

FLUID MANAGEMENT

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The goals of perioperative fluid management are purported to provide appropriate amounts of parenteral fluid to maintain intravascular volume and cardiac preload, oxygen-carrying capacity, optimal coagulation status, acid-base homeostasis, and electrolyte balance. Just how these goals may be achieved remains controversial and often elusive. Over the past few years there has been a paradigm shift in perioperative fluid management not only in quantity but also in quality owing in part to changes in surgical and anesthetic techniques and also to the status of the patient population.

BACKGROUND

Prior to the explanation of the heart and vascular system by Harvey in 1628, little was understood about the circulation.¹ The need for intravenous fluid replacement probably started during the cholera epidemic that broke out in India in 1827, spreading to Russia in 1829 and to England in 1831, finally reaching the United States in 1832.²

O'Shaughnessy, a recent Edinburgh graduate, performed an analysis on the blood and excreta of several victims and concluded that the blood . . .

“has lost a large proportion of its water . . . it has lost also a great proportion of its neutral saline ingredients.”² . . . the indications of cure . . . are two in number—viz. 1st to restore the blood to its natural specific gravity; 2nd to restore its deficient saline matters . . . the first of these can only be effected by absorption, by imbibition, or by the injection of aqueous fluid into the veins. . . . When absorption is entirely suspended . . . in those desperate cases . . . the author recommends the injection into the veins of tepid water holding a solution of the normal salts of the blood.”³

Although intravenously administered anesthetics used to induce anesthesia became a standard approach during the second half of the 20th century, intravenous fluid

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infusions were restricted to extreme and complicated cases. Rather, through the 1950s it was standard practice to secure a vein with a right-angle steel needle. A moveable arm with a rubber patch on the outside of the skin was then moved to cover the hole of the needle within the vein. Should fluid or blood be required, small amounts could be injected via syringe or by presterilized and packaged infusion sets. These sets did not have filters when blood was given.

OVERVIEW OF FLUID AND ELECTROLYTE PHYSIOLOGY

Water, the major component of fluid compartments in the body, makes up about 60% of body weight or 600 mL/kg. In a 70-kg individual that would represent about 40 L. Age, gender, adiposity, and physical activity are major factors that alter these percentages. Body water is divided between intracellular (66%) and extracellular (34%) spaces, separated by water-permeable cell membranes. The extracellular compartment comprises blood volume (60 to 65 mL/kg) and the interstitial fluid volume (120 to 165 mL/kg). The percentage of plasma, the noncellular component of blood, is a fraction of the blood, as measured by the hematocrit, and averages about 30 to 35 mL/kg. About 15% of blood is in the arterial side and 85% in the venous (and capillary) side. The higher oncotic pressure of plasma due to the protein content (20 mm Hg greater than interstitial pressure) helps to maintain intravascular volume. Daily maintenance requirements for adults approximate 1.5 to 2.5 L of water, 50 to 100 mEq sodium, 50 to 100 g glucose, and 40 to 80 mEq potassium.⁴ The normal electrolyte composition in body compartments is shown in Table 23.1.

PERIOPERATIVE FLUID BALANCE

Traditionally, preoperative fasting produces a fluid deficit, which is calculated as the maintenance fluid requirement

multiplied by the duration of fasting since fluid intake. After fasting for 8 to 10 hours, the normal state after sleep, requirements in the noncomatose individual may be little more than 250 mL. Very few patients are likely to require 1500 to 2000 mL fluid within the first 1 to 2 hours of surgery. Preoperative fasting causes a slight decrease in extracellular fluid while maintaining intravascular volume.⁵ Current fasting requirements encourage clear fluids for up to 2 hours before anesthesia. The use of evanescent anesthetics ensures a rapid return to consciousness. Also, insensible losses are decreased with laparoscopic incisions and by constant irrigation of the wound. The preoperative use of bowel preps has also decreased significantly. Finally, antidiuretic hormone release during anesthesia severely curtails the ability of the kidneys to remove excess fluid.

