Treatment of severe hypovolemia or hypovolemic shock in adults

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INTRODUCTION

Fluid resuscitation is the mainstay of therapy in patients with severe hypovolemia. Although no clear definition exists, severe hypovolemia may be present when loss of blood or extracellular fluids results in decreased peripheral perfusion. Hypovolemic shock is considered present when severe hypovolemia results in organ dysfunction as the result of inadequate tissue perfusion. In patients with severe hypovolemia or hypovolemic shock, delayed fluid therapy can lead to ischemic injury and irreversible shock with multiorgan system failure.

Treatment of severe hypovolemia and hypovolemic shock are discussed here. Etiologies, manifestations, and diagnosis of volume depletion and maintenance fluid therapy are discussed separately. (See "Etiology, clinical manifestations, and diagnosis of volume depletion in adults" and "Maintenance and replacement fluid therapy in adults".)

PRINCIPLES OF MANAGEMENT

Management of hypovolemia involves assessing and treating the underlying cause, identifying electrolyte and acid-base disturbances, and assessing and treating the volume deficit, all of which influence the choice of fluid and rate at which it should be administered.

Identify and treat the etiology — Clinicians should identify the etiology (or etiologies) contributing to hypovolemia so that therapies can be directed at the underlying cause of volume loss. Potential etiologies of hypovolemia include gastrointestinal, renal, skin, hemorrhage, and third-space losses. Therapies may include anti-emetics to treat vomiting, cessation of diuretics, or controlling bleeding. Further details regarding etiology and diagnosis of hypovolemia are discussed separately. (See "Etiology, clinical manifestations, and diagnosis of volume depletion in adults".)

Identify electrolyte and acid-base disturbances — Biochemical analysis will alert the clinician to electrolyte (eg, hypo- or hypernatremia, hypo- or hyperkalemia) and acid-base disturbances (eg, contraction alkalosis, metabolic acidosis) which may affect choice of replacement fluid and rate of repletion. In some cases, an arterial blood gas may be needed if mixed acid-base disturbance is suspected. (See "Overview of the treatment of hyponatremia in adults" and "Treatment of hypernatremia in adults" and "Clinical manifestations and treatment of hypokalemia in adults" and "Treatment and prevention of hyperkalemia in adults" and "Simple and mixed acid-base disorders" and "Potassium balance in acid-base disorders".)

Assess the volume deficit — Clinical assessment involves estimating pre- and post-deficit body weight, if known, as well as assessment of clinical and laboratory parameters including the blood pressure, jugular venous pressure, urine sodium concentration, urine output, lactate, and, if bleeding has not occurred, the hematocrit. Ultrasonographic assessment of collapse of the inferior vena cava on inspiration may be useful in some situations. Assessing volume deficit is discussed separately. (See "Maintenance and replacement fluid therapy in adults", section on 'Volume deficit' and "Novel tools for hemodynamic monitoring in critically ill patients with shock", section on 'Vena cava assessment'.)

CHOICE OF REPLACEMENT FLUID

For patients with hypovolemic shock, the three major classes of replacement fluids are:

- Crystalloid solutions (eg, saline solutions, buffered [ie, also known as balanced or chloride-restrictive] solutions [eg, Lactated Ringer, Plasma-Lyte, bicarbonate buffered 0.45 percent saline]). Hartmann solution is the same as Lactated Ringer, although small differences in the sodium, chloride, and calcium concentrations may exist across commercial formulations.
- Colloid-containing solutions (eg, albumin solutions, hyperoncotic starch, dextran, gelatin).
- Blood products (eg, packed red blood cells) or blood substitutes.

The choice of replacement fluid depends in part upon the type of fluid that has been lost [1]. For example, blood components are indicated in patients who are bleeding. Isotonic crystalloids are generally preferred for the management of patients with severe volume depletion not due to bleeding. (See "Indications and hemoglobin thresholds for RBC transfusion in adults" and "Massive blood transfusion" and "Approach to shock in the adult trauma patient".)

The components and physiologic effects of commonly administered fluids are provided in the tables (table 1 and table 2 and table 3).

Hemorrhagic shock

Blood products — The mainstay of therapy for patients with intravascular volume depletion due to bleeding is the replacement of volume loss with blood products, typically packed red blood cells. Patients may receive fluid replacement, usually with crystalloid (eg, 0.9 percent saline), while waiting for blood products to be delivered to the bedside. The management of patients with hemorrhagic shock is discussed separately. (See "Initial management of moderate to severe hemorrhage in the adult trauma patient".)

Blood substitutes — Acellular, oxygen carrying resuscitation fluids may be an alternative when blood transfusion is not immediately available or when patients refuse blood products due to religious beliefs. This subject is discussed separately. (See "Oxygen carriers as alternatives to red blood cell transfusion".)

