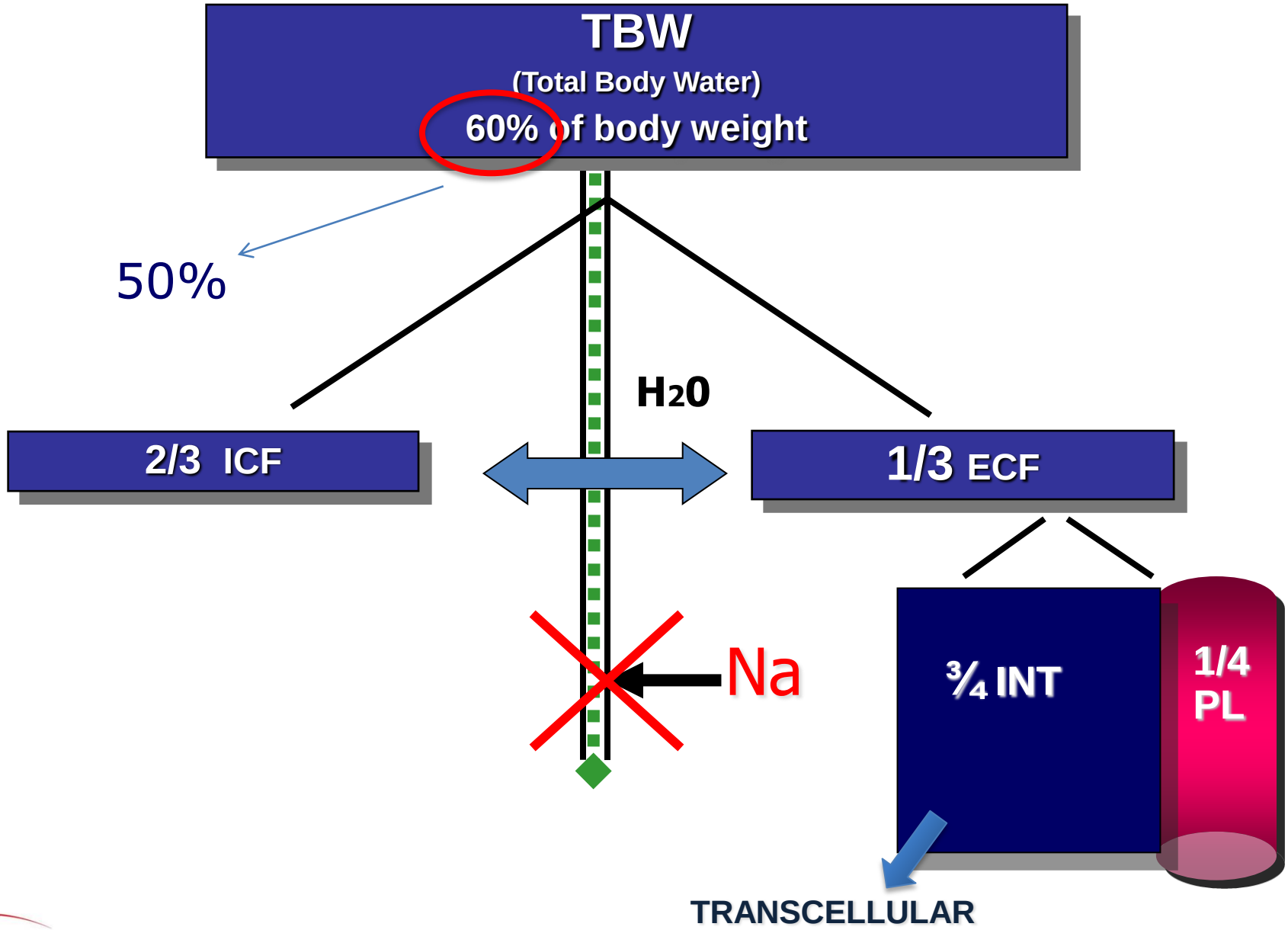
Captain’s speaking

Fluids should be administered with the same caution that is used with any intravenous drug.

Fluid resuscitation is a component of a complex physiological process.

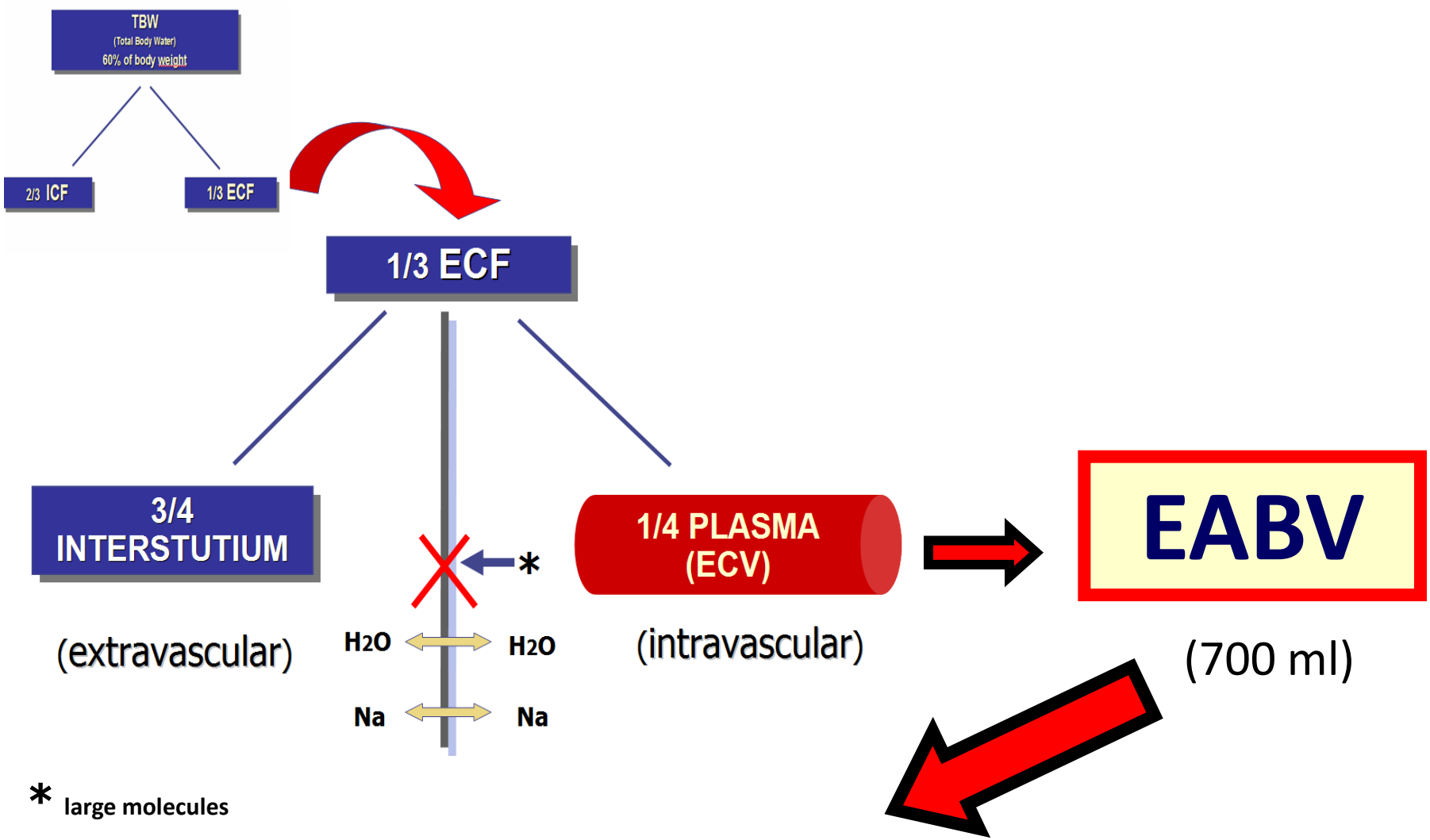
Fluid requirements change over time in critically ill patients.

Myburgh J, Mythen M N Engl J Med 2013;369:1243-51


TBW
(Total Body Water)
60% of body weight
50%
H2O
2/3 ICF
1/3 ECF
Na
¾ INT
1/4 PL
TRANSCELLULAR

ECF volume

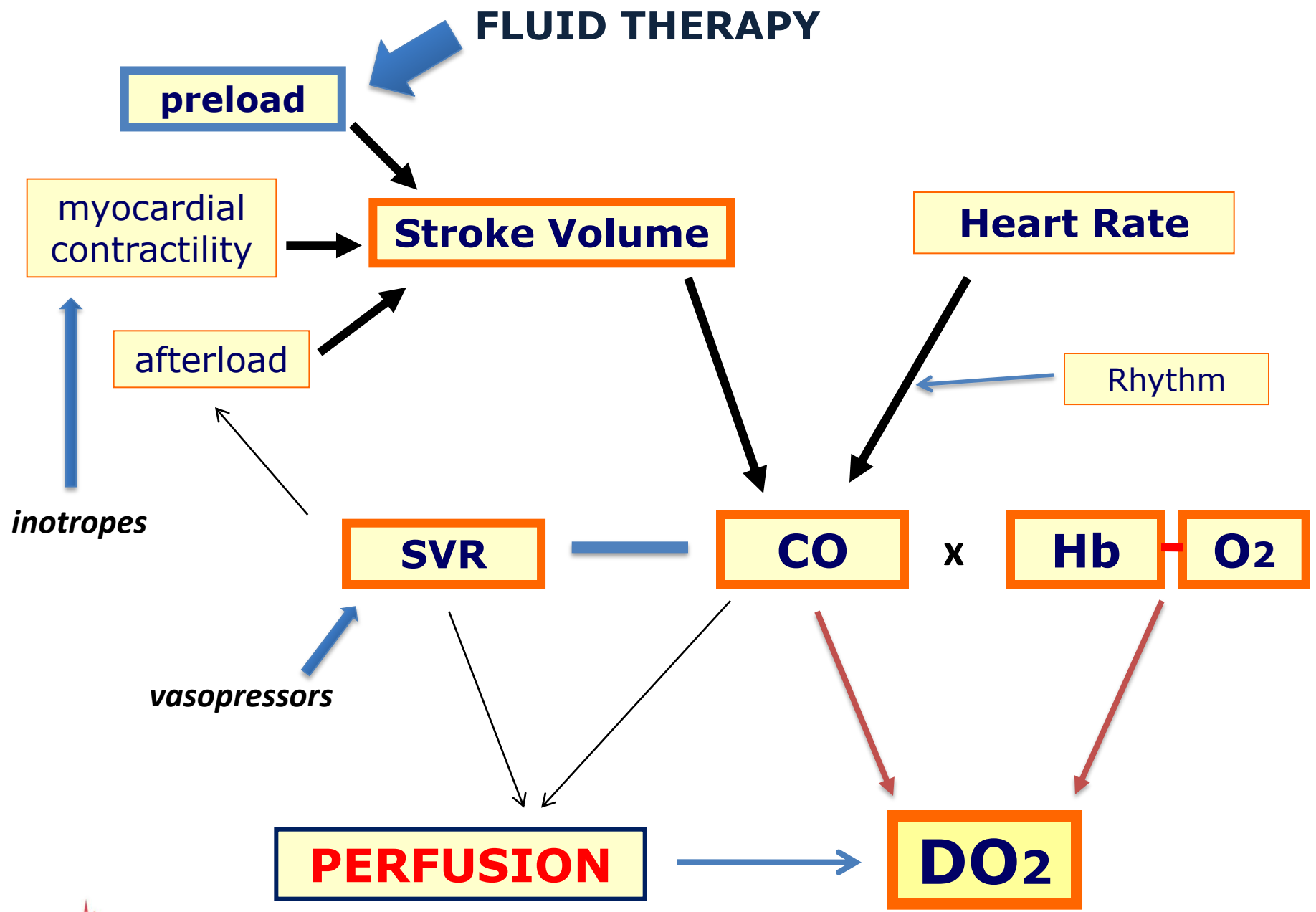
EABV


TBW
(Total Body Water)
60% of body weight
2/3 ICF
1/3 ECF
1/3 ECF
3/4
INTERSTUTIUM
(extravascular)
1/4 PLASMA
(ECV)
(intravascular)
EABV
(700 ml)
H2O
H2O
Na
Na
* large molecules
Tissues Perfusion

$$DO_2 = CO \times CaO_2$$

The primary function of the cardiovascular system:

delivery oxygen for utilization by the parenchymal cells for their metabolic needs to sustain organ function.


