

Crystalloid solutions

Thassayu Yuyen M.D. FRCAT

Department of Anesthesiology
Faculty of Medicine, Siriraj Hospital
Mahidol University

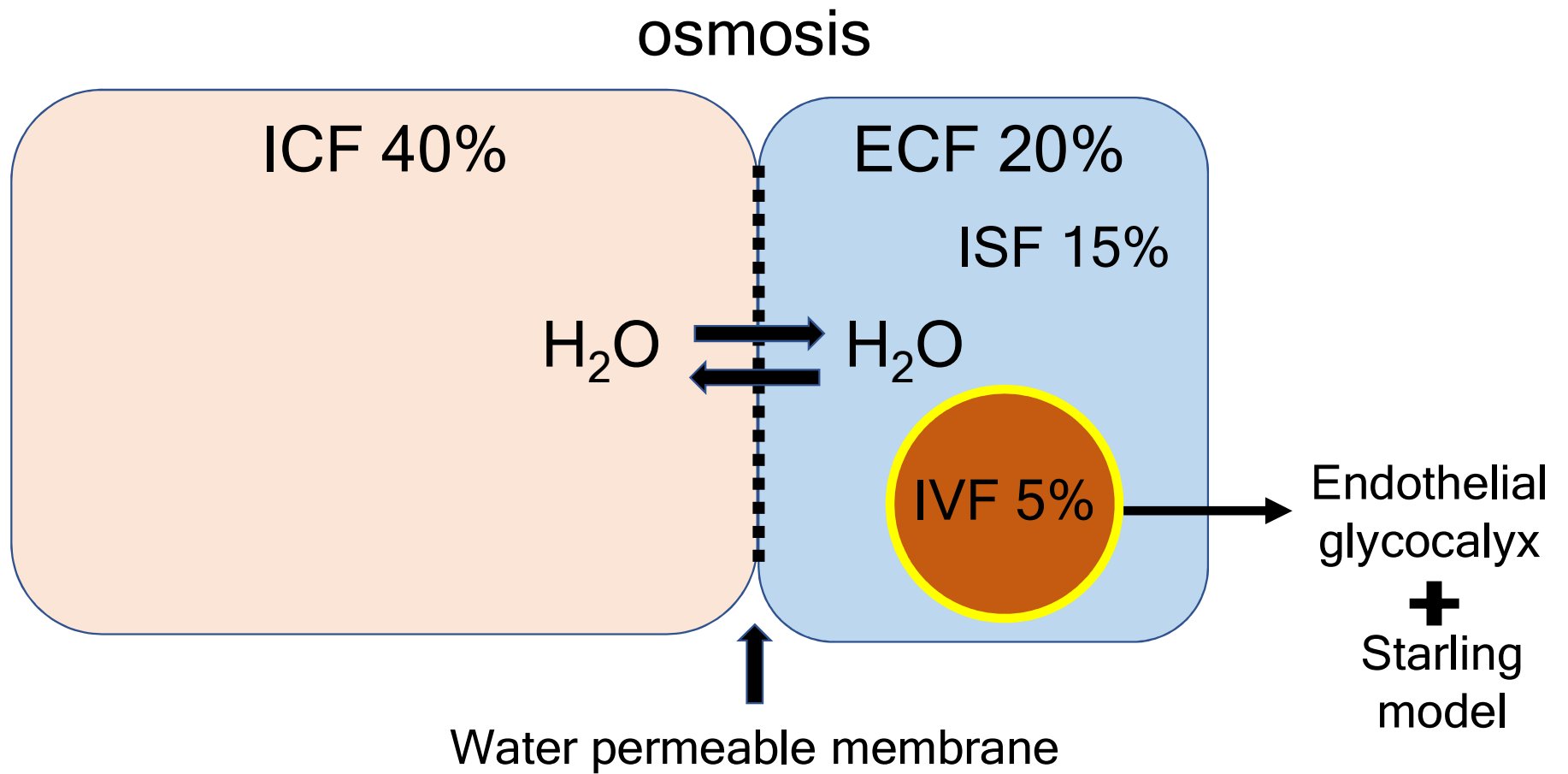
Outline

- Basic science related to fluid therapy
- Principle of fluid therapy
- Crystalloid vs Colloid
- NSS vs BSS

Outline

- Basic science related to fluid therapy
- Principle of fluid therapy
- Crystalloid vs Colloid
- NSS vs BSS

Total body water = 60% of BW

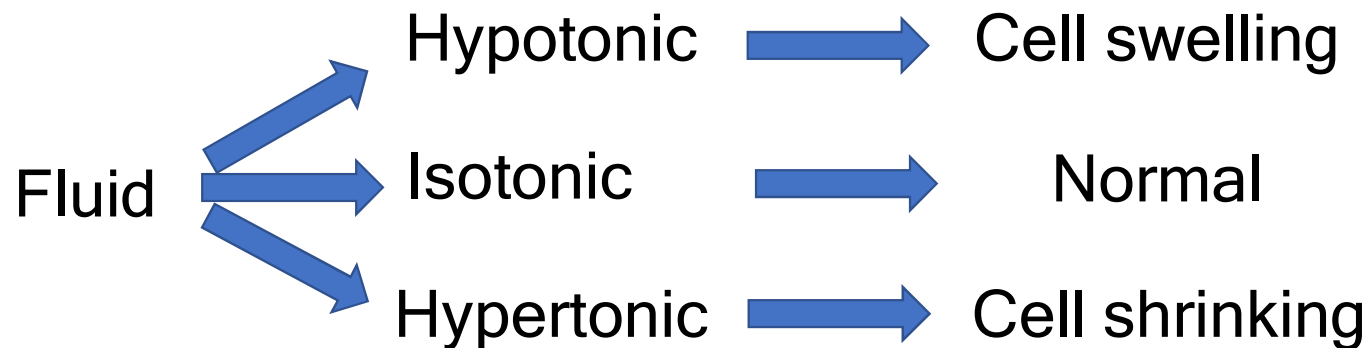


Serum osmolality

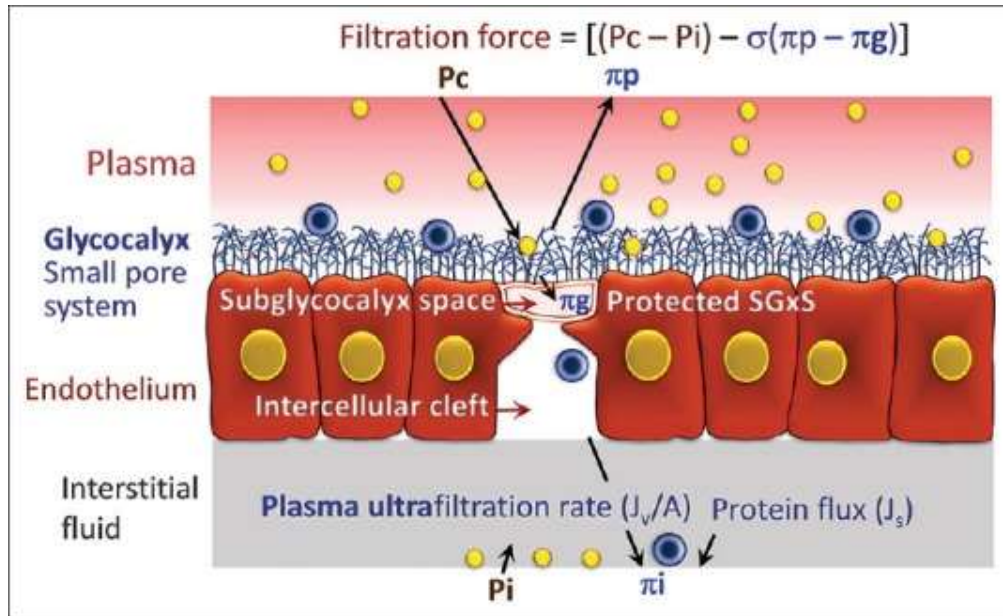
$$(2 \times \text{Na}) + \text{Glu}/18 + \text{BUN}/2.8$$

Normal range 285-305 mOsm/L

Effective serum osmolality
“Tonicity”