The concept of the “third space” grew out of a study in the 1960s with two groups of patients: group 1 consisted of 5 patients undergoing minor surgery with general anesthesia (cyclopropane and ether); group 2 (13 patients) had elective major surgical procedures (cholecystectomy, gastrectomy, and colectomy). Plasma volume, red blood cell mass, and extracellular fluid volumes were measured in all patients on two occasions during the operative period by using ¹³¹I-tagged serum albumin, ⁵¹Cr-labeled red blood cells, and ³⁵S-tagged sodium sulfate. The authors determined that the loss of functional extracellular fluid in group 2 was due to an internal redistribution because of surgery; in other words, there is a “third space” that must be replaced.⁶ This conclusion was argued by Moore who wrote that the redistribution was due to antidiuretic hormone release and that intravenous fluid administration should follow a more restricted approach.⁷ Although both groups later recommended moderation, the concept of the “third space” became firmly established. Although inadequate fluid administration can be harmful, excessive fluid replacement is also associated with poorer outcome. Although the concept of the “third space” may have some validity, its overall validity has been questioned.⁸

Currently, patients undergoing major surgical procedures do require fluid replacement based mainly on losses from the surgical site as well as hourly needs, which will be defined later.

Table 23.1 Normal Electrolyte Composition in Body Compartments

Electrolyte	Plasma Fluid (mEq/L)	Intracellular Fluid (mEq/L)	Extracellular Fluid (mEq/L)
Sodium	142	10	140
Potassium	4	150	4.5
Magnesium	2	40	2
Calcium	5	1	5
Chloride	103	103	117
Bicarbonate	25	7	28

Modified from Rhoades RA, Tanner GA. *Medical Physiology*. Boston: Little Brown; 1995.

FLUID REPLACEMENT SOLUTIONS

Many crystalloid and colloid solutions are available and appropriate for adults (Table 23.2). Blood and blood products are discussed in Chapter 24. The British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients contains many evidence-scored recommendations to assist in intravenous fluid management.⁴ However, controversy in fluid replacement is still common, and many recommendations are seriously challenged.⁹

Crystalloids

Crystalloids are grouped as balanced, isotonic, hypertonic, and hypotonic salt solutions in water, depending on the amount of electrolytes they contain. They cross rapidly from the vascular to the interstitial spaces (e.g., gut, lungs, dependent parts) with only about one third remaining intravascular.

Balanced Salt Solutions

The electrolyte composition of balanced salt solutions is similar to that of extracellular fluid. Examples include lactated Ringer solution (similar to Hartmann solution), Plasma-Lyte, and Normosol. These solutions are hypotonic with respect to sodium. The added buffer (e.g., lactate) is metabolized *in vivo* to generate bicarbonate. They each contain small amounts of other electrolytes such as potassium, magnesium, and calcium. A Cochrane database review concluded that the administration of buffered fluids is equally safe as nonbuffered saline-based fluids and is associated with less metabolic derangements, especially hyperchloremia and metabolic acidosis.¹⁰

Normal Saline

Normal saline (0.9% NaCl) is hypertonic with equal concentrations of Na⁺ and Cl⁻ even though the plasma concentration of Na⁺ normally is 40 mEq/L higher than that of Cl⁻. Concerns have been raised that normal saline, which is probably the most widely used of all solutions for resuscitation, is associated with significant hyperchloremic metabolic acidosis and the need for renal replacement therapy, as compared to resuscitation with balanced crystalloid

solutions.^{4,11} These effects may well be dose dependent and in otherwise healthy individuals may be of no clinical significance.⁹ Avoiding an increased Cl⁻ concentration or using fluids that lessen the increase in Cl⁻ reduces the risk of renal dysfunction, infections, and possibly even death.¹² Either normal saline or Plasma-Lyte may be used for diluting packed red blood cells, but lactated Ringer solution should be avoided as it contains calcium.

Hypertonic Saline

Use of hypertonic solutions generally is restricted to specific situations such as control of intracranial hypertension or the need for rapid intravascular resuscitation. The sodium concentrations range from 250 to 1200 mEq/L; the inverse relation between the concentration of sodium and the amount of fluid required is due to the osmotic gradient from the intracellular to the extracellular spaces. Patients predisposed to tissue edema might benefit from use of a hypertonic solution. However, the half-life of hypertonic solutions is similar to that of isotonic solutions. Sustained expansion of plasma volume is not achieved unless colloids are present. Also, the osmolarity may cause hemolysis at the point of injection.

