxyethyl starches (Hetastarch®)

Where the IV fluid goes

Crystalloids	Colloids
NS, RL	Albumin, HES
75 % Extravascular 25 % Intravascular/ Plasma Volume	Almost 100 % Intravascular/ Plasma Volume

Table 1. **Comparative summary of crystalloid and colloid solutions**

Crystalloid solution	Colloid sollution
Half-life of 30-60 minutes	Half-life of several hours or days
Three times the volume needed for replacement	Replaces fluid volume for volume
Excessive use can cause peripheral and pulmonary oedema	Excessive use can precipitate cardiac failure
Molecules small enough to freely cross capillary walls, so less fluid remains in the intravascular spaces	Molecules too large to cross capillary walls, so fluid remains in intravascular spaces for longer
Inexpensive	More expensive than crystalloids
Non-allergenic	Risk of anaphylactic reactions
Suitable for vegetarian or vegan patients	Some preparations unsuitable for vegetarian or vegan patients

Source: Adapted from Pryke (2004)

Table 4.8 Approximate distribution of 1 L of IV fluids in body compartments

Fluid	Intracellular (mL)	Interstitial (mL)	Intravascu (mL)
D5W	664	252	84
Normal saline (0.9%)	0	752	248
Ringer's lactate	0	752	248
Albumin (5%)	0	100	900
Albumin (25%)	0	−3,000[a]	4,000
Hetastarch (6%)	0	0	1,000
Dextran-40	0	−1,000[a]	2,000
Packed RBC	0	0	250

[a]Fluid movement from interstitial to intravascular (plasma) compartment

Normal saline is not Normal !

Solute	Plasma	Crystalloids			
		Normal Saline	Ringer's Lactate	Hartmann's Solution	Plasma-Lyte
Na^+	135 - 145	154	130	131	140
K^+	4.0 - 5.0	0	4.5	5	5
Ca^{2+}	2.2 - 2.6	0	2.7	4	0
Mg^{2+}	1.0 - 2.0	0	0	0	1.5
Cl^-	95 - 110	154	109	111	98
Acetate	0	0	0	0	27
Lactate	0.8 - 1.8	0	28	29	0
Gluconate	0	0	0	0	23
Bicarbonate	23 - 26	0	0	0	0
Osmolarity	291	308	280	279	294
Colloid	35 - 45	0	0	0	0
Osmolarity (mOsm/L); Colloid (g/L); All other solutes (mmol/L)					

	Tonicity	Osm mosm/L	Na meq/L	Cl meq/L	K meq/L	Buffer
Plasma	✅	290	140	103	4	Bicarbonate (HCO3)
Plasma-Lyte	✅	294	140	98	5	Gluconate, acetate
0.45% Saline (1/2 NS)	↓	154	77	77	0	
0.9% Saline (NS = normal saline)	✅	308	154	154	0	
2% Saline	↑	684	342	342	0	NephSim
3% Saline	↑	1027	513	513	0	www.nephsim.com
5% Dextrose (D5W)	↓	253	0	0	0	
Ringer's Lactate	✅	273	130	109	4	Lactate
D5W + 150 meq NaHCO3	✅	480	150	0	0	HCO3
1/2 NS + 75 meq NaHCO3	✅	304	152	77	0	HCO3

✅ = isotonic

Tonicity ≠ Osmolarity

Tonicity = [effective osmoles]; **Osmolarity (Osm)** = [effective osmoles] + [ineffective osmoles]

Dextrose is an ineffective osmole!

What's in a fluid?

	Tonicity	Osmolality mOsm/L	Na meq/L	Cl meq/L	K meq/L	Buffer
0.45% Saline (1/2 NS)	↓	154	77	77	0	
5% Dextrose (D5W)	↓	253	0	0	0	
Ringer's Lactate	✓	273	130	109	4	Lactate
Plasma	✓	290	140	103	4	HCO3
Plasma-lyte	✓	294	140	98	5	Gluconate, acetate
0.9% Saline (NS)	✓	308	154	154	0	
D5W + 150 meq NaHCO3	✓	480	150	0	0	HCO3
3% Saline	↑	1027	513	513	0	