FLUID THERAPY
preload
myocardial contractility
Stroke Volume
Heart Rate
afterload
Rhythm
inotropes
SVR
CO
x
Hb
O2
vasopressors
PERFUSION
DO2

Perfusion, DO_2….

The **microcirculation** may be the right target.

The microcirculation is the **ultimate destination of blood flow to the tissues** to transport oxygen for utilization by the parenchymal cells for their metabolic needs to sustain their support of organ function and defines the **primary function of the cardiovascular system.**

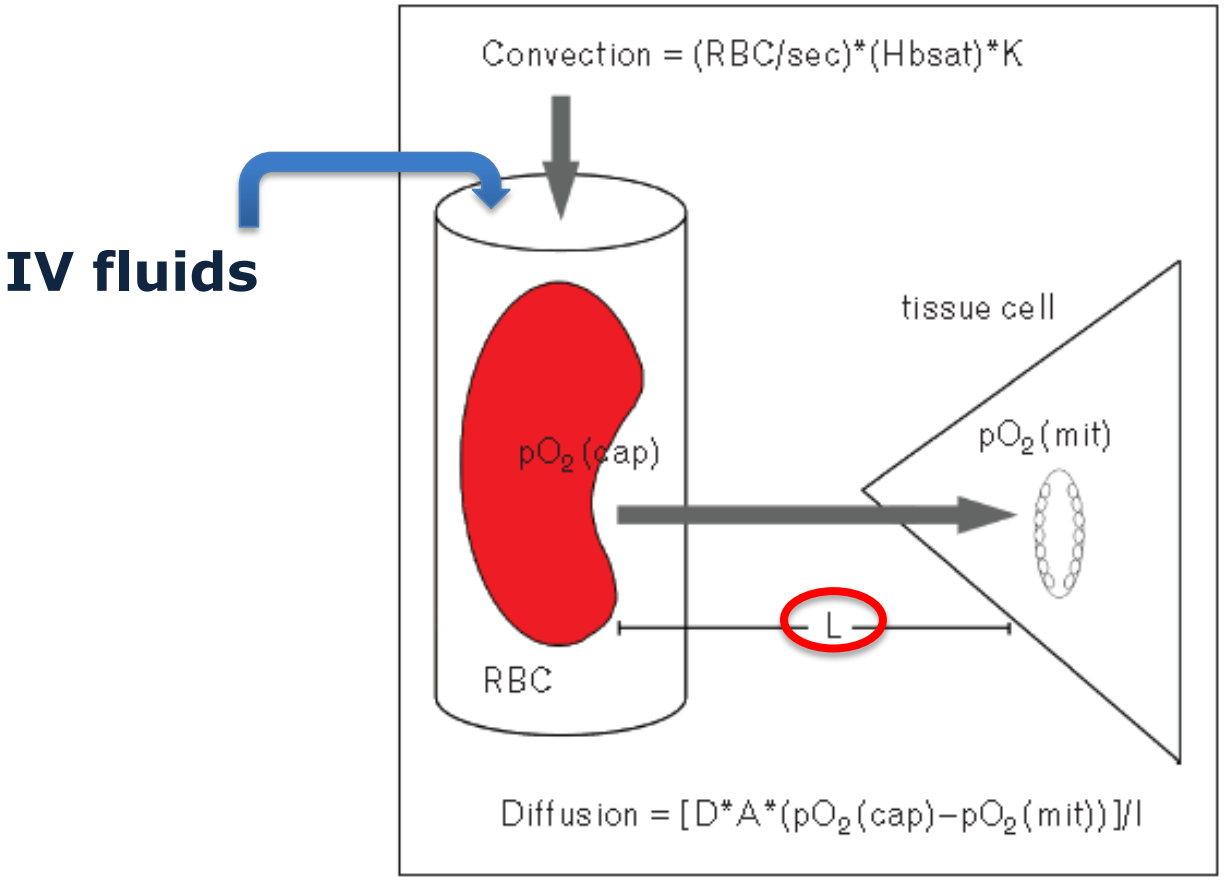
Ince C Curr Opin Crit Care 2014, 20:301–308

In the setting of **sepsis**, the endothelium and vasculature are under assault by activated leukocytes, inflammatory mediators, and reactive oxygen species that ***cause microcirculatory dysfunction*** in advance of organ failure.

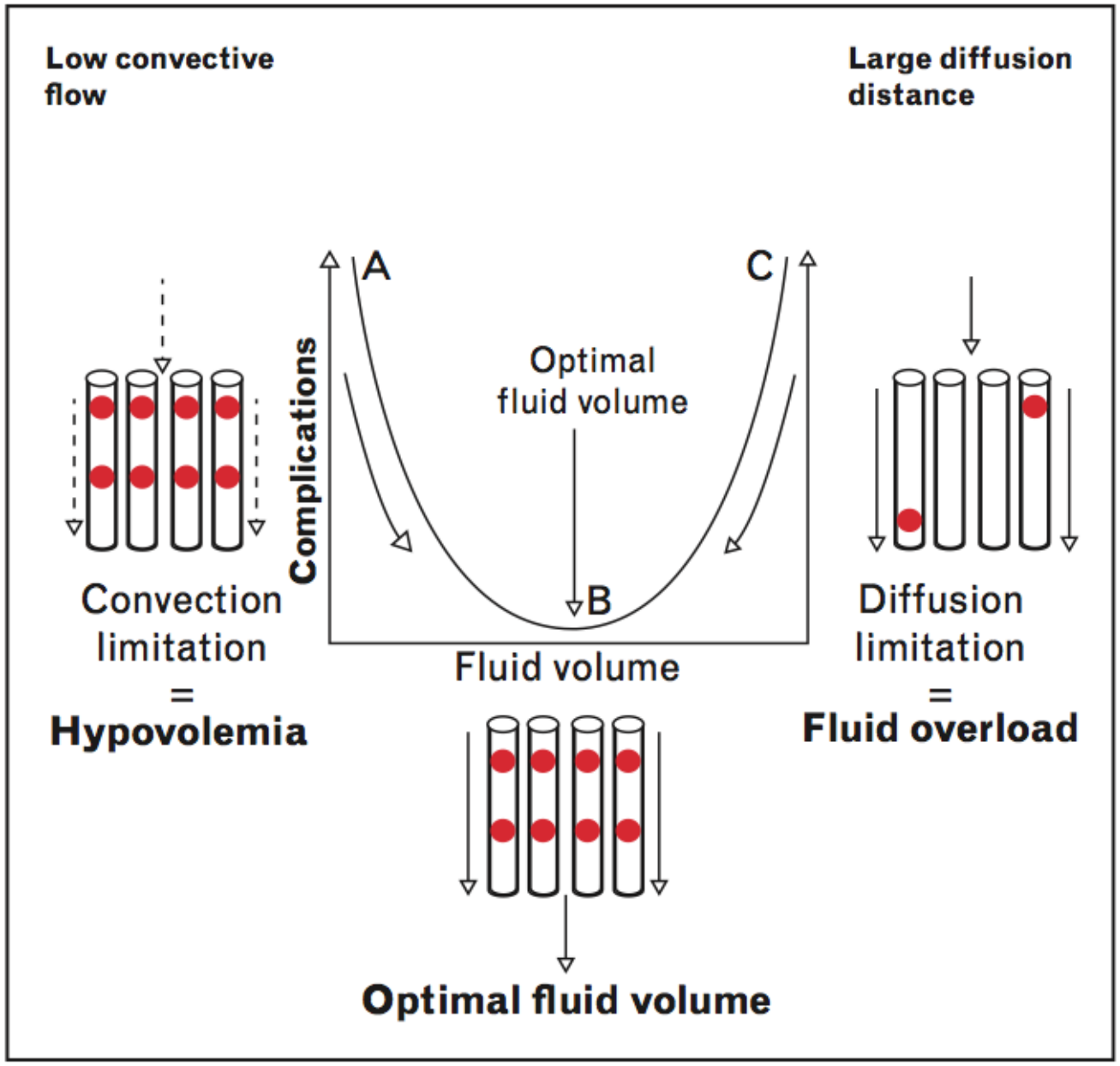
A *compromised microcirculation is no longer able to regulate blood flow distribution*, resulting in ***functional shunting*** where the **oxygen need of the parenchymal cells is not met by adequate delivery.**

Ince C *Critical Care 2013, 17(Suppl 1):S9*

Too little volume is **low microcirculatory blood flow** and **too much volume** as a ***dilution of the capillaries***, resulting in **increased diffusion distances**.



Ince C Curr Opin Crit Care 2014, 20:301–308



Ince C Curr Opin Crit Care 2014, 20:301–308

Sepsis is associated with a **decrease in capillary density** in association with an increase in heterogeneity of perfusion because of the presence of intermittently or not perfused capillaries in close proximity to well perfused capillaries.