Nonhemorrhagic shock — In patients with nonhemorrhagic shock, isotonic or near-isotonic crystalloids (eg, 0.9 percent saline solutions with or without dextrose, buffered crystalloids [eg, Lactated Ringer, Plasma-Lyte, bicarbonate buffered 0.45 percent saline]) and colloid-containing solutions (eg, albumin solution, hyperoncotic starch, dextran, gelatin) can be used to effectively replace the extracellular fluid deficit. Hyperoncotic starch solutions, although effective, should be avoided since they increase the risk of acute kidney injury (AKI), need for renal replacement therapy, and mortality [2-6].

First-line: Crystalloid solutions — In general, for patients with severe volume depletion or hypovolemic shock not due to bleeding, crystalloids are typically preferred over colloid-containing solutions. Among the crystalloids, normal saline (ie, 0.9 percent saline) is the most commonly used solution for initial repletion since data have failed to show consistent superiority of buffered crystalloids when compared with saline, especially when volumes ≤2 L are being administered. However, several factors influence the choice between 0.9 percent saline and buffered crystalloids, which are discussed below. (See 'Choosing between 0.9 percent saline and buffered crystalloid' below.)

Data that support the value of **crystalloid solutions over colloid-containing solutions** include the following:

- In a 2013 nine-year, multicenter, open-label trial (CRISTAL), 2857 patients with hypovolemic shock due to any cause were randomly assigned to resuscitation with intravenous crystalloid (mostly 0.9 percent saline) or colloid solutions (eg, albumin, gelatin, hetastarch) [7]. There was no difference in 28-day mortality or need for renal replacement therapy between the groups. However, patients treated with colloids had more days free of mechanical ventilation (13.5 versus 14.6 days) and vasopressor therapy (15.2 versus 16.2 days), as well as a lower 90-day mortality (31 versus 34 percent). The open-label design, lengthy study period (2003 to 2012), and heterogeneity of fluids that were compared between the groups, limit confidence in a possible benefit of colloid solutions in this population. (See 'Second-line: Colloid solutions' below.)

- A 2006 multicenter trial (SAFE) randomly assigned nearly 7000 hypovolemic medical and surgical intensive care unit (ICU) patients to fluid resuscitation using either 4 percent albumin solution (colloid) or 0.9 percent saline (crystalloid) [8]. All-cause mortality at 28 days, multiorgan failure, the duration of hospitalization, and effect upon systemic pH were similar in both groups [9]. No differences were observed in subgroup analyses of patients with and without sepsis [10]. However, in patients with head trauma, resuscitation with albumin was associated with higher mortality than resuscitation with 0.9 percent saline [11]. (See 'Albumin' below.)

- Meta-analyses of studies older than SAFE confirm a similar lack of benefit and/or harm from colloid-containing solutions compared with crystalloids. For example, one analysis reported a 4 percent increase in mortality [12] and another reported no difference in mortality [13] in patients given albumin compared with crystalloids (mostly 0.9 percent saline).

Choosing between 0.9 percent saline and buffered crystalloid — Normal saline (0.9 percent saline) is hyperchloremic relative to plasma, such that large volume resuscitation using 0.9 percent saline may be associated with the development of a hyperchloremic metabolic acidosis (table 1) [14-16]. This has led to suggestions that isotonic fluids with lower chloride concentration be used instead of 0.9 percent saline for large volume resuscitation; such fluids are termed buffered, balanced, or chloride-restrictive crystalloids and include fluids such as Lactated Ringer solution (or Hartmann solution), 0.45 percent saline solution with 75 mmol/L of sodium bicarbonate, or Plasma-Lyte. A list of commonly administered crystalloids and their electrolyte content relative to plasma can be viewed in the table (table 1).

We believe the choice between buffered solutions and normal saline is individualized and informed by factors including patient chemistries, estimated volume of resuscitation, potential adverse effect of the solution used (eg, hyponatremia [Lactated Ringer] and hyperchloremic acidosis [normal saline]), as well as institutional and clinician preference. Following initial resuscitation, we have a low threshold to re-evaluate the type of fluid administered depending upon the patient's response and development of adverse effects. As an example, patients with hypernatremia in association with hypovolemia may benefit from fluids with lower concentrations of sodium or supplemental free water, while those with symptomatic acute hyponatremia may benefit from hypertonic saline. Similarly, in patients with hyperchloremic acidosis, buffered crystalloids may be preferred, while 0.9 percent saline may be preferred in those with metabolic alkalosis. Potassium-containing solutions such as Lactated Ringer are traditionally avoided in patients with hyperkalemia; however, data in patients undergoing renal transplantation suggest that Lactated Ringer does not significantly increase the potassium level when compared with normal saline [17,18]. (See "Treatment of hypernatremia in adults" and "Overview of the treatment of hyponatremia in adults" and "Clinical manifestations and treatment of hypokalemia in adults" and "Treatment and prevention of hyperkalemia in adults" and "Treatment of metabolic alkalosis".)

