Fluids and Electrolytes

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LEARNING OBJECTIVES

1. Demonstrate an understanding of the composition of body fluids, fluid regulation, and fluid requirements in pediatric patients.
2. Assess laboratory data and physical signs and symptoms in the evaluation of fluid status and dehydration.
3. Devise intravenous fluid regimens for pediatric patients on the basis of age, clinical status, and identified needs.
4. Evaluate electrolyte status and recommend appropriate treatment for electrolyte abnormalities in pediatric patients.

ABBREVIATIONS IN THIS CHAPTER

AVP	Arginine vasopressin
ECF	Extracellular fluid
ICF	Intracellular fluid
TBW	Total body water

Table of other common abbreviations.

INTRODUCTION

Water, a primary component of body fluids, is the most abundant substance in the body. Water plays a vital role in several physiologic processes such as digestion, absorption and use of nutrients, distribution, waste excretion, and perfusion and maintenance of hemodynamics (Jain 2015; Schmidt 2010). Homeostasis of fluids and electrolytes occurs by complex systems that ensure proper functioning. Pediatric patients undergo rapid growth and development associated with changing pharmacokinetics from birth to adulthood. An understanding of these ongoing dynamic changes is essential for maintaining a patient's fluid balance, avoiding fluid and electrolyte derangements, and optimizing pharmacotherapy. For example, total body water (TBW) and hydration status affect the pharmacokinetics of medications by altering the volume of distribution, and for select medications, electrolytes may influence drug therapy or vice versa (Meyers 2009). This chapter focuses on the homeostasis and therapeutic management of fluids and electrolytes in various pediatric populations as well as select electrolyte abnormalities in pediatric patients.

FLUIDS

Composition of Body Fluids

Fluid Distribution/TBW

Total body water as a percentage of body weight changes during development from childhood into adulthood and depends on factors such as age, weight, sex, and percentage of body fat (Table 1) (Jain 2015; Schmidt 2010). Total body water is separated into three compartments: transcellular fluid (TCF) (e.g., synovial, pleural, CSFs), extracellular fluid (ECF), and intracellular fluid (ICF) (Schmidt 2010). Because the percentage of TCF is low (e.g., 1.5%–2.5% of TBW) and does not significantly contribute to fluid losses, this compartment will not be a focus of further discussion. The ECF/ICF ratio varies

throughout life, with a higher ECF/ICF ratio earlier in development. Variations in the ECF/ICF ratio with aging are secondary to changes in cellular growth, muscle mass, level of hydration, nutritional status, and renal function/urinary output. Clinical status and disease states such as nephrotic syndrome, liver failure, and protein-losing enteropathy can also alter the ECF/ICF ratio. By adolescence/adulthood, about two-thirds of TBW is distributed to the ICF, with the remainder in the ECF. Within the ECF, 75% of fluid is in the interstitial fluid compartment (i.e., between cells in the extravascular), with 25% circulating intravascularly (Figure 1). The changing TBW composition was shown in an NPR segment titled *Born Wet, Human Babies Are 75 Percent Water. Then Comes Drying*, which aired November 2013.

BASELINE KNOWLEDGE STATEMENTS

Readers of this chapter are presumed to be familiar with the following:

- Physiologic, pharmacokinetic, and pharmacodynamic differences across the pediatric age spectrum
- Common terminology used to describe fluid, electrolyte, and acid-base imbalances in pediatric patients
- Knowledge of pediatric renal function throughout development
- General knowledge regarding the homeostatic mechanisms involved in maintaining sodium and water balance/metabolism in pediatric patients
- Medications influencing fluid, electrolyte, and acid-base status
- General approach to managing electrolyte disturbances in pediatric patients

Table of common pediatric laboratory reference values.

ADDITIONAL READINGS

The following free resources have additional background information on this topic:

- Kearns GL, Abdel-Rahman A, Alander SW, et al. Developmental pharmacology-drug disposition, action, and therapy in infants and children. N Engl J Med 2003;349:1157-67.
- Buckley MS, Leblanc JM, Cawley MJ. Electrolyte disturbances associated with commonly prescribed medications in the intensive care unit. Crit Care Med 2010;38:S253-64.
- Segar JL. Renal adaptive changes and sodium handling in the fetal-to-newborn transition. Semin Fetal Neonatal Med 2017;22:76-82.
- Rhoda KM, Porter MJ, Quintini C. Fluid and electrolyte management: putting a plan in motion. JPEN J Parenter Enteral Nutr 2011;35:675-85.

Osmotic Equilibrium

Osmotic equilibrium is maintained in the body by three primary principles: hydrostatic pressure, oncotic pressure, and capillary permeability. Differences in solute composition are secondary to sodium (main extracellular cation), potassium (primary intracellular cation), and the sodium-potassium-adenosine triphosphatase (Na^+-K^+-ATPase) pump, which maintains sodium and potassium concentrations using cellular energy (Jain 2015; O'Brien 2014; Schmidt 2010). Water distribution between ECF and ICF is regulated by osmotic pressure (Schmidt 2010). Factors affecting this distribution include (1) transmembrane ion channels and electrochemical gradients and (2) semipermeable membranes that maintain osmotic equilibrium (O'Brien 2014). Cellular membranes are relatively impermeable to large anions and proteins but are freely permeable to water.

Osmolality is the concentration of all solutes in a given weight of water (Jain 2015). Sodium, glucose, and urea are the primary osmoles in blood, leading to the following equation for calculating osmolality:

calculated serum osmolality

$$= 2\ Na^+\ \frac{mmol}{L} + \frac{glucose\ \frac{mg}{dL}}{18} + \frac{BUN\ \frac{mg}{dL}}{2.8}$$

Normal values are 275–295 mOsm/kg. Hyper- and hypo-osmolality occur when the equilibrium is disturbed. Hyperosmolality (serum osmolality greater than 295 mOsm/kg) results from a relative deficiency of water to solute in the ECF. Hyperosmolality may occur when water intake is decreased or if water excretion is increased. Potential causes of hyperosmolality include diabetes insipidus, osmoreceptor dysregulation (rare), acute tubular necrosis, burns, GI illness, and iatrogenic causes. Hypo-osmolality (serum osmolality less than 275 mOsm/kg) is an indicator of excess water compared with solute in the ECF. Hypo-osmolality may occur secondary to increased TBW or depletion of body solutes, or a combination of the two. Common causes are syndrome of inappropriate antidiuretic hormone secretion, salt-losing nephropathy, diuretic use, mineralocorticoid deficiencies, GI illnesses, nephrotic syndrome, heart failure, and cirrhosis.

Fluid Regulation (Hypervolemia/Hypovolemia)

Water metabolism is a balance between intake and output. Intake consists of unregulated factors (ingested water in foods and liquids), water generated from the oxidation of ingested macronutrients, and regulated factors (consumption in response to thirst) (Jain 2015; Schmidt 2010). The

Table 1. Age-Related Changes in TBW

	Neonate (% body weight)	Infant (% body weight)	1 Yr (% body weight)	Adolescent/ Adult (% body weight)
TBW	23–27 wk GA: 85–90 28–32 wk GA: 82–85 36–40 wk GA: 71–76	~70	~60	~60 (male) ~55 (female)
Extracellular fluid	23–27 wk GA: 60–70 28–32 wk GA: 50–60 36–40 wk GA: ~40	~70	~55	~30
Intracellular fluid	23–27 wk GA: 30–40 28–32 wk GA: 40–50 36–40 wk GA: 60	~30	~45	~70
Transcellular fluid	~2.5	~2	~1.8	~1.7

GA = gestational age; TBW = total body water.

Information from: Jain A. Body fluid composition. Pediatr Rev 2015;36:141-52; O'Brien F, Walker IA. Fluid homeostasis in the neonate. Pediatr Anesth 2014;24:49-59; and Schmidt GL. Fluids and electrolytes. In: Corkins M, ed. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition, 2010:87-102.

sensation of thirst is controlled by the activation of baroreceptors, release of angiotensin II, increase in serum tonicity, and activation of osmoreceptors in the anterior hypothalamus (Jain 2015). Output/excretion is the main regulator of water metabolism. Water loss occurs through insensible losses by skin, respiratory, and GI and through sensible losses such as urinary excretion. The main driving factor for water output occurs by physiologic feedback through the activity of antidiuretic hormone/arginine vasopressin (AVP), renin-angiotensin-aldosterone system (RAAS), and other compounds such as natriuretic peptides and prostaglandins (Jain 2015; O'Brien 2014; Schmidt 2010).

Hypovolemia, defined as a decrease in TBW, causes an increased serum osmolarity, which results in the release of two hormones: AVP and aldosterone (Jain 2015). Arginine vasopressin is synthesized in the hypothalamus and

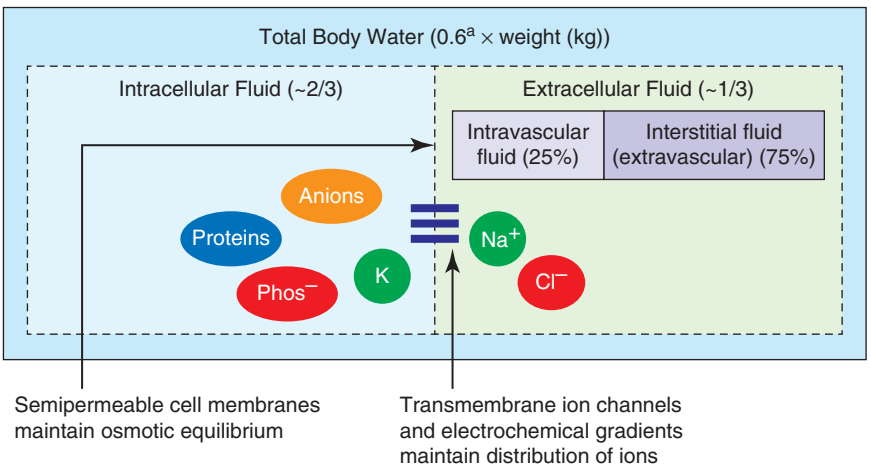


Figure 1. Body distribution of fluid and solutes in adolescents/adults.

