13 Fluid and Electrolyte Therapy in Children

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Introduction

The prescription of fluid and electrolyte therapy is a common task for the pediatric clinician. The clinical situations requiring such therapy are myriad and range from the urgent in cases of children with circulatory collapse to the more mundane in children with mild dehydration from gastroenteritis. Superimposed on the simple provision of any set amount of water and salts are the changes in normal physiology and homeostatic mechanisms that accompany both acute and chronic illness. Recognition of each child's individual clinical situation and each situation's ultimate goal in respect to hydration or volume resuscitation is crucial for the provision of the correct combination of fluid and electrolytes in the proper amount of time.

In the eighteenth century, attempts to replace the profound enteral losses of salt and water from cholera infection led to an initial understanding of the morbidity and mortality that accompanies significant perturbations in fluid and electrolyte balance (1). The recognition that affected patients improved with repeated infusions of a saline solution became an impetus to define fluid and electrolyte needs in healthy individuals and to develop clinical parameters for fluid and electrolyte therapy. The understanding gained from clinical observations in epidemics of cholera and other diarrheal illness came to be generalized to other conditions in which there was an element of dehydration or poor circulation and ultimately helped to define the threshold for the minimum daily provision of fluid and electrolytes – so-called maintenance requirements – as well as a threshold of maximal tolerance.

By the early twentieth century, clinicians began more frequently to use such techniques as intraperitoneal injection of saline or intravenous infusion of isotonic solutions to try to restore circulation in children with volume compromise (2, 3). Additionally, spearheaded by Gamble and colleagues, fluid spaces in terms of intracellular and extracellular compartments were defined and the kidney's role in the regulation of overall body volume and specific gradients of solute between these fluid spaces were elucidated (4, 5). These early studies established the basis for all modern fluid and electrolyte therapies.

By the middle of the twentieth century, Holliday and colleagues devised simplified equations to link average daily metabolic rate to daily fluid requirements, and the practice of calculating daily fluid and electrolyte needs for an ill child based on continuing or "maintenance" needs and past and current losses or "deficits" was taught as the gold standard to minimize complications and improve clinical outcomes (6). Although the need to make exceptions to this approach in situations with reduced urine output or non-osmotic stimulated antidiuretic hormone activity was clearly stated, emphasis on these empiric equations led to relatively formulaic hydration protocols regardless of specific clinical condition. Moreover, in children requiring rehydration, a tradition of fluid therapy grounded on the so-called "deficit therapy" approach became widespread (7, 8).

Reassessment of this traditional approach, again spawned in large measure by Holliday's work, has come to appreciate that such elaborate maneuvers are often unnecessary and that reassessment of a child's response to any initial fluid therapy is crucial to the assessment of its adequacy and applicability (9). Moreover, increasing recognition that the use of oral rehydration solutions are a simple, safe, and efficacious alternative for most children in need of fluid and electrolyte therapy has also impacted this tradition of precisely calculated intravenous fluid volumes (10).

Nonetheless, there continues to be a place for such careful assessment and prescription of fluid and electrolyte therapy, especially in children with non-diarrheal illness (11). In more complex disorders of fluid and electrolyte pathophysiology, such as seen in critically ill children with sepsis, burns, trauma, or postoperatively, an understanding of the distribution of body fluids, usual fluid and electrolyte requirements, and the effect of disturbances in normal homeostatic balance remain vital to the correct prescription of therapy and the proper assessment of response. Such an understanding resonates

louder when approaching the care of a child with renal disease. Frequently, the presence of a preexisting renal condition or the development of acute kidney injury complicates the fluid and electrolyte management of the child. Standard approaches to fluid therapy assume that normal renal homeostatic mechanisms will come into play with the provision of adequate water and electrolytes. Such approaches are ill advised for the child with renal disease in whom such regulation may be deranged. Similarly, these approaches may have limited value with the critically ill child in whom normal fluid and electrolyte homeostasis may also be altered. In these circumstances, the clinician needs to approach fluid and electrolyte therapy systematically and with attention to individual clinical circumstance. Otherwise, in the absence of a customized prescription, the possibility arises that a therapeutic intervention may be deleterious, given preexisting reduced tolerance to alterations in body fluid volume, composition, or distribution.

Lastly, with improvements in long-term management strategies, many children with severe chronic disease are living longer lives, often surviving into adulthood. As a result, there is also an increasing population of children and adolescents with conditions such as chronic pulmonary disease, complex congenital cardiac disease, and chronic kidney disease who may require fluid and electrolyte therapy for support through an acute illness or during medical or surgical procedures when usual oral or enteral hydration may be contraindicated. For these children with more fragile clinical states, hydration must also be tailored to individual need and tolerance, and clinicians cannot rely on the formulaic prescription of water and electrolytes. In this regard, these children with significant chronic disease pose a special challenge to a medical community that often wishes to simplify or standardize approaches to care across a spectrum of patients. In addition, they also demonstrate why a well grounded understanding of volume balance and appreciation of both normal and aberrant physiology is critical to the clinician who is regularly prescribing fluid and electrolyte therapy.

Total Body Water

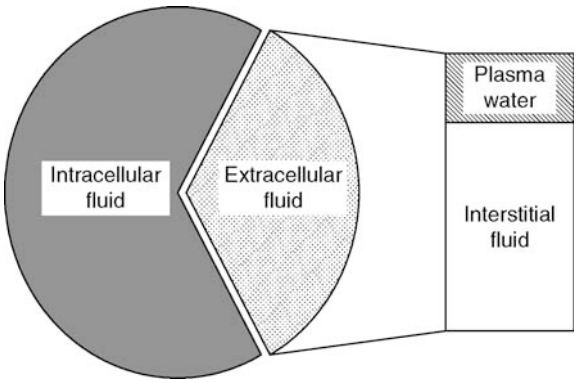
Extracellular and Intracellular Fluid Compartments

Although water makes up a large component of body weight, the exact proportion in each child varies with age, body size, and body composition. Early in gestation, 90% of the weight of the developing fetus may be water. By the first weeks of the third trimester, total body water (TBW) of the developing fetus approximates 80% of body weight in kilograms. This percentage falls to 70–75% in term infants, 65–70% in toddlers and young children, and eventually to 60% in older children and adolescents. Lean individuals have more body water than obese individuals and adolescent boys with increasing muscle mass tend to have more total body water than less muscular adolescent girls. Although 60% is the usual benchmark for estimating TBW in older children and adults, the actual percentage may be lower, especially in less well-conditioned individuals and the elderly (12).

Body water is found in both intracellular and extracellular compartments (*Fig. 13-1*). The intracellular compartment consists of the water within the cells of the body, comprising about two-thirds of TBW or 40% of body weight. The extracellular compartment comprises one-third of TBW or 20% of body weight. The extracellular compartment is divided into the interstitial fluid that bathes all cells and the plasma water that is carried intravascularly. The increased TBW seen in young children is the result of a relatively increased surface area as compared to body weight that accounts for an overall increased extracellular compartment (13).

The boundary between the intracellular and extracellular compartments is the cell membrane. Input or output from the body proceeds via some interface with the extracellular compartment. For instance, intravenous electrolyte solutions are infused into the extracellular intravascular space and their subsequent delivery intracellularly depends

Figure 13-1
Total body water: Fluid compartments and solute composition.



on a host of factors that influence transport across the cell membrane.

Since most cell membranes are readily permeable to water, the distribution of water between the intracellular and extracellular spaces reflects osmotic forces. In each body space there is a solute that is primarily sequestered within that compartment and that maintains its osmotic gradient (14, 15). For instance, activity of the sodium-potassium pump found in cell membranes leads to an increased concentration of potassium intracellularly and an increased concentration of sodium in the interstitial fluid. Thus, sodium serves as the effective osmole interstitially and potassium intracellularly. Similarly, plasma proteins, most notably albumin, exert an osmotic force to maintain water intravascularly. Hydrostatic perfusion pressure counterbalances this osmotic force by pushing water across the capillary from the lumen to the interstitium. Changes in the distribution of effective osmoles can result in redistribution of water between intracellular and extracellular spaces.

A dynamic equilibrium exists between the intracellular and extracellular spaces. Diffusional gradients, osmotic forces, and the activity of cellular transporters all combine to establish the composition differences between body compartments. Since the intracellular space cannot be directly accessed, its composition can be altered only by affecting the extracellular space and its subsequent communication with the cell. Any intake by ingestion or infusion into the extracellular space will result in a new equilibrium being established with the intracellular space as solute and fluid comes to be exchanged. Ultimately, the final equilibrium is a result of complex biochemical, electrical, and physical interactions.

Communication between the cellular spaces can be bidirectional. In other words, there can be exchange from the intracellular space to the extracellular space allowing for transfer or release of cell metabolites. In addition, since the extracellular space can communicate with the external milieu, output from the extracellular space to the external milieu results in effective excretion from the body. No direct communication exists, however, between the intracellular space and the external milieu. Any output from the cells themselves is mediated via the cell's direct ability to interface with the interstitial fluid or the plasma water.

Any impairment in the patient's normal homeostatic mechanisms regulating fluid and electrolyte balance will have a striking impact on the patient's total body water and its extracellular and intracellular constituents. An example of this disruption of normal balance is the development of hypertension frequently seen in individuals with progressive chronic kidney disease. As glomerular filtration rate falls, the ability of the kidney to excrete free water (CH_2O) also declines. Frequently, this change is in the setting of a decreasing number of effectively functioning nephrons with concomitant impairment of overall tubular solute excretion, most notably salt. Superimposed on this baseline tendency for dysregulation of solute and water balance may be clinical factors such as circulatory failure and decreased effective arterial volume leading to further renal salt and water retention. This salt and water overload leads to chronic expansion of TBW and mediates systemic hypertension with expansion of the extracellular volume compartment. Appropriate therapy in this instance would include use of diuretics to reduce the total body burden of salt and water and to restore the total body water to a more physiologic state. In this instance, failure to appreciate the preexisting expansion of the total body water because of chronic salt and water overload could prove deleterious to the patient if management did not include some measure to reduce the salt and water overload. This example also underscores the concept that fluid and electrolyte therapy may involve the removal of solute and water as well as the more usual notion that it is solely concerned with the correction of deficits of electrolytes and volume.

Effective Circulating Volume

Effective circulating volume is a more abstract concept than the division of body water into intracellular and extracellular fluid compartments. As the vascular volume circulates, oxygen and nutrients get delivered to the intracellular space and cellular metabolites get cleared from the intracellular space. The effective circulating volume refers to that portion of the extracellular vascular space that actually perfuses the tissues and accomplishes such an exchange.

Any compromise in this exchange proves deleterious to usual cell homeostasis and, as a result, the body constantly senses and regulates effective perfusion of fluid through the intravascular space. Homeostatic feedback mechanisms include baroreceptors that respond to the stretch of specialized areas of the carotid arteries and the atrium. Hypoperfusion of these areas decreases stimulation of the stretch receptors, triggering the secretion of vasopressin that increases water reabsorption in the most distal nephron and expands the vascular volume.

Similarly, in response to glomerular hypoperfusion, there is not only decreased afferent arteriolar stretch but also decreased glomerular filtration and delivery of sodium to the macula densa. These stimuli both can lead to the secretion of renin from the juxtaglomerular cells of the afferent arteriole. Renin release initiates a cascade resulting ultimately in increased aldosterone-mediated sodium and water reabsorption from the kidney as well as increased angiotensin-mediated vasoconstriction and sodium and water uptake.

Effective circulating volume should be considered the product of multiple factors, not the least of which include the size of the vascular space and the influence of various regulatory hormones. As a component of the extracellular body water, the size of the vascular space often parallels the size of the extracellular space. The size of the vascular space and the adequacy of the effective circulating volume do not, however, always vary coordinately. The extracellular space may be replete or expanded and the actual effective circulating volume decreased. For instance, children with significant liver disease are often edematous, due to sodium retention and expansion of the interstitial component of the extracellular space. The intravascular component of their extracellular space may also be expanded as a result of factors resulting in avid salt and water reabsorption by the kidney. But, because of portal hypertension, splanchnic vessel congestion, and multiple arteriovenous spider angiomas that are seen with this condition, much of the expanded intravascular volume is ineffective – it does not serve to perfuse the tissues and accomplish effective cellular exchange. Thus, these children act as if they are volume depleted: they avidly reabsorb any filtered sodium and excrete small volumes of urine and they vigorously continue to expand their already over expanded extracellular space by reabsorbing even more salt and water in response to the effects of renin and ADH. Similarly, this paradoxical state of sodium avidity and ADH-mediated water reabsorption characterizes children with nephrotic syndrome or with cardiac failure despite their preexisting expansion of the extracellular space.

In managing all aspects of a patient's fluid and electrolyte therapy, the clinician must accurately assess both the patient's current extracellular volume status and effective circulating volume and reconcile these with potential causes of volume loss. At all times, it is crucial to maintain an effective circulating volume and to make therapeutic decisions based on the unique clinical circumstances facing the patient. Such management may require rather disparate therapeutic interventions. For instance, expansion of the extracellular volume with vigorous rehydration may be called for in a child with poor perfusion secondary to gastroenteritis-induced dehydration whereas another child with equally poor perfusion due to cardiodynamic compromise may be intravascularly replete and require the initiation of pressor therapy and another child with edema from relapsed nephrotic syndrome may actually require fluid and salt restriction. These examples underscore that loss of effective circulating volume generally arises as a result of one or more broad perturbations in the extracellular fluid compartment that impacts effective perfusion (*Table 13-1*). In hospitalized children where there may be both aberrant disease related physiology and iatrogenic derangements of regulatory response, the causes of effective volume perturbations may be even more complex.

Clinical signs and symptoms of effective circulating volume loss may be subtle. At times, there may be preservation of effective circulating volume in the face of an overall depleted extracellular fluid compartment. Failure to initiate appropriate fluid and electrolyte therapy in such a circumstance may result in eventual compromise of the effective circulating volume. Important initial clinical signs to assess in any patient being evaluated for fluid therapy include pulse rate and capillary refill. Tachycardia and sluggish refill generally precede more obvious signs of ineffective circulation such as hypotension and oliguria. Clinical symptoms may also be non-specific and include fatigue and lethargy that are often attributed to an underlying illness rather than volume depletion. Proper restoration of effective circulating volume or extracellular fluid compartment depletion requires an understanding of baseline fluid and electrolyte needs as well as consideration of any extenuating clinical circumstances unique to the patient in question.

Table 13-1

Alterations in effective circulating volume

Cause	Mechanism
Contracted extracellular fluid space	Water or sodium chloride deficit
Massive vasodilatation	Loss of vascular tone sustaining perfusion pressure
Loss of intravascular osmotic pressure	Osmotic fluid losses into interstitium
Overfill of the intravascular space	Hydrostatic fluid losses into interstitium
Hemorrhage	Direct loss of blood and plasma water

Water and Electrolyte Requirements

Maintenance Therapy

The concept of maintenance therapy refers to that amount of water and electrolytes required to replace usual daily losses and to maintain an overall net balance of no water or electrolytes gained or lost. Such needs are a function of homeostatic and environmental factors and vary from day to day and from child to child. In the average child with adequate access to water and food, these maintenance needs are generally readily met (6, 16). In the ill or hospitalized child who requires therapeutic intervention and in whom there may be ongoing aberrant physiology, these needs must be considered when clinicians prescribe fluid therapy.

