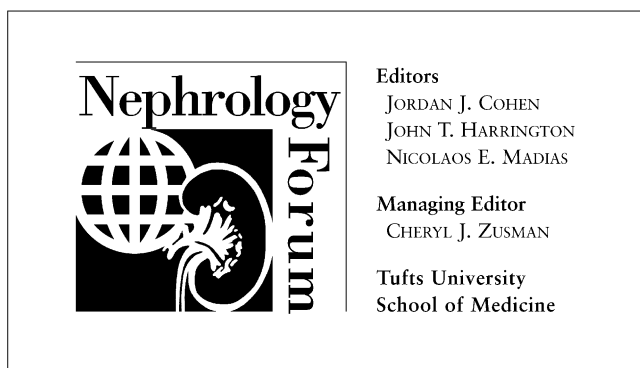


Pediatric hydration therapy: Historical review and a new approach

Principal discussant: AARON L. FRIEDMAN

Brown Medical School, and Hasbro Children's Hospital, Providence, Rhode Island



blood pressure, 90/64 mm Hg while seated; heart rate, 120 beats/min; and respiratory rate, 24 breaths/min. His skin was warm without rashes or edema. The head, ears, eyes, nose, and throat revealed a somewhat dry oral mucosa but no other abnormal findings. His neck was supple without significant lymphadenopathy or thyromegaly. Chest examination revealed normal lung sounds with no murmur. The abdomen was slightly distended and tympanic with active bowel sounds and no organomegaly or masses. There was no costovertebral angle tenderness. The patient had very slight peri-anal redness; the rest of the genitourinary exam was normal. His joints were not red, full, or tender, and he had full range of motion of his arms and legs.

Urinalysis revealed a specific gravity of 1.020; 1+ protein, and negative for blood, bilirubin, glucose, leukocyte esterase, and nitrate; trace ketones; 1 to 2 white blood cells/high-power field, and 1 granular cast. Blood studies disclosed: sodium, 128 mEq/L; potassium, 3.6 mEq/L; chloride, 98 mEq/L; bicarbonate, 18 mmol/L; serum creatinine, 0.7 mg/dL; and blood urea nitrogen, 26 mg/dL.

The parents were concerned because the child continued to vomit.

DISCUSSION

DR. AARON L. FRIEDMAN (*Sylvia Kay Hassenfeld Professor and Chairman, Department of Pediatrics, Brown Medical School and Hasbro Children's Hospital, Providence, Rhode Island*): This clinical scenario, common in pediatrics, reflects a typical problem in fluid and electrolyte management. Why should this become the subject of a Nephrology Forum? Isn't this issue well understood not only by nephrologists but by a large percentage of other clinicians? Is there anything new in the arena of the management of fluid and electrolyte disorders? The following discussion not only addresses these questions but also looks at the physiology that underlies our understanding of fluid and electrolyte disorders, especially those associated with abnormalities of body fluid compartments as manifested by physical findings and abnormal extracellular electrolyte concentrations.

CASE PRESENTATION

A 4-year-old boy weighing 15 kg presented with a 3-day history of vomiting, decreased appetite, and 2 days of non-bloody diarrhea. He was "warm to the touch" according to the parents, but no direct measurement of temperature was taken. An older sibling had had a similar illness 5 days prior to the onset of vomiting by the patient.

For the previous 2 days, the patient had ingested only water, apple juice, and non-cola soft drinks. The parents believed that his urine output had dropped but only in the previous 12 hours. The patient's past medical history and review of systems were unremarkable. He took no medications on a chronic basis, although acetaminophen in appropriate doses was used by the family "when the child felt warm" (2–3 times/day).

On physical examination, he was mildly irritable and appeared somewhat uncomfortable while sitting quietly on his parent's lap. The oral temperature was 38.2°C;

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In the preface to his remarkable book, *The Kidney: Structure and Function in Health and Disease* [1], Homer Smith quotes Claude/Bernard (1878): “Higher animals have really two environments: a milieu exterieur in which the organism is situated, and a milieu interieur in which the tissue elements live. The living organism does not really exist in the milieu exterieur (the atmosphere if it breathes, salt or fresh water if that is its element) but in the liquid which surrounds and bathes all the tissue elements. . . the milieu interieur surrounding the organs, the tissues and their elements never varies; atmospheric changes cannot penetrate beyond it and it is therefore true to say that the physical conditions of the environment are unchanging in the higher animal. . . . Here we have an organism which has enclosed itself in a kind of hothouse. . . . *All the vital mechanisms, however varied they may be, have only one object, that of preserving constant the conditions of life in the internal environment.*”

Smith’s footnote on this paragraph ends with, “His concept of the constancy of the internal environment was, however, perhaps his greatest contribution.” Haldane has said, “No more pregnant sentence was ever formed by a physiologist.” Fluid and electrolyte management is a quintessential example of “preserving constant the conditions of life,” in other words, homeostasis.