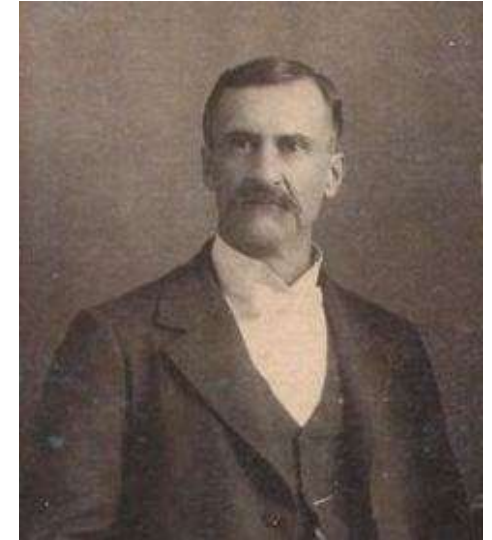
Endothelial glycocalyx



Nature Reviews Nephrology volume 14, pages541-557 (2018)

Outline

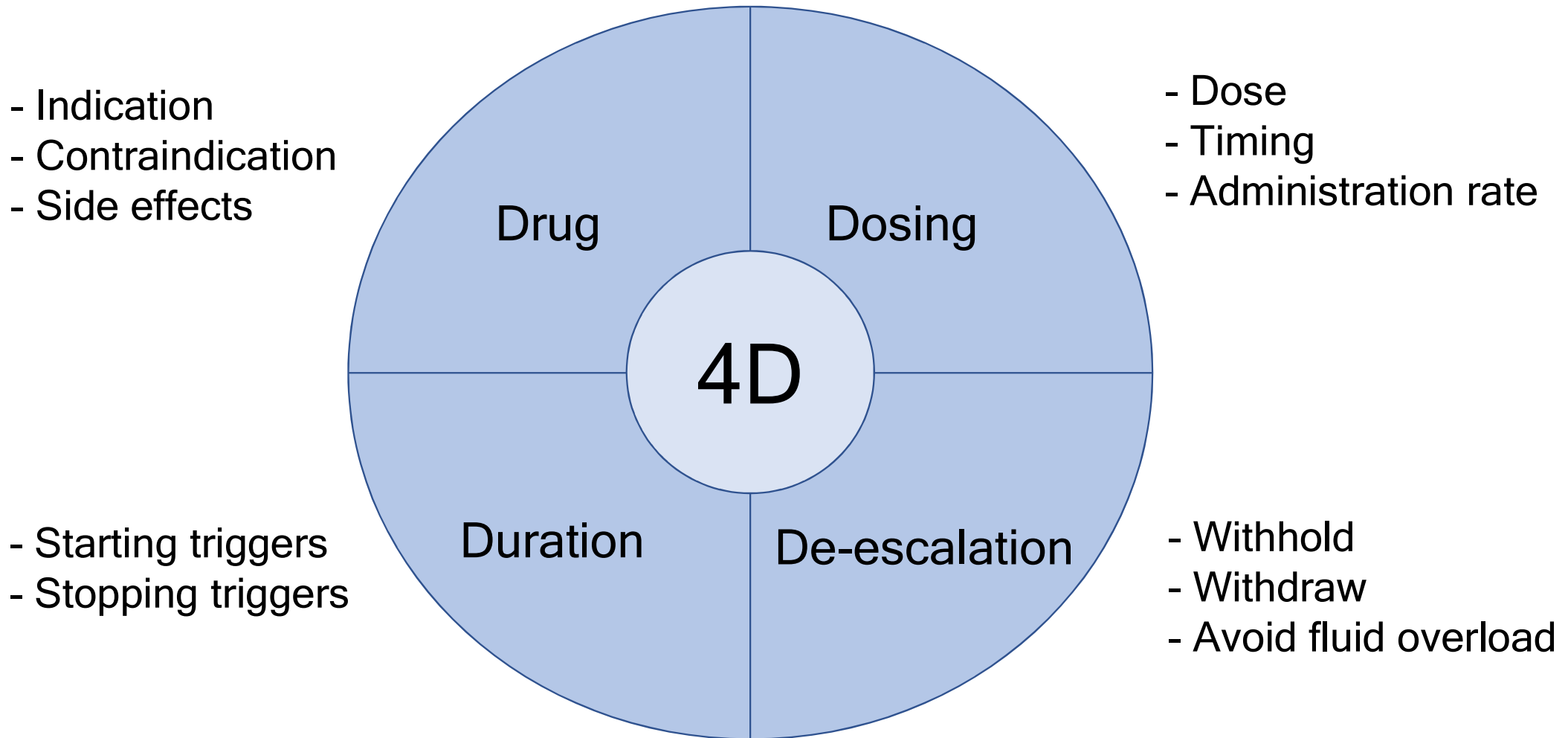
- Basic science related to fluid therapy
- Principle of fluid therapy
- Crystalloid vs Colloid
- NSS vs BSS



“injecting a weak saline solution into the veins of the patient [had] the most wonderful and satisfactory effect...”

- 1832 : Cholera epidemic, Thomas Latta, Robert Lewins
- 1900 : Identical blood group transfusion
- 1936-1939 : Spanish Civil War, blood transfusion program
- 1939-1945 : Second World War, plasma for volume expansion
- 1941 : attack on Pearl Harbor, human albumin

Fluid = drug



Indications

Resuscitation

- Correct an intravascular volume deficit or acute hypovolemia
- Focus on rapid restoration of circulating volume

Maintenance

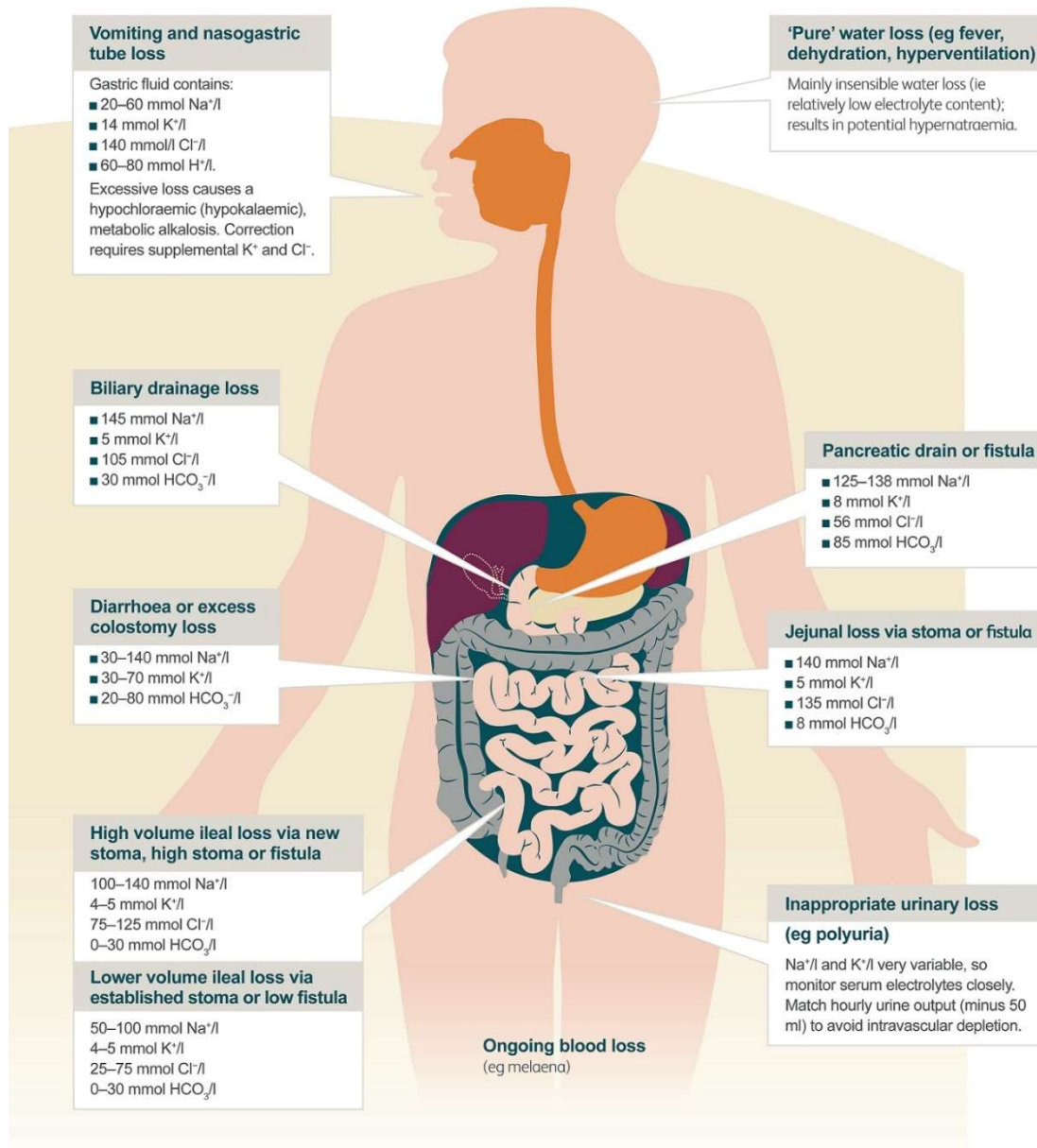
- Hemodynamically stable patients that are not able/allowed to drink water in order to cover daily requirement of water and electrolytes
- Deliver basic electrolytes and glucose for metabolic needs