DE Backer D et al. Virulence 5:1, 73–79; January 1, 2014

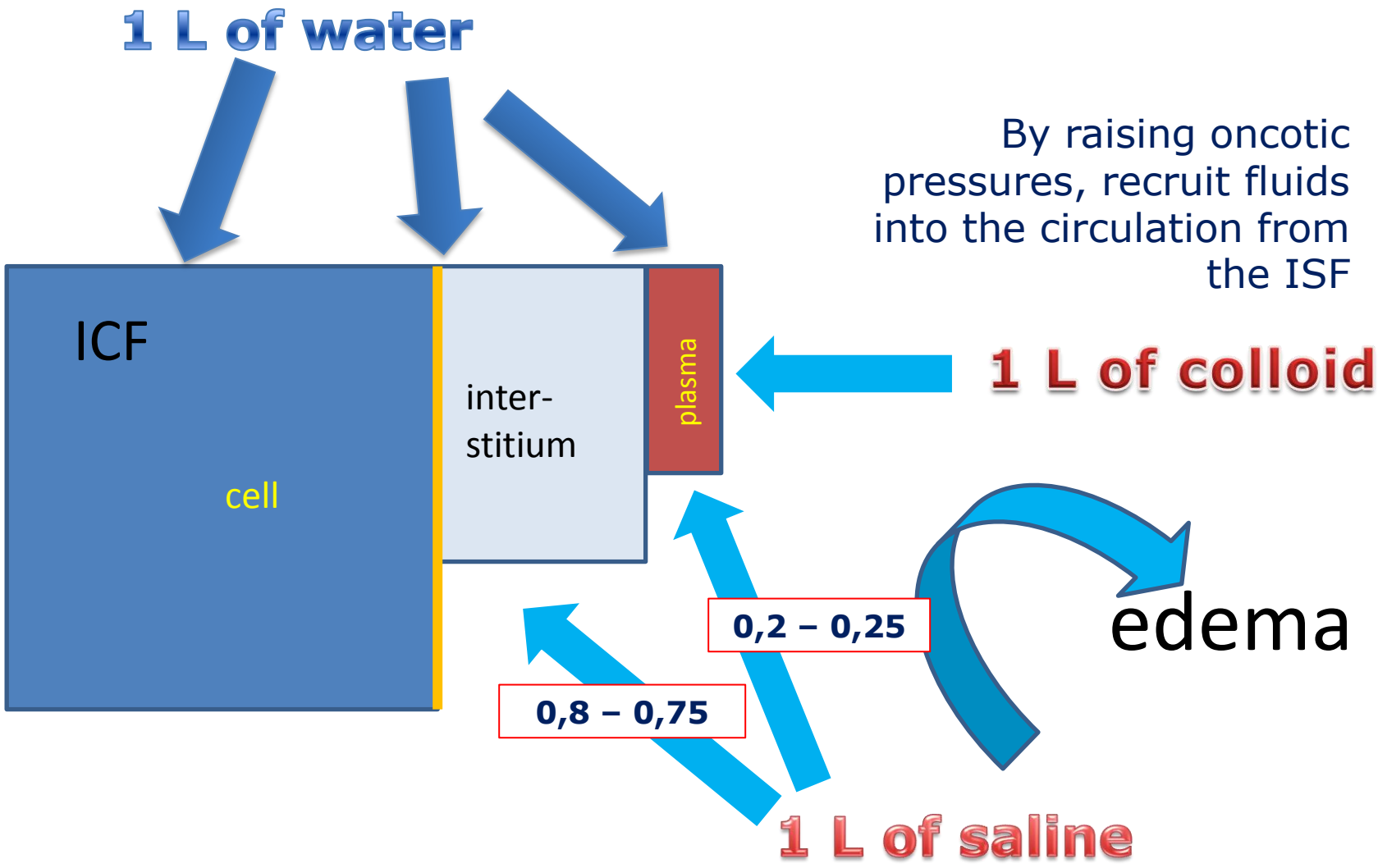
Pathophysiologic Alterations in the ISF Associated with Critical Illness

In **sepsis** there are **increases in the extracellular body water during the acute phase of the inflammatory response**.

Elderly patients with sepsis demonstrate increases in extracellular water and **increasesing extracellular water are associated with worse outcome.**

Major blunt trauma display similar pathophysiologic changes.

Interstitium. Venkatesh B et al Crit Care Med 2010; 38[Suppl.]:S630–S636



Classic model

The end of the crystalloid era?

Twiglwy AJ, Hillman KM Anaesthesia 1985;40(9):860-71

Is it the end of the road for synthetic starches in critical illness?

Prowler & Pearse , Editorial, BMJ 2013;346:f1805

The preferred use of colloidal solutions is based on **rationales that are not supported by clinical evidence**.

Hartog CS et al Anesth Analg 2011;112:156 –64

The *common belief* that **3 to 4 times more crystalloids than colloids are needed** to achieve similar hemodynamic effects is **not supported by this clinical observation**

Schortgen F, Brochard L Crit Care Med 2012 40;9:2709-10

Evidence that colloids provide better survival is lacking

Consensus statement of the ESICM task force on colloid volume therapy in critically ill patients

Intensive Care Med 2012; 38:368–383

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The *Committee confirmed that* ***HES*** *solutions* ***must no longer be used to treat*** *patients with* ***sepsis or burn injuries or critically ill patients,*** *because of an* ***increased risk of kidney injury and mortality***.

However the PRAC agreed that *HES could continue to be used in patients with* ***hypovolaemia caused by acute blood loss*** where treatment with alternative infusions solutions known as 'crystalloids' alone are not considered to be sufficient.

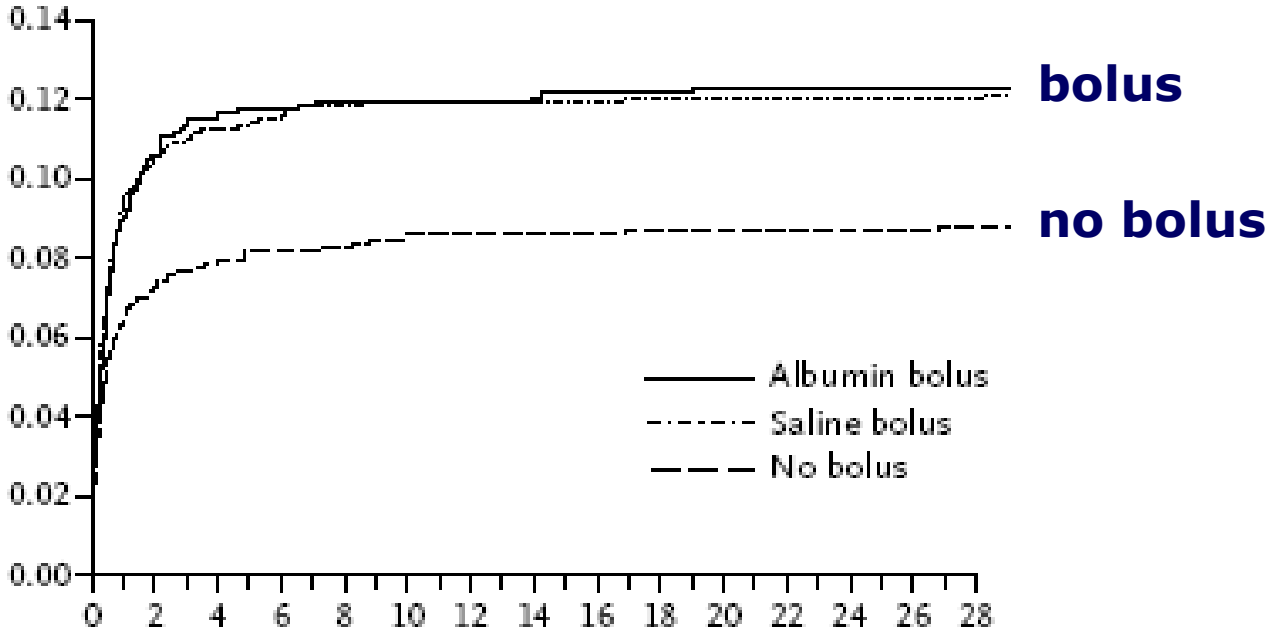
11.11.2013

An African Lesson

Fluid **E**xpansion **a**s **S**upportive **T**herapy

(FEAST) trial

Maitland K, Kiguli S, Opoka RO, et al.
Mortality after fluid bolus in African children with severe infection
N Engl J Med 2011, 64:2483-2495.



the trial was stopped **after the recruitment of 3141 patients when bolus-fluid resuscitation with albumin or saline was shown to increase the absolute risk of death** at 48 hours by **3.3** % and the risk of death, neurologic sequelae, or both at 4 weeks by **4%**.

The cause of excess deaths was **primarily refractory shock and not fluid overload.**

These features are consistent with a potential **cardiotoxic or ischemia-reperfusion injury** following resuscitation with boluses of intravenous fluid.

Myburgh and Finfer BMC Medicine 2013, 11:67

… **interruption of genetically determined catecholamine-mediated host defense responses** by the rapid increase in plasma volume, which might result in a ***reperfusion injury.***

….. transient hypervolemia or hyperosmolality **might exacerbate capillary leak** in patients who are susceptible to intracranial hypertension or pulmonary edema, with fatal consequences.

Myburgh JA N Engl J Med 2011;364:2543-44

The pathophysiology of ***the host response to stress*** includes activation of the neurohumoral system that is targeted at **conserving both sodium and water**.

The **amount and type of fluid administered** by clinicians to critically ill patients ***affects this acute adaptative response*** and , through this, may affect subsequent survival and recovery.

Saxena MK Crit Care Res 2013 15; 2:75-76

…**discontinuation of the practice of bolus- fluid resuscitation** in patients with febrile illness due to medical causes and impaired perfusion or compensated shock **must be recommended**.

Myburgh JA N Engl J Med 2011;364:2543-44

A critique of fluid bolus resuscitation in severe sepsis

Hilton and Bellomo Critical Care 2012, 16:302

…. recommendations are only based on **expert opinion** and **lack adequate experimental or controlled human evidence**.

Fluid resuscitation for people with sepsis.

It’s time to challenge our basic assumptions

Another question we must consider is whether fluid resuscitation to maintain cardiac output is the right thing to do in the first place.

Brown SGA BMJ. 2014 Jul 22;349:g4611

Fluid resuscitation in **septic shock**: a positive fluid balance and elevated CVP are associated with increased mortality

Boyd A Crit Care Med 2011; 39:259 –265

Emerging data from basic and clinical science have *challenged* the **dogma of large-volume fluid resuscitation** in ***trauma***.

Douzinas EE Crit Care Med 2012 Vol. 40, No. 4

Current evidence indicates that initial **liberal fluid resuscitation** strategies *may be* associated with **higher mortality** in injured patients.

Wang CH et al Crit Care Med. 2014 Apr;42(4):954-61

It is time to go back to basics and challenge our entrenched assumption that fluid resuscitation is beneficial for people in septic shock, rather than continue to argue over which fluid works best.