Our understanding of body fluid physiology clearly has advanced since Bernard’s description, although his picture of the fluid that surrounds cells—“a kind of hothouse”—is a wonderfully vivid picture. What is our present understanding of body fluid compartments, how has it evolved, and how does this understanding inform fluid and electrolyte management?

Historical review

In 1878, Bernard had little data upon which to make his statement about the internal milieu of higher organisms. In the early 20th century, physiologists began to construct a more complete picture of body fluid compartments. Gamble et al embarked on studies in 1914 that culminated in a seminal manuscript published in 1928 [2]. They introduced the concept of extracellular fluid (ECF), and carefully described the electrolyte composition of extracellular space. They derived this basic description while studying the influence of fasting (used to treat seizures) on acid-base status in children. That study plus later studies by Gamble and Ross [3] described the renal response to ECF depletion. The kidney’s ability to respond seemed “designed” to minimize ECF loss because severe ECF reduction is life threatening. These studies formed the foundation of body fluid physiology and our therapeutic approach to maintaining body fluid homeostasis.

In the 1940s, Gamble described extracellular fluid as an “enclosed sea” [4]. The total volume of ECF in adults was measured using the volume of distribution of inulin

after a 2-hour intravenous infusion at approximately 150 to 160 mL/kg [including plasma volume (PV) and interstitial fluid (ISF)] [5]. Since then, our view of ECF has undergone further refinement. First, more recent measurements of ECF using 6-hour chloride equilibration techniques found that earlier measurements did not fully account for ISF in skin and connective tissue. This changed the total recognized volume of ECF to approximately 270 mL/kg in adults [6] and 300 mL/kg in children [7]. Second, ECF obviously is not really a “sea” but, to a large degree, a gel. The ISF of muscle and other organs is a complex collagen matrix that provides structure to the ISF, limiting the effect of gravity. It imposes structural integrity on intercellular and intercapillary space, allowing for nutrient delivery to cells and removal of the end products of metabolism [8]. In skin and connective tissue, a somewhat different but equally important collagen-proteoglycan gel comprises the ISF. This gel is especially important in structure and function of connective tissue and bone [9]. This gel backbone slows the exchange of fluid between the plasma and interstitial space and limits the “collapse” of the interstitial space when dehydration occurs.

The complex interaction of the fluid exchange between plasma and the interstitium involves hydrostatic and interstitial pressures (Starling forces); filtration coefficients, size and charge of proteins and other solutes; and gravity and lymphatic flow, to name a few. Discussion of this complex association is beyond the scope of this report but is reviewed elsewhere [7, 10–12]. Essential to a discussion of fluid therapy is an understanding that ISF serves as a reservoir and that in episodes of dehydration ISF is transferred to the plasma, offsetting the loss of fluid from the plasma volume.

The infusion of fluids to more rapidly restore fluids in patients with diarrhea and dehydration did not wait for an understanding of body fluid physiology and body fluid compartments. The first reported case of the use of fluid therapy appeared in the *Lancet* in 1832 [13]. Latta reported using a solution of salt, sodium bicarbonate, and water to replace diarrheal losses in a cholera patient. This technique was not incorporated into practice until 60 to 70 years later, however, when sterile distilled water and improved equipment made the infusion of fluids safer. In 1918, Blackfan and Maxcy reported using intraperitoneal injections of saline to treat dehydration from diarrheal illnesses [14]. In 1931, Karelitz and Schick used continuous intravenous drips to treat dehydration [15]. The success of these techniques in children was quite impressive given the difficulty at that time with infusion techniques. Concepts regarding body fluid compartments and body fluid physiology were still in their formative years.

Our modern-day view of intravenous fluid therapy and oral rehydration therapy (ORT) is based on our understanding of fluid compartments. The definition and

quantitative understanding of ECF as described by Gamble was an important milestone. In 1960, Darrow, a major contributor to our understanding of body fluid physiology and its correction during dehydration, described Gamble's work on ECF as his greatest contribution and one that forms the basis for modern fluid therapy [16].