Replacement

- Correct existing or developing deficits that cannot be compensated by oral intake alone
- Mimic the fluid that has been lost

Replacement fluids

- Correct existing or developing deficits that cannot be compensated by oral intake alone
- Mimic the fluid that has been lost



Maintenance Intravenous Fluids in Acutely Ill Patients

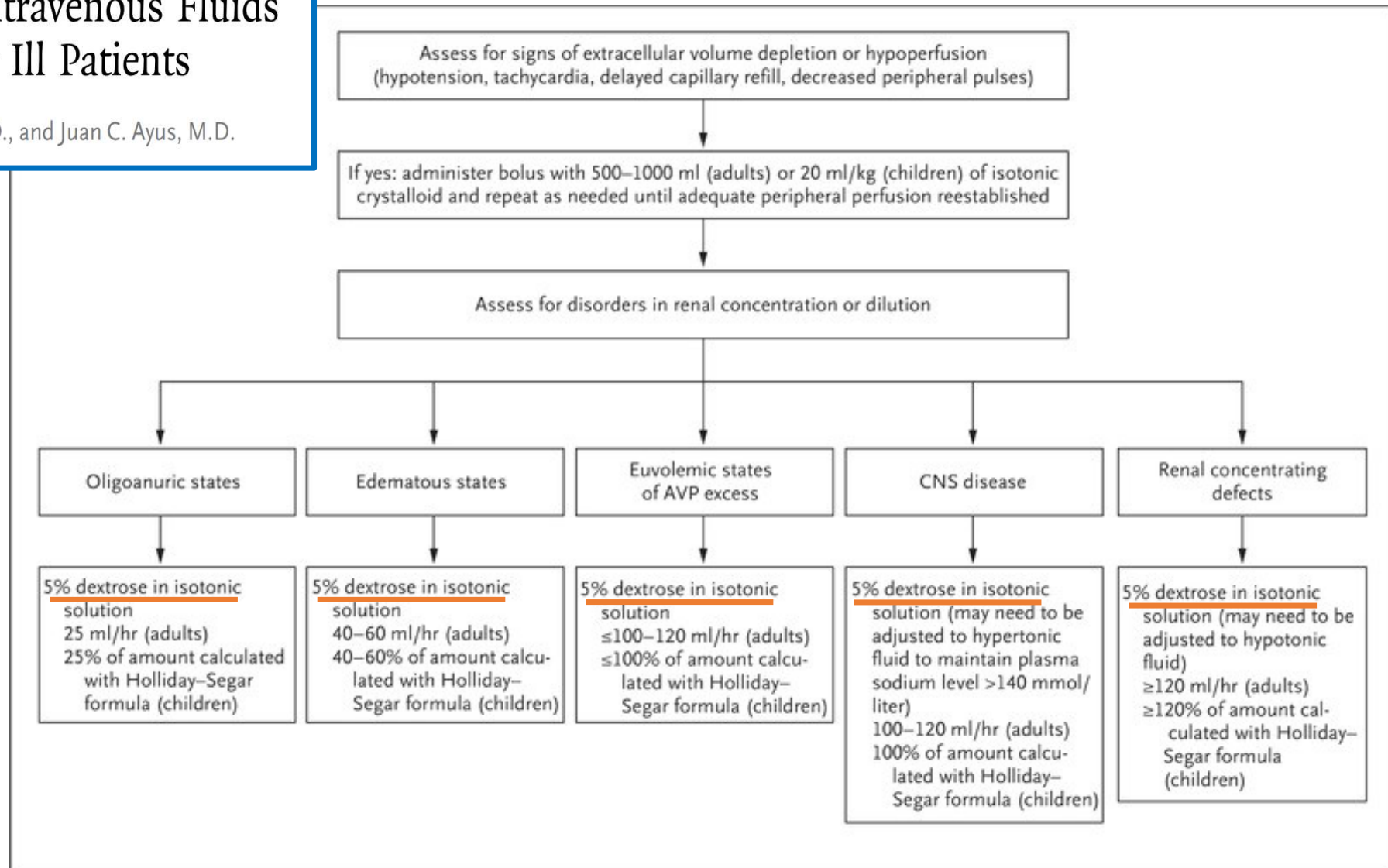
Michael L. Moritz, M.D., and Juan C. Ayus, M.D.

Benefit

Prevention of hospital acquired hyponatremia

Risk

- Volume excess
- Hyperchloremia



Resuscitation Fluids

John A. Myburgh, M.B., B.Ch., Ph.D., and Michael G. Mythen, M.D., M.B., B.S.

**Crystalloid
(isotonic)**

Colloid

Blood

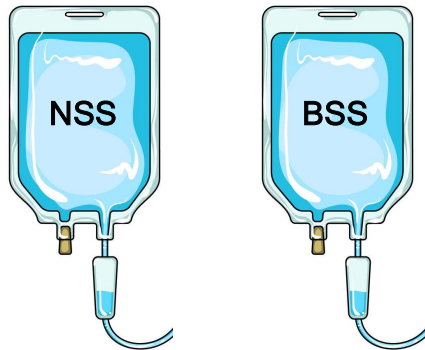
The ideal

- Predictable and sustainable
- Similar chemical composition to ECF
- Metabolized and excreted without accumulation
- Not produce adverse metabolic or systemic effects
- Cost-effective in terms of improving patient outcomes

Outline

- Basic science related to fluid therapy
- Principle of fluid therapy
- **Crystalloid vs Colloid**
- NSS vs BSS

- Solutions of ions
- capable of passing through semipermeable membranes



**Crystalloid
(isotonic)**

Colloid

- Suspensions of molecules within a carrier solution
- incapable of crossing the intact semipermeable capillary membrane



HES

Gelatin

Dextran

ICF

ISF

IVF

Volume sparing effect
1:3 ratio

Evidence from studies
1:1.4 ratio

Crystalloid vs Colloid

	Albumin		HES			Colloid
Study	SAFE	ALBIOS	WISEP	6S	CHEST	CRISTAL
Author Year	Finfer S 2004	Caironi P 2014	Brunkhorst FM 2008	Perner A 2012	Myburgh JA 2012	Annane D 2013
Design	Multicenter RCT	Multicenter RCT	Multicenter, 2-by-2 RCT	Multicenter, blinded RCT	Multicenter, blinded RCT	Multicenter, pragmatic RCT
Population	ICU	Severe sepsis	Severe sepsis	Severe sepsis	ICU	ICU
Intervention (N)	4% albumin (3,497)	20% albumin + crystalloid (910)	10% HES (275)	6% HES 130/0.42 (398)	6% HES 130/0.4 (3,358)	Colloid, 70% use HES (1,414)
Comparison (N)	NSS (3,500)	Crystalloid (908)	Ringer's lactate (262)	Ringer's acetate (400)	NSS (3,384)	Crystalloid (1,413)
Renal outcome	N/A	21.9% vs 22.7% (p=0.71)	34.9% vs 22.8% (p=0.002)	Doubling Scr 41% vs 35% (p=0.08)	RIFLE-R: 54% vs 57.3% (p=0.007) RIFLE-I: 34.6% vs 38% (p=0.005) RIFLE-F: 10.4% vs 9.2% (p=0.12)	N/A
RRT	Duration RRT 0.48 vs 0.39 (p=0.41)	Use of RRT 24.6% vs 21.4% (p=0.11)	Use of RRT 31% vs 18.8% (p=0.001)	Use of RRT 22% vs 6% (p=0.04)	Use of RRT 7% vs 5.8% (p=0.04)	11.3% vs 11.94% (p=0.90)
Mortality	28 days: 20.9% vs 21% (p=0.87)	28 days: 31.8% vs 32% (p=0.94)	28 days: 26.7% vs 24.1% (p=0.48)	90 days: 51% vs 43% (p=0.03)	90 days: 18% vs 17% (p=0.26)	28 days: 25.4% vs 27% (p=0.26)

