Edward Sumner MA BM BCh FRCA

[redacted]

Telephone/Fax [redacted]

Mobile

E-mail

February 26th 2006

D/Sergeant William Cross
Fermanagh District Command Unit
48 Queen Street
Enniskillen
BT74 7JR

Dear Mr Cross,

Re: Adam Strain

Further to our meetings of 22nd and 23rd February 2006, I will answer your points in writing:

In my opinion it should be standard practice to take base-line readings of blood gases and electrolytes as soon as possible as vascular access has been achieved. This would be particularly important in a child who has been dialysed overnight and who is scheduled for a kidney transplant. It was an error of judgement not to do this, especially as they had tried to obtain blood in the immediate preoperative period.

In my opinion it was an error of judgement to regard the CVP reading of 17 as the baseline. This initial high reading could be explained by the large volume of fluids given by this stage.

Overall the management of the haemoglobin was fine, even though the level fell from 10.5 to around 6. This can be explained by gradual blood loss and also dilution. Blood transfusion brought the level back to normal for Adam. The low reading for sodium at 0930 can be explained by the dilution by large volumes of dextrose/saline. It is impossible to be dogmatic, but at this stage it might have been too late to reverse the effects of the acute sodium dilution.

It is my opinion that there was fluid overload in the early stages of the operation.

HPPF does contain sodium so would help to raise the serum sodium level, though is usually given for blood volume replacement.

It is common knowledge that it is advisable to have a full circulation during a renal transplant to fill the new kidney, which, in a child is usually relatively large and to

maintain a rather high venous pressure (10-12) to prevent kinking of the venous anastomosis. It is not possible to put an exact figure on the extra volume of fluid necessary, but is in the order of 10-20% extra.

The concept of tonicity is explained in the enclosed paper "Prevention of Hospital-Acquired Hyponatremia" Isotonic; Fluids having the same tonicity as the intra-cellular fluid have 154mmol/l. In this respect dextrose/saline is isotonic when outside the body, but as soon as it is given intravenously, it becomes hypotonic as the dextrose is rapidly metabolised, leaving just water.

The comment by Moritz and Ayus is not actually polarised in my opinion, but stresses that problems can also occur if other solutions are used. They stress the need for monitoring of sodium levels.

Point 8: Monitoring signs of pulse and blood pressure were fine, but the CVP readings were not. Again, this relates to the fact that it was assumed that the initial reading was erroneous and was therefore used as the base-line.

Point 9: I am not a nephrologist but in my opinion the care given to Adam during this period was first-rate. At that stage the sodium was low – either from increased output (losses via the kidney) or reduced intake. Because this was a chronic situation the cells are able to adapt over a period of time and no harm is done.

I hope this is satisfactory.

Please come back to me if you have further questions.

Yours sincerely

Edward Sumner
Consultant paediatric anaesthetist

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Prevention of Hospital-Acquired Hyponatremia: A Case for Using Isotonic Saline

Michael L. Moritz, MD*, and Juan Carlos Ayus, MD‡

ABSTRACT. *Objective.* The current standard of care in pediatrics is to administer hypotonic saline in maintenance parenteral fluids. The safety of this approach has never been evaluated.

Methods. A review of the literature reveals that the administration of hypotonic fluids is potentially dangerous and may not be physiologic for the hospitalized child.

Results. There have been >50 reported cases of neurologic morbidity and mortality, including 26 deaths, in the past 10 years resulting from hospital-acquired hyponatremia in children who were receiving hypotonic parenteral fluids. Common childhood conditions requiring parenteral fluids, such as pulmonary and central nervous system infections, dehydration, and the postoperative state, are associated with a nonosmotic stimulus for antidiuretic hormone production, which can lead to free water retention and hyponatremia. Children are at particularly high risk of developing symptomatic hyponatremia as they have a larger brain-to-skull size ratio.