Brown SGA BMJ. 2014 Jul 22;349:g4611

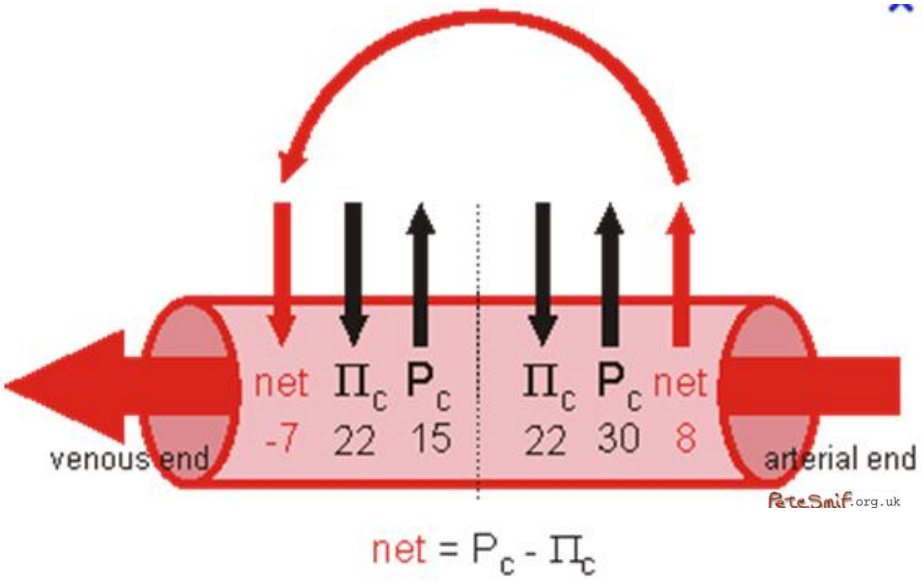
RSE&GM

Revised Starling equation (**RSE**) and the glycocalyx model (**GM**) of transvascular fluid exchange: **an improved paradigm for prescribing intravenous fluid therapy**

WoodcockTE, Woodcock TM
British Journal of Anaesthesia 108 (3): 384–94 (2012)

Levick R, Michel CC
Cardiovascular Research (2010) 87, 198–210

Driving pressure across capillary wall



$$J = K_f ([P_c - P_i] - \sigma [\Pi_c + \Pi_i])$$

K_f(P_{HS} capillary - P_{HS} interst) - σ(P_o capillary - P_o interst)

P_c= hydrostatic capillary pressure

P_i= hydrostatic interstitial pressure

Π_c = oncotic capillary pressure

Π_i= oncotic interstitial pressure

K_f = filtration co-efficient

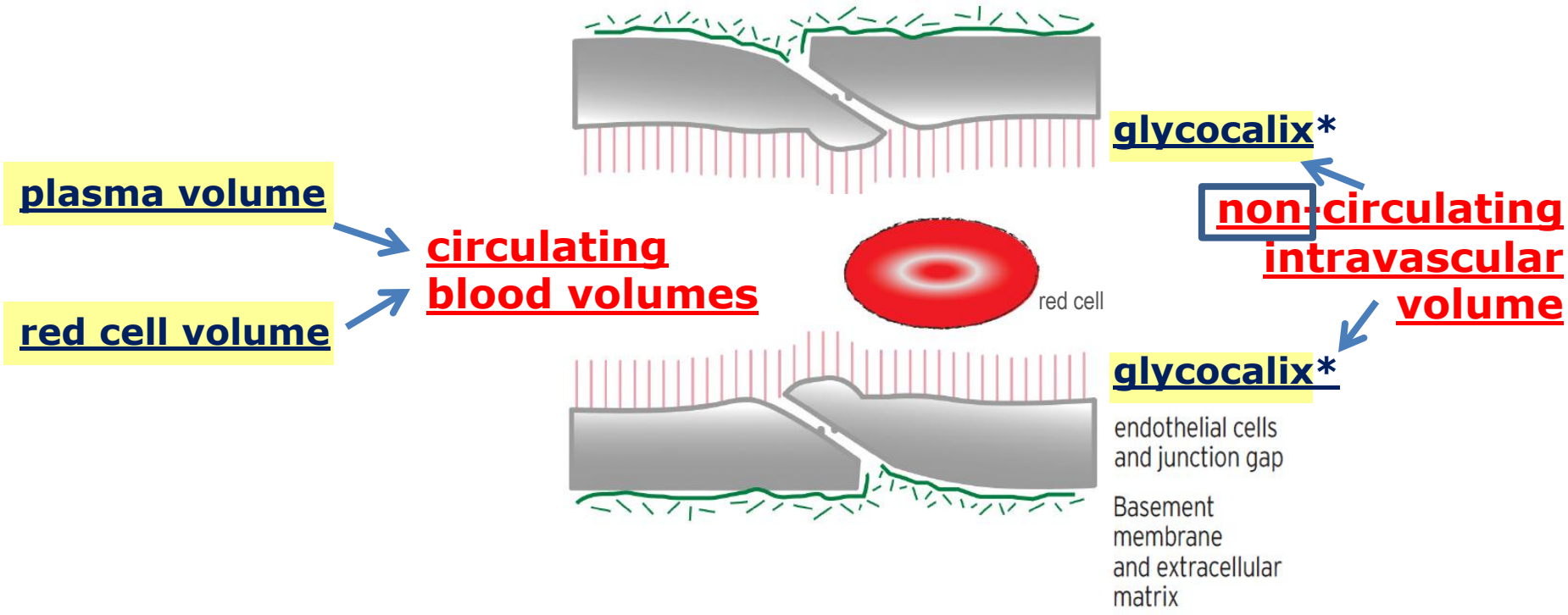
σ = reflection co-efficient

…a negatively charged, extracellular coating that has a mesh-like structure of glycoproteins, proteoglycans, glycosaminoglycans, and plasma proteins including albumin.

Brown SGA BMJ. 2014 Jul 22;349:g4611

There are three intravascular volumes:

- plasma volume
- red cell volume
- glycocalix



* *1.5 litres of the intravascular volume in health*

from Woodcock, modified

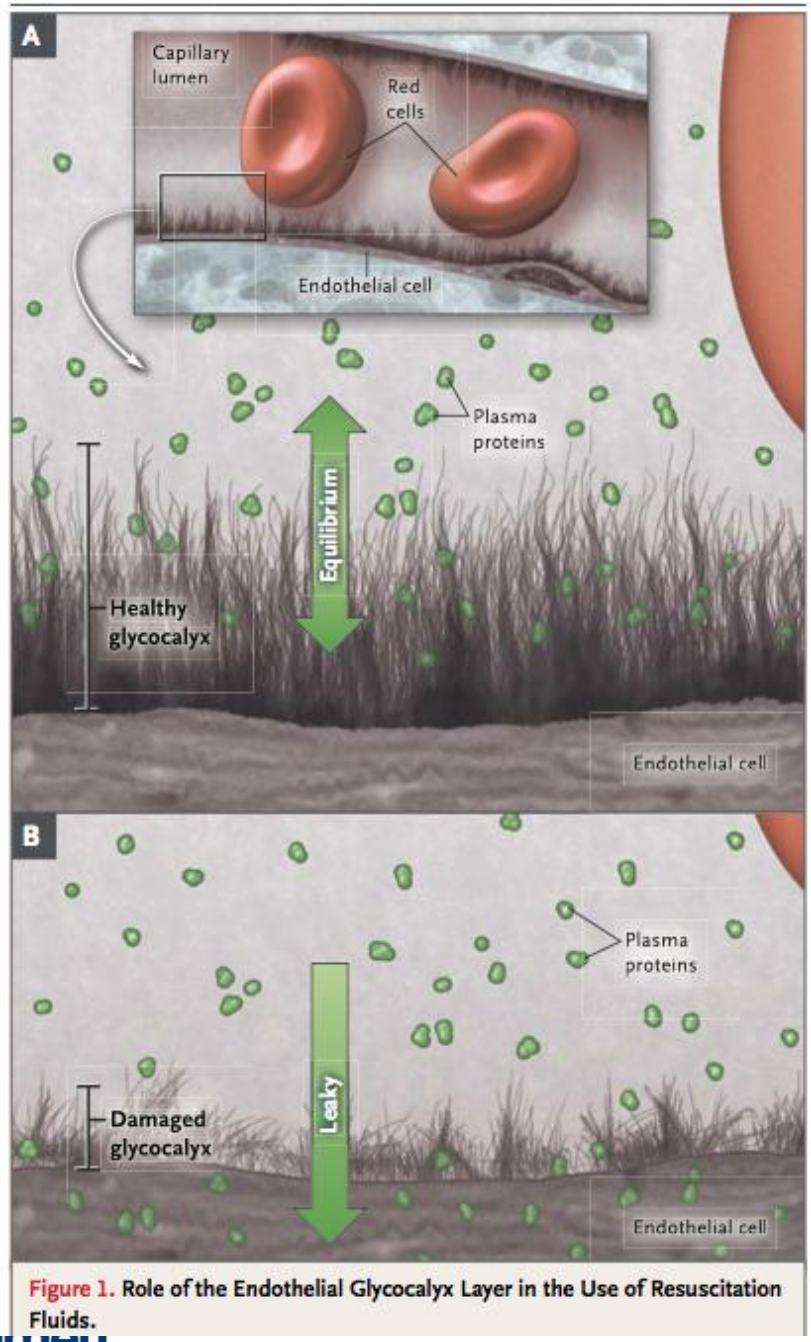


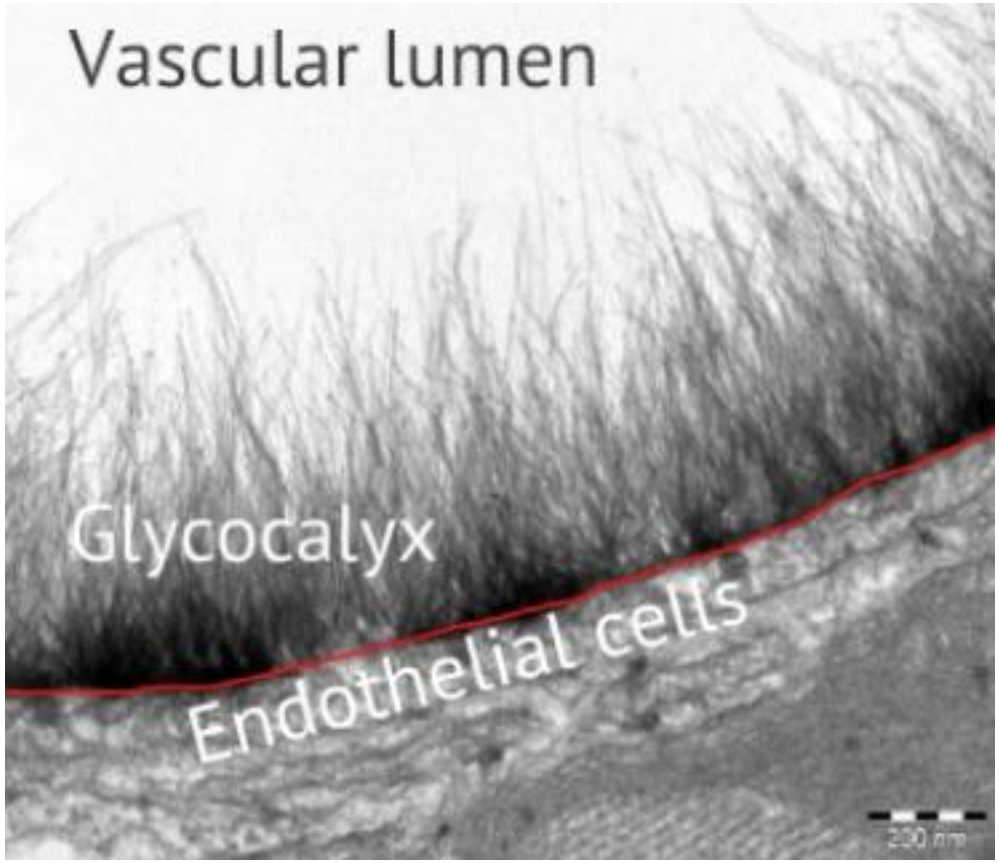
Figure 1. Role of the Endothelial Glycocalyx Layer in the Use of Resuscitation Fluids.

endothelial glycocalyx layer, a web of membrane-bound glycoproteins and proteoglycans on endothelial cells, key determinant of membrane permeability in various vascular organ systems.

healthy endothelial glycocalyx layer

damaged endothelial glycocalyx layer

N Engl J Med 2013;369:1243-51.