The rationale for this recommendation is based upon the lack of an ideal standard crystalloid resuscitation solution that is suitable for all patients and data that suggest potential benefit from buffered crystalloids, particularly in those in whom **large** volumes of fluids are administered (eg, ≥2 L). Data to support our approach to this choice include the following:

- Two major trials reported modest benefit from the use of balanced crystalloids in critically ill and non-critically ill patients. A trial including 15,802 adults in five intensive care units in one institution found that balanced crystalloids (Lactated Ringer solution or Plasma-Lyte A) resulted in a modest reduction in a composite outcome of death from any cause at 30 days, new renal replacement therapy, or persistent renal dysfunction, when compared with 0.9 percent saline (14.35 versus 15.4 percent), but no significant difference in the rates of the individual components of the outcome were found [19]. The response was variable among subgroups. For example, a pre-specified analysis of patients with sepsis (who received higher volumes than the median of approximately 1 L) found infusion of balanced crystalloids to be associated with a lower 30-day mortality (25.2 versus 29.4 percent; adjusted odds ratio 0.8, 95% CI 0.67 to 0.94), while minimal benefit was seen in other subpopulations. No differences in in-hospital death, ICU- ventilator- or vasopressor-free days, rates of stage-2 or higher AKI, or creatinine levels before discharge were reported. Another parallel trial including 13,347 non-critically ill patients treated in the emergency department and subsequently hospitalized outside the ICU found that

compared with 0.9 percent saline, buffered crystalloids did not affect the number of hospital-free days but did result in a modest reduction in the composite outcome of death from any cause, new renal replacement therapy, or persistent renal dysfunction (4.7 versus 5.6 percent) without significant difference in the individual outcomes [20]. Although well-conducted, both of these studies were criticized for issues including small median volumes of infusion, heterogeneity of the populations studied, and a response in a composite outcome that was marginal [21].

- By contrast, two other major trials reported no difference in mortality or AKI when buffered solutions or 0.9 percent saline was used. The first, a two-by-two-factorial-design randomized trial (BaSICS) of over 11,000 critically ill patients, compared fluid resuscitation using either saline or buffered crystalloid solution (in a blinded comparison) and faster versus slower fluid administration (in an open-label comparison) [22,23]. Most patients had undergone elective surgery, and the remainder were a mix of medical and emergency surgery patients. No difference was reported for 90-day mortality (26 percent [buffered solutions] versus 27 percent [saline]; adjusted hazard ratio [HR] 0.97, 95% CI 0.90-1.05), incidence of AKI, or need for replacement therapy [22]. Similarly, giving a fast bolus (999 mL/hour) or slow infusion (333 mL/hour) had no effect on mortality or rate of AKI [23]. Only small volumes of fluid were administered (1.5 L by first day after enrollment; 2.9 L by day 3), which was equal and supported by similar chloride levels among the groups, a feature that may limit generalizability for patients in whom larger volumes of fluid are administered; thus, whether more aggressive resuscitation measures would have resulted in a difference is unknown. Further confounding the outcome is that two-thirds of patients received more than 1 L of fluid prior to randomization, which may or may not have been the same as that administered during the study. The trial may also have been underpowered to detect a difference since the mortality was lower than that predicted. While a prespecified subgroup analysis reported that patients with traumatic brain injury (TBI) who were treated with buffered solutions had a higher mortality compared with those treated with saline (31.3 versus 21.1 percent; HR 1.48, 95% CI 1.03-2.12), these data may be explained by the tonicity of the balanced solutions used rather than the anion composition and are hypothesis-generating only.

- In keeping with the above trial, an additional randomized trial of 5037 critically ill patients (almost half of whom had sepsis) reported no difference in the mortality or incidence of AKI among patients treated with either 0.9 percent saline or Plama-Lyte-148, a balanced salt solution [24]. However, limitations include a reduction in the recruitment target and unavailable data on some of the patients.

- However, one meta-analysis of 13 randomized trials (including all the major trials referenced above [19,20,22-24]) suggested a probable benefit from balanced solutions [25]. Using the six trials that were at low risk of bias (34,450 patients), use of balanced solutions resulted in a 4 percent reduction in the risk of death at 90 days when compared with 0.9 percent saline. However, the impact of balanced crystalloids ranged from a 9 percent relative reduction to a 1 percent relative increase in the risk of death (risk ratio [RR] 0.96, 95% CI 0.91-1.01), limiting the certainty of the effect. The risk of developing AKI was also reduced (RR 0.96, 95% CI 0.89-1.02), but the impact on the need for renal replacement therapy was less certain (RR 0.95, 95% CI 0.81-1.11).