Conclusions. The administration of isotonic saline in maintenance parenteral fluids is the most important prophylactic measure that can be taken to prevent the development of hyponatremia in children who receive parenteral fluids. *Pediatrics* 2003;111:227–230; *hyponatremia, child, treatment, fluid, intravenous, encephalopathy.*

ABBREVIATIONS. ADH, antidiuretic hormone; SIADH, syndrome of inappropriate secretion of antidiuretic hormone.

From the *Division of Nephrology, Department of Pediatrics, Children's Hospital of Pittsburgh, University of Pittsburgh School Medicine, Pittsburgh, Pennsylvania; and ‡Department of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, Texas.

Received for publication Mar 25, 2002; accepted Jul 8, 2002.

Reprint requests to (M.L.M.) Division of Nephrology, Children's Hospital of Pittsburgh, 3705 Fifth Ave, Pittsburgh, PA 15213-2583. E-mail: moritm@chp.edu

The basic principles for prescribing maintenance parenteral fluids in children were laid down in the 1940s and 1950s and culminated with Holliday and Segar's landmark paper in 1957[1] describing a simple formula for determining the maintenance need for water in children and recommending the use of a hypotonic saline solution, equivalent to 0.2% sodium chloride in 5% dextrose in water. Since that time, recommendations for prescribing maintenance parenteral fluid therapy have remained unchanged.[2] Although Holliday and Segar's formula for determining water needs clearly has passed the test of time, their recommendations for prescribing hypotonic saline need to be reassessed. Increasing evidence has shown that hypotonic maintenance fluids can lead to potentially fatal hyponatremia in cases of excess antidiuretic hormone (ADH) production.[3–6] Although it is well-established that isotonic saline should be used for fluid resuscitation in children to raise circulatory volume while preventing the development of hyponatremia,[7] it has not been an accepted practice to use isotonic saline as a maintenance fluid. We review the evidence supporting our view that isotonic saline should be used in favor of hypotonic saline in maintenance fluids in hospitalized children, who are prone to have an increase in ADH production, as this is least likely to result in hyponatremia.

WHY HYPOTONIC MAINTENANCE PARENTERAL FLUIDS ARE CURRENTLY USED

Maintenance needs for water in children have been shown to parallel energy metabolism.[8–10] Maintenance requirements for electrolytes are less clear. Holliday and Segar[1] conceded this point, writing, "With respect to maintenance needs for electrolytes, less precise data are available and figures considerably in excess of minimum requirements are readily handled." In 1953, Talbot et al[11] recognized the potential danger of administering hypotonic fluid in states of ADH excess, stating that the "administra-

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tion of dextrose in water solution at a rate of more than approximately 1100 mL/M^2/24 hrs may induce water intoxication" and that the "risk of water intoxication may be reduced to small proportions by the administration of 100 or more mosm of organic solute to each liter of solution." The safety of administering maintenance hypotonic parenteral fluids has never been evaluated prospectively, and Holliday and Segar noted that approximately one third of children and adults receiving parenteral therapy had urinary concentration outside of a desirable range.

NB

The primary basis for the current recommendation of prescribing 3.0 and 2.0 mEq/100 kcal/24 h sodium and potassium, respectively, in maintenance fluids is that this roughly reflects the electrolyte composition of breast and cow milk.[8–10] This electrolyte composition will also result in a urine osmolality of approximately 400 mOsm/kg/H_2O, which was believed to be ideal, as it is between the range of urinary concentrating capacity.[11] Although it has been well-established that isotonic saline could be tolerated without any adverse effects, the use of isotonic saline has been avoided to prevent excess urinary water losses in conditions with impaired renal concentrating ability and to prevent the development of postoperative edema.[9–11] Whereas these recommendations may be appropriate for the healthy child, they may not apply to ill children, who are much more likely to have a nonosmotic stimulus for ADH production (Table 1). At the time that these recommendations were made, it was not yet fully appreciated that many conditions could lead to impaired free water excretion as a result of ADH excess. It is our intent to alert physicians to the potential dangers of using hypotonic maintenance fluids in children who may have an impaired ability to excrete free water, as this can lead to clinically significant hyponatremia.