To assist in estimating maintenance needs, fluid and electrolyte requirements are typically calculated based on weight or surface area, but individual clinical circumstance must be considered when making such calculations (17). For instance, the 20-kg child who is well will require a far different "maintenance" quantity of fluid and electrolytes than the 20 kg child who is tachypneic and febrile or the 20 kg child who is anuric and on a ventilator in the pediatric intensive care unit. Careful clinical assessment of the patient's volume status and close attention to the balance of overall daily input and output will prove more useful at arriving at a correct estimate of daily fluid and electrolyte needs than merely using mathematical equations without clinical correlation. With these caveats in mind, it is nonetheless a common clinical practice to make certain empirical assumptions regarding daily needs for water and the major electrolytes.

Historically, daily maintenance water needs have been estimated based on energy expenditure (*Table 13-2*) (6, 16). For each kilocalorie of energy expended daily, 1 mL of water must be provided. Based on the computed energy expenditure of the average hospitalized patient, for the first 10-kg of body weight, 100 mL of water per kg is provided daily. For the next 10 kg of body weight, 50 mL of water per kg is provided daily, and for every kg of body weight in excess of 20 kg, 20 mL of water per kg is provided daily. In addition, in the process of oxidation of carbohydrate and fat, approximately 15 mL of water is generated for every 100 kcal of energy produced. This water of oxidation contributes significantly to overall water balance.

Maintenance water losses occur from urine output and from insensible sources that are almost exclusively evaporative and respiratory losses. In the child with average metabolic demands, for every 100 kcal of energy expended, 100 mL of water must be ingested. Oxidative metabolism generates 15 mL of water in the course of producing the 100 kcal of energy. Of this 115 mL of water, 40 mL is lost insensibly and 75 mL is lost as urine output. Overall, net water balance, composed of 100 mL ingested, 15 mL generated and 115 mL excreted, becomes equilibrated.

Table 13-2
Relationship of body weight to metabolic and maintenance fluid needs

Body Weight (kg)	Metabolic needs[a] (kcal/day)	Maintenance fluid needs[b]	
		mL/day	mL/h
5	500	500	20
10	1,000	1,000	40
15	1,250	1,250	50
20	1,500	1,500	60
30	1,700	1,700	70
40	1,900	1,900	80
50	2,100	2,100	90
60	2,300	2,300	95
70	2,500	2,500	105

[a]Based on 100 kcal/kg for first 10 kg of body weight + 50 cal/kg for next 10 kg of body weight + 20 cal/kg for next 50 kg of body weight
[b]Based on need of 1 mL of water to metabolize 1 kcal of energy
As described in (6)

Clinical factors can have a striking impact on insensible water losses (*Table 13-3*). Fever increases insensible losses by more than 10% per degree Celsius. Premature infants with relatively increased surface areas for size can have insensible losses two to threefold higher than baseline, especially if they are on open warmers or under phototherapy. On the other hand, children on ventilators providing humidified oxygen may have half the insensible losses of a non-ventilated child.

Similarly, urinary water output can vary tremendously. A child with a renal concentrating defect or ADH unresponsiveness may have urinary water losses of several liters per day, whereas an oligoanuric child will have no appreciable urinary water losses. In any child with normal renal function, even in the setting of maximal ADH stimulation, there is a minimal volume of urinary water obligatory to excrete the osmotic load ingested by the diet and generated by basal metabolism. As a result, even the child concentrating urine to 1,200–1,400 mOsm/L will lose nearly 25 mL of urinary water per 100 kcal of energy expended (6).

Table 13-3

Factors affecting insensible water losses

Increased losses	% Change	Decreased losses	% Change
Prematurity	100–300	Enclosed incubator	25–50
Radiant warmer	50–100	Humidified air	15–30
Phototherapy	25–50	Sedation	5–25
Hyperventilation	20–30	Decreased activity	5–25
Increased activity	5–25	Hypothermia	5–15
Hyperthermia	12%/°C		

Recent reports contend that the relationships between energy expenditure and water requirements demonstrated by hospitalized children at bed rest do not apply to anesthetized or critically ill children (18). For instance, in infants and children studied during general anesthesia, energy expenditure was half that of awake children at bedrest. On the other hand, water needs for cell metabolism was increased over baseline by about 60%, leaving the overall relationship between water needs and caloric expenditure similar in both situations. In some critically ill children, maintenance volumes may need to be reduced by 40–50% to prevent positive water balance (19).

Serum Osmolality

Water homeostasis maintains a stable serum osmolality. Serum concentrations of sodium, glucose, and urea nitrogen determine serum osmolality (20). Serum osmolality is estimated by the equation: (2 × serum Na) + (serum glucose/18) + (BUN/2.8), where the serum sodium is measured in mEq/L and the glucose and BUN in mg/dL. In the majority of children with no functional renal impairment and normal glucose metabolism, the contributions of BUN and glucose to the effective osmolality are small and the serum osmolality can be estimated by doubling the serum sodium concentration (21, 22). Thus, most children have a serum osmolality between 270 and 290 mOsm/L, corresponding to serum sodium values of 135–145 mEq/L.

Chemoreceptors in the hypothalamus constantly sense serum osmolality and respond to even small variations towards either limit of normal by adjusting ADH release from the posterior pituitary. Changes in osmolality in the setting of hypovolemia augment ADH release further. ADH effect on water permeability of the collecting tubule is a principal influence on the regulation of water balance.

Alterations in water intake or excretion result in the development of hypo- or hyperosmolality as the usual ratio of extracellular solute to water is perturbed. Since sodium is the largest component of extracellular osmolality, its concentration can be influenced profoundly by changes in water metabolism. An understanding of this link between water regulation and serum sodium values is crucial when prescribing fluid and electrolyte therapy. Most importantly, the clinician must recognize that hypo- or hypernatremia is usually a manifestation of impaired water regulation and that therapy must address regulation of water balance rather than alterations in body sodium stores.

Water Homeostasis in Acutely Ill Children or During the Perioperative Period

In ill children, there are multiple causes of both physiologic and aberrant vasopressin effect as listed in *Table 13-4* (23). As a result, if these children receive hypotonic intravenous fluids for prolonged periods of time or in volumes exceeding those generally recommended, there is the risk of acute hyponatremia. After volume resuscitation with isotonic fluids, most hospitalized children have traditionally been provided hypotonic fluids for their maintenance therapy. Given the tendency for ill children to have vasopressin effect independent of the usual osmotic and volume related stimuli, over the last decade some have suggested that isotonic fluids may be safer alternatives and should be continued as the source of maintenance fluid even after acute volume repletion (24).

Similarly, some have called for using isotonic saline as the intravenous fluid of choice whenever a maintenance infusion is needed in setting like the perioperative period when oral hydration has been held and when high ADH levels may come to be expected because of pain or anxiety. In these instances, children could receive intravascular volume expansion with an initial infusion of 20–40 mL/kg over a period of a few hours and then continued on isotonic saline as dictated by clinical circumstance, rather than the transition to fluids with more free water content.

Table 13-4
Common causes of vasopressin effect in hospitalized children

Category	Specific etiology
Physiologic	Hyperosmolar state, hypovolemia
Pulmonary	Pneumonitis, pneumothorax, asthma, bronchiolitis, cystic fibrosis
Drug effect	Narcotics, barbiturates, carbamazepine, vincristine, cyclophosphamide
Metabolic	Hypothyroidism, hypoadrenalism, porphyria
CNS	Infection (meningitis or encephalitis), tumor, trauma, hypoxia, shunt malfunction, nausea, pain, anxiety

Proponents of this routine believe it would decrease the overall numbers of hospitalized children who develop hyponatremia and prevent hyponatremia-related central nervous system damage (25).

Others have claimed that long term maintenance infusions of isotonic saline to all ill or perioperative patients may result in sodium loading in children who do not have triggers for water retention (8, 26). Moreover, hypernatremia has been described in some children receiving less sodium than that provided in these maintenance isotonic infusions (27). These cases of hypernatremia are often a result of an underlying renal concentrating defect, related to significant free water loss from sources other than urine, or resulting from aggressive fluid restriction (28). Children with certain renal or cardiopulmonary problems may be especially sensitive to such sodium loads and may more readily develop unintended sequelae of such sodium provision (29).

Several studies have shown that children with acute illness requiring emergency department evaluation or hospitalization do seem to be at risk for hyponatremia. In one study of 103 children admitted to a German pediatric hospital, nearly 80% had elevated serum ADH levels and increased plasma renin activity, independent of the underlying illness. As expected with ADH release, plasma osmolality was reduced significantly in comparison to a group of well children (23). In another report from a Canadian pediatric center, fewer than 5% of children were hyponatremic at presentation to the emergency department, but nearly 10% became hyponatremic after hospital admission, most as a consequence of excess free water provision by aggressive intravenous hydration with hypotonic fluid. Hospitalized children who became hyponatremic received on average three-times the volume of electrolyte free water than their hospitalized colleagues who remained eunatremic and were also three-times more likely to receive fluids at a rate that exceeded recommended maintenance rates (30).

A retrospective analysis of postoperative admissions to a pediatric ICU found that 11% of children manifested hyponatremia (serum sodium <130 mEq/L) during their ICU stay (31). Of those children with hyponatremia, although there was a trend towards an increased incidence in children receiving hypotonic fluids in comparison to children given isotonic solutions, there was no statistical difference demonstrated in the incidence of what the authors termed either moderate (<130 mEq/L) or severe (<125 mEq/L) hyponatremia. No children developed any neurologic sequelae or other morbidity. Children did have serum electrolytes assayed four times daily, however, so this vigilance likely resulted in clinical interventions to prevent exacerbating hyponatremia.

A prospective randomized study of 102 children with gastroenteritis at an Australian children's hospital demonstrated that the risk of developing hyponatremia decreased with provision of isotonic saline (32). Eunatremic children at presentation were most protected from subsequent falls in serum sodium when provided isotonic (0.9% NaCl) versus hypotonic (0.45% NaCl) intravenous solutions. Urinary biochemistry demonstrated that in the face of isotonic fluid provision hyponatremic children were more likely to retain sodium and bring their serum sodium values closer to normal, whereas children with normal serum sodium values already at presentation were able to excrete excess sodium appropriately and prevent hypernatremia.

A meta-analysis of six studies comparing hypotonic and isotonic maintenance intravenous solutions in children suggested that no single fluid composition or rate is ideal for all children but that an isotonic or nearly isotonic solution may prove less likely to cause symptomatic hyponatremia in acute illness and the perioperative period (33). Despite this growing body of literature to suggest that isotonic fluids may be preferable in many situations where non-osmotic ADH effect can be expected, children are still commonly prescribed hypotonic fluid therapy. A recent survey of anesthesiologists in the United Kingdom found that 60% were still prescribing hypotonic fluids for children intraoperatively, with 75% prescribing such fluids in the postoperative period (34).

Maintenance Electrolyte Therapy

Estimates for the maintenance requirements of the major electrolytes sodium, potassium, and chloride can also be

made based on metabolic demands and daily water needs (6). For sodium and chloride, approximately 2–3 mEq/100 mL of daily water requirement is needed with 1–2 mEq of potassium for each 100 mL of daily water need. Again, these estimates require adjustment based on clinical circumstance but the daily intake of most healthy individuals contains more than adequate electrolytes for maintenance needs. Although at times there can be significant electrolyte losses through the skin or the gastrointestinal tract, most electrolyte losses are urinary (17, 35). In the setting of anuric renal failure and no concomitant electrolyte losses from other sources, a much lower level of maintenance electrolyte supplementation is needed and patients may maintain adequate electrolyte balance with water supplementation alone to provide insensible fluid losses.

As with provision of water, in children who require electrolyte therapy their electrolyte prescription must be tailored to their individual needs. For the provision of sodium and chloride, this requires careful assessment of the extracellular fluid space, especially the effective circulating volume. Providing too little sodium chloride results in volume contraction and circulatory compromise; providing too much causes volume overload and sequelae such as hypertension and edema.

Similarly, inappropriate potassium supplementation may have significant clinical ramifications. In children with diminished renal function or who are at risk of hyperkalemia for other reasons, it is usually appropriate to forego any maintenance potassium supplementation. When supplementation is given acutely, it is important to monitor serum potassium values closely. When chronic potassium supplementation is needed, there should continue to be periodic assessments. A course of supplemental potassium administered orally is safer than a bolus intravenous injection; intravenous potassium supplements rarely need to exceed 0.5 mEq/kg/h (20).

Perturbations in Fluid and Electrolyte Homeostasis

Alterations in Water Balance, Serum Sodium, and Cell Volume

As discussed above, the regulation of osmolality is achieved by alterations in water intake and excretion. Serum sodium levels often vary with these alterations in water balance. Generally, serum sodium is kept regulated at levels between 135 and 145 mEq/L. A serum sodium value below 130 mEq/L or above 150 mEq/L is out of the range of normal homeostasis and most often indicates a problem with water balance.

Since sodium is the major extracellular osmole, alterations in serum sodium can result in water flux between the intracellular and extracellular spaces. Because significant water movement into or out of cells could prove deleterious to cell function, cell volume is closely regulated to minimize such shifts (36). For instance, with hyponatremia there is decreased effective osmolality in the extracellular space. As a result, water can shift from the plasma into the intracellular space and cell swelling will occur. To counterbalance such swelling, the cell acutely regulates its volume by transporting electrolytes, especially potassium, from the intracellular space into the extracellular space, thereby decreasing the osmotic gradient for water transfer. Over several days, when faced with chronic hyponatremia or chronic hypoosmolality, the cells will also achieve effective volume regulation by losing organic osmolytes such as taurine and inositol, thereby further diminishing the osmotic gradient for water transfer into the cell (37).

With hypernatremia, the osmotic gradient favors water movement out of the cells and into the extracellular space and, without protective mechanisms, cells will shrink. Again, there are both acute and chronic mechanisms minimizing these changes in cell volume. Acutely, there is transport of electrolytes intracellularly, whereas with time there is stimulation of the production of organic idiogenic osmoles (37, 38). Together, these act to blunt the loss of intracellular volume that would otherwise occur.

Changes in serum sodium values evolving slowly and reflecting chronic processes tend to be better tolerated clinically than acute alterations. Such slow changes allow for maximal counter-regulation and fewer clinical sequelae. On the other hand, profound sudden alterations – serum sodium values falling below 120 mEq/L or above160 mEq/L – are often accompanied by dramatic neurologic complications directly related to the acute changes in cell volume in the central nervous system.

These regulatory mechanisms must also be kept in mind when formulating specific therapeutic intervention. Acute perturbations can be corrected more rapidly than chronic conditions because the full gamut of responses to the imbalance has yet to come into play.

Hyponatremia: Initial Approach

Hyponatremia is usually defined as a serum sodium value less than 130 mEq/L. Depressed serum sodium values are likely to be the result of persistent ADH effect and a

relative surfeit of water for solute in the extracellular space; hyponatremia uncommonly arises secondary to depleted salt stores alone.

Infrequently, pseudohyponatremia may be seen. Pseudohyponatremia is not a depletion of sodium stores but a change in the usual make-up of the extracellular space such that the relative concentration of sodium is now depressed because of the pathologic elevation of another solute. Common etiologies of pseudohyponatremia include hypergylcemia, hyperlipidemia, and hyperproteinemia. In these clinical conditions, serum sodium values tend to be only modestly depressed. Since there is no underlying true anomaly in sodium or water stores in these conditions, the serum sodium need not be addressed with any therapeutic maneuvers. With the introduction of ion sensitive electrodes for the measurement of plasma sodium concentration, pseudohyponatremia related to the presence of confounding factors in the laboratory assay is much less commonly encountered.