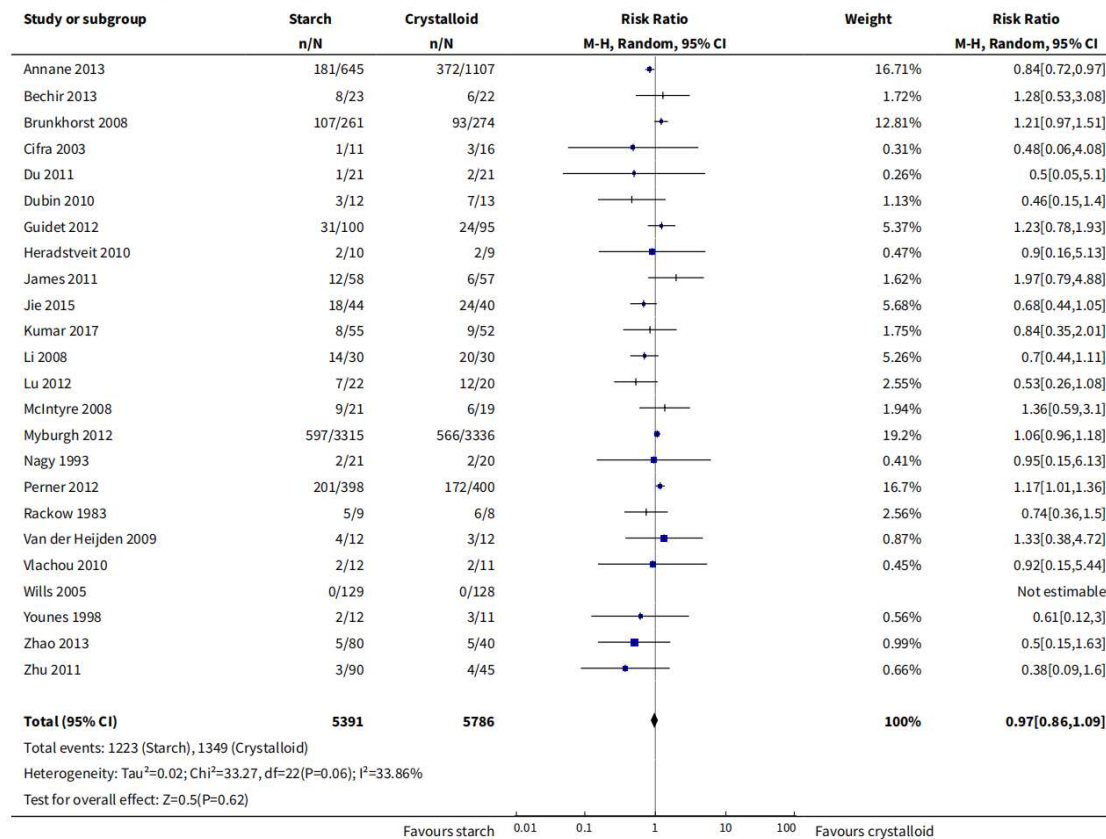
Colloids versus crystalloids for fluid resuscitation in critically ill people (Review)



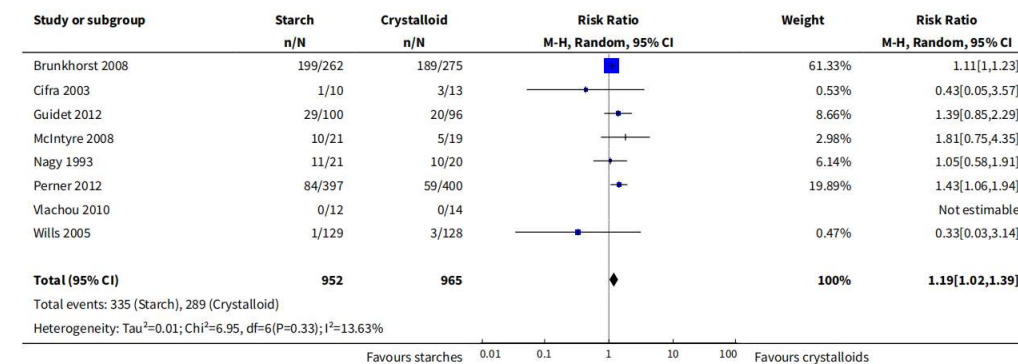
Cochrane Database of Systematic Reviews

Lewis SR, Pritchard MW, Evans DJW, Butler AR, Alderson P, Smith AF, Roberts I

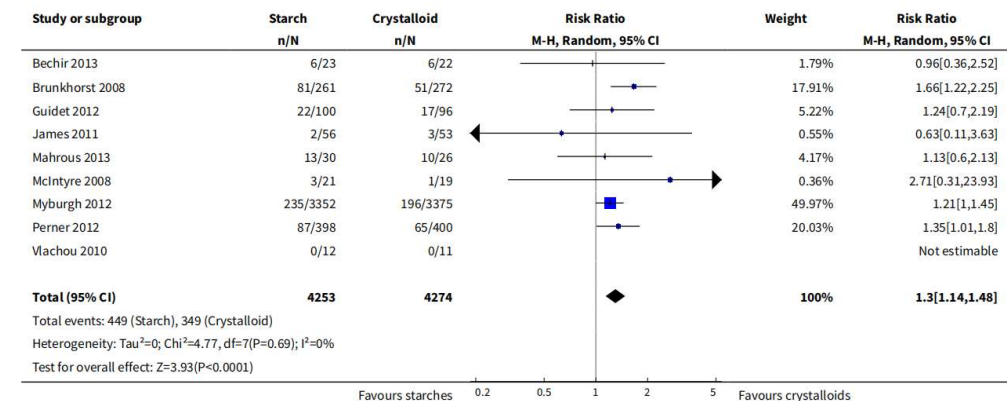
Analysis 1.1. Comparison 1 Starches vs crystalloid, Outcome 1 Mortality at end of follow-up.



Analysis 1.4. Comparison 1 Starches vs crystalloid, Outcome 4 Transfusion of blood product.



Analysis 1.5. Comparison 1 Starches vs crystalloid, Outcome 5 Renal replacement therapy.



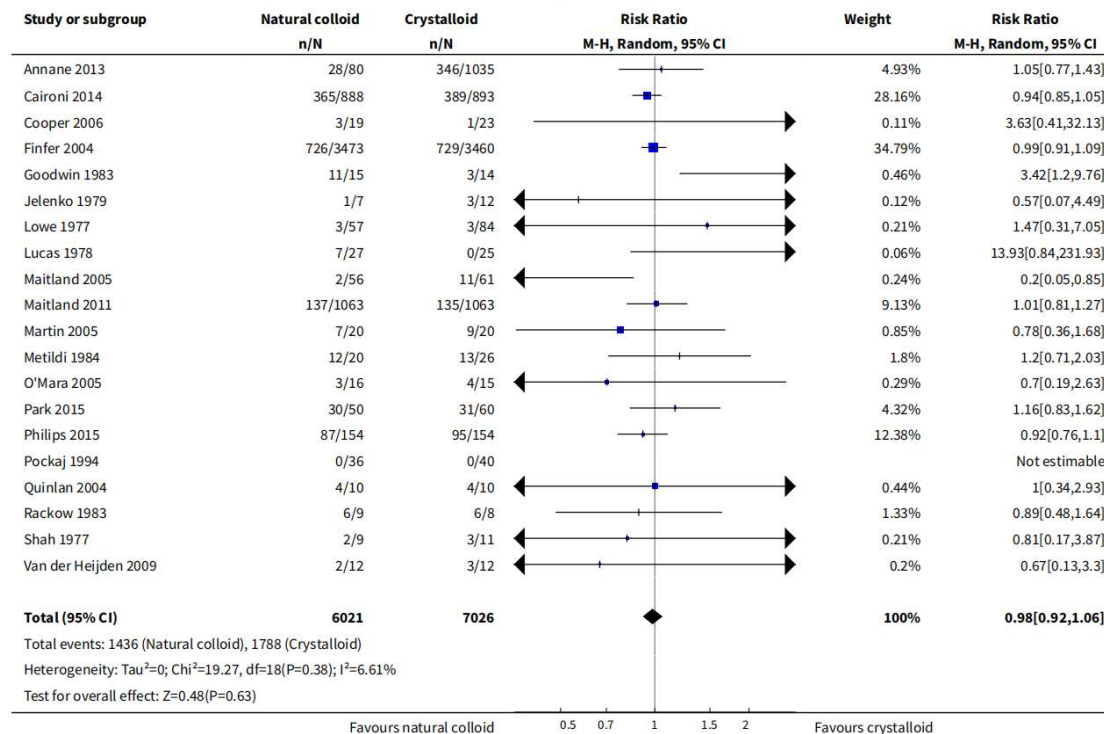
Colloids versus crystalloids for fluid resuscitation in critically ill people (Review)