[a]Correction factor varies across age and sex (see Table 1).

Information from: Jain A. Body fluid composition. Pediatr Rev 2015;36:141-52; O'Brien F, Walker IA. Fluid homeostasis in the neonate. Pediatr Anesth 2014;24:49-59; and Schmidt GL. Fluids and electrolytes. In: Corkins M, ed. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition, 2010:87-102.

stored in the pituitary. Arginine vasopressin is superbly sensitive, with small alterations in serum osmolality (e.g., 1%) leading to large, minute-to-minute changes in AVP release and physiologic responses. The AVP that is released from the posterior pituitary interacts with the AVP V2 receptors in the kidneys. This interaction stimulates the insertion of aquaporin 2 channels on the luminal surface of the collecting tubules, leading to increased free water reabsorption. Aldosterone is also released through the RAAS. Detection of a low ECF leads to the release of renin, which converts angiotensin I to angiotensin II. Angiotensin II leads to vasoconstriction and the release of aldosterone, which causes sodium and water reabsorption in the distal convoluted tubules of the kidneys (Jain 2015). Clinical scenarios that may result in hypovolemia include bleeding/blood loss, GI illnesses such as vomiting and/or diarrhea, burns, excessive sweating or diuresis, and diabetes insipidus. In such cases, the disease state overwhelms the body's natural process for regulating volume (Powers 2015).

Hypervolemia, defined as an increase in TBW, causes a decreased serum osmolality and reduced AVP concentrations (Schmidt 2010). Under normal circumstances, hypervolemia leads to decreased thirst and increased excretion of water by the kidneys. However, in certain clinical situations such as heart failure, hypervolemia does not inhibit AVP, which results in continued volume expansion and hyponatremia. Hypervolemia may also be caused by conditions such as kidney or liver failure, sepsis, and syndrome of inappropriate antidiuretic hormone secretion.

Fluid Considerations: Historical Perspective and Maintenance Requirements

Maintenance fluid therapy is necessary to maintain fluid homeostasis and is a requirement for all patients. The main objective in maintenance fluid therapy is to provide adequate fluid to replace normal, ongoing physiologic losses (Holliday 1957). Maintenance fluid therapy does not replace deficits or ongoing additional losses and does not provide nutritional support.

Fluid therapy was described in the literature as early as 1918 in pediatric patients with dehydration (Bailey 2010). In the early 20th century, work focused on expanding the understanding of fluid composition and estimating fluid needs. In 1957, Holliday and Segar published a practical method for evaluating and calculating fluid status, which became and continues to be the basis for prescribing intravenous fluids (Table 2) (Meyers 2009; Holliday 1957). Holliday and Segar proposed that because insensible loss of water paralleled energy metabolism, fluid needs were derived from a function of energy metabolism. This method equates the kilocalories expended with fluid requirements: for each 100 kcal used in metabolism, 100 mL of fluid is needed to replace losses.

Compared with adult patients, children have higher requirements for maintenance fluid (on a milliliter/kilogram/day basis) because of increased metabolic rates, higher body surface area/weight ratios, and higher respiratory rates. Various methods can be used to estimate maintenance fluid requirements. However, the Holliday-Segar and the 4-2-1 methods (see Table 2) are most commonly used in practice today. Although these calculations are reasonable for providing estimates of fluid requirements, individualized and tailored therapy for overall fluid requirements must account for the patient's underlying clinical condition. Certain conditions, such as gastroschisis, burn injury, and hypermetabolic states, increase fluid needs. Other conditions, such as cardiac or respiratory disorders, decrease fluid requirements. Estimates of maintenance fluid needs are used initially, with close monitoring of fluid therapy used thereafter (e.g., laboratory values, vital signs, clinical signs, and symptoms of volume status) and alterations made on the basis of individual responses to therapy.

Table 2. Common Methods to Estimate Maintenance Fluid Requirements in Pediatric Patients[a]

Method to Estimate Maintenance Fluid Needs	Details	Pros	Cons
Holliday-Segar (daily requirement)	0–10 kg: 100 mL/kg/day > 10 kg to ≤ 20 kg: [1000 mL + (50 mL x each kg > 10 kg)]/day > 20 kg: [1500 mL + (20 mL x each kg > 20 kg)]/day	Simple calculation	Does not account for abnormal clinical circumstances
4-2-1 (hourly requirement)	0–10 kg: 4 mL/kg/hr > 10 kg to ≤ 20 kg: 40 mL/hr + (2 mL/hr x each kg > 10 kg) > 20 kg: 60 mL/hr + (1 mL/hr x each kg > 20 kg)		

[a]Excludes neonates.

Special Population Consideration: Neonates

Fluid homeostasis in the neonatal patient must account for the demands of transitioning from intrauterine to extrauterine existence as well as rapid growth and development (O'Brien 2014). During fetal development, the fluid and electrolyte balance depends on the placenta; postnatally, the neonate must regulate the balance of fluid and electrolytes. Premature neonates rely on immature organ and hormone systems to adapt to this change (Chow 2008). Maintaining nutrition and hydration, preventing dehydration, and avoiding fluid overload are challenges that must be considered during the early neonatal period.

Postnatal adaptation depends on intrauterine growth as well as gestational age (Chow 2008). Under normal physiologic conditions, within the first 24–48 hours of early postnatal period, natriuresis and diuresis occur by excretion of sodium and water through the kidneys. The contraction of ECF because of water loss results in a reduction of body weight of 5%–15% (O'Brien 2014; Oh 2012; Meyers 2009). Premature neonates and/or those who are small for gestational age have a larger percentage of TBW, as well as immature skin barriers and a higher body surface area/weight ratio. As such, the percentage of weight loss is inversely related to gestational age and birth weight (Oh 2012; Chow 2008). The processes of natriuresis and diuresis contribute to reduced incidence rates of complications of prematurity such as patent ductus arteriosus, necrotizing enterocolitis, bronchopulmonary dysplasia, and intracranial hemorrhage, each associated with poor neurodevelopmental outcomes (Oh 2012). As such, a goal of fluid and electrolyte therapy during the neonatal period is to allow these processes to occur in order to avoid fluid retention and concomitant complications. Avoiding fluid retention and concomitant complications is achieved through the careful provision of volume and electrolytes (Chow 2008).

Volume delivery must account for neonatal renal function. Neonatal kidneys are immature, and function depends on the level of prematurity (Chow 2008). During fetal development, nephrogenesis occurs at 4–5 weeks' gestation, yet the development of nephrons does not begin until 20–22 weeks' gestation, with completion at 34–35 weeks' gestation. Neonates also cannot excrete excess fluid and electrolytes because of tubular immaturity, high ECF volume, and decreased response to aldosterone. In addition, the neonatal RAAS is altered because AVP concentrations are higher in the first 24 hours of life (O'Brien 2014; Oh 2012; Chow 2008). Volume delivery early in life is typically 60–100 mL/kg/day, depending on the level of prematurity. If excessive volume is provided during the early neonatal period, fluid retention can occur, rather than contraction of the ECF, thus leading to poor outcomes (O'Brien 2014; Oh 2012). Underlying medical conditions are important to consider during volume delivery. For example, children born with cardiac or pulmonary disorders require more conservative fluid provision. Conversely, those born with gastroschisis require higher fluid intake because of fluid loss in utero.

Volume provision also depends on external factors during the neonatal period. Incubators and radiant warmers provide a thermoregulated environment for the premature neonate; however, they may lead to increased insensible water losses (Chow 2008). Phototherapy also affects insensible water loss. These challenges can be overcome by adjusting humidity within the environment or altering fluid therapy to make up for the additional losses.

Early provision of electrolytes should be avoided until renal function is established. Early administration of sodium can lead to fluid retention and, for the reasons stated earlier, is avoided until renal function is established. Exceptions include gastroschisis, in which children may be born with a sodium deficit because of intestinal fluid loss during fetal development. To avoid hyperkalemia and its associated complications, potassium should not be added to neonatal fluids until the urinary output is established.

Hypoglycemia can also be harmful in neonatal patients (Bailey 2010). Neurodevelopmental impairment, one of the most harmful effects of hypoglycemia, can occur if hypoglycemia is left untreated. Therefore, a higher dextrose content is required in the neonatal period to maintain euglycemia. The typical fluid administered within the first 24–48 hours consists of dextrose 10% without added electrolytes, at restricted volumes (60–100 mL/kg/day). Once renal function and diuresis occurs, fluid volume can be liberalized, and sodium, potassium, and other electrolytes can judiciously be added.

Altered Maintenance Needs in the Surgical Patient

For the surgical patient, preoperative fasting may place children at a fluid deficit because of ongoing insensible losses and urinary output in the absence of intake (Bailey 2010). In the 1970s, periods of fasting were prolonged, and various strategies were proposed to make up for these deficits such as bolus dosing and/or increasing maintenance needs by multiplying by a factor. However, in the past 30 years, preoperative fasting guidelines have been liberalized to allow shorter periods of reduced intake. Still, in some clinical scenarios, children may be fasting for longer than 2 hours and go into an operation already at a deficit. Pre-, intra-, and postoperative fluid provision must account for the patient's individual fluid status, losses during surgery, and postoperative recovery.