To clarify the etiology of the hyponatremia, the clinician should assess the patient's extracellular volume status and determine if it is decreased, normal, or increased. Then, by measuring urine sodium excretion and determining the renal response to the hyponatremia, it becomes easier to determine if the patient should receive sodium and water or if sodium and water restriction is the appropriate therapy (*Table 13-5*).

Table 13-5
Etiology of hyponatremia

Circulating volume	Urinary Na (mEq/L)	
	≤ 20	≥ 20
Decreased	Burns	Adrenal insufficiency
	Cystic fibrosis	Diuretics –early
	Diuretics – late	Salt wasting
	Gastroenteritis	
Normal or Increased	Cardiac failure	Renal failure
	Hepatic cirrhosis	SIADH
	Nephrotic syndrome	Water intoxication

Hyponatremia: Decreased Volume Status and Urine Na ≤ 20 mEq/L

Decreased circulating volume is usually seen with states of significant sodium loss. The most common site of this loss is the gastrointestinal tract as a result of vomiting, diarrhea, or tube drainage. The renal response to the decreased effective circulating volume involves increased activity of the renin-angiotensin axis and relatively high levels of aldosterone and angiotensin. As a result, urine sodium values are generally low (<20 mEq/L) and water reabsorption in the distal nephron is facilitated by high levels of ADH. In the face of continuing sodium losses exceeding intake, this state of vigorous ADH effect leads to a relative excess of water and concomitant hyponatremia.

A similar clinical state of hyponatremia can also be seen in cystic fibrosis where there are increased skin losses of sodium and chloride, with bleeding, with burns, and with certain losses of fluid from the intravascular space of the extracellular fluid into the interstitial space ("third-spacing") as can occur post-operatively, in conditions of vascular leak such as sepsis, or with peritonitis. Such hyponatremia can also be seen following a period of diuretic therapy. In response to chronic diuretic-mediated volume contraction, the mechanisms outlined above come into play. Thiazide diuretics, especially in combination with a loop diuretic such as furosemide, are particularly prone to inducing such hyponatremia.

The appropriate therapeutic response to these conditions is the provision of sodium and water either by use of intravenous saline solutions or oral electrolyte solutions. This results in restoration of sodium balance and volume expansion.

Hyponatremia: Decreased Volume Status and Urine Na ≥ 20 mEq/L

Decreased circulating volume with a random urinary sodium excretion >20 mEq/L is indicative of renal salt wasting, either from an intrinsic tubulopathy or from early diuretic effect. Less commonly, adrenal insufficiency can cause sodium wasting from the cells of the distal nephron. Such a deficiency can arise from an intrinsic endocrine defect such as congenital adrenal hyperplasia related to 21-hydroxylase deficiency, from some secondary impairment of adrenal function caused by infection, bleeding, or malignancy, or from pharmacologic adrenal suppression without adequate replacement therapy. In the setting of adrenal insufficiency, provision of appropriate adrenal hormone replacement as well as adequate sodium and water proves therapeutic. With renal salt wasting, supplementation with sodium and any other electrolytes exhibiting impaired renal reabsorption is useful.

Hyponatremia: Normal or Expanded Volume and Urine Na ≤ 20 mEq/L

Normal or increased circulating volume and random urine sodium excretion <20 mEq/L can be seen in conditions where there is an excess of both total body water and total body sodium. The three major disorders that cause this type of hyponatremia are the nephrotic syndrome, hepatic failure related to cirrhosis, and cardiac failure. In all these conditions, there is a state of sodium and water avidity related to high levels of ADH and aldosterone. Most commonly, this is in the setting of preexisting total body sodium overload as evidenced by edema. In all of these conditions, despite the increased extracellular or circulating volume, the effective circulating volume is often depressed. As a result of this ineffective perfusion of the tissues, sodium and water avidity is only heightened by stimulation of the renin-aldosterone-angiotensin axis, further exacerbating the total body excess of salt and water. Appropriate therapy includes striking a balance between interventions promoting the maintenance of effective circulating volume and restricting the provision of excess water and sodium which will only contribute to further total body water and sodium overload.

Hyponatremia: Normal or Expanded Volume and Urine Na ≥ 20 mEq/L

Hyponatremia in the setting of normal or increased effective circulating volume is always related to persistent ADH effect (15). If the random urine sodium value is >20 mEq/L, the most common clinical scenario is the syndrome of inappropriate antidiuretic hormone secretion or SIADH. SIADH can arise from disparate clinical conditions including the postoperative child, the child with significant pain, or the child with pulmonary disease. As described earlier, ill children are at risk for both inappropriate ADH secretion and inappropriate ADH effect (39). In SIADH, despite a state of hypo-osmolality, the urine is inappropriately concentrated as a result of an inability to suppress ADH secretion and block ADH-mediated water reabsorption from the distal nephron. Appropriate therapy for SIADH includes restricting water intake and attending to any underlying clinical factors predisposing to this syndrome. Provision of fluids containing higher concentrations of sodium will not necessarily increase serum sodium without attention to concomitant water restriction.

Normal or increased extracellular volume and high urine sodium concentration can also be seen in the setting of renal failure as both glomerular filtration and water clearance falls while the fractional excretion of sodium rises. A more unusual cause of this form of hyponatremia is polydipsia, usually psychogenic in nature. Such water intoxication is rare in children but can occasionally be seen with emotional or psychiatric illness in older children or with infants inappropriately provided large volumes of water or very hypotonic fluid in a repetitive fashion by a caretaker. In both these circumstances, restriction of the volume of free water ingested on a daily basis may be beneficial.

Hypernatremia

Hypernatremia is defined as a serum sodium value greater than 150 mEq/L. Generally, even higher serum sodium values can be tolerated with the most significant clinical and neurologic effects not occurring until sodium values exceed 160 mEq/L. As with hyponatremia, it has long been recognized that hypernatremia is more commonly a reflection of a problem with water balance rather than a sodium imbalance (40). In most instances, the patient has a relative deficiency of water for normal extracellular solute content.

Since sodium is the major determinant of plasma osmolality, as serum sodium levels rise, serum osmolality concomitantly increases. Increases in serum osmolality are sensed by hypothalamic osmoreceptors, triggering ADH release from the posterior pituitary as serum osmolality increases over 280 mOsm (41). Increased serum osmolality also causes a sensation of thirst. Thus, in the normal state, as serum osmolality increases, there is increased fluid intake mediated by thirst in the setting of high ADH levels. This results in increased reabsorption of free water from the cortical collecting duct and re-equilibration of serum sodium levels and serum osmolality before clinically significant hypernatremia or hyperosmolality occurs.

Outside infancy, hypernatremia as a result of sodium excess or salt poisoning is infrequent. Its major cause is improper preparation of powdered or liquid concentrated formula resulting in a hypertonic, hypernatremic solution. Since infants do not have free access to water, they cannot respond to their increasing sense of thirst as they develop such hypernatremia. As caregivers continue to provide the same incorrectly prepared formula for further feedings, there is further salt loading. In addition, young

infants are unable to excrete sodium loads as efficiently as older children and this limits the intrinsic renal response. Iatrogenic sodium loading can also be seen in children who receive large doses of sodium bicarbonate because of persistent acidosis, during a resuscitation, or in children who have been given inappropriate amounts of sodium in peripheral nutrition. Iatrogenic sodium loading can also be seen in the child who has received repeated large volumes of blood products, generally isotonic or sodium-rich solutions.

Children who have hypernatremia from sodium excess should exhibit the physical signs and symptoms of an expanded extracellular space. They frequently have peripheral edema and may have hypertension or symptoms of pulmonary edema. These children can respond to therapy aimed at augmenting sodium elimination. The use of diuretics and the provision of adequate free water decrease the total body sodium burden. Rarely, dialysis may be necessary when the hypernatremia must be corrected rapidly (42, 43).

Hypernatremia as a result of salt loading is rare and the pediatric clinician is much more likely to see hypernatremia stemming from a free water deficit or a combined water and sodium deficit where the water losses exceed the sodium losses. Hypernatremia secondary to a water deficit arises in the setting of inadequate access to water or some impairment in ADH release or response. It is uncommon to see hypernatremia secondary to poor water intake except in infants or young children who cannot get water for themselves in response to their sense of thirst (44). As for ADH-related anomalies, there are many causes of central or nephrogenic diabetes insipidus (45). Again, given normal access to water, it is rare for the older child to develop hypernatremia even with an impairment in the ADH axis because of the strong drive to drink in response to thirst (46). In very young children with diabetes insipidus, however, the issue of access to water arises and hypernatremia may be a concern. Such hyponatremia can also be seen in the postoperative state in children with concentrating defects who are not allowed to drink by mouth and who are receiving a prescribed volume of fluid based on a presumed ability to concentrate urine and conserve water.

The most common etiology of hypernatremia in children is the loss of hypotonic fluid, that is fluid with a relative excess of water for its sodium content. In these situations, the total body water is decreased more than the total body sodium. The usual clinical scenario leading to such a condition is viral diarrheal illness in the setting of poor water intake or persistent vomiting. In this condition, there is loss of stool with a sodium content generally <60 mEq/L. These children tend to excrete small volumes of concentrated urine with urine sodium content <20 mEq/L, underscoring the fact that they are conserving both water and sodium. Their hypernatremia is not a manifestation of a total body excess of sodium but a depletion of sodium that is overshadowed by a larger relative depletion of body water. Therapy is aimed at restoring water and sodium balance by providing back the hypotonic fluid which was initially lost either by the use of intravenous saline solutions or with oral electrolyte therapy.

Fluid Replacement Therapy

Most commonly, the prime goal of fluid replacement therapy is restoration of an adequate effective circulating volume. In its absence, significant metabolic derangements can occur that then exacerbate perturbations in fluid and electrolyte homeostasis. The volume of fluid replacement required varies with the extent and etiology of the compromised circulation. In many children with acute illness, there may be an element of decreased effective volume that is mild and difficult to appreciate by clinical examination. Expansion of extracellular volume with infusion or ingestion of 20–40 mL/kg of fluid over a few hours often results in better perfusion and improved clinical appearance from presentation. Urine output tends to remain normal in these situations speaking against persistent non-osmotic ADH activity that would encourage volume overload (47).

Children with mild dehydration, manifesting with <5% weight loss, will usually respond to 30–50 mL/kg of fluid. In the setting of more significant compromise of effective volume such as with loss of vascular tone in sepsis or a systemic inflammatory response, more than 200 mL/kg may be needed to achieve hemodynamic stability and effective perfusion. In most situations other than outright shock, the clinician can approach fluid resuscitation with either intravenous or oral rehydration therapy.

Assessment of Volume Depletion

In estimating the severity of dehydration, a change in weight from baseline is the most objective measure (48). As rehydration proceeds, following weights on a serial basis becomes an important adjunct in assessing the efficacy of fluid repletion. If no baseline weight is known, the clinican

will use various parameters based on history and physical examination to judge the severity of dehydration (*Table 13-6*). Children with mild dehydration will have minimal clinical signs and only a modest decline in urine output. As dehydration becomes more significant, more classical findings such as dry mucous membranes, tenting skin, sunken eyes, and lethargy become prominent. With profound dehydration, there is anuria, marked alterations in consciousness, and hemodynamic instability.

A capillary refill time greater than 2 s has long been touted as a useful physical finding pointing towards effective volume depletion (49). Unfortunately, delayed capillary refill is neither a sensitive nor specific marker of dehydration (50, 51). It may be most useful if normal, as this does seem to exclude reliably severe dehydration. In a prospective cohort study of dehydrated Egyptian children between 3 and 18 months of age, the best correlation between clinical assessment of degree of dehydration and actual volume depletion came in children who had clinical parameters of significant dehydration such as prolonged skinfold tenting, a dry mouth, sunken eyes, and altered sensorium (52). Similarly, in a review of pre-school children with dehydration, the best clinical indicators of volume depletion – decreased skin turgor, poor peripheral perfusion, and Kussmaul breathing – accompanied more significant dehydration, underscoring the difficulty with which mild degrees of dehydration may be estimated by the clinician without access to prior weights (53).

A study of 97 American children given intravenous fluids in an emergency department for rehydration underscored the difficulty in assessing accurately even severe dehydration by standard clinical estimates (54). Physicians' initial estimate of dehydration compared to the actual percent loss of body weight varied dramatically, with a sensitivity of 70% for severe dehydration (>10% loss) but only 33% for moderate dehydration (6–10% loss). This study suggested that adding a serum bicarbonate level to the assessment may be useful, increasing the sensitivity of the clinical scales to 100% in severe dehydration and 90% in moderate dehydration if standard clinical features and a serum bicarbonate <17 mEq/L were found.

Other studies have found that laboratory studies by themselves are poor indicators of the degree of dehydration. In 40 children receiving intravenous fluids for dehydration, pre-hydration assessment of serum BUN, creatinine, uric acid, anion gap, venous pH, and venous base deficit were made as well as assessment of urinary specific gravity, urinary anion gap, and fractional excretion of sodium. Only the serum BUN/Cr ratio and serum uric acid significantly correlated with increasing levels of dehydration, but both lacked sensitivity or specificity for detecting more than 5% dehydration (55). Similarly, in a retrospective review of 168 dehydrated children, elevated serum urea levels and depressed serum bicarbonate levels were found to be useful adjuncts to clinical evaluation in accurately assessing the degree of dehydration but were not by themselves predictive (56).

In fact, with viral gastroenteritis, the most common cause of dehydration in children, there rarely is a significant laboratory anomaly despite clinically detected

Table 13-6

Clinical assessment of dehydration

	Degree of dehydration		
	Mild	Moderate	Severe
Vital signs			
Pulse	Normal	Rapid	Rapid and weak
Blood pressure	Normal	Normal to slightly low	Shock
Weight loss			
Infant	<5%	10%	>15%
Older child	<3%	6%	>9%
Mucous membranes	Tacky	Dry	Parched
Skin turgor	Slightly decreased	Decreased	Tenting
Eye appearance	Normal tearing	Decreased tearing ± sunken	No tears + very sunken
Capillary refill	Normal	Delayed (>3 s)	Very delayed (>5 s)
Urine output	Decreased	Minimal	Anuric

volume depletion, as underscored by a cohort of children from the United Kingdom admitted for rehydration due to viral gastroenteritis in whom only 1% of admitted children had an electrolyte derangement (57–59).

In children with volume depletion accompanying trauma, sepsis, surgery, or underlying renal dysfunction, it would be more likely to find perturbations in electrolyte and acid-base status. Thus, in the absence of a straightforward case of mild to moderate diarrheal dehydration, it is general consensus that blood should be obtained for assessment of electrolytes, bicarbonate, and renal function to help guide specific fluid and electrolyte therapy (60, 61)

As the child is volume resuscitated, it is important to reassess the child's clinical status. Initial estimates of degree of dehydration may need to be adjusted if the child is not showing progressive improvement. Most clinicians follow parameters such as general appearance and sensorium, change in weight from initiation of rehydration, and urine output and urine osmolality. In children with some types of renal dysfunction, there may often be an underlying chronic urinary concentrating defect. In these children, relatively dilute urine flow may be maintained even in the face of clinical dehydration and markers other than urine output and osmolality should be followed.