Darrow contributed significantly to our understanding of body fluid physiology and what it took to repair alterations in body fluids. His concept of "deficit therapy" as part of fluid therapy has been an important fixture in most prescriptions of fluid therapy. Deficit therapy is a method of replacing *previous* losses from the extracellular and intracellular fluid spaces. It is a slow form of fluid replacement therapy calculated over several hours or even days, depending on the severity of the dehydration and severity of the electrolyte derangements. Experiments performed in the 1930s demonstrated a redistribution of total body water following a change in ECF volume as well as changes in ECF electrolyte composition. Using a clever experimental technique, Darrow and Yannet demonstrated that a change in ECF electrolyte levels, specifically hyponatremia and the resultant hypotonicity, produced a loss in both ECF and intracellular fluid (ICF). Therefore, correction of the full electrolyte loss of salt and water depletion requires replenishment of the ICF component of total body water as well as the ECF. Restoration of ECF alone, although helpful, would not suffice. These findings introduced the concept of deficit therapy [17, 18].

Darrow et al added two other important concepts to fluid therapy. The first was tying the "maintenance" allowance of water in a 24-hour period to metabolic rate rather than body weight. Maintenance therapy is the provision of fluid and electrolytes to replace anticipated losses from breathing, sweating, and urine output. It is usually calculated to replace the *upcoming* 24 hours of water and electrolyte losses. This concept became the basis for maintenance fluid requirements termed the "Holliday-Segar method," a guide for 24-hour total water requirements for children [19]. Darrow's second important contribution was recognizing the importance of potassium deficiency in dehydration, especially diarrheal dehydration, and noting that potassium deficiency was a significant component of metabolic alkalosis often associated with extracellular volume contraction [20].

The importance of potassium deficiency logically led to another critical change in fluid therapy: the addition of potassium to parenteral fluid therapy regimens. Darrow et al recognized that potassium loss was indeed part of the dehydration of diarrhea, then a common cause of dehydration and death [21, 22]. The addition of potassium in parenteral fluid significantly improved survival rates in children with diarrheal dehydration. Darrow et al understood that parenteral fluid therapy with potassium needed to be given slowly to avoid the risk of hy-

Table 1. Twenty-four-hour maintenance water requirement in children

Holliday-Segar	
≤10 kg	100 mL/kg/24 hr
11–20 kg	1000 mL + 50 mL/kg/24 hr for each kg from 11–20
>20 kg	1500 mL + 20 mL/kg/24 hr for each kg >20
Simplified method (based on Holliday-Segar)	
<10 kg	4 mL/kg/hr
11–20 kg	40 + 2 mL/kg/hr for each kg between 11–20
	60 + 1 mL/kg/hr for each kg >20
Body surface area method	
	1500 mL/m ² /24 hr
	$BSA \sqrt{\frac{wt(kg) \times (ht)cm}{3600}}$
Adult estimate	
	2–3 L/24 hrs

perkalemia [23]. Thus, deficit therapy became a slower form of fluid replacement therapy designed to expand extracellular fluid and to replace sodium and potassium losses.

Maintenance therapy and deficit therapy

The net result of more than half a century of clinical studies is a formulaic view of fluid and electrolyte therapy. Physicians now understand the concepts of maintenance therapy and deficit (rehydration) therapy. Maintenance therapy (for upcoming losses) and deficit therapy (for previous losses) are calculated as part of overall fluid therapy. We define maintenance therapy as the fluid and electrolyte requirements needed by the average individual with normal ICF/ECF volumes over a 24-hour period. Intravenous fluids are generally used when a patient is unable to take oral fluids for 24 to 48 hours or more. In children, especially in premature babies, infants, and young children, the inability to ingest fluids for even 8 to 12 hours can be sufficient to require intravenous maintenance fluids. An examination of a number of commonly used resources points to three methods for determining maintenance water requirements in children: the Holliday-Segar formula, a simplified Holliday-Segar formula, and a formula based on body surface area for children more than 10 kg [24–27] (Table 1).

Maintenance electrolyte requirements in children are generally considered 3 mEq of sodium, 2 mEq of chloride, and 2 mEq of potassium for every 100 mL of maintenance IV fluid. Meeting these requirements is most easily accomplished by using a solution that contains a small amount of carbohydrate, 5% dextrose, plus 0.25 normal saline plus 20 mEq/L of potassium chloride. Interestingly, in adult patients, the most commonly suggested maintenance solution is 5% dextrose, plus 0.45 normal saline

plus 20 to 30 mEq/L of potassium chloride [26, 27]. The precise reason for the higher sodium content in adults is unclear, although some references allude to the greater risk of hyponatremia in the elderly. One common mistake in the pediatric age group is providing electrolytes on a per kilogram basis as opposed to per 100 mL of maintenance IV fluid.