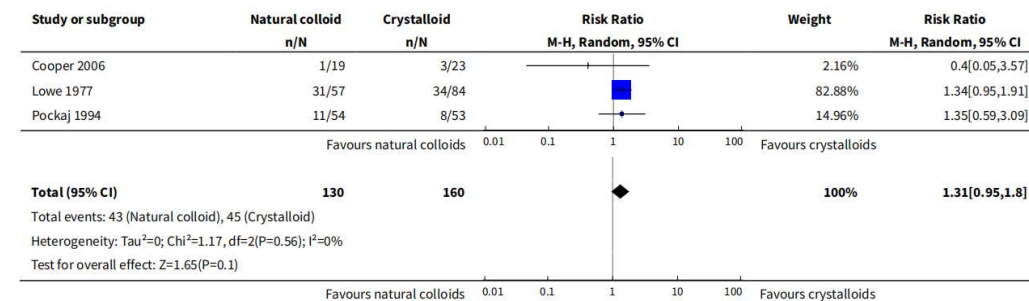
Cochrane Database of Systematic Reviews

Lewis SR, Pritchard MW, Evans DJW, Butler AR, Alderson P, Smith AF, Roberts I

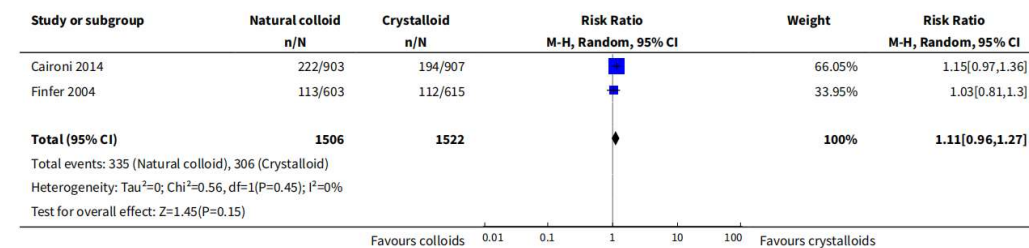
Analysis 4.1. Comparison 4 Albumin or FFP vs crystalloid, Outcome 1 Mortality at end of follow-up.



Analysis 4.4. Comparison 4 Albumin or FFP vs crystalloid, Outcome 4 Transfusion of blood product.



Analysis 4.5. Comparison 4 Albumin or FFP vs crystalloid, Outcome 5 Renal replacement therapy.



Recommendation

- No benefit of colloid over crystalloid in reducing mortality rates
- HES increase AKI, rate of RRT
- High cost of albumin



Crystalloid as initial fluid resuscitation


SSC guideline 2016

F. FLUID THERAPY

1. We recommend that a fluid challenge technique be applied where fluid administration is continued as long as hemodynamic factors continue to improve (BPS).
2. We recommend crystalloids as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock (strong recommendation, moderate quality of evidence).
3. We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock (weak recommendation, low quality of evidence).
4. We suggest using albumin in addition to crystalloids for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock when patients require substantial amounts of crystalloids (weak recommendation, low quality of evidence).
5. We recommend against using hydroxyethyl starches (HESs) for intravascular volume replacement in patients with sepsis or septic shock (strong recommendation, high quality of evidence).
6. We suggest using crystalloids over gelatins when resuscitating patients with sepsis or septic shock (weak recommendation, low quality of evidence).

Ongoing studies - Albumin in septic shock

ALBumIn Italian Outcome Septic Shock-BALANCED Trial (ALBIOSS-BALANCED) (ALBIOSS-BAL)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated  by the U.S. Federal Government. [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT03654001


[Recruitment Status](#)  : Recruiting
[First Posted](#)  : August 31, 2018
[Last Update Posted](#)  : April 23, 2021
See [Contacts and Locations](#)

ALBIOSS-BALANCED

Sponsor:

Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico

Albumin Replacement Therapy in Septic Shock (ARISS)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated  by the U.S. Federal Government. [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT03869385

[Recruitment Status](#)  : Recruiting
[First Posted](#)  : March 11, 2019
[Last Update Posted](#)  : June 29, 2021
See [Contacts and Locations](#)

ARISS

Sponsor:

Jena University Hospital

REVIEW

Open Access

Resuscitation Fluid Choices to Preserve the Endothelial Glycocalyx



Elissa M. Milford^{1,2*} and Michael C. Reade^{3,4}

- While FFP has been identified as the most effective, further work is needed to establish the mechanisms, and to determine whether glycocalyx repair improves clinical outcomes.
- A fluid resuscitation strategy that protects and repairs the endothelial glycocalyx may prove to be the most effective

Outline

- Basic science related to fluid therapy
- Principle of fluid therapy
- Crystalloid vs Colloid
- **NSS vs BSS**