Normal saline (crystalloid) — For most patients, normal saline (0.9 percent saline) (table 1), which contains 154 mEq/L of sodium chloride, is an effective and inexpensive initial resuscitation fluid for the management of patients with hypovolemia and hypovolemic shock not due to bleeding [7,8,12,13,26,27]. This assessment is based upon several trials and meta-analyses which consistently report that although colloids expand plasma volume more effectively than isotonic crystalloids, clinically meaningful outcomes are similar [7-13,26,27]. Data that compare buffered crystalloids and 0.9 percent saline and the factors that influence the decision regarding the choice between 0.9 percent saline and buffered crystalloids are discussed above. (See 'First-line: Crystalloid solutions' above and 'Choosing between 0.9 percent saline and buffered crystalloid' above.)

Complications of 0.9 percent saline include hyperchloremic acidosis and peripheral edema.

- Hyperchloremic acidosis is due to the high concentrations of chloride relative to that in plasma and may be resolved by the administration of buffered crystalloid, provided continued fluid resuscitation is required. Hyperchloremia associated with 0.9 percent saline has also been associated with hyperkalemia due to transcellular shifts of potassium. For example, in patients undergoing renal transplantation, 0.9 percent saline administration has been associated with more cases of hyperkalemic acidosis than Lactated Ringer [17,18].

- Peripheral edema occurs because of the significant extravascular distribution of normal saline when compared with colloids (table 2 and table 3); for this reason, it has been estimated that 1.5 to 3 times as much saline must be given when compared with colloid-containing solutions [8,28-30]. However, this is not necessarily deleterious, since fluid loss also leads to an interstitial fluid deficit that is repaired by saline administration.

Buffered crystalloid — Buffered crystalloids are a reasonable alternative as either the initial resuscitation fluid or as a secondary fluid to be used if large volumes of resuscitation

fluids are necessary or if hyperchloremic acidosis is a concern. Several buffered crystalloids are available (table 1). Some of these have a lower sodium concentration than 0.9 percent saline, and were associated with greater hyponatremia than saline in the SMART/SALT-ED trials [19,20]. Although buffered fluids also contain small amounts of potassium, their contribution to extracellular potassium concentration is small unless very large volumes are infused. Buffered crystalloids have nearly the same plasma-expanding properties as isotonic crystalloid solutions (table 2 and table 3).

As with 0.9 percent saline, administration of buffered crystalloids may be associated with the development of peripheral edema. Because the available buffered crystalloids are modestly hypotonic, they are more commonly associated with development of hyponatremia. Data that compare buffered crystalloids and 0.9 percent saline and the factors that influence the decision regarding the choice between 0.9 percent saline and buffered crystalloids are discussed above. (See 'Choosing between 0.9 percent saline and buffered crystalloid' above.)

Second-line: Colloid solutions — Colloid-containing solutions are rarely used as first-line resuscitative fluids for the management of hypovolemia and hypovolemic shock not due to bleeding. However, some clinicians advocate the administration of colloid solutions, particularly albumin, in those with limited response to crystalloid solutions or those in whom hypoalbuminemia is thought to be contributing to shock, although data to support these indications are limited. Hyperoncotic starch should, in general, be avoided since its use is associated with an increased risk of kidney dysfunction and mortality. (See 'Fluids to avoid: hyperoncotic starch (colloid)' below.)

The rationale for the administration of colloid is that colloids result in more rapid plasma volume expansion than saline, since the colloid solution is more likely to remain in the vascular space (in contrast to saline, three-quarters of which enters the interstitium) (table 2 and table 3). Although rapid plasma expansion can be achieved with colloid-containing solutions, randomized trials and meta-analyses have failed to convincingly demonstrate a consistent clinically meaningful benefit derived from this advantage [7-9,12,13,26,28,31-37] and some older studies suggest possible harm [11,12]. Data to support this lack of clear benefit from the administration of colloid-containing solutions are discussed above. (See 'First-line: Crystalloid solutions' above.)

Albumin — The use of hyper-oncotic (20 to 25 percent) albumin has been used in individuals with intravascular volume depletion but total body volume overload, such as patients with cirrhosis. However, little data exists to support this strategy. Details regarding the management of cirrhosis are discussed separately. (See 'Chronic liver disease' below and "Ascites in adults with cirrhosis: Initial therapy" and "Cirrhosis in adults: Overview of

complications, general management, and prognosis" and "Hyponatremia in patients with cirrhosis".)

Several formulations of albumin are available. Intravenous albumin can expand the intravascular volume effectively but it is expensive and data have not shown consistent benefit with its use as an initial resuscitation fluid compared with crystalloids (see 'First-line: Crystalloid solutions' above). While it was originally thought that albumin might avoid the dilutional hypoalbuminemia typically seen with isotonic crystalloid [38] and therefore protect against the effect of pulmonary edema, this advantage has not been proven to be true [39-41].