Five Percent Dextrose

Five percent dextrose is similar to free water as the dextrose is metabolized. It is iso-osmotic and does not cause hemolysis. With the realization that hyperglycemia is associated with poor outcome and the stress of the operative period causes blood sugar levels to increase, 5% dextrose solutions are seldom used currently except for the treatment and/or prevention of hypoglycemia or hyponatremia.

Table 23.2 Composition of Replacement Fluids

Fluid	Na (mEq/L)	K (mEq/L) (g/L)	Glucose (g/L)	Osm	pH	Other
5% Albumin	145 ± 15	<2.5	0	330	7.4	COP 32-35 mm Hg
Plasmanate	145 ± 15	<2.0			7.4	COP 20 mm Hg
10% Dextran 40	0	0	0	255	4.0	
HES 450/0.7	154	0	0	310	5.9	
0.9% NaCl	154	0	0	308	6.0	
Lactated Ringer	130	4	0	273	6.5	Lactate 28 mEq/L
5% Dextrose	0	0	50	252	4.5	
D5LR	130	4	50	525	5.0	
D50.45% NaCl	77	0	50	406	4.0	
Normosol-R	140	5	0	294	6.6	Mg 3 mEq/L, acetate 27 mEq/L, gluconate 23 mEq/L
Plasma-Lyte A	140	5	0	295	7.4	

COP, Colloid oncotic pressure; D5LR, 5% dextrose in lactated Ringer's solution; D50.45% NaCl, 5% dextrose in 0.45% NaCl; HES, hydroxyethyl starches; Osm, osmolarity.

From Kaye AD. Fluid management. In Miller RD, Pardo MC Jr, eds. *Basics of Anesthesia*. 6th ed. Philadelphia: Elsevier; 2011:364.

Colloids

Colloid solutions, albumin, and starches contain large-molecular-weight substances that remain in the intravascular space for significantly longer periods than crystalloids. The synthetic starches have little to no risk of infection, but allergic reactions can occur. They are more expensive than crystalloids but less expensive with fewer risks than with blood replacement.

Albumin

Albumin is supplied as a 5% or 25% solution. Albumin comprises about 50% of plasma proteins. The initial volume of distribution is equivalent to the plasma volume, and it remains in the intravascular space for a longer duration than crystalloids. Preparation removes viruses and bacteria. There is little effect on coagulation.

Dextran

First discovered by Pasteur as a microbial product in wine, dextrans are complex branched polysaccharides composed of chains of lengths varying from 3 to 2000 kilodaltons (kDa). The two used medically are dextran 40 (40 kDa) and dextran 70 (70 kDa). Dextrans are used as antithrombotics to reduce blood viscosity, and as intravascular volume expanders in hypovolemia. Dextrans are synthesized from sucrose by lactic acid bacteria, such as *Leuconostoc mesenteroides* and *Streptococcus mutans*. The antithrombotic effect is due to binding of erythrocytes, platelets, and vascular endothelium, increasing the electronegativity and reducing erythrocyte aggregation and platelet adhesiveness. Dextrans also reduce factor VIII-Ag von Willebrand factor and, hence, platelet function. By inhibiting α_2 -antiplasmin, dextran serves as a plasminogen activator, and so possesses thrombolytic features. Dextrans remain intravascular, are potent osmotic agents, and have been used to treat hypovolemia, although less so nowadays. The hemodilution caused by intravascular volume expansion also improves blood flow, which provides a theoretical advantage in promoting patency of microanastomoses and reducing thrombosis. However, a recent study did not find antithrombotics, including dextrans, of value in improving free flap survival.¹³

Both solutions are degraded to glucose. Side effects include anaphylactic or anaphylactoid reactions in about 1:3300 administrations, increased bleeding times, and rarely, noncardiogenic pulmonary edema.