Crystalloid

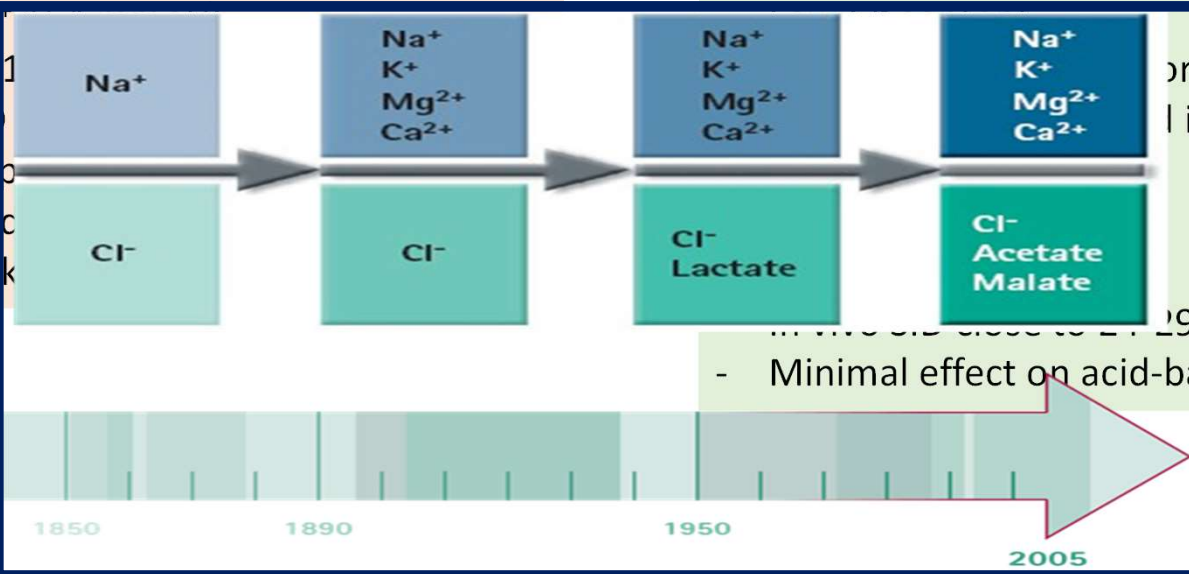
Abnormal

0.9% NaCl

Balanced

- a/k/a Normal saline

- Na⁺
- Cl⁻
- SID
- Hypo
- acc
- Risk

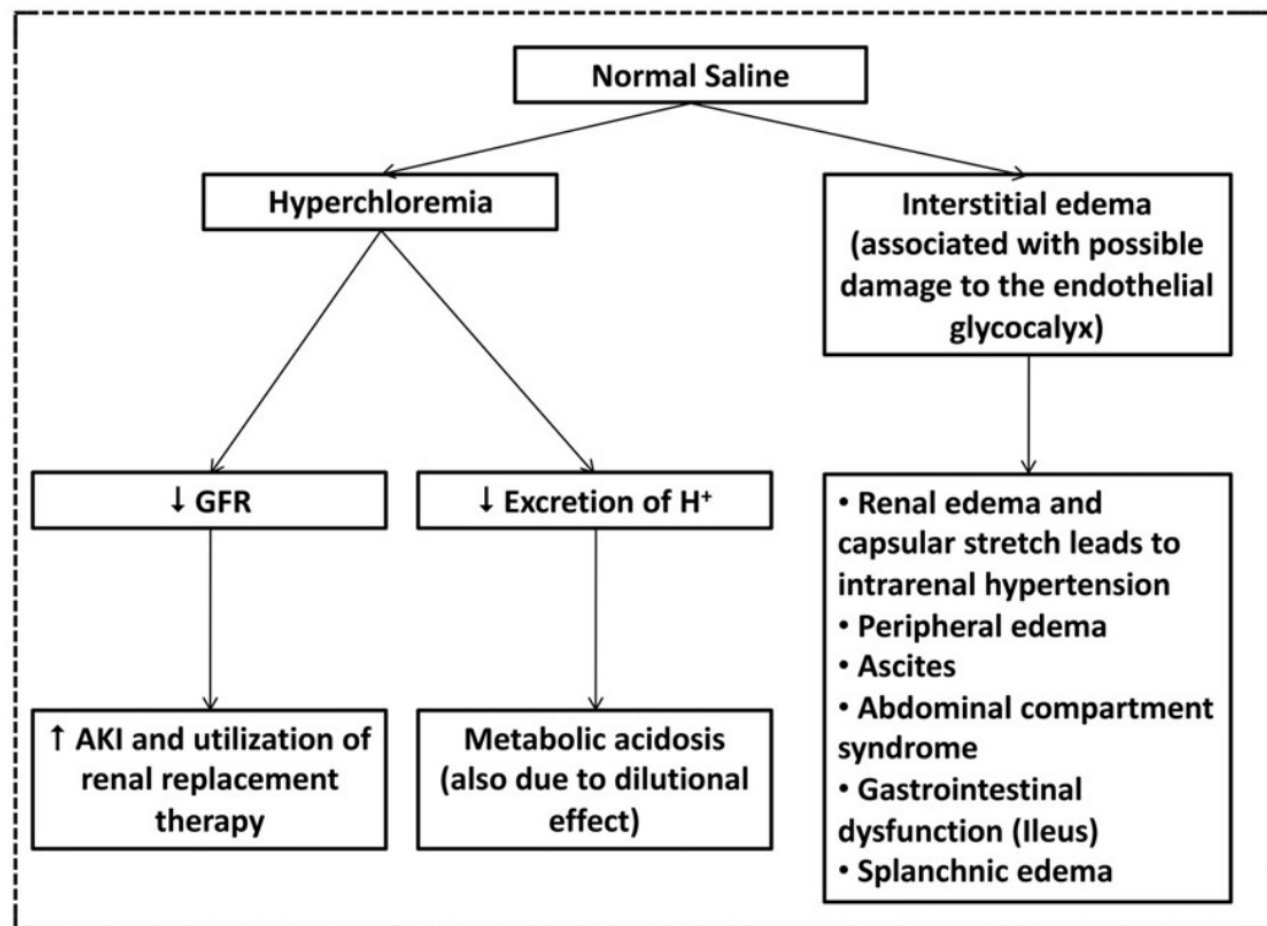
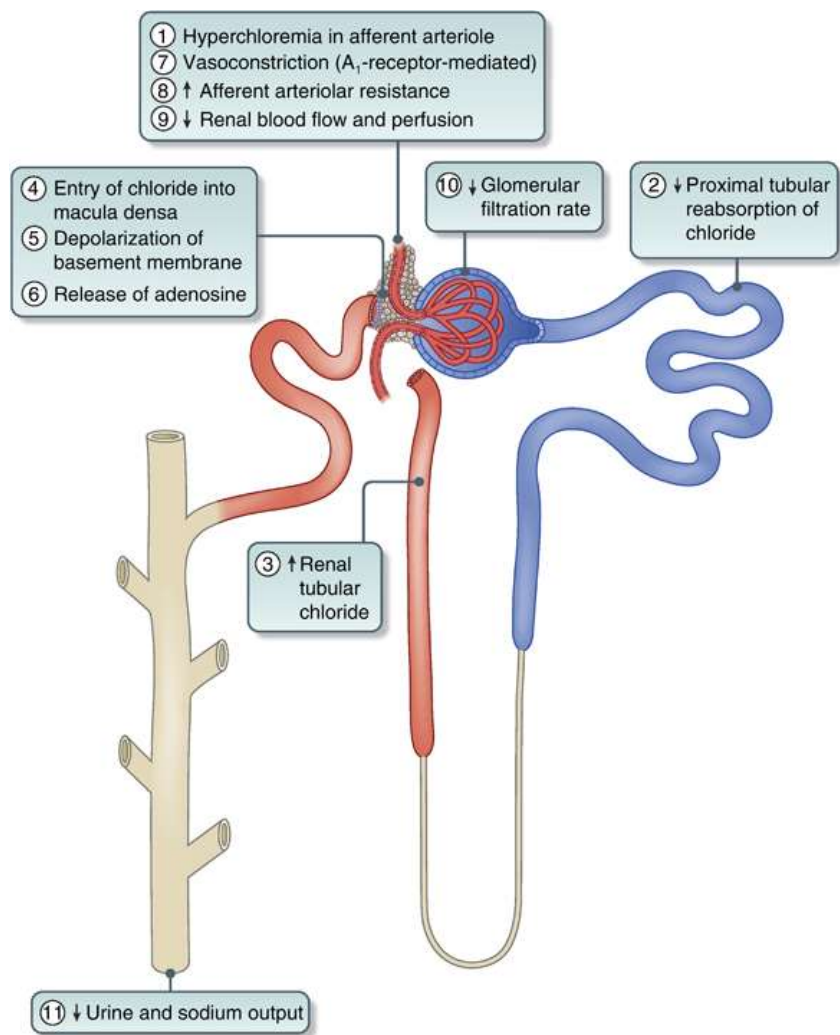


- a/k/a Buffered crystalloids

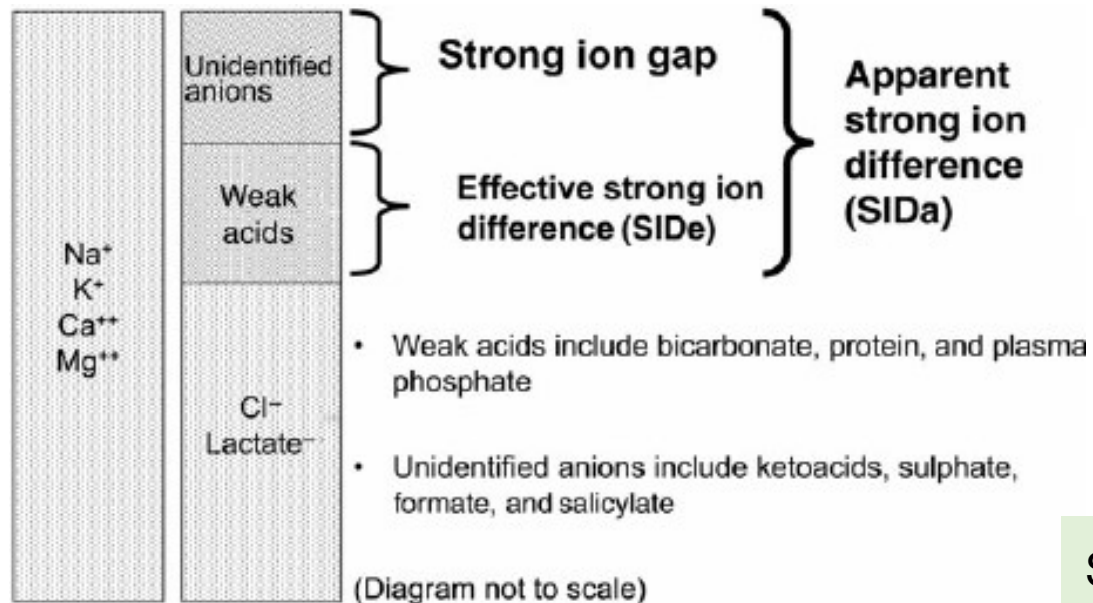
or buffers
into HCO₃⁻

- Minimal effect on acid-base status

Solute (mmol/L)	Plasma	0.9% NaCl	RLS	Acetar	Sterofundin ISO®	Plasmalyte 148®
Na ⁺	136 - 145	154	130	130	145	140
K ⁺	3.5 - 5.0		4	4	4	5
Mg ²⁺	1.0 - 2.0				1	1.5
Ca ²⁺	2.2 - 2.6		3	2.7	2.5	
Cl ⁻	98 - 106	154	109	109	127	98
Gluconate						23
Acetate				28	24	27
Lactate			28			
Malate					5	
eSID	42	0	28	28	25.5	50
Theoretical osmolarity (mOsm/L)	291	308	273	273	309	295
Measured osmolality (mOsm/kg H ₂ O)	287	286	256	256	287	271
pH	7.35-7.45	4.5-7.0	5.0-7.0	6.7-7.0	5.1-5.9	4.0-8.0