Glucose management is critically important for the surgical patient, with keen attention paid to managing hyper- and hypoglycemia. If ischemia and hypoxia are present, hyperglycemia may lead to the accumulation of lactate because of decreased metabolism, resulting in a decrease in serum pH and ultimately cellular death. Hyperglycemia may also lead to dehydration and electrolyte abnormalities. Because of the potential for these harmful effects, dextrose in maintenance

fluids in the operating room is administered cautiously for the otherwise healthy surgical pediatric patient. However, for surgical neonates and those at high risk of hypoglycemia, intravenous fluids typically contain dextrose.

Postsurgical patients are also at risk of hyponatremia and acid-base abnormalities after surgical procedures (Sümpelmann 2017). Intraoperative fluid and electrolyte losses contribute to these risks, in addition to the release of antidiuretic hormone (Oh 2016). Factors such as duration and type of surgery influence the degree of risk, with children undergoing neurosurgical procedures at a relatively higher risk (Williams 2016; Edate 2015; Belzer 2014). Choice of fluid and volume provided must account for the risk of hyponatremia and acid-base status, and patients should be monitored closely during the postoperative period for fluid and electrolyte derangements, with individualized adjustments made on the basis of clinical status.

Intravenous Fluid Choices/Considerations

The provision of intravenous fluid therapy to pediatric patients is lifesaving; however, like all pharmacotherapy, several risks are possible, such as inaccurate volume provided, inappropriate fluid choice, risk of extravasation, or mechanical complications such as thrombosis and infection (McNab 2016). The pediatric pharmacist must understand intravenous fluid therapy to mitigate these risks. Intravenous fluids fall into two broad categories: colloids and crystalloids.

Colloids vs. Crystalloid Fluid

Colloid fluids may be natural (e.g., albumin, blood products) or synthetic (e.g., hydroxyethyl starches, dextrans, and gelatins [not available in the United States]) (Table 3) (Bailey 2010). Colloids may be chosen when intravascular volume expansion is desired and for acute resuscitation. Compared with crystalloids, a higher proportion of the administered dose stays within the vasculature. Colloids can also pull fluid (water) from the extravascular space into the vasculature for intravascular volume expansion. However, for patients with sepsis, capillary leak, and/or "third spacing," colloids may worsen edema. Capillary leak may allow colloids to leak into the interstitial space, which then also results in the drawing of water into the interstitial compartment because of increased osmolality. Of the colloids, albumin is the most commonly used, especially in neonates and infants. However, strong data supporting its use for general fluid resuscitation are lacking, and in some patient populations (e.g., those with traumatic brain injury), albumin may be harmful (Bailey 2010). Synthetic colloids are not well studied in the pediatric population, and the existing literature suggests a greater potential for adverse events. Studies of adult patients have led to the recommendation that in most cases, crystalloids are preferred to colloids for fluid resuscitation because of decreased cost, lower risk of adverse events, and lack of proven efficacy of colloids over crystalloids. This lack of strong evidence supporting the use of colloids over crystalloid fluids has led to

Table 3. Summary of Select Colloids

Colloid	Select Details	Potential Adverse Events
Albumin gold standard	Derived from pooled human plasma Molecular weight: 69 kDa 5% albumin: Osmotically equivalent to an equal volume of plasma 25% albumin: Osmotically 5 x greater than an equal volume of plasma Both albumin 5% and albumin 25% contain 130–160 mEq/L of sodium	Anticoagulation (weak effect) Allergic reactions Select products contain aluminum; caution should be used in patients with renal impairment as well as in premature neonates, especially if concomitantly on parenteral nutrition (daily aluminum content > 4–5 mcg/kg/day is associated with CNS and bone toxicities)
Hydroxyethyl starches	Synthetic colloid/modified natural polysaccharide Molecular weight varies: < 70 kDa, 130–270 kDa, > 450 kDa Expands plasma volume for 2–6 hr Typically contains 140–154 mEq/L of sodium	Anticoagulation Renal toxicity Pruritus
Dextran	Water-soluble glucose polymer Molecular weight varies: 40 kDa, 70 kDa Expands plasma for 5–6 hr (Dextran 70), 3–4 hr (Dextran 40) Can be in D_5W or NaCl	Anticoagulation (strong effect) Anaphylactic reactions

D_5W = 5% dextrose in water; NaCl = sodium chloride.

Information from: Bailey AG, McNaull PP, Jooste E, et al. Perioperative crystalloid and colloid fluid management in children: where are we and how did we get here? Anesth Analg 2010;110:375-90.

Table 4. Summary of Select Crystalloids

Fluid	Osmolarity (mOsm/L)	Sodium (mEq/L)	Chloride (mEq/L)	Other
D_5W only	252	—	—	Dextrose 5 g/100 mL
0.9% NaCl	308	154	154	—
0.45% NaCl	154	77	77	—
D_5W + 0.225% NaCl	329	38.5	38.5	Dextrose 5 g/100 mL
D_5W + 0.45% NaCl	406	77	77	Dextrose 5 g/100 mL
Lactated Ringer	273	130	109	Potassium 4 mEq/L Lactate 28 mEq/L Calcium 2.7 mg/dL
Plasma-Lyte A	294	140	98	Potassium 5 mEq/L Magnesium 3 mEq/L Acetate 27 mEq/L Gluconate 23 mEq/L

varying recommendations. The 2000 International Guidelines for Neonatal Resuscitation no longer recommend albumin as the fluid of choice for initial volume expansion because of its limited availability, possibility for infectious complications, and possible association with increased mortality (Neirmeyer 2000).

Crystalloid fluids are the mainstay of intravenous fluid therapy. Table 4 summarizes the various crystalloid fluids currently used. In addition to estimating fluid needs, Holliday and Segar estimated electrolyte requirements (see the Electrolytes section), which are theoretically met using hypotonic crystalloid fluids infused at maintenance rates, namely dextrose 5% in 0.225% sodium chloride or dextrose 5% in 0.45% sodium chloride, plus 20–40 mEq/L of potassium chloride, depending on renal function and potassium status. Crystalloids have become the mainstay of maintenance intravenous fluid therapy and have remained as such for the past 50-plus years. However, according to more recent data, applying the Holliday-Segar method as well as fluid choice may not be appropriate in all clinical scenarios today. The choice of maintenance fluid depends on the patient's clinical status, the patient's laboratory values, and institutional practice. In addition, after original estimates and empiric fluid selections, the choice of ongoing fluid must be individualized and tailored to meet patient-specific needs.

Hypotonic vs. Isotonic Fluids

Crystalloid fluids have historically been chosen on the basis of Holliday-Segar estimates, which account for maintenance electrolyte requirements (Meyers 2009). When Holliday-Segar estimated pediatric electrolytes in the 1950s, requirements were suggested to fall between what would be consumed from breast milk and adult requirements (McNab 2016). As such, for the past 50-plus years, dextrose 5% in 0.45% sodium chloride or dextrose 5% in 0.225% sodium chloride has been the mainstay of therapy, which, when given at maintenance rates, provides about 2–4 mEq/kg of sodium per day. However, this may not be appropriate for all patients today.

Tonicity is the ability of fluid to exert an osmotic force and influence the movement of fluid across cellular membranes (McNab 2016). Crystalloids can be categorized as hypotonic, isotonic, or hypertonic. The traditional fluids (as discussed earlier) are considered hypotonic. Although conventionally hypertonic compared with plasma, once administered, cells rapidly uptake dextrose; this almost-immediate dextrose metabolism reduces the tonicity of the fluid, which in essence becomes equivalent to 0.45% or 0.225% sodium chloride without dextrose. Thus, these fluids are considered hypotonic. When hypotonic fluids are administered, an osmotic gradient is created, which can drive fluid from the intravascular space into the intracellular space because intracellular osmolality is greater than intravascular (and interstitial) osmolality. In severe cases, cerebral edema, brain hypoperfusion, and neurologic damage may occur. In a typically healthy child, the renal system will compensate for reduced serum sodium through alterations in AVP release. However, in acutely ill patients, the AVP response may be blunted, leading to hyponatremia and poor clinical outcomes. This concept has called into question the appropriateness of the traditional hypotonic fluids historically suggested by Holliday-Segar for use in hospitalized pediatric patients today. Several case reports outlining poor clinical outcomes associated with hyponatremia in hospitalized patients as well as studies comparing hypotonic fluids with isotonic fluids have been published over the past 20 years. Because of study heterogeneity, no clear

consensus regarding the optimal crystalloid fluid has been developed to date.

A 2014 Cochrane review evaluated 10 trials in which most patients (n=1106) were children (3 months to 18 years of age) (McNab 2014). Most studies included in the analysis were of surgical and ICU patients, and data were limited beyond 24 hours. The primary end point, risk of developing hyponatremia (serum sodium less than 135 mEq/L), was halved in those receiving isotonic fluid compared with those receiving hypotonic fluids (RR 0.48; 95% CI, 0.38–0.6). The risk of hypernatremia was unclear from this investigation. Because adverse events associated with either fluid were rare, comparative safety determinations are not possible from this study. Although limitations exist in the interpretation and clinical application of data from this systematic review, isotonic fluids may be preferable to hypotonic fluids, at least during the first 24 hours of hospitalization of surgical or critically ill patients.