Hydroxyethyl Starch

Hydroxyethyl starches (HES) are nonionic starch derivatives and were one of the most frequently used intravascular volume expanders. These synthetic colloids are modifications of natural polysaccharides. They are characterized by concentration and molecular weight. Six percent solutions are isotonic. Molecular weights vary from under 70 kDa to over 450 kDa. The molar

substitution and C2/C6 ratios are also factors. The molar substitutions refer to the number of hydroxyethyl residues per 10 glucose subunits. Preparations with 7 hydroxyethyl residues per 10 glucose units (a ratio of 0.7) are hetastarches. The larger the molecular weight and molar substitution, the longer the duration of the increase in intravascular volume effect but at the expense of more side effects. The C2/C6 ratio describes the pattern of hydroxyethyl substitution on specific carbon atoms of the HES glucose subunits. HES preparations with higher C2/C6 ratios are more resistant to breakdown by amylase, and have a prolonged duration of effect without an increase in side effects. Several preparations are available: Hespan (B. Braun Medical Inc.) is 6% HES 450/0.7; Hextend (Biotime Inc.) is 6% HES 670/0.7; Voluven (Fresenius Kabi) is 6% HES 130/0.4 in 0.9% NaCl, or Volvulyte (Fresenius Kabi) is 6% HES 130/0.4 in a balanced electrolyte solution. Pentastarch is a subgroup of HES with 5 hydroxyethyl groups out of each 11 hydroxyls, giving it approximately 50% hydroxyethylation, which compares with tetrastarch at 40% and HES at 70% hydroxyethylation, respectively.

HES interferes with von Willebrand, factor VIII, and platelet function. The dose-dependent risk of dilutional coagulopathy differs between colloids (dextran > hetastarch > pentastarch > tetrastarch, gelatins > albumin). Monitoring for early signs of side effects can include use of rotational thromboelastometry/thromboelastography to assess the deterioration not only in clot strength but also in clot formation and in platelet interaction.¹⁴

Higher molecular weight preparations may have side effects related to the solvent, as Hespan is dissolved in saline and Hextend in a balanced salt solution. The most common complication associated with HES administration is pruritus, which occurs in up to 22% of patients.

A systematic review of HES administration in intensive care unit (ICU) patients requiring intravascular volume resuscitation revealed an association of HES use and risk of mortality and acute kidney injury.¹⁵ The FDA (Food and Drug Administration) accordingly issued a black box warning in 2013, advising that HES solutions not be used in adult critically ill patients, including those with sepsis.¹⁶

The choice of fluid for intravenous administration should be guided by the cause of the hypovolemia, the cardiovascular state of the patient, and the renal function, as well as the serum osmolarity, comorbid conditions, and any coexisting acid-base and electrolyte disorders.¹⁷

Crystalloids Versus Colloids

The debate over crystalloid versus colloid persists and has stimulated many clinical studies—primarily in the adult critical care patient population. The fundamental principles are described in this section (also see Chapter 41).

Crystalloids dilute plasma proteins and decrease plasma oncotic pressure. Fluid is extravasated to interstitial compartments causing edema of the gastrointestinal tract and all dependent parts and extra lung fluid. Colloids given after blood loss in a ratio of 1:1 restores intravascular blood volume more rapidly. Colloids, although remaining in the vascular space longer, have more complications and are expensive. A Cochrane review of 78 randomized controlled trials of intravascular fluid resuscitation in critically ill patients concluded that resuscitation with colloid (albumin mainly) did not reduce the risk of death and HES might increase mortality rate.¹⁸ Another Cochrane study of kidney function in patients receiving HES versus other fluid therapies for volume depletion reviewed over 40 randomized controlled trials. HES use was associated with increased risk of acute kidney injury and need for renal replacement therapy.¹⁹ A safe volume of HES was not determined. The Surviving Sepsis Campaign (SSC) has issued international guidelines regarding management of patients with severe sepsis and septic shock, including the management of fluid therapy.²⁰ Recommendations include use of crystalloids as the initial fluid choice, avoidance of HES fluids, and use of albumin when patients require substantial amounts of crystalloid. The Saline versus Albumin Fluid Evaluation (SAFE) study of albumin versus saline for intravascular fluid resuscitation in the ICU evaluated almost 7000 patients in a randomized controlled trial. At 28 days, there was no difference in outcomes (including death, ICU length of stay, or organ failure), but a small subgroup of patients with traumatic brain injury had increased mortality rate after resuscitation with albumin.²¹

Although the aforementioned studies are primarily in the adult critical care population, they may be relevant in the perioperative setting as well, especially for complex or prolonged surgical procedures.