HOSPITAL-ACQUIRED HYPONATREMIA

In 1957, the same year that Holliday and Segar published their paper on maintenance water needs, Schwartz et al[12] described the first case of "the syndrome of inappropriate secretion of antidiuretic hormone" (SIADH).[13] SIADH is a disorder that can lead to hyponatremia as a result of the nonphysiologic secretion of ADH, which leads to free water retention followed by a natriuresis that maintains fluid balance at the expense of serum osmolality. SIADH is 1 of the most common causes of hyponatremia in both children and adults in a hospital setting.[14] It has been reported in numerous conditions but primarily affects children with central nervous system and pulmonary disorders and as a side effect of medications. Many common childhood conditions that require parenteral fluids cause SIADH, such as pneumonia,[15] bronchiolitis,[16] asthma,[17] positive pressure ventilation, CNS infections,[18] and head trauma.[19] Other stimuli for ADH release that can lead to hyponatremia in children are emesis, pain, stress, and hypoxia.[20] There are many clinical settings where children are at risk for developing hyponatremia as a result of nonosmotic stimuli for ADH release (Table 1).

A common reason that hospitalized children receive parenteral fluids is to treat isotonic dehydration. Although isotonic saline is recommended for acute volume expansion, hypotonic fluids with 0.45% sodium chloride are currently recommended for the remainder of the deficit therapy.[21] Volume depletion is a potent stimulus for ADH production. The administration of hypotonic fluids to children with dehydration can result in acute hyponatremia secondary to free water retention.[22] Hypotonic fluids are even recommended as parenteral fluid therapy in children with meningitis.[23] Such children frequently have dehydration in addition to other nonosmotic stimuli for ADH production, and the administration of hypotonic fluids can lead to worsening neurologic deterioration secondary to the development of hyponatremia.

Postoperative children are at especially high risk for developing hyponatremia, and there have been many associated fatalities.[3,17,24–30] Contributing factors to hyponatremia in the postoperative setting comprise a combination of nonosmotic stimuli for ADH release, such as subclinical volume depletion, pain, nausea, stress, edema-forming conditions, and the administration of hypotonic fluids. The postoperative nonosmotic stimuli for ADH release typically resolve by the third postoperative day but can last until the fifth postoperative day.[17] The most important factors that lead to postoperative hyponatremia are the failure to recognize the compromised ability of the patient to maintain water balance and the administration of hypotonic fluids.

There have been >50 reported cases of neurologic morbidity and mortality, including 26 deaths, resulting from hospital-acquired hyponatremia in children who were receiving hypotonic fluids.[3–5,15,26–29,31–34] More than half of these cases occurred in the post-

TABLE 1. Clinical Settings of Increased ADH Release in Children

Hemodynamic Stimuli for ADH Release (Decreased Effective Circulation Volume)	Nonhemodynamic Stimuli for ADH Release
Hypovolemia	Central nervous system disturbances
Nephrosis	Meningitis, encephalitis, brain tumors, head injury
Cirrhosis	Pulmonary disease
Congestive heart failure	Pneumonia, asthma, bronchiolitis
Hypoaldosteronism	Cancer
Hypotension	Medications
Hypoalbuminemia	Cytoxan, Vincristine, Morphine
	Nausea, emesis, pain, stress
	Postoperative state

TABLE 2. Electrolyte-Free Water in Parenteral Fluids

Intravenous Fluid	Sodium (mEq/L)	Osmolality (mOsm/kg/H_2O)	% Electrolyte-Free Water*
5% Dextrose in water	0	252	100
0.2% Sodium chloride in 5% dextrose in water	34	321	78
0.45% Sodium chloride in 5% dextrose in water	77	406	50
Lactated Ringer's	130	273	16
5% Dextrose Lactated Ringer's	130	525	16
0.9% Sodium chloride in 5% dextrose in water	154	560	0