Vascular lumen
Glycocalyx
Endothelial cells
200 nm

Proposed functions include

- **maintenance of the vascular permeability** barrier
  mediation of shear-stress-dependent nitric oxide production
  retention of vascular protective enzymes (e.g. superoxide dismutase)
- **retention of coagulation inhibition factors** (e.g. antithrombin, the protein C system and tissue factor pathway inhibitor)
- **modulation of the inflammatory response** by preventing leukocyte adhesion and binding various ligands (e.g. chemokines, cytokines and growth factors)

Capillary leak

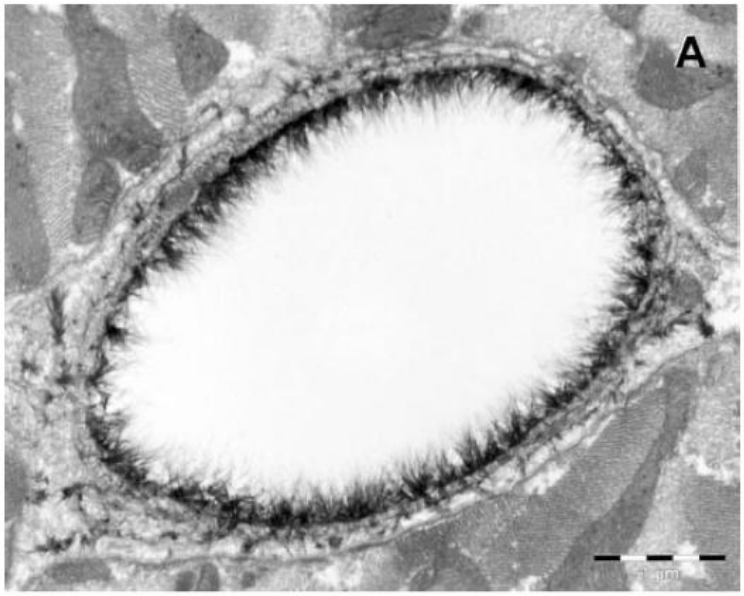
Oedema

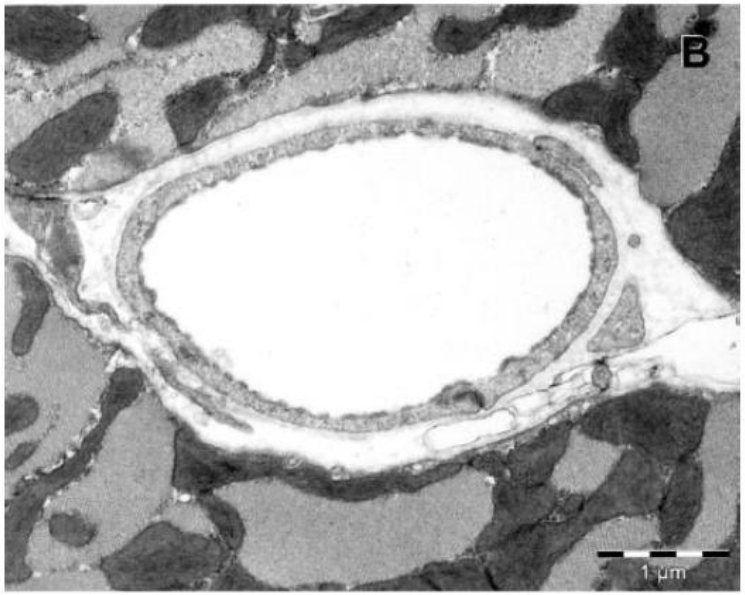
Inflammation

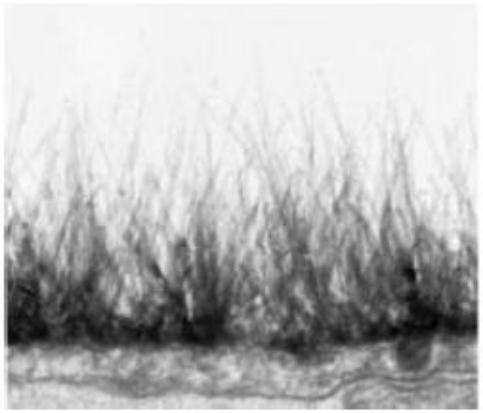
Hypercoagulation

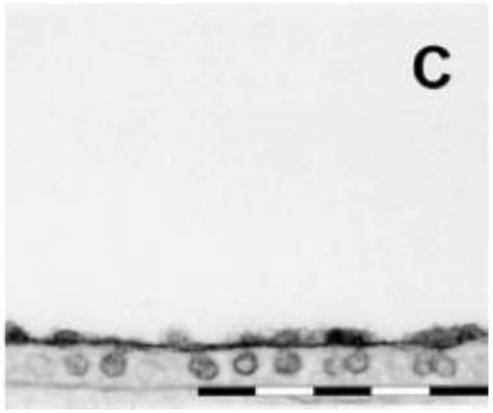
Platelet hyperaggregation

Loss of vascular responsiveness









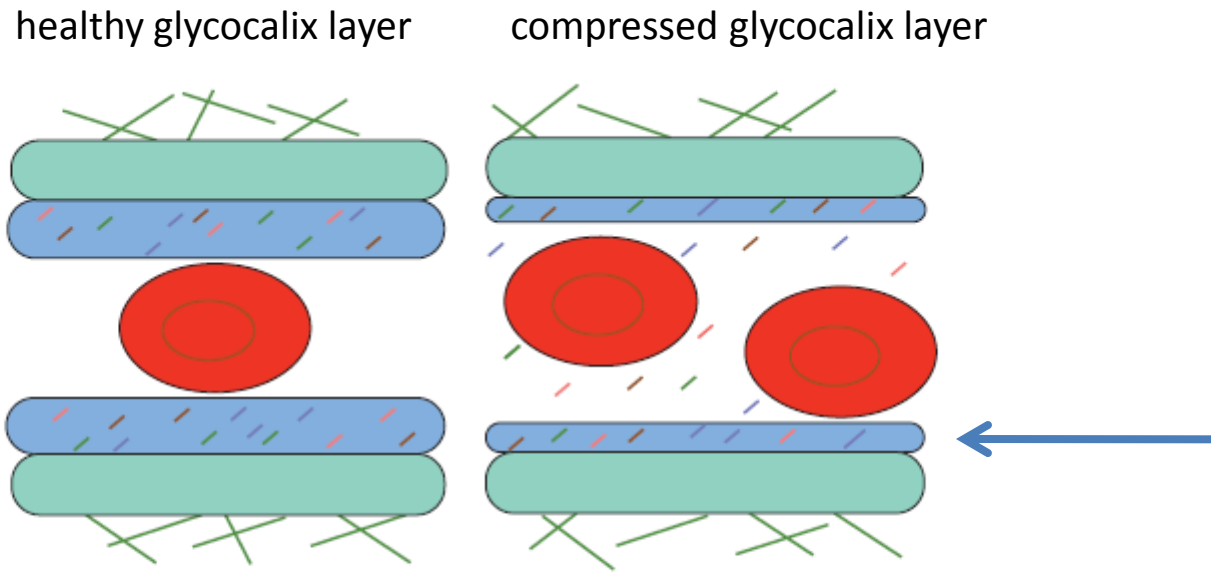
The glycocalyx is a fiber matrix of proteoglycans and glycoproteins lining the luminal aspect of capillaries.

It contains several types of glycosaminoglycans and is only semi- permeable to albumin, so that filtered fluid within the interendothelial clefts is almost albumin free.

Van den Berg BM et al. Circ Res. 2003;92:592-594.

It is hydrophilic, helps maintain the function of the endothelial barrier, provides a range of immunomodulating functions, and **inhibits coagulation**.

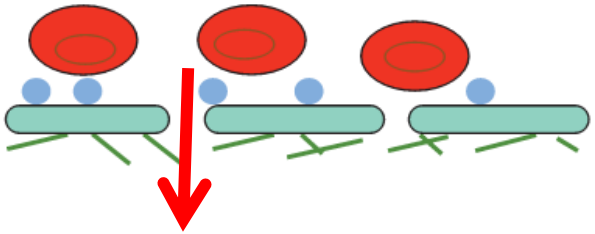
Brown SGA BMJ. 2014 Jul 22;349:g4611



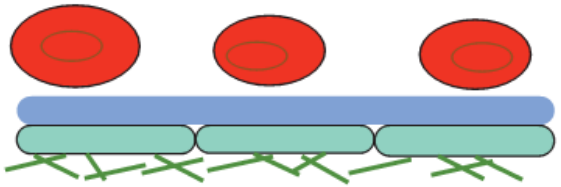
Compaction of the glycocalyx layer increases plasma volume and the red cell dilution volume independently of changes in intravascular volume.

Woodcock TE, Woodcock TM British Journal of Anaesthesia 108 (3): 384–94 (2012)

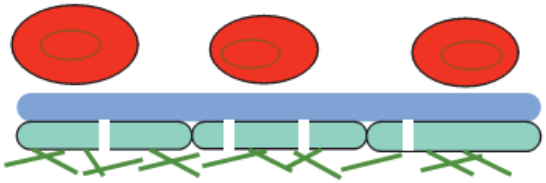
Sinusoidal
(***liver***, spleen, marrow)



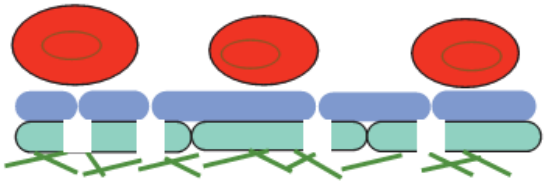
Non-fenestrated
(***CNS***, muscle, connective, ***lung***)



Fenestrated
(endocrine, choroid plexus, ***gut*** *mucosa*)



Fenestrated
(***glomerular***)



Woodcock TE, Woodcock TM British Journal of Anaesthesia 108 (3): 384–94 (2012)

- ***nonfenestrated capillaries*** normally ***filter fluid*** to the ISF throughout their length.

- ***absorption*** **through venous capillaries and venules *does not occur*.**

- ***COP opposes, but does not reverse, filtration.***

- ***most of the filtered fluid returns to the circulation as lymph.***

British Journal of Anaesthesia 108 (3): 384–94 (2012)

Plasma proteins, including *albumin*, escape to the interstitial space by a relatively small number of large pores, which are responsible for the **increased transcapillary flow (Jv**) observed in the early stage of **inflammation**.