Oral Rehydration Therapy

Although oral rehydration with electrolyte solutions is a safe, efficacious, and convenient way to treat mild to severe volume depletion, parenteral fluid and electrolyte therapy has been the mainstay of medical treatment for most children presenting with fluid and electrolyte imbalances (62–65). Especially underutilized in North America, oral therapy has proved successful in clinical settings worldwide in resuscitating children of all ages with profound fluid and electrolyte anomalies, and short of significant circulatory compromise, can be used as first line therapy in all fluid and electrolyte aberrations (66, 67). An example of a situation calling for oral rehydration in the following clinical scenario:

A healthy 4-year old girl presents to her pediatrician's office following 3 days of a febrile illness. For most of this time, her appetite has been severely depressed and her parents estimate that she has only had a few cups of fluid in the last 12 h. Yesterday, she vomited once and today has had an additional episode of emesis. She has continued to urinate, although less frequently and with smaller volumes. On physical examination, the girl looks unhappy but non-toxic and alert. Initially, her pulse is 120 but, after acclimation to the examination, it has decreased to 100 beats per min. Her sitting blood pressure is 80/50 and she will not cooperate with attempts at orthostatic vital signs. Her mucous membranes are somewhat dry and her weight today is 15 kg, exactly the same as her weight at a well child examination 6 months previously. The parents are concerned that she is becoming dehydrated.

Primary care and emergency department physicians face such clinical scenarios regularly. An otherwise healthy child with an apparent viral illness causing mild to moderate dehydration will frequently be treated by intravenous therapy with the contention that oral rehydration will rarely succeed, will be too labor intensive, or will take too much time. In fact, such children are excellent candidates for oral rehydration. In most developed countries where a viral disease is thought to be the etiology of the dehydration and there is little concern about a cholera-like enteritis, solutions with sodium contents from 30 mEq/L to 90 mEq/L have been shown for years to be efficacious for oral rehydration (68–71).

With this girl, given the history and physical examination, it is unlikely that any clinically significant electrolyte perturbations will be found, so there is little indication for assaying electrolytes or renal function prior to starting oral rehydration (57–59). The family is given a commercially available oral rehydration solution containing 75 mEq/L Na, 20 mEq/L K, 30 mEq/L citrate, and 2.5% glucose. They are asked to provide 1 L of fluid (50 mL/kg) to the child over the next 4 h. The child should be offered small aliquots of fluid very often – 5 mL every 1–2 min at initiation. If this regimen is tolerated with no vomiting, the aliquots may be gradually increased in volume and the frequency reduced, aiming to deliver at least the prescribed total volume over about 4 h. After her rehydration, the child should subsequently continue to be provided free access to fluid and resume an age-appropriate diet. If, on the other hand, there are any further episodes of vomiting, then for each episode of emesis an additional 120–240 mL of oral rehydrating solution should be given, again with the goal to complete rehydration and resume usual fluid intake and nutrition.

The initial provision of oral fluid given often in small volumes is far more likely to be well tolerated by the dehydrated child than larger aliquots. If families are unwilling to provide the fluid in this manner, a nasogastric tube may be placed for continuous infusion of rehydrating solution.

Although occasional children may fail this approach and require intravenous rehydration, most children with mild to moderate rehydration can be rehydrated orally.

A guide for the volumes of fluid to provide and the duration of rehydration can be found in Table 13-7.

The first oral rehydration solutions were developed in the 1940s at academic medical centers. Within 10 years, a commercial preparation formulated as a powder meant to be mixed with water was available, but its use became associated with an increased incidence of hypernatremia (72). Several factors contributed to the development of this problem: the preparation was sometimes incorrectly administered as the powder itself or improperly diluted with too little water; when correctly reconstituted, the solution had a final carbohydrate concentration of 8% predisposing to an osmotic diarrhea; and it was a common practice at that time for parents to use high solute fluids such as boiled skim milk as an adjunctive home remedy. Taken together, these early experiences contributed to reluctance to use oral rehydration solutions on the part of many clinicians.

Over time, there came to be a better understanding of the physiology of water and solute absorption from the gut. Of prime importance was the recognition that many substances actively transported across intestinal epithelium had an absolute or partial dependence on sodium for absorption and that sodium itself was actually better reabsorbed in their presence (73–75). This led to the routine introduction of glucose into oral rehydration solutions in a fixed molar ratio of no more than 2:1 with sodium. Moreover, it became clear that the sodium/glucose cotransporter remained intact not only in the face of enterotoxic-gastroenteritis such as seen with cholera or *Eschericia coli* but also in more common viral and bacterial enteritides (66, 67).

The World Health Organization (WHO) and the United Nations Children's Fund have championed the use of a rehydrating solution that includes: Na 90 mmol/L, Cl 80 mmol/L, K 20 mmol/L, base 30 mmol/L, and glucose 111 mmol/L (2%). This WHO solution has proved useful in many clinical trials rehydrating children and has also been shown to reduce the morbidity and mortality associated with diarrheal illness regardless of its etiology (68, 69).

Most commercially available oral rehydration solutions differ from WHO solution in that they have a somewhat higher carbohydrate content, a lower sodium content, and a higher carbohydrate to sodium ratio (Table 13-8). Some preparations are available as powder and other as ready to drink formulations. Some manufacturers have also used rice solids as a carbohydrate source instead of glucose.

Many of these formulation changes arose from concerns that using an oral rehydrating solution with a sodium content >60 mmol/L would prove problematic in developed countries where most gastroenteritis is viral in nature and has a lower sodium content than the secretory diarrheas seen in less developed areas. Some clinicians

Table 13-7

Oral rehydration for previously healthy, well-nourished children

Type of dehydration	Rehydration phase	Rehydration duration	Replacement of ongoing losses	Nutrition
Mild (<5%)	30–50 mL/kg ORT	3–4 h	60–120 mL ORS for each diarrheal stool or episode of emesis[a]	Continue breast milk or resume age appropriate usual diet
Moderate (5–10%)	50–100 mL/kg ORT	3–4 h	As above	As above
Severe (>10%)	100–150 mL/kg ORT	3–4 h	As above with use of nasogastric tube if needed	As above
Evidence of shock	20 mL/kg 0.9% NaCl or Lactated Ringers IV	Repetitive infusions until perfusion restored then transition to ORT 100 mL/kg over 4 h	As above with use of nasogastric tube if needed or consideration of further IV therapy	As above
Accompanying Hypernatremia	Per type of dehydration	At least 12 h for ORT. Monitor fall in serum Na	As above	As above

ORT, Oral Rehydration Therapy with fluid containing 45–90 mmol/L Na, 90 mmol/L glucose, 20 mmol/l K, 10–30 mmol/L citrate; IV, Intravenous infusion

[a]For children >10 kg, aliquots for replacement of ongoing losses should be doubled to 120–240 mL rehydration solution for each stool or emesis

Table 13-8

Oral rehydration solutions

	Concentration (mmol/L)					
Product						
	Na	Sugar	K	Cl	Base	Osmolality (mOsm/L)
WHO ORS[a]	90	111	20	80	30	311
CeraLyte 90[a]	90	220[b]	20	80	30	275
Low-Na ORS[a]	75	75	20	65	30	245
Rehydralyte	75	140	20	65	30	300
CeraLyte 70[a]	70	220[b]	20	60	30	230
CeraLyte 50[a]	50	220[b]	20	40	30	200
CeraLyte 50 lemon	50	170[b]	20	40	30	200
Enfalyte	50	170	25	45	34	167
Pedialyte	45	140	20	35	30	254

[a]Provided as powder. Needs to be reconstituted with water
[b]Contains rice-syrup solids substituted for glucose

feared that, if minimally dehydrated children losing small amounts of sodium in their stools were exclusively provided WHO solution, hypernatremia might ensue without provision of excess free water. A few early studies did document iatrogenic hypernatremia related to such rehydration techniques (76). In cases of mild dehydration stemming from causes other than secretory diarrhea, solutions with lower sodium contents may be as useful and, in fact, solutions with sodium content ranging from 30 to 90 mmol/L have proved quite effective in this setting (70, 71, 77). A more recent meta-analysis of studies focused on the safety and efficacy of oral rehydration solution in well nourished children living in developed countries documented little evidence that WHO solution was more likely to cause aberrations in serum sodium than lower sodium containing oral rehydration solutions (78). Why ingestion of lower tonicity oral rehydration fluids would be less problematic than infusion of similar tonicity intravenous fluid is not clear, but does again underscore the safety of oral rehydration.

Oral Rehydration with Fluids Other than ORS

Despite the efficacy and widespread availability of commercial oral rehydration solutions and the ease with which other electrolyte solutions can be mixed at home with recipes requiring few ingredients other than water, sugar, and salt, there are many children who are still given common household beverages in attempts at rehydration. In children with dehydration and electrolyte losses from vomiting or diarrhea, most common beverages do not contain adequate sodium or potassium supplementation. Moreover, the base composition and the carbohydrate source are often sub-optimal for the dehydrated child, especially in the setting of diarrheal illness (*Table 13-9*). Similarly, most beverages marketed as sports drinks for "rehydration" following exercise are also deplete of sufficient electrolytes given that the electrolyte composition of sweat is many fold lower than the composition of gastrointestinal fluid. In prescribing oral rehydration to children in an ambulatory setting, the clinician should be specific to the family as to the appropriate fluid and volume for the child to ingest, emphasizing the need to use a fluid with appropriate electrolye content if there is concern about evolving imbalances in sodium, potassium, or bicarbonate homeostasis.

Oral Rehydration and Serum Sodium Abnormalities

Although oral rehydration is often considered for children with modest dehydration and no presumed electrolyte anomalies, oral rehydration with WHO or WHO-like solution has also been used in cases of dehydration accompanied by hyponatremia or hypernatremia (79, 80). Although most children with severe hypernatremia (>160 mEq/L) can be successfully rehydrated orally, there have been reports of seizures, generally as a result of too rapid correction of serum sodium stemming from the

Table 13-9

Composition of common oral fluids[a]

Fluid	Na (mEq/L)	K (mEq/L)	Source of base	Carbohydrate (g/100 mL)
Apple juice	<1	25	Citrate	12
Orange juice	<1	55	Citrate	12
Milk	20	40	Lactate	5
Cola	2	<1	Bicarbonate	10
Ginger ale	4	<1	Bicarbonate	8
Kool-Aid	<1	<1	Citrate	10
Gatorade	20	2.5	Citrate	6
Powerade	10	2.5	Citrate	8
Jello	25	<1	Citrate	14
Coffee	<1	15	Citrate	<0.5
Tea	2	5	Citrate	10

[a]Adapted in part from data found in (74)

provision of supplemental water in addition to the glucose-electrolyte solution (79–81). In those cases, the average serum sodium fell by 10–15 mEq/L over 6 h rather than over 24 h as advised. In follow-up studies, no seizure activity was seen in a similar cohort of hypernatremic children who received 90 mmol/L Na rehydration solution alone at a rate calculated to replace the infant's deficit over 24 h (79). It is important for the practitioner to remember that once peripheral perfusion has been stabilized with initial volume expansion, there is no benefit to correcting any deficit rapidly and taking 24–48 h may be a more prudent course in the face of significant electrolyte anomalies.

Oral Rehydration Schemes

Several oral rehydration schemes have been shown to be quite effective and well tolerated. In one approach used extensively in developing countries, the patient's volume deficit is calculated on the basis of weight loss and clinical appearance (82). The volume deficit is doubled; this is the target rehydration volume to be given over 6–12 h. Two-thirds of this volume is given as a glucose-electrolyte solution containing 90 mmol/L Na over 4–8 h; once this has been ingested, the remaining volume is provided as water alone over 2–4 h. In cases of suspected or confirmed hypernatremia with serum sodium exceeding 160 mEq/L, the volume deficit would not be doubled and would be administered as 90 mmol/L Na glucose-electrolyte solution alone over 12–24 h. Patients who refuse to take fluids by mouth have nasogastric tubes placed. With this approach, successful oral rehydration is the rule; 95% of children are fully rehydrated without the need for intravenous therapy.

An alternative approach has been to have the child begin by taking 15 mL/kg/h of a 60–90 mmol/L Na rehydration solution by mouth or nasogastric tube (83). The solution is given in small frequent quantities and increased up to 25 mL/kg/h until hydration has improved at which point solid feedings are reintroduced and volumes of 5–15 mL/kg of rehydration solution offered after feeds until the volume deficit has been delivered.

Over two decades ago, the American Academy of Pediatrics issued guidelines for the treatment of fluid and electrolyte deficits with oral rehydration solutions (66). Children with acute dehydration and extracellular volume contraction were to be provided 40–50 mL/kg of a glucose-electrolyte solution containing in each liter 75–90 mmol Na, 110–140 mmol glucose (2–2.5%), 20 mmol potassium, and 20–30 mmol base. This volume was to be administered over 3–4 h and then once there has been amelioration of the extracellular volume contraction, the child would be changed to a maintenance solution with 40–60 mmol/L Na at half the rate. If the child was still thirsty on this regimen, there should be free access to supplemental water or low-solute fluid such as breast milk.

Based on much of this published clinical experience, an evidence-based guideline for treating dehydration in children from industrialized European countries was created in the late 1990s, recommending oral rehydrating solution containing 60 mmol/L of sodium, 90 mmol/L of glucose, 20 mmol/L of potassium, and 10–30 mmol/L

of citrate with rehydration occurring over 3–12 h utilizing from 30 to 150 mL/kg of fluid depending on the degree and type of dehydration (48).

In 2004, the American Academy of pediatrics updated its oral rehydration recommendations and endorsed guidelines promulgated by the Center for Disease Control and Prevention (84, 85). Minimal dehydration in children weighing less than 10 kg was to be treated with provision of 60–120 mL of oral rehydration fluid for each watery stool or each episode of vomiting. In larger children, twice this volume would be provided. For children with more moderate dehydration, 50–100 mL/kg of oral rehydration solution would be given over 2–4 h to account for estimated fluid deficit and ongoing losses would be treated with the 60–240 mL per stool or emesis depending on size. Nursing babies would continue to receive breast milk as desired and formula fed babies would be provided age appropriate diet as soon as they had been rehydrated. For severely dehydrated children, a combination of intravenous hydration with isotonic fluids and prompt transition to oral rehydration solution by mouth or nasogastric tube was recommended. Overly restricted diets were to be avoided during gastrointestinal illness and attention to adequate caloric intake emphasized (see *Table 13-7*).

Use and Acceptance of Oral Rehydration Solutions

Despite the availability of guidelines for oral rehydration and their endorsement by professional organizations, a minority of American academic pediatricians, private practitioners, and pediatric house staff acknowledged utilizing oral rehydration (70). Although oral rehydration schemes have been shown to be used significantly more frequently by emergency room physicians who were familiar with the American Academy of Pediatrics recommendations, even in this group oral therapy was underutilized in children with all degrees of dehydration. Worldwide, WHO estimates that fewer than 25% of patients who could benefit from oral rehydration are actually treated with such therapy (86). Moreover, even in areas of the world such as Bangladesh, where oral rehydration has been championed by both local and international medical agencies for decades, its use is still suboptimal (87, 88). Among practitioners, there may also be generational differences in the use of oral rehydration therapy. In a national survey of Amercian pediatric emergency department physicians, although there was no difference in the baseline knowledge of published data in this field or acceptance of its validity, recent graduates of training programs were much more likely to use oral rehydration for more advanced cases of clinical dehydration than their older colleagues (89).