I offer this seemingly elementary, but often neglected, material here for two reasons. First, maintenance fluid should be viewed as no more than the usual water and electrolyte requirements for the next 24 hours in an otherwise normal individual. It takes into account average water and electrolyte losses in urine and feces (sensible losses) and insensible losses (water lost in evaporation across the skin and in expired air) as well. But one must keep in mind exceptions to maintenance requirements. Fluid requirements increase in patients with high solute loads, such as glucosuria and diabetic ketoacidosis, or severe catabolism with high protein losses, such as burns or crush injuries. Other examples include uncontrolled diabetes insipidus with very high urinary losses of water and increased insensible losses from fever or an increased respiratory rate. Decreased free water requirements result from excessive antidiuretic hormone (ADH) secretion, which leads to a concentrated urine (for example, SIADH). Excess ADH secretion can result from postoperative stress, persistent nausea, coma, head injury, and positive pressure ventilation, to name just a few underlying stimuli. Oliguria, as a result of renal insufficiency, also can reduce maintenance requirements, and situations of decreased insensible loss, such as ventilator use with fully humidified air, will lower maintenance fluid requirements. Second, in hospitalized patients, as a means of increasing urine output, the total fluid intake often is calculated as a multiple of maintenance fluid requirements. For example, certain oncology protocols specify that a patient receive 1 1/2 or 2 times maintenance fluid as a way of assuring high fluid intake and high urine volumes. While simple, this use of the term "maintenance" is inappropriate. Complicated patients on protocols often have other medical problems that call for a different electrolyte solution; indeed, if one wants to maintain a diuresis, abundant evidence indicates that water alone and/or solutions such as normal saline are better choices.

I must comment on a recent report analyzing maintenance fluid therapy. Moritz and Ayus cite articles in which hyponatremia in hospitalized patients has caused brain damage or even death [28]. Most of the patients were admitted for acute medical or surgical illnesses, diarrheal dehydration, or even elective surgery [29, 30]. These authors conclude that hypotonic maintenance therapy is responsible for these episodes of hyponatremia, and state that therefore fluid therapy for hospitalized children should comprise isotonic saline.

This approach is problematic. Most reports of hyponatremia as a result of fluid therapy have involved specific situations in which maintenance therapy was applied erroneously [31]. In some cases, maintenance therapy was estimated or was indexed to body weight and not metabolic rate; thus, too much electrolyte-free water was provided to the patient. In others, maintenance therapy was used as a deficit therapy for which it was not designed. In some instances, the average maintenance therapy prescribed for the patient was inappropriate because the patient had reduced urine output due to stress-induced diuresis, which limited electrolyte-free water excretion. In these situations, the more appropriate response is to calculate maintenance therapy (Table 1) and to provide such a therapy only for maintenance and not for repair of deficits. Finally, in instances in which a reduction in electrolyte-free water excretion can be anticipated, such as stress (surgery and postoperative care), nausea and vomiting, the use of certain medications, or head injury, average maintenance therapy should be reduced to one half to two thirds of that calculated for the patient.

For one specific type of patient, the use of isotonic saline as an intravenous solution does have some validity. Patients undergoing elective surgery can have an intravenous catheter placed prior to surgery that can be infused with isotonic saline at a "keep open" rate so that fluid can be administered to replace fluids lost during surgery. During surgery, isotonic saline or lactated Ringer's solution can be used to maintain perfusion or to replace blood or fluid losses; an intravenous catheter also ensures access for drug administration. After surgery, if fluid therapy is needed, isotonic saline or lactated Ringer's solution should be provided at one-half the average maintenance because of anticipated stress-induced antidiuresis. Clearly, episodes of hyponatremia induced by inappropriate fluid therapy have and will make their way into the literature. However, administration of high volumes of isotonic solution that results in peripheral edema, heart failure, or hypertension are not likely to appear in the literature but could very easily result from the recommendation of using isotonic fluids or maintenance therapy.

Rapid rehydration therapy: A new approach

In dehydrated (volume-depleted) patients, certain basic tenets apply regarding management. First, one must estimate the degree of dehydration to be able to determine the prescription for rehydration, including amount of fluid, type of electrolyte solution, and mode of administration. In children, clinical signs have been adopted as a standard method for determining degree of dehydration (percentage of body weight lost) (Table 2).

The majority of dehydrated patients whom physicians see have suffered acute fluid loss from an illness that

Table 2. Clinical signs of dehydration

	Mild	Moderate	Severe
Weight	1% to 5% 1–5% decrease	6% to 9% 6–9% decrease	10% to 15% 10%–15% decrease
Skin: turgor	Normal	Tenting	None
Skin: touch	Normal	Dry	Clammy
Buccal mucosa: lips	Moist	Dry	Parched
Buccal mucosa: eyes	Normal	Intermediate	Sunken
Pulse	Regular	Increased	Very rapid
Urine output	Normal	Reduced	Oliguria
Babies			
Fontanelle	Flat	Soft	Sunken
Aspect	Consolable	Irritable	Lethargic

generally has lasted less than one week. This is important because most of the fluid lost by that patient comes from the ECF. Estimates made by Gamble [32] suggest that fluid losses occurring in fewer than 3 days are between 75% to 100% from the ECF; between 3 to 7 days, the figure is probably closer to 60% to 75% from ECF. Fluid losses for longer than 7 days are a combination of ECF (50%) and ICF (50%).