Others — While colloid-containing solutions other than albumin and hyperoncotic starch (eg, dextran, gelatin), are effective expanders of intravascular volume, they have not been sufficiently studied for recommendations to be made regarding their administration. While in the past dextran has been used to inhibit platelet function, they are no longer used to treat hypovolemia [42].

Fluids to avoid: hyperoncotic starch (colloid) — Hyperoncotic starch solutions are not recommended for patients with hypovolemia. Concern has been raised about risks associated with the use of hyperoncotic starch solutions (eg, pentastarch, hydroxyethyl starch [HES]) (table 2 and table 3). Use of hyperoncotic starch solutions has been associated with increased risk of AKI, and in some studies, increased mortality [2-5,37,43-48]. The lack of benefit and potential adverse effects of starch solutions for critically ill patients, including the subgroup with septic shock, are illustrated by the following:

- In a randomized trial, 7000 ICU patients were assigned to receive 6 percent HES or 0.9 percent saline for all fluid resuscitation until ICU discharge [46]. Compared with patients resuscitated with 0.9 percent saline, there was an increased risk of AKI requiring renal replacement therapy in the HES group (7 versus 5.8 percent), but not an increased mortality risk.

- In two subsequent meta-analyses, one of which excluded seven trials that were retracted due to scientific misconduct of one investigator, compared to conventional fluid resuscitation regimens, HES was associated with increased risk of mortality (relative risk ranging from 1.08 to 1.09), and treatment with renal replacement therapy (relative risk ranging from 1.09 to 1.25) [4,5].

- Similarly, in the randomized 6S trial that compared HES with the crystalloid, Lactated Ringer, for volume expansion in patients with severe sepsis and septic shock, patients receiving HES had a higher mortality and a greater likelihood of needing renal replacement therapy [48]. This trial is discussed in more detail separately. (See "Evaluation

and management of suspected sepsis and septic shock in adults", section on 'Intravenous fluids (first three hours)'.)

INITIAL RATE OF FLUID REPLETION

The rate of fluid repletion should be individualized depending upon the underlying etiology and rate of fluid loss, estimated total body deficit, underlying electrolyte abnormalities, and predicted future losses, which can be hard to predict if fluid loss continues from persistent bleeding or third space sequestration. While there is no one ideal initial rate, many clinicians model the rate of fluid administration on rates similar to those recommended in patients with sepsis and septic shock, although data to support this strategy is lacking. Further details on rate of fluid repletion in patients with sepsis are provided separately. (See "Evaluation and management of suspected sepsis and septic shock in adults", section on 'Volume'.)

Ensuring adequate intravenous access for fluid resuscitation is important and for those with massive hemorrhage adhering to massive transfusion protocols is advised. Further details are provided separately. (See "Evaluation and management of suspected sepsis and septic shock in adults", section on 'Establish venous access' and "Initial management of moderate to severe hemorrhage in the adult trauma patient", section on 'Predicting the need for massive transfusion'.)

MONITORING THE RESPONSE

Following the response to fluid administration is necessary to prevent irreversible shock and to prevent over resuscitation and iatrogenic hypervolemia. Irreversible shock is associated with loss of vascular tone, a drop in systemic vascular resistance, pooling of blood in the capillaries and tissues, an impaired response to vasoactive medications, and multiorgan failure. Clinical parameters including heart rate, blood pressure, urine output, skin turgor, mucus membrane integrity, and mental status should be continuously followed during fluid replacement to assess the efficacy of volume replacement. For most patients, the period of observation lasts for the duration of fluid resuscitation (eg, 6 to 48 hours, longer for ongoing fluid loss). While there are no recommended ideal measurable targets for patients with hypovolemia, many clinicians use parameters extrapolated from patients with sepsis and septic shock (eg, mean arterial pressure 65 to 70 mmHg, no greater than 70 mmHg, urine output >0.5 mL/kg/hour), the details of which are discussed separately. (See "Evaluation and management of suspected sepsis and septic shock in adults", section on 'Clinical'.)

Measuring laboratory parameters including chemistries and lactate level within 6 hours and urinary sodium within 24 hours of replacement may also be useful. If, for example, the urine sodium concentration remains below 15 mEq/L (15 mmol/L), then the kidney is sensing persistent volume depletion and more fluid should be given. Use of the urine sodium concentration does **not** apply to edematous patients with heart failure or cirrhosis in whom the urine sodium concentration is a marker of effective circulating volume depletion but not of the need for more fluid or more salt.

FOLLOW-UP

Patients who respond to therapy — In most patients, an immediate clinical response to fluid administration is appreciated by clinical examination and laboratory findings. The decision to maintain or stop fluids is dependent upon the robustness of the clinical response as well as any predicted continued loss of fluids and the ability of the patients to maintain their own oral fluid intake.