British Journal of Anaesthesia 108 (3): 384–94 (2012)

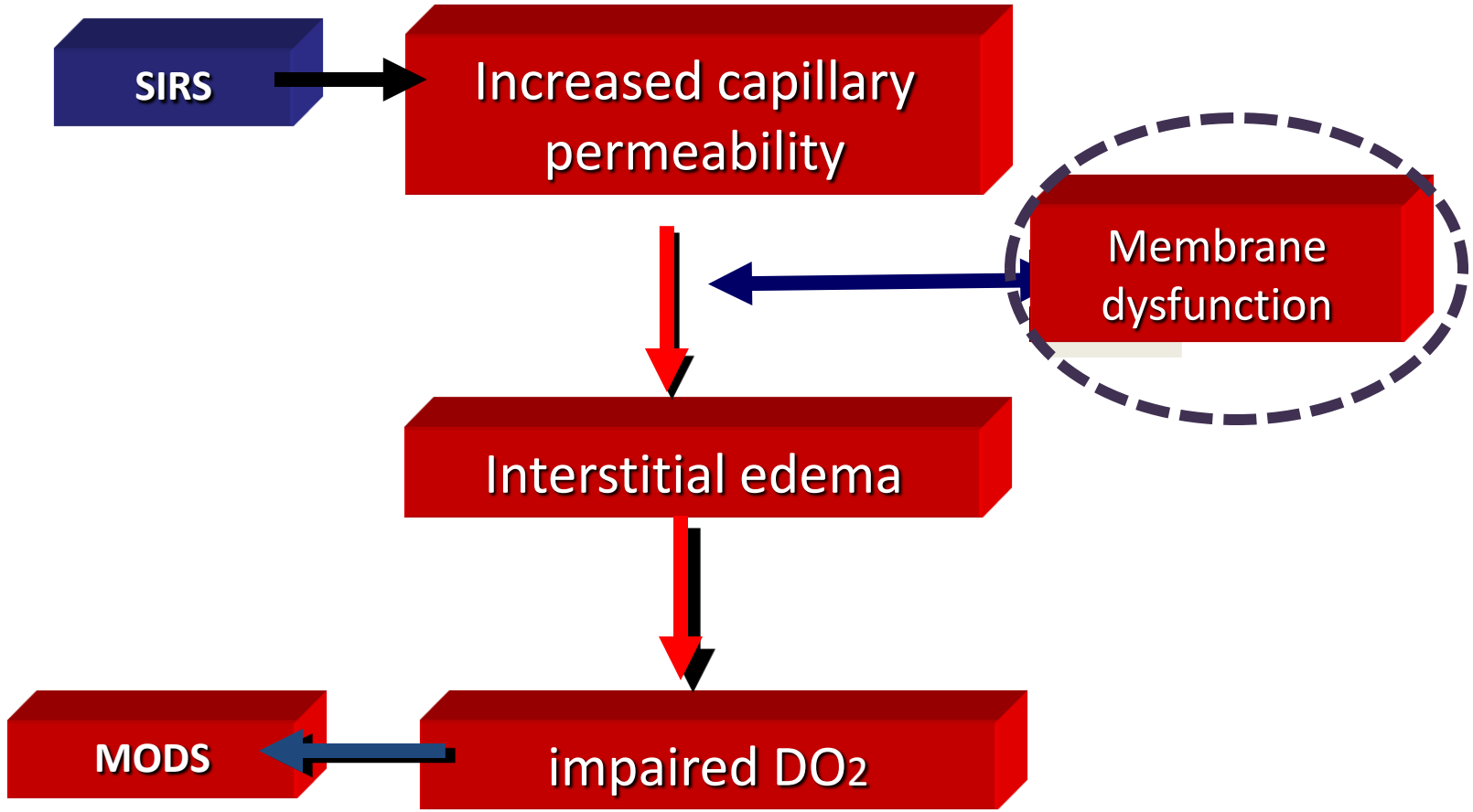
It appears, on the evidence from human studies to date, that the ***EGL is compromised in systemic inflammatory states*** such as

diabetes, hyperglycaemia, surgery, trauma, and ***sepsis***

Br J Anaesth 108 (3): 384–94 (2012)

A range of insults has been associated with **degradation of the glycocalyx**, including inflammatory mediators or even natriuretic peptides associated with acute iatrogenic hypervolaemia.

Edwards and Mythen Extreme Physiology & Medicine 2014, 3:16


SIRS
Increased capillary permeability
Membrane dysfunction
Interstitial edema
impaired DO2
MODS

Rapid crystalloid infusion in volunteers results in elevated plasma levels of hyaluronic acid and may therefore be injurious

Woodcock TE, Woodcock TM British Journal of Anaesthesia 108 (3): 384–94 (2012)

Acute myocardial infarction is associated with endothelial glycocalyx and cell damage and a parallel increase in circulating catecholamines

Ostrowski SR *Critical Care* 2013, **17**:R32 doi:10.1186/cc12532

Rapid infusion of fluids has been linked with glycocalyx degradation.

Brown SGA BMJ. 2014 Jul 22;349:g4611

Effects of glycocalyx damage:

- capillary leak
- edema
- **hypercoagulability**
- inflammation
- loss of vascular responsiveness
- **platelet aggregation**

Tradizionalisti → Omeostasi

Modernisti

Post-modernisti → **Allostasi**

The ***allostatic concept*** emphasizes that the *brain predicts the most likely demand during a stress response*, and therefore modifies physiological variables to **values that match anticipated demand.**

Healthy **physiological values routinely targeted** in the critically ill are not related to these anticipatory demands and are thus likely to be **inappropriate**.

Cuesta JM, Singer M Crit Care Med 2012; 40:1-7

A more efficient strategy is for the brain to continuously moni-tor many parameters and use its stored knowledge to ***predict what values will most likely be needed***; then it sets them promptly by controlling the neuroendocrine and autonomic systems. This strategy of predictive regulation has been termed ***allostasis***, meaning "**stability through change**."

Sterling P JAMA Psychiatry 2014 71;10: 1192-93

Il problema ETIC

Early trauma induced coagulopathy

ATC

Acute Traumatic Coagulopathy

J Trauma 2003; 54:1127–1130

severe multitrauma

systemic inflammatory response

lethal triad

hypothermia, coagulopathy, and acidosis

Coagulopathy on admission is associated with a 25–40% mortality in the trauma population

Feinman M et al Curr Opin Crit Care 2014, 20:366 – 372

INJURY-RELATED FACTORS CONTRIBUTING TO ACUTE TRAUMATIC COAGULOPATHY

Consumption and loss

Dilution *(Dilution is aggravated by replacement of lost whole blood with crystalloid, colloid and red cell transfusion)*

Hormonal and cytokine-induced changes

Hypoxia, acidosis and hypothermia

Immune system activation

Cap A, Hunt B. Curr Opin Crit Care 2014, 20:638 – 645

Although early trauma-induced coagulopathy (ETIC) was more prevalent in severely injured patients, patients with an injury severity score less than 16 still had an 11% incidence of ETIC.

Macleod JB et al. Injury 2014; 45:910 – 915

Early dysfunction and decrease in activity of clotting factors is, ***in part***, due to **hemodilution**.

It is postulated that **decreasing the amount of crystalloid** administration early in trauma can help prevent this phenomenon.

Shaz BH et al. J Trauma 2011; 70:1401 – 1407

…investigators have suggested that **much of the decrease in coagulopathy and mortality** from hemorrhage attributed to massive transfusion protocols and higher plasma and platelet ratios is actually a result of a ***decrease in early crystalloid volumes***

Duchesne JC et al J Trauma Acute Care Surg 2013;75:76 – 82.

Holcomb JB et al. The PRospective && Observational Multicenter Major Trauma Transfusion (PROMMTT) study. J Trauma Acute Care Surg 2013; 75 (Suppl 1):S1–2.

--->*PROPPR study.*

Dilution is aggravated by replacement of lost whole blood with crystalloid, colloid and red cell transfusion.

The **volume of fluid** administered both in vitro and in vivo is proportional to the resultant coagulopathy.

Cap A, Hunt B. Curr Opin Crit Care 2014, 20:638 – 645
Maegele M et al. Injury 2007; 38:298 – 304
Bolliger D et al. Br J Anaesth 2009; 102:793 – 799

Prehospital use of nonsteroidal anti- & inflammatory drugs (NSAIDs) is associated with a reduced incidence of trauma-induced coagulopathy.

Neal MD et al. Ann Surg 2014.

.

Prehospital NSAID use was independently associated with a 72% lower risk of trauma-induced coagulopathy (TIC), providing additional evidence that TIC and inflammation are linked.

Hemostatic resuscitation than with traditional methods **does not seem to correct hypoperfusion or coagulopathy during acute traumatic hemorrhage**. Lactate levels remain elevated and coagulopathy parameters remain deranged until bleeding is controlled.

Hemostatic resuscitation is neither hemostatic nor resuscitative in trauma hemorrhage.
Khan S et al. J Trauma Acute Care Surg 2014; 76:561–568.

Prehospital intravenous **fluid administration** is associated with **higher mortality** in trauma patients: a National Trauma Data Bank analysis.

Haut ER et al Ann Surg 2011; 253:371 – 377

Although a definitive cut-off amount is yet to be determined, **aggressive i.v. fluid resuscitation in the prehospital setting should be avoided**, with studies suggesting that a restrictive fluid strategy should be employed.

Feinman M et al Curr Opin Crit Care 2014, 20:366 – 372

ED crystalloid resuscitation of

1.5 l or more

is associated with increased mortality in elderly and nonelderly trauma patients.

Ley EJ et al. J Trauma 2011; 70:398–400

"Should we just carry on doing ***what we have always done***, which is essentially giving **too much fluid**?"

"Or should we make some effort to be a bit more thoughtful in what we are doing and r**educe the amount of fluid?**

Finfer S Issue 1 18 March 2014 ISICEM News

Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis (**VISEP**) trial *(HES 200/0.5-0.6)*

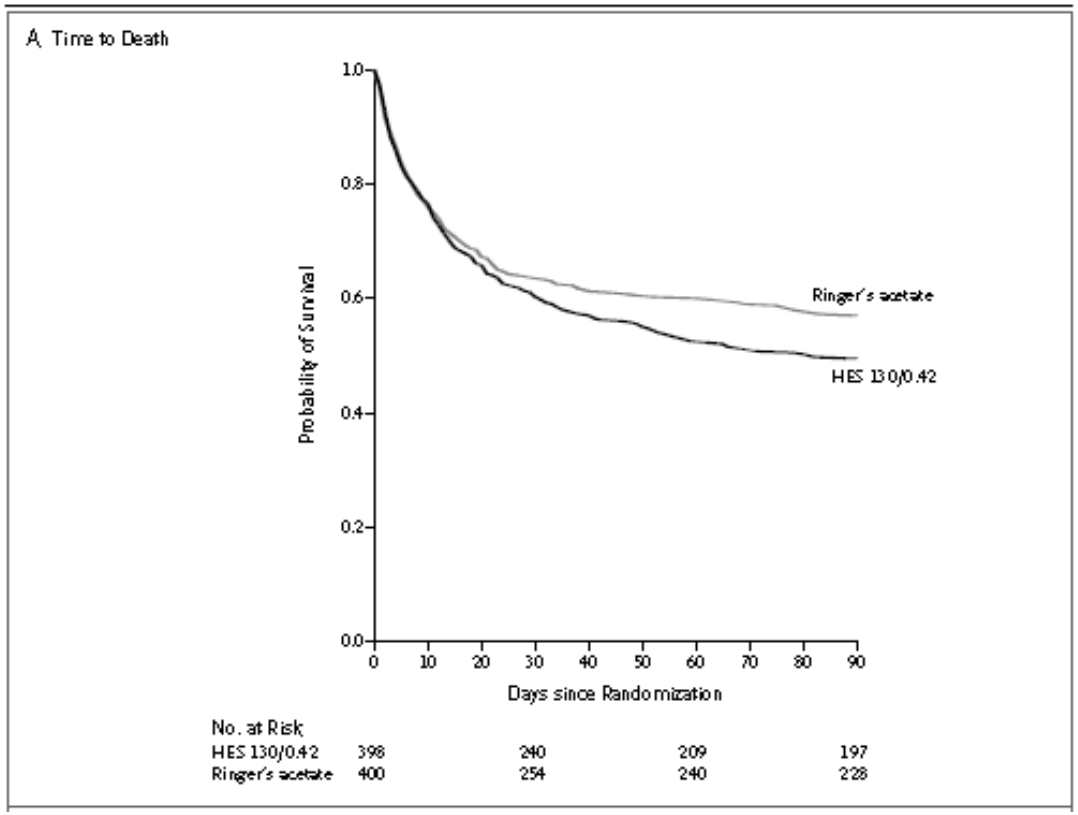
….***stopped early for safety reasons***.