* Based on a sodium plus potassium concentration in the aqueous phase of plasma of 154 mEq/L, assuming that plasma is 93% water with a serum sodium of 140 mEq/L and a potassium concentration of 4 mEq/L.

operative setting in previously healthy children who underwent minor surgery. Arieff et al[3] reported on 16 previously healthy children who died or experienced permanent neurologic damage as a result of hyponatremic encephalopathy soon after receiving hypotonic fluids after minor surgical procedures or for the treatment of common childhood infections. McJunkin et al[5] and Moritz and Ayus[6] noted that the major factor that results in neurologic deterioration in children with La Crosse encephalitis was mild hyponatremia developing after the administration of hypotonic fluid. Halberthal et al[4] reported on 23 children, without an underlying disease that impaired water handling, who developed acute symptomatic hyponatremia after the administration of hypotonic fluids. Hyponatremia in these cases seemed to be attributable to a combination of hypotonic fluid administration and ADH excess. The above authors and others[30,35] have cautioned against the routine use of hypotonic maintenance fluids in children.

Children are at particularly high risk for developing symptomatic hyponatremia as they develop hyponatremic encephalopathy at higher serum sodium concentrations than adults and have a poor prognosis if timely therapy is not instituted. This seems to be attributable to the higher brain-to-skull size ratio in children, which leaves less room for brain expansion.[3,36] Children achieve adult brain size by 6 years of age, whereas full skull size is not achieved until 16 years of age. Female adolescents may also be at increased risk of developing hyponatremic encephalopathy, as women of reproductive age are >30 times more likely to develop hyponatremic encephalopathy than are men, as a result of diminished ability to adapt to hyponatremia by decreasing brain volume.[36,37]

Hyponatremic encephalopathy can be difficult to recognize in children, as the symptoms can be variable and do not correlate with either the serum sodium concentration or the rapidity of development of hyponatremia.[3] The most consistent symptoms of hyponatremia are headache, nausea, vomiting, emesis, and weakness. Advanced symptoms are signs of cerebral herniation, with seizures, respiratory arrest, noncardiogenic pulmonary edema,[38,39] dilated pupils, and decorticate posturing.[3] Failure to recognize hyponatremic encephalopathy and initiate appropriate therapy will result in a poor neurologic outcome.[3,29]

WHY ISOTONIC MAINTENANCE PARENTERAL FLUIDS SHOULD BE USED

The administration of isotonic maintenance fluids is the most important prophylactic measure that can be taken to prevent the development of hyponatremia in children who are receiving parenteral fluids. Commonly used intravenous fluids have a significant amount of free water that can contribute to hyponatremia (Table 2); therefore, they should be used with caution in maintenance fluids, to mix intravenous medications or to keep a vein open. Even isotonic saline can lead to hyponatremia if excessive fluid is administered in the presence of a fixed urine osmolality with impaired urinary dilution.[40] If an isotonic solution of 300 mOsm/kg/H_2O is administered in a state of excess vasopressin, such as SIADH or the postoperative state, for which the urine osmolality may be fixed at 500 mOsm/kg/H_2O, then a natriuresis that will result in the generation and retention of free water and the development of hyponatremia will ensue. An isotonic solution will have approximately 154 mEq/L monovalent cations, sodium plus potassium, as the average concentration of sodium plus potassium in the aqueous phase of plasma is 154 mEq/L. Although no 1 fluid rate or composition will be appropriate for all children, isotonic saline in 5% dextrose in water seems to be the safest fluid composition in most hospitalized patients. If potassium chloride is to be added to the parenteral fluids, then the sodium concentration can be lowered proportionally to maintain isotonicity. Lactated ringers with 20 mEq/L potassium chloride in 5% dextrose in water would also be an isotonic fluid. Physicians must assess children carefully to choose the most appropriate parenteral fluid rate and composition before initiating therapy. The maintenance fluid requirements of the term and preterm neonate may differ from the older child as a result of unique physiologic issues, and our recommendations do not extend to this group of patients. Children with ongoing free water losses or a free water deficit will require a more hypotonic fluid. In children with illnesses that can lead to fluid overload, such as nephrosis, cirrhosis, congestive heart failure, and glomerulonephritis, both sodium and fluid restriction is of paramount importance to avoid worsening fluid overload and the development of hyponatremia. Hospitalized children who are receiving parenteral fluid therapy should be considered at risk for developing hyponatremia and monitored closely