Strong ion difference (SID)



$$\text{SID} = (\text{Na}^+ + \text{K}^+ + \text{Ca}^{2+} + \text{Mg}^{2+}) - (\text{Cl}^- + \text{Lactate})$$

$$\text{pH} = \text{pK}_1' + \log[\text{SID} - A_{\text{tot}} / (1 + 10^{\text{pK}_a - \text{pH}})] / (S \times \text{PCO}_2)$$

Ideal solution : $\text{SID} = \text{baseline HCO}_3$

$\text{SID} < \text{baseline HCO}_3$

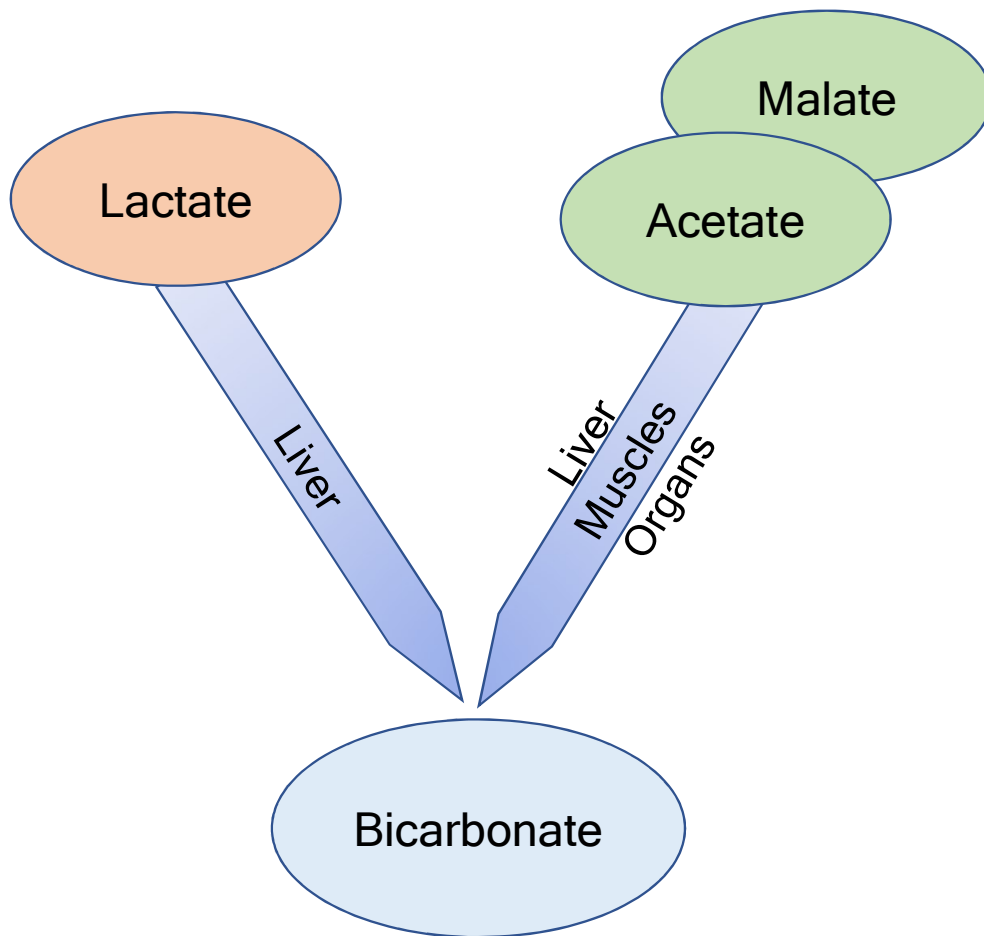
Acidosis

$\text{SID} > \text{baseline HCO}_3$

Alkalosis

- 0.9% NaCl \rightarrow SID = 0
- Large amount > 40 ml/kg/hr or > 3L in 2 hrs
- Hyperchloremic metabolic acidosis

Bicarbonate precursors




	Acetate	Lactate
Metabolism	Fast (min)	slow
Tissue (normal)	All	Liver
Tissue (shock)	All	-
RQ	0.5	0.67
Oxygen consumption (mol O ₂ /mol)	2	3
Myocardial depression, vasodilatation	++	-
Hyperglycemia	↔	↑
Lactate assay	↔	↑

Study	SPLIT	SALT	SALT-ED	SMART
Author Year Country	Paul Y 2015 New Zealand	MW Semler 2015 USA	WH Self 2018 USA	MW Semler 2018 USA
Design	Multicenter RCT Double blind	Single center RCT	Single center, crossover RCT	Single center, crossover RCT
Population	Mixed ICU	Medical ICU	ER + Ward (Non-ICU)	ICU
Intervention (N) Volume	Plasma-Lyte148 (1,067) 2,000 ml (1,000-3,500)	LRS or Plasma-Lyte A (520) 1,617 ml (500-3,628)	LRS or Plasma-Lyte A (6,708) 1,089 ml (1,000-2,000) > 2,000 ml = 32.9%	LRS or Plasma-Lyte A (7,942) 1,000 ml (0-3,210)
Comparison (N) Volume	0.9% NaCl (1,025) 2,000 ml (1,000-3,250)	0.9% NaCl (454) 1,424 ml (500-3,377)	0.9% NaCl (6,639) 1,071 ml (1,000-2,000) > 2,000 ml = 32.4%	0.9% NaCl (7,860) 1,020 ml (0-3,500)
Composite outcome		MAKE-30* 24.6% vs 24.7% (p=0.98)	MAKE-30 4.7% vs 5.6% (p=0.01) OR 0.82 (0.70-0.95)	MAKE-30 14.3% vs 15.4% (p=0.04) OR 0.90 (0.82-0.99)
Renal outcome	Incidence of AKI 9.6% vs 9.2% (p=0.77)	AKI stage 2 or greater 26% vs 28.4% (p=0.39)	AKI stage 2 or greater 8.0% vs 8.6% (p=0.14)	AKI stage 2 or greater 10.7% vs 11.5% (p=0.09)
RRT	Use of RRT 3.3 vs 3.4 (p=0.91)	Use of RRT 4.6% vs 3.1% (p=0.22)	Use of RRT 0.3% vs 0.5%	Use of RRT 2.5% vs 2.9% (p=0.08)
Mortality	28 days: 7.6% vs 8.6% (p=0.40)	30 days: 13.8% vs 15% (p=0.62)	30 days: 1.4% vs 1.5%	30 days: 10.3% vs 11.1% (p=0.06)

*MAKE-30 : death at 30 days, new RRT, final creatinine > 200% of baseline

Ongoing trial: Balanced solutions vs 0.9% NaCl

Plasma-Lyte 148® versUs Saline Study (PLUS)

 The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

Sponsor:

The George Institute

Collaborators:

Australian and New Zealand Intensive Care Society Clinical Trials Group
Baxter Healthcare Corporation

ClinicalTrials.gov Identifier: NCT02721654


Recruitment Status ⓘ : Active, not recruiting

First Posted ⓘ : March 29, 2016

Last Update Posted ⓘ : April 22, 2021

PLUS

Balanced Solution Versus Saline in Intensive Care Study (BaSICS)

 The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

Sponsor:

Hospital do Coracao

Information provided by (Responsible Party):

Hospital do Coracao

ClinicalTrials.gov Identifier: NCT02875873

Recruitment Status ⓘ : Completed

First Posted ⓘ : August 23, 2016

Last Update Posted ⓘ : April 19, 2021

BaSICS

Perioperative administration of buffered versus non-buffered crystalloid intravenous fluid to improve outcomes following adult surgical procedures (Review)



**Cochrane
Library**

Cochrane Database of Systematic Reviews

Bampoe S, Odor PM, Dushianthan A, Bennett-Guerrero E, Cro S, Gan TJ, Grocott MPW, James MFM, Mythen MG, O'Malley CMN, Roche AM, Rowan K, Burdett E

Author's conclusion

- Moderate-quality evidence to support the safety of buffered fluids in terms of their **low risk of precipitating electrolyte disturbance**.
- Perioperative buffered fluid resuscitation is associated with **hyperchloremic metabolic acidosis in a reduced proportion of patients** when compared with non-buffered fluid resuscitation.
- **Buffered fluids are appropriate for fluid replacement during surgery** and should be considered especially for patients with, or at risk of, metabolic derangement



Intravenous fluid therapy in the perioperative and critical care setting: Executive summary of the International Fluid Academy (IFA)

Manu L. N. G. Malbrain^{1,2,3*†} , Thomas Langer^{4,5†}, Djillali Annane⁶, Luciano Gattinoni⁷, Paul Elbers⁸, Robert G. Hahn⁹, Inneke De laet¹⁰, Andrea Minini¹, Adrian Wong¹¹, Can Ince¹², David Muckart^{13,14}, Monty Mythen¹⁵, Pietro Caironi^{16,17†} and Niels Van Regenmortel^{10,18†}

