Critical Care

FAST FACTS

A brief refresher with useful tables, figures, and research summaries

Resuscitation Fluids and Blood Transfusion

Intravascular volume repletion is crucial to resuscitating critically ill adults. Fluids, electrolytes, and blood products have historically been given liberally because they were considered natural and essential elements of human physiology, but increasingly we are recognizing that, like other medications, they must be administered with careful consideration of indication, type, dose, frequency, and adverse effects. In this section, we review the following topics:

- Resuscitation Fluids
- Blood Transfusion

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Resuscitation Fluids

An ideal intravenous (IV) fluid does not exist for all situations, but data gathered over the past 15 years have transformed our understanding of safe and appropriate fluid resuscitation. Keep the following evidence-based principles in mind as you select the best option for your patient:

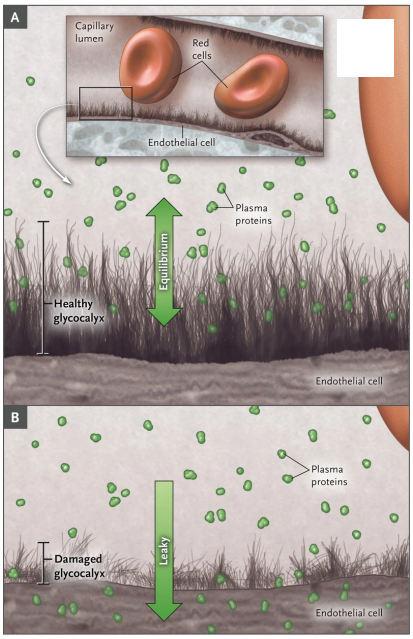
1. Colloids are not superior to crystalloids in most cases and may be harmful in some situations.

- Colloids, such as albumin and blood, exert higher oncotic pressure and theoretically are retained entirely in the vasculature. Consequently, to achieve the same hemodynamic change, a smaller amount of colloid than crystalloid should be required (often described in a 1:3 ratio). However, in practice, the observed difference is smaller, likely due to increased vascular permeability (see figure below).
- Albumin also has theoretical benefits of being an antioxidant, an anti-inflammatory, a carrier for drugs, and an acid–base buffer. Derived from blood, it is expensive to produce and distribute.
- Because data from a meta-analysis suggested that giving albumin-containing fluid increased mortality, investigators conducted the randomized SAFE trial that compared 4.0% albumin and 0.9% normal saline in approximately 7000 adult ICU patients and found no difference in 28-day mortality.
- A post-hoc analysis of the SAFE trial in patients with traumatic brain injury showed higher 24-month mortality with albumin.
- Because results from the SAFE trial suggested a possible benefit from albumin in the subgroup of patients with severe sepsis, the ALBIOS trial compared 20% albumin plus crystalloid versus crystalloid alone in ICU patients with severe sepsis. Subgroup analysis suggested a

benefit from albumin in patients with septic shock, compared with patients without septic shock.

- Semisynthetic colloids were created to circumvent the availability and expense of albumin. However, one semisynthetic colloid, hydroxyethyl starch (HES), has been associated with increased mortality and adverse events. HES is not recommended for fluid resuscitation, and other semisynthetic colloids should be used with caution.
- Albumin is beneficial in select situations, such as reducing the incidence of renal impairment and death in patients with cirrhosis and spontaneous bacterial peritonitis.

Role of the Endothelial Glycocalyx Layer in the Use of Resuscitation Fluids



(Source: Resuscitation Fluids. N Engl J Med 2013.)

2. Among crystalloids, different solutions have different adverse-event profiles.

- Normal saline (0.9% sodium chloride [NaCl]) has higher concentrations of Na and Cl (154 mEq/L) than plasma.

Large-volume infusion leads to hyperchloremic metabolic acidosis (owing to a compensatory decrease in bicarbonate concentration and acid-buffering capacity), renal vasoconstriction, acute kidney injury, and hyperkalemia.

- Balanced solutions (e.g., lactated Ringer solution or Plasma-Lyte A) have more physiologic concentrations of Na and Cl and contain lactate or acetate as anionic buffers (bicarbonate is unstable in plastic containers) as well as potassium (K) and other cations. Large-volume infusion may lead to hyponatremia and metabolic alkalosis. But the jury is still out regarding whether balanced solutions are better than normal saline:
    - Two pragmatic single-center clinical trials (SMART) and SALT-ED) that compared normal saline to balanced solutions found that balanced solutions were associated with a small but significant decrease in major adverse kidney events. Study clinicians could choose saline for patients with relative contraindications to balanced solutions (e.g., hyperkalemia and brain injury when hypernatremia may be preferred to reduce brain swelling).
    - In a more recent study (PLUS), no difference in mortality or acute kidney injury was reported in critically ill patients who received normal saline or balanced solutions.
    - However, a recent meta-analysis that included the PLUS data suggested a slight benefit from balanced salt solutions.
- In the open-label multicenter BICAR-ICU trial, treatment with 4.2% bicarbonate solution to increase pH >7.3 in patients with severe metabolic acidosis (pH <7.2) and sequential organ failure assessment (SOFA) score >3 or lactate >2 mm/L did not improve mortality at 28 days or reduce organ failure at one week. However, patients with acute kidney injury (Acute Kidney Injury Network [AKIN]