N Engl J Med. 2008;358:125-139

…from 6% *HES 130/0.4* to 4% *gelatins* to *crystalloids* only

Fluid resuscitation with *only crystalloids* was **equally effective**, resulted in a more positive fluid balance only on the first 2 days, and was associated with a **lesser incidence of acute kidney injury**.

Bayer 0 et al. Crit Care Med 2011; 39:1335–1342



Scandinavian
Starch for **S**evere
Sepsis/**S**eptic
Shock Trial

(**6S**)

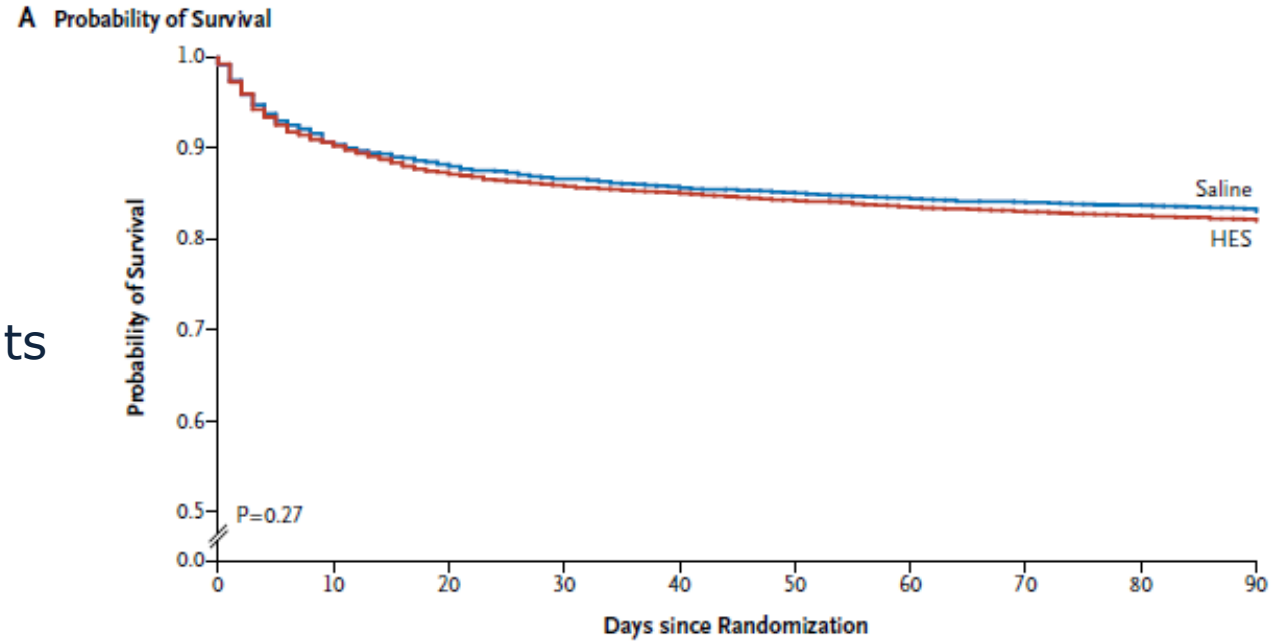
804 patients with severe sepsis

HES 130/0.42 vs. Ringer's acetate

<u>increased risk of death at day 90</u> and more likely to require renal-replacement therapy

Perner A et al. N Engl J Med 2012;367:124-34.

7000 ICU patients



…**not evidence that resuscitation with 6% HES (130/0.4), as compared with saline, in the ICU provides <u>any clinical benefit to the patient</u>.**

…**<u>increased rate of renal replacement therapy</u>.**

CHEST Myburgh J et al NEJM 2012;367(20):1901-1911.

ESICM Consensus statement

We **recommend**

not to use HES with molecular weight ≥200 kDa and/or degree of substitution 0.4 in patients with ***severe sepsis or risk of acute kidney injury***

and **suggest not to use 6% HES 130/0.4 or gelatin** in these populations.

…**not to use colloids in patients with head injury** and not to administer gelatins and HES in organ donors.

Intensive Care Med (2012) 38:368–383

…**no evidence** from RCTs that resuscitation with **colloids reduces the risk of death**, compared to resuscitation with crystalloids…

…the use of **HES might increase mortality.**

…**it is hard to see how their continued use in clinical practice can be justified**.

Cochrane Database of Systematic Reviews, 28 feb **2013**, Issue 2.

…unlikely therefore that HES provides **overall clinical benefit for patients with sepsis.**

Haase N, Perner A et al BMJ 2013;346:1839

In acutely ill surgical and intensive care patients, fluid resuscitation with **6 % HES 130 increased the use of renal replacement therapy and mortality**.

Gattas DJ et al. Intensive Care Med (2013) 39:558-568

Clinical use of HES for acute volume resuscitation is not warranted due to **serious safety concerns.**

Zarychanski R et al JAMA. 2013;309(7):678-688

….no data from high-quality trials showing that 6 % HES 130 improves any patient-important outcome, and there are **clear signals of harm.**

Perner A, Reinhart K Intensive Care Med (2013) 39:782–783

6 % HES as part of initial fluid resuscitation for severe sepsis was associated with **harm and, as alternatives exist, in our view <u>should be avoided.</u>**

Patel A et al. Intensive Care Med may 2013,39:811-822

Fluid resuscitation practice with HES is associated with an **increase in AKI incidence, need of RRT, RBC transfusion, and 90-day mortality in patients with sepsis.**

Serpa Neto A et al J Crit Care. 2014 Feb;29(1):185.e1-7.

The CRISTAL Randomized Trial
Effects of Fluid Resuscitation With Colloids vs Crystalloids on Mortality in Critically Ill Patients Presenting With Hypovolemic Shock

open- labeled fluids
recruitment period of 9 years

INTERVENTIONS Colloids (n = 1414; gelatins, dextrans, hydroxyethyl starches, or 4% or 20% of albumin) or crystalloids (n = 1443; isotonic or hypertonic saline or Ringer lactate solution) for all fluid interventions other than fluid maintenance throughout the ICU stay.

Among ICU patients with hypovolemia, the use of colloids compared with crystalloids **did not result in a significant difference in 28-day mortality.**

Annane D et al. JAMA 2013;310:1809-17

…***HES solutions should not be used for more than 24 hours*** and t patients' kidney function should be monitored for at least 90 days.

In addition, the PRAC requested that further studies be carried out on the use of these medicines in ***elective surgery and trauma patients.***

EMA 11.11.2013

To the Executive Director of the European Medicines Agency

We are concerned that the European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee's (PRAC) recent conclusions on the use of hydroxyethyl starch (HES) **will result in harm to patients**.

R. Bellomo
J. Bion
S. Finfer
J. Myburgh
A. Perner
K. Reinhart
on behalf of all co-signatories

Br J Anaesth 2014 Mar;112(3):595-600

Counter statement to open letter to the Executive Director of the European Medicines Agency concerning the licensing of hydroxyethyl starch solutions for fluid resuscitation.

BJA doi:10.1093/bja/aeu217

Retrospective analyses in observational studies found the use of **gelatin** to be associated with ***increased renal impairment*** and the ***need for transfusion products*** in patients with severe sepsis and cardiac surgery.

Considering that the use of non-protein colloids is not associated with improved clinical outcomes, potentially **harmful effects of gelatins should be carefully explored**

Thomas-Rieddel Intensive Care Med (2012) 38:1134–1142

All of the evidence was of very low quality.

NICE Intravenous Fluid therapy, dec 2013

Albumin

…in view of the **absence of evidence of a mortality benefit** from albumin and the **increased cost** compared to alternatives such as saline, it would seem reasonable that albumin should ***only be used within the context of well concealed and adequately powered RCT*.**

Cochrane Database of Systematic Reviews. 11, 2012

SAFE (**S**aline *vs* **A**lbumin **F**luid **E**valuation) Study.

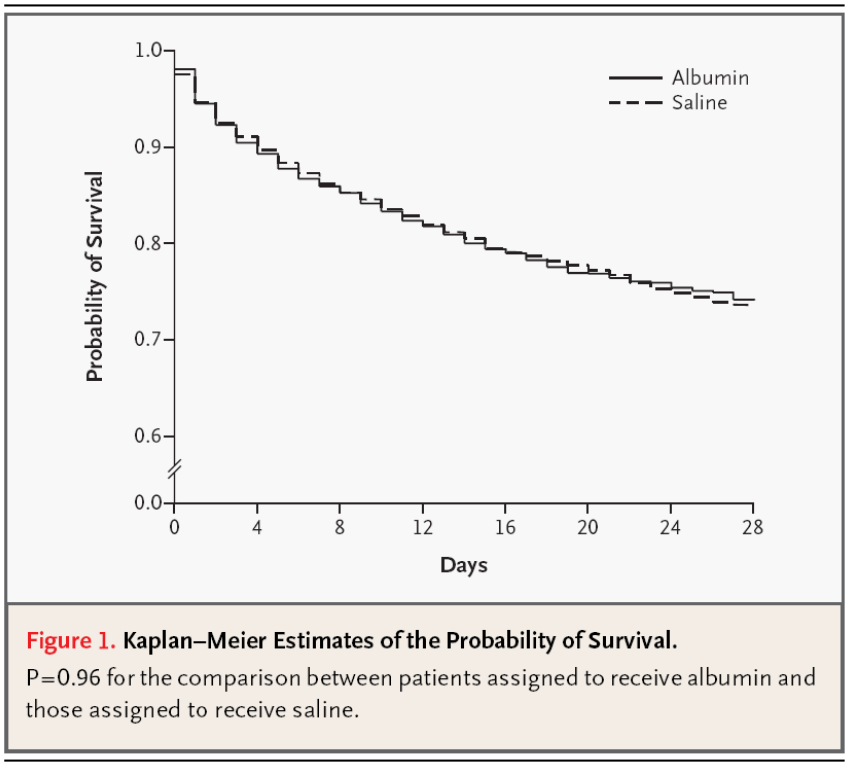


Figure 1. Kaplan–Meier Estimates of the Probability of Survival.
P=0.96 for the comparison between patients assigned to receive albumin and those assigned to receive saline.