When utilized according to these schemes, oral rehydration has been demonstrated to be almost universally successful in achieving some degree of volume repletion (90). Other advantages to oral therapy include the safety and stability of the product despite lengthy shelf storage, its ability to be administered readily by the child's caretaker in nearly any locale, and avoidance of the discomfort and potential complications associated with intravenous catheter placement (91). In developed countries, there has been the concern that some powdered ORS formulations may not be looked upon by parents as a convenient hydration solution since they involves preparation. In fact, in a randomized controlled trial of an urban pediatric clinic and a suburban medical practice in the United States, parents were as equally satisfied with the ease of administration and effectiveness of a powdered solution as a commercially prepared ready to drink solution (92).

Oral rehydration is somewhat less successful in hospitalized children than in children treated in an ambulatory setting (90). This difference may be directly related to the degree of dehydration or other complicating clinical issues leading to hospital admission. Moreover, the relatively labor intensive slower approach to oral rehydration may be problematic in medical facilities with time constraints or space limitations (91, 93).

Frozen flavored oral rehydration solutions may be more readily accepted than conventional unflavored liquid electrolyte solutions. Their use resulted in higher rates of successful rehydration in children with mild to moderate dehydration, even if these children initially failed conventional oral rehydration (91). Frozen flavored rehydration solution is now commercially available in many parts of the world, as is a variety of flavored rehydration solutions.

Another potential issue with oral rehydration is that its use does not alter the natural course of the child's illness. For instance, in gastroenteritis with dehydration, by far and away the most common illness requiring rehydration in children, oral rehydration does not lower stool output or change the duration of diarrheal illness (94). As a result, caretakers may abandon oral rehydration because the child continues to have symptoms, failing to appreciate the benefits of ongoing hydration. Oral rehydrating solutions have been formulated with lower electrolyte composition and different carbohydrate moieties with the goal to reduce the osmolarity of solutions and potentially augment fluid absorption from the small intestine (78). The rice based oral solutions have been studied most

extensively. In these solutions, glucose is substituted with 50–80g/L of rice powder. In a meta-analysis of 22 randomized clinical trials comparing rice based solution to conventional glucose containing solutions, stool output dramatically decreased in children with cholera given rice based hydration but did not change in children with other bacterial or viral enteritides (95).

There are some reports that suggest that providing children with non-cholera enteritis with reduced osmolarity rehydration solution may be beneficial. A study of 447 boys less than 2 years of age admitted for oral rehydration were assigned to either receive WHO solution (osmolarity 311 mmol/L) or a solution containing less sodium and chloride (osmolarity 224 mmol/L). Children who received the lower osmolarity solution had reduced stool output, reduced duration of diarrhea, reduced rehydration needs, and reduced risk of requiring intravenous fluid infusion after completion of oral hydration (96). A meta-analysis of 9 trials comparing WHO solution to reduced osmolarity rehydration solution concluded that children admitted for dehydration had reduced needs for intravenous fluid infusion, lower stool volumes, and less vomiting when receiving the reduced osmolarity solution (97).

Intravenous Therapy

Although absolute indications for parenteral intravenous therapy are limited, they do include significantly impaired circulation or overt shock. In addition, there are occasional children who are truly unable to sustain an adequate rate of oral fluid intake despite concerted effort or have such persistent losses that parenteral therapy comes to be necessary. The mainstays of fluid therapy in children are saline or buffered saline crystalloid solutions. Isotonic versions of these crystalloids are used for volume resuscitation and hypotonic saline solutions may be used in addition to provide supplemental maintenance hydration. In addition to crystalloid solutions, there are several colloid fluids that are also used by many clinicians. *Table 13-10* lists the electrolyte content of some of the more common intravenous solutions used for pediatric fluid therapy.

Table 13-10

Composition of common intravenous fluids

Fluid	Osmolarity (mOsm/L)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	Buffer (source) (mEq/L)	Mg (mEq/L)	Ca (mEq/L)	Dextrose (g/L)
Chrystalloids								
0.9% Saline	308	154	0	154	0	0	0	0
Lactated ringers	275	130	4	109	28 (lactate)	0	3	0
D5 0.45% Saline	454	77	0	77	0	0	0	50
D5 0.22% Saline	377	38	0	38	0	0	0	50
5% Dextrose water	252	0	0	0	0	0	0	50
Normosol	295	140	5	98	23 (gluconate) 27 (acetate)	3	0	0
Plasma-Lyte	294	140	5	98	23 (gluconate) 27 (acetate)	3	0	0
Colloids								
5% Albumin	309	130–160	<1	130–160	0	0	0	0
25% Albumin	312	130–160	<1	130–160	0	0	0	0
Fresh frozen plasma	300	140	4	110	25 (bicarbonate)	0	0	0
3.5% Hemaccel	301	145	5	145	0	0	6	0
6% Hetastarch	310	154	0	154	0	0	0	0
Dextran 40 or 70	310	154	0	154	0	0	0	0

Choice and Volume of Parenteral Fluid

Children with significant extracellular volume contraction (greater than 10% acute weight loss in an infant or 6% weight loss in an older child) should receive an isotonic crystalloid solution such as 0.9% saline (154 mEq/L NaCl) or Lactated Ringer's (130 mEq/L NaCl) at a rate of 20 mL/kg over 30–60 min. In some children, even more rapid infusions or serial provision of such aliquots may be necessary to restore effective volume. Children with less pronounced dehydration may not exhibit signs or symptoms of volume contraction. In certain situations, however, it may be clinically warranted to provide them with an initial rapid intravenous bolus to initiate rehydration therapy.

Concomitant with the placement of intravenous access, blood should be obtained for determination of serum electrolytes, osmolality, and renal function. Given that dehydrated children often have high levels of vasoactive hormones and high vasopressin levels, it is most circumspect to establish baseline electrolyte levels since it is possible to alter electrolyte balance rapidly with intravenous therapy. In the face of inadequate tissue perfusion, a parenteral fluid infusion should begin immediately prior to the return of any pertinent laboratory results. If hemorrhagic shock is suspected, resuscitation with packed red blood cells is optimal. In cases of severe volume depletion, if the child does not improve with the initial 20-mL/kg crystalloid bolus, this should be repeated up to two additional times. In children who have not improved despite administration of 60 mL/kg of total volume over an hour or in children in whom underlying cardiac, pulmonary, or renal disease may make empiric aggressive rehydration more problematic, consideration should be given to placement of a central monitoring catheter to more accurately assess intravascular volume and cardiac dynamics (98). In some instances of profound ineffective circulating volume, such as might accompany certain cases of sepsis, initial volume resuscitation may require sequential infusions of fluid ultimately exceeding 100 mL/kg.

Within minutes of infusion of a crystalloid fluid, it becomes distributed throughout the extracellular space. Since this involves equilibration of the fluid between the two components of the extracellular space – the intravascular and interstitial spaces – actually only one-third to one-quarter of infused crystalloid stays in the blood vessels (99). This accounts for the need to give large volumes of crystalloid in the setting of circulatory collapse and leads some to suggest that colloid solutions such as 5% or 10% albumin should play a role in resuscitation (100, 101).

Colloid Solutions and Volume Resuscitation

The use of colloid solutions for volume resuscitation is controversial. Colloids were once included in a number of widely promulgated guidelines for the care of patients in emergency facilities and intensive care units both for hemorrhagic shock prior to the availability of blood and for non-hemorrhagic shock as an adjunct to crystalloid use (102). Types of colloid utilized included 5% albumin, fresh frozen plasma, modified starches, dextrans, and gelatins. These guidelines, generally aimed toward the fluid resuscitation of adults, were composed despite the prior publication of a systematic review of randomized controlled trials that demonstrated no effect on mortality rates when colloids were used in preference to crystalloids (103). Moreover, there is a distinct cost disadvantage to using colloid solutions.

Subsequent systematic reviews have looked at this issue anew. In one meta-analysis of 38 trials comparing colloid to crystalloid for volume expansion, there was no decrease in the risk of death for patients receiving colloid (102). In the other review, albumin administration was actually shown to increase mortality by 6% compared to crystalloid (104). Proposed mechanisms contributing to this worse outcome include anticoagulant properties of albumin (105) and accelerated capillary leak (106).

A drawback of all these systematic reviews, however, has been the limited number of studies that included children other than ill premature neonates. As a result, generalization of these results from ill adults may not be germane to all critically ill volume depleted children. For instance, a report of 410 children with meningococcal disease suggests that albumin infusion in this population may not have been harmful, as case fatality rates were lower than predicted (107). Overall, however, there seems to be no substantive data to support the routine use of colloid to complement or replace crystalloid in fluid resuscitation. Rather, repetitive infusions of large volumes of crystalloid seem to be well tolerated in volume depleted children, do not seem to predispose to excessive rates of acute respiratory distress syndrome or cerebral edema, and in some conditions such as sepsis, play an important role in improved survival (108). A recent survey of pediatric anesthesiologists in western Europe reported that colloid solutions are being used less frequently in infants and older children and suggested that familiarity with some of the issues raised in these systematic reviews are affecting practice patterns (109).

Repetitive infusions of crystalloid may also prove problematic in some children. Most notably, if very large volumes of 0.9% saline are used acutely for volume

resuscitation, it is not unusual for children to develop a hyperchloremic metabolic acidosis. This occurs as acidotic peripheral tissues begin to reperfuse and already depleted extracellular bicarbonate stores are diluted by a solution with an isotonic concentration of chloride (98, 110). This acidosis can be ameliorated by supplemental doses of bicarbonate as well as the addition of supplemental potassium as needed. There is sometimes a tendency for clinicians to react to the hyperchloremic metabolic acidosis with further saline bolus infusions. In the face of corrected hypoxia or hypovolemia, however, such maneuvers may only exacerbate the chloride driven acidosis (111). This hyperchloremic acidosis is seen less frequently when Ringer's lactate solution is used as the resuscitation fluid because of the metabolic conversion of lactate to bicarbonate. In the setting of significant preexisting acidosis or underlying hepatic dysfunction preventing the metabolism of lactate, infusion of Ringer's lactate solution may, however, exacerbate an acidosis.

With the recent suggestion that some children with acute illness or following surgery may benefit from a prolonged period of isotonic fluid infusion given high levels of ADH and the possibility for hyponatremia developing with hypotonic fluid therapy, some have expressed concern that a hyperchloremic acidosis may develop in these children. In a prospective randomized study of more than 100 children with gastroenteritis given isotonic intravenous rehydration and maintenance therapy, there was no tendency for the development of hyperchloremic acidosis even after a day of isotonic fluid provision. Although serum chloride levels did tend to increase in these children, serum bicarbonates also improved, potentially related to improved effective volume and subsequent better tissue perfusion (112). Similarly, in children post cardiac surgery who were given isotonic solutions for their maintenance fluid needs, although there was a tendency for a hyperchloremic acidosis to develop, there seemed to be no significant clinical ramifications and long-term outcomes were similar to children who did not develop hyperchloremic acidosis (113).

Large volume infusion of blood may also predispose to electrolyte anomalies as well as manifestations of citrate toxicity. If aged whole blood is infused, there is the possibility that a large potassium load will be delivered to the patient as potassium over times migrates down its concentration gradient from less viable erythrocytes into plasma. Since most patients receive packed red blood cells instead of whole blood, this potential problem is minimized since little plasma is infused and, thus, the relatively small amount of infused potassium can be accommodated by intracellular movement.

Citrate is used as the anticoagulant in stored blood. Since citrate complexes with calcium, there can be a fall in ionized calcium levels if large volumes of blood are infused rapidly or if there are concomitant perturbations in calcium homeostasis. Similarly, citrate may complex with magnesium and magnesium depletion may occur. The liver usually metabolizes infused citrate into bicarbonate. Alkalosis may, thus, occur if large volumes of citrate are metabolized. In the setting of hepatic dysfunction, however, citrate will not be metabolized and serves as an acid load and will help create an acidosis or exacerbate any underlying acidosis.

Regardless of the initial infusion with either colloid or crystalloid, once sufficient volume to restore circulatory integrity has been infused, less rapid volume expansion is necessary. During this phase, the rapidity of fluid repletion is most probably not a concern unless there are severe underlying aberrations in the serum sodium or serum osmolality. In the absence of these derangements or profound volume deficit, if the child has improved significantly with the initial parenteral volume expansion, attempts should be made to reinstitute oral rehydration. Prolonged intravenous therapy rarely should be necessary.

Rapid Rehydration

Over the last decade, a scheme of rapid intravenous resuscitation and follow-up oral rehydration has been adopted by many pediatric emergency departments to treat children with up to 10% dehydration secondary to vomiting and gastroenteritis (114). After infusion of 20–30 mL/kg on intravenous crystalloid, the child is allowed to take up to several ounces of a standard oral rehydration fluid, and if this intake is tolerated without vomiting for 30–60 min, then discharged home to continue rehydration, initially with a prescribed volume of standard rehydration solution.

If the child does not tolerate oral rehydration or if there are such significant electrolyte anomalies that there are concerns regarding potential adverse CNS sequelae of too rapid rehydration, then intravenous rehydration may be the best route for continued hydration. It is rare for children to become symptomatic from serum sodium aberrations until levels less than 120 mEq/L or greater than 160 mEq/L are reached. Children who have had very sudden fluxes in electrolytes may become symptomatic earlier. On the other hand, children whose severe sodium abnormalities are thought to be more chronic in nature must be treated in a more controlled fashion since they are at higher risk for developing CNS symptoms during treatment.

The vast majority of children treated in emergency facilities for volume repletion do well with such rapid rehydration. These children are generally healthy with normal cardiac and renal function and have developed extracellular volume depletion relatively rapidly. As a result, they suffer no ill effects from rapid rehydration. In fact, the clinical success of this aggressive restoration of extracellular volume underlies the calls to reexamine the traditional deficit therapy approach to rehydration with its tedious calculations of fluid and electrolytes losses and requirements (9, 115).

Symptomatic Hyponatremia

In the setting of symptomatic hyponatremia, especially if the child has seizures, it is important to raise the serum sodium approximately 5 mEq/L acutely. Generally, this results in stabilization of the clinical situation and allows for further evaluation and treatment of the child in a less urgent fashion. This is one of the few situations in which hypertonic saline (3% saline) should be utilized.

To calculate the proper volume of 3% saline to infuse, the child's TBW must be multiplied by the 5 mEq/L-desired increase in serum sodium to determine the amount of sodium (in mEq) to infuse. Since every mL of 3% saline contains 0.5 mEq of sodium, doubling the number of mEq of sodium needed results in the proper milliliter volume of 3% saline to infuse. Thus, in the 20 kg child, the TBW is approximately 12 L (0.6 L/kg × 20 kg) and the desired sodium dose would be 60 mEq (12 L × 5 mEq/L). If 120 mL of 3% saline were infused, the serum sodium would be expected to rise by approximately 5 mEq/L. The infusion should be given at a rate to increase the serum sodium by no more than 3 mEq/L/h and is often given more slowly over the course of 3–4 h (116). If the child continues to be symptomatic from hyponatremia after this infusion, additional 3% saline may be given until the symptoms improve or the serum sodium is in the 120 to 125 mEq/L range. At that point, further correction of the hyponatremia should consist of a slower infusion of more dilute saline to cover the sodium deficit, the sodium maintenance needs, and any volume deficit. Consideration of the role of ADH and prior excess free water provision should also be considered in determining the volume and tonicity of fluid to be provided.