through daily weights, fluid balance, blood pressure, observing for signs of edema, and monitoring the serum sodium concentration. Isotonic saline seems to be the preferred fluid for administration to hospitalized patients, as they are at high risk for developing hyponatremia as a result of factors that lead to ADH excess.

ACKNOWLEDGMENTS

We thank Demetrius Ellis, MD, for editorial comments.

REFERENCES

1. Holliday MA, Segar WE. The maintenance need for water in parenteral fluid therapy. *Pediatrics*. 1957;19:823–832
2. Chesney RW. The maintenance need for water in parenteral fluid therapy. *Pediatrics*. 1998;102:399–400
3. Arieff AI, Ayus JC, Fraser CL. Hyponatraemia and death or permanent brain damage in healthy children. *BMJ*. 1992;304:1218–1222
4. 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
5. Mcjunkin JE, de los Reyes EC, Irazuzta JE, et al. La Crosse encephalitis in children. *N Engl J Med*. 2001;344:801–807
6. Moritz ML, Ayus JC. La Crosse encephalitis in children. *N Engl J Med*. 2001;345:148–149
7. Jackson J, Bolte RG. Risks of intravenous administration of hypotonic fluids for pediatric patients in ED and prehospital settings: let's remove the handle from the pump. *Am J Emerg Med*. 2000;18:269–270
8. Wallace WM. Quantitative requirements of infant and child for water and electrolyte under varying conditions. *Am J Clin Pathol*. 1953;23:1133–1141
9. Darrow DC, Pratt EL. Fluid therapy, relation to tissue composition and expenditure of water and electrolyte. Council on Food and Nutrition. *JAMA*. 1950;143:365–373
10. Darrow DC, Pratt EL. Fluid therapy, relation to tissue composition and expenditure of water and electrolyte. Council on Food and Nutrition. *JAMA*. 1950;143:432–439
11. Talbot NB, Crawford DJ, Butler AM. Medical progress: homeostatic limits to safe parenteral fluid therapy. *N Engl J Med*. 1953;249:1100–1108
12. Schwartz WB, Bennett W, Curelop S, Bartter FC. A syndrome of renal sodium loss and hyponatremia probably resulting from inappropriate secretion of antidiuretic hormone. *Am J Med*. 1957;23:529–542
13. Bartter FC, Schwartz WB. The syndrome of inappropriate secretion of antidiuretic hormone. *Am J Med*. 1967;42:790–806
14. Wattad A, Chiang ML, Hill LL. Hyponatremia in hospitalized children. *Clin Pediatr (Phila)*. 1992;31:153–157
15. Dhawan A, Narang A, Singhi S. Hyponatraemia and the inappropriate ADH syndrome in pneumonia. *Ann Trop Paediatr*. 1992;12:455–462
16. Poddar U, Singhi S, Ganguli NK, Sialy R. Water electrolyte homeostasis in acute bronchiolitis. *Indian Pediatr*. 1995;32:59–65
17. Burrows FA, Shutack JG, Crone RK. Inappropriate secretion of antidiuretic hormone in a postsurgical pediatric population. *Crit Care Med*. 1983;11:527–531
18. Cotton MF, Donald PR, Schoeman JF, Van Zyl LE, Anlbers C, Lombard CJ. Raised intracranial pressure, the syndrome of inappropriate antidiuretic hormone secretion, and arginine vasopressin in tuberculous meningitis. *Childs Nerv Syst*. 1993;9:10–15; discussion 15–16
19. Padilla G, Leake JA, Castro R, Ervin MG, Rose MG, Leake RD. Vasopressin levels and pediatric head trauma. *Pediatrics*. 1989;83:200–205
20. Robertson GL, Berl T. Pathophysiology of water metabolism. In: Brenner BM, ed. *The Kidney*. 1. Philadelphia, PA: WB Saunders Co; 1996: 873–928