In patients in the ICU, use of either 4 % **albumin** or normal **saline** for fluid resuscitation results in **similar outcomes at 28 days**

SAFE N Engl J Med 2004, 350:2247-56

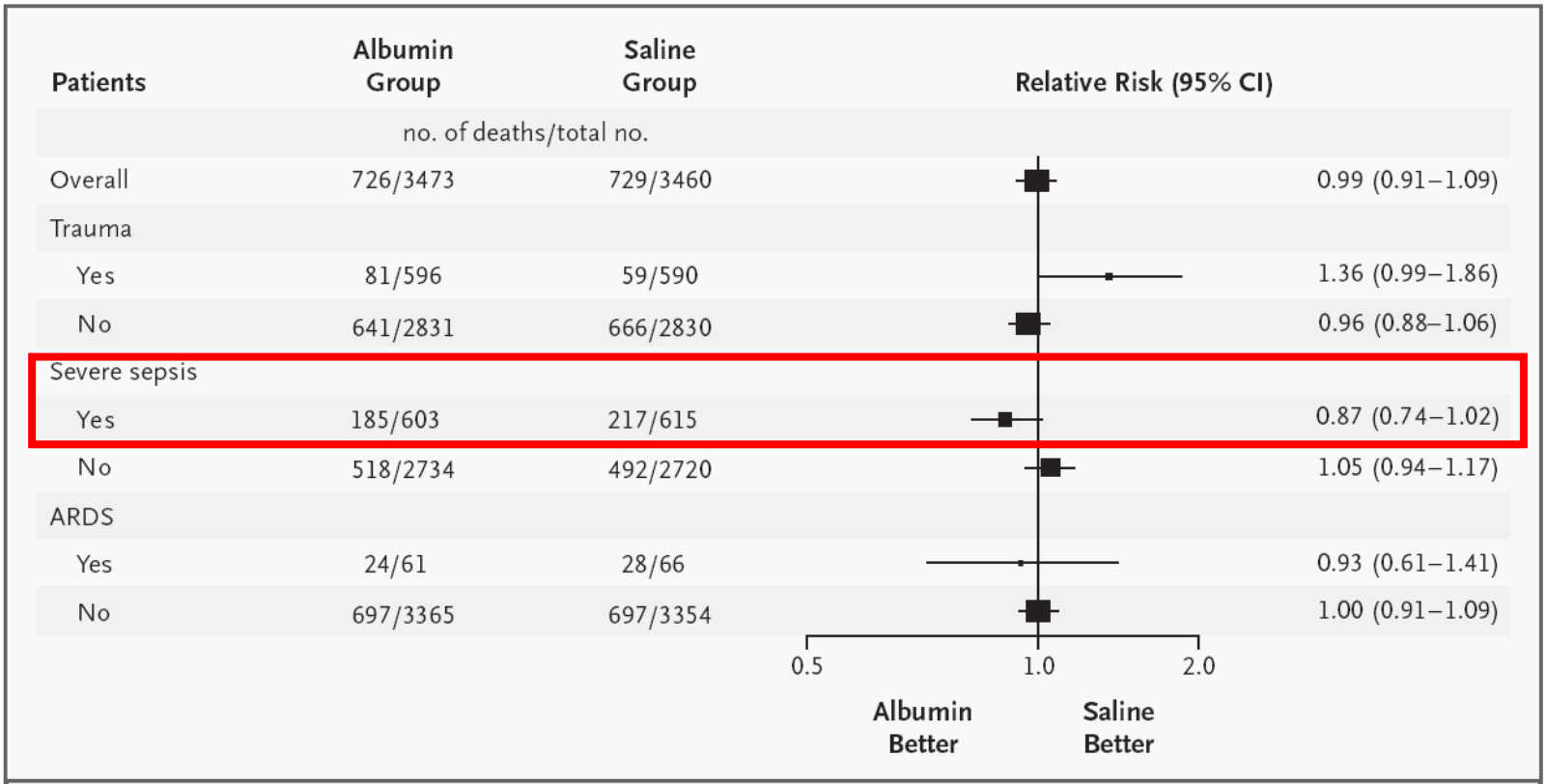


Figure 2. Relative Risk of Death from Any Cause among All the Patients and among the Patients in the Six Predefined Subgroups.

The size of each symbol indicates the relative number of events in the given group. The horizontal bars represent the confidence intervals (CI). ARDS denotes the acute respiratory distress syndrome.

SAFE N Engl J Med 2004, 350:2247-56

Less SAFE than presumed?

In this post hoc study of critically ill patients with ***traumatic brain injury***, fluid resuscitation with albumin was associated with higher mortality rates than was resuscitation with saline.

Crit Care Med 2011 Vol. 39, No. 6:1584-85

Neither of these differences in these subgroups reached statistically significance even without correction for multiple testing**.**

NICE Intravenous Fluid therapy, dec 2013

ALBIOS

Albumin Replacement in Patients with Severe Sepsis or Septic Shock

Caironi P et al. N Engl J Med 2014; 370:1412-1421

In patients with severe sepsis, albumin replacement in addition to crystalloids, as compared with crystalloids alone, **did not improve the rate of survival at 28 and 90 days**.

Post hoc univariate and multivariate analyses of data from the 1121 patients with ***septic shock showed significantly lower mortality at 90 days in the albumin group***.

Conversely, in the subgroup of patients with ***severe sepsis without shock, mortality appeared to be higher among those who were treated with albumin***.

Caironi P et al. N Engl J Med 2014; 370:1412-1421

Randomised trials of human albumin for adults with sepsis

As part of fluid volume expansion and resuscitation (with or without improvement of baseline hypoalbuminaemia), pooled human albumin solutions **did not reduce all-cause mortality in adults with sepsis of any severity, including septic shock**, in the critical or intensive care setting
A signal towards harm was not detected.

Patel A. BMJ. 2014 Jul 22;349:g4561.

Saline is not “physiologic”

The forgotten ion: chloride

The end of saline solutions?

Lactated Ringer's solution is perfectly reasonable as an alternative, and if clinicians were to make that change, one would expect to see a drop in the rate of AKI and dialysis.

J.Kellum

A chloride-restrictive intravenous fluid strategy has been shown to be associated with decreased renal injury in a pre– and post–intensive care unit

Yunos NM et al. JAMA. 2012;308:1566-72.

the prevailing hypothesis is that their superiority is due to hyperchloremia's potential to induce renal vasoconstriction.

Among critically ill adults with sepsis, resuscitation with **balanced fluids** was associated with a lower risk of in-hospital mortality. If confirmed in randomized trials, this finding could have significant public health implications, as crystalloid resuscitation is nearly universal in sepsis.

Raghunatan K et al *Crit Care Med* 2014; 42:1585–1591

Where Is the Balance?

Which crystalloid should clinicians use as we await more definitive evidence?

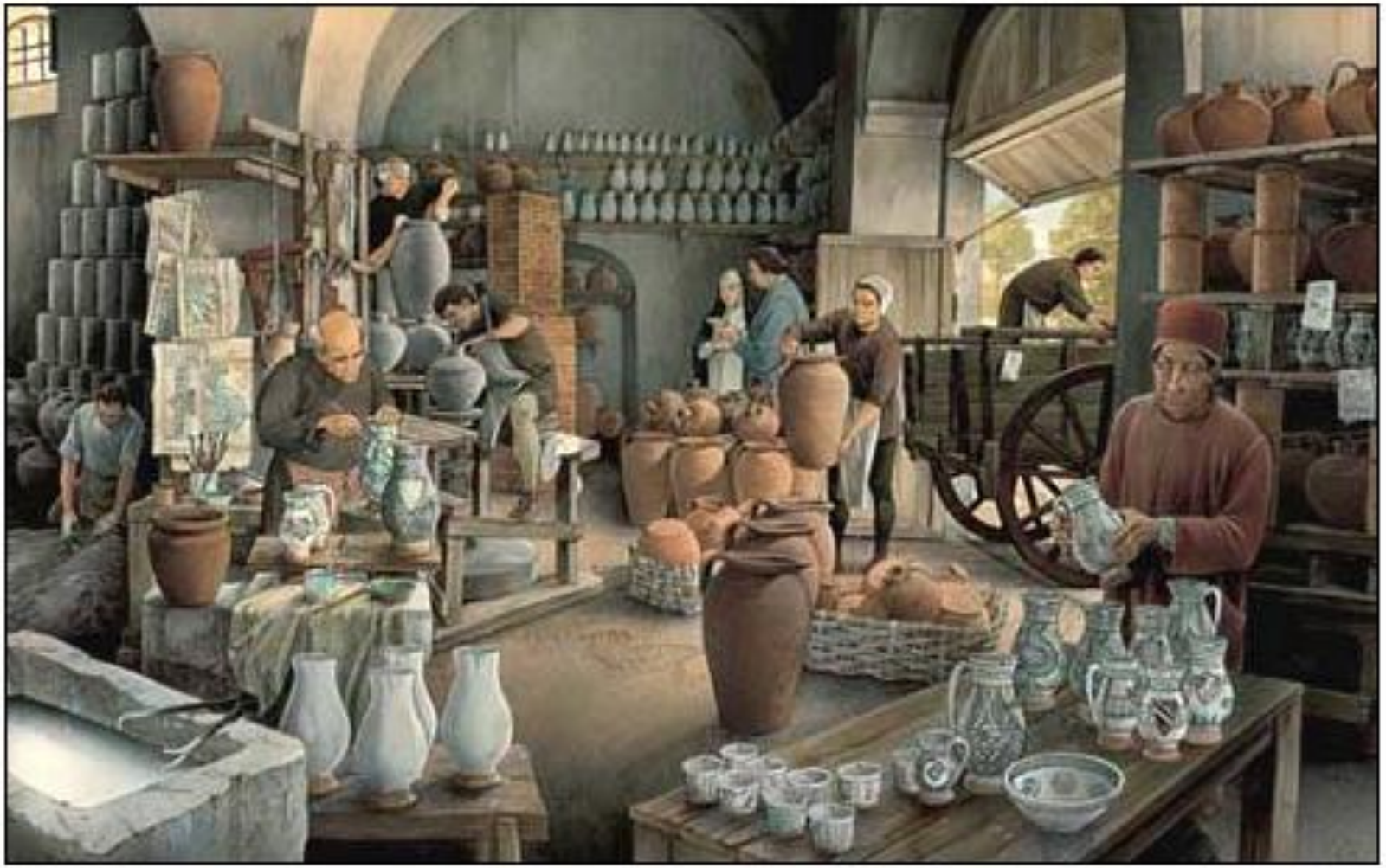
Some might argue that, because nothing indicates that unbalanced is better than balanced, balanced solutions should be the choice.
Perhaps we should use balanced crystalloids just to resuscitate patients with shock who are likely to require large quantities of fluids?

Dellinger Ann Intern Med 2014

Saline versus plasma-lyte A in initial & resuscitation of trauma patients: a randomized trial.

Young JB et al. Ann Surg 2014; 259:255– 262

This is the first randomized controlled trial to compare normal saline to plasma-lyte for the resuscitation of trauma patients. Patients given plasma-lyte A had improved acid-base status and less hyperchloremia at 24 h after injury. Additional studies are needed to determine if these laboratory findings translate into mortality benefit.



	ml	€
NaCl 0,9%	1000	0.72
NaCl 0,9%	500	0.43
Ringer Ac	500	0.48
Voluven 500 ml	500	6.27
Alb 20% 50 ml	20	15.20
Emagel 500 ml	500	3.69

AOU, Udine, Italy 2012