The importance of rapid ECF replacement was nicely demonstrated by Holliday et al in their examination of the literature about three forms of shock—burns, hemorrhagic shock, and septic shock [33]. In shock, the ECF, especially ISF, moves into the injured area in the case of a burn, into the circulation in the case of hemorrhagic shock, or as a maldistribution of extracellular and plasma fluid in the case of septic shock. In each instance, patients improve and mortality rates decline in the presence of a rapid, generous expansion of the ECF so that both plasma and ISF volumes are expanded. Often, the total fluid amount given in the first 6 to 12 hours approximates 100 mL/kg of an ECF-type fluid, such as normal saline or lactated Ringer's solution. The major take-home lesson is the benefit of rapid restoration in ECF volume.

Can the lessons learned from rapid ECF replacement in shock be useful in more common dehydration conditions? I believe that the answer is yes. As early as the 1970s, Hirschhorn et al demonstrated success using a more rapid ECF restoration regimen than that used following Darrow's deficit approach [34]. The report documents the use of ORT for children with diarrheal dehydration. The arguments for more rapid ECF rehydration regimen were (1) improved gastrointestinal perfusion, allowing earlier oral feeding; (2) improved renal perfusion, allowing more rapid correction of sodium, potassium, and acid-base abnormalities, often without special measures for achieving these corrections; and (3) an excellent recovery rate with a low morbidity and mortality rate [30]. The volumes provided to accomplish this type of rehydration were equivalent to 100 to 120 mL/kg of normal

saline in the first 24 hours. This time period needed with oral replacement is longer than that with intravenous replacement.

The American Academy of Pediatrics (AAP), in a subcommittee report on acute gastroenteritis, reviewed the management of diarrhea and offered recommendations for its therapy in 1996 [36]. The committee defined dehydration as shown in Table 2, recommended that only infants with moderate (6% to 9%) or severe (greater than 10%) dehydration should have serum chemistries determined, and recommended the initial use of intravenous rehydration in patients with severe dehydration. In the description of intravenous rehydration, they noted that, "a common recommendation is to give 20 mL/kg (of normal saline or lactated Ringer's solution) during a 1-hour period. However, larger quantities and much shorter periods of administration may be required (to achieve rehydration)." They further defined rehydration as (1) restoration of skin turgor and weight; (2) recovery of alertness; (3) tolerance to oral intake of formula; and (4) correction of serum chemistries.

As I discussed, the important message from the treatment of shock is that rapid ECF volume replenishment improves patient outcomes [37–40]. This along with work by Hirschhorn [34] and the AAP management recommendation for dehydration [36] provides convincing evidence for rapid extracellular volume restoration that cannot be obtained by the usual deficit therapy. I suggest a revised approach to the therapy of rehydration—here termed "rapid rehydration therapy." This approach is consistent with recommendations already promulgated [36] and takes into account the advantages of rapid ECF volume restoration noted earlier. (1) In patients with mild dehydration, oral rehydration therapy (up to 50 mL/kg over 12 to 24 hours) alone should be sufficient. (2) In patients with moderate dehydration, oral rehydration therapy (25 to 50 mL/kg over 6 to 12 hours) should be sufficient. However, if intravenous rehydration is utilized, ECF should be rapidly restored by administering lactated Ringer's solution at 40 mL/kg in 1 to 2 hours, with the initiation of ORT after completion of the intravenous infusion. (3) In patients with severe dehydration, weight loss of 10% or greater, impaired circulation (as measured by rapid pulse and a reduced capillary fill time), and evidence of ISF fluid loss (including loss of skin turgor and sunken eyes), ECF should be rapidly restored via administration of intravenous lactated Ringer's solution and/or normal saline at 40 mL/kg over 1 to 2 hours; if skin turgor, alertness, or pulse do not return to normal by the end of the infusion, one should infuse an additional bolus of 20 to 40 mL/kg over 1 to 2 hours. ORT then can be initiated as soon as oral intake is tolerated. Oral rehydration solutions with lower sodium concentrations (45–60 mEq/L) are appropriate for patients with mild to moderate dehydration, but higher sodium concentrations

Table 3. Fluid replacement therapy

Moderate dehydration ~7% (70 mL/kg)			
Wt (15 kg)	Water mL	Na ⁺ mEq	K ⁺ mEq
Maintenance (Holliday-Segar)	1250	37	25
Deficit (1000) (Darrow)			
ECF 75%	700	114	
ICF 25%	250		37
Additional Na ⁺ ^a		63	
Total	2250	214	62

D₅ 0.45 NS + 30 mEq KCl/L at 100 mL/hr for 24 hours.