A similar systematic review of randomized trials of hospitalized children 1 month to younger than 19 years compared isotonic fluids with hypotonic fluids (Padua 2015). Compared with the 2014 Cochrane review, two additional studies were included for analysis; however, the additional included population was similar (e.g., most were critically ill) (Padua 2015; McNab 2014). Of importance, studies that included patients with dysnatremia secondary to disorders including heart failure, renal dysfunction, and liver disease or those who required fluid resuscitation or replacement therapy were excluded from the analysis. Eleven studies evaluating 1095 medical and surgical patients 3 months to 18 years of age were included in the analysis. The risk of developing hyponatremia or severe hyponatremia was significantly reduced in those who received isotonic maintenance fluids (RR 0.5; 95% CI, 0.4–0.62 and RR 0.21; 95% CI, 0.1–0.45, respectively). Of studies that reported mean plasma sodium concentrations (n=7), patients receiving hypotonic fluid had significantly lower serum sodium concentrations as well as decreased sodium concentrations from baseline. However, isotonic fluids did not increase the risk of hypernatremia compared with hypotonic fluids.

In a 2015 study, authors evaluated the administration of isotonic (sodium chloride 0.9% in dextrose 5%) compared with hypotonic (sodium chloride 0.45% in dextrose 5%) maintenance fluids in hospitalized pediatric patients (non-ICU patients) (Friedman 2015). Children 1 month to 18 years of age with normal baseline serum sodium concentrations (135–145 mEq/L) receiving 80%–120% of maintenance fluid needs were randomized to receive either isotonic fluids or hypotonic fluids for 48 hours. One hundred ten children with a median age of 4.5 years (range 0.1–17.2 years) were enrolled in the study. The two groups had similar baseline characteristics. The primary outcome measure, mean (SD) serum sodium concentration at 48 hours, was similar between the two groups (isotonic 139.9 [2.7] mEq/L vs. hypotonic 139.6 [2.6] mEq/L, p=0.6). The secondary outcome measures of serum sodium at 24 hours and change in weight were also similar between groups. A post hoc exploratory analysis showed significant differences in serum sodium change from baseline, with those in the hypotonic group having a decrease in serum sodium compared with baseline values. No patient had significant adverse events attributable to the study.

From this review of available data on the subject, no clear consensus or generalization can be made for all hospitalized patients. However, evidence suggests that isotonic fluids in critically ill children, at least during the first 24 hours of hospitalization, are more appropriate and possibly safer than traditional hypotonic fluids with respect to serum sodium concentrations (Wang 2014). Other outcomes such as hospital length of stay and mortality have not specifically been evaluated. For noncritically ill children, the evidence is less clear, and therapy should be individualized according to clinical presentation. Specific considerations may be required because many factors may affect the risk of hyponatremia. Postsurgical patients may be at an increased risk of hyponatremia with the administration of hypotonic fluids because of increased extrarenal losses of electrolytes and increased release of AVP (Bailey 2010). Sex and age differences also exist with respect to hyponatremia and associated risks. Estrogen may impair the brain's ability to adapt to hyponatremia (Bailey 2010). Postmenarchal females are at a higher risk than males. Before puberty, all children are at a higher risk than adults of cerebral edema in the setting of hyponatremia because of the relative inability of the developing brain to adapt to hyponatremia/excess free water and a higher brain-to-skull ratio. Additional well-designed trials are necessary, focused on select patient populations, to further delineate the optimal empiric maintenance fluid.

Fluid Considerations: Management of Dehydration/Correction of Deficits

Guiding Principles

Fluid deficits are defined as losses of fluid above what is expected through insensible and sensible losses. Deficits may occur for a variety of reasons such as GI illness, blood loss, respiratory disease (asthma/pneumonia/bronchiolitis), neurologic disease, or inadequate intake over a period (Meyers 2009). Dehydration is one of the main causes of pediatric morbidity and mortality, with infants and very young children at greatest risk (Powers 2015). Hypovolemia and dehydration occur when fluid losses exceed the replacement rate. If water and electrolytes are not replaced in a timely and adequate fashion, circulating volume decreases, organ and tissue perfusion is compromised, and negative clinical outcomes occur.

Clinical Evaluation and Assessment of Severity

Clinical evaluation of the patient thought to have fluid deficit should include a physical examination of overt signs and symptoms of dehydration (Table 5). When a pre-illness/baseline weight is known, the degree of dehydration and the

Table 5. Clinical Signs, Symptoms, and Correlates of Dehydration[a]

Clinical Signs	Mild Dehydration	Moderate Dehydration	Severe Dehydration
Pulse	Full, normal rate	Slightly increased	Rapid, weak
Systolic blood pressure	Normal	Normal-low	Shock
Urinary output	Normal or decreased	Markedly decreased (e.g., < 1 mL/kg/hr)	Anuric
Weight loss	3%–5%	6%–10%	9%–15%
Thirst	Slight	Moderate	Intense
Behavior	Normal	Irritable	Irritable/lethargic
Mucosa	Normal/slightly dry	Dry	Extremely dry
Tears	Present	Reduced	Absent
Eyes	Normal	Deep set	Markedly sunken
Skin turgor	Normal	Decreased	Tenting/increased
Skin	Normal	Cool	Cool, mottling
Fontanelle	Flat	Reduced	Sunken
Capillary refill	2–3 s	> 5 s	> 8 s

[a]Capillary refill time, skin turgor, and vital signs may be the most useful individual signs of dehydration; however, scales based on a combination of physical findings are more predictive than individual signs.

Information from: Merck Manual: Dehydration in Children; and Canavan A, Arant BS. Diagnosis and management of dehydration in children. Am Fam Physician 2009;80:692-6.

estimated volume required to restore euvolemia can be calculated using the following equations:

$$\%\ dehydration = \frac{[(pre\text{-}illness\ weight\ (kg)) - (illness\ weight\ (kg))] \times 100}{pre\text{-}illness\ weight\ (kg)}$$

$$fluid\ deficit\ (L) = \%\ dehydration \times pre\text{-}illness\ weight\ (kg) / 100$$

Of importance, signs and symptoms of dehydration must continually be reevaluated because the previously mentioned calculations are only estimates. Thus, therapy should be adjusted as necessary throughout the patient's clinical course. Assessment of laboratory values, including acid-base status and serum electrolytes, must also be included in the evaluation of dehydration (Powers 2015). This is especially important in children requiring intravenous fluid therapy to make up for fluid deficits.

Classification of Dehydration

Once dehydration is confirmed, the type of dehydration must be determined: isonatremic, hyponatremic, or hypernatremic (Meyers 2009). A comprehensive review of managing each type of dehydration is beyond the scope of this chapter. Table 6 provides an overview of the three main types of dehydration.

Management of Dehydration

A guiding principle of managing dehydration is to recognize the degree and type of dehydration and then to restore fluid and electrolyte deficits. It is also crucial to meet maintenance needs and address any additional ongoing losses (Powers 2015).

Mild to moderate dehydration can be managed using appropriate oral rehydration solution therapy, such as the WHO oral rehydration solution or Pedialyte (Powers 2015). Liquids such as juice, sports beverages, and milk are not appropriate oral fluids for dehydration because of inappropriate glucose and electrolyte composition; however, children who are breastfed human milk may continue to breastfeed if the cause of dehydration is diarrheal illness. For mild dehydration, 50 mL/kg over 4 hours is provided in small aliquots (Meyers 2009). For moderate dehydration, 100 mL/kg is provided over 4 hours.

For patients with more severe dehydration or those who cannot be rehydrated enterally, intravenous fluids are used to restore fluid homeostasis. The general approach to restoring fluid balance can be broken into three phases: phase 1, acute resuscitation (i.e., fluid bolus); phase 2, the first 8 hours of therapy; and phase 3, the next 16 hours (Meyers 2009). Isotonic crystalloid fluids such as normal saline or lactated Ringer solution, or colloids such as blood or 5% albumin are administered at a dose of 10–20 mL/kg over 30–60 minutes when acute resuscitation is warranted to correct for hemodynamic instability. Fluid choice depends on the clinical situation

Table 6. Types of Dehydration

	Hyponatremic Dehydration	Isonatremic Dehydration (most common)	Hypernatremic Dehydration
Serum sodium	< 130 mEq/L	130–150 mEq/L	> 150 mEq/L
Losses	Solute loss is greater than water loss	Equal water and solute loss	Water loss is greater than solute loss
Associated conditions	Cerebral salt wasting Overaggressive diuresis	Secretory diarrhea	Viral gastroenteritis Poor breastfeeding Diabetes insipidus
Management	IV rehydration: • Unstable initial: 20-mL/kg bolus of 0.9% NS • If acute symptoms such as seizures, sodium bolus (see the Hyponatremia section) may be given • Fluid choice must account for sodium and potassium deficits Do not correct sodium faster than 12–15 mEq/L/24 hr	Mild to moderate: Oral rehydration can be considered Moderate to severe: IV rehydration generally required • Unstable initial: 20-mL/kg bolus of 0.9% NS • Replace 50% deficit over 8 hr, followed by remaining 50% over next 16 hr • Combine with maintenance fluids + replacement fluids	IV rehydration: • Unstable initial: 20-mL/kg bolus of 0.9% NS • Fluid choice must account for serum sodium as well as free-water deficit (typically dextrose 5% in 0.225% or 0.45% NS)

IV = intravenous(ly); NS = normal saline (0.9% NaCl).