Asymptomatic Hyponatremia

If a child has severe hyponatremia but is not symptomatic, there is no need to administer hypertonic saline based solely on a laboratory anomaly. With or without symptoms, in cases of severe hyponatremia the child should be carefully evaluated as to the etiology of the hyponatremia, keeping in mind that hyponatremia tends to result from an imbalance of water regulation. If this is the case, free water should be restricted and appropriate supplementation with intravenous saline solutions begun to provide maintenance sodium requirements of approximately 2–3 mEq/kg/day and any ongoing losses of sodium.

Besides these maintenance sodium needs, if the child has an element of dehydration, every kilogram of body weight lost from baseline represents a 1 L deficit of nearly normal saline from the total body water as well. These losses are often referred to as isotonic losses. These account for a sodium deficit of 154 mEq/L that also must be included in the calculations for sodium replacement.

In the setting of hyponatremic dehydration, there have been additional sodium losses as well. Generally, these occur as viral diarrheal stool losses with a sodium content $\leq$60 mEq/L are replaced with fluids with a lower sodium content. To estimate these sodium losses, the difference between the child's desired serum sodium and current serum sodium is multiplied by the child's estimated TBW. This product represents the hyponatremic sodium losses that must be added to the maintenance sodium needs, any ongoing losses, and the sodium losses that accompanied weight loss. An example of the calculations and therapeutic maneuvers that need to be considered with significant hyponatremia is presented in the following case study:

A girl who normally weighs 10 kg suddenly develops generalized seizures and is brought by ambulance to the emergency department. She has had a week of gastroenteritis, has felt warm to touch, and has been drinking water and apple juice only, refusing any other liquids or any solid food for several days. Intravenous access is placed and lorazepam is administered and the seizure activity stops. The emergency department physician orders serum chemistries and the child is weighed and found to be 8.8 kg. A bolus infusion of 200 mL of 0.9% NaCl is administered over the next 30–60 min after which the girl appears well perfused but she is still lethargic. The serum sodium is then reported to be 112 mEq/L. While further evaluation of the child's overall status is ongoing, it is important to begin correcting the symptomatic hyponatremia.

The child has actually already received approximately 30 mEq of sodium in the 0.9% NaCl bolus given because of her dehydration and poor perfusion. Given her TBW of roughly 5.5 L (wt in kg × 0.6 L/kg), this should result in an increase in her serum sodium by approximately 5 mEq/L.

Since the child has had hyponatremic seizures and is still exhibiting some central nervous system effect with her lethargy, it is prudent to raise the serum sodium by 5 mEq/L so that it will be in the 120–125 mEq/L range. Since she is hemodynamically stable, it is also best not to provide an excess of further volume until the child undergoes imaging to assess for cerebral edema, especially given the history of seizures, lethargy, and hyponatremia. By using a small volume of hypertonic saline, the serum sodium can be raised in a controlled manner while further evaluation of the child continues. It would take about 22 mEq of sodium (TBW × desired increase in serum sodium = 5.5 L × 5 mEq/L) to accomplish the desired elevation. Since each mL of 3% saline contains about 0.5 mEq of sodium, a total of 44 mL of 3% saline could be infused over approximately 3–4 h.

In addition to this acute management to restore initial circulation and perfusion and to raise the serum sodium to a safer level, plans must be formulated to attend to the patient's overall volume and sodium deficit. To prescribe the proper follow-up intravenous fluid, the patient's water and electrolyte deficits at presentation must be reconciled with his therapy thus far.

The child's water deficit is 1.2 L, reflecting the 1.2-kilogram weight loss. She has "maintenance" water needs of an additional 1 L/day based on her normal weight of 10 kg. She is having no other ongoing water losses and has already received nearly 250 mL in intravenous fluid in the form of 0.9% NaCl and 3% NaCl. Her current water needs are thus 1,950 mL.

The child's normal "maintenance" sodium needs are 30 mEq/day (3 mEq/kg/day). She has lost 1.2 kilograms of isontonic fluid in body weight that represents 185 mEq of sodium. In addition, she has hyponatremic sodium losses that have arisen as her diarrheal stool that contained sodium was replaced with water alone. To calculate these needs, her normal total body water needs to be multiplied by the difference in her serum sodium from a normal value of 135 mEq/L. Her TBW is 6 L (TBW = 0.6 L/kg × 10 kg) and the difference in serum sodium is 23 mEq/L (135 mEq/L − 112 mEq/L); her hyponatremic losses are therefore 138 mEq (6 L × 23 mEq/L). Total sodium needs are thus 30 mEq of maintenance, 185 mEq of isotonic losses, and 138 mEq of hyponatremic losses or a total of 353 mEq. She has already received 52 mEq of sodium from the 400 mL of 0.9% NaCl given in the emergency department. Her current sodium needs are thus just about 300 mEq.

To choose the proper solution for this child, the deficit of 1,950 mL of water should contain 300 mEq of sodium. This is best approximated by 0.9% NaCl with its NaCl content of 154 mEq/L NaCl. In the past, it has been suggested that half of the fluid and sodium deficit be replaced over 8 h and the remainder over the ensuing 16 h. Although such a plan can be followed, there is little evidence that more rapid correction of the hyponatremia is harmful except if the patient has been symptomatic with hyponatremia or has profound asymptomatic hyponatremia of chronic duration. In these cases, it is safest to plan to correct the serum sodium by no more than 12–15 mEq/L over 24 h. More rapid correction has resulted in osmotic demyelination injury to the brain with devastating long-term neurologic outcomes (116–118).

Severe Hypernatremia

With hypernatremia, therapy is again guided by the clinical situation and provision of intravenous fluid is usually reserved for those children with very elevated serum sodium values who are not considered candidates for oral rehydration therapy. In cases of hypernatremia due to salt poisoning, there should be signs of overhydration and volume expansion. Excretion of sodium should be enhanced by using a loop diuretic to augment urine sodium losses and by replacing urine output with free water. If the patient has significant underlying renal or cardiac compromise, dialysis and ultrafiltration may be necessary to correct the water and electrolyte imbalance (42, 43). With hypernatremia and volume expansion from salt excess, it will be detrimental to provide further intravenous saline.

In hypernatremia accompanied by volume loss, any significant alterations in effective circulation should be addressed with 20 mL/kg bolus infusions of an isotonic crystalloid solution until effective peripheral perfusion is restored. Then, further provision of water and sodium should be provided based on calculated water and sodium needs. In the majority of cases, with mild elevations in serum sodium and minimal degrees of dehydration, the actual calculation of deficits is probably unnecessary since the child will be hemodynamically stable and a candidate for exclusive oral rehydration. In situations where there is profound hypernatremia or circulatory compromise, it remains necessary, however, to be able to calculate a free water deficit to tailor intravenous rehydration therapy. An example of such a situation is outlined in the following clinical scenario:

After 2 days of refusing to nurse, a 5 kg infant boy with a viral syndrome presents to an emergency department in shock, 15% dehydrated with a weight of 4.25 kg and a

serum sodium of 170 mEq/L. He receives 300 mL of 0.9% NaCl urgently and further therapy is now planned.

The child has lost 750 g of weight. Since this is hypernatremic dehydration, there has been loss of water in excess to salt. Thus, part of the weight loss represents isotonic losses but a larger proportion represents free water loss. The child's free water deficit can be calculated by the equation:

$$[(\text{Serum Na actual})/(\text{serum Na desired}) \times \text{total body water}] - \text{total body water}$$

Substituting the appropriate data for this baby:

$$[(170/145) \times (0.6 \times 4.25)] - (0.6 \times 4.25) = [1.2 \times 2.55] - 2.55 = 0.51\text{L}]$$

Thus, of this baby's 750-mL fluid deficit due to dehydration, 510 mL is free water and 240 mL is normal saline.

Too rapid correction of the baby's serum sodium with free water could result in cerebral edema as the water infused into the extracellular space follows osmotic forces and moves into the intracellular space. In cases of hypernatremia where the serum sodium exceeds 160 mEq/L, it is considered safest to correct the serum sodium by no more than 15 mEq/day. In this boy's case, this would mean that correction to a serum sodium in the normal range would take about 2 days.

If the fluid and electrolyte therapy must be given intravenously, the appropriate prescription again depends on calculation of water and sodium requirements and deficits. His original fluid deficit was 750 mL and his maintenance water needs are estimated at 500 mL/day. Thus, over the next 2 days, the fluid needs to replace the deficit and provide maintenance would be 1,750 mL. Of this volume, sthe baby has already received 300 mL of fluid in the emergency department so a net deficit of 1,450 mL now exists.

The baby has maintenance sodium needs of 15 mEq/day (3 mEq/kg/day). His sodium deficit reflects only the isotonic fluid losses that have been estimated above at 240 mL of normal saline or 37 mEq of sodium. Thus, over the next 2 days, his sodium needs are 67 mEq of which he has already received more than 45 mEq in the emergency department due to initial volume expansion.

Initiating an infusion of 30 mL an hour of free water should result in the slow and steady correction of the hypernatremia over 2 days by providing the nearly 1.5 L of free water that the child requires to replace losses and provide ongoing needs. The serum sodium should be monitored every 4 h initially and if it is falling faster than desired (about 0.5 mEq/hour) then sodium should be added to the rehydration fluid.

Fluid and Electrolyte Therapy with Renal Dysfunction

Impact of Kidney Disease

Children with compromised renal function often manifest a reduced tolerance for changes in total body water as well as changes in the composition or distribution of volume between the intracellular and extracellular body spaces. Similarly, alterations in electrolyte balance are more likely problematic because normal homeostatic mechanisms are frequently perturbed. Especially in the child with marked nephrosis or significant impairment in renal clearance, it becomes vital to approach the provision of fluids and electrolytes with great care.

As far as fluid therapy is concerned, of utmost importance is the recognition that the concept of maintenance fluids or electrolytes pre-supposes normal renal function. Roughly two-thirds of any daily maintenance fluid prescription is to replace urinary water losses. Similarly, urinary electrolyte losses figure prominently in daily electrolyte balance. In the setting of oliguria or anuria, provision of maintenance fluids could contribute to and, potentially, exacerbate volume overload and maintenance electrolyte therapy could result in electrolyte anomalies.

Fluid and electrolyte needs of the child with renal dysfunction are better considered in the context of the child's current volume status and electrolyte needs. For instance, in symptomatic volume depletion with decreased circulatory perfusion, volume expansion would be initiated regardless of urine output. Once volume replete, the child's needs could be reassessed along with his current renal function. The child who is volume overloaded would best be managed by fluid restriction and provision of only insensible losses of approximately 300 mL/m^2. Insensible fluid losses should be considered essentially electrolyte free water. The child who is volume replete should be kept volume replete. This is most readily accomplished by providing a combination of insensible losses as free water and any other volume losses (urine output, diarrheal stool, surgical drain output, emesis) on an additional milliliter for milliliter basis. If there are significant ongoing losses from a single source, the electrolyte composition of this fluid can be assayed so that the replacement fluid may more accurately reflect the electrolyte losses. Otherwise, a solution of 0.45% NaCl can be used initially and altered as the clinical situation continues to develop and further electrolyte determinations are made.

If the child's volume status or the adequacy of renal function is difficult to discern initially, it is best to provide the child with replacement of both insensible and ongoing losses. This approach should maintain the child's current volume status and allow for further determination of the appropriateness of more vigorous hydration or conversely fluid restriction as the clinical situation clarifies. Monitoring the child's weight on at least a daily basis and documenting the child's total fluid intake and output will also assist in arriving at a proper hydration regimen.

Assessing the child's current electrolyte status and monitoring the loss of electrolytes in the urine or in any other source of significant output will help tailor the daily electrolyte prescription. An understanding of the pathophysiology underlying the child's renal dysfunction will also be useful. The child who has profound tubular electrolyte losses will require more sodium on a daily basis than the child who is edematous and total body salt overloaded from his nephrotic syndrome. The child with chronic renal insufficiency and hypertension mediated by long-standing salt and water overload may actually benefit from diuretic therapy to remove salt and water rather than any further volume expansion with saline.

Certainly the provision of supplemental potassium to the child with renal dysfunction must be done judiciously. The oliguric or anuric child should receive no potassium until it is well documented that serum potassium levels are low or that there are extrarenal potassium losses (for instance losses from diarrheal stool). The child with marginal renal function should receive small amounts of potassium (approximately 1 mEq/kg/day) with at least daily assessment of electrolyte balance to determine adequacy and appropriateness of continued potassium supplementation.

Fluid and Electrolyte Therapy in the Pediatric Intensive Care Unit

Critically ill children present a challenge to the clinician attempting to prescribe appropriate fluid and electrolyte therapy. Oftentimes, there may be acute kidney injury or multiorgan failure complicating management decisions. With such children, rote reliance on standard equations or practice guidelines to prescribe fluid and electrolyte therapy may create significant fluid and electrolyte anomalies. Rather than prescribing set maintenance requirement of fluid or electrolytes, the clinician should assess the patient's individual fluid and electrolyte needs in the context of the underlying pathophysiology, the current volume status, the efficacy of tissue perfusion, the current ventilatory requirements, and the current renal function. Whenever there is concern about incipient or exacerbating fluid overload, it is important to review the volume and type of fluids being provided. Maximizing the concentration of continuous medication drips and assessing medication compatibility for simultaneous infusions are important steps in limiting total daily fluid input. Initially, it is crucial in these critically ill children to ascertain that their intravascular space is replete to help maintain hemodynamic stability. Once a patient is felt to be intravascularly replete, maintaining euvolemia by providing insensible water losses as well as replacing any ongoing fluid and electrolyte losses should maintain fluid and electrolyte balance.

Oftentimes, despite a desire to limit fluids in the critically ill child, medication requirements, nutritional needs, and hemodynamic insufficiency may result in very large daily fluid loads. There may also be situations in which increased vascular permeability or "leak" causes a critically ill child to become massively volume overloaded but with a decreased effective circulating volume. In other words, renal and tissue perfusion may be sluggish because fluid has leaked from the intravascular space into the interstitial space. In this setting, there may be need to continue to administer large volumes of fluid to maintain circulatory integrity with the knowledge that such infusions will only exacerbate the total body fluid overload. Aggressive diuretic therapy may prove useful especially if renal function is not compromised. Combination diuretic therapy utilizing agents that work at separate sites along the renal tubule may be necessary. Ultimately, the use of either periodic or continuous ultrafiltration may be beneficial to these patients by allowing ongoing fluid administration but limiting the daily imbalance between fluid intake and output. Ultrafiltration may be accomplished via peritoneal dialysis, by intermittent hemodialysis with ultrafiltration, or by utilizing one of the slow continuous ultrafiltration techniques now known as continuous renal replacement therapy (CRRT)). The recognition that volume overload has a deleterious effect on many aspects of patient management and seems to be a strong prognostic indicator of poor ultimate outcome has led some to suggest that early ultrafiltration should be considered in critically ill patients (119).