21. Roberts KB. Fluid and electrolytes: parenteral fluid therapy. *Pediatr Rev*. 2001;22:380–387
22. Gregorio L, Sutton CL, Lee DA. Central pontine myelinolysis ... a previously healthy 4-year-old child with acute rotavirus gastroenteritis. *Pediatrics*. 1997;99:738–743
23. Kaplan SL. Bacterial meningitis and septicemia beyond the neonatal period. In: Burg DF, Ingelfinger JR, Wald ER, Polin RA, eds. *Gellis & Kagan: Current Pediatric Therapy*. Philadelphia, PA: WB Saunders Co; 1999:27–30
24. Lieh-Lai MW, Stanitski DF, Sarnaik AP, et al. Syndrome of inappropriate antidiuretic hormone secretion in children following spinal fusion. *Crit Care Med*. 1999;27:622–627
25. Chen MK, Schropp KP, Lobe TE. Complications of minimal-access surgery in children. *J Pediatr Surg*. 1996;31:1161–1165
26. Armour A. Dilutional hyponatraemia: a cause of massive fatal intraoperative cerebral oedema in a child undergoing renal transplantation. *J Clin Pathol*. 1997;50:445–446
27. Eldredge EA, Rockoff MA, Medlock MD, Scott RM, Millis MB. Postoperative cerebral edema occurring in children with slit ventricles. *Pediatrics*. 1997;99:625–630
28. Hughes PD, McNicol D, Mutton PM, Flynn GJ, Tuck R, Yorke P. Postoperative hyponatraemic encephalopathy: water intoxication. *Aust N Z J Surg*. 1998;68:165–168
29. McRae RG, Weinsburg AJ, Chung KW. Iatrogenic hyponatremia: a cause of death following pediatric tonsillectomy. *Int J Pediatr Otorhinolaryngol*. 1994;30:227–232
30. Judd BA, Haycock GB, Dalton RN, Chantler C. Antidiuretic hormone following surgery in children. *Acta Paediatr Scand*. 1990;79:461–466
31. Sonker D, Easi T, Lurie S, Feld S, Savir I. Symptomatic hyponatraemia due to inappropriate antidiuretic hormone secretion following minor surgery. *Can J Anaesth*. 1991;38:225–226
32. Paut O, Reinaud C, Lagier P, Fortier G, Camboulives J. [Severe hyponatremic encephalopathy after pediatric surgery: report of seven cases and recommendations for management and prevention]. *Ann Fr Anesth Reanim*. 2000;19:467–473
33. Talmaciu M, Paut O, Dedil S, Fortier G, Viard L, Camboulives J. [Severe postoperative hyponatremia: role of prolonged fasting and perfusion of hypotonic solution]. *Ann Pediatr*. 1994;41:153
34. Keating JP, Schears GJ, Dodge PR. Oral water intoxication in infants. An American epidemic. *Am J Dis Child*. 1991;145:985–990
35. Judd BA, Haycock GB, Dalton N, Chantler C. Hyponatraemia in premature babies and following surgery in older children. *Acta Paediatr Scand*. 1987;76:385–393
36. Arieff AI, Kozniewska E, Roberts TP, Vexler ZS, Ayus JC, Kucharczyk J. Age, gender, and vasopressin affect survival and brain adaptation in rats with metabolic encephalopathy. *Am J Physiol*. 1995;268:R1143–R1152
37. Ayus JC, Wheeler JM, Arieff AI. Postoperative hyponatremic encephalopathy in menstruant women. *Ann Intern Med*. 1992;117:891–897
38. Ayus JC, Arieff AI. Pulmonary complications of hyponatremic encephalopathy. Noncardiogenic pulmonary edema and hypercapnic respiratory failure. *Chest*. 1995;107:517–521
39. Ayus JC, Varon J, Arieff AI. Hyponatremia, cerebral edema, and noncardiogenic pulmonary edema in marathon runners. *Ann Intern Med*. 2000;132:711–714
40. Ayus JC, Caramico CI. Sodium and Potassium Disorders. *Textbook of Critical Care*. Philadelphia, PA: WB Saunders Co; 2000:853–861