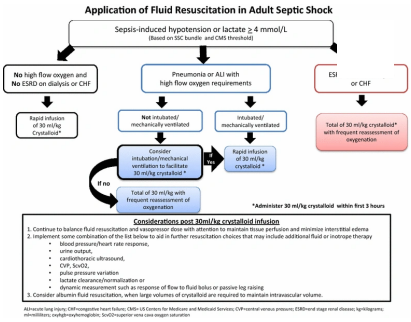
score, 2–3) showed improved mortality and a reduction in organ failure. Adverse effects of bicarbonate infusion included metabolic alkalosis, hypernatremia, and hypocalcemia.

3. Patients' fluid requirements depend on the clinical circumstances, and conservative fluid administration may be beneficial.

- Excessive fluid administration can lead to tissue edema and organ dysfunction, especially in situations with increased vascular permeability from inflammation (see figure above). In the past, early aggressive hydration was the gold standard for patients with acute pancreatitis. However, results from the recently published WATERFALL trial showed that early aggressive hydration led to a higher incidence of fluid overload without a change in other clinical outcomes.
- In the FACCT trial, a conservative fluid-management strategy (central venous pressure [CVP] goal <4 mm Hg) was associated with improved outcomes in patients with acute respiratory distress syndrome (ARDS). However, the mean time to intervention was 43 hours after ICU admission, when most patients are past the acute phase of sepsis.
- In contrast, for the initial resuscitation of patients with sepsis-induced hypoperfusion, the 2021 Surviving Sepsis Campaign guideline recommends ≥30 mL/kg of crystalloids within the first 3 hours, followed by fluids administered guided by frequent reassessments of how a patient might improve (see algorithm below).
    - Several metrics can be used at the bedside to determine if a patient is fluid responsive, and dynamic measures are recommended over static parameters or physical exam alone (e.g., passive leg raise, pulse pressure variation with ventilation, and change in CVP). Passive leg raise may be the

most reliable test (positive likelihood ratio, 11) according to a recent review.

Application of Fluid Resuscitation in Adult Septic Shock



(Source: A Users' Guide to the 2016 Surviving Sepsis Guidelines. Intensive Care Medicine 2017. © SCCM and ESICM 2017 with permission of Springer.)

Blood Transfusion

Blood transfusion is also often required in critically ill patients, but growing evidence supports the safety of conservative transfusion thresholds (hemoglobin concentration <7 g/dL), reducing the need for blood transfusion in critically ill patients and avoiding unnecessary risks.

- The 1999 TRICC trial found no difference in mortality or severity of organ dysfunction between a restrictive (hemoglobin <7 g/dL) and liberal (hemoglobin <9 g/dL) transfusion threshold in a general population of patients in the ICU.
- The 2014 follow-up TRISS trial compared the same restrictive or liberal transfusion thresholds as the 1999 TRICC trial but in patients with septic shock. This trial also found no difference in mortality and ischemic events between the two transfusion thresholds.
- Note: Patients with acute coronary syndrome were excluded from the TRISS trial, and evidence is lacking for

this patient population and other populations, including patients with hematologic disorders, cancer, thrombocytopenia, or acute neurologic disorders.

- The AABB (formerly the American Association of Blood Banks) recommends a restrictive hemoglobin threshold <7 g/dL for adults who are hemodynamically stable, including critically ill patients, and a threshold of <8 g/dL for those with underlying cardiovascular disease. The Society of Critical Care Medicine recommends a similar threshold of <7 g/dL for general critically ill patients and those with stable cardiac disease who are hemodynamically stable, and to reserve the <8 g/dL threshold for patients with acute coronary syndrome.
- Ultimately, the hemoglobin threshold **should not be the only trigger** for transfusion. Blood transfusion is preferred for resuscitation of patients with hemorrhagic shock and indicated for anyone with hemodynamic instability or inadequate oxygen delivery.

The risks associated with blood transfusion are generally low. See Transfusion Reactions in the Hematology rotation guide for more information.