Information from: Powers KS. Dehydration: isonatremic, hyponatremic and hypernatremic recognition and management. Pediatr Rev 2015;36:274-85.

and the source of fluid loss. Boluses may be repeated two or three times to adequately restore perfusion (e.g., resolution of tachycardia and hypotension and improved capillary refill). During this resuscitation phase, clinicians should also monitor for and avoid over-resuscitation (e.g., rales, hepatomegaly). During phase 2, one-third of maintenance fluid plus one-half of the remaining deficit (subtract the volume provided from the boluses given in phase 1) is administered over 8 hours. During phase 3, two-thirds of maintenance fluid plus the remaining deficit is provided over the next 16 hours. Fluid choice depends on the type of dehydration and the patient's individual laboratory values. For patients with hypernatremic or hyponatremic dehydration, serum sodium must not be corrected faster than 12 mEq/L/day because of the risks of cerebral edema or central pontine myelinolysis, respectively.

Fluid Consideration: Replacement Fluid Therapy

Replacement fluid therapy accounts for ongoing losses such as vomiting, diarrhea, suctioning, chest tubes, and shunts (Powers 2015; Meyers 2009). For patients with ongoing losses, the amount and type of fluid loss is evaluated, which then guides the fluid choice. The most precise way of determining the type of fluid for replacement fluids is a laboratory analysis of electrolyte composition. However, this is costly and not always clinically feasible. For practicality, reference tables are used, with the choice of crystalloid fluid closely mimicking the type of fluid lost (Table 7). In clinical practice, replacement fluid may be given on a milliliter/milliliter basis or as a proportion of losses (e.g., 0.5 mL for each 1 mL lost) (Powers 2015). If ongoing losses are consistent and stable, daily totals may be added to the patient's maintenance needs, simplifying the fluid regimen. Although certain fluids contain electrolytes such as potassium, many institutions do not allow potassium to be added to replacement fluids for safety reasons.

ELECTROLYTES

The electrolytes (sodium, potassium, magnesium, calcium, phosphorus) are essential to maintain normal biochemical reactions and homeostatic functioning (Table 8). Electrolytes work in concert to maintain cell membrane functions, nerve conductivity, muscle contractility, hormonal activity, bone structure, and fluid and acid-base homeostasis. Both serum electrolyte balance and normal balance are guided by renal function (Meyers 2009). Under normal processes, the electrolyte balance is maintained. However, clinical conditions and medications can cause electrolyte abnormalities. In assessing electrolytes, three basic steps guide therapy: determine the cause, classify it as acute or chronic, and determine a therapeutic plan to manage the electrolyte abnormality. In the following discussion, each electrolyte will be reviewed, with summaries of normal function, excess, and deficits.

Table 7. Approximate Electrolyte Composition of Body Fluids

	Gastric	Ileostomy	Diarrhea	Sweat	Bile	Pancreatic	Small Bowel	Burns
Na (mEq/L)	20–80	45–135	10–90	10–30	120–140	120–140	100–140	140
K (mEq/L)	5–20	3–15	10–80	3–10	5–15	5–15	5–15	5
Cl (mEq/L)	100–150	20–115	10–110	10–35	80–120	90–120	90–130	110
Example empiric fluid choice	0.45% NaCl				0.9% NaCl			

Information from: Davenport M, Syed SHS. Fluids, electrolytes, and dehydration. In: Sinha CK, Davenport M, eds. Handbook of Pediatric Surgery. London: Springer-Verlag London, 2010:9-19.; and Lam WM. Fluids and electrolytes. In: Benavides S, Nahata MC, eds. Pediatric Pharmacotherapy. Lenexa, KS: American College of Clinical Pharmacy, 2013:290-304.

Table 8. Overview of Electrolytes and Management of Deficiencies

	Normal Daily Requirements	Treatment of Deficit (Oral)	Treatment of Deficit (IV)
Sodium	2–5 mEq/kg/day	2–5 mEq/kg/day in divided doses	Calculation of deficit: Dose (mEq of sodium) = [desired serum sodium (mEq/L)* – actual serum sodium (mEq/L)] x K x wt (kg) K = 0.6 (males), 0.5 (females) *For acute correction, desired sodium should be 125 mEq/L
Potassium	Neonate: 2–6 mEq/kg/day Children: 2–3 mEq/kg/day	2–5 mEq/kg/day in divided doses, not to exceed 1–2 mEq/kg/dose	0.5–1 mEq/kg/dose, infuse at 0.3–0.5 mEq/kg/hr (maximum dose/rate 10–20 mEq/hr) *For rates > 0.5 mEq/kg/hr, continuous cardiac monitoring is recommended (not to exceed 1 mEq/kg/hr or 40 mEq/hr)
Magnesium	0.3–0.5 mEq/kg/day (1 mEq = ~12 mg of elemental magnesium)	10–20 mg elemental / kg/dose up to four times per day (oral replacement is challenging because of GI intolerance)	2.5–5 mg of elemental magnesium kg/dose Infuse slowly, generally over 1–4 hr Preferred salt for IV replacement is magnesium sulfate, dosed as follows: 25–50 mg/kg/dose every 6–12 hr for two or three doses; then recheck serum concentration; maximum dose: 2000 mg/dose
Calcium	Neonates: 200 mg/day (elemental) Children: 700–1300 mg/day	(dose expressed as elemental calcium) 50–150 mg/kg/day in four to six divided doses	Calcium gluconate: 200 mg/kg every 6–12 hr (neonates) 200–500 mg/kg/day as continuous infusion or in four divided doses (infants, children, adolescents) Maximum single dose: 1000 mg (infants/children), 2000–3000 mg (adolescents/adults) Calcium chloride: 10–20 mg/kg/dose every 4–6 hr (neonates) 10–20 mg/kg/dose every 4–6 hr (infants, children, adolescents) Maximum single dose: 1000 mg
Phosphorus	1–2 mmol/kg/day	0.08–0.32 mmol/kg/day	0.5–2 mmol/kg/day in divided doses

Sodium

Primary Physiologic Function and Normal Homeostasis

Sodium (typical range 135–145 mEq/L) is the most abundant cation in the body; it plays three main functions: fluid balance, osmotic regulation, and maintenance of membrane potential (Schmidt 2010). Sodium excretion, rather than intake, primarily regulates sodium homeostasis. The RAAS and glomerular filtration rate (GFR) are the main contributors to regulation of sodium homeostasis, with RAAS activation leading to increased renal tubular sodium reabsorption. Changes in GFR affect the amount of sodium that is filtered. Other factors such as intrarenal blood flow, renal prostaglandins, and natriuretic peptides also play a role, albeit more limited, in sodium regulation. The Na^+-K^+-ATPase pump maintains cellular membrane potential (Schmidt 2010). Under normal physiologic circumstances, the body's sodium intake matches sodium losses.

Hypernatremia

Hypernatremia is defined as a serum sodium concentration greater than 145 mEq/L (Schmidt 2010). Causes of hypernatremia include, but are not limited to, dehydration, GI illness, fever, lack of intake, and medications such as diuretic therapy and hypertonic saline. Hypernatremia presents with increased thirst, fatigue, restlessness, and muscle irritability (Rhoda 2011). In severe hypernatremia, cerebral cellular dehydration can occur, which can progress to hemorrhage, neurologic sequelae such as seizures, coma, and death (Powers 2015; Rhoda 2011). Management of hypernatremia relies on first identifying the underlying cause and then correcting it. For example, if hypernatremia is caused by the lack of oral intake of fluid resulting in dehydration, correcting the dehydration will correct the serum sodium. Likewise, if diuretic therapy is the cause, adjusting the medication, if possible, will correct this electrolyte abnormality. If the serum sodium is greater than 160 mEq/L, correction should not occur faster than 0.5 mEq/L/hour over 48 hours to avoid the risk of cerebral edema and possibly death.

Hyponatremia

Hyponatremia is defined as a serum sodium concentration less than 135 mEq/L (Schmidt 2010). Hyponatremia is one of the most common electrolyte disturbances. Many causes are possible, including diarrhea, dehydration, enterocutaneous fistulas, and loop and thiazide diuretic use. Common signs and symptoms of hyponatremia include headache, GI symptoms such as nausea, myopathy, lethargy, and restlessness. Severe hyponatremia (serum sodium less than 125 mEq/L) places patients at risk of CNS symptoms such as lethargy and seizures (Meyers 2009). Treatment of hyponatremia involves judicious administration of intravenous fluids to correct fluid and sodium balance. For patients with acute symptoms, faster correction of the sodium deficit using normal saline or hypertonic saline to prevent symptoms is warranted. Sodium deficit in milliequivalents is calculated as follows:

Sodium deficit
= [(*desired sodium concentration*)
– (*current sodium concentration*)] *x k x weight* (*kg*)

where K is 0.6 (males) and 0.5 (females).

Acute hyponatremia without associated end-organ effects (e.g., seizure) should be corrected no faster than 0.5 mEq/L/hour, or around 12 mEq/L/24 hours, to avoid the development of central pontine myelinolysis. Patients should be monitored every 2–4 hours when symptomatic and every 4–8 hours when asymptomatic (Rhoda 2011).

Potassium

Primary Physiologic Function and Normal Homeostasis

Potassium (typical range 3.5–5 mEq/L, depending on age) is the primary intracellular cation in the body; it plays essential roles in cellular metabolism and maintains membrane potential as well as promotes neuromuscular and cardiac function (Rhoda 2011; Schmidt 2010). Potassium homeostasis is primarily maintained through renal elimination, which varies depending on serum concentrations as well as the release of aldosterone and angiotensin II. Nonrenal mechanisms such as hormones, acid-base status, and osmolality also play a role in potassium regulation (Rhoda 2011). Medications such as diuretics or nephrotoxic agents can affect potassium balance (Rhoda 2011).