"Human progress can be compared to a storm-lashed sea; men must commit a thousand errors to arrive at the truth."

—Arj Turgot (1751)

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COMMENTARY

Opinions expressed in this commentary are those of the author and not necessarily those of the American Academy of Pediatrics or its Committees.

Reducing Errors in Fluid Therapy Management

ABBREVIATION. ECF, extracellular fluid.

The article by Moritz and Ayus in this month's issue of *Pediatrics*[1] noted errors in fluid therapy management causing hyponatremia, brain damage, and death in previously well children who had been hospitalized with an acute illness or for elective surgery. The authors have done a service in calling attention to the problem. However, their proposal to avoid this complication, using 0.9% saline rather than standard 0.25% saline[2] for meeting maintenance fluid needs would, in our view, do more harm than good. The risk for other errors would increase.

Many children who were cited in their report suffered because of egregious errors in management, not from conventional fluid therapy.[3] Children with acute problems that require fluid therapy commonly have central nervous system, pulmonary, or gastrointestinal illness; injuries requiring surgery; or are admitted for elective surgery. Some have plasma dislocated to interstitial fluid from accompanying inflammation, whereas others have losses of extracellular fluid (ECF) or a prolonged period with little or no intake. These factors elicit a nonosmotic stimulus to antidiuretic hormone secretion that impairs free water clearance,[4] making these children vulnerable to hyponatremia.

Current practice would promptly treat many of these children initially by expanding ECF volume with 20 to 40 mL/kg 0.9% saline, minimizing this vulnerability. For those going to surgery, current practice would continue the infusion of 0.9% saline throughout surgery in the event of shock, need for intravenous medication, or an unanticipated error in infusion. An additional safeguard would be to give half the average recommended maintenance fluid (50 instead of 100 mL/100 kcals per day) for the first day and monitor serum sodium daily should the need for fluid therapy continue.

Our recommendations are broader than those of Moritz and Ayus[1] to avoid other errors in fluid therapy. These errors include hypernatremia, inadequate expansion of ECF in dehydration and shock, and gross overload of circulation in patients whose prescriptions are not properly indexed to the patient's size or clinical state.

Hypernatremia, like hyponatremia, is a cause of brain injury and death.[5] The common cause of hypernatremia is excess salt intake. Because hypernatremia is reported in children with sodium chloride intakes[6] well below those that would follow from the recommendations of Moritz and Ayus,[1] their regimen would incur that risk.

In the last few decades, it has become standard practice to give more generous prescriptions of 0.9% saline to infants with moderate to severe dehydration.[7] We have recommended giving 60 to 100 mL/kg in the first 2 to 4 hours.[8] Other physicians treating children with burn[9] or septic shock[10] have recommended giving 60 to 200 mL/kg in 2 to 4 hours to restore circulation. These regimens more quickly restore perfusion of the gastrointestinal tract and kidneys; early oral feedings then are readily tolerated and acute acidosis is quickly repaired. The nonosmotic stimulus to antidiuretic hormone release is removed; mortality is decreased.