Maintenance — Once clinically stable, fluid repletion is often maintained for a short period at a rate lower than the initial rate, and occasionally with a different solution, depending upon complications of fluid resuscitation that may be evident. Further details regarding maintenance fluids are discussed separately. (See "Maintenance and replacement fluid therapy in adults".)

Cessation — Once fluids have been adequately repleted (usually 3 to 48 hours) and it has been determined that maintenance fluids are not needed, fluids may be stopped.

Over resuscitation — Some patients may show evidence of over resuscitation such as pulmonary edema. Although peripheral edema is a marker of fluid overload, it should not be used as the sole marker for adequate fluid resuscitation or fluid overload since peripheral edema is often due to acute dilutional hypoalbuminemia. The decision to diurese patients should be individualized and depends upon several factors including the need for supplemental oxygen, presence of respiratory failure, or lower extremity discomfort from edema.

Patients who fail therapy — While most patients respond to fluid resuscitation, some patients demonstrate a poor or no improvement in clinical or biochemical parameters within the first 1 to 6 hours of treatment. Such patients may require additional testing and/or monitoring (to investigate other potential etiologies for shock and to assess for fluid-responsiveness), or an empiric trial of alternative resuscitation fluid such as albumin. Rarely, when hypovolemic shock is refractory to aggressive fluid administration, vasopressors are added to maintain tissue perfusion.

Alternative resuscitation fluid — For those who initially fail with or develop a complication from 0.9 percent crystalloid, some experts may empirically switch to or add a colloid, such as albumin, although data to support this strategy are lacking.

Additional testing and monitoring — Additional testing may be needed to revisit the diagnosis of hypovolemic shock and to investigate contributions from other etiologies of shock (eg, vasogenic from sepsis or cardiogenic from heart failure). (See "Evaluation of and initial approach to the adult patient with undifferentiated hypotension and shock".)

Additional monitoring may also be appropriate. For example, measurement of the central venous pressure (CVP) may help direct therapy. Alternative methods of monitoring volume status and fluid-responsiveness may also be considered including pulmonary arterial venous catheterization (eg, patients with underlying cardiopulmonary disease), pulse contour analysis, passive leg raising, and point-of-care ultrasonography, all of which require intensive care unit admission. Details of CVP and alternate forms of measuring volume status are provided separately. (See "Evaluation and management of suspected sepsis and septic shock in adults", section on 'Hemodynamic' and "Novel tools for hemodynamic monitoring in critically ill patients with shock" and "Pulmonary artery catheterization: Indications, contraindications, and complications in adults".)

Vasopressors — Vasopressors (eg, norepinephrine) generally should not be administered, since they do not correct the primary problem and, in the absence of adequate resuscitation, tend to further reduce tissue perfusion [49]. However, in patients with refractory shock, vasopressors may be administered while ongoing measures are being taken to treat hypovolemia. (See "Use of vasopressors and inotropes".)

SPECIAL POPULATIONS

Individual populations of patients with hypovolemia due to specific etiologies may need special attention.

Acute pancreatitis — Patients with acute pancreatitis can lose significant volumes of fluid into the third space such that aggressive fluid resuscitation with crystalloid is the cornerstone of therapy. Details regarding fluid choice and rate of repletion are discussed separately. (See "Management of acute pancreatitis", section on 'Fluid replacement'.)

Sepsis — Most patients with sepsis are treated with crystalloids and a similar lack of clear benefit for the colloid, albumin, has been demonstrated in that population, the details of which

are discussed separately. (See "Evaluation and management of suspected sepsis and septic shock in adults", section on 'Choice of fluid'.)

Lactic acidosis — Patients with marked hypoperfusion may develop lactic acidosis, leading to a reduction in extracellular pH below 7.10. Some have advocated addition of sodium bicarbonate to the replacement fluid in this setting, in an attempt to correct both the acidemia and the volume deficit, although the optimal approach is controversial. Data to support bicarbonate therapy in lactic acidosis are discussed separately. (See "Bicarbonate therapy in lactic acidosis".)

Acute respiratory distress syndrome — Patients with acute respiratory distress syndrome (ARDS) commonly have hypovolemia in association with the etiology inducing ARDS (eg, pancreatitis). Fluid management in patients with ARDS is discussed separately. (See "Acute respiratory distress syndrome: Fluid management, pharmacotherapy, and supportive care in adults", section on 'Conservative fluid management'.)

Trauma — Fluid resuscitation in patients with hypovolemic shock due to trauma is discussed separately. (See "Initial management of moderate to severe hemorrhage in the adult trauma patient", section on 'Intravenous fluid resuscitation'.)

Diabetic ketoacidosis — Fluid management in patients with diabetic ketoacidosis and hyperosmolar hyperglycemic state is discussed separately. (See "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Treatment".)