Hyperkalemia

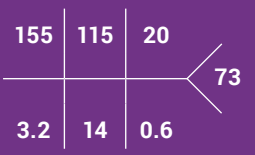
Hyperkalemia is defined as a serum potassium concentration greater than 4.7–5.9 mEq/kg, depending on age (Schmidt 2010). Because potassium is the primary intracellular cation, pseudohyperkalemia should be ruled out before making an assessment. For example, hemolysis that occurs as a result of laboratory blood tests may falsely elevate serum potassium concentrations. Common causes of hyperkalemia include medications (e.g., potassium-sparing diuretics), excessive potassium intake, dehydration, altered renal function or metabolic acidosis, burns, and hemolysis. Common signs and symptoms of elevated potassium include muscle weakness or cramping, twitching, and ascending paralysis. When serum potassium is greater than 6 mEq/L, changes in cardiac conductivity are possible, leading to arrhythmias (Rhoda 2011; Schmidt 2010; Meyers 2009). Hyperkalemia is one of the most dangerous electrolyte derangements because of these effects. When managing hyperkalemia, all sources of potassium intake must be assessed and adjusted, including dietary sources as well as medications. Pharmacologic management of hyperkalemia includes agents that shift potassium intracellularly (i.e., dextrose/insulin, albuterol, sodium bicarbonate) and agents that eliminate potassium

Patient Care Scenario

A 4-month-old girl (weight 6.1 kg) presents to the pediatrician with a 5-day history of diarrhea, described by her mother as 7 or 8 large, watery stools per day. At her well-child physical examination last month, the child weighed 6.5 kg. Her mother reports that she has done her best to keep up with the fluid loss by giving the child small sips of oral rehydration fluid. The child has been refusing enteral nutrition but has tolerated the sips of rehydration fluid. Her mother is afraid that the child cannot keep up with fluid intake enterally. Today, the child has only had one wet diaper and no loose stools, and she has been inconsolable.

Physical examination findings consistent with dehydration include heart rate 150 beats/minute, blood pressure within normal limits, dry mucosa, decreased skin turgor, capillary refill 6 seconds, and temperature 102.4°F (39.1°C).

Laboratory tests show the following:



Estimate this patient's fluid requirements to correct her fluid deficit and recommend an appropriate replacement rate.

ANSWER

Step 1: Determine whether emergency management is necessary.

When assessing whether a fluid bolus is required, the level of dehydration should be assessed, together with an evaluation for signs of shock, unconsciousness, or severe electrolyte disturbances. Although this patient presents with moderate dehydration and identified electrolyte derangements of concern for hypernatremia, she is currently hemodynamically stable. Therefore, a fluid bolus (emergency management) may not be required in this scenario.

Step 2: Estimate the fluid requirements.

To estimate fluid requirements, the percent dehydration and fluid deficit must first be calculated:

$$\%\ dehydration = \frac{[(pre\text{-}illness\ weight\ (kg)) - (illness\ weight\ (kg))]}{pre\text{-}illness\ weight\ (kg)} \times 100$$

$$= (6.5\ kg - 6.1\ kg)/6.5\ kg \times 100$$

$$= 6.15\%$$

$$Fluid\ deficit\ (L) = \%\ dehydration \times pre\ illness\ weight\ (kg)/100$$

$$= 6.15\% \times 6.5\ kg/100$$

$$= 0.4\ L\ (400\ mL)$$

For hypernatremic dehydration, a free-water deficit should be included in the estimate of fluid deficit. Various equations exist for this calculation of free-water deficit. Here, the free-water deficit is calculated with the equation below (Lam 2013).

$$Free\text{-}water\ deficit = 4\ mL \times actual\ serum\ sodium\ \frac{mEq}{L} - desired\ serum\ sodium\ \frac{mEq}{L} \times body\ weight\ (kg)$$

$$= 4\ mL \times (155 - 145) \times 6.5\ kg = 260\ mL.$$

Of note, a serum sodium of 145 mEq/L was chosen as the desired serum sodium in order to avoid over-correction of sodium.

Therefore, the total fluid deficit is 660 mL. Then, calculate maintenance fluid requirements: 100 mL/kg x 6.5 kg = 650 mL/day needed to meet maintenance requirements.

Next, calculate ongoing losses. In this case, ongoing losses are estimated with each watery stool. The patient's mother reports that she has had no watery stools today; therefore, this will not be added to the calculation right now. However, if loose stools continue, these should be estimated and added into the calculations.

Step 3: Determine the replacement rate.

The total fluid required for the next 24 hours is as follows:

	Fluid Needs	
	Fluid deficit Maintenance Total	400 mL + 260 mL = 660 mL 650 mL 1310 mL
Replacement for first 8 hr	1/2 of fluid deficit 1/3 of maintenance Total	330 mL 217 mL *547 mL* *(68.4 mL/hr)*
Replacement for next 16 hr	1/2 of fluid deficit 2/3 of maintenance Total	330 mL 433 mL *763 mL (47.7 mL/hr)*

When choosing the crystalloid fluid to use, sodium and potassium requirements should be included. In this case, the most clinically appropriate fluid would likely be 5% dextrose in water in 0.225% sodium chloride plus 20 mEq/L of potassium chloride or 5% dextrose in water in 0.45% sodium chloride plus 20 mEq/L of potassium chloride, depending on what is known about the patient. Based on available data, the use of isotonic fluids may not be clinically warranted given that this patient is not critically ill. After the first 12–24 hours, the comprehensive metabolic panel should be repeated, with fluid therapy adjusted on the basis of laboratory and physical examination findings. To avoid complications, serum sodium should not be corrected faster than 12 mEq/L/day.

1. Lam WM. Fluids and electrolytes. In: Benavides S, Nahata MC, eds. Pediatric Pharmacotherapy. Lenexa, KS: American College of Clinical Pharmacy, 2013:290-304.
2. Meyers RS. Pediatric fluid and electrolyte therapy. J Pediatr Pharmacol Ther 2009;14:204-11.
3. Powers KS. Dehydration: isonatremic, hyponatremic and hypernatremic recognition and management. Pediatr Rev 2015;36:274-85.

from the body (i.e., sodium polystyrene sulfonate, loop diuretics). Calcium, which stabilizes the cardiac myocytes, may be used in symptomatic patients for cardioprotective purposes. In severe cases, dialysis may be required to remove potassium from the body.

Hypokalemia

Hypokalemia (serum sodium of less than 3.4 mEq/L) may be caused by medications (e.g., loop and thiazide diuretics, antibiotics, amphotericin B), metabolic alkalosis, inadequate intake, hypomagnesemia, hyperaldosteronism, refeeding syndrome, and GI losses (Schmidt 2010). Although symptoms are nonspecific, presentation may include constipation/ileus, dysrhythmias, paralysis, muscle necrosis, and possibly, in severe cases, death. Management includes supplementing potassium either orally or intravenously, depending on severity. If the patient has a functioning GI tract and is asymptomatic, oral supplementation is preferable in order to avoid rapid overcorrection; however, oral potassium is irritating to the GI tract. Sustained release products may help mitigate GI upset in patients able to swallow tablets. When intravenous potassium is used, infusion rates should not exceed 0.5 mEq/kg/hour unless the patient is on a continuous cardiac monitor. Because potassium supplementation is irritating to veins, peripheral fluid concentration must not exceed 0.06 mEq/mL. Patients should be monitored carefully during potassium supplementation at intervals of 2–4 hours to assess the need for ongoing supplementation. Finally, if hypomagnesemia is present, magnesium concentrations must be corrected concomitantly.

Magnesium

Primary Physiologic Function and Normal Homeostasis

Magnesium (typical range 1.6–2.3 mg/dL, depending on age) has important physiologic functions such as acting as an essential cofactor for hundreds of enzymatic reactions, including glucose, fatty acid, DNA, and protein metabolism (Schmidt 2010). Magnesium also plays a role in the Na^+-K^+-ATPase pump with downstream functions on neuromuscular transmission, vasomotor tone, cardiac excitability, and muscle contraction. Magnesium is also an important component of bone (more than 50% of magnesium resides in the bone) as well as parathyroid hormone secretion. Homeostasis is maintained through the GI tract, renal system, and bone through the parathyroid hormone. Magnesium is absorbed in the jejunum, with absorption inversely proportional to intake. Around 30%–40% of dietary magnesium is absorbed through the GI tract, with the remainder excreted in the stool (Rhoda 2011). If dietary intake is low, magnesium will be leached from the bone to maintain normal circulating concentrations (Schmidt 2010).

Hypermagnesemia

A serum magnesium concentration greater than 2.4 mg/dL defines hypermagnesemia (Schmidt 2010). Common causes include excessive supplementation, renal disease, laxative overuse, and/or increased intake of magnesium-containing antacids (Rhoda 2011). Typically, mild hypermagnesemia is tolerated well, but when serum magnesium concentrations exceed 3 mg/dL, neurologic, neuromuscular, and cardiac symptoms may be present (Schmidt 2010). Other signs and symptoms include nausea, sweating, flushing, muscular weakness, hypotension, and bradycardia. In severe cases when cardiac abnormalities are present, intravenous calcium should be administered to stabilize the cardiac muscle, and in some cases, dialysis may be required. Most cases, however, are mild and can be managed by decreasing magnesium intake or administering diuretic therapy. In the neonatal population, hypermagnesemia may result from the placental transfer of magnesium from mothers who have received high-dose magnesium sulfate to prevent premature labor. For infants born prematurely, magnesium concentrations should be assessed before magnesium is administered in intravenous fluids or parenteral nutrition.