Patients needing fluid therapy today are more likely to include children with chronic disease: bronchopulmonary dysplasia, asthma, congenital heart disease, and renal insufficiency. These patients have lower tolerance for excess water or saline.

The maintenance regimen we proposed in 1957,[2] indexing maintenance requirements to estimated calorie expenditure,[4] antedated the introduction of rapid ECF expansion. Oral rehydration therapy, which has been introduced since then, has shortened the course of intravenous fluid therapy—often to less than a day. However, for those needing parenteral fluid therapy for longer periods, the original regimen remains appropriate.

The electrolyte intakes per 100 kcals proposed by this maintenance regimen are: sodium, 3; potassium, 2; chloride, 2 meq/100 cals per day.[2] These intakes were questioned by Moritz and Ayus[1] as, perhaps, too little. The sodium and chloride intakes are twice that provided by human milk and are adequate unless losses of body fluids are appreciable.

The current practices we cite minimize the risk for hyponatremia and do not incur the risk of hyper-

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Reprint requests to (M.A.H.) 1515 Oxford St. Apt 1A, Berkeley, CA 94709.
E-mail: mahillas@uclink.edu

7–10 kg: 100 kcals/kg; 12–20 kg: 1000 kcals + 100 kcals/2 kg > 10; 25–70 kg: 1500 kcals + 100 kcals/5 kg > 20 kg. For example, 17kg: 1100 kcals; 25 kg: 1600 kcals; 45 kg: 2000 kcals; 70 kg: 2500 kcals

natremia. They set standards for rapid ECF expansion when that is indicated and limit overload that causes pulmonary congestion. These principles are a safer preventive for hyponatremia than using 0.9% saline for maintenance therapy.

MALCOM A. HOLLIDAY, MD
Department of Pediatrics
University of California, San Francisco
San Francisco, CA 94143

WILLIAM E. SEGAR, MD
AARON FRIEDMAN, MD
Department of Pediatrics
University of Wisconsin
Madison, WI 53792-4108

REFERENCES

1. Moritz ML, Ayus JC. Prevention of hospital acquired hyponatremia: a case for using isotonic saline in maintenance fluid therapy. *Pediatrics*. 2003;111:227–230
2. Holliday MA, Segar WE. The maintenance need for water in parenteral fluid therapy. *Pediatrics*. 1957;19:823–832
3. Arieff AI, Ayus JC, Fraser CL. Hyponatremia and death or permanent brain damage in healthy children. *BMJ*. 1992;304:1218–1222
4. Holliday MA. Extracellular fluid and its proteins: dehydration s. and recovery. *Pediatr Nephrol*. 1999;13:989–995
5. Finberg L. Hypernatremic (hypertonic) dehydration in infants. *N Engl J Med*. 1973;288:196–198
6. Friis MN, Segar WE. The association of various factors with hypernatremic diarrheal dehydration. *Am J Dis Child*. 1972;97:298–302
7. Hirshhorn N. The treatment of acute diarrheal dehydration in children: an historical and physiological perspective. *Am J Clin Nutr*. 1980;30:637–663
8. Holliday MA, Friedman AL, Wassner SJ. Extracellular fluid restoration in dehydration: a critique of rapid versus slow. *Pediatr Nephrol*. 1999;13:292–297
9. Carvajal HF. Fluid resuscitation of pediatric burn victims: a critical appraisal. *Pediatr Nephrol*. 1994;8:357–366
10. Carcillo JA, Davis AL, Zaritsky A. Role of early fluid resuscitation in pediatric septic shock. *JAMA*. 1991;266:1242–1245

HYPE JUMPS AHEAD OF EVIDENCE

"... Medical practice, as it so often does, got ahead of medical science. We made observations and developed hypotheses—and then forgot to prove them... There is a tendency, driven by wishful thinking combined with good marketing and media hype, to jump ahead of the medical evidence."

Love SM. Preventive medicine, properly practiced. *New York Times*. July 16, 2002

Submitted by Student

COMMENTARY

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