Chronic liver disease — Fluid management in patients with intravascular hypovolemia who have chronic liver disease is challenging, since most are also total body sodium and fluid overloaded with interstitial edema and/or ascites. In general, these patients should be managed using a similar strategy to that in noncirrhotic patients. However, particular attention needs to be paid to avoiding and managing hyponatremia and to managing third space sequestration with diuresis and paracentesis. The intermittent administration of hyperoncotic (20 to 25 percent) albumin as a resuscitative fluid is poorly studied but used by experts to limit fluid retention in this population [50]. (See "Hyponatremia in patients with cirrhosis" and "Ascites in adults with cirrhosis: Initial therapy".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer

short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Dehydration in children (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **General principles** – Rapid volume repletion is indicated in patients with severe hypovolemia or hypovolemic shock. Delayed therapy can lead to ischemic injury and possibly to irreversible shock and multiorgan system failure. Management of hypovolemia involves assessing and treating the underlying cause, identifying electrolyte and acid-base disturbances, and assessing the volume deficit, all of which influence the choice of fluid and rate at which it should be administered. (See 'Introduction' above and 'Principles of management' above.)

- **Initial approach** – For patients with intravascular volume depletion due to bleeding, fluid loss is repleted with blood products, typically packed red cells. Patients may receive fluid replacement with crystalloid (eg, 0.9 percent saline), while waiting for blood products. (See "Initial management of moderate to severe hemorrhage in the adult trauma patient" and 'Hemorrhagic shock' above.)

- **Replacement fluid** – For patients with severe non-hemorrhagic hypovolemia or non-hemorrhagic hypovolemic shock:

  - We recommend initial fluid replacement with an isotonic crystalloid solution rather than a colloid-containing solution (**Grade 1B**) based upon the rationale that randomized trials and meta-analyses have demonstrated no consistent clinically meaningful benefit from colloids when compared with crystalloids. (See 'First-line: Crystalloid solutions' above.)

  - Among crystalloids, the choice between buffered solutions and normal saline is individualized and informed by factors including patient chemistries, estimated volume of resuscitation, potential adverse effect of the solution used (eg, hyponatremia

[Lactated Ringer], and hyperchloremic acidosis [normal saline]), as well as institutional and clinician preference. The clinician should have a low threshold to re-evaluate the type of fluid administered depending upon the patient's response and development of adverse effects. The rationale for this recommendation is based upon the lack of an ideal standard crystalloid resuscitation solution and data that suggest potential benefit from buffered crystalloids, particularly when large volumes of fluids are administered (eg, >2 L). (See 'Choosing between 0.9 percent saline and buffered crystalloid' above.)

- Colloid-containing solutions are rarely used as first-line resuscitative fluids for the management of non-hemorrhagic hypovolemia and hypovolemic shock. However, some clinicians advocate the administration of colloid solutions, particularly albumin, in those with a limited response to crystalloid solutions or those in whom hypoalbuminemia is thought to be contributing to shock, although data to support these indications are limited. (See 'Second-line: Colloid solutions' above.)

- For patients with severe hypovolemia and hypovolemic shock, we recommend against the use of hyperoncotic starch solutions due to an increased risk of acute kidney injury and death (**Grade 1B**). (See 'Fluids to avoid: hyperoncotic starch (colloid)' above.)

- **Rate of fluid repletion** – The rate of fluid repletion should be individualized depending upon the underlying etiology and rate of fluid loss, estimated total body deficit, predicted future losses, and underlying electrolyte abnormalities. While there is no one ideal initial rate, many clinicians model the rate of fluid administration on rates similar to those recommended in patients with sepsis and septic shock, although data to support this strategy are lacking. (See 'Initial rate of fluid repletion' above and "Evaluation and management of suspected sepsis and septic shock in adults", section on 'Volume'.)

- **Monitoring the response** – Clinical parameters including heart rate, blood pressure, urine output, skin turgor, mucus membrane integrity, and mental status should be continuously followed during fluid replacement to assess the efficacy of volume replacement and avoid over resuscitation. Chemistries, lactate, and urinary sodium should also be intermittently followed (within 6 to 24 hours). While there are no recommended ideal measurable targets for patients with hypovolemia, many clinicians use parameters extrapolated from patients with sepsis and septic shock. (See 'Monitoring the response' above and "Evaluation and management of suspected sepsis and septic shock in adults", section on 'Monitor response'.)

- **Follow-up** – In most patients, an immediate clinical response to fluid administration is appreciated, such that fluids can be weaned and/or stopped. However, for patients who

fail to respond, additional testing and monitoring (to investigate other potential etiologies for shock and/or to assess for fluid-responsiveness), or an empiric trial of an alternative resuscitation fluid such as albumin may be required. Rarely, vasopressors are added in shock refractory to aggressive fluid resuscitation so that tissue perfusion can be maintained. (See 'Follow-up' above.)