Hypomagnesemia

Hypomagnesemia is defined as magnesium concentrations less than 1.3 mg/dL (Schmidt 2010). Common causes of hypomagnesemia include decreased intake, excessive renal/GI loss, and intracellular shifts of magnesium. Hypomagnesemia occurs in patients with acute tubular necrosis, renal tubular acidosis, hyperaldosteronism, and Bartter syndrome and in the setting of select medications (e.g., tacrolimus, cyclosporine, aminoglycosides). Hypomagnesemia is common in hospitalized patients and is associated with apathy, depression, muscle weakness, ataxia, muscle cramps, and cardiac complications. Hypomagnesemia is also associated with other electrolyte derangements such as hypokalemia and hypocalcemia. Because of poor GI tolerance of magnesium, the intravenous route is preferred for acute management, with a maximum infusion rate of 0.1 mEq/kg/hour because of dose-dependent renal absorption. Monitoring should occur 2–4 hours after magnesium dosing, with additional doses provided as required to maintain normal magnesium concentrations. During administration, hemodynamics, specifically blood pressure, should be monitored. For patients requiring home administration or ongoing magnesium supplementation, oral/enteral administration is acceptable.

Calcium

Primary Physiologic Function and Normal Homeostasis

Calcium (typical range 6.2–11 mg/dL, depending on age) is one of the most abundant ions in the body; it is required for proper neuromuscular activity, integrity of membranes, endocrine function, coagulation, and bone metabolism (Schmidt 2010).

The parathyroid gland is primarily responsible for controlling serum calcium concentrations; when serum concentrations are low, parathyroid hormone is released, which increases bone resorption, renal conservation, and activates vitamin D, which improves calcium retention from the GI tract. When concentrations are high, calcitonin is released from the thyroid, which inhibits bone resorption and increases renal elimination. Calcium is found in the body as complexed, protein bound, or ionized and is primarily located in the teeth and bone.

Hypercalcemia

Hypercalcemia definitions depend on normal values for age as well as nutritional factors such as circulating albumin. Corrected calcium is calculated as follows:

$$\textit{Corrected calcium} = \textit{measured total calcium}\ \frac{mg}{dL}$$

$$+\ 0.8\ \ 4\ -\ \textit{albumin}\ \frac{g}{dL}$$

Although hypercalcemia may be the result of increased dietary intake, increased vitamin A or D concentrations, renal dysfunction, or certain medications (e.g., calcium-containing antacids, vitamin A or D supplementation), the primary cause of hypercalcemia is hyperparathyroidism or cancer with bone metastases (Schmidt 2010). Patients with hypercalcemia may present with fatigue, nausea or vomiting, constipation, and confusion. In severe cases, cardiac conductivity abnormalities may be present. In mild to moderate cases of hypercalcemia, fluid therapy is first line and usually effective. For severe cases, intravenous fluid therapy, loop diuretics, and dialysis therapy may be needed to prevent dysrhythmias, kidney failure, and death.

Hypocalcemia

Hypocalcemia is defined as a corrected calcium or ionized calcium below age-appropriate normal values (Schmidt 2010). Although the equation above can be used to calculate corrected calcium, when possible an ionized calcium level should be obtained for greater accuracy. Hypocalcemia can result from low vitamin D intake or deficiency, hyperphosphatemia, decreased parathyroid hormone activity, blood transfusions, and rhabdomyolysis. Medications such as diuretics and anticonvulsants can also cause aberrations in calcium concentrations. Patients with hypocalcemia present with symptoms such as hypotension, decreased cardiac contractility and QT interval prolongation, muscle cramps, and seizures. In hypocalcemia, hypomagnesemia must also be assessed for and corrected, if present. For neonates receiving parenteral nutrition, hypocalcemia may result from an inability to provide adequate amounts of calcium because of intravenous fluid compatibility issues. Depending on the severity of hypocalcemia, treatment involves oral or intravenous calcium supplementation.

Phosphorus

Primary Physiologic Function and Normal Homeostasis

The main intracellular anion, phosphorus (typical range 2.7–9 mg/dL, depending on age), is critically important for maintaining cellular function, bone and cell membrane composition, pH, energy (ATP), and all physiologic functions requiring energy (Schmidt 2010). Homeostasis is maintained through GI absorption, renal excretion, and parathyroid hormone activity.

Hyperphosphatemia

Serum values above age-expected normal concentrations define hyperphosphatemia (Schmidt 2010). Hyperphosphatemia can be caused by metastatic calcifications, hypocalcemia, or hypoxemia (Rhoda 2011). Most hyperphosphatemia is tolerated well, and many patients may be asymptomatic (Schmidt 2010). However, symptoms, when present, often include anorexia, nausea and vomiting, dehydration, poor appetite, neuromuscular symptoms, and tachycardia (Rhoda 2011; Schmidt 2010). Of greatest concern is metastatic calcifications, which occur when serum calcium is also elevated. Hyperphosphatemia is managed by implementing a low-phosphorus diet and/or adding phosphate binders (Rhoda 2011). If low volume is suspected, volume repletion may be required. In severe cases, dialysis may be needed.

Hypophosphatemia

Hypophosphatemia is defined by serum concentrations less than 2.7–4.5 mg/dL, depending on age (Schmidt 2010). This condition is common in critically ill children as well as in those who are malnourished or having refeeding syndrome. Hypophosphatemia may also be present in patients receiving phosphate binders or those with alkalosis. Clinical signs include, but are not limited to, neurologic and neuromuscular symptoms and cardiac, respiratory, or hematologic dysfunction. If presentation and symptoms are mild, management typically consists of oral replacement. When larger doses are needed, however, GI tolerance is poor. Therefore, intravenous supplementation is required when moderate or severe hypophosphatemia is present. Patients should be monitored every 2–4 hours when intravenous doses are used.

CONCLUSION

The practicing pediatric pharmacist plays a key role in assessing and managing fluids and electrolytes across the age spectrum. A solid foundation in understanding the composition of body fluids, fluid requirements, and regulations; assessing and managing dehydration, understanding the physiologic functions of electrolytes, and managing electrolyte derangements is critical. In addition to providing direct patient care, pharmacists are involved in developing clinical

Practice Points

When approaching fluid and electrolyte therapy in the pediatric population, practitioners should consider the following practice points:

- **The composition of body fluids and regulation of fluids changes across development. Age-appropriate fluid calculations and estimates should be done when designing fluid regimens for pediatric patients, considering unique patient characteristics and clinical status.**
- **Crystalloid fluids are the mainstay of therapy for most clinical conditions; however, colloids may be considered when intravascular volume expansion is clinically warranted.**
- **Crystalloid fluids have historically been chosen on the basis of Holliday-Segar estimates; however, a growing body of evidence suggests that use of isotonic fluids is more appropriate in hospitalized, critically ill children.**
- **Pediatric patients are at greater risk of dehydration than adolescent and adult counterparts. The approach to managing dehydration must account for an assessment of severity, source of fluid and electrolyte loss, and classification of dehydration, followed by a comprehensive approach to management that addresses route of administration, maintenance fluid requirements, and ongoing losses.**
- **Normal serum electrolyte values must be maintained for normal biochemical reactions and homeostatic functioning. Knowledge of each electrolyte's physiologic functions, the monitoring parameters, and the main causes of electrolyte derangements is important for the practicing pediatric pharmacist.**

practice guidelines, policies, and procedures; managing fluid and electrolyte product shortages; and providing continuous quality improvement efforts. An understanding of these practices ensures optimal care across a dynamically changing population from the neonatal period through adolescence/adulthood. Furthermore, a pediatric pharmacist can work on collaborative teams to develop research and evidence as it pertains to managing fluid and electrolytes in 21st-century medicine.

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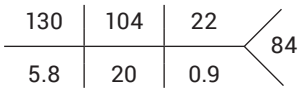
Self-Assessment Questions

1. A 6-year-old girl (weight 22.5 kg) is admitted for a 2-day history of nausea and vomiting secondary to a viral gastroenteritis. Before this illness, she weighed 23 kg. Her laboratory test results are as follows:



   Which one of the following best assesses this patient's clinical state based on serum osmolality?
   A. Relative deficiency of water compared with solute
   B. Relative deficiency of solute compared with water
   C. Equal deficiency of water and solute
   D. Dynamic shift of water and solute from extracellular fluid to intracellular fluid

2. An 8-year-old girl (weight 27 kg) presents to the ED with complaints of generalized abdominal pain and malaise for the past 3 days. These symptoms have steadily increased during the past 24 hours such that she cannot tolerate oral intake and has a decreased appetite. She is given a diagnosis of acute appendicitis and admitted to the general ward. The patient will be treated medically rather than surgically. Physical examination reveals heart rate 100 beats/minute, respiratory rate 20 breaths/minute, and blood pressure 120/75 mm Hg. The ED physician consults you for assistance. Which one of the following crystalloids, in addition to potassium chloride 20 mEq/L, is best to recommend as this patient's initial maintenance fluid?

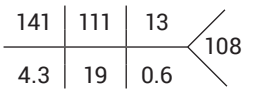
   A. Dextrose 5% in 0.9% sodium chloride
   B. Dextrose 5% in 0.45% sodium chloride
   C. Dextrose 10% in 0.9% sodium chloride
   D. Dextrose 10% in 0.45% sodium chloride

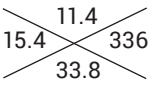
3. Which one of the following patients would be most likely to benefit from initiation of isotonic fluids?