If ultrafiltration is initiated, extreme vigilance is necessary to prevent exacerbation of intravascular depletion and the development of pre-renal azotemia or frank renal failure. Special care must be taken with the continuous modalities to insure that ultrafiltration rates are

periodically reassessed and readjusted. Furthermore, because the electrolyte losses that accompany the ultrafiltration of fluid are isotonic, the electrolyte content of infused fluids must be adjusted to match the composition of the ultrafiltrate, especially if there is no component of dialysis ongoing that may blunt the development of serum electrolyte anomalies. As a result, serum electrolyte values need to be followed in a serial fashion with periodic review and readjustment of the composition of supplemental intravenous fluids.

Abnormalities in Serum Sodium Complicated by Kidney Injury

Because of the important contribution of serum sodium to serum osmolality, alterations in serum sodium, especially coupled with alterations in BUN related to renal failure, can complicate the usual approach to a child with fluid and electrolyte anomalies. Generally, there are greater concerns with hypernatremia and renal failure since the need to correct the sodium in a slow fashion can be problematic when renal replacement therapy needs to be initiated for clearance of urea. Balancing the correction of sodium and the hyperosmolar state with the clearance of urea requires a carefully considered plan that is grounded in a firm understanding of fluid and electrolyte homeostasis.

In most cases of hypernatremia related to severe dehydration, some degree of acute kidney injury is present. This renal dysfunction is usually "pre-renal" in nature, a result of a decreased effective circulating volume rather than an intrinsic glomerular or tubular disorder. Most often, in the course of rapid restoration of perfusion and early rehydration, urine output increases and azotemia begins to resolve.

Alternatively, there are occasional cases in which due to intrinsic renal dysfunction or acute tubular necrosis, the renal insufficiency will not respond to volume infusion and, in fact, the provision of excess volume may contribute to significant volume overload. In these cases, there may be need to consider some form of renal replacement therapy to assist in the controlled correction of fluid and electrolyte derangements, especially if the renal failure is oliguric or anuric in nature. Such an example is detailed in the following case study:

A 15-year-old boy presents with several weeks of polyuria, severe weight loss, fatigue, and poor oral intake. He is diagnosed as having diabetes mellitus with ketoacidosis by his pediatrician and referred to an emergency department for management. At this point, his serum sodium is 154 mEq/L, his creatinine is 3.0 mg/dL, and his BUN is 30 mg/dL. In the emergency department, the child receives several bolus infusions of normal saline supplemented with sodium bicarbonate and is started on an insulin drip. He is admitted and continues to receive brisk intravenous hydration with normal saline with bicarbonate supplementation per a practice guideline for treating children with diabetic ketoacidosis. He is noted to be oliguric and this does not improve with several more h of hydration with normal saline following the guideline hydration recommendations. The next morning, laboratory values reveal a serum sodium of 165 mEq/L, a creatinine of 4.5 mg/dL, and a BUN of 50 mg/dL. He has made only 75 mL of urine in the last 8 h and is developing some mild peripheral edema.

In this case, the renal insufficiency and poor urine output have complicated the usual management of diabetic ketoacidosis and has exacerbated an underlying hypernatremia. Given the patient's evolving renal failure, it is not feasible to provide the necessary volume of free water to correct the hypernatremia without contributing to further volume overload. Because of the apparent progressive renal failure, it would also be useful to correct the hypernatremia in case dialysis becomes necessary for urea clearance. By performing controlled ultrafiltration on the patient and replacing back the volume ultrafiltered with free water, the serum sodium could be corrected without exacerbating the volume status.

With a serum sodium of 165 mEq/L and an estimated TBW of 42 L (70 kg $\times$ 0.6 L/kg), this boy has free water needs of 7.5 L to lower his serum sodium to the 140 mEq/L range ([165/140 $\times$ 42]–42). Since the patient is now significantly hypernatremic and has been subject to various fluid and electrolyte shifts as his diabetic ketoacidosis has been treated, it would be prudent to correct his serum sodium by no more than 10–12 mEq/day over the course of 3 days. Thus, if the boy undergoes ultrafiltration with a goal of 2.5 L removed daily, and the ultrafiltration volume each day is replaced back totally as free water, the serum sodium should be in the normal range in 3 days' time. The ultrafiltration goal could be achieved over the course of a few hours each day if the patient were hemodynamically stable or over a more prolonged period of time each day if there were concerns regarding hypotension. Thus, either a conventional hemodialysis set up could be used for relatively rapid ultrafiltration only or a continuous filtration circuit for either rapid or slow filtration.

Since the fluid removed in ultrafiltration is isonatremic to the serum sodium, the sodium concentration of each liter of ultrafiltrate should mirror the serum sodium

concentration at the time of ultrafiltration. Thus, on the initial day of ultrafiltration, each liter of ultrafiltrate would contain a sodium content of 165 mEq/L. By providing back the volume ultrafiltered each day as free water, the serum sodium content could be expected to fall, in this case, by about 8–10 mEq/L/day.

It is important to recognize that free water must be provided back to the patient to make up for the ultrafiltration losses. Otherwise, since the ultrafiltrate is isotonic, there will be no change in the serum sodium concentration and the ultrafiltration may potentially exacerbate the renal failure by depleting the intravascular space and the effective circulating volume.

Moreover, it is also important to recognize that the boy's overall daily fluid needs will be greater than the daily ultrafiltration volume alone since maintenance fluid requirements and any ongoing fluid losses must also be considered. Since the boy is in renal failure, his maintenance fluid needs can be scaled back to insensible losses of 300 mL/m^2/day and, in this case, there are no ongoing losses. Thus, each day for the next 3 days this 70-kg patient needs to receive approximately 500 mL/day of insensible losses and 2,500 mL/day of ultrafiltration replacement or a total of 3,000 mL/day. His maintenance sodium requirements are 3 mEq/kg/day. Although it may seem counterintuitive to provide a hypernatremic patient with maintenance sodium, disregarding these requirements will result in a more rapid correction of the hypernatremia than desired. If the child were to receive a saline infusion of 0.45% NaCl at a rate of 125 mL/h, this will provide just over 3 mEq/kg/day of sodium in a total volume of 3 L/day.

If the child with hypernatremia has profound renal failure and requires dialysis for urea clearance, the dialysis prescription must take into account the need to correct the serum sodium slowly. Normally, regardless of the modality of renal replacement therapy, most dialysate contains sodium isotonic to the normal serum sodium range. It may prove detrimental, however, to dialyze a patient who is very hypernatremic against a dialysate with a sodium concentration 30 mEq/L or more less than the patient's serum sodium concentration. The diffusional gradient during dialysis would lead to more rapid correction of the serum sodium than the desired drop of approximately 1 mEq every 2 h.

Although most hemodialysis machines can be readjusted so that the dialysate produced will have a sodium content as high as the low to mid-150s, this still may not reduce the gradient sufficiently in cases of severe hypernatremia. In those situations, by maximizing the sodium concentration of the dialysate and by performing dialysis for limited amounts of time, one could minimize the drop in serum sodium. Still, there would need to be frequent assessments of the serum sodium concentration, and overall clearance may need to be sacrificed to prevent too rapid correction of the serum sodium and a rapid concomitant decrease in the serum urea that may increase the chances for dialysis dysequilibrium.

Alternatively, a continuous hemodiafiltration technique such as continuous venovenous hemodiafiltration (CVVHDF) could be performed. By asking the hospital pharmacy to increase the sodium content of the dialysate and replacement fluid to within 10–12 mEq/L of the serum sodium concentration, the diffusional gradient for sodium clearance could be minimized. Then, by making appropriate adjustments in the sodium content of the dialysate as the serum sodium falls, the serum sodium levels could be reduced gradually by 10–12 mEq/L/day while at the same time adequate urea clearance and ultrafiltration for most situations would be achieved.

Peritoneal dialysis has also been used in cases of severe hypernatremia (120–122). Again, the concentration of sodium in the dialysate may need to be adjusted upwards in severe hypernatremia to prevent too rapid clearance of sodium. In addition, since the degree of clearance and ultrafiltration may not be as precisely controlled as with hemodialysis or hemodiafiltration, frequent assessment of electrolyte values will be necessary. Manipulation of dwell volumes and dwell times will also influence overall clearance and the use of smaller dwell volumes for longer periods of time will help to minimize sodium clearance.

In contradistinction to hypernatremia, since hyperosmolality is less common with hyponatremia, in some ways it is easier to employ renal replacement therapy in the setting of severe hyponatremia and concomitant renal insufficiency. Again, the focus needs to be on the rapidity of the correction of the serum sodium. In conditions of severe but asymptomatic hyponatremia of some chronicity, the rate of correction of serum sodium should parallel the rate of correction recommended in hypernatremia – approximately 10–12 mEq/L/day. Correction of chronic hyponatremia at a more rapid rate has been associated with the development of central pontine demyelinosis.

All of the manipulations described above for hypernatremia and renal failure can be utilized with hyponatremia and renal failure, with the understanding that the dialysate sodium concentration should now not exceed the serum sodium value by 10–12 mEq/L. Conventional hemodialysis machines can be adjusted to produce dialysate with a sodium concentration as low as the mid-120s. In the very rare situation in which a child with profound hypernatremia (<110 mEq/L) were being hemodialyzed,

brief hemodialysis runs may be necessary initially to prevent too rapid correction of the serum sodium level and the attendant risk of central pontine demyelinosis. If dialysate is being custom prepared for peritoneal dialysis or hemodiafiltration, precise alterations in the electrolyte content can be made more readily to reduce the sodium gradient.

The local resources, the training of ancillary staff, the unique circumstances of each patient, and the comfort of the clinician with different modalities of renal replacement therapy will guide the choice of therapy when faced with renal failure and significant serum sodium anomalies. The actual modality of renal replacement therapy utilized is less important than careful attention to the rate of correction of the electrolyte anomaly, to the rate of urea clearance being achieved, and to the clinical response of the patient to on-going therapy.

References

1. Cosnett JE. The origins of intravenous therapy. *Lancet* 1989;1:768–771.
2. Blackfan KD, Maxcy KF. Intraperitoneal injection of saline. *Am J Dis Child* 1918;15:19–28.
3. Karelitz S, Schick B. Treatment of toxicosis with the aid of a continuous intravenous drip of dextrose solution. *Am J Dis Child* 1932;42:781–802.
4. Gamble JL. Early history of fluid replacement therapy. *Pediatrics* 1953;11:554–567.
5. Holliday MA. Gamble and Darrow: pathfinders in body fluid physiology and fluid therapy for children, 1914–1964. *Pediatr Nephrol* 2000;15:317–324.
6. Holliday MA, Segar WE. The maintenance need for water in parenteral fluid therapy. *Pediatrics* 1957;19:823–832.
7. Holliday MA. Body fluid physiology during growth. In Clinical Disorders of Fluid and Electrolyte Metabolism, 2nd edn, Maxwell MH, Kleeman CR (eds.). chapter 13. New York, McGraw-Hill, 1972.
8. Holliday MA, Ray PE, Friedman AL. Fluid therapy in children: facts, fashions, and questions. *Arch Dis Child* 2007;92:546–550.
9. Holliday M. The evolution of therapy for dehydration: should deficit therapy still be taught? *Pediatrics* 1996;98:171–177.
10. Gavin N, Merrick N, Davidson B. Efficacy of glucose-based oral rehydration therapy. *Pediatrics* 1996;98:45–51.
11. Schwartz R. Comments from another student of Gamble and Darrow on fluids. *Pediatrics* 1996;98:314.
12. Cumlea WC, Schubert CM, Sun SS et al. A review of body water status and the effects of age and body fatness in children and adults. *J Nutr Health Aging* 2007;11:111–118.
13. Yoshioka T, Iitaka K, Ichikawa I. Body fluid compartments. In Pediatric Textbook of Fluids and Electrolytes. Ichikawa I (ed.). Baltimore, Williams and Wilkins, 1990, pp. 14–20.
14. Ritchie RF, Ledue TB, Craig WY. Patient hydration: a major source of laboratory uncertainty. *Clin Chem Lab Med* 2007;45:158–166.
15. Rose BD, Rennke HG. Regulation of salt and water balance. In Renal Pathophysiology – The Essentials. Rennke HG, Denker BM (eds.). Philadelphia, Lippincott Williams and Wilkins, 2006, pp. 31–69.
16. Talbot NB, Crawford JD, Butler AM. Homeostatic limits to safe parenteral fluid therapy. *N Engl J Med* 1953;248:1100–1108.
17. Friedman AL, Ray PE. Maintenance fluid therapy: what it is and what it is not. *Pediatr Nephrol* 2008;23:677–680.
18. Murat I, Dubois MC. Perioperative fluid therapy in pediatrics. *Pediatr Anesth* 2008;18:363–370.
19. Choong K, Bohn D. Maintenance parenteral fluids in the critically ill child. *J Pediatr (Rio J)* 2007;83(2suppl):S3–S10.
20. Rasouli M, Kalantari KR. Comparison of methods for calculating serum osmolality: multivariate linear regression analysis. *Clin Chem Lab Med* 2005;43:635–640.
21. Trachtman H. Sodium and water homeostasis. *Pediatr Clin North Am* 1995;42:1343–1363.
22. Rose BD, Rennke HG. Disorders of water balance: hyponatremia, hypernatremia, and polyuria. In Renal Pathophysiology – The essentials. Rennke HG, Denker BM (eds.). Philadelphia, Lippincott Williams and Wilkins, 2006, pp. 69–99.
23. Gerigk M, Gnehm HE, Rascher W. Arginine vasopressin and renin in acutely ill children: implication for fluid therapy. *Acta Paediatr* 1996;85:550–553.
24. Halberthal M, Halperin ML, Bohn D. Lesson of the week: acute hyponatraemia in children admitted to hospital: retrospective analysis of factors contributing to its development and resolution. *BMJ* 2001;322:780–782.
25. Moritz ML, Ayus JC. Prevention of hospital acquired hyponatremia: a case for using isotonic saline in maintenance fluid therapy. *Pediatrics* 2003;111:227–230.
26. Holliday MA, Segar WE, Friedman A. Reducing errors in fluid therapy management. *Pediatrics* 2003;111:424–425.
27. Franz MN, Segar WE. The association of various factors with hypernatremic diarrheal dehydration. *Am J Dis Child* 1972;97:298–302.
28. Moritz ML, Ayus JC. Preventing neurological complications from dysnatremias in children. *Pediatr Nephrol* 2005;20:1687–1700.
29. Holliday MA, Friedman AL, Segar WE et al. Acute hospital-induced hyponatremia in children: a physiologic approach. *J Pediatr* 2004;145:584–587.
30. Horn EJ, Geary D, Robb M et al. Acute hyponatremia related to IV fluid administration in hospitalized children: an observational study. *Pediatrics* 2004;113:1279–1284.
31. Au AK, Ray PE, McBryde KD et al. Incidence of postoperative hyponatremia and complications in crucially ill children treated with hypotonic and normotonic solutions. *J Pediatr* 2008;152:33–38.
32. Neville KA, Verge CF, Rosenberg AR et al. Isotonic is better than hypotonic saline for intravenous rehydration of children with gastroenteritis: a prospective randomized study. *Arch Dis Child* 2006;91:226–232.
33. Choong K, Kho ME, Menon K et al. Hypotonic versus isotonic saline in hospitalized children: a systematic review. *Arch Dis Child* 2006;91:828–835.
34. Way C, Dhamrait R, Wade A et al. Perioperative fluid therapy in children: a survey of current prescribing practices. *Br J Anaesth* 2006;97:371–379.
35. Choi M, Szerlip HM. Sodium and volume homeostasis. In Workshops in Fluid and Electrolyte Disorders. Szerlip HM, Goldfarb S (eds.). New York, Churchill Livingstone, 1993, pp. 1–24.
36. Pasantes-Morales H, Lezama RA, Ramos-Mandujano G et al. Mechanisms of cell volume regulation in hypo-osmolality. *Am J Med* 2006;119:S4–S11.
37. Strange K. Cellular volume homeostasis. *Adv Physiol Educ* 2004;28:155–159.