PERIOPERATIVE FLUID STRATEGIES

Although it might seem simple to arrive at a fluid management formula that could be applied universally in the perioperative setting, many difficulties have arisen. First, there has been little consensus as to what represents liberal (20 mL/kg/h), standard (5 to 10 mL/kg/h), or restrictive fluid replacement (2 to 5 mL/kg/h). Most studies have not been standardized, so reasonable comparisons cannot be performed. The specific clinical targets are also open to speculation (Box 23.1). Many clinicians are unwilling to change established protocols in their practice. There is no clear differentiation between major and minor surgery. Perhaps the target that has been most closely associated with adverse outcome is that of weight gain. A small study of primarily postcardiac surgery ICU patients demonstrated increased mortality rate in the patients with the greatest postoperative weight

Box 23.1 Study Targets

Weight gain	Need for revision surgery
Postoperative nausea and vomiting	Speed of wound healing
Pain	Infection
Tissue oxygenation	Cardiovascular complications
Postoperative ileus	Length of hospital stay
Pneumonia	Development of coagulopathies

increase during their ICU stay.²² Although this does not demonstrate a cause-effect relationship, it does raise the question of “how much is too much fluid?” By way of contrast, for healthy patients having minor elective surgery (e.g., young women undergoing short gynecologic procedures), liberal fluid administration (20 to 30 mL/kg) was associated with less nausea and vomiting and improved pain control.⁸

How did perioperative fluid management evolve? Following the discovery of the “third space” by Shires and associates⁶ in the 1960s, protocols were developed to compensate for it and for other supposed intraoperative requirements. The 4:2:1 or 100-50-20 rule was developed and has remained in general use despite its lack of relevance to current anesthetic practice.²³ Fluids are infused depending on weight: 4 mL/kg/h for the first 10 kg, 2 mL/kg/h for the next 10 kg, and finally 1 mL/kg/h thereafter; or looking at daily replacement, 100 mL/kg for the first 10 kg, 50 mL/kg for the next 10 kg, and 20 mL/kg for weight over that. Holliday’s article²³ of almost 60 years ago was intended as a general guide to daily needs of children and was not meant specifically for intraoperative application. It was based on three theories from even earlier work:

1. Surface area can estimate water expenditure.²⁴
2. Caloric needs depend on age, weight, activity, and food.²⁵
3. Urinary output and insensible losses correspond to age.²⁶

“Rules” for fluid replacement, therefore, were developed without scientific evidence, and much information was based on unpublished data. Apart from the fact that the formulas were not meant for adults, anesthetic and surgical techniques have changed drastically. The relevance in today’s practice should be questioned.

A recent meta-analysis shows that larger fluid volumes are required to meet the same targets if a goal-directed approach is used with crystalloids than with colloids, with an estimated ratio of 1.5 (1.36-1.65).²⁷ Again, there is little consistency among studies and the reasons behind such heterogeneity are unclear. The suggested crystalloid-colloid ratio has decreased over the years as less crystalloid is infused. Differences in ratios correlate mainly with the concentration of albumin solutions.