- **Balanced solutions** → avoid fluid-induced metabolic acidosis and excessive chloride loading
- **Excessive chloride** → detrimental effect on renal function, even at low doses.
- The use of **balanced solutions**, particularly in patients that potentially **need a significant amount of intravenous fluids**, seems to be a reasonable pragmatic choice.
- **Saline** → considered in hypovolemic hyponatremia or hypochloremic metabolic alkalosis
- The patient's serum Cl⁻ is an important factor to determine the appropriate type of fluids



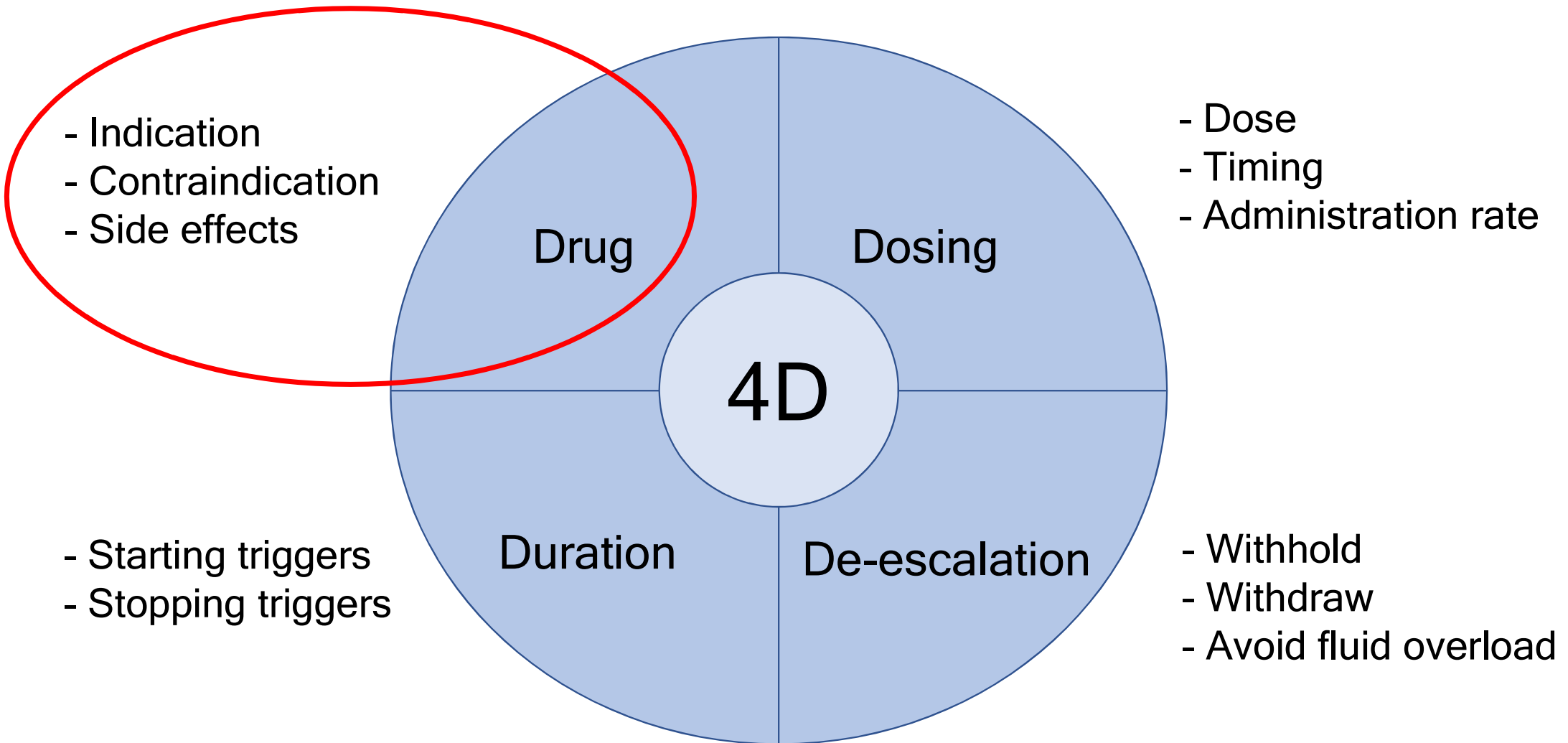
Balanced Crystalloid Solutions

Matthew W. Semler¹ and John A. Kellum²

¹Division of Allergy, Pulmonary and Critical Care Medicine, Vanderbilt University Medical Center, Nashville, Tennessee; and ²The Center for Critical Care Nephrology, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania

- Balanced crystalloids rather than saline may have the potential to reduce morbidity and mortality for critically ill patients.
- For patients undergoing major surgery, randomized trials have found that **balanced crystalloids** cause **less hyperchloremic metabolic acidosis** and **reduce the need for vasopressors**
- Among acutely ill adults in the ED or ICU, data from several recent large randomized trials suggest that using **balanced crystalloids decreases the risk of death or severe kidney dysfunction**.

Fluids are drugs



Phases of fluid therapy

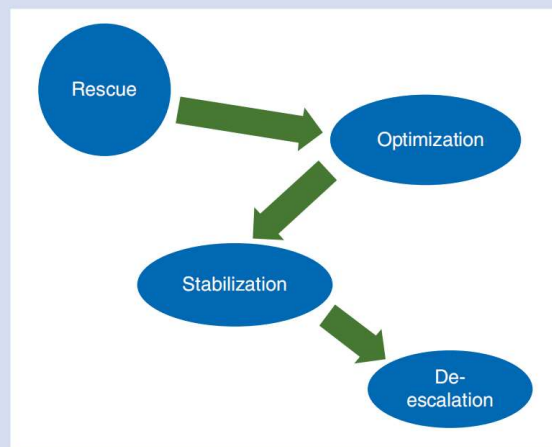


Fig 1 Relationship between the different stages of fluid resuscitation. Reproduced with permission from ADQI (www.ADQI.org).

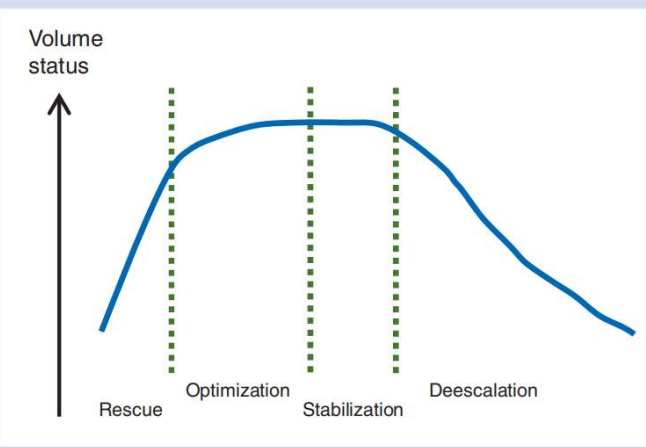


Fig 2 Patients' volume status at different stages of resuscitation. Reproduced with permission from ADQI (www.ADQI.org).

Table 1 Characteristics of different stages of resuscitation: 'Fit for purpose fluid therapy'. GDT, goal directed therapy; DKA, diabetic keto acidosis; NPO, nil per os; ATN, acute tubular necrosis; SSC, surviving sepsis campaign

	Rescue	Optimization	Stabilization	De-escalation
Principles	Lifesaving	Organ rescue	Organ support	Organ recovery
Goals	Correct shock	Optimize and maintain tissue perfusion	Aim for zero or negative fluid balance	Mobilize fluid accumulated
Time (usual)	Minutes	Hours	Days	Days to weeks
Phenotype	Severe shock	Unstable	Stable	Recovering
Fluid therapy	Rapid boluses	Titrate fluid infusion conservative use of fluid challenges	Minimal maintenance infusion only if oral intake inadequate	Oral intake if possible Avoid unnecessary i.v. fluids
Typical clinical scenario	<ul style="list-style-type: none"> - Septic shock - Major trauma 	<ul style="list-style-type: none"> - Intraoperative GDT - Burns - DKA 	<ul style="list-style-type: none"> - NPO postoperative patient - 'Drip and suck' management of pancreatitis 	<ul style="list-style-type: none"> - Patient on full enteral feed in recovery phase of critical illness - Recovering ATN
Amount	Guidelines, for example, SSC, pre-hospital resuscitation, trauma, burns, etc.			