- **Special populations** – Individual populations of patients with hypovolemia due to specific etiologies may need special attention including patients with acute pancreatitis, sepsis, lactic acidosis, acute respiratory distress syndrome, trauma, diabetic ketoacidosis, hyperosmolar hyperglycemic state, and chronic liver disease. (See 'Special populations' above.)

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Topic 1607 Version 55.0

GRAPHICS

Comparison of plasma with commonly used intravenous solutions

	Sodium	Potassium	Calcium	Magnesium	Chloride	Acetate
Plasma	135-145 mEq/L	3.5-5.0 mEq/L	2.2-2.6 mEq/L 4.4-5.2 mg/dL 1.1-1.3 mmol/L	0.8-1.0 mEq/L 1.0-1.2 mg/dL 0.4-0.5 mmol/L	94-111 mEq/L	–
Plasma water*	145-156 mEq/L	3.8-5.4 mEq/L	2.4-2.8 mEq/L 4.8-5.6 mg/dL 1.2-1.4 mmol/L	0.9-1.1 mEq/L 1.1-1.3 mg/dL 0.5-0.6 mmol/L	101-119 mEq/L	–
Intravenous solutions						
▪ Sodium chloride injection, USP[1]	154 mEq/L	–	–	–	154 mEq/L	–
▪ Lactated Ringer's injection, USP[2]	130 mEq/L	4.0 mEq/L	2.7 mEq/L 5.4 mg/dL 1.4 mmol/L	–	109 mEq/L	–
▪ Plasma-Lyte A[3]	140 mEq/L	5.0 mEq/L	–	3.0 mEq/L 3.7 mg/dL 1.5 mmol/L	98 mEq/L	27 mEq/L
▪ 0.45% Sodium chloride injection, USP[1] with added sodium bicarbonate[4] ¶	141 mEq/L	–	–	–	72 mEq/L	–

* Plasma is approximately 93% aqueous; concentrations in plasma water calculated as plasma concentration ÷ 0.93.

¶ This solution can be mixed by adding 75 mL of 8.4% sodium bicarbonate ($NaHCO_3$) to 1 liter of 0.45% normal saline.

Data from:

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Graphic 117769 Version 1.0

Physiological characteristics and clinical effects of commonly used intravenous solutions

	Available solutions			
	Albumin solutions		Starches¶	
	4, 5 percent	20, 25 percent	3, 6, 10 percent Hetastarch	10 percent Pentastarch
Molecular weight, average (kD)	69	69	450	280
Osmolality, mOsm/L	290	310	300-310	326
COP, mm Hg	20-30	70-100	23-50	23-50
Maximum volume expansion,* percent	70-100	300-500	100-200	100-200
Duration of volume expansion, h	12-24	12-24	8-36	12-24
Plasmatic half-life, h	16-24	16-24	50	2-12
Potential for adverse reactions	+	+	++	++
Possible side effects	Allergic reactions	Allergic reactions	Renal dysfunction	Renal dysfunction
	Transmitted infection	Transmitted infection	Coagulopathy	Coagulopathy
			Pruritus	Pruritus
			Anaphylactoid reactions	Anaphylactoid reactions

COP: colloid osmotic pressure.

* Expressed as a percentage of administered volume.

¶ Starches are rarely used due to increased mortality and renal dysfunction associated with their use.

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Graphic 60477 Version 3.0

Physiological characteristics and clinical effects of commonly used intravenous solutions, continued

	Available solutions				
	Dextrans¶		Gelatins	Crystalloids	
	10 percent Dextran-70	3 percent Dextran-60, 6 percent Dextran-70	Succinylated and cross-linked: 2.5, 3, 4 percent Urea-linked: 3.5 percent	Normal saline	Ringer's lactate
Molecular weight, average (kD)	40	70	30-35	0	0
Osmolality, mOsm/L	280-324	280-324	300-350	285-308	250-273
COP, mm Hg	20-60	20-60	25-42	0	0
Maximum volume expansion,* percent	100-200	80-140	70-80	20-25	20-25
Duration of volume expansion, h	1-2	8-24	4-6	1-4	1-4
Plasmatic half-life, h	4-6	12	2-9	0.5	0.5
Potential for adverse reactions	+++	+++	++	+	+
Possible side effects	Anaphylactoid reactions Allergic reactions Interference with blood crossmatching	Anaphylactoid reactions Allergic reactions Interference with blood crossmatching	High calcium content (urea-linked forms) Anaphylactoid reactions	Hyperchloremic metabolic acidosis	Hyperkalemi

COP: colloid osmotic pressure; maximum volume expansion: the degree of expansion of circulatory volume divided by infused volume.

* Expressed as a percentage of administered volume.

¶ Dextrans are rarely used due to increased mortality and renal dysfunction associated with their use.

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