Table 23.3 Assumptions Underlying “Classic” Approaches to Perioperative Fluid Management

Assumption	Problems With Assumption
The patient is fasted preoperatively and is thus hypovolemic.	BUT current fasting guidelines allow water ingestion up to 2 hours prior to surgery. The so-called fluid deficit in elective surgery is negligible.
Insensible losses continue during surgery and must be accounted for.	BUT with laparoscopic and other minimally invasive surgery there is little insensible loss.
Fluid shifts to the “third space” must be replaced.	BUT it is unlikely that the “third space” exists.
Blood loss must be replaced with three to four times the amount of crystalloid.	BUT there should be an assessment of fluid responsiveness to guide administration of fluid after blood loss.
Hypotension following induction of anesthesia is due to vasodilation, and the vascular space must be filled.	BUT anesthetic-induced vasodilation is better managed with vasopressors and/or lighter anesthesia to maintain peripheral vascular resistance.
Urine output must be taken into consideration and replaced.	BUT antidiuretic hormone excretion (ADH) during surgery makes urine output as a guide very unreliable.
Even if the patient has an excessive intravascular volume, the kidneys will regulate.	BUT the kidneys are already stressed by ADH, and it may take days or weeks to excrete a large fluid load.

Intraoperative Fluids

Several previous assumptions regarding preoperative fluid therapy need to be modified. Some of these assumptions are listed in [Table 23.3](#).

Based on current findings, appropriate fluid replacement strategies for elective surgical procedures should consider the following principles:

1. No excessive administration of intravenous fluids at the start of a case or prior to epidural analgesia
2. No fluid replacement of “third space” or urine output
3. Replacement of surgical blood loss on a 1:1 basis with colloid
4. Use of colloid on a restricted basis for hypovolemia
5. Limit volume of crystalloids administered intraoperatively (e.g., limit to 100 to 200 mL/hr in the adult)
6. Preference for balanced salt solutions rather than normal saline
7. Postoperative restriction of fluids and use of diuretics if weight gain exceeds 1 kg

Monitoring Adequacy of Fluid Replacement

Assessment of the adequacy of intravascular volume is essential in assuring appropriate vascular volume, cardiac function, and tissue oxygenation. Traditional measurements such as arterial blood pressure and heart rate react slowly to changes in intravascular volume, depending also on contractility and compensation.^{28,29} Unfortunately, these measurements may not change with an intravascular fluid challenge, especially in elderly patients or those receiving cardiovascular medications (also see

[Chapters 25 and 35](#)). Surgical stimulation and anesthetic drugs can also impact these basic vital signs without changing intravascular volume status. Central venous pressure (CVP) records pressure from the right atrium and does not reliably indicate circulating blood volume or intravascular volume responsiveness. CVP may remain “normal” long after both blood pressure and heart rate have declined. The use of pulmonary artery catheters has decreased in frequency of use. Serial hemoglobin levels are also notoriously subject to intraoperative variability.

Arterial pulse pressure variation induced by mechanical ventilation has been appreciated for decades as an indicator of “fluid responsiveness.” Computerized analyses that incorporate information from the pulse oximeter arterial waveform provide an estimate of stroke volume variability and a prediction of response to intravascular fluid challenge. Several commercial monitors are available including Edwards Vigileo, System-Flo Trac, and Lidco, among others.^{30,31} Also, transesophageal echocardiography (TEE) can be used to assess cardiac output and preload in order to guide fluid therapy (also see [Chapter 20](#)). A combination monitor of TEE and pulse pressure variation (PPV) is available as the Cardio-EDM.³² Other monitors incorporate sensors on endotracheal tubes, and on finger probes again measuring PPV. Thus, intravascular fluid versus vasopressor therapy can be tailored to a patient’s needs rather than general application of formulas.

Although controversy still exists as to how much and which fluids to use, the current recommendations are becoming clearer. Older formulas have little or no place in currently practiced perioperative care. Our standard monitors do not give accurate information and should be supplemented with newer techniques such as pulse pressure or stroke volume variation measurements. Above all, patients must be treated as individuals and their complete

history and physical examination taken into account to allow sound clinical judgment to prevail.

QUESTIONS OF THE DAY

1. What is the rationale for intravenous fluid replacement of the so-called preoperative fasting deficit? Do clinical studies support this practice?
2. What metabolic abnormalities are associated with normal saline administration, as compared to balanced salt solutions?

3. What are the potential adverse affects of hydroxyethyl starch (HES) administration? Which patient populations should not receive HES solutions?
4. What common assumptions about perioperative fluid management should be challenged?

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