^aAdditional Na⁺ (135–128) × 15 (body weight in kg) × 0.6 (total body water = 60% of body weight) = 63.

(75–90 mEq/L) are best suited for patients with severe dehydration and/or persistent diarrhea [33].

Let's return to today's patient. This little boy has moderate dehydration as defined in Table 2. Routine fluid replacement therapy for the first 24 hours would accomplish the desired effect of providing the patient with both maintenance and deficit (rehydration) fluid, although completion of rehydration would take most of the first 24-hour period (Table 3).

Maintenance following the Holliday-Segar method for a 15 kg child equals 1250 mL of water (1000 mL for the first 10 kg plus 50 mL/kg for the next 5 = 1250 mL). Maintenance sodium is 3 mEq/100 mL fluid = 37 mEq of sodium; maintenance potassium is 2 mEq/100 mL fluid = 25 mEq of potassium. In addition, standard deficit therapy would require 1 L of fluid (7% of 15 kg) with 75% calculated as ECF replacement (given the length of time of illness). Therefore, 750 mL of NS that would provide 114 mEq of sodium (0.75 × 154 mEq of sodium) is recommended. Twenty-five percent is calculated as ICF replacement; ICF contains approximately 150 mEq of potassium per liter, so 250 mL would require approximately 37 mEq of potassium. Finally, the patient's serum sodium is 128 mEq/L. To bring a 15 kg child with a serum sodium of 128 to a serum sodium in the normal range—135 mEq/L—would require an additional 63 mEq (see Table 3 for calculation). In total, fluids required for maintenance plus deficit therapy can be obtained by a solution that approximates 0.45 normal saline (NS) with 30 mEq/L of potassium. In 24 hours, 2250 mL of solution would be needed; therefore, an infusion rate near 100 mL/hr would provide maintenance plus deficit for this patient.

If intravenous therapy were used, the first step would be to provide the patient with 40 mL/kg of NS or lactated Ringer's (LR) solution as rapidly as possible (for example, over 1 to 2 h). Based on a weight of 15 kg (15 × 40 mL), this patient would require 600 mL of water, approximately 78 mEq LR, and 92 mEq of sodium using NS. We'd then give him ORT, and his feedings would begin as quickly as tolerated; 600 mL of an "ECF-like solution" would rapidly restore nearly all the extracellular fluid losses. The rest of the rehydration of ECF as well as ICF,

Table 4. "Revised rehydration therapy"

Stepwise approach	
Moderate dehydration ~7% (70 mL/kg), 15 kg patient	
1.	IV + oral route
	a. IV: 40 mL/kg normal saline (NS) or lactated Ringer's (LR) over 1–2 hours = 600 mL
	b. ORT
2.	Oral rehydration therapy (ORT)—WHO formula (≥60 mEq NaCl/L) IV + oral route
3.	IV only
	a. 40 mL/kg NS or LR over 1–2 hours
	b. Additional bolus 10–20 mL/kg NS or LR to normalize cardiovascular signs, if needed
	c. Start maintenance fluids as in Table 3 over 24 hours. Replace additional sodium and potassium if needed as in Table 3.

along with the provision of potassium, would be accomplished more slowly by the oral rehydration fluid. Finally, if for some reason deficit (rehydration) and maintenance therapy needed to be provided intravenously only, we first would give 40 mL/kg of NS or LR over 1 to 2 hours. Thus, nearly all the calculated ECF loss would be replaced. If the patient still appeared to need further IV replacement (for example, if he were tachycardic), we then would administer an additional 10 to 20 mL/kg bolus of NS or LR over 1 to 2 hours to complete extracellular fluid volume replacement. Over the next 16 to 24 hours, maintenance fluids (Holliday-Segar method), perhaps with additional sodium and potassium replacement, would be used.

Let me summarize. Extracellular fluid volume restoration plays a major, if not predominant, role in the therapy of most patients with dehydration. What I have termed "rapid rehydration therapy" aims at a rapid restoration of ECF (followed by maintenance therapy) and is both safe and effective for the overwhelming majority of patients. It is now time for us to refine our understanding of the treatment of dehydration and to recognize that "rapid rehydration therapy," as opposed to "deficit therapy," is the more appropriate treatment for children with dehydration.