38. DePetris L, Luchetti A, Emma F. Cell volume regulation and transport mechanisms across the blood-brain barrier: implications for the management of hypernatremic states. *Eur J Pediatr* 2001;160:71–77.
39. Rose BD. Hypoosmolal states – hyponatremia. In Clinical Physiology of Acid–Base and Electrolyte Disorders, 5th edn. New York, McGraw-Hill, 2001, pp. 696–745.
40. Conley SB. Hypernatremia. *Pediatr Clin North Am* 1990;37:365–372.
41. Robertson GL. Physiology of ADH secretion. *Kidney Int* 1987;32: (suppl 21): S20–S26.
42. Yang CW, Kim YS, Park IS, Chang YS, Yoon YS, Bang BK. Treatment of severe acute hypernatremia and renal failure by hemodialysis. *Nephron* 1995;70:372–373.
43. Pazmino PA, Pazmino BP. Treatment of acute hypernatremia with hemodialysis. *Am J Nephrol* 1993;13:260–265.
44. Molteni KH. Initial management of hypernatremic dehydration in the breastfed infant. *Clin Pediatr (Phila)* 1994;33:731–740.
45. Carr M, Gill D. Polyuria, polydipsia, polyposia: "Mummy I want a drink". *Arch Dis Child Educ Pact Ed* 2007;92:ep139–ep143.
46. Robertson GL. Abnormalities of thirst regulation. *Kidney Int* 1984;25:460–469.
47. Holliday MA, Friedman A, Segar WE et al. Avoiding hospital-induced hyponatremia: a physiological approach. *J Pediatr* 2004;145:584–587.
48. Murphy MS. Guidelines for managing acute gastroenteritis based on a systematic review of published research. *Arch Dis Child* 1998;79:279–284.
49. Saavedra JM, Harris GD, Li S, Finberg L. Capillary refilling (skin turgor) in the assessment of dehydration. *Am J Dis Child* 1991;145:296–298.
50. Gorelick MS, Shaw KN, Baker MD. Effects of ambient temperature on capillary refill in children. *Pediatrics* 1993;92:699–702.
51. Baraff LJ. Capillary refill: is it a useful clinical sign? *Pediatrics* 1993;92:723–724.
52. Duggan C, Refat M, Hashem M, Wolff M, Fayad I, Santosham M. How valid are clinical signs of dehydration in infants? *J Pediatr Gastroenterol Nutr* 1996;22:56–61.
53. Mackenzie A, Barnes G, Shann F. Clinical signs of dehydration in children. *Lancet* 1989;2:605–607.
54. Vega RM, Avner JR. A prospective study of the usefulness of clinical and laboratory parameters for predicting percentage of dehydration in children. *Pediatr Emerg Care* 1997;13:179–182.
55. Teach SJ, Yates EW, Feld LG. Laboratory predictors of fluid deficit in acutely dehydrated children. *Clinical Pediatr (Phila)* 1997;36:395–400.
56. Yilmaz K, Karabocuoglu M, Citak A, Uzel N. Evaluation of laboratory tests in dehydrated children with acute gastroenteritis. *J Paediatr Child Health* 2002;38:226–228.
57. Conway SP, Phillips RR, Panday S. Admission to hospital with gastroenteritis. *Arch Dis Child* 1990;65:579–584.
58. Jenkins HR, Ansari BM. Management of gastroenteritis. *Arch Dis Child* 1990;65:939–941.
59. Ellis ME, Watson B, Mandal BK, Dunbar EM, Mokashi A. Contemporary gastroenteritis of infancy: clinical features and prehospital management. *BMJ* 1984;288:521–523.
60. Armon K, Stephenson T, McFaul R, Eccleston P, Werneke U. An evidence and consensus based guideline for acute diarrhoea management. *Arch Dis Child* 2001;85:132–141.
61. American Academy of Pediatrics. Provisional Committee on Quality Improvement Subcommittee on Acute Gastroenteritis. Practice parameter: the management of acute gastroenteritis in young children. *Pediatrics* 1996;97:424–436.
62. US Department of Health and Human Services. The management of acute diarrhea in children: oral rehydration, maintenance, and nutritional therapy. *MMWR Mor Mortal Wkly Rep* 1992;41:1–20.
63. Pierce NF, Sack RB, Mitra R, Banwell JG, Brigham KL, Fedson DS, Mondal A. Replacement of electrolyte and water losses in cholera by an oral glucose-electrolyte solution. *Ann Intern Med* 1969;70:1173–1181.
64. Mahalanbais D, Wallace CK, Kallen RJ, Mandel A, Pierce NF. Water and electrolyte losses due to cholera in small children and infants: a recovery balance study. *Pediatrics* 1970;45:374–385.
65. Pizzaro D, Posada G, Mata L, Nalin D, Mohs E. Oral rehydration of neonates with dehydrating diarrhoea. *Lancet* 1979;2:1209–1210.
66. American Academy of Pediatrics Committee on Nutrition. Use of oral fluid therapy and posttreatment feeding following enteritis in children in a developed country. *Pediatrics* 1985;75:358–361.
67. Santosham M, Greenough WB. Oral rehydration therapy: a global perspective. *J Pediatr* 1991;118:S44–S51.
68. World Health Organization. Treatment and prevention of dehydration in diarrheal disease. A guide for use at the primary level. Geneva: WHO, 1976.
69. World Health Organization. Cholera: can rehydration therapy be improved? *WHO Drug Informtaion* 2000;14:88.
70. Snyder JD. Use and misuse of oral therapy for diarrhea: comparisons of US practices with American Academy of Pediatrics recommendations. *Pediatrics* 1991;87:28–33.
71. Santosham M, Daum RS, Dillman L et al. Oral rehydration therapy of infantile diarrhea: a controlled study of well nourished children hospitalized in the United States and Panama. *N Engl J Med* 1986;306:1070–1076.
72. Finberg L. The role of oral electrolyte-glucose solutions in hydration for children – international and domestic aspects. *Pediatrics* 1980;96:51–54.
73. Nalin DR, Cash RA, Islam R, Molla M, Phillips RA. Oral maintenance therapy for cholera in adults. *Lancet* 1968;2:370–372.
74. Hirschhorn N, Kinzie JL, Sachar D, Northrup RS, Taylor JO, Ahmad SZ, Phillips RA. Decrease in net stool output in cholera during intestinal perfusion with glucose containing solutions. *N Engl J Med* 1968;279:176–181.
75. Phillips RA. Water and electrolyte losses in cholera. *Fed Proc* 1964;23:705–712.
76. Nalin DR, Harland E, Ramlal A, Swaby D, McDonald J, Gangarosa R, Levine M, Akierman A, Antoine M, Mackenzie K, Johnson B. Comparison of low and high sodium and potassium content in oral rehydration solutions. *J Pediatr* 1980;97:848–853.
77. Leung AKC, Taylor PG, Geoffroy L, Darling P. Efficacy and safety of two oral solutions as maintenance therapy for acute diarrhea. *Clinical Pediatrics* 1988;27:359–364.
78. Hahn S, Kim S, Garner P. Reduced osmolarity oral rehydration solution for treating dehydration caused by acute diarrhoea in children. *Cochrane Database Syst Rev* 2002;1:CD002847.
79. Pizarro D, Posada G, Levine MM. Hypernatremic diarrheal dehydration treated with "slow" (12-hour) oral rehydration therapy: a preliminary report. *J Pediatr* 1984;104:316–319.
80. Pizarro D, Posada G, Villavicencio N, Mohs E, Levine MM. Oral rehydration in hypernatremic and hyponatremic diarrheal dehydration. *Am J Dis Child* 1983;137:730–734.
81. Pizarro D, Posada G, Villavicencio N, Mohs E, Levine MM. Oral rehydration in hyper- and hyponatremic diarrheal dehydration. *Am J Dis Child* 1983;137:730–734.
82. Pizarro D, Posada G, Levine MM, Mohs E. Oral rehydration of infants with acute diarrhoeal dehydration: a practical method. *J Trop Med Hyg* 1980;83:241–245.

83. Wittenberg DF, Ramji S. Paediatric diarrhoea – rehydration therapy revisited. *S Afr Med J* 1995;85:655–658.
84. American Academy of Pediatrics. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. *Pediatrics* 2004;114:507.
85. King CK, Glass R, Bressee JS et al. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. *MMWR Recomm Rep* 2003;52(No. RR-16):1–16.
86. Avery ME, Snyder JD. Oral therapy for acute diarrhea: the underused simple solution. *N Engl J Med* 1990;323:891–894.
87. Tanzi VL. An econometric study of the adoption of oral rehydration solution in Bangladesh. *Dissertation Abstracts International* 1999;60:1563.
88. Chowdhury AM, Karim F, Sarkar SK, Cash RA, Bhuiya A. The status of ORT (oral rehydration therapy) in Bangladesh: how widely is it used? *Health Policy Plan* 1997;12:58–66.
89. Bender BJ, Ozuah PO, Crain EF. Oral rehydration therapy: is anyone drinking? *Pediatr Emerg Care* 2007;23:624–626.
90. Gavin N, Merrick N, Davidson B. Efficacy of glucose-based oral rehydration therapy. *Pediatrics* 1996;98:45–51.
91. Santucci KA, Anderson AC, Lewander WJ, Linakis JG. Frozen oral hydration as an alternative to conventional enteral fluids. *Arch Pediatr Adolesc Med* 1998;152:142–146.
92. Ladinsky M, Duggan A, Santosham M, Wilson M. The World Helath Organization oral rehydration solution in US pediatric practice: a randomized trial to evaluate parent satisfaction. *Arch Pediatr Adolesc Med* 2000;154:700–705.
93. Provisional Committee on Quality Improvement. Subcommittee on Acute Gastroenteritis. Practice parameter: the management of acute gastroenteritis in young children. *Pediatrics* 1996;97:424–436.
94. Rabbani GH. The search for a better oral rehydration solution for cholera. *N Engl J Med* 2000;342:345–347.
95. Fontaine O, Gore SM, Pierce NF. Rice-based oral rehydration solution for treating diarrhoea. *Cochrane Database Syst Rev* 2000;2:CD000567.
96. International Study Group on Reduced-Osmolarity ORS Solutions. Multicentre evaluation of reduced-osmolarity oral rehydration salts solution. *Lancet* 1995;345:282–285.
97. Hahn S, Kim Y, Garner P. Reduced osmolarity oral rehydration solution for treating dehydration due to diarrhoea in children: systematic review. *BMJ* 2001;323:81–85.
98. Brierley J, Carcillo J, Choong K et al. Clinical practice parameter for hemodynamic support of pediatric and neonatal shock: 2007 update from the American College of Critical Care Medicine. *Crit Care Med* 2009;37:666–688.
99. Chappell D, Jacob M, Hoffman-Kiefer K et al. A rational approach to perioperative fluid management. *Anesthesiology* 2008;109:723–740.
100. Awazu M, Devarajan P, Stewart CL, Kaskel F, Ichikawa I. "Maintenance" therapy and treatment of dehydration and overhydration. In Pediatric Textbook of Fluids and Electrolytes. Baltimore, Williams and Wilkins, 1990, pp. 417–428.
101. Tullis JL. Albumin. 2. Guidelines for clinical uses. *JAMA* 1977;237: 460–463.
102. Alderson P, Schierhout G, Roberts I, Bunn F. Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database Syst Rev* 2000;2:CD000567.
103. Bisonni RS, Holtgrave DR, Lawler F, Marley DS. Colloid versus crystalloids in fluid resuscitation: an analysis of randomized controlled trials. *J Fam Pract* 1991;32:387–390.
104. The Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients. *Cochrane Database Syst Rev* 2000(2):CD001208.
105. Soni N. Wonderful albumin? *BMJ* 1995;310:887–888.
106. Fleck A, Raines G, Hawker F, Trotter J, Wallace P, Ledingham I, Calman KC. Increased vascular permeability: a major cause of hypoalbuminaemia in disease and injury. *Lancet* 1985;1:781–784.
107. Nichani S. Albumin: saint or sinner? *Arch Dis Child* 1999;81:189.
108. Carcillo JA, Fields AI. American College of Critical Care Medicine Task Force Committee Members. Clinical practice parameters for hemodynamic support of pediatric and neonatal patients in septic shock. *Crit Care Med* 2002;30:1365–1378.
109. Soderlind M, Salvignol G, Izard P, Lonnqvist PA. Use of albumin, blood transfusion and intraoperative glucose by APA and ADARPEF members: a postal study. *Paediatr Anaesth* 2001;11: 685–689.
110. Hirschhorn N. The treatment of acute diarrhea in children: an historical and physiological perspective. *Am J Clin Nutr* 1980; 33:637–663.
111. Skellett S, Mayer A, Durward A, Tibby SM, Murdoch IA. Chasing the base deficit: hyperchloraemic acidosis following 0.9% saline fluid resuscitation. *Arch Dis Child* 2000;83:514–516.
112. Neville KA, Verge CF, Rosenberg AR et al. Is hyperchloraemic acidosis a problem in children with gastroenteritis rehydrated with normal saline? Authors' reply. *Arch Dis Child* 2007;92:466.
113. Durward A, Tibby SM, Skellett S et al. The strong ion gap predicts mortality in children following cardiopulmonary bypass surgery. *Pediatr Crit Care Med* 2005;6:281–285.
114. Reid SR, Bonadio WA. Outpatient rapid intravenous rehydration to correct dehydration and resolve vomiting in children with acute gastroenteritis. *Ann Emerg Med* 1996;28:318–323.
115. Holliday MA, Friedman AL, Wassner SJ. Extracellular fluid restoration in dehydration: a critique of rapid versus slow. *Pediatr Nephrol* 1999;13:292–297.
116. Oh MS, Kim H-J, Carroll HJ. Recommendations for treatment of symptomatic hyponatremia. *Nephron* 1995;70:143–150.
117. Pradhan S, Jha R, Singh MN, Gupta S, Phadke RV, Kher V. Central pontine myelinolysis following 'slow' correction of hyponatremia. *Clin Neurol and Neurosurg* 1995;97:340–343.
118. Faber MD, Kupin WL, Heilig CW, Narins RG. Common fluid-electrolyte and acid-base problems in the intensive care unit: selected issues. *Semin Nephrol* 1994;14:8–22.
119. Mehta RL. Fluid balance and acute kidney injury: The missing link for predicting adverse outcomes. *Nat Clin Prac Nephrol* 2009;5: 10–11.
120. Miller NI, Finberg L. Peritoneal dialysis for salt poisoning. *N Engl J Med* 1960;263:1347–1350.
121. Finberg L, Kiley J, Luttrell CN. Mass accidental salt poisoning in infancy. *JAMA* 1963;184:187–190.
122. El-Dahr S, Goez RA, Campbell FG et al. Rapid correction of acute salt poisoning by peritoneal dialysis. *Pediatr Nephrol* 1987;1: 602–604.