   A. A day-of-life 1 neonate with gastroschisis in the neonatal ICU.
   B. An 11-year-old prepubescent girl on the general ward for gastrostomy tube placement
   C. A 16-year-old postmenarche female adolescent admitted to the general ward for UTI management
   D. A 13-year-old male adolescent admitted for surgical repair of pectus excavatum

4. A 10-year-old boy (weight 32 kg) has had gastroenteritis for the past 4 days. His baseline weight is 33 kg. He has been unable to tolerate oral intake because of persistent nausea and diarrhea. He now presents to the pediatrician's office for a complete evaluation. On examination, the patient feels warm to the touch. His initial temperature on admission was 97.7°F (36.5°C). However, during this visit, his temperature increased to 101.3°F (38.5°C). His heart rate is 132 beats/minute, respiratory rate 33 breaths/minute, and blood pressure 110/72 mm Hg, with pulse oximetry 96%.

   Laboratory values:





   Ca: 10.4 mg/dL

   Which one of the following best assesses this patient's fluid deficit and initial approach to treatment?
   A. 3% deficit; oral rehydration can be considered at 100 mL/kg given over 4 hours in the pediatrician's office.
   B. 900-mL deficit; patient should be admitted for intravenous rehydration: dextrose 5% in 0.9% sodium chloride given at 110 mL/hour for 8 hours.
   C. 1000-mL deficit; patient should be admitted for intravenous rehydration: dextrose 5% in 0.45% sodium chloride given at 135 mL/hour for 8 hours, followed by 103.8 mL/hour for 16 hours.
   D. 1000-mL deficit; 20-mL/kg bolus of normal saline, followed by oral rehydration in pediatrician's office.

Questions 5–7 pertain to the following case.

K.T. is a 2-year-old girl (weight 15 kg) who presents to the ED at the children's hospital with a 6-day history of emesis and poor enteral intake. She is lethargic, with dry mucous membranes; her mother reports that K.T. last urinated over 24 hours ago. A pre-illness weight is unknown; however, given the physical examination, she is estimated to be 6% dehydrated. Laboratory test results show a serum sodium of 151 mEq/L. K.T. receives a diagnosis of hypernatremic dehydration and is given a 20-mL/kg normal saline bolus.

5. Given this information, which one of the following options best describes the appropriate estimated maintenance, remaining deficit (after the saline bolus), and total fluid requirements for K.T. over the next 24 hours?

   A. Maintenance 1300 mL; deficit 900 mL; total needs 2200 mL
   B. Maintenance 1500 mL; deficit 600 mL; total needs 2100 mL
   C. Maintenance 1300 mL; deficit 600 mL; total needs 1900 mL
   D. Maintenance 1500 mL; deficit 900 mL; total needs 2400 mL

6. K.T. continues to have bouts of emesis, once admitted. To replace ongoing losses, the attending physician would like to replace each emesis on a 1-mL/1-mL basis. Given the source of fluid loss, which one of the following fluid options would be most appropriate to replace K.T.'s ongoing losses?

   A. Dextrose 5% in 0.45% sodium chloride plus potassium chloride 20 mEq/L
   B. 0.9% sodium chloride plus potassium chloride 20 mEq/L
   C. Lactated Ringer Solution
   D. 0.45% sodium chloride

7. K.T.'s second set of laboratory tests 8 hours after rehydration therapy is initiated show a serum magnesium concentration of 1.2 mg/dL. The attending physician asks you about magnesium supplementation. Which one of the following is best to recommend for K.T.?

   A. Magnesium chloride 64-mg elemental tablet; 2 tablets by mouth once; recheck laboratory values in 4 hours.
   B. Magnesium chloride 200-mg/mL injection; 40 mg intravenously every 4 hours; recheck laboratory values in 24 hours.
   C. Magnesium gluconate 27.5-mg elemental tablet; 5 tablets by mouth every 6 hours for four doses; recheck laboratory values in 24 hours.
   D. Magnesium sulfate 1000 mg/100 mL; 4.5 mL intravenously once; recheck laboratory values in 4 hours.

8. A patient with hypernatremia is being evaluated during rounds in the pediatric ICU. The medical resident, concerned about potential neurologic morbidity because of sustained elevated serum sodium concentrations greater than 155 mEq/L, changes dextrose 5% in 0.225% sodium chloride to dextrose 5% in water. Which one of the following is most accurate regarding the resident's action?

   A. The order is appropriate with the change to dextrose 5% in water; patients with hypernatremia should not receive additional sodium until serum sodium concentrations have decreased below 150 mEq/L.
   B. The order is inappropriate; dextrose 5% in 0.225% sodium chloride was appropriate as initially ordered; rapid over-correction of serum sodium can lead to cerebral edema and seizures.
   C. The order is inappropriate and should be changed to dextrose 5% in 0.9% sodium chloride; new evidence supports the use of isotonic fluids in critically ill children.
   D. The order is inappropriate; dextrose 5% in 0.225% sodium chloride was appropriate as initially ordered; rapid over-correction of serum sodium can lead to central pontine myelinolysis.

9. A 3-year-old girl presents for her annual physical examination in the pediatric special needs clinic. Her medication list shows tacrolimus, hydrochlorothiazide, acetaminophen, polyethylene glycol 3350, and ranitidine. The attending physician plans to obtain laboratory values at today's visit. Which one of the following sets of electrolytes is most likely to be affected by this patient's current medication regimen?

   A. Potassium, sodium, calcium
   B. Potassium, phosphorus, calcium
   C. Magnesium, sodium, potassium
   D. Magnesium, sodium, phosphorus

10. A 12-year-old girl with a history of anorexia was admitted to the pediatric ICU after being found unresponsive in the girl's restroom at school. On admission, hemodialysis is initiated because of profound electrolyte abnormalities that are unresponsive to initial fluid management. Which one of the following electrolyte abnormalities best justifies acute initiation of hemodialysis in this patient?

    A. Hypermagnesemia
    B. Hyperkalemia
    C. Hypercalcemia
    D. Hypernatremia

11. A day-of-life zero neonate is born at 37 weeks' gestational age (birth weight 2.2 kg) with gastroschisis. She had a large abdominal defect in utero. Her intestinal contents could not be reduced at birth, and she will remain in the neonatal ICU sedated with a silo in place. Which one of the following initial fluid orders is best to recommend for this patient?

    A. Dextrose 10% at a rate of 5.5 mL/hour
    B. Dextrose 10% in 0.45% sodium chloride at a rate of 7.3 mL/hour
    C. Dextrose 10% in 0.225% sodium chloride at a rate of 9.2 mL/hour
    D. Dextrose 10% in 0.225% sodium chloride plus 20 mEq/L potassium chloride at a rate of 8.3 mL/hour

Questions 12 and 13 pertain to the following case.

J.E. is an 11-year-old girl (dosing weight 32.1 kg; today's weight 31.8 kg) with ulcerative colitis. She presents 3 days after a diverting ileostomy, which has been putting out 500–600 mL/day since the operation. J.E. has been and is currently receiving dextrose 5% in 0.9% sodium chloride plus 40 mEq/L of potassium chloride at 75 mL/hour. This morning during rounds, she is lethargic, with complaints of nausea as well as muscle aches. Vital signs show an elevated heart rate, and her blood pressure is soft. Capillary refill is 7 seconds. Laboratory tests are ordered.

12. Which one of the following best assesses J.E.'s current symptoms?

    A. Hypernatremic dehydration because of the administration of isotonic fluid for more than 48 hours post-hospitalization
    B. Hyponatremic dehydration because of ongoing ileostomy losses
    C. Hyperkalemia because of the administration of intravenous fluids containing 40 mEq/L of potassium chloride
    D. Hypocalcemia because of poor vitamin D absorption from her GI tract and overall poor nutritional status secondary to her colitis

13. J.E.'s laboratory test results show a serum sodium concentration of 130 mEq/L. Which one of the following is best to recommend to replace J.E.'s deficit?

    A. Continue current intravenous fluid but increase the rate to 113 mL/hour for 24 hours; then recheck serum sodium in 12 hours.
    B. Place a central line and administer 186 mL of sodium chloride 3% once over 30 minutes; recheck laboratory values in 24 hours.
    C. Continue current intravenous fluid but provide a one-time bolus of 0.9% sodium chloride; recheck laboratory values in 4 hours.
    D. Continue current intravenous fluids, administer sodium chloride 2 g orally every 12 hours for three doses; then recheck laboratory values 4 hours after the last dose.

14. A day-of-life zero female neonate (weight 3.1 kg) is born at term with long-gap esophageal atresia. She will receive maintenance intravenous fluids before a gastrostomy tube is placed. Which is the most appropriate fluid and rate to recommend for this patient?

    A. Dextrose 5% in 0.225% sodium chloride plus potassium chloride 20 mEq/L
    B. Dextrose 5%
    C. Dextrose 10% in 0.225% sodium chloride plus potassium chloride 20 mEq/L
    D. Dextrose 10%

15. A 13-year-old female adolescent (weight 39 kg) is admitted after a motor vehicle crash. On arrival at the ED, she is unresponsive and found to have several traumatic injuries with blood loss. Laboratory test results include Na 136 mEq/L, K 2.9 mEq/L, Cl 92 mEq/L, HCO_3 22 mEq/L, BUN 18 mg/dL, SCr 1.1 mg/dL, glucose 88 mg/dL, albumin 3.4 mg/dL, and Hgb 8 mg/dL. En route to the hospital, the patient received three 20-mL/kg normal saline boluses; however, on arrival, her blood pressure is 80/66 mm Hg. Which one of the following would be most appropriate for this patient's acute resuscitation?

    A. 25% albumin; 20 mL/kg
    B. 5% albumin; 20 mL/kg
    C. 0.9% sodium chloride; 20 mL/kg
    D. Packed RBCs; 20 mL/kg