QUESTIONS AND ANSWERS

DR. TODD VARNES (*Department of Pediatrics, University of Wisconsin Children's Hospital, Madison, Wisconsin*): When we prescribe intravenous fluid, on occasion we also suggest using additional fluids to replace a portion of ongoing daily losses. But that seems akin to the deficit approach: we're putting back what we think the patient will lose. How should we best handle the issue of ongoing daily losses?

DR. FRIEDMAN: The point you're raising is a third component to fluid therapy. What we've talked about is maintenance therapy and replacement of deficits, that is, replacing what was lost. However, when you anticipate ongoing losses such as continued diarrheal losses, what

do you do about the ongoing losses? When a predictable amount is going to be lost during a 24-hour period, you should build that into the patient's fluid therapy. It's not replacing a previous loss, and it's not providing maintenance fluids; rather it's simply keeping up with an ongoing loss, which makes sense.

DR. BRANDON NATHAN (*Department of Pediatrics, University of Wisconsin Children's Hospital*): My question relates to hyponatremic dehydration. Is there a level at which we need to be conservative about rehydration therapy? How low can the serum sodium concentration fall before one has to be more concerned about providing a more aggressive rehydration approach with isotonic fluids, as you suggested? Considering the potential risks of central pontine myelinolysis (CPM), can one continue using normal saline or Ringer's lactate?

DR. FRIEDMAN: I'm glad you asked that. The literature reveals that clinicians fear that changing the sodium concentration too rapidly in either direction is a risk. If the patient has hypernatremic dehydration, lowering the serum sodium level too rapidly can induce cerebral edema; and in hyponatremia, if you raise the serum sodium level too rapidly or increase the osmolality too fast, you run the risk of causing CPM. It's an interesting discussion; CPM is a very uncommon result in children, and it appears to be an issue that involves the adult brain more than the child's brain [33]. Presumably the risk is there in children; however, children at risk usually are patients with long-standing illness in whom hypotonicity, not volume depletion, is the issue. CPM does not result from the restoration of extracellular volume from low to normal.

DR. JOHN T. HARRINGTON (*Dean Emeritus, Tufts-New England Medical Center, Boston, Massachusetts*): Let me add a comment regarding volume status in patients with CPM. A lot of work done over the past 15 to 20 years showed that adult patients who have rapid correction of severe hyponatremia develop CPM. Most of these patients have been hypotonically volume expanded, not depleted. In most patients who are hypotonic and volume depleted, restoration of ECF volume corrects the hyponatremia by inhibiting secretion of antidiuretic hormone. Electrolyte-free water is excreted in the urine, and serum sodium concentration returns to normal. These volume-depleted patients are not the problem; the problem is non-volume-depleted patients who are hyponatremic. When hyponatremia is rapidly corrected in that setting, given the changes in cerebral osmolality 2 to 3 days later, one can produce CPM.

DR. ROBERT BENJAMIN (*Department of Pediatrics, University of Wisconsin Children's Hospital*): In the emergency room, the topic of oral rehydration therapy comes up time and again. We recommend Pedialyte[®], even though this solution might not be as effective as the World Health Organization (WHO) formula, which contains 60 to 90 mEq/L of sodium. Can you suggest other solutions

or tell us where we might find other information that we can share with our patients? The other problem besides choosing an appropriate rehydration solution is ensuring that the patient does not vomit. Even when patients are <10% dehydrated, we have the problem of treating a dehydrated-looking 13-month-old who has no visible vasculature, but we are forced to administer fluid intravenously nonetheless, because the child continues to vomit.

DR. FRIEDMAN: That's the most common feature of many patients who have gastroenteritis with diarrhea and continued vomiting. This problem has been examined around the world because cholera is not the only thing that results in diarrheal dehydration. Frequent feeding of small volumes does result in children being rehydrated. The attempt to get many ounces of fluid into a patient in one sitting doesn't work. Small, frequent amounts work best, and it's labor intensive. You can set an IV at a certain rate and walk away and the patient will receive fluids. Oral rehydration does keep people out of the hospital, it does rehydrate them, and it's quite effective. I think the reason Pedialyte[®] works most of the time is that for mild to moderate dehydration, even a solution containing 40 to 45 mEq/L of a sodium solution will be sufficient. It's only when the patient is more severely dehydrated and has a rapid pulse and changing blood pressure that oral rehydration might not be fast enough. That is the time when I think utilization of rapid rehydration provided intravenously (rapid rehydration) approach, followed by oral rehydration is sensible. Hirschhorn makes an important point: reperfusion of the gut and reperfusion of the kidney make a difference to how much one can consume orally [34]. Dr. Tuffli, you might want to comment.