↓ = hyPOtonic
✓ = ISOtonic
↑ = hyPERtonic

Adapted from www.nephsim.com

Theoretical Distribution of IV Fluids

		1L D5W	1L of 1/2 NS	1L NS or LR	1u pRBC	25g albumin (colloid)
ICF		667	333	0	0	0
ECF	INTERSTITIUM	250	500	750	0	0 (colloids draw water from the interstitium into the plasma)
	PLASMA	83	167	250	300	450 (short half-life)

*All values reported in "mL"

Characteristics of some crystalloids

	NaCl 0.9%	Lactated Ringer's	Hartmann's	Rehydrating III	Plasma Lyte	Sterofundin ISO	Dextrose 5%
Na^+	154	130	131	140	140	145	0
K^+	0	4	5	10	5	4	0
Ca^{2+}	0	3	4	5	0	5	0
Mg^{2+}	0	0	0	3	3	2	0
Cl^-	154	109	111	103	98	127	0
In-vivo SID	0	28	29	55	50	29	0

Normal saline indications

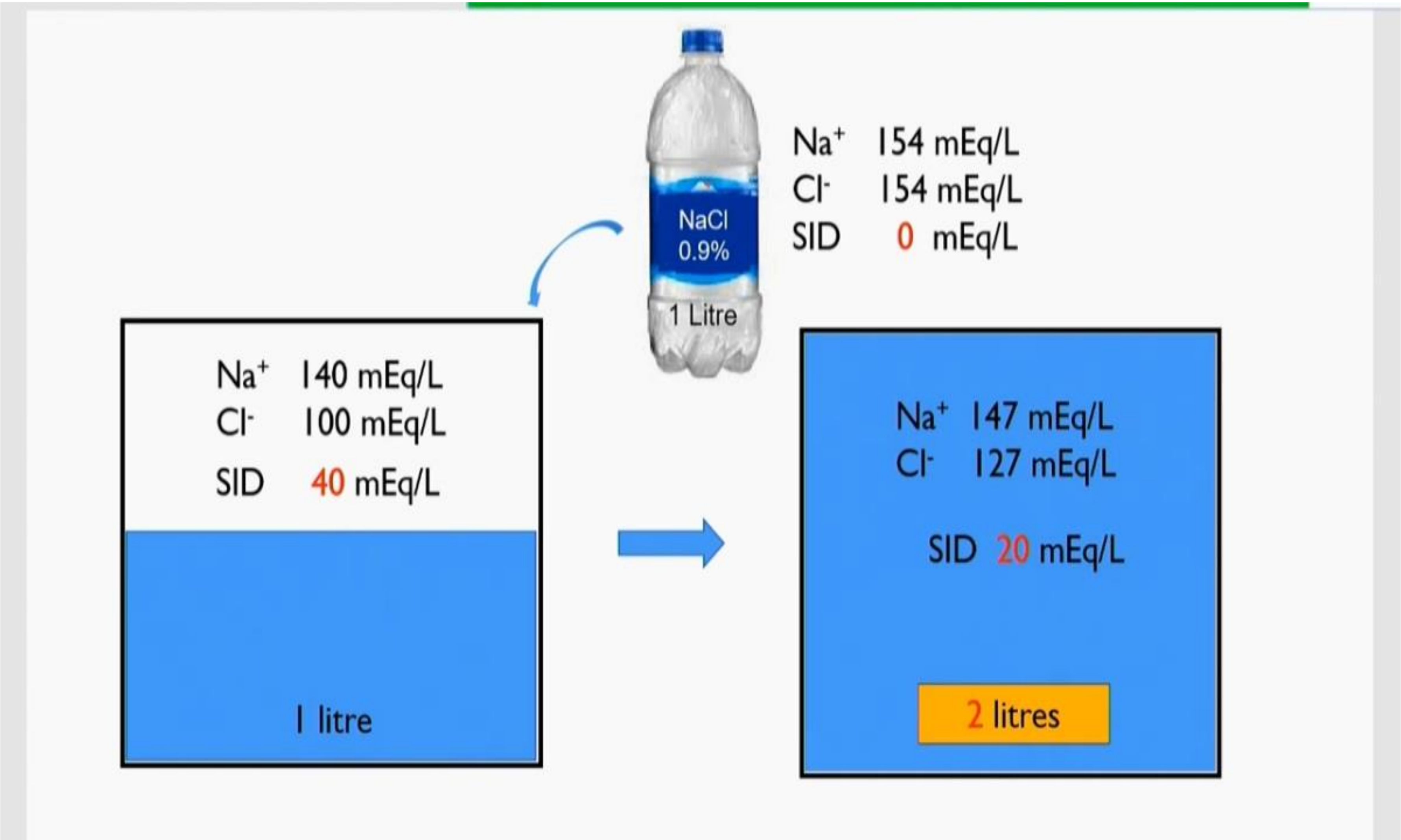
- **1. Hypovolemia shock, hypovolemic hyponatremia,...**
- **2. Sepsis**
- **3. Hypercalcemia**
- **4.Metabolic alkalosis (saline responsive)**
- **5.HRS**
- **6. Maintenance fluid in neurosurgery and brain edema**
- **7. Packed RBC cell infusion**
- **8. Fluid for drugs infusion**
- **9. Contrast nephropathy prophylaxis**

.10. Rhabdomyolysis,DKA

Normal saline side effects

Metabolic	• Hyperchloremic acidosis • ↑Need for buffers to correct acidosis
Body water	• Possible damage to the endothelial glycocalyx • ↑Interstitial fluid volume leading to edema
Renal	• Renal edema and capsular stretch leading to intrarenal tissue hypertension • Renal vasoconstriction, ↓renal blood flow and renal tissue perfusion • ↓Glomerular filtration rate, urine volume, and sodium excretion
Gastrointestinal	• Gastrointestinal edema, intestinal stretch • Ileus, impaired anastomotic healing
Hematological	• ↑Intraoperative blood loss • ↑Need for blood product transfusion
Clinical outcomes	• ↑Postoperative complications • ↑Mortality • ↑Incidence of acute kidney injury and need for renal replacement therapy

Normal saline and Hyperchloremic metabolic acidosis



Stewart Approach

During crystalloid infusion we affect 2 variables!

(at constant PCO_2)

SID

If SIDinf < SIDplas	→ ↓ pH
If SIDinf > SIDplas	→ ↑ pH
If SIDinf = SIDplas	→ ~ pH

A_{TOT}

↓ A_{TOT} → ↑ pH

Balance between these effects?

Lactate ringer

- **Can you use LR in patients with liver failure? Probably not.** Lactate is converted to pyruvate in the liver, generating a bicarbonate ion. In liver failure, it is presumed this is inhibited and LR is generally contraindicated in cirrhosis and liver failure.[33]
- **Can LR cause lactic acidosis? No.** The lactate in LR is sodium lactate, not lactic acid, so it cannot cause lactic acidosis. It can, however, increase the serum lactate, so some caution should be used when using lactate to judge the adequacy of resuscitation.[34]
- **Is LR contraindicated in hyperkalemia? No.** LR has 4 mmol/L of potassium, so diluting plasma with a normal potassium should not raise the serum potassium. Additionally, because NS causes a nonanion gap metabolic acidosis, this may cause movement of potassium from inside to outside of the cell. In studies of LR versus NS following kidney transplant, there was less hyperkalemia with LR.[35,36]
- **Can you run LR with a blood transfusion? No.** Blood transfusions use citrate anticoagulation to prevent clotting. The calcium in LR is the antidote to citrate and could inadvertently cause the blood to clot.

Table 4.4 Indications for dextrose in water (D5W)

1. To replace deficits of total body water in treatment of hypernatremia
2. To provide energy and prevent starvation ketosis
3. To treat hypoglycemia
4. To mix with amino acid solution in total parenteral nutrition
5. *Do not* give D5W to a patient with syndrome of inappropriate antidiuretic hormone because serum [Na^+] may become dangerously low
6. *Do not* give D5W alone to expand the ECF volume in a hypovolemic patient or to a patient with hypokalemia

Table 4.7 Indications for albumin

1. To expand plasma volume when crystalloids have failed to correct acutely diminished intravascular volume
2. To treat severe edematous patients with nephrotic syndrome resistant to potent diuretic therapy
3. To prevent hemodynamic instability and acute kidney injury following large volume (>5 L) paracentesis
4. To prevent renal impairment and mortality in patients with spontaneous bacterial peritonitis
5. To treat cirrhotic patients with hypoalbuminemia and hypovolemia
6. To treat hepatorenal syndrome with other agents (midodrine, octreotide)
7. To replace plasma volume during plasmapheresis
8. *Do not* use to treat hypoalbuminemia due to malnutrition unless the patient has protein-losing enteropathy
9. *Do not* use routinely in critically ill patients with hypovolemia, burns, or hypoalbuminemia because albumin administration does not *reduce* mortality

Colloid fluid: Hydroxyethyl starch (voluven)

EMA	FDA
Contraindications before 2013	**Contraindications before 2013**
Renal failure (with oliguria or anuria)	Renal failure (with oliguria or anuria)
Patients on dialysis	Hypersensitivity
Hypersensitivity	Congestive heart failure
Congestive heart failure	Treatment of lactic acidosis
Hyperhydration states (including pulmonary edema)	Patients on dialysis
Intracranial bleeding	Clinical conditions with volume overload
Severely impaired hepatic function	
Hyperkalemia	
Severe hypernatremia or hyperchloremia	
Clinical conditions with volume overload	
Additional contraindications in 2013	**Additional contraindications in 2013**
Critically ill patients	Critically ill adult patients
Sepsis	Sepsis
Burn injuries	Renal dysfunction
Renal impairment	Severe liver disease
Renal replacement therapy	Pre-existing coagulation/bleeding disorders
Severe coagulopathy and bleeding	Patients undergoing open heart surgery in association with cardiopulmonary bypass
Organ transplant patients	
Additional contraindications in 2018	**No update**
Fluid maintenance therapy	
Dehydrated patients	
Cerebral hemorrhage	

Crystalloids or colloids: which is better?

2004

SAFE TRIAL

A comparison of albumin and saline for fluid resuscitation in the intensive care unit

multicenter, double-blind, randomized controlled trial

Objective: To compare the effect of fluid resuscitation with albumin as compared with saline on mortality in a heterogeneous population of patients in the ICU

6997 patients

Inclusion criteria: Patients ≥18 years who had been admitted to ICU and required fluid administration to maintain or increase intravascular volume

Albumin group (n=3497) VS **Saline group (n=3500)**

PRIMARY OUTCOME

Albumin	Outcome	Saline
20.9	Death from any cause at 28-days % RR 0.99; 95% CI, 0.91 to 1.09; P=0.87	21.1

SECONDARY OUTCOMES

Albumin	Outcome	Saline
6.5	Length of stay in ICU (in days) Diff 0.24; 95% CI, -0.06 to 0.54; P=0.44	6.2
4.5	Duration of mechanical ventilation (in days) Diff 0.19; 95% CI, -0.08 to 0.47; P=0.74	4.3
0.48	Duration of renal-replacement therapy (in days) Diff 0.09; 95% CI, -0.0 to 0.19; P=0.41	0.39

Conclusion: In patients in the ICU, use of either 4 percent albumin or normal saline for fluid resuscitation results in similar outcomes at 28 days.

The SAFE Study Investigators NEJM 2004; 350:2247-2256 | Summary by Dr.Shreyash Bhoyar, MBBS Visualmed

ARTICLES | VOLUME 4, ISSUE 10, P818-825, OCTOBER 01, 2016

Hydroxyethyl starch versus saline for resuscitation of patients in intensive care: long-term outcomes and cost-effectiveness analysis of a cohort from CHEST

Colman Taylor, PhD • Kelly Thompson, MPH • Prof Simon Finfer, MD • Alisa Higgins, MPH • Prof Stephen Jan, PhD • Qiang Li, MBiostat • et al. Show all authors

Published: June 17, 2016 •

DOI: https://doi.org/10.1016/S2213-2600(16)30120-5 •

Interpretation

Although longer term clinical outcomes did not differ between patients resuscitated with hydroxyethyl starch or saline in the ICU, from a health-care payer's perspective, the probability that hydroxyethyl starch is cost effective in these patients is low.

Randomized Controlled Trial

Effects of fluid resuscitation with colloids vs crystalloids on mortality in critically ill patients presenting with hypovolemic shock: the CRISTAL randomized trial

Djillali Annane et al. JAMA. 2013.

Conclusions and relevance: Among ICU patients with hypovolemia, the use of colloids vs crystalloids did not result in a significant difference in 28-day mortality. Although 90-day mortality was lower among patients receiving colloids, this finding should be considered exploratory and requires further study before reaching conclusions about efficacy.

Balanced solutions or normal saline: which is better?

Major trials on balanced solution versus 0.9% saline on kidney outcomes

Infographic by Priti Meena, MD, FASN @Priti899

	SALT-ED 2018	SMART 2018	BaSICS 2021	PLUS 2022
	n = 13,347	n = 15,802	n = 11,052	n = 5037
Site	Single-center site	Single-center site	Multi-center site	Multi-center site
Comparative arms	Plasma-Lyte A and RL vs 0.9% saline	Plasma-Lyte A and RL vs 0.9% saline	Plasma-Lyte 148 vs 0.9% saline	Plasma-Lyte 148 vs 0.9% saline
Major outcomes	Median hospital-free days to day 28; MAKE within 30 days	MAKE within 30 days; in-hospital mortality	90-Day survival; incidence of AKI and need for KRT	90-Day survival; receipt of new KRT
Setting	Emergency	ICU	ICU	ICU
Design of trial	RCT non- blind	RCT non- blind	RCT double-blind	RCT double-blind
Result	No difference in hospital-free days; lower MAKE-30 in balanced solutions group	Lower composite outcome of death and MAKE-30 with balanced solutions group	No difference in survival at 90 days; no difference in incidence of AKI or need for KRT	No difference in survival at 90 days; no difference in incidence of AKI or need for KRT
Bottom line	Balanced solutions safer for kidneys than 0.9% saline in emergency department setting	Balanced solutions safer for kidneys; decreased the composite outcome of death compared with 0.9% saline	Use of balanced salt solutions did not reduce mortality or kidney outcomes when compared with 0.9% saline in critically ill.	Use of balanced salt solutions did not reduce mortality or kidney outcomes when compared with 0.9% saline in critically ill.

RL, Ringer's lactate.

Important considerations in fluids therapy

Important considerations

Normal saline (0.9% NaCl) →
- Hyperchloremic metabolic acidosis
- Renal vasoconstriction and decline in eGFR
- Impaired coagulation
- Upregulation of pro-inflammatory pathways

Ringer's Lactate →
- Avoid in patients with chronic liver disease
- Hyperglycemia
- Intravascular crystallization when used along with blood products
- Allergic reactions

Hartmann's solution →
- Intravascular crystallization when used along with blood products
- Lactic acidosis

Plasmalyte →
- Metabolic alkalosis
- False positive galactomannan antigen test result

Special scenarios

5% dextrose → preferred in
- Hypoglycemia
- Hypernatremia
- Hyperkalemia

Hypertonic saline (3% NaCl) → preferred in
- Hyponatremia
- Cerebral edema

Conclusion:

- 1. Fluids are drugs.
- 2. Answer these questions before start fluid therapy: which fluid? How much? How about
- fluid responsiveness ?
- 3. Normal saline is not Normal and has Supra physiological chloride and PH =5.5 .
- 4. Large (more than 30 cc / kg) and rapid infusion of Normal saline may induce Hyperchloremic metabolic acidosis and hyperkalemia and AKI.

.5. Crystalloids or colloids: which is a better solution?

- Answer is Crystalloids.

Conclusion :

6. The results of studies about normal saline vs balanced Crystalloids are controversial.

In non critically ill patients especially With Cl> 110 meq/l or cr> 1.5 mg/dl Balanced fluids were safer for kidney(SALT_ED trial 2018) .

In critically ill patients balanced fluids group had lower mortality and MAKE_ 30 outcomes and more safety for kidney (SMART trial 2018).

In two recent RCT (BASICS 2021 and PLUS 2022) there were no differences between balanced fluids and normal salin in 90 days mortality rate and incidence of AKI and need to KRT in critically ill patients.