DR. GORDON TUFFLI: To optimize electrolyte absorption from the gut, you need equimolar amounts of glucose. Pedialyte[®] doesn't provide equimolar amounts of glucose and sodium. The WHO rehydration packets are equimolar, but they are not readily available at drug stores or pharmacies. Our patients' parents come to us for help; they want us to prevent them from having to stay up all night. Asking them to administer a teaspoon or two of fluid every 5 minutes is just not going to be greeted with much enthusiasm, and my guess is that compliance will be less than maximal. It is difficult in our society to achieve good rehydration by the oral route, but it can be done more effectively with solutions other than Pedialyte.

DR. HARRINGTON: Could you lay out the underlying rationale for using glucose in oral rehydration therapy? What is the true relationship between glucose and gastrointestinal sodium transport?

DR. FRIEDMAN: It's a really interesting story. In the 1920s and 1930s, physicians believed that if we could just give fluids orally instead of intravenously, we could rehydrate patients. So the original solutions were approximately D5-half-normal saline. Unfortunately, there was

an increase in mortality rates when that solution was used, and that problem set back oral rehydration therapy for a generation. Dr. Tuffli alluded to the finding that the problem was too much glucose. Therefore, a solution that was more like D2, just 2% glucose, would be very effective because the transporter for glucose in the gut is a sodium-dependent transporter. If you could maximize the glucose that was absorbed, glucose would not be provided to the colon as a substrate for natural growth and also would not serve as an osmotic agent and produce more diarrhea. Sodium transport and glucose transport together were improved when the concentration of glucose and the concentration of sodium were equimolar. That's the key point. After that was determined, oral rehydration solutions became much more commonly used and, of course, much more effective.

DR. HARRINGTON: I was struck by your comment on fluid/electrolyte replacement, that is, that we don't look at the other half of it—salt and water overload—for example, pulmonary edema. Some time ago, I was interested in hospital-acquired hyperkalemia [41]. It was clear from the literature that the most potent single drug that caused death in hospitals was potassium, particularly intravenous potassium; yet we all use it like candy. Has anyone systematically analyzed the issue of sodium overload in patients treated with “deficit therapy” rather than your newly proposed “rapid rehydration therapy”?

DR. FRIEDMAN: I haven't, and I don't know of any studies on this issue.

DR. CHRISTOPHER BIRN (*PGY-3 Pediatric Resident, University of Wisconsin Children's Hospital*): I'd like to return to oral rehydration. One problem I often encounter is a dehydrated child who won't take Pedialyte. These patients sometimes will drink half-strength Gatorade or half-strength juice. What should I recommend to the parents? Is half-strength Gatorade or is juice sufficient, or is water all right? Or should I push harder for the Pedialyte? Should I just tell them to come in for the IV because what they're doing is not going to be effective?

DR. FRIEDMAN: Obviously, lots of children have diarrhea and vomiting and they get by without receiving intravenous fluids. With a self-limited illness, one improves with time as long as the dehydration is not too severe. Parents have used tricks, like freezing Pedialyte and using that as a Pedialyte Popsicle; some people say that that approach works. If you're trying to give small amounts of fluid in frequent intervals as opposed to trying to give six ounces at once, there seems to be more success. I don't know what to tell you. Have you ever tasted Pedialyte? You all should taste it at least once. It's very salty.

The last point is that dehydrated patients do feel better after receiving IV saline. Patients feel better and probably will be able to ingest additional fluids orally if they are

rehydrated. But IV rehydration is not that simple either. Say your patient is a 13-month-old, pudgy child. You're looking for a vein so you can administer 40 mL/kg of normal saline. It takes a lot of time and effort to place an IV in a busy clinic or emergency room. It's not simple any way you look at it, but basically, the more fluid you can get into the patient, the faster you'll be able to get more in orally because of improved gut function.

DR. HARRINGTON: The *Boston Globe* recently ran a remarkable story about a marathon runner who died after the race with severe hyponatremia. That doesn't make sense to those of us from the pre-Gatorade generation, because if you run a marathon, you sweat, and you lose hypotonic fluids. The serum sodium concentration should rise, not fall. This unfortunate woman obviously had release of antidiuretic hormone from running, stress, and volume depletion; she drank too much hypotonic fluid, became hyponatremic, and died shortly after the race. That is an extreme example of why we're so concerned about hyponatremia.

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*Reprint requests to Dr. A. Friedman, Department of Pediatrics, Brown Medical School, Hasbro Children's Hospital, 593 Eddy Street, Providence, RI 02903.
E-mail: afriedman@